Conclusion regarding the peer review of the pesticide risk assessment of the active substance Carbofuran[1]

(Question No EFSA-Q-2009-496)

Issued on 16 June 2009

SUMMARY

Carbofuran is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[2], as amended by Commission Regulation (EC) No 1490/2002[3]. 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, Belgium, 2004), 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 carbofuran in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 3 August 2004. Following a quality check on the DAR, the peer review was initiated on 17 August 2004 by dispatching the DAR for consultation of the Member States and the applicants FMC Chemical sprl and Dianica S.A. 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.

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

[2] OJ No L 53, 29.02.2000, p. 25

[3] OJ No L 224, 21.08.2002, p. 25

A discussion of the outcome of the consultation of experts took place with representatives from the Member States on 8 June 2006 leading to the conclusions as laid down in the EFSA conclusion issued on 28 July 2006 (EFSA Scientific Report (2006) 90).

Following the Commission Decision of 13 June 2007 (2007/416/EC)[4] concerning the non-inclusion of carbofuran 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: operator, worker and bystander exposure; the risks to birds, mammals, and aquatic organisms; the possible impact on non-target arthropods.

Belgium, being the designated rapporteur Member State, submitted the additional report (Belgium, 2008) on carbofuran to the EFSA on 5 January 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 18 March 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.

The peer review was initiated on 18 March 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 April/May 2009.

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

The original conclusion from the review was reached on the basis of the evaluation of the representative uses as an insecticide as proposed by the applicants, which comprise incorporation into soil (at drilling) to control soil insects where maize, sugar beet and sunflower will be grown, at an application rate of 0.6 kg carbofuran per hectare. Carbofuran can be used as an acaricide, insecticide and nematicide. It should be noted that during the peer review process only the use as insecticide was evaluated. The conclusion of the peer review of the resubmission was reached on the basis of the

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

evaluation of the representative use as an insecticide as proposed by the applicant, which comprises mechanical incorporation into soil (at drilling) to control soil insects in sugar beet at an application rate of 0.6 kg carbofuran per hectare, applied once every 3 years.

It should be noted that the conclusion has only been updated in relation to the risk assessment of the representative use presented in the additional report, i.e. only the use on sugar beet at an application rate of 0.6 kg carbofuran per hectare. It should also be noted that the proposal by the applicant for a reduced application rate of 60 g a.s./ha was rejected by the rapporteur and was not considered in the peer review.

The representative formulated products for the evaluation in the original review were Furadan 5G, a granule (GR) and Diafuran 5G, a microgranule (MG). Both were registered in some Member States of the EU.
The representative formulated product for the evaluation under the resubmission was Furadan 5G, a granule (GR) containing 50 g/kg carbofuran.
There are methods available to monitor all compounds given in the respective residue definitions for food of plant and animal origin, environmental matrices, body fluids and tissues, however data gaps were identified for additional validation data for the hydrolysis step of the monitoring methods for plant and animal matrices and for an ILV for the method in plants. 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.

Carbofuran is rapidly and completely absorbed and excreted in the rat. It is very toxic by ingestion (LD_{50} 7 mg/kg bw) and by inhalation (LC_{50} 0.05 mg/L) whereas toxicity during dermal exposure is moderate (LD_{50} 1000-2000 mg/kg bw). Carbofuran is not a skin irritant, eye irritant, or skin sensitizer, but mortality was reported after exposure to eyes. The proposed **classification is T^+, R28/R26 "Very toxic if swallowed and via inhalation", Xn, R21 "Harmful in contact with skin" and T, 39/41 "Danger of very serious irreversible effects" and "Risk for serious damage to eyes".**
The critical target is inhibition of brain and erythrocyte (RBC) acetylcholinesterase (AChE). The overall oral short term no-observed-adverse-effect-level (NOAEL) is 0.1 mg/kg bw/day from the 1-year dog studies with the NOAELs of 0.1 and 0.25 mg/kg bw/day, based on RBC AChE inhibition and clinical signs of neurotoxicity and testicular degeneration. It is genotoxic *in vitro* but negative in *in vivo* studies. The relevant long term NOAEL is 0.462 mg/kg bw/day from the rat study. Carbofuran induced decreased body weight in pups as well as pup survival at parental toxic doses. Results from the open literature demonstrated that *in utero* or lactational exposure to carbofuran during whole gestation or lactation period caused testicular and spermatotoxicity in pups at dose levels of 0.4

mg/kg bw not associated with inducing general toxic effects, these effects were reproduced in a more recent study with dietary administration, however, the effects were far less pronounced and occurred only at systemically toxic doses (18 mg/kg bw/day); they were not reproduced upon gavage administration. Therefore, no classification regarding reproduction toxicity was proposed. At the occasion of the resubmission of carbofuran, new sets of acute neurotoxicity studies were assessed. No NOAEL could be established in pups at post natal day 11 (PND11) based on a significant inhibition of the brain acetylcholinesterase, the low-observed-adverse-effect-level (LOAEL) was 0.03 mg/kg bw. In young adult rats, the NOAEL was 0.03 mg/kg bw; overall, clinical signs were observed from 0.3 mg/kg bw onwards.

The human study (1976) was not considered as scientifically valid. The metabolites 3-hydroxy-carbofuran[5] and 3-keto-carbofuran[6] are very toxic and toxic (LD_{50} of 8 and 107 mg/kg bw, respectively), the hydroxy metabolite is genotoxic as well *in vitro* (Ames test and mouse lymphoma cells assay). The metabolites 3-hydroxy-carbofuran-phenol[7], 3-keto-carbofuran-phenol[8] and carbofuran-phenol[9] are harmful if swallowed.

The dermal absorption value for the granular formulation, Furadan 5G, is 5 % based on *in vivo* (default value of 10 %) and *in vitro* studies (rate of absorption 2x higher in rat than in human skin).

The acceptable daily intake (ADI) and acute reference dose (ARfD) are 0.00015 mg/kg bw/day based on the LOAEL of 0.03 mg/kg bw in pups from the acute neurotoxicity studies and a safety factor of 200. The acceptable operator exposure level (AOEL) is 0.0003 mg/kg bw/day, based on the NOAEL of 0.03 mg/kg bw in young adults from the acute neurotoxicity studies and a safety factor of 100 applied.

The estimated operator exposure according to the US PHED (Pesticide Handler's Exposure Database) is below the AOEL i.e. 95 % if personal protective equipment (PPE) as gloves, normal work wear and respiratory protective equipment (RPE) are worn during loading and spreading of the product and assuming an application rate of 0.6 kg carbofuran/ha and a maximum work rate of 10 ha/day. Worker exposure is unlikely to occur, as the formulation is incorporated by mechanical means into the soil when sowing. The granular formulation is applied by ground-directed equipment that is nearly dust free; therefore, the level of bystander exposure to vapour or airborne particles at the time of application is likely to be negligible.

The metabolism, distribution and residue behaviour of carbofuran was investigated in various crops and with different methods of application. Moreover, studies with benfuracarb and carbosulfan, of which carbofuran is the main metabolite, were considered applicable to address residue behaviour of carbofuran.

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[5] 3-hydroxy-carbofuran: 3-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl methylcarbamate
[6] 3-keto-carbofuran: 2,2-dimethyl-3-oxo-2,3-dihydro-1-benzofuran-7-yl methylcarbamate
[7] 3-hydroxy-carbofuran-phenol: 2,2-dimethyl-2,3-dihydro-1-benzofuran-3,7-diol
[8] 3-keto-carbofuran-phenol: 7-hydroxy-2,2-dimethyl-1-benzofuran-3(2*H*)-one
[9] carbofuran-phenol: 2,2-dimethyl-2,3-dihydro-1-benzofuran-7-ol

Based on all available data the metabolic pathway of carbofuran in soil applied uses can be considered as sufficiently investigated. Carbofuran and 3-OH-carbofuran and 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 low and mostly 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, carbofuran undergoes an extensive metabolisation. 3-OH-carbofuran free and conjugated was considered the relevant residue in animal matrices to assess consumer exposure and consumer risk. Further clarification on the ratio of free and conjugated residues in animal matrices was required by the experts in PRAPeR 70 (data gap). This might be important information to conclude on an animal residue definition for monitoring. For the time being no MRLs can be proposed for plant and animal commodities, because amongst others, the residue definition for monitoring could not be agreed due to outstanding data.

The data gaps identified by the meeting PRAPeR 70 do not permit finalisation of the consumer risk assessment. 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-OH 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 in both models. As agreed by the meeting PRAPeR 70 the risk assessment could be further refined in terms of residues in processed sugar beet.

However, 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.

To mitigate the identified risk it was 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.

On basis of the laboratory degradation experiments, carbofuran is from low to very high persistent in soil under aerobic conditions. In one of the experiments the metabolite 3-keto-carbofuran exceed the 10 % AR. Carbofuran-phenol reached the 9 % AR at the end of one of the aerobic experiments and the transformation product 3-OH-carbofuran was identified as a minor metabolite in various experiments (max 1.32 % AR).

Additionally, the rapporteur Member State included in the list of end points degradation parameters obtained in the studies performed with benfuracarb and carbosulfan. Three experiments resulted in significantly longer DT_{50} values than the other soil incubations. The EPCO/PRAPeR expert meetings (EPCO 31, September 2005; PRAPeR 62, January 2009 and PRAPeR 67, May 2009) agreed to use these values in the exposure assessment, however the RMS disagreed with the use of these values for the resubmission.

Only carbofuran-phenol was identified as major metabolite in the validated anaerobic study. In this anaerobic study carbofuran is low persistent.

In the field studies performed with parent carbofuran in USA metabolites 3-OH-carborfuran, 3-keto carbofuran and carbofuran-phenol were analyzed for. Results were only reported as total carbamate for some of the trials and it is not possible to know the exact amount of each metabolite. In other trials, 3-OH-carborfuran is found at levels up to the 3 % of the total residue and 3-keto-carbofuran at levels up to approx. 20 % of the total residue. Carbofuran-phenol is not found above the LOD in any of the trials.

Summaries of some field studies performed carbosulfan (EU, reported in the carbosulfan DAR) as parent compound were provided by one applicant. Addendum including the data from these studies has been provided by the rapporteur Member State in April 2006; however the complete assessment of the studies is still missing. Half life of carbofuran in the EU trials (where it appears as metabolite of carbosulfan) ranges between 1.3 to 71.9 d. Half life of carbofuran in the USA sites (where it is applied as parent compound), assessed as relevant for the EU climatic conditions by the rapporteur Member State, ranges between 5 and 121 d. However, only the carbosulfan field studies performed in EU were used by the rapporteur Member State in the risk assessment of carbofuran. The expert meeting 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 not been assessed and peer reviewed. The expert meeting EPCO 31 agreed also that it is necessary to determine whether the studies from the USA are acceptable for the EU risk assessment. In the additional report for carbofuran (November 2008) the RMS stated that the field studies performed in the USA were of limited quality, therefore these results were not used in the final risk assessment. Moreover an assessment of the experiment, resulting in a DT_{50} of 71.9 days, was provided. The RMS conclusion in this assessment was that this experiment is not accepted anymore and for PECsoil calculation the second longest DT_{50} of 27 days was used from the data set of the EU field studies.

Based on the available information, carbofuran was considered stable to photolysis in soil.

No information on the degradation rate of metabolites was available in the original DAR, but for the resubmission, laboratory degradation experiments were submitted for the metabolites 3-OH-carbofuran, 3-keto-carbofuran and carbofuran-phenol. Carbofuran-phenol and 3-OH-carbofuran exhibited very low persistence, while 3-keto-carbofuran exhibited very low to low persistence.

Carbofuran is classified as very high mobile compound. A data gap was set in 2006 for batch adsorption/desorption studies on carbofuran soil metabolites, which were included in the additional report. 3-OH-carbofuran exhibits very high to high and 3-keto-carbofuran exhibits very high to low mobility in soil, while carbofuran-phenol exhibits medium to low mobility.

An aged column leaching study shows that carbofuran and its metabolites (3-keto-carbofuran and carbofuran-phenol) are mobile and may leach under the conditions of the experiments.

In aqueous buffer solutions, carbofuran is stable at pH 4 and degrades with half lives of 28 – 45.7 d at pH 7 and 0.1 d at pH 9. Carbofuran-phenol was the major hydrolysis product identified. Photolysis may contribute only slightly to the degradation of carbofuran in water. Carbofuran is not readily biodegradable according the available study.

Dissipation of carbofuran in the water sediment was investigated in two studies with a total of three systems. In an acidic system carbofuran degraded in the whole system with a half life of approximately 70 days (normalized to 20 °C). Mineralization was low and bound residue reached a maximum level of 32.8 % AR. In the neutral or alkaline systems carbofuran dissipated from the water phase with half lives of 6.9-8.5 days and degraded in the whole system with half lives of 9 – 11.6 d. Carbofuran-phenol was the only major metabolite found in the water-sediment systems. Bound residues reached maximum of 74 -78 % AR at the end of the study (102 d). These experiments seem to indicate that the degradation of carbofuran may be pH dependent in water sediment systems.

Additionally, degradation parameters obtained in the studies performed with benfuracarb and carbosulfan were included in the list of end points.

No suitable PECsw and PECsed calculations were available in 2006, but for the resubmission, calculations based on the FOCUS recommendations were performed.

FOCUS modelling for estimation PECgw were performed in the original DAR in 2005 and in the additional report (November 2008), however some input parameters used for these simulations were questioned. The simulations were repeated with the agreed parameters (note that most of the FOCUS input parameters for carbofuran were already agreed in January 2009, when benfuracarb was discussed) and the results are included in an addendum. These simulations were accepted by the expert meeting (PRAPeR 67).

Parent 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 0.19-7.21 µg/L using the PEARL model, and 7 out of the 9 modelled FOCUS scenarios with the range of 0.48-1.2 µg/L using the PELMO model, when annual application was simulated. Only the Porto (PEARL) or Porto and Thiva (PELMO) FOCUS scenarios resulted PECgw <0.1µg/L (0.037 µg/L, 0.018 µg/L and 0.003 µg/L, respectively).

When triennial application was simulated by FOCUS PEARL, 7 out of the 9 modelled FOCUS scenarios exceeded the 0.1µg/L parametric drinking water limit (0.38-1.26 µg/L), and again Porto and Thiva FOCUS scenarios resulted PECgw <0.1µg/L (0.018 µg/L and 0.056 µg/L, respectively).

The PECgw for the metabolites simulated exceeded the 0.1µg/L parametric drinking water limit only in a few cases of FOCUS simulations except the annual simulation with PEARL for 3-keto-carbofuran, where 6 out of the 9 results were above the trigger of 0.1 µg/L. However, it is noted that the simulations for the metabolites were regarded as extreme worst case, as 100 % formation was assumed (which would be expected to be lower in reality).

In summary, the potential for groundwater exposure from the applied for intended uses by carbofuran 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 carbofuran according to uniform principles.

Carbofuran is not expected to be prone to long range transport through the air compartment.

A high risk to birds and mammals was identified. The suggested refinements of the risk assessment were not sufficiently supported by data (e.g. PT, PD refinement) or had some shortcomings (e.g. residue trials, lower application rates used in the risk assessment). The experts in the PRAPeR 68 meeting were concerned that the TERs were below the trigger even when the not justified refinements of PD and PT values were included in the TER calculation. The experts expressed their doubts that a safe use could be demonstrated even with further refinement of the risk assessment. The TERs were below the trigger of 100 and 10 for aquatic invertebrates with FOCUS step3 PECsw for the application rate of 600 g a.s./ha for the drainage scenarios (D3, D4). The exposure of the aquatic environment was negligible for the FOCUS run-off scenarios (R1, R3). The TERs for carbofuran were below the trigger of 100 and 10 for aquatic invertebrates with FOCUS step3 PECsw for the application rate of 600 g a.s./ha. Therefore the aquatic risk assessment needs further refinement. A high risk was indicated in extended laboratory studies and semi-field tests with non-target arthropods. A field study was submitted where recovery was observed. However, the study was conducted at an application rate of 375 g a.s./ha which was too low to cover the intended rate of 600 g a.s./ha. The long-term TERs were below the trigger of 5 for earthworms. A field study with the formulation Marshall 25 CS (a.s. carbosulfan) was suggested to address the long-term risk to earthworms. Uncertainties remain whether the exposure from in-furrow application (high concentrations locally) would lead to higher risk than even distribution of the active substance. A high risk was indicated in the first-tier risk assessment for soil non-target macro-organisms. Recovery was observed also for soil dwelling arthropods in the above mentioned field study. Since the application rate was too low the risk to soil dwelling non-target macro organisms was considered not sufficiently addressed.

The risk to bees, non-target plants and biological methods of sewage treatment was assessed as low for the representative use evaluated.

Key words: carbofuran, peer review, risk assessment, pesticide, insecticide, acaricide, nematicide

TABLE OF CONTENTS

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. Carbofuran 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 carbofuran, hereafter referred to as the draft assessment report, to the EFSA on 3 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 applicants FMC Chemical sprl and Dianica S.A. 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 on 28 July 2006 (EFSA Scientific Report (2006) 90).

Following the Commission Decision of 13 June 1007 (2007/416/EC)[10] concerning the non-inclusion of carbofuran 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

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

data in response to the areas of concern identified in the review report as follows: operator, worker and bystander exposure; the risks to birds, mammals, and aquatic organisms; the possible impact on non-target arthropods.

Belgium, being the designated rapporteur Member State, submitted the additional report on carbofuran to the EFSA on 5 January 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 18 March 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.

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

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It should be noted that the conclusion has only been updated in relation to the risk assessment of the representative uses presented in the additional report, i.e. only the use in sugar beet at application rates of 0.6 kg carbofuran per hectare. It should also be noted that the proposal for a reduced granular dose rate of 60 g a.s./ha corresponding to the doses used for seed treatment was considered not acceptable and not considered in the peer review. A list of relevant end points for the active substance as well as the formulation is provided in appendix A.

The documentation developed during both the initial and the resubmission 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 review and resubmission)
- the resulting reporting table (rev. 1-1 of 14 June 2005) and (rev. 1-1 of 20 March 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 18May 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 addendum (compiled version of May 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 documents of the peer review report and the final addendum developed and prepared during the course of the initial review process are made publicly available as part of the background documentation to the original conclusion, *EFSA Scientific Report* (2006) 90, 1-88, finalised/issued on 28 July 2006.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

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

Carbofuran belongs to the class of benzofuranyl methylcarbamate insecticides such as carbosulfan and benfuracarb. It belongs also to the classes of carbamate acaricides and carbamate nematicides. Carbosulfan is a systemic insecticide with contact and stomach action. It inhibits the acetylcholinesterase (AChE) in the nervous system.

The representative formulated products for the evaluation were Furadan 5G, a granule (GR) and Diafuran 5G, a micro granule (MG), containing 50.5 g/kg (pure) carbofuran for Diafuran 5G and 50.27 g/kg (pure) for Furadan 5G, respectively. Both were registered in some Member States of the EU. The representative formulated product for the evaluation under the resubmission was Furadan 5G, a granule (GR) containing 50 g/kg carbofuran.

The representative uses evaluated during the original submission comprise applications by incorporation into soil (at drilling) to control soil insects in maize, sugar beet and sunflower, in all EU, at an application rate of 0.6 kg carbofuran per hectare. Carbofuran can be used as acaricide, insecticide and nematicide. It should be noted that during the peer review process only the use as insecticide was evaluated.

The representative use evaluated during the resubmission comprises application by mechanical incorporation into soil at drilling, to control soil insects in sugar beet, in all EU, at an application rate of 0.6 kg carbofuran per hectare. The use on maize and sunflower are no longer supported. It should also be noted that the proposal by the applicant for a reduced application rate of 60 g a.s./ha was rejected by the rapporteur and was not considered in the peer review.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of carbofuran as manufactured should not be less than 960 g/kg for the technical material of Dianica and 980 g/kg for the technical material of FMC. It should be noted that the rapporteur Member State regarded the technical materials as equivalent based on SANCO/10597/2003 rev.2 (for details see Volume 4, C.1.2.5). This assessment was accepted without question during the peer review process.

There is no FAO specification available. The technical materials contain no relevant impurities.

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 carbofuran or the respective formulations.

The main data regarding the identity of carbofuran and its physical and chemical properties are given in appendix 1.

Adequate analytical methods are available for the determination of carbofuran in the technical material and in the representative formulation (HPLC-UV, CIPAC Method 276/TC/(M)/3, 276/GR/(M)/3) as well as for the determination of the respective impurities in the technical material (GC-FID, HPLC-UV).

Sufficient test 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.

The experts at PRAPeR 70 meeting (May 2009) agreed that the residue definition for monitoring in food of plant and animal origin should preferably be the same as for the risk assessment.

An HPLC-MS/MS method is available that claims to monitor both free and conjugated 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), identified data gaps for the validation of the efficiency of the hydrolysis step in the method and for an ILV for the monitoring method.

The Dutch multiresidue method M-1 (GC) covers carbofuran in non-fatty matrices and M-2, S-1 (HPLC-PCD with fluorescence detection) covers carbofuran and 3-hydroxy carbofuran in cereals, fruits and vegetables. The German multiresidue method DFG S19 (GC) covers carbofuran in maize and sugar beet and method 658-(344) (GC) covers 3-hydroxy carbofuran in rape seed and tomatoes. In conclusion, a published multi-residue methods allowing determination of all compounds included in the proposed residue definitions in all matrix groups is not available.

An HPLC post-column derivatization method with fluorescence detection that claims to monitor both free and conjugated residues of carbofuran and 3-hydroxy carbofuran in products of animal origin with LOQs of 0.05 mg/kg (meat, eggs) and 0.025 mg/kg (milk) respectively, however the experts at PRAPeR 70 meeting (May, 2009) identified a new data gap to address the efficiency of the hydrolysis step to release the 3-hydroxy carbofuran conjugates in animal matrices in the method of analysis for monitoring.

For the environmental matrices the proposed residue definition for monitoring is carbofuran.

An adequate GC-MS method is available to monitor residues of carbofuran in soil with a LOQ of 0.007 mg/kg. It should be noted that HPLC-MS/MS methods are also available to monitor carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol in soil with LOQs of 0.01 mg/kg for each analyte. Several methods are available to monitor residues of carbofuran in water by GC-MS with a LOQ of 0.05 µg/L, or HPLC-MS/MS with a LOQ of 0.1 µg/L. It should also be noted that HPLC-MS method also exists for monitoring carbofuran, 3-hydroxy carbofuran, carbofuran-phenol in drinking water, groundwater and surface water with LOQs of 0.1 µg/L for each analyte.

Residues of carbofuran in air can be monitored by HPLC-UV with a LOQ of 0.6 µg/m^3.

Residues of carbofuran and metabolites 3-hydroxy carbofuran, 3-keto carbofuran and carbofuran-7-phenol in body fluids and tissues can be determined by HPLC-MS/MS with LOQs of 50 µg/L in blood and urine and LOQs of 0.01 mg/kg in tissues, respectively.

2. Mammalian toxicology

Carbofuran was discussed at EPCO expert meeting for mammalian toxicology (EPCO 33) in September, 2005. The rapporteur Member State has provided an addendum which is dated August 2005, which was not available for the other MSs during the discussions at the experts´ meeting but was used as a support for discussions at the meeting.

Carbofuran was re-discussed during the PRAPeR 69 (round 14) expert meeting on mammalian toxicology based on the additional report (revised draft assessment report of March 2009) provided by the RMS upon a resubmission application. The discussion focused on the AOEL and dermal absorption values, and on operators risk assessment, as the remaining open issues (effects on the male reproductive system, further neurotoxicity studies, ADI and ARfD values) had been agreed during the PRAPeR teleconference TC04 in January 2009 on benfuracarb[11] for which carbofuran is the main metabolite and for which the same data/information were available.

There are two applicants FMS and Dianica and the rapporteur Member State has evaluated the two data packages. Most of the toxicology studies have a purity of 94-97 %, irrespectively if it is a FMC or Dianica source. In the 1980's FMC developed a more efficient method for producing carbofuran, which is of higher quality (> 98 %) but has several minor new impurities. After consultation with the US EPA, comparative acute oral toxicity data was generated for the revised technical material together with genotoxicity. These additional studies demonstrated that the new material did not pose any additional acute toxicological risk.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Carbofuran is rapidly and completely absorbed and excreted, up to 92 % of the dose after 96 hours in urine. Most of the carbofuran (83 %) was excreted within 32 hours.
Distribution is rapid; 1 hour after oral administration liver contains the highest amount. Carbofuran does not accumulate.
Carbofuran is metabolized to 3-hydroxy-carbofuran[12] which is further conjugated to glucuronic acid and excreted in bile. Enterohepatic recirculation of this metabolite is suggested. 3-hydroxy-carbofuran is also hydrolyzed in 3-hydroxy-carbofuran-phenol[13] or hydroxylated in 3-keto-carbofuran[14], the later being itself hydrolyzed in 3-keto-carbofuran-phenol[15]. The three metabolites of 3-hydroxy-carbofuran are conjugated and excreted in urine mainly.
Carbofuran can also undergo oxidation of its carbamate moiety giving N-OH-methylcarbofuran,[16] further hydroxylated in 3-OH-N-OH-methyl-carbofuran.[17] Hydrolysis of the carbamate moiety gives rise to CO_2 excreted in expired air.

2.2 ACUTE TOXICITY

Carbofuran is very toxic by ingestion (LD_{50} 7 mg/kg bw) and by inhalation (LC_{50} 0.05 mg/L). Onset of clinical signs, significant for an acetyl cholinesterase (AChE) inhibitor, is rapid, within 1 hour, and resulted in tremors, oral discharge, fasciculation, swollen cheeks, chromodacryorrhea and perinea staining. Ataxia and convulsions were noted at the highest tested doses. Deaths were very acute in

[11] EFSA Scientific Report (2009) 239, 1-107: Peer review of the pesticide risk assessment of the active substance benfuracarb, re-issued on 18 February 2009
[12] 3-hydroxy-carbofuran: 3-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl methylcarbamate
[13] 3-hydroxy-carbofuran-phenol: 2,2-dimethyl-2,3-dihydro-1-benzofuran-3,7-diol
[14] 3-keto-carbofuran: 2,2-dimethyl-3-oxo-2,3-dihydro-1-benzofuran-7-yl methylcarbamate
[15] 3-keto-carbofuran-phenol: 7-hydroxy-2,2-dimethyl-1-benzofuran-3(2*H*)-one
[16] N-OH-methylcarbofuran: 2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl (hydroxymethyl)carbamate
[17] 3-OH-N-OH-methyl carbofuran: 3-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl (hydroxymethyl)carbamate

nature as evidenced by their occurrence within one hour of dosing. For surviving animals, recovery was evident within 2 days.

The toxicity during dermal exposure is moderate (LD_{50} 1000-2000 mg/kg bw). Carbofuran from Dianica induced mortality in rabbits after dermal application of 1 and 2 g/kg bw.

Carbofuran is not a skin irritant, eye irritant or skin sensitizer. However, mortality was reported after instillation of 0.1 g carbofuran (FMC) in eyes. Therefore, the compound should be classified T, R39-41 as warning as long as no other more specific classification exists.

Classification for acute toxicity is needed and the proposed risk phrases are: T^+, R28/R26 "Very toxic if swallowed and via inhalation", Xn, R21 "Harmful in contact with skin" and T, 39/41 "Danger of very serious irreversible effects" and Risk for serious damage to eyes"

2.3 SHORT TERM TOXICITY

Overall, inhibition of brain and RBC AChE was not always seen, while inhibition in plasma was more frequently observed. Toxicity of carbofuran was evaluated in rats and dogs in doses ranging from 1 to 6000 ppm.

<u>Oral exposure, rat</u>

In the 90-day dietary study, the most sensitive parameter was a brain AChE inhibition in the brain already observed at the lowest dose. Although no clinical signs of neurotoxicity were apparent, no NOAEL could be defined.

A 60-day oral rat study was reported in the open literature. In this study, clinical signs of neurotoxicity were evident at 0.8 mg/kg bw/day but effects on AChE were not measured. Chemical and histopathological alterations indicate testicular damage and toxic effects on sperm. A NOAEL of 0.1 mg/kg bw/day is proposed.

<u>Oral exposure, dog</u>

A 14-day dietary study in dogs was performed. At the top dose of 1000 ppm, dogs showed muscle tremors, emesis and salivation. Body weight losses were noted. Food intake was depressed notably from 56 ppm onwards. While plasma AChE was inhibited from the lowest dose, RBC cholinesterase remained unchanged at the time of measurement.

In a 4-week dog study, mortality was reported at 6000 ppm and clinical signs of neurotoxicity were evident from 200 ppm onwards (Dianica). A dose-related body weight loss was apparent.

Another 4-week study by FMC (Belgium 2006, Vol3 B.6.3.1) was discussed at the EPCO 33 experts´ meeting and the experts agreed with the conclusion that the NOAEL was < 5 ppm i.e. 22 mg/kg bw/day based on clinical signs and > 20 % decreased erythrocyte AChE activity, brain was not measured. The study is summarized in the addendum from August 2005.

A 90-day dog study was reported by the JMPR in 1996 (Belgium 2004, Vol3 B.6.3.2.2). Clinical signs of neurotoxicity were reported at the lowest tested dose of 10 ppm. Dose-related inhibition of plasma and erythrocyte AChE activity was observed in all treated groups. However, there was no inhibition of brain AChE activity by the end of the treatment. A NOAEL was not defined due to the inhibition of erythrocyte AChE activity (> 20 % in males only, not statistically significant) in combination with the increased salivation was seen at the lowest tested dose. Thus, NOAEL is < 10 ppm i.e. 0.41 mg/kg bw/day.

Two 1-year dog studies were reported: one exposure via the diet and one with capsules. Symptoms of neurotoxicity such as emesis, tremors, salivation, loose stool and lethargy as well as brain AChE inhibition were observed at 500 ppm (13 mg/kg bw/day). Plasma AChE inhibition, in a dose-related manner, was noted at 10, 20 and 500 ppm. RBC AChE was sometimes inhibited at 500 ppm. The NOAEL is 0.1 mg/kg bw/day.
In the second study (FMC), testicular degeneration was observed at the mid and high dose without any severe systemic toxicity observed at least at the mid dose. At the top dose the body weight was reduced by 35 %. The results on testicular degeneration were discussed at the EPCO 33 experts´ meeting. It was confirmed that degeneration was observed in 2/6 dogs at the 20 ppm dose (0.5 mg/kg bw/day), and at 500 ppm in 4/5 dogs and that the NOAEL in this study is 0.25 mg/kg bw/day. The study is summarized in more details in the addendum from August 2005.

In conclusion, the overall relevant oral short term NOAEL is 0.1 mg/kg bw/day based on the 1-year dog studies based on the NOAELs of 0.1 and 0.25 mg/kg bw/day based on RBC AChE inhibition and clinical signs of neurotoxicity and testicular degeneration, respectively. The results of the 60-day rat study published in the open literature came to a comparable NOAEL value based on testicular toxicity (see 2.6, below).

Dermal exposure, rabbit

Two 21-day rabbit dermal toxicity studies were provided. One rabbit died after exposure to 400-mg/kg bw/day and dose-related inhibition of brain cholinesterase was observed at 100 and 400-mg/kg bw/day. The NOAEL is 25 mg/kg bw/day.

2.4 GENOTOXICITY

In the DAR the genotoxic properties of carbofuran were studied in 15 *in vitro* studies (of which four Ames tests) and 7 *in vivo* studies. The purity of the test material is between 96 % and 99 % (one 80 %) or carbofuran technical (4 studies) and sometimes not specified (3 studies).

In vitro tests:

Carbofuran gave positive responses in 2 out of 4 Ames tests. However, negative results were observed with carbofuran from Dianica.

Two mutation assays on the V79 cell line reported by Dianica were negative. Two mouse lymphoma tests were realized with carbofuran from FMC. Positive results were reported in the first test with and w/o S9 mix. The positive response w/o S9 mix was confirmed in the second assay.
From these tests, it appears that carbofuran from FMC is able to induce gene mutations in *in vitro* tests, while carbofuran from Dianica was negative.

Chromosome aberrations or DNA damage were not noted for either the FMC source or the Dianica source.

In vivo studies:
Micronuclei mice bone marrow cells were not reported during carbofuran exposure (Dianica). Carbofuran (FMC) did not induce chromosome aberrations *in vivo,* although the studies showed some deficiencies. A new *in vivo* chromosomal aberration study in mice was provided. The preliminary results showed that no chromosomal aberrations were induced.
However, in the open literature positive results have been demonstrated although in a different strain than used by either FMC or Dianica.
In conclusion, the genotoxic potential of carbofuran was discussed at the EPCO 33 experts´ meeting and it was concluded that the data presented were adequate. It was agreed that carbofuran is genotoxic *in vitro* but negative in *in vivo* studies.

2.5 LONG TERM TOXICITY

Four long term studies were evaluated two in the rat and two in the mouse. Neoplasms and non-neoplastic histological changes, by type, incidence and/or degree of severity, in rats and mice, which died, killed moribund, and those killed following 24 months of study were considered to represent spontaneous lesions and to be unrelated to the administration or exposure to carbofuran.

Overall, carbofuran did not induce carcinogenicity in rats or mice. The relevant long term NOAEL is 10 ppm i.e. 0.462-mg/kg bw/day from the rat study

2.6 REPRODUCTIVE TOXICITY

Two multigeneration studies in the rat in order to determine the reproductive effects of carbofuran are presented in the DAR, one from Dianica and one from FMC.
In a two-generation study (Dianica), the NOAEL for reproduction is 20 ppm i.e. 2.9 mg/kg bw/day, based on decreased body weight in pups at 50 ppm and reduced survival of the F1a, F2a and F3a at lactation, the parental NOAEL is also 20 ppm i.e. 1.2 mg/kg bw/day based on body weight gain and food consumption (Belgium 2004, Vol3 B.6.6.1.1, first study).
In the three-generation study (FMC), the NOAEL for both parental and reproduction is 1.2 mg/kg bw/day, based on decreased body weight and reduced survival of the F1a, F2a and F3a at lactation day 4 in pups at 100 ppm (Belgium 2004, Vol3, B.6.6.1.1, second study).

Results from the open literature demonstrated that *in utero* or lactational exposure to carbofuran during whole gestation or lactation period caused testicular and spermatotoxicity in pups at dose levels of 0.4 mg/kg bw not associated with inducing general toxic effects. Degeneration of some of the seminiferous tubules, disturbed spermatogenesis, degenerative changes in Sertoli cells and depletion of a variety of other cell types without affecting testicular weight were reported. In a 60-day rat exposure study (Belgium 2004, Vol3, B.6.6.1.2, first study), testicular and toxic effects on sperm were observed at 0.2 mg/kg bw/day and the NOAEL is 0.1 mg/kg bw/day.

The relevance of the testicular effects was discussed at the EPCO 33 experts' meeting in 2005 also in the light of the findings in the 1-year dog study. It was agreed that the endpoints in the multigeneration studies normally do not cover sperm parameters and thus male fertility. The rapporteur Member State presented a discussion paper from the applicant on the reproduction toxicity studies in the addendum from August 2005. At the time of the expert meetings it was highlighted that spermatogenesis study in rats was ongoing (Dianica) but not completed. The experts then agreed to propose the classification of Reproduction Toxic Category 3, R62, based on the available data, but final decision was to be made by ECB.

The new study was provided to the RMS and summarized in the revised version of the DAR of November 2008. The study was conducted to examine if the effects on the male reproductive system were reproducible in rats using both the dietary (for 10 weeks) and gavage administration (for 60 days). The NOAELs in this study were 0.2 mg/kg bw/day when administered by gavage, based on transient clinical signs (hypoactivity, tremor and hypersalivation) at 0.8 mg/kg bw/day and 3 mg/kg bw/day with gavage administration, based on decreased body weight and testicular findings, including increased γ-GT observed at 18 mg/kg bw/day, the highest dose tested. The study showed that the testicular findings were reproducible in the dietary administration; however, the effects were far less pronounced and occurred only at systemically toxic dose (18 mg/kg bw/day). With gavage administration, the histopathological effects were not replicated. Therefore, the experts at the PRAPeR teleconference T04/09 agreed that no classification was triggered related to this end-point. In March 2006, the ECB classification meeting had reached the same conclusion, based on the same data and this decision was included in the Commission Directive 2009/2/EC of 15 January 2009.

The <u>teratogenic or developmental effects</u> of carbofuran were studied in five studies in rat and in the rabbit.

In rats, at doses of 2 mg/kg bw/day onwards, decreased body weights of pups were noted. In addition, slight increases although not statistically significant of skeletal variations were observed at doses > 1 mg/kg bw/day. As they were associated with foetal reduced body weight, these results might imply a sign of developmental adverse effect. The developmental NOAEL is 1 mg/kg bw/day and the maternal NOAEL is 0.1 mg/kg bw/day based on clinical signs.

In rabbits, at doses from 0.12- to 2.5-mg/kg bw/day, clinical signs of neurotoxicity, bw gain alteration and mortality were evident at 2 mg/kg bw/day. No teratogenic effects were observed. Reproductive parameters were not modified. Slight increases in misaligned sternebrae, not reaching statistical significance, were observed in one study. The developmental and maternal NOAEL is 0.5 mg/kg bw/day.

2.7 NEUROTOXICITY

Carbofuran was investigated for delayed neurotoxicity in hens at doses ranging from 0.5- to 2-mg/kg bw/day. No signs of development of ataxia were seen in birds at the highest dose. While NTE was not altered, AChE was decreased at 2 mg/kg bw/day. Minimal histological lesions in brain, spinal cord and sciatic nerve were seen at 1 mg/kg bw/day. Carbofuran did not induce delayed neurotoxicity in hens.

In a 13-week rat study, clinical signs of neurotoxicity appeared at 500 and 1000 ppm and FOB testing revealed biologically significant differences. No treatment-related lesions were noted in the nervous system of rats receiving 1000 ppm. In this study, while the NOAEL systemic toxicity was < 50 ppm, the NOAEL for neurotoxicity is 50 ppm (3.2 mg/kg bw/day).

At the occasion of the resubmission of carbofuran, FMC notified the existence of comparative acute neurotoxicity studies, conducted after the submission of the original EU DAR. As the rapporteur Member State suspected that these studies could have an impact on the original reference doses of carbofuran, they were requested and evaluated in the revised DAR of November 2008. These studies were conducted to establish the lowest relevant neurotoxicity NOAEL in post natal day 11 (PND11) in pups or young adult rats. Overall, clinical signs were observed from 0.3 mg/kg bw onwards. But no NOAEL could be established in pups based on a significant inhibition of the brain acetylcholinesterase (statistically significant decrease of 20 % compared to the controls), the LOAEL was 0.03 mg/kg bw. The rapporteur Member State proposed to apply a curve-fitting to estimate the NOAEL using the data in the dose-response curve, and to estimate the benchmark dose at the 10 % response level (BMD_{10}). This approach resulted in a value of 0.017-0.020 mg/kg bw which supports a 2x assessment factor on the LOAEL to derive a NOAEL. This approach was agreed by the experts during the PRAPeR teleconference in January 2009 on benfuracarb.

2.8 FURTHER STUDIES

Human study

A study on human volunteers was carried out in 1976. According to the rapporteur Member State, and confirmed by the experts (EPCO 33 meeting), the study is not scientifically valid. Effects are observed in the placebo group as well. Although there was a decreased activity in plasma AChE activity evident at 0.25 mg/kg bw no clear correlation could be established.

Mechanism study

Carbofuran suspended in corn oil and administered via gastric intubation to neonates, weanling and adult rats caused depression of plasma, red blood cells and brain cholinesterase activity. There were no differences in sensitivity to AChE inhibition with age.

Metabolites

All metabolites presented below were found in the rat metabolism study. The acute toxicity studies are all performed by FMC and the tests on genotoxicity by Dianica.

3-OH-carbofuran	oral toxicity in the same range as carbofuran LD_{50} 8.3 mg/kg bw (**T^+; R28**). Positive in Ames test, strain TA 1537 with S9 mix and in TK locus in L5178Y mouse lymphoma cells assay with and without S9 mix.
3-OH-carbofuran-7-phenol	oral LD_{50} 1654 mg/kg bw (**Xn; R22**).
3-keto carbofuran	oral LD_{50} 107 mg/kg bw (**T; R25**).
3-keto-carbofuran-7-phenol	oral LD_{50} >800 mg/kg bw (**Xn; R22**).
carbofuran 7-phenol[18]	oral LD_{50} 1743 mg/kg bw (**Xn; R22**). Negative in Ames test

2.9 MEDICAL DATA

Low number carbofuran intoxications have been reported. The majority of the incidents resulted from maintenance or equipment cleaning work. Under normal work conditions, employees wear rubber gloves, long sleeve shirts, eye protection and head covering.

2.10 DERMAL ABSORPTION

No *in vivo* studies were provided for the granular formulation Diafuran 5G but a paper from the open literature submitted (Belgium 2004, Vol3, B.6.12.1a). If a default would have been used it should have been 100 % based on the physical chemical properties according to the guidance document on dermal absorption. However, the dermal absorption value of 10 % for the formulation was proposed by the rapporteur Member State based on the results from the *in vivo* study from open literature in combination with the *in vitro* results. The dermal absorption studies were discussed at the EPCO 33 expert meeting (2005). The Shah study was performed on rats with carbofuran solubilized in acetone,

[18] Carbofuran-7-phenol: 2,2-dimethyl-2,3-dihydro-1-benzofuran-7-ol

which would implicate a worst case scenario. The absorption was 2 % at 6 hours and 18 % at 100 hours. An *in vitro* study (Dianica) with 5 % granular formulation, demonstrated 1.25 % in rat skin and 0.6 % in human skin. Furthermore, an additional recent study on rat skin from the open literature showed results in the same range although based on the penetration rates. The estimated absorption is 1.3 % and 0.25 % for low and high dose, respectively (Belgium 2004, Vol3, B.6.12.2a, second study). The EPCO 33 meeting agreed to the proposal of 10 % based on the *in vitro* study (Dianica) supported by results from the open literature and that it could be considered as a conservative approach.

During the re-submission, a new comparative *in vitro* study conducted with the representative formulation Furadan 5G on both rat and human skin was provided by FMC and assessed in the revised DAR of November 2008. The RMS proposed a value of 3 % dermal absorption based on both *in vivo* and *in vitro* studies where 6.19 % of the dose is absorbed *in vivo* in the rat, and a correction factor of 2 is used, based on the ratio observed in the *in vitro* study. However, the experts at PRAPeR 69 considered the drawbacks from the *in vivo* study (mainly urinary excretion showing possible further absorption after 24 h), and agreed with a more conservative value of 10 % default value derived from the *in vivo* study (as was concluded during the EPCO 33 meeting). The correction factor of 2 resulting from the *in vitro* comparison of dermal absorption between rat and human skin was agreed. Therefore, the estimated dermal absorption value to be used in the risk assessment is **5 %**.

2.11 Acceptable daily intake (ADI), Acceptable operator Exposure Level (AOEL) and Acute reference dose (ARfD)

Provisional reference values were set at the EPCO 33 experts' meeting in 2005 due to the uncertainties existing at the time over adverse effects on the male reproductive system. The provisional ADI and AOEL were set at 0.001 mg/kg bw/day, with the safety factor of 100 applied, based on the NOAELs of 0.1 mg/kg bw/day from the 1-year dog studies where testicular degeneration was observed at 0.5 mg/kg bw/day and inhibition of AChE at 1 mg/kg bw/day.
The provisional ARfD was 0.001 mg/kg bw, with the safety factor of 100 applied. The ARfD was based on the NOAEL of 0.1 mg/kg bw/day in the developmental study in rat where neurotoxic signs were observed in the dams at 0.3 mg/kg bw/day as well as mortality at 1 mg/kg bw/day.

During the re-submission (revised DAR of November 2008), it was concluded that the testicular damage and toxic effects on sperm were not replicated in a more recent study in rats, however, the absence of similar findings in the rat did not discount the effects observed in the dog. Newly submitted acute neurotoxicity studies were evaluated, which were considered relevant for the setting of reference doses.

ADI

During the re-submission, a new ADI was proposed by the RMS, based on the LOAEL of 0.03.mg/kg bw observed in PND11 pups in the newly submitted acute neurotoxicity studies for which a significant inhibition of the brain AChE of 20 % was observed. The use of a supplementary 2x assessment factor was supported by a benchmark dose approach for a 10 % decrease of brain AChE, resulting in an overall assessment factor of 200. This approach was agreed by the experts during the teleconference T04/09 on benfuracarb.

The ADI is 0.00015 mg/kg bw/day with a safety factor of 200 applied.

AOEL

During the PRAPeR 69 meeting, the experts discussed whether the pups at post natal day 11 (PND11) or the young adults effects relating to the reduction of the brain AChE from the new set of rat acute neurotoxicity studies should be taken into consideration for the establishment of the AOEL. The experts agreed that the effects obtained in PND11-21 rats are representative for human neonates brain development stage and that it would be very unlikely that woman in late stages of pregnancy would be exposed to carbofuran applications. Therefore the NOAEL of 0.03 mg/kg bw from the young adult rats was used as a basis for setting the AOEL.

The AOEL is 0.0003 mg/kg bw/day with a safety factor of 100 and no correction for enteral resorption applied.

ARfD

The approach followed by the RMS to propose the ADI is applicable to the ARfD setting and was agreed by the experts at the teleconference 04/09 on benfuracarb. The ARfD is based on the LOAEL of 0.03 mg/kg bw resulting from the newly submitted acute neurotoxicity studies in rat.

The ARfD is 0.00015 mg/kg bw with a safety factor of 200 applied.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The estimated operator exposure is made for the application of Furadan 5G using tractor-mounted granule applicator by placement in the open furrow directly behind each drill coulter. Furadan 5G is a granular formulation, containing 50 g carbofuran/kg, the maximum application rate is 600 g carbofuran/ha.

Operator exposure

The operator exposure was estimated using the American Pesticide Handlers exposure Database (PHED) as the standard models, the UK-POEM and the German model, do not have scenarios representative for granular formulations. The RMS presented new calculations in the addendum of May 2009 (revised DAR) based on the AOEL of 0.0003 mg/kg bw/day, dermal absorption of 5 % agreed during the PRAPeR 69 experts meeting, work rate of 10 ha/day, and the total amount handled of 6 kg/day (for sugar beet). The body weight for operators was assumed to be 70 kg. In the calculation on the basis of the PHED without respirator, the estimated exposure exceeds the AOEL (655 %). However, it should be noted that PPE in the PHED studies only refers to gloves and normal work wear worn during loading and application operations. Furthermore, as carbofuran is highly toxic via the inhalatory route, additional respiratory protective equipment (RPE) is applicable; a half mask with respiratory filter (EN 149, FFP2) conferring a protection of 90 % was assumed with this RPE. The estimated exposure is below the AOEL i.e. 95 % only if PPE and respiratory protective equipment (RPE) are worn and the 75th percentile is considered, see table below.

Estimated operator exposure presented as % of the AOEL (0.0003 mg/kg bw/day) for an application rate of 0.6 kg carbofuran/ha and a work rate of 10 ha/day, according to calculations with the PHED model.

Model	No PPE	With PPE:	With PPE and RPE:
PHED (75th percentile)	-	655 %	95 %

PPE (personal protective equipment): gloves, RPE (respiratory protection equipment) used during loading and spreading of the product

Considering the proximity between operator exposure and the AOEL value, and the nature of the critical effects, the experts at PRAPeR 69 meeting considered that the restriction to the uses supported in this assessment (according to the GAP table, granule formulation to be dropped into seed furrow by mechanical incorporation) should be emphasized.

The UK-POEM and the German model are not appropriate for this representative use and several assumptions are needed. Although calculations were provided by the RMS, the experts at PRAPeR 69 considered that they should not be included into this assessment.

Worker exposure

Worker exposure is unlikely to occur, as the formulation is incorporated mechanical means into the soil when sowing.

Bystander exposure

The granular formulation is applied by ground-directed equipment that is nearly dust free; therefore, the level of bystander exposure to vapour or airborne particles at the time of application is likely to be negligible.

3. Residues

Carbofuran was discussed in the experts' meeting for residues in September 2005 (EPCO 34)

The representative use for inclusion of carbofuran in Annex I of 91/414/EEC is an in-furrow granular application to maize, sugar beet and sun flower.

The assessment of data in a resubmitted dossier of carbofuran was discussed in the expert meeting on residues in May 2009 (PPAPeR 70) on the basis of the additional report (revised DAR) of November 2008 and the Addendum of April 2009, considering the notified use in sugar beet with granular application at drilling.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

A number of studies on uptake, translocation and metabolism of carbofuran in plants and numerous publications on soil and plant metabolism of carbofuran were submitted by the two applicants. In addition, studies and trials with carbosulfan and benfuracarb have been considered also applicable since carbosulfan and benfuracarb degrade rapidly into carbofuran in plants and soil.
Only some of the available studies and reports were considered of acceptable quality by the RMS. These are taken into consideration in this conclusion.
As all the available metabolism studies do not sufficiently address the nature of residues in the representative crops (no or very limited identification of residues was performed in the mature crop parts) further data were considered necessary in order to definitely clarify the residue of concern in food and feed.
Therefore, in the resubmission dossier new metabolism studies with carbofuran on maize and maize seedlings, sugar beet and sugar beet seedlings with application to the seed bed were submitted.
Moreover, the need for further residue trials across all crops intended for use as well as for data on rotational crops was identified in the previous review process. Additional data to address these requirements were made available in the resubmission dossier.
It is also noted that, in addition, data and information submitted on the active substances benfuracarb and carbosulfan as well as publicly available evaluation reports on carbofuran, carbosulfan and benfuracarb were included in the peer review conducted on carbofuran, if these data and information were considered to be appropriate but more critical or adverse.

3.1.1. PRIMARY CROPS

A) The following paragraphs summarise the considerations, discussions and conclusions on carbofuran on the basis of the available data and information at the time of the first review process of carbofuran in 2005/2006.

It should be noted that the conclusions drawn at the time of the first peer review of carbofuran as presented here below will require reconsideration because:

1) more recent data generated with methods of improved analytical performance as well as adverse data have become available since

2) the toxicological reference values for carbofuran have been significantly lowered on the basis of new toxicological data and therefore the angle of viewing the residue data has changed (e.g. trigger and threshold values applied in a previous assessment are no longer appropriate).

However, the following information is kept for historical reference:

Metabolism studies with radio labelled carbofuran were submitted on maize and soybean involving a pre-planting soil application and on potatoes involving a post-emergence application. Moreover, the metabolism of carbosulfan and carbofuran was studied comparatively in rice plants following a soil application. The study indicated a common metabolic degradation pathway for both of the two active substances and supports the idea that studies with carbosulfan could be used to evaluate the metabolic behaviour of carbofuran in plants. Thus, in addition, metabolism studies with carbosulfan in sugar beet following soil application and a foliar treatment were evaluated. (all studies FMC)

In a study in soybeans and mungbeans with carbofuran and in cabbage with benfuracarb, uptake and translocation of radioactivity was investigated. However, the identity of metabolites was not investigated in these studies (Dianica) and thus, they could not be used to establish a metabolic profile in plants.

In the study on maize carbofuran and its metabolite 3-OH-carbofuran were the predominant compounds recovered in forage and silage (up to *ca* 18 and 25% TRR respectively). The total residue in grain was very low, and no further identification of the grain residues was performed.

In potato plants carbofuran was rapidly metabolized as it was not detected in the mature potato tubers, and only a small amount was recovered in the immature foliage. In the mature tubers, the major part of the radioactivity was allocated to phenol metabolites, with carbofuran-7-phenol and 3-OH-7-phenol being the predominant compounds (*ca* 45 % and 13 % TRR respectively). In the immature foliage samples, the major constituent of the residues were the 3-OH-carbofuran (*ca* 23 % TRR) and 5-OH-carbofuran[19] (*ca* 35 % of the TRR).

In the study on soybean carbofuran and 3-OH-carbofuran were major components of the total residues in forage (*ca* 11 % and 27 % of TRR respectively) while in mature beans and hay carbofuran was extensively degraded (<1% TRR) and 3-OH-carbofuran was present at levels <10% TRR. Several metabolites were formed and were present in free and conjugated form. The increasing amount of radioactivity that could not be released from the samples indicated that carbofuran was gradually metabolised into compounds that were most likely incorporated into naturally occurring plant constituents.

In the comparative study on rice plants carbofuran (*ca* 41 %TRR) and 3-OH carbofuran (*ca* 26% TRR) were the major compounds of the total residue in immature plants at approximately two weeks following a carbofuran application. In plants treated in the same manner with carbosulfan, the latter was only present at trace levels (0.2 % of the TRR) while carbofuran and 3-OH carbofuran accounted for *ca* 45 % and 20 % of TRR respectively. Minor components including 3-keto-carbofuran and phenol metabolites were also identified in both experiments. However, levels of phenol metabolites increased with time and became equivalent to the levels of carbofuran and 3-OH carbofuran at PHI

[19] 5-OH-carbofuran: 2,3-dihydro-2,2-dimethyl-5-hydroxy-7-benzofuranyl-N-methylcarbamate

30. The metabolic picture and even the level of metabolites were found to be very similar in immature rice plants treated with either carbofuran or carbosulfan. In mature rice grain no characterisation of metabolites was attempted.
In the study on sugar beet with carbosulfan, 3-OH-carbofuran, 3-OH-7-phenol and 3-keto-7-phenol were major compounds in the leaves, accounting for up to *ca* 17%, 14% and 23% of the total residue, respectively, whereas the level of carbosulfan and carbofuran was minor (together less than 3% TRR). No metabolite identification was performed in the roots of plants treated with carbosulfan.

From the available data it can be concluded that the degradation and metabolisation of carbofuran in plants following a soil application proceeds primarily via hydroxylation on the furan ring to yield the major metabolite 3-OH-carbofuran, which forms due to successive oxidation and hydrolysis steps 3-keto-carbofuran, 2-hydroxymethyl-3-keto-carbofuran[20] and the phenol metabolites 3-OH-7-phenol and 3-keto-7-phenol. Two other dependent degradation routes in plants were the aromatic hydroxylation of carbofuran to 5-OH-carbofuran and a direct hydrolysis of carbofuran to carbofuran 7-phenol.
The carbofuran metabolites 3-OH-carbofuran and 3-keto-carbofuran were considered as toxicologically relevant. The phenol metabolites 3-OH-7-phenol, 3-keto-7-phenol and carbofuran 7-phenol were tested regarding their acute toxicity and considered of lower toxicity than carbofuran and 3-OH-carbofuran. (refer to 2.8)
Considering the level of occurrence and the toxicological relevance of carbofuran and its 3-hydroxyl metabolite it is proposed to define the residue for risk assessment purposes as carbofuran and 3-OH carbofuran, expressed as carbofuran (soil applied uses). The same residue definition should apply for monitoring purposes.

Residue trial data with carbofuran under field conditions from both European regions were submitted by both applicants on sugar beet and maize, and on sunflower by the applicant Dianica. Carbofuran and 3-OH-carbofuran are the residues determined with a LOQ of 0.05 mg/kg per compound in FMC trials, and except from few cases with a LOQ of 0.01 mg/kg per compound in Dianica trials.
In addition residue trials with carbosulfan on sugar beet and maize from both European zones were submitted by the applicant FMC. Based on the molecular weight of carbosulfan and carbofuran it was extrapolated, that studies performed with carbosulfan at application rates of 1 kg a.i./ha can be considered equivalent to the one with carbofuran at the proposed rate of 0.6 kg a.i./ha. Carbosulfan, carbofuran and 3-OH-carbofuran are the residues determined with a LOQ of 0.05 mg/kg per compound in these trials.

[20] 2-hydroxymethyl-3-keto-carbofuran: 2,3-dihydro-2,2-dimethyl-3-oxo-7-benzofuranyl-N-hydroxymethylcarbamate

It is noted that for most of the representative uses the data set of trials submitted by both applicants is incomplete according to current requirements, and thus the available data permit only a provisional assessment.

The data indicate residues being below the respective LOQ for both analytes in maize grain. In maize silage positive residues (0.03 mg/kg) were found in Northern and Southern European trials (Dianica). Since trials with carbosulfan in maize (FMC) were considered adequate to prove the residue situation for carbofuran uses, the following is noted: trials with a lower carbosulfan application rate as considered applicable above have not been included in the assessment by the RMS. However, in these trials positive residues of carbofuran and 3-OH-carbofuran (up to 0.14 mg/kg) were found in whole plants with cobs at harvest and should be considered when assessing livestock dietary burden (refer to EFSA conclusion regarding carbosulfan).

In sugar beet, together with carbosulfan data, a complete data set (FMC) has been submitted for Northern Europe, but limited data are available for Southern Europe. Even though in these trials residues in roots were mainly below the respective LOQ, residues might reach or exceed the LOQ (HR 0.11 mg/kg carbofuran and 3-OH-carbofuran). In residue trials submitted by the applicant Dianica no residues above the LOQ of 0.02 mg/kg were found in sugar beet roots as opposed to sugar beet leaves (0.034 mg/kg), while the number of trials was very limited for N-EU and S-EU. Taken all the available results on sugar beets from both applicants together (complete data set) EPCO 34 considered 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 and a potential requirement for a full set of residues studies per applicant could not be waived by the experts. To allow a final decision on whether additional trials are required a clearer presentation of the all results from sugar beet trials in an addendum was felt necessary by the experts. Even though the experts’ conclusion was not disputed during EPCO 34, RMS indicated prior to the final discussion of carbofuran in the evaluation meeting its disagreement with a requirement of further residue trials in sugar beet.

In four available trials in sunflower seed (Dianica) from Southern Europe the carbofuran and 3-OH-carbofuran residues were below the respective LOQ, whereas data for Northern Europe still need to be generated.

The investigation of effects of industrial or household processing on the nature and the level of the residue was not triggered for the representative uses.

B) The following text reflects the most recent considerations, discussions and conclusions on carbofuran on the basis of current data and information (resubmission procedure):

In the resubmission dossier new metabolism studies with carbofuran on maize and maize seedlings, sugar beet and sugar beet seedlings with application to the seed bed were submitted. Upon evaluation of these studies in the additional report the RMS concluded as follows:

The studies on maize seedlings and sugar beet seedlings were mainly destined to be used in the ecotoxicology assessment and were therefore not considered representative for the consumer risk assessment.

In the study on maize, treated at approx. the normal field rate (1N) and at an exaggerated rate (5N) characterization of the radioactive residues was performed only on maize silage. No characterization was attempted on mature maize straw and grain although those matrices were extracted according to the same pattern as for the silage and the level of radioactivity was higher in those matrices. Also on maize silage information about the nature of the metabolites was limited. There was no further clarification provided or requested since maize is not a supported use in the resubmission procedure.

A new study on sugar beet, treated at the normal field rate (1N) and at an exaggerated rate (4N), was submitted. Total radioactive residues in both sugar beet roots and leaves/tops from the normal dose (1N) treatment accounted for 0.031 and 0.024 mg ^{14}C-Carbofuran equiv./kg, respectively. Radioactive residues were characterized in sugar beet roots and tops/leaves without any further identification. Therefore the study does not provide any new information with regard to identity of residues in sugar beet at harvest.
The RMS concluded that with regard to the notified use, a complete metabolic pathway of carbofuran in mature sugar beet leaves/tops and roots could not be established based on the available metabolism studies. The RMS did not expected a different degradation of carbofuran to occur in sugar beet than in other crops studied and thus proposed to maintain the residue definitions as established in the previous peer review procedure on carbofuran (see above).

To assess the notified representative use in sugar beet treated at furrow in the resubmission dossier, the experts in the meeting PRAPeR 70 focussed their considerations on metabolism studies with soil application, and out of them mainly on data in crops / crop groups relevant to the scenario currently under evaluation.
Reference was made to the experts' discussion on the active substance benfuracarb and its metabolite carbofuran in particular in the teleconference meeting TC05 in January 2009. In the TC05 meeting, metabolism studies in sugar beet and in cabbage with a treatment at sowing were assessed. Moreover an evaluation by the JMPR (1997) on metabolism studies in maize, potato and soya plants with soil application were considered. Carbofuran, 3-keto-carbofuran, 3-hydroxy-carbofuran and the phenol metabolites and their conjugated forms were present at non negligible levels at late sampling intervals and also at harvest. Based on the findings the experts in the TC05 meeting agreed that carbofuran and 3-hydroxy carbofuran conjugates should be included in the residue definition for risk assessment with regard to the use of benfuracarb in brassica vegetable crops.

Hence, in PRAPeR 70 the experts agreed that due to the similarity of the scenario and data considered for the benfuracarb application on brassica crops (sugar beet data, cabbage data and JMPR evaluation) the same residue definition for risk assessment should be applied to the carbofuran use in sugar beet, i.e. sum of carbofuran and 3-hydroxy carbofuran, both free and conjugated expressed as carbofuran.

The experts discussed the necessity to also include these 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. However, it was suggested that preferably the residue definition for monitoring should be the same as established for risk assessment, i.e. should include conjugated residues of carbofuran and 3-hydroxy carbofuran.

In total 11 new - GAP conform - residue trials in sugar beet and fodder beet were submitted with carbofuran (four in N-EU and seven in S-EU) and seven new trials in sugar beet with carbosulfan (all S-EU). The crop received one application of either carbofuran or carbosulfan into the furrow at sowing. Residues of carbosulfan, carbofuran and 3-hydroxy carbofuran in sugar/fodder beet tops/leaves and roots were determined with a limit of quantification (LOQ) of 0.005 mg/kg for each analyte.

The experts in PRAPeR 70 discussed whether the analytical method used in the residue trials has also determined residues according to the new established residue definition for risk assessment (including conjugated residues of carbofuran and 3-hydroxy carbofuran), but 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.
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 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

It is noted that with the resubmission dossier also new residue trial data in sunflower and maize were submitted. Though the RMS has presented them in the additional report, they have not been peer reviewed as they are not relevant in terms of the currently notified use on sugar beet in the resubmission dossier.

To address the nature and level of residues upon household and industrial processing the applicant has submitted a position paper referring to hydrolysis studies performed with carbosulfan at pH 5, 7 and 9 at room temperature (25°C). These tests are not in compliance with the guidelines for generation of residue processing data. Even though sugar beet processing is conducted at merely alkaline conditions, the experts in PRAPeR 70 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.

However, considering the harsh conditions in sugar beet processing and the crystallisation steps, virtually no residues are expected to occur in refined sugar. The majority of the experts were of the opinion that it would be acceptable to use an input value of zero to reflect expected residue intake through processed sugar beet (sugar) in the consumer intake assessment.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

During the first peer review on carbofuran the RMS considered studies in succeeding crops or a waiting period for planting succeeding crops unnecessary since soil degradation studies indicate that carbofuran is declined by more than 90% within 100 days. However, carbofuran degradation in soil seemed to vary highly in the different tests. The available degradation studies in soil gave contradictory results; carbofuran was shown to be low to moderate persistent or high persistent. (refer to 4.1.1).

Thus the experts' meeting for residues EPCO 34 concluded that there is a need to address residues of carbofuran in succeeding crops.

In a position paper (additional report Nov 2008) the applicant argued that no such data is required since the DT90 for carbofuran would not trigger rotational crop studies. This position was supported by the rapporteur Member State.

In the context of the assessment of benfuracarb the DT90 of carbofuran was re-discussed by 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 of November 2008.

Upon application of carbofuran to the soil at the recommended field rate (0.6 kg a.s./ha) 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 results will be provided in the final report; however from the interim report plant back 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 toxicological reference values for 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.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

A) The following paragraphs summarise the considerations, discussions and conclusions on carbofuran on the basis of the available data and information at the time of the first review process of carbofuran in 2005/2006.

It should be noted that the conclusions drawn at the time of the first peer review of carbofuran as presented here below will require reconsideration because

1) the livestock dietary burden as the prerequisite to assess residues in food of animal origin has changed due to amended notified uses and new residues data relevant in terms of animal feeding

2) the toxicological reference values for carbofuran have been significantly lowered on the basis of new toxicological data and therefore the angle of viewing the studies has changed (e.g. trigger and threshold values applied in a previous assessment are no longer appropriate)

However, the following information is kept for historical reference:

In terms of the representative uses, all concerned crops are considered potential feed items. However, based on the currently available residue data significant residues may only be expected from the use on sugar beet and maize. Residues of carbofuran and 3-OH-carbofuran above the respective LOQ were determined in sugar beet roots and tops and in maize plants with cobs and maize silage. A reassessment of the livestock dietary burden requested by EPCO 34 and submitted by the RMS in the addendum of February 2006, was not peer reviewed.

Livestock animal metabolism of carbofuran was studied in lactating goats and laying hens (FMC). Metabolism studies with benfuracarb (Dianica) administered to lactating cows and goats were considered appropriate by the applicant to address carbofuran metabolism in ruminants based on the argumentation that an identical metabolic pattern was found in rats following administration of benfuracarb and carbofuran, respectively.

In the study with lactating goats (FMC) the animals were orally dosed with carbofuran radio labelled in the phenyl-ring for 7 consecutive days. The chosen dose rate corresponds to a theoretical overdosing factor of at least 50N, with regard to the estimated maximum residues level in the total diet of cattle, assuming a diet composition containing sugar beets roots and tops or alternatively maize silage.

The majority of the administered radioactivity (94% of total dose) was rapidly excreted. Only a low amount (0.3% of total dose) was excreted with the milk and residue levels reached a plateau after 5 days, amounting to 0.35 mg/kg. The TRR in tissues and organs were low and residues did not appear to accumulate in fat tissues (<0.01 of total dose). Total residues above 0.01 mg/kg have only been found in liver (0.14 mg/kg) and kidney (0.27 mg/kg). Upon characterisation of residues in milk, liver and kidney, 3-OH-carbofuran as a toxicologically relevant metabolite has been identified at levels of 4-11% TRR in either matrix. Phenol compounds made up a major part of the radioactive residue in liver (15%), kidney (16%) and milk (54%). Carbofuran per se was not identified in any of the analysed samples.

In the studies with benfuracarb in cows and goats (Dianica) the investigation of metabolic degradation was not attempted in milk, tissues and organs. However, the level of total residues in milk and edible tissues was determined in the study with goats, and only low amounts of radioactivity were recovered in milk and no residues were detected in edible tissue. The highest chosen dose rate in the study corresponds to a theoretical overdosing factor of at least 20 N with regard to the estimated maximum residues level in the total diet of cattle. The metabolic pattern was investigated only in urine and indicated an extensive metabolisation into mainly 3-OH-Carbofuran and phenol metabolites through oxidation and hydrolysis steps. Neither benfuracarb nor carbofuran was present in urine. The submitted studies with benfuracarb are not appropriate to establish a complete picture of the metabolic pathway of carbofuran in ruminants, including a metabolic pattern in edible animal matrices, and to conclude on potential relevant metabolites in order to define a residue for risk assessment purposes.

Dietary intake of carbofuran/3-OH-carbofuran residues by poultry does not exceed 0.1 mg/kg total diet. Nevertheless metabolism studies with carbofuran in laying hens were submitted by both applicants and evaluated in the DAR. A metabolic pattern in poultry tissue and organs was only established in one of these studies (FMC) and was found to be very similar to that observed in the goat.

Based on the available data it is concluded that in livestock animals, carbofuran undergoes an extensive metabolisation proceeding primarily via hydroxylation on the furan ring to yield the major metabolite, 3-OH-carbofuran, followed by hydrolysis and oxidation steps to 3-keto-carbofuran and phenol derivatives (3-OH-7-phenol and 3-keto-7-phenol). A direct hydrolysis of carbofuran releases carbofuran 7-phenol. The phenols occurred mainly as conjugates in animal matrices.

No residue definition for animal matrices was proposed by the RMS, however, based on the available data EPCO 34 proposed to define the residue for animal product as 3-OH-carbofuran for risk assessment purposes. The same definition should apply for monitoring if necessary for future uses.

In a feeding study in lactating cows with carbosulfan (FMC) the level of carbosulfan, carbofuran and their pertinent metabolites (3-keto-carbofuran, 3-OH-carbofuran, carbofuran 7-phenol, 3-keto-7-phenol-carbofuran, 3-OH-7-phenol carbofuran) was determined.
No significant total residues or residues of individual metabolites <0.01 mg/kg are expected to occur in edible animal matrices taking into account the residue situation for the representative use proven by the data currently available. Thus, no MRLs for animal matrices are currently proposed.

B) The following text reflects the most recent considerations, discussions and conclusions on carbofuran on the basis of current data and information (resubmission procedure):

Livestock may be exposed to residues as defined in the 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 highest residues of carbofuran and 3-hydroxy carbofuran found in sugar beet in supervised residue trials. Though residues in rotational crops relevant in animal diet have not been considered, the available estimates are not expected to change significantly since critical residue levels have already been used in the feed categories green forage and root and tuber crops. 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.
On the basis of the livestock dietary intake assessment conducted by the RMS the trigger value of 0.1 mg/kg diet is exceed for dairy and beef cattle when intakes are considered on a dry matter basis.
Given the very low toxicological reference values for carbofuran and its metabolite 3-hydroxy carbofuran the experts in PPAPeR 70 agreed that it might be also necessary to assess potential residues in all animal products, even if the trigger value of 0.1 mg/kg diet was not exceeded for poultry and pig.

Two metabolism studies in poultry are available with carbofuran (1970 and 1994). However information is poor in the older study from 1970 which had been classified by the RMS as of limited utility during the first peer review of carbofuran.

Metabolism in lactating ruminants was studied with carbofuran, and with benfuracarb and carbosulfan for which carbofuran is the main metabolite. Information on residues in edible animal commodities was very limited in the study with benfuracarb. The study with carbosulfan was presented by the RMS in the Addendum of April 2009 on the basis of the 1997 JMPR evaluation and could only be used as far as it provided adverse information to the data submitted by the applicant.

Hence, the experts focussed mainly on the more recent metabolism study with carbofuran in poultry and the carbofuran metabolism study in lactating goats (both 1994), each study conducted over a period of 7 consecutive days.

Plateaus in milk and eggs were reached within the dosing period and thus accumulation of residues in animal matrices is not expected. The metabolite identification in animal matrices was considered sufficient. The majority of the total residue in tissues and organs was recovered as the carbofuran phenol metabolites, indicating extensive metabolism of carbofuran in the animals. Carbofuran itself was detected only in milk, in extremely low amounts. Of the toxicological relevant compounds 3-OH carbofuran was the most pertinent residue in edible animal matrices.

In these studies samples were analysed using an analytical method including a hydrolysis steps (acidic and enzymatic). Thus the sum of free and conjugated carbofuran and 3-hydroxy carbofuran, respectively, was determined and reported, but the respective of ratio free and conjugated compound remains unknown. The rat metabolism data indicate that conjugates are present in urine in faeces, and therefore it is reasonable to assume conjugates were also present in edible animal matrices. A data gap was identified for the applicant to address the amount of conjugates in the livestock metabolism studies.

On the basis of the available data the following residue definition for animal matrices was agreed for risk assessment: 3-hydroxy carbofuran free and conjugated expressed as carbofuran.

For monitoring the experts suggested to set the same residue definition as for risk assessment. It was however 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.

The experts reviewed the estimated levels of relevant residues in food of animal origin (addendum of April 2009). Though a ruminant feeding study is available it could not be used to derive residue levels for consumer risk assessment since the LOQ was considered to high (0.05 and 0.025 mg/kg for tissues and milk respectively) with regard to the low toxicological reference values of carbofuran and the 3-hydroxy carbofuran metabolite, respectively. For this reason residue levels were assessed on the basis of the animal metabolism studies and according to the estimated livestock dietary burden. These levels were used to conduct a provisional consumer risk assessment.

MRLs for food of animal origin can currently not be proposed due to necessary clarification with regard to the analytical method and residue definition for monitoring.

3.3. CONSUMER RISK ASSESSMENT

Note: Superseded by an updated risk assessment based on new data, only kept for historical reference:

To assess consumer risk the dietary intake of the sum of carbofuran and 3-OH-carbofuran residues was estimated and compared with the toxicological reference values of carbofuran. This approach can be considered appropriate as the metabolite 3-OH-carbofuran is assumed to be of comparable toxicity as carbofuran based on acute toxicity studies, however it should be noted that no long-term studies with 3-OH-carbofuran are available. It is also stressed that the carbofuran reference values were only provisionally agreed by EPCO 33 (refer to 2.11). Furthermore it is noted that following the experts' discussion and decisions, no updated risk assessment was submitted by the RMS. The initially presented risk assessment by RMS is summarised below for the sake of transparency, but should not be considered as agreed on.

In the chronic exposure assessment the TMDI was estimated based on the FAO/WHO GEMS/Food European Diet, the German diet and the UK PSD consumer exposure model and with the proposed MRLs for sugar beet, maize and sunflower seed. The estimated dietary intake of carbofuran and 3-OH-carbofuran residues ranges from *ca* 1% to 38% of the provisionally allocated ADI for carbofuran of 0.001 mg/kg bw/day, for the considered consumer groups.

The acute exposure assessment for consumers is based on JMPR FAO/WHO guidelines and UK PSD consumption figures for adults and toddlers. As highest residues (HR) the respective LOQs for carbofuran and 3-OH-carbofuran in the supervised residue trials have been applied. The estimates of acute dietary intake of carbofuran and 3-OH-carbofuran residues reached at the highest 102% of the provisionally allocated ARfD for carbofuran of 0.001 mg/kg bw/day for toddlers consuming maize.

The slight exceedance of the ARfD appears to be a theoretical concern due to limitations of the sensitivity of the analytical methods applied in some of the available residue trials (FMC). Considering the high acute toxicity of carbofuran and 3-OH-carbofuran it is advised to attempt a lower LOQ in the residue trials still to be generated.

Recent state of consumer dietary risk assessment:

Due to the data gaps identified by the meeting PRAPeR 70 the consumer risk assessment cannot be finalized, and therefore no updated assessment was submitted by the RMS after the meeting.

For discussion in the meeting PRAPeR 70 the RMS has provided a comprehensive dietary exposure and risk assessment for consumers using both the EFSA PRIMo and the UK model in the Addendum of April 2009.

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-OH-carbofuran is assumed to be of comparable toxicity as carbofuran based on acute toxicity studies.

An **exceedance of the ADI** was noted for UK toddlers in both models (EFSA PRIMo 173% ADI; UK model 101% ADI). As agreed by the meeting PRAPeR 70 the risk assessment could be further refined when residues in sugar are not considered at the level of the LOQ of the analytical method for sugar beet, but at a level of 0 mg/kg.

However, 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 proposed to consider as 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.

Based on the available data no further refinement of the consumer risk assessment is currently possible.

Finally, it was noted by the expert meeting in fate and behaviour PRAPeR 67 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 8 out of 9 scenarios (refer to 4.2.2.). In some of the scenarios the trigger of 0.1 µg/L may also be exceeded for the toxicolically 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[21] 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 the metabolites 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.

Tab. 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	1.6643	0.0437	0.1176	0.061	40.3	0.182	**121**	0.272	**182**
Hamburg	1.5890	0.0495	0.2085	0.061	40.7	0.183	**122**	0.275	**183**
Jokioinen	1.6238	0.0391	0.0651	0.057	38.3	0.172	**115**	0.258	**172**
Kremsmuenster	1.2330	0.0334	0.1093	0.046	30.4	0.137	91.1	0.205	**137**
Okehampton	1.2805	0.0366	0.1185	0.048	31.7	0.143	95.1	0.214	**143**
Piacenza	2.3195	0.0738	0.4252	0.093	62.0	0.279	**186**	0.418	**279**
Porto	0.0366	0.0008	0.0013	0.001	0.9	0.004	2.6	0.006	3.9
Sevilla	7.2117	0.1587	0.212	0.252	**168**	0.756	**504**	1.134	**756**
Thiva	0.1936	0.0054	0.0171	0.007	4.8	0.021	14.3	0.032	21.5

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

3.4. PROPOSED MRLS

The following MRLs were proposed on the basis of the first peer review of carbofuran. 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.
For the time being no MRLs can be proposed for plant and animal commodities.

The provisional MRLs as presented here below are kept solely for historical reference.

MRLs for carbofuran residues, defined as sum of carbofuran and 3-OH carbofuran expressed as carbofuran equivalents have been proposed by RMS at LOQ level. This fact results in different MRLs proposed by the RMS for the same crop, since the proposal is based on the respective LOQ reached in the residue trials submitted by the two different applicants.

Sugar beet	0.02* mg/kg (based on Dianica studies); 0.1* mg/kg (based on FMC studies)
Maize	0.02* mg/kg (based on Dianica studies); 0.1* mg/kg (based on FMC studies)
Sunflower seed	0.02* mg/kg (based on Dianica studies)

It is noted that the data base (per applicant), the MRL proposals are derived from, is not complete according to current requirements and consequently the MRL proposals should be considered as provisional. Moreover, following the conclusion of EPCO 34 on the residue situation in sugar beet the MRL proposal at LOQ level might need to be reconsidered.

4. Environmental fate and behaviour

In the frame of the first peer review of carbofuran, the fate and behaviour in the environment was discussed in the meeting of experts EPCO 31 (September 2005) on the basis of the DAR (March 2005), the carbofuran Reporting and Evaluation tables and the updated List of End Points (August 2005). An addendum to the fate and behaviour chapter has been provided on 18 May 2006. When reported, the information in the addendum has 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 were considered neither evaluated nor peer-reviewed in the first conclusion (July 2006).

For the resubmission, the RMS prepared an additional report (November 2008) 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 an addendum was prepared for the meeting of experts in March 2009. The additional report (November 2008) and this addendum (March 2009) were the bases of the second peer review and second expert discussion on the fate and behaviour of carbofuran in the environment in the meeting of experts PRAPeR 67 (April 2009). Additionally, some expert discussion on the carbofuran fate and behaviour in the environment took place during the peer review on benfuracarb (PRAPeR 62, January 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 of degradation in soil

A number of studies to address the carbofuran metabolism in soil were submitted by the two applicants of carbofuran on their respective dossiers and summarized by the rapporteur Member State in the DAR (March 2005). Only some of them were considered of acceptable quality. These are taken into consideration in this conclusion.

Metabolism of carbofuran was investigated in four soils under dark aerobic conditions at 20 ºC (Dianica, Völk, S., 2002). The soils covered a range of pH values (5.7-7.5), clay contents (9 - 34.2 %) and organic carbon contents (1.3 - 3.0 %). No metabolites reaching levels above 10%AR were found in these experiments. One experiment was repeated at 10 ºC in which metabolite 3-keto-carbofuran reached a 7.7 % AR at the end of the study (56 d). Some minor metabolites (< 2.5) were detected but not characterized. Unextractable residue amounted up to 57.7 % AR and mineralization reached a maximum of 66.3 % AR after 120 d.

Another study (FMC, Saxena A M *et al* 1994) was performed under dark aerobic conditions at 25 ºC with one soil (sandy loam, clay 11 %, OC 0.7 %) at two different pHs: 5.7 and 7.7 (the soil with pH 7.7 was prepared by adding lime to the collected soil with pH 5.7). In this study metabolite 3-keto-carbofuran reached a maximum of 12.41 % AR after 181 d. Other minor metabolites identified were 3-OH-carbofuran (max 1.32 % AR after 122 d), 3-keto-7-phenol and carbofuran-phenol.

An additional aerobic soil metabolism study (FMC, Schocken, M. J., 1989) is available. Additionally to the same metabolites, 3-OH-7-phenol carbofuran were identified. In this case 3-OH-carbofuran reached a maximum of 0.9 % AR and carbofuran-phenol a maximum of 9 % AR at the end of the study (184 d). None of the other maximum appearance of any identified metabolite was higher than 2 % AR.

An aerobic / anaerobic study is available (FMC, Matt F J, 1986) where the same minor metabolites identified in the previous studies are found. 3-keto-carbofuran reached a maximum of 6.2 % AR at the day of 31 of this study. All the other maximum appearance of any identified metabolite was less than 3 % AR (aerobic phase).

The mineralization in these previous three studies was between 0.7-14.6 % AR after day 112-120 days and the unextractable residues reached 7.7-94 % AR after 112 or 89 days (in the study where the unextractable residues reached the maximum of 94% on the day of 89, the unextractable residues decreased to 84.8% to the study end at 120 days).

Only one of the anaerobic studies submitted in the dossier was found acceptable by the rapporteur Member State and summarized in the DAR (Dianica, A Van der Gaauw, 2002). The study was performed in one soil (pH 7.4, clay 21.9 %, OC 1.2 %) under dark anaerobic conditions at 20 ºC. Only carbofuran-phenol was identified as major metabolite in this study (max. 62.9 % AR after 28 d). Another metabolite fraction M4 reached a maximum at the end of the study (max. 8.9 % AR after 120 d) but was shown to contain several compounds. Mineralization was low (CO_2 6.1 % AR after 120 d) and bound residues reached a maximum of 62.7 % AR after 120 d.

Photolysis of carbofuran in soil was investigated in two studies. In one of the studies (FMC, McGovern, P.A. *et al*, 1989) the same minor metabolites already identified under aerobic conditions were found (< 5 % AR). In the other study (van de Gaaw, A., 2002) only parent carbofuran was found.

In the field studies performed with parent carbofuran in USA (FMC) metabolites 3-OH-carborfuran, 3-keto-carbofuran and carbofuran-phenol were analyzed. Results are only reported as total carbamate for some of the trials and it is not possible to know the exact amount of each metabolite. In other trials 3-OH-carborfuran is found at levels up to the 3 % of the total residue and 3-keto-carbofuran at levels up to approx. 20 % of the total residue (max 0.079 mg / kg). Carbofuran-phenol is not found above the LOD in any of the trials.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The rate of degradation of carbofuran was investigated in the same studies used to establish the route of degradation. Carbofuran was shown to be low to moderate persistent ($DT_{50\ 20\ °C}$ = 9.5-19.4 d; Dianica, Völk, S., 2002) or high persistent ($DT_{50\ 25\ °C}$ = 149 – 321 d; FMC, Saxena A M *et al* 1994 / $DT_{50\ 25\ °C}$ = 352 d; FMC, Schocken, M. J., 1989 / $DT_{50\ 10\ °C}$ = 110 d; Dianica, Völk, S., 2002) in soil depending on the study. In the soil degradation study under anaerobic conditions carbofuran is low persistent ($DT_{50\ anaerobic\ 20\ °C}$ = 7.6 d).

Additionally, the rapporteur Member State included in the list of end points (of the original DAR in 2005) degradation parameters obtained from other studies where carbofuran appeared as metabolite of benfuracarb or carbosulfan. However, finally these data were not included in the list of end points of the EFSA conclusion (2006) due to the lack of adequate study summaries, availability of the degradation parameters or the unacceptability of some of these studies.

For the resubmission of the dossier of carbofuran, FMC reanalysed and normalised (to FOCUS reference conditions) all of the available data for carbofuran and its precursors (carbosulfan and benfuracarb) according to the FOCUS kinetic guidance document. This reanalysis for all the experiments, where the degradation of carbofuran was adequately investigated and the experiment was regarded as valid by the previous peer review of carbofuran, carbosulfan or 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 high persistence of carbofuran (Saxena A M *et al* 1994 and Schocken, M. J., 1989; Additional report of carbofuran, Annex B, B.8.1.1.1). 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.

The rapporteur Member State did not agree with the use of the three long DT_{50} values (151 d, 54.5 d and 387 d; refitted and normalized to FOCUS reference conditions) from the experiments that indicated a potential high persistence of carbofuran (Saxena A M *et al* 1994 and Schocken, M. J., 1989; Additional report of carbofuran, Annex B, B.8.1.1.1). Therefore the RMS presented an evaluation of the distribution of the available soil DT_{50} values in the addendum for the carbofuran additional report (March 2009), however no new scientific argumentation supporting the exclusion of these values was provided. The meeting of experts PRAPeR 67 (April 2009) discussed and confirmed that the degradation parameters derived from these studies (by Saxena and Schocken) should be used in the FOCUS modelling.

Whereas in one of the studies photolysis seems to contribute to the dissipation of carbofuran (FMC, McGovern, P.A. *et al*, 1989) the other study shows that carbofuran is stable to photolysis (van de Gaaw, A., 2002). Due to the fact that the former study presents some drawbacks, this assessment will consider carbofuran as stable to photolysis in soil.

Summaries of some field studies performed either with carbofuran (USA) or carbosulfan (EU, reported in the carbosulfan DAR from 2004) as parent compound were provided by one applicant (FMC, Mol, 2002 and Taylor and Houseman, 1982). Addendum including the data from carbosulfan studies has been provided by the rapporteur Member State in April 2006; however, the complete assessment of the studies is still missing in this addendum. Half life of carbofuran in the EU trials (where it appears as metabolite of carbosulfan) ranges between 1.3 to 71.9 d. Half life of carbofuran in the USA sites (where it is applied as parent compound), assessed as relevant for the EU climatic conditions by the rapporteur Member State, ranges between 5 and 121 d. However, only the field studies performed in EU were used by the rapporteur Member State in the risk assessment. The meeting of the 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 was not assessed and peer reviewed, however the meeting of experts (EPCO 31, September 2005) agreed that it is necessary to determine whether the studies from the USA sites are acceptable for the EU risk assessment.

PEC soil for carbofuran presented in the original DAR (March 2005) are based on the worst case EU field half life (DT_{50} = 71.9 d) determined for carbofuran in the carbosulfan field studies, however the meeting of the experts (EPCO 31, September 2005) was not able to conclude the appropriateness of using this value due to the lack of relevant information for the field studies in the DAR. In the additional report for carbofuran the RMS stated that the field studies performed in the USA were of limited quality therefore these results were not used in the final risk assessment. Moreover an assessment of the experiment resulted the DT_{50} of 71.9 days was provided. The conclusion of the RMS in this assessment was that this experiment is not accepted anymore and for PECsoil calculation the second longest DT_{50} of 27 days was used from the data set of the EU field studies. This is in line with the conclusion of the PRAPeR 62 (January 2009) expert meeting (on benfuracarb), where this issue was also discussed.

No information on the degradation rate of metabolites was available in the original DAR, therefore a data gap was set for the rate of degradation in soil for 3-OH-carbofuran, 3-keto-carbofuran and carbofuran-phenol.

The additional report prepared for the resubmission contained summaries of acceptable studies regarding the degradation of these metabolites in three aerobic soils (pH 5.7-6.9, OC content 1.02-2.29%, clay content 7.9-42%). The DT_{50} of 3-OH-carbofuran was less than one day in all the three soils. The geometric mean derived after the normalisation to FOCUS reference conditions (20°C and -10kPa soil moisture) of the three SFO values was 0.41 day. The SFO DT_{50} values of 3-keto-carbofuran were between 1.54 and 8.12 days. The geometric mean after normalisation to FOCUS reference conditions was 3.01 days. Additionally, the degradation of the minor soil metabolite carbofuran-phenol was also investigated in the three soils. The results indicated that the DT_{50} of this metabolite is less than one day. However in light of the relatively high vapour pressure (estimated by QSAR modelling) of this metabolite, it was questioned whether these results can be regarded as reliable degradation endpoint. The meeting of experts PRAPeR 67 (April 2009) discussed and agreed that in this case, where the use of the soil degradation/dissipation endpoint for this metabolite is limited to the PECsw/sed calculation by the FOCUS Step 1 and 2 tools only, the use of these study results is acceptable. It should be noted that the meeting of experts PRAPeR 67 finally recommended another approach to calculate PECsw and PECsed values (see point 4.2.1), but the meeting conclusion above is still appropriate.

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

An acceptable batch adsorption / desorption study (Dianica; Mamouni, 2002) is available for carbofuran in four soils. Carbofuran may be classified as very high mobile compound (K_{oc} = 17 – 28 mL / g). The study presented by the other notifier is of limited acceptability, but the results are in the same range. A data gap for further batch adsorption / desorption studies on carbofuran soil metabolites was deemed to be necessary to complete the FOCUS-GW calculations by the meeting of MS experts (EPCO 31, September 2005). The additional report for carbofuran included batch adsorption/desorption studies for three metabolites (3-OH-carbofuran, 3-keto-carbofuran and carbofuran-phenol) in three soils. Due to the fast degradation observed in the experiments especially for 3-OH-carbofuran and 3-keto-carbofuran, reliable Freundlich isotherms were not established for these metabolites. The calculated K_{doc} values for 3-OH-carbofuran were in the range of 43-62 mL/g (mean 55 mL/g). Due to the fast degradation in aqueous solution, the reliability of the measured adsorption potential of this metabolite to soil, at least for one of the three experiments was questioned. The RMS agreed that the results of this experiment might be refitted further, but considered that the assumptions applied in the FOCUS modelling were sufficiently worst-case. The meeting of experts PRAPeR 67 (April 2009) agreed that the use of the mean K_{doc} value of 55 mL/g is supported. The K_{doc} values for 3-keto-carbofuran were in the range of 47.5-504 mL/g (mean 330.5 mL/g) (note: the dataset of 3-keto-carbofuran is a mix of one K_{doc} value and two K_{Foc} values). Additionally, the adsorption/desorption of the minor soil metabolite carbofuran-phenol was also investigated in three soils. The calculated K_{Foc} values varied from 444 to 1810 mL/g (mean 1031 mL/g) (1/n 0.407-0.751).

An aged column leaching study in four soils is available (FMC, Saxena, A. M. *et al* 1994 b). This study shows that carbofuran and its metabolites (3-keto-carbofuran and carbofuran-phenol) are mobile and may leach under the conditions of the experiments.

The rapporteur Member State proposed in the original DAR (March 2005) a data requirement for a lysimeter study. In the additional report two lysimeter studies were presented, but none of them were regarded as conclusive regarding the leaching potential of carbofuran or its metabolites.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Two acceptable hydrolysis studies are available (FMS and Dianica). In sterile aqueous buffer solutions at 25 ºC, hydrolysis of carbofuran is pH dependent. Carbofuran is stable at pH 4 and degrades with half lives of 28 – 45.7 d at pH 7; 2.7 d at pH 8; and 0.1 d at pH 9. Transformation product carbofuran-phenol was the major hydrolysis products identified. Carbofuran-phenol was shown to be stable to hydrolysis at pH 4 and 7, whereas degrades hydrolyses slowly at pH 9 (DT_{50}= 278 d).

Only one of the aqueous photolysis studies available was considered acceptable by the rapporteur Member State (Dianica, van der Gaaw, A., 2002). Photolysis may contribute only slightly to the degradation of carbofuran in water.

Carbofuran is not readily biodegradable according the available study.

Dissipation of carbofuran in the water sediment was investigated in two studies with a total of three systems. The first study (FMC, Saxena A.M., Marengo, J. R., 1994) was performed on a dark aerobic system with pond sediment (pH 5.3) and water (pH 6.1) at 25 ºC during 30 d. Carbofuran dissipates from the surface water by degradation and partition to the sediment. The carbofuran degraded in the whole system with a first order half life of approximately 41 d (note that this value was the first estimation from the original DAR in 2004). Transformation products 3-OH-carbofuran and 3-keto-carbofuran were found both in the water and the sediment phase at low levels (≤ 0.31 % AR). Mineralization was low (CO_2 = 1.87 % AR at the end of the study) and bound residue reached a maximum of level of 33 % AR. The rapporteur Member State required in the DAR a new water/sediment study or additional information on carbofuran-phenol metabolite and on the degradation rate of carbofuran. In 2006, EFSA recalculated the half life ($DT_{50\ \text{whole system}}$ = 44.6 d) by non-linear regression that passed the χ^2 test with an error level of 6.8 %. Fitting was not very good and it was found that it would be necessary to have more data points at longer times to have a reliable half life. However, the available data clearly indicated that the half life must be longer than 30 d for this system. For the resubmission, in the additional report, this value was refitted resulting the DT_{50} of 47.24 days and normalized from 25°C to 20°C resulting the DT_{50} of 70 days (whole system, 20°C) (note that the DT_{50} of 70 days seems to be the results of the temperature normalization of the value of 44.6 days using the new Q10 of 2.58, rather than the normalization of the value of 47.2 days using the old Q10 of 2.2). Clarification on metabolite carbofuran-phenol seemed to be related to the high levels of this metabolite found in the second replicate of the days 20 and 30. These high levels (water phase 5.9 %AR, sediment phase 17.6 %AR) were explained due to a problem with the trapping system that produced a change of pH from acidic to alkaline in the water sediment systems. Available water sediment study under alkaline conditions already showed the faster degradation of carbofuran and the formation of this metabolite at high levels. Therefore, EFSA did not consider this data requirement essential to finalize the EU risk assessment. A position paper from one of the applicants was included in the additional report, but regarded as not useful to clarify the pH dependency by the meeting of experts PRAPeR 67 (April 2009).

Another water sediment study (Dianica; Diehl M., 2002) was performed in two dark aerobic systems obtained from a river (water: pH 8.2; sediment: 7.45) and a pond (water: pH 7.0; sediment: 7.08). In these systems, carbofuran dissipated from the water phase with half lives of 5.3-6.9 d and degraded in the whole system in with half lives of 7.8 – 11.6 d. For the resubmission, in the additional report, these results were refitted, which resulted the water phase half lives of 6.9-8.5 days and the whole system half lives of 9.04-11.6 for carbofuran in these water-sediment systems. From this study, the degradation of carbofuran-phenol in the whole system was also recalculated and the half-life was found to be 1.69-1.86 days. These refitted values are included in the Appendix A of this conclusion

together with results from the additional reports of carbosulfan and benfuracarb. The only major metabolite found in the water phase was carbofuran-phenol (max. 12.0 % AR after 4 d). Only carbofuran reached levels above 10 % AR in the sediment. Some minor metabolite fractions were identified but not characterized. Bound residues reached maximum of 74 -78 % AR at the end of the study (102 d).
These experiments seem to indicate that the degradation of carbofuran may be pH dependent in water sediment systems.
An anaerobic water / sediment study was available and summarized in the DAR but not employed for the risk assessment of the EU representative uses.

In the original dossiers (2002) the two applicants proposed different approaches to estimate the potential contamination of surface water. None of these approaches followed the FOCUS SW scheme since the input parameters selected to calculate PEC_{SW} and the assumptions made were not fully justified. The rapporteur Member State considered in the original DAR (2005) that more appropriate PEC_{SW} calculations were necessary to finalize the assessment of the EU representative uses and proposed the use of FOCUS SW scheme. FOCUS modelling for estimation PECsw and PECsed were performed in the additional report (November 2008), however many input parameters (e.g. soil DT_{50}, K_{doc}/K_{Foc}, 1/n) were commented by several MS and EFSA and deviated from the conclusion of the meeting of PRAPeR 62 (January 2009), when the input parameters for FOCUS modelling for carbofuran and its metabolites had already been agreed. In the addendum prepared for the additional report a new FOCUS modelling was included. For this modelling the input parameters which were criticized were changed to the agreed values, but three additional parameters (DT_{50} for the water phase for carbofuran, the Q10 value and the vapour pressure data for all the metabolites) were also changed although these changes were not required previously. The impact of these changes was discussed by the experts at the meeting of PRAPeR 67 and it was agreed that these changes have presumably negligible impact on the outcome of the modelling in this case. Therefore the use of the PECsw and PECsed values presented in the addendum (March 2009) in the risk assessment was agreed by the meeting. The change of the DT_{50} for the water phase for carbofuran (based on whole system value) from 70 days to 15.3 days was checked by EFSA after the meeting of experts and it was found that the change of this value resulted no change in 2 out of the 3 PECsw values (D3 ditch, D4 stream; global max. values) and in one case (D4 pond) the PEC value increased from 0.103 to 0.139 μg/L (note: for the results of the so called runoff scenarios this value has no impact at all in this case).
The appropriateness of the model approach used for carbofuran-phenol was also discussed. The meeting of experts (PRAPeR 67) agreed that the use of the FOCUS step 1 and 2 tools is not suitable in this case, because the exposure of the water body is modelled via the soil; however this metabolite is formed only in the water-sediment systems. Therefore the meeting recommended the use of the parent Step 3 PEC values in the risk assessment for this metabolite as a conservative estimate after

the potential correction for molar weight and maximum occurrence in the water-sediment studies (12% in water, 17.6% in sediment).

Whereas exposure of surface water to the active substance is not excluded, the meeting of MS experts (EPCO 31, September 2005) agreed that exposure to the formulations in its integrity may be excluded when the product are used according the GAP (incorporated into soil) for the representative uses. Therefore, no specific ecotoxicological studies with the formulation need to be required to assess the risk of the representative uses to the aquatic environment.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Potential groundwater contamination by the carbofuran and its metabolites 3-OH-carbofuran and 3-keto-carbofuran (soil metabolites containing the toxosphore carbamate) was not appropriately addressed by any of the applicants.

The meeting of the experts (EPCO 31, September 2005) identified a data gap for FOCUS PEC_{GW} taking into account all the information available on the rate of degradation of carbofuran and to address the potential groundwater contamination by carbofuran soil metabolites.

FOCUS modelling for estimation PECgw were performed in the additional report (November 2008), however many input parameters (e.g. soil DT_{50}, K_{doc}/K_{Foc}, 1/n, soil incorporation depth, plant uptake factor, Q10 value, vapour pressure and formation fraction of the metabolites) were commented by several MS and EFSA and/or deviated from the conclusion of the meeting of PRAPeR 62 (January 2009), when the input parameters for FOCUS modelling for carbofuran and its metabolites had already been agreed. In the addendum prepared for the additional report new FOCUS modelling was included. In this modelling the agreed parameters were used, however the used Q10 value, the formation fractions of the metabolites and the issue of the available different set of vapour pressure data for the metabolites were discussed in details. The meeting of experts PRAPeR 67 (April 2009) agreed that the PECgw modelling presented in the addendum (March 2009) is accepted. All the input parameters which were questioned were either changed to the accepted value, or have negligible effect to the outcome of the modelling or regarded as conservative input value (especially regarding to the metabolites).

In these simulations the applied for representative use of soil incorporation (incorporation depth 7cm, dose 600 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 (only for PEARL) application scheme using the following input parameters: carbofuran single first order DT_{50} 14 days (median of the normalised laboratory values, n=17), K_{Foc} 22 mL/g, 1/n=0.96; 3-OH-carbofuran single first order DT_{50} 0.41 days, K_{doc} 55 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 carbofuran 1. Additionally, the metabolite carbofuran-phenol was also modelled (DT_{50} 1 day, K_{Foc} 1031 mL/g, 1/n=0.9, formation fraction from carbofuran 1).

Parent 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 0.19-7.21 µg/L using the PEARL model, and 7 out of the 9 modelled FOCUS scenarios with the range of 0.48-1.2 µg/L using the PELMO model, when annual application was simulated. Only the Porto (PEARL) or Porto and Thiva (PELMO) FOCUS scenarios resulted PECgw <0.1µg/L (0.037 µg/L, 0.018 µg/L and 0.003 µg/L, respectively).

When triennial application was simulated by FOCUS PEARL 7 out of the 9 modelled FOCUS scenarios exceeded the 0.1µg/L parametric drinking water limit (0.38-1.26 µg/L), and again Porto and Thiva FOCUS scenarios resulted PECgw <0.1µg/L (0.018 µg/L and 0.056 µg/L, respectively).

The PECgw for the metabolites simulated exceeded the 0.1µg/L parametric drinking water limit only in a few cases of FOCUS simulations except the annual simulation with PEARL for 3-keto-carbofuran, where 6 out of the 9 results were above the trigger of 0.1 µg/L (for details see the addendum for carbofuran additional report, March 2009). However it is noted that the simulations for the metabolites were regarded as extreme worst case, as 100 % formation was assumed, while the observed maximum occurrences or the assumed formations in soil are significantly lower.

It is noted that in the addendum (March 2009) FOCUS simulations with the dose 60 g/ha were also summarized however these simulations were not considered by the RMS regarding the applied for representative uses.

4.3. Fate and behaviour in Air

Vapour pressure of carbofuran is in the range of 10^{-5} – $2.25 \cdot 10^{-4}$ Pa and Henry law constant in the range of $5 \cdot 10^{-5}$ to $1.58 \cdot 10^{-4}$ $Pa \cdot m^3 \cdot mol^{-1}$ under common environmental temperatures (20 – 25 ºC). Half life in air due to photochemical degradation was estimated to be less than five hours. Carbofuran is not expected to be prone to long range transport through the air compartment.

5. Ecotoxicology

Carbofuran 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. An addendum to the chapter on ecotoxicology has been provided on 18 May 2006. The information in the addendum has been summarized too briefly to draw any conclusion on its reliability. Carbofuran was resubmitted, peer-reviewed and discussed in the PRAPeR expert meeting for ecotoxicology (PRAPeR 68) in May 2009 on the basis of the additional report from November 2008, update April 2009 and the addendum to Volume 3, B9 from April 2009.

5.1. RISK TO TERRESTRIAL VERTEBRATES

A risk assessment for birds and mammals was conducted according to SANCO/4145/2000. Inconsistencies with regard to the size and weight of the granules were noted during the peer-review. The applicant did not provide detailed information on the granule size and this needs to be clarified further. The risk assessment was based on a granule size of 0.4-0.85 mm and an average weight of 0.87 mg. The loading of one granule was assumed to be 0.0437 mg a.s./granule.

The number of granules to reach the acute and dietary LD_{50} dose was calculated to be 0.2 and 0.5 granules for a 15 g bird indicating a potential high risk to birds.

Two field monitoring studies were submitted. One was assessed as inconclusive by the rapporteur Member State. Slightly higher mortality of birds and mammals was observed in fields treated with Furadan 5 G. The study indicated a high risk to sparrows and mice within the first 4 days after the application.

A test on the acceptance of the granules was conducted with bobwhite quail (*Colinus virginianus*). The birds were exposed to treated seeds and granules (spread on the floor of the aviaries) equivalent to an application rate of 12 kg Diafuran 5 G/ha (the maximum recommended dose) and at dose rates equivalent to 93% and 99% incorporation into the soil. In the group exposed to the highest dose rate one bird was found dead. Severe sub lethal effects were observed in birds exposed to treated seedlings and granules equivalent to the highest recommended dose without incorporation of granules and at 93% incorporation efficiency. It is difficult to quantify the observed sub lethal effects in terms of potential adverse effects in the field. However, the study gives an indication that severe sub lethal effects may occur at the proposed GAPs which could lead to an increased mortality in the natural environment. A new study with the granular formulation Curaterr GR5 and house sparrow was included in the resubmission. The test should simulate exposure via grit uptake. Grit particles were placed on the soil surface together with 36 Curaterr GR5 granules/m^2. No mortality was observed in the study. However The RMS concluded that extrapolation to a real field situation is difficult. The applicant provided a probabilistic risk assessment for the uptake of granules. Two scenarios were simulated a “worst case” and an “average case”. The principle of the probabilistic risk assessment was agreed by the experts as a relevant way to refine the acute risk assessment. However the experts identified uncertainties related to the input parameters and noted that several input parameters were clearly not worst case although this was claimed by the applicant for the “worst case” scenario. Sources uncertainty were e.g. only one trial with relatively few sampling points was available to derive the numbers of granules on the soil surface, spills were not taken into account in the simulations. In the field trial no granules were found on the surface in the middle of the field but high numbers of granules were found at the end of the row. In the “worst case” scenario it was assumed that the birds visit all area with the same frequency and in the “average case” scenario it was assumed that the frequency of bird visits correlates to the size of the areas. The experts questioned this assumption since the field margins may be visited more frequently by small birds seeking grit, particularly if there are structures like hedges. In the calculations it was assumed that the loading of the granules was 0.0185 mg a.s./granule while the worst case would be 0.0437 mg a.s./granule. PT values were included in the simulation. However these PT values were collected for a situation with established crops and therefore are considered not suitable for refinement of the risk of uptake of granules as grit. Clarification on the granule size is still needed. This information is important to know the size overlap with preferred grit particles of different birds. The experts did not accept the uncertainties in the input parameters taking into consideration the very high acute toxicity of carbofuran to birds. A data gap was identified to further address the risk from uptake of granules.

A high risk to birds was identified in the first-tier risk assessment for the uptake of contaminated food items (sugar beet seedlings, earthworms and arthropods). Reduced PD and PT values were suggested in the refined risk assessment together with measured residues in food items. A residue trial in sugar beet was conducted at an application rate of 600 g a.s./ha. The metabolite 3-OH carbofuran which contains still the carbamate moiety was not measured in the trial. The applicant suggested an extrapolation factor of 6.13 to account for the content of 3-OH carbofuran. This was rejected by the RMS because of the high variability in the content of 3-OH carbofuran observed (the highest factor for extrapolation to the total of carbofuran and 3-OH carbofuran was 25.2). The extrapolation factor of 2.5 suggested for benfuracarb was not accepted because it was derived from residue trials with a different crop (cabbage) and the data from the sugar beet trial indicate that the extrapolation factor for sugar beet would be greater. The risk assessment was based on carbofuran content only. However, taking only the carbofuran concentration into account, would clearly lead to an underestimation of the risk from residues in seedlings. In order to refine the risk assessment for the application rate of 60 g a.s./ha the applicant suggested that the residue values could be divided by 10 to extrapolate to the lower application rate. The RMS did not agree to such a linear relation between application rate and residues, because it is only based on two residue trials and there was more than 50% variation in the measured residues in the trials. Furthermore the plant uptake curve is not known and the plateau of the uptake rate could have been reached at an application rate of 600 g a.s./ha or lower. The experts agreed to the RMS that such a linear extrapolation to a lower application rate is uncertain. A data gap was identified for further residue trials in accordance with the GAP use and at different field conditions. The concentrations of carbofuran and its metabolite 3-OH carbofuran should be measured in these trials.

A residue trial with arthropods was conducted with an application rate of 375 g a.d./ha. Extrapolation to a higher rate was considered to be possible for spray applications. However for granular formulations this was considered more difficult. The residues which can be found on insects are very much dependent on their behaviour. Sampling was done by pitfall traps. Therefore only surviving and mobile insects were caught and analysed. Since carbofuran is an insecticide it is likely that at least some insects are killed by the active substance. The dead insects could potentially carry higher residues but would not be caught in the pitfall traps. The content of 3-OH carbofuran was not measured. The experts were of the opinion that the provided residue data will probably underestimate exposure. A data gap was suggested to carry out arthropod residue trials with the correct application rates, with behavioural observations and including residues on dead arthropods and to include 3-OH carbofuran in the measurements.

The residues in earthworms were measured in the same study as for arthropods. 3-OH carbofuran was not measured. It was noticed that the earthworms were rinsed and stored alive overnight before analysis. Rinsing and storing for one night has probably reduced the residue levels in earthworms and would lead to an underestimation of the exposure. Furthermore data on precipitation during the field trial should be followed because rainfall will probably affect the disintegration of granules and release of the active substance. The experts suggested a data gap for new residue trials with earthworms at the correct application rates and without rinsing the earthworms before analysis. The metabolite 3-OH carbofuran also needs to be measured.

Refinement of PD and PT values were suggested on the basis of general information on the landscape and food composition but no data (field observations and telemetry studies) were provided to support the suggested PD and PT refinement. However, even with the proposed PT, PD refinement the resulting TERs were below the trigger of 10 and 5. The experts pointed out that targeted studies should be carried out to investigate the food consumption of focal species in fields with sugar beet seedlings.

The acute risk to birds from uptake of contaminated food items was further refined by body burden modelling for yellow wagtail (*Motacilla flava*) and wood pigeon (*Columba palumbus*) according to the opinion on pirimicarb (PPR-Panel 2005). Several input parameters were highly uncertain or clearly not worst-case values. The concentrations in the food items were based on an application rate of 400 g a.s./ha instead of 600 g a.s./ha. The half life of ADME processes (assimilation, distribution, metabolisation, excretion) was based on recovery of acetylcholine esterase activity as a surrogate of ADME processes. The PPR opinion on pirimicarb suggests that the avoidance threshold dose should be between the NOEL and LOEL for food uptake. The avoidance threshold dose suggested by the applicant was assumed to be 0.3 x HD5 (mean 5th percentile of the LD50) and 0.5 x HD5. The worst case value would have been 0.9 x HD5. The studies on which the avoidance delay time was base on were not made available to the RMS. Taking all uncertainties into account the experts were of the opinion that the refined risk assessement was not acceptable.

The long-term endpoint for birds proposed by the RMS did not include the parental mortality. The experts were of the opinion that parental mortality cannot be disregarded since it will also affect reproduction. No long-term reproductive NOEL could be derived from the reproduction study because parental mortality was observed even at the lowest tested dose. It was not clear if the effects of carbofuran are only acute effects. In order to avoid animal testing it was agreed to use the LC10 of 0.64 mg a.s./kg bw/d from a 14 day dietary study as a surrogate for the long-term NOEL together with a safety factor of 10 to account for the shorter exposure period compared to the long-term study. The TERs were significantly below the trigger of 10 indicating a high long-term risk to birds.

The number of granules to reach the acute LD_{50} and the long-term NOAEL was calculated to be 1.82 for a small mammal of 15 g indicating a potential high acute risk to mammals. The RMS provided a risk assessment for unintentional uptake of granules according to the EPPO scheme which resulted in an acceptable risk to mammals. The experts agreed to the risk assessment.
The first tier TERs for the uptake of residues in food items were significantly below the trigger values of 10 and 5. The refined risk assessment was based on measured residues in sugar beet seedlings, earthworms and arthropods. The residue values were not accepted to be used in the risk assessment (see discussion above for birds).

Refinement of PD and PT was suggested by the RMS for hare (*Lepus europaeus*) and common shrew (*Sorex araneus*). The refinements were based on general information of food composition during the year. For hare it was suggested to use a PD of 0.4 for dicotyledon leaves (only sugar beet leaves) and 0.6 as untreated feed (monocotyledonous leaves) in the risk assessment. For shrew the PD was 0.8 for earthworms and 0.2 for arthropods. It was noted by the experts that there these refinements include some uncertainty since the data were not derived from targeted studies on sugar beet fields. However, even with the proposed refinement the resulting TERs were below the trigger values of 10 and 5.

The acute risk assessment for hare was further refined by body burden modelling analogous to birds (see above). It was not clear from where the feeding rate per minute was derived from. The modelling was done for 400 g a.s/ha instead of 600 g a.s./ha and the endpoint used was slightly wrong (5.5 instead of 5.3). The experts noted that smaller mammals would not be covered by the refined risk assessment for hare. The above mentioned input parameters were uncertain and/or do not present a realistic “worst case” scenario. Therefore the refinement was not accepted.
A data gap was identified for the applicant to further address the risk to mammals from uptake of residues in contaminated food items. The choice of the long-term endpoint for mammals was discussed in the expert meeting. The experts raised concerns since the long-term endpoint NOAEL of 0.71 mg a.s./kg bw/d was the average of endpoints from different studies where different effects were observed. The experts suggested that the final endpoint for the ecotoxicological risk assessment should be chosen after the long-term endpoints were confirmed by the experts on mammalian toxicology. The long-term endpoint of 0.1 mg a.s./kg bw/d based on neurotoxic and testicular effects was confirmed by the experts on toxicology. However the long-term TERs were below the trigger also with the originally proposed long-term NOAEL of 0.71 mg a.s./kg bw/d.

A new risk assessment for birds and mammals for the uptake of contaminated drinking water was provided in the addendum. The calculation followed the suggestions of the PPR-Panel on the science behind the guidance document on risk assessment for birds and mammals (PPR-Panel 2008). The resulting acute TER for small granivorous mammals was 20 but the acute TER for birds was significantly below the trigger of 10. However, the formula was developed for spray applications and the RMS was of the opinion that the risk may be overestimated. The experts in the meeting noted that a high risk could prevail for situations where puddles are formed at locations where high numbers of granules are left on the soil surface (e.g. end of row).

Overall it was concluded that a high risk to birds and mammals was indicated for the representative use evaluated. The experts expressed their doubts that a safe use could be demonstrated even with further refinement of the risk assessment.

5.2. RISK TO AQUATIC ORGANISMS

Aquatic invertebrates were the most sensitive group of aquatic organisms tested. The acute and long-term TERs were above the Annex VI trigger for fish, algae and sediment dwellers with FOCUS step3 PECsw. The TERs were below the trigger for crustaceans (*Daphnia magna*, *Ceriodaphnia dubia*) in the FOCUS scenarios which are based on drainage (D3, D4). The exposure via run-off was neglgible in the FOCUS run-off scenarios R1 and R3.

No further refinement of the aquatic risk assessment was provided and a high risk to the aquatic environment cannot be excluded for the representative use of carbofuran at an application rate of 600 g a.s./ha for environmental conditions represented by the FOCUS drainage scenarios.

The risk from the metabolites 3-keto-karbofuran, 3-OH-carbofuran and carbofuran-phenol was assessed as low.

Overall it can be concluded that a high risk to aquatic organisms cannot be excluded for the application rate of 600 g a.s./ha and environmental conditions represented by the FOCUS drainage scenarios (D3, D4). Further refinement of the risk assessment is needed. The risk was considered to be low for environmental conditions represented by the run-off scenarios (R1 and R3).

5.3. RISK TO BEES

Carbofuran is very toxic to bees with acute oral and contact LC_{50} values ranging from 0.0357 µg a.s./bee to 0.05 µg a.s./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

Effects of >50% were observed in extended laboratory studies and semi-field tests with the ground dwelling beetles *Aleochara bilineata* and *Poecilus cupreus* and the fromulation Curaterr GR5. A field study was conducted at an application rate of 375 g a.s./ha where recovery was observed within 2 months of all invertebrate taxa investigated. The application rate in the field study does not cover the

the supported use of 600 g a.s./ha in sugar beet. Therefore a data gap remains to address the risk to non-target arthropods for an application rate of 600 g a.s./ha.

5.5. RISK TO EARTHWORMS

The acute risk to earthworms was assessed as low but the long-term TER values were below the trigger of 5 indicating a high long-term risk to earthworms. A data requirement for a field study was identified in the original DAR. FMC submitted a position paper and an argumentation for using the earthworm field study with carbosulfan in June/July 2005. A position paper was submitted for the use of Diafuran 5G by Arysta in August 2005. The rapporteur Member State concluded in the addendum of May 2006 that the information provided by the applicants is not sufficient to address the potential high long-term risk to earthworms.

In the risk assessment it was referred to a field study with the formulation Marshall25CS (a.s. carbosulfan) to address the long-term risk to earthworms. Carbosulfan degrades rapidly to its primary metabolite carbofuran and therefore the study was suggested to be of use in the risk assessment for carbofuran. The application rate was 1.3 kg carbosulfan/ha leading to initial measured concentrations of 0.6 mg carbosulfan/kg wet soil and 2.8 mg carbofuran/kg wet soil. A severe impact on earthworm populations was observed after application of the product. Earthworm populations recovered 6 months after the date of application. The measured concentration of 2.8 mg carbofuran/kg wet soil would cover the PECsoil of 0.8 mg carbofuran/kg dry soil. However it was noted that the PECsoil was calculated for an even distribution of the active substance in the field, while in reality there will be high concentrations locally due to the in furrow application. It was unclear whether this would have a greater impact on the earthworm populations than an even distribution of the a.s. over the whole field surface. A study (Broadbent and Tomlin; 1982) was mentioned in the DAR where more severe effects were observed in studies with even distribution of the test substance. However the study was not submitted and no study summary was made available in the DAR. Since this study is of importance for drawing a final conclusion the experts in the meeting suggested a data gap for the submission of this study.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

Laboratory studies with the formulation Furadan 5G and *Folsomia candida* and *Hypoaspis aculeifer* were submitted. The NOECs (reproduction) were 0.21 mg a.s./kg dry soil and 10.4 mg a.s./kg dry soil. The resulting TERs based on the initial PECsoil of 0.8 mg a.s./kg dry soil were 0.26 and 13 indication a potential high risk to collembola. Collembola were also investigated in the field study with non-target arthropods (see above). Recovery was observed in this study but the application rate of 375 g a.s./ha does not cover the the supported use of 600 g a.s./ha in sugar beet. Therefore the risk to other soil non-target macro organisms needs to be addressed further (data gap).

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects on soil respiration and nitrification were observed after 28 days of exposure to a concentration of 0.8 and 4 mg carbofuran/kg soil equivalent to an application rate of 12 kg Furadan 5G/ha and 60 kg Furadan 5G/ha. A strong impact on nitrogen turnover was observed at days 7 and 14. However, the risk to soil micro-organisms is considered to be low for the representative uses since the nitrogen level in the treated samples was similar to controls after 28 days.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

No risk assessment has been conducted for other non-target organisms. Since the applicants did not provide any data on the risk to non-target organisms a data requirement was set. Position papers were submitted by the applicants of the original dossier. The rapporteur Member State agreed to the argumentation of the applicants that the risk to non-target plants is low (insecticide, acetylcholine esterase inhibitor, no exposure of off-field areas).

Due to the mode of application (in furrow) exposure of non-target plants was assumed to be negligible suggesting a low risk to non-target plants. A new study on the efficacy of carbofuran against southern corn rootworm (*Diabrotica undecempunctata*) and cotton aphid (*Aphis gossypii*) was submitted. The study confirmed the activity of cabofuran and its metabolites 3-hydroxy-carbofuran, 3-keto-carbofuran against these species. The metabolite 7-phenol had low or no activity. The study was not considered further in the risk assessment since these species are considered as target organisms.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No inhibitory effects on the respiration of activated sewage sludge was observed up to the highest tested dose of 10,000 mg carbofuran/L. Therefore the risk to biological methods of sewage treatment is considered to be low for all representative uses.

6. RESIDUE DEFINITIONS

6.1 SOIL

Definitions for risk assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran

Definitions for monitoring: carbofuran

6.2. WATER

6.2.1. GROUND WATER

Definitions for exposure assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran

Definitions for monitoring: carbofuran (as marker compound); in case of carbofuran is found, it is recommended to analyse for 3-OH-carbofuran and 3-keto-carbofuran as well

6.2.2. Surface water

Definition for risk assessment
in surface water: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran phenol
in sediment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran phenol.
Definition for monitoring: carbofuran; in case of carbofuran is found, it is recommended to analyse for 3-OH-carbofuran and 3-keto-carbofuran as well

6.3 Air

Definitions for risk assessment: carbofuran
Definitions for monitoring: carbofuran

6.4 Food of plant origin

Definitions for risk assessment: carbofuran and 3-hydroxy carbofuran, both free and conjugated expressed as carbofuran (uses with soil application)
Definitions for monitoring: open - pending submission of further data with regard to the efficiency of the analytical method to determine conjugated residues, preferably carbofuran and 3-hydroxy carbofuran, free and conjugated expressed as carbofuran (uses with soil application)

6.5 Food of animal origin

Definitions for risk assessment: 3-hydroxy carbofuran, free and conjugated expressed as carbofuran
Definitions for monitoring: open - pending clarification of the efficiency of the analytical method to determine 3-hydroxy carbofuran and conjugated 3-hydroxy carbofuran, but preferably also 3-OH carbofuran, free and conjugated expressed as carbofuran

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
carbofuran	Low to very high persistent Single first order DT_{50lab}5.7-387 days, normalized to 20°C and -10kPa soil moisture $DT_{50field}$ = 1.3 —27 days (SFO)	A high long-term risk to earthworms was identified in a first tier risk assessment. Recovery was observed in a field study. However a final conclusion on the risk to earthworms can only be drawn after submission of supporting data (see List of studies to be generated, still ongoing or available but not peer reviewed)
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.
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.

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**
Carbofuran	Very high mobile (K_{oc} = 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, 7 of 9 scenarios (PEARL) with triennial applications. Trigger 0.75 µg/L exceeded for 4 of 9 scenarios (PELMO), or 7 of 9 scenarios (PEARL) with annual applications, 2 of 9 scenarios (PEARL) with triennial applications.	Yes	Yes	Carbofuran is very toxic to aquatic organisms. The TERs with FOCUS step3 PECsw value indicated a potential high acute and chronic risk for aquatic invertebrates
3-OH-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 applications. Note: simulations were regarded as extreme worst case simulations.	Yes	Relevant Very toxic (LD_{50} 8.3 mg/kg bw) It is genotoxic *in vitro* (Ames test and mouse lymphoma cells assay)	Very toxic to aquatic organisms (*Ceriodaphnia dubia* EC50 = 0.023 mg/L). The TERs exceeded the trigger of 100 with FOCUS step3 PECsw.

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
3-keto-carbofuran	Very high to low mobility (Kdoc = 47.5–504 mL/g) Mobile according aged column leaching experiment	FOCUS: Yes, trigger 0.1 µg/L exceeded for 2 of 9 scenarios (PELMO), or 6 of 9 scenarios (PEARL) with annual applications, 1 of 9 scenarios (PEARL) with triennial applications. Note: simulations were regarded as extreme worst case simulations.	Yes	Relevant Toxic (LD_{50} 107 mg/kg bw) No studies on genotoxicity available	Very toxic to aquatic organisms (*Ceriodaphnia dubia* EC50 = 0.049 mg/L). The TERs exceeded the trigger of 100 with FOCUS step3 PECsw..

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Carbofuran (water and sediment)	Carbofuran is very toxic to aquatic organisms. The risk assessment of the RMS which was based on FOCUS step 3 PECsw value indicated a potential high acute and chronic risk for aquatic invertebrates.
3-OH-carbofuran	Very toxic to aquatic organisms (*Ceriodaphnia dubia* EC50 = 0.023 mg/L). The TERs exceeded the trigger of 100 with FOCUS step3 PECsw.
3-keto-carbofuran	Very toxic to aquatic organisms (*Ceriodaphnia dubia* EC50 = 0.049 mg/L). The TERs exceeded the trigger of 100 with FOCUS step3 PECsw.

Carbofuran-phenol	Carbofuran-phenol was about 3 orders of magnitude less toxic to aquatic organisms compared to carbofuran. The TERs exceeded the trigger of 100 with FOCUS step3 PECsw (for the parent carbofuran)

Air

Compound (name and/or code)	**Toxicology**
Carbofuran	Very toxic during acute inhalation (LC_{50} 0.05 mg/L) T^+; R26

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

- 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).
- Data to address the efficiency of the hydrolysis step to release the 3-hydroxy carbofuran conjugates in animal matrices in the method of analysis for monitoring (relevant for all representative uses evaluated, data gap identified by PRAPeR 70 meeting (May, 2009), date of submission unknown; refer to chapter 1 and 3).
- A data requirement was identified for the applicant to address the amount of conjugates in the livestock metabolism studies (relevant for all representative uses evaluated; data gap identified by PRAPeR 70 meeting (May, 2009)no submission date proposed by the applicant, refer to 3.2)
- 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 PRAPeR 70 meeting (May, 2009)no submission date proposed by the applicant, refer to 3.1)
- A data requirement 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 PRAPeR 70 meeting (May, 2009); no submission date proposed by the applicant, refer to 3.1.2)
- The risk to birds from uptake of granules, treated seedlings and contaminated earthworms and arthropods needs to be addressed. (relevant for the representative use assessed; data gap identified in the DAR and confirmed in the PRAPeR 68 expert meeting in May 2009; refer to point 5.1).
- Residue trials with sugar beet seedlings, earthworms and arthropods are required to refine the risk assessment for birds and mammals. These trials should be conducted at the correct application rates and should also include measurements of the metabolites which contain the carbamate moiety. (relevant for the representative use assessed; data gap identified in the DAR and confirmed in the PRAPeR 68 expert meeting in May 2009; refer to point 5.1).
- The risk to mammals needs to be addressed further. (relevant for the representative use assessed; data gap identified in the PRAPeR 68 expert meeting in May 2009; refer to point 5.1).

- The aquatic risk assessment needs to be refined further for aquatic invertebrates since the TERs were below the Annex VI trigger values of 100 and 10 with FOCUS step3 PECsw for the drainage scenarios (D3, D4). Exüposure of the aquatic environment is negligable for the run-off scenario. (refer to point 5.2). Dat gap identified by EFSA.
- The risk to non-target arthropods needs to be addressed further for the application rate of 600 g a.s./ha. (relevant for the representative use assessed; data gap identified in the DAR and confirmed in the PRAPeR 68 expert meeting in May 2009; refer to point 5.4).
- The study of Broadbent and Tomlin, 1982 should be submitted to address the long-term risk to earthworms (relevant for the representative use assessed; data gap identified in the PRAPeR 68 expert meeting in May 2009; refer to point 5.5).
- The risk to soil non-target macro-organisms needs to be addressed further for the application rate of 600 g a.s./ha (including the metabolite 3-keto-carbofuran). (relevant for the representative use assessed; data gap identified in the PRAPeR 68 expert meeting in May 2009; refer to point 5.6).

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The original conclusion from the review was reached on the basis of the evaluation of the representative uses as an insecticide as proposed by the applicants, which comprise incorporation into soil (at drilling) to control soil insects where maize, sugar beet and sunflower will be grown, at an application rate of 0.6 kg carbofuran per hectare. Carbofuran can be used as an acaricide, insecticide and nematicide. It should be noted that during the peer review process only the use as insecticide was evaluated. The conclusion of the peer review of the resubmission was reached on the basis of the evaluation of the representative use as an insecticide as proposed by the applicant, which comprises mechanical incorporation into soil (at drilling) to control soil insects in sugar beet at an application rate of 0.6 kg carbofuran per hectare, applied once every 3 years.

It should be noted that the conclusion has only been updated in relation to the risk assessment of the representative use presented in the additional report, i.e. only the use on sugar beet at an application rate of 0.6 kg carbofuran per hectare. It should also be noted that the proposal by the applicant for a reduced application rate of 60 g a.s./ha was rejected by the rapporteur and was not considered in the peer review.

The representative formulated products for the evaluation were Furadan 5G, a granule (GR) and Diafuran 5G, a microgranule (MG). Both were registered in some Member States of the EU.

The representative formulated product for the evaluation under the resubmission was Furadan 5G, a granule (GR) containing 50 g/kg carbofuran.

There are methods available to monitor all compounds given in the respective residue definitions for food of plant and animal origin, environmental matrices, body fluids and tissues; however data gaps were identified for additional validation data for the hydrolysis step of the monitoring methods for plant and animal matrices and for an ILV for the method in plants. 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.

Carbofuran is rapidly and completely absorbed and excreted in the rat. It is very toxic by ingestion (LD_{50} 7 mg/kg bw) and by inhalation (LC_{50} 0.05 mg/L) whereas toxicity during dermal exposure is moderate. Carbofuran is not a skin irritant, eye irritant, or skin sensitizer but mortality was reported after exposure to eyes. The proposed classification is T^+, R28/R26 "Very toxic if swallowed and via inhalation", Xn, R21 "Harmful in contact with skin" and T, 39/41 "Danger of very serious irreversible effects" and Risk for serious damage to eyes".

The critical target is inhibition of brain and RBC acetylcholinesterase. The overall oral short term NOAEL is 0.1 mg/kg bw/day based on the 1-year dog studies. It is genotoxic *in vitro* but negative in *in vivo* studies. The relevant long term NOAEL is 0.462 mg/kg bw/day from the rat study. Carbofuran induced decreased body weight in pups as well as pup survival at parental toxic doses. Results from the open literature demonstrated that carbofuran caused testicular and spermatotoxicity in pups at dose levels of 0.4 mg/kg bw not associated with inducing general toxic effects, these effects were reproduced in a more recent study with dietary administration, however, the effects were far less pronounced and occurred only at systemically toxic doses (18 mg/kg bw/day); they were not reproduced upon gavage administration. Therefore, no classification regarding reproduction toxicity was proposed. At the occasion of the resubmission of carbofuran, new sets of acute neurotoxicity studies were assessed. No NOAEL could be established in pups at post natal day 11 (PND11) based on a significant inhibition of the brain acetylcholinesterase, the LOAEL was 0.03 mg/kg bw. In young adult rats, the NOAEL was 0.03 mg/kg bw; overall, clinical signs were observed from 0.3 mg/kg bw onwards.

The metabolites 3-OH-carbofuran and 3-keto carbofuran are very toxic and toxic (LD_{50} of 8 and 107 mg/kg bw, respectively), the hydroxy metabolite is genotoxic as well *in vitro* (Ames test and mouse lymphoma cells assay). The metabolites 3-OH-carbofuran-7-phenol, 3-keto-7-phenol and carbofuran 7-phenol are harmful if swallowed.

The dermal absorption value for the granular formulation, Furadan 5G, is 5 %.

The acceptable daily intake (ADI) and acute reference dose (ARfD) are 0.00015 mg/kg bw/day with a safety factor of 200 applied; the acceptable operator exposure level (AOEL) is 0.0003 mg/kg bw/day, applying a safety factor of 100.

The estimated operator exposure according to the US PHED data is below the AOEL i.e. 95 % if personal protective equipment (PPE) as gloves, normal work wear and respiratory protective equipment (RPE) are worn during loading and spreading of the product and assuming an application rate of 0.6 kg carbofuran/ha and a maximum work rate of 10 ha/day. Worker exposure is unlikely to occur, as the formulation is incorporated by mechanical means into the soil when sowing. The granular formulation is applied by ground-directed equipment that is nearly dust free; therefore, the level of bystander exposure to vapour or airborne particles at the time of application is likely to be negligible.

The metabolism, distribution and residue behaviour of carbofuran was investigated in various crops and with different methods of application. Moreover, studies with benfuracarb and carbosulfan, of which carbofuran is the main metabolite, were considered applicable to address residue behaviour of carbofuran.

Based on all available data the metabolic pathway of carbofuran in soil applied uses can be considered as sufficiently investigated. Carbofuran and 3-OH-carbofuran and 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 low and mostly 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, carbofuran undergoes an extensive metabolisation. 3-OH-carbofuran free and conjugated was considered the relevant residue in animal matrices to assess consumer exposure and consumer risk. Further clarification on the ratio of free and conjugated residues in animal matrices was required by the experts in PRAPeR 70 (data gap). This might be important information to conclude on an animal residue definition for monitoring. For the time being no MRLs can be proposed for plant and animal commodities, because amongst others, the residue definition for monitoring could not be agreed due to outstanding data.

Te data gaps identified by the meeting PRAPeR 70 do not permit finalisation of the consumer risk assessment. 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-OH 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 in both models. As agreed by the meeting PRAPeR 70 the risk assessment could be further refined in terms of residues in processed sugar beet.

However, 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.

To mitigate the identified risk it was suggested to restrict crop rotation to cereals only, but further data and assessment of the proposed scenario would be necessary in order to conclude if this mitigation would be effective.

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. For the applied for intended uses, the potential for groundwater exposure by carbofuran 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 extreme 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.
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 according to uniform principles.

A high risk to birds and mammals was identified. The suggested refinements of the risk assessment were not sufficiently supported by data (e.g. PT, PD refinement) or had some shortcomings (e.g. residue trials, lower application rates used in the risk assessment). The experts in the PRAPeR meeting were concerned that the TERs were below the trigger even when the not justified refinements of PD and PT values were included in the TER calculation. The experts expressed their doubts that a safe use could be demonstrated even with further refinement of the risk assessment. The TERs were below the trigger of 100 and 10 for aquatic invertebrates with FOCUS step3 PECsw for the application rate of 600 g a.s./ha for the drainage scenarios (D3, D4), the exposure of aquatic organisms for the FOCUS run-off scenarios (R1, R3) was negligible. Therefore the aquatic risk assessment needs further refinement. A high risk was indicated in extended laboratory studies and semi-field tests with non-target arthropods. A field study was submitted where recovery was observed. However, the study was conducted at an application rate of 375 g a.s./ha which was too low to cover the intended rate of 600 g a.s./ha. The long-term TERs were below the trigger of 5 for earthworms. A field study with the formulation Marshall25CS (a.s. carbosulfan) was suggested to address the long-term risk to earthworms. Uncertainties remain whether the exposure from in-furrow application (high concentrations locally) would lead to higher risk than even distribution of the active substance. A high risk was indicated in the first-tier risk assessment for soil non-target macro-

organisms. Recovery was observed also for soil dwelling arthropods in the above mentioned field study. Since the application rate was too low the risk to soi dwelling non-target macro organisms was considered not sufficiently addressed.
The risk to bees, non-target plants and biological methods of sewage treatment was assessed as low for the representative use evaluated.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Appropriate PPE as well as RPE (respiratory protective equipment) are considered in order to have an estimated operator exposure below the AOEL according to the PHED data (treated area 10 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 by mechanical incorporation) is emphasized by the experts on mammalian toxicology, refer to 2.12.

CRITICAL AREAS OF CONCERN

- An intake concern has been identified for consumers, mainly due to exposure to residues in succeeding crops. With the available data further refinement is not possible.
- The potential for groundwater exposure by 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 carbofuran and metabolites 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 7 out of the 9 presented FOCUS groundwater scenarios).
- A high risk to birds and mammals. The suggested refinements of the risk assessment were not sufficiently supported by data (e.g. PT, PD refinement) or had some shortcomings (e.g. extrapolation of residue trials, lower application rates used in the risk assessment). The TERs were below the trigger even when the not justified refinements of PD and PT values were included in the TER calculation. The experts expressed their doubts that a safe use could be demonstrated even with further refinement of the risk assessment.
- The risk to aquatic organisms. (The TERs were below the trigger of 100 and 10 for aquatic invertebrates with FOCUS step3 PECsw for the application rate of 600 g a.s./ha for the drainage scenarios (D3, D4), the exposure for the FOCUS run-off scenarios (R1, R3) was negligible.

- The risk to non-target arthropods. (A high risk was indicated in extended laboratory studies and semi-field tests, a field study where recovery was observed was conducted at an application rate of 375 g a.s./ha which was too low to cover the inteded rate of 600 g a.s./ha.)
- The risk to soil non-target macro-organisms. (A high risk was indicated in the first-tier risk assessment, a field study where recovery was observed was conducted at an application rate of 375 g a.s./ha which was too low to cover the inteded rate of 600 g a.s./ha.)

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APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

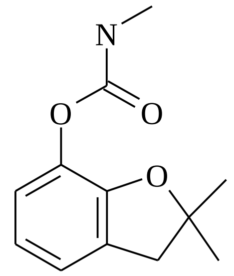
Active substance (ISO Common Name) ‡	Carbofuran
Function (*e.g.* fungicide)	Insecticide, acaricide, nematicide

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 methylcarbamate
Chemical name (CA) ‡	2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate
CIPAC No ‡	276
CAS No ‡	1563-66-2
EEC No (EINECS or ELINCS) ‡	EINECS 216-353-0
FAO Specification (including year of publication)‡	not available
Minimum purity of the active substance as manufactured (g/kg) ‡	*Arysta* : 960 g/kg *FMC* : 980 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	None
Molecular formula ‡	$C_{12}H_{15}NO_3$
Molecular mass ‡	221.3 u

Structural formula ‡



Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	*Arysta* : melting point 153.1 °C (98.2%) *FMC* : melting range 151.2 – 153.7 °C (99.3%)
Boiling point (state purity) ‡	*Arysta* : boiling with partial decomposition at 276 °C (98.2%) *FMC* : boiling at 254.1 °C (no decomposition) (99.6%)
Temperature of decomposition (state purity)	*Arysta* : boiling with partial decomposition at 276°C (98.2%) *FMC* : boiling at 254.1 °C (no decomposition) (99.6%)
Appearance (state purity) ‡	*Arysta* : white crystalline solid, odourless (purified a.s.) *FMC* : off-white powder, aromatic acid-like odour (99.3%)
Vapour pressure (state temperature, state purity) ‡	*Arysta* : 2.25×10^{-4} Pa at 20°C (98.2%) *FMC* : 8×10^{-5} Pa at 25 °C (99.9%)
Henry's law constant ‡	*Arysta* : 1.58×10^{-4} Pa.m^3.mol^{-1} at 20 °C *FMC* : 5×10^{-5} Pa.m^3.mol^{-1} at 25 °C
Solubility in water (state temperature, state purity and pH) ‡	*Arysta* : 315 mg/L at 19.5 ± 2.0 °C, no effect of pH (99.9%) *FMC* : 322 mg/L at 20.0 ± 0.5 °C, no effect of pH (99.3%)
Solubility in organic solvents (state temperature, state purity) ‡	*Arysta*: (98.2% pure)

	solubility at 20 °C (g/L)
n-heptane	0.1
xylene	7.8
1,2-dichloroethane	106.5
methanol	71.0
acetone	107.0
ethyl acetate	66.9

FMC : (98.5% pure)

	solubility at 20 °C (g/L)
n-heptane	0.13
xylene	8.0
1,2-dichloroethane	91.0

	methanol 72.8 acetone 103.4 ethyl acetate 56.1
Surface tension (state concentration, temperature and purity)‡	*Arysta* : 48.9 mN/m at 20.3 °C (90% saturated solution) (98.2%) *FMC* : 54.7 mN/m at 20 °C (90% saturated solution) (98.5%)
Partition co-efficient (state temperature, pH and purity) ‡	*Arysta* : log P_{OW} = 1.8 at 20 °C, no effect of pH (99.9%) *FMC* : log P_{OW} = 1.62 at 22 °C, no effect of pH (99.3%)
Dissociation constant (state purity) ‡	*Arysta* : no pKa in environmentally relevant pH range *FMC* : no pKa in environmentally relevant pH range
UV/VIS absorption (max.) incl. ε (state purity, pH) ‡	*Arysta* : (99.9% pure) in neutral methanol : λ_{max} 276 nm; ε = 2.80 x 10^3 $L.mol^{-1}.cm^{-1}$ at λ 290 nm : ε = 2.51 x 10^2 $L.mol^{-1}.cm^{-1}$ in acidic methanol : no significant difference in spectrum in alkaline methanol : spectrum differs from that in neutral/acidic conditions (λ_{max} 243 and 291 nm) due to Carbofuran degradation *FMC* : (99.6% pure) in neutral methanol : λ_{max} 277 nm; ε = 3.28 x 10^3 $L.mol^{-1}.cm^{-1}$ at λ 290 nm : ε = 500 $L.mol^{-1}.cm^{-1}$ in acidic methanol : no significant difference in spectrum in alkaline methanol : spectrum differs from that in neutral/acidic conditions (λ_{max} 245 and 292 nm) due to decomposition
Flammability (state purity)‡	*Arysta* : not highly flammable; not auto-flammable (98.2%) *FMC* : not highly flammable; not auto-flammable (98.5%)
Explosive properties (state purity)‡	*Arysta* : no explosive properties (statement) *FMC* : no explosive properties (98.5%)

Oxidising properties (state purity)‡	*Arysta* : no oxidising properties (statement) *FMC* : no oxidising properties (98.5%)

Summary of uses supported by available data (carbofuran) *

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation: Type (d-f)	Formulation: Conc. of as (i)	Application: method kind (f-h)	Application: growth stage & season (j)	Application: number min max (k)	Application: interval between applications (min)	Application rate per treatment: kg as/hL min max	Application rate per treatment: water L/ha min max	Application rate per treatment: kg as/ha min max	PHI (days) (l)	Remarks: (m)
Sugar Beet BEAVA	EU	FURADAN 5G - FMC	F	*Elateridae spp.* *Scutigerella spp.* *Atomaria linearis* *Aphis spp.* *Blaniulus spp.Oscinella frit* *Phyllocnistis spp.*	G	50 g/kg	mechanical incorporation into soil	At drilling	1	na	na	na	0.06 (not acceptable, see point 2.1.3 in level 2) 0.6 (proposed by FMC in its original submission)	PHI : not applicable as applied at drilling	Granule dropped into seed furrow. Soil then folded over to cover. Applied every 3 years (Yearly application is not acceptable) [1]

[1] A high risk and/or data gaps were identified in section 3 and 5

(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

* Uses for which the risk assessment cannot be concluded are marked grey.

Methods of Analysis

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

Technical as (principle of method)	*Arysta* : CIPAC Method 276/TC/(M)/3 : HPLC-UV (ISTD) *FMC* : HPLC-UV
Impurities in technical as (principle of method)	*Arysta* : GC-FID Karl Fischer *FMC* : HPLC-UV
Plant protection product (principle of method)	*Arysta, FMC* : CIPAC Method 276/GR/(M)/3 : HPLC-UV (ISTD)

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		OPEN (pending information on the efficiency of the hydrolysis step of the analytical method). And additional ILV data.
Food of animal origin		OPEN (pending information on the efficiency of the hydrolysis step of the analytical method).
Soil (and sediment)		carbofuran
Water	surface	carbofuran
	drinking/ground	carbofuran
Air		carbofuran
Body fluids and tissues		Carbofuran, 3-hydroxy carbofuran and 3-keto carbofuran

Monitoring/Enforcement methods

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	*FMC:* 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: ILV and efficiency of hydrolysis step
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	HPLC-PCD with Flu (carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran); LOQ = 0.05 mg/kg (meat, eggs) LOQ = 0.025 mg/kg (milk)

	OPEN: efficiency of hydrolysis step
Soil (principle of method and LOQ)	*Arysta:* LC-MS/MS (carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol); LOQ = 0.01 mg/kg (for each analyte) *FMC* : LC-MS/MS (carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol); LOQ = 0.01 mg/kg (for each analyte); HPLC-PCD with Flu (carbofuran) and GC-MS (dibutylamine); LOQ = 0.005 mg/kg; GC-MS (Carbofuran) and HPLC-Flu (dibutylamine); LOQ = 0.007 mg/kg (Carbofuran), 0.01 mg/kg (dibutylamine)
Water (principle of method and LOQ)	*Arysta*: HPLC-MS (carbofuran, 3-hydroxy carbofuran, carbofuran-phenol); LOQ = 0.1 µg/L (for each analyte, drinking water, groundwater, surface water) LC-MS/MS (carbofuran, carbofuran-7-phenol); LOQ = 0.1 µg/L (for each analyte, surface water) *FMC* : HPLC-MS (carbofuran, 3-hydroxy carbofuran, carbofuran-phenol); LOQ = 0.1 µg/L (for each analyte, drinking water, groundwater, surface water); HPLC-PCD with Flu (carbofuran, 3-hydroxy carbofuran); LOQ = 0.1 µg/L (drinking water, surface water); GC-MS (carbofuran); LOQ = 0.05 µg/L (for each analyte, surface water)
Air (principle of method and LOQ)	HPLC-UV (carbofuran) LOQ = 0.6 µg/ m^3
Body fluids and tissues (principle of method and LOQ)	*Arysta* : LC-MS/MS (Carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol); LOQ = 50 µg/L (blood, urine), 0.01 mg/kg (tissues); LC-MS/MS (Carbofuran); LOQ = 50 µg/L (fluids), 0.1 mg/kg (tissues) *FMC* : LC-MS/MS (Carbofuran, 3-hydroxy carbofuran, 3-

	keto carbofuran, carbofuran-7-phenol); LOQ = 50 µg/L (blood, urine), 0.01 mg/kg (tissues); HPLC-PCD with Flu (Carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran); LOQ = 0.05 mg/kg (tissues, blood)

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 in mammals (Annex IIA, point 5.1)

Rate and extent of absorption ‡	83-92 % (urine and air) within 32 hour (0.4 mg/kg bw, rat)
Distribution ‡	Large, highest residue in liver
Potential for accumulation‡	No evidence of accumulation
Rate and extent of excretion ‡	92 % of phenyl part within 48 h mainly via urine (89 %) and faeces (2.5 %); carbamate moiety excreted within 32 h in air as CO_2
Metabolism in animals ‡	Oxidation at C-3, generating 3-OH-metabolites, further oxidation (3-ketocarbofuran) and/or excretion as conjugates Hydrolysis of carbamate bond into CO_2
Toxicologically relevant compounds ‡ (animals and plants)	Carbofuran and metabolites with the carbamate moiety
Toxicologically relevant compounds ‡ (environment)	Carbofuran and metabolites with the carbamate moiety

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	7 mg/kg bw	**T^+, R28**
Rat LD_{50} dermal ‡	1000< LD50<2000 mg/kg bw	**Xn, R21**
Rat LC_{50} inhalation ‡	0.05 mg/L (13 mg/kg bw)	**T^+ R26**
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant, but mortality reported (rabbits)	**T; R39/41**
Skin sensitisation ‡	Non-sensitiser (Bühler and M&K)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Testicular degeneration, clinical signs of neurotoxicity related to AChE inhibition (rats and dogs)	
Relevant oral NOAEL ‡	0.1 mg/kg bw/day, 1-year dog and 60 day, rat (published study)	
Relevant dermal NOAEL ‡	25 mg/kg bw/day (21 day, rabbit)	
Relevant inhalation NOAEL ‡	No data - not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

	Positive results in bacterial tests; Negative in *in vivo* tests	

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

Target/critical effect ‡	Body weight and AChE inhibition	
Relevant NOAEL ‡	10 ppm (0.462 mg/kg bw/day) (2-year rat)	
Carcinogenicity ‡	No carcinogenic potential	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Testicular and sperm toxicity (published study) Reduced offspring weight and survival in multigeneration rat study	
Relevant parental NOAEL ‡	0.2 mg/kg bw/d (by gavage, 60-day, rat) 1.2 mg/kg bw/day (multigeneration)	
Relevant reproductive NOAEL ‡	0.2 mg/kg bw/d (by gavage, 60-day, rat) 1.2 mg/kg bw/day (multigeneration)	
Relevant offspring NOAEL ‡	1.2 mg/kg bw/day (multigeneration)	

Developmental toxicity

Developmental target / critical effect ‡	Foetotoxicity and developmental neurotoxicity at maternal toxic doses (rat)	
Relevant maternal NOAEL ‡	0.1 mg/kg bw (rat) 0.5 mg/kg bw/d (rabbit)	
Relevant developmental NOAEL ‡	1 mg/kg bw/day (rat) 0.5 mg/kg bw/d (rabbit)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	LOALEL= 0.03 mg/kg bw (NOAEL*= 0.015 mg/kg bw), rat pups (brain AChE inhibition) NOAEL= 0.03 mg/kg bw, adult rats (brain AChE inhibition)	
Repeated neurotoxicity ‡	NOAEL = 50 ppm (3.2 mg/kg bw/day) 90-day, rat study	
Delayed neurotoxicity ‡	No delayed neuropathy in hens NOAEL neurotoxicity= 0.5 mg/kg bw (hens)	

*** application of AF = 2 on LOAEL**

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	There were no differences in sensitivity to carbofuran's induced AChE inhibition with age	
Studies performed on metabolites or impurities ‡		
3-OH-carbofuran	Rat LD_{50} oral: 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**
3-keto-carbofuran	Rat LD_{50} oral: 107 mg/kg bw	**T, R25**
3-OH-7-phenol	Rat LD_{50} oral: 1654 mg/kg bw	**Xn, R22**
3-keto-7-phenol	Rat LD_{50} oral: > 800 mg/kg bw	**Xn, R22**
7-phenol-carbofuran	Rat LD_{50} oral: 1743 mg/kg bw negative in Ames test	**Xn, R22**

Medical data ‡ (Annex IIA, point 5.9)

	Low number of carbofuran intoxications has been reported. The majority of the incidences resulted from maintenance of equipment cleaning work.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.00015 mg/kg bw/day	Acute rat neurotoxicity study (with pups)	200*
AOEL ‡	0.0003 mg/kg bw/day	Acute rat neurotoxicity study (with young adults)	100
ARfD ‡	0.00015 mg/kg bw	Acute rat neurotoxicity study (with pups)	200*

***2× (LOAEL bridging), 100× (default)**

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Furadan 5G, 50 g carbofuran/kg, granule)	5% supported by published results from open literature *in vivo* and comparative *in-vitro* studies (human/rat skin) with Furadan 5G

Exposure scenarios (Annex IIIA, point 7.2)

Operator	<u>Granular formulations: PHED model:</u>	% of AOEL
	Gloves	655 %
	Gloves+ respirator during loading	95 %
Workers	formulation is incorporated into soil by mechanical means during sowing: no exposure	
Bystanders	formulation is applied by ground directed equipment that is nearly dust free: no exposure	

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

	RMS/peer review proposal	
Substance classified (carbofuran)*	**T+;**	Very toxic
	R21	Harmful in contact with skin
	R26/28	Very toxic by inhalation and if swallowed
	R39/41	Danger of very serious irreversible effects/risk for serious damage to eyes

* ECB voted not to classify carbofuran as R62 (Commission Directive 2009/2/EC of 15 January 2009)

Residues

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

Plant groups covered	maize (C), potatoes (R), soybeans (P/O) (soil applied carbofuran) Sugar beet (R), rice(C) (soil applied carbosulfan) The metabolism of Carbofuran could be considered as completely investigated in potato and soybean.
Rotational crops	Interim results of a confined accumulation study in rotational crops (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.
Plant residue definition for monitoring	Open (pending information on the efficiency of the hydrolysis step in the analytical method). Preferably, the same as for risk assessment. Open (pending information
Plant residue definition for risk assessment	Sum of Carbofuran and 3–OH-carbofuran, both 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 (carbofuran)
Animal residue definition for monitoring	Open (pending information on the efficiency of the hydrolysis step in the analytical method). Preferably, the same as for risk assessment.
Animal residue definition for risk assessment	3-OH-carbofuran, 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)	No.

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

	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)

	FMC[1] Carbofuran and its relevant metabolites 3-keto-carbofuran and 3-hydroxy-carbofuran were stable in all the tested matrices (alfalfa, corn, oranges, peanut, potato, sugar beet, sorghum, cow milk and muscle) for at least 26 months except 3-keto-carbofuran on sugar beet tops that showed to be stable for 11 months of storage period. ***ARYSTA*** Residues of Carbofuran and 3-OH-carbofuran in maize (corn and silage), sunflower (seeds) and sugar beet (leaves with tops and roots) under frozen storage conditions (-20 °C) were considered as stable for a minimum of 12 months.

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: yes	Poultry: No	Pig: Yes[2]
Muscle	0.000083*	-	-
Liver	0.00005*	-	-

[2] A metabolism study in pigs was not required as metabolic pathways in rat and in goat were considered as similar. For the same reason, a feeding study in pigs is not required even if intake calculations for pigs indicated that non negligible exposure can be expected.

Kidney	0.0003*	-	-
Fat	0.000083*	-	-
Milk	0.0003*	-	-
Eggs	-	0.000008*	-

* calculated on the basis of the metabolsm studies, considering the estimated dietary burden

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

Crop	Northern or Southern Europe	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL (mg/kg)	STMR (mg/kg) (b)
Sugar beet	NE	***Carbosulfan residue data :*** Samples of sugar/fodder leaves/tops and roots at normal harvest time (PHI values ranging between 92 and 182 days) were analysed for carbosulfan and its metabolites carbofuran and 3-OH-carbofuran. Decay curves are given with last sampling 139 to 172 days after the application. *North, sugar beet, 0.6 kg a.s./ha, 1 application after sowing, PHI not applicable (FMC): **root: -carbofuran + 3-OH-carbofuran expressed as carbofuran equiv.: 11 x <0.1, 0.112 mg/kg **Leaves/tops: -carbofuran + 3-OH-carbofuran expressed as carbofuran equiv.: 12 x <0.1 mg/kg Carbofuran residue data: *North, sugar beet, 0.5-0.930 kg a.s./ha, 1 application at seeding, PHI not applicable (FMC): **root: -carbofuran + 3-OH-carbofuran expressed as carbofuran equiv: 5 x <0.1 mg/kg ** Leaves/tops: -carbofuran + 3-OH-carbofuran expressed as carbofuran equiv: 5 x <0.1 mg/kg	Trials performed in accordance with the critical GAP. Confirmation required whether the results were generated with a method of analysis that is validated for the full residue definition for risk assessment (i.e. inlcuding conjugates)	PRAPeR 70: currently unable to propose	0.01[1]

[1] Based on the residue showing no residue at LOQ 0.01 mg/kg (sum of carbofuran + 3-OH-carbofuran)

Crop	Northern or Southern Europe	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL (mg/kg)	STMR (mg/kg) (b)
		(Residue trials added in November 2008) *North, sugar beet, 0.6 kg carbofuran/ha, 1 application at seeding, PHI not applicable (FMC): **root: -carbofuran + 3-OH-carbofuran expressed as carbofuran equiv: 4 x <0.01 mg/kg ** Leaves/tops: -carbofuran + 3-OH-carbofuran expressed as carbofuran equiv: 4 x <0.01 mg/kg *North, sugar beet, 0.6025 kg a.s./ha, 1 application at seeding, PHI not applicable (Arysta): **root: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: <0.02 mg/kg ** Top and leaves: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: <0.02 mg/kg			
Sugar beet	SE	***Carbosulfan residue data :*** *South, sugar beet, 0.628-0.674 kg a.s./ha, 1 application, PHI not applicable (FMC): **root: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: 4 x <0.1 mg/kg ** Leaves/tops: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: 4 x <0.1 mg/kg *(Residue trials added in November 2008)* *South, sugar/fodder beet, 0.750-1.056 kg carbosulfan/ha, 1 application, PHI not applicable (FMC): **root: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: 7x <0.01 mg/kg			

Crop	Northern or Southern Europe	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL (mg/kg)	STMR (mg/kg) (b)
		** Leaves/tops: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: 7 x <0.1 mg/kg ***Carbofuran residue data:*** *South, sugar beet, 0.6 kg a.s./ha, 1 application at seeding, PHI not applicable (FMC): **root: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: <0.1 mg/kg ** Leaves/tops: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv:* <0.1 mg/kg *South, sugar beet, 0.6025 kg a.s./ha, 1 application at seeding, PHI not applicable (Arysta): **root: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: 4 x <0.02 mg/kg ** Top and leaves: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: 3 x <0.02, 0.034 mg/kg *(Residue trials added in November 2008)* *South, sugar beet, 0.628-1.053 kg carbofuran/ha, 1 application at seeding, PHI not applicable (FMC): **root: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: 7 x <0.01 mg/kg ** Leaves/tops: -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv*: 7 x <0.1 mg/kg			

(a) : Number of trials in which particular residue levels were reported.
(b) : Supervised Trials Median Residue : The median residue level estimated on the basis of supervised trials relating to the critical GAP

Consumer risk assessment[25] (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.00015 mg/kg bw/day
TMDI (European Diet) (% ADI)	***FMC*** *a) EFSA model for chronic and acute risk assessment – rev. 2a*

MS diet	Highest calculated TMDI values in % of ADI
UK, Toddler	172.9

b) UK Model:
101 % of the ADI (toddlers)

NEDI (% ADI)	-
Factors included in NEDI	-
ArfD	0.00015 mg/kg bw/day
Acute exposure (% ARfD)	***FMC*** EFSA model for chronic and acute risk assessment – rev. 2a

MRL 0.01* mg/kg	Commodities	Highest % of ARfD/ADI
IESTI 1 children	Sugar beet (root)	425.7
IESTI 2 children	Sugar beet (root)	425.7
IESTI 1 adult	Sugar beet (root)	172.9
IESTI 2 adult	Sugar beet (root)	172.9

The ARfD is significantly exceeded for numerous leafy and roots/tubers crops [26] consumed by children and by adults/ the general population.
b) UK model

[26] (> 1000% ARfD scarole, kale, >500% ARfD Chinese cabbage, potatoes, lettuce, >200% ARfD spinach, chard, carrots, purslane, celeriac, swedes, > 100% ARfD beetroot, salsify, parsnips, turnips)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Exceedances of the ARfD were observed for all the categories of UK consumers when consuming sugar beet roots, other root/tuber and leafy crops.
There is no acute intake concern for refined sugar. Both for the 2 models (EFSA PRIMo and UK model), there is no acute intake concern for animal matrices and cereal crops consumed by the different categories of consumers and according to the different European diets.

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
At PRAPeR 70, the experts agreed that no novel metabolites (other than recovered in plant metabolism studies) is expected to coour during sugar beet root processing. Considering the crystallisation step in the sugar beet process, no residues are expected in refined sugar.			

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

Proposed MRLs[27] (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Expression of the residue	**MRLs (mg/kg)**
pending data on efficiency of the hydrolysis step of the analytical method for montioring (proposed: Sum of Carbofuran and 3-OH-carbofuran both free and conjugated expressed as carbofuran equivalents)	PRAPeR 70: MRLs could not be proposed for food of plant and animal origin (pending the efficiency of the hydrolysis step to release the conjugates in the analytical methods).

[27] ~~provisonal due to incomplete data base~~

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

When appropriate, the name of the data provider is given between brackets

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

Mineralization after 100 days	26.9-66.3% after 120 days d, [^{14}C- phenyl ring]-label, 20°C (n= 4) (Arysta) 0.7-14.6% AR after day 112-120 days, [^{14}C- phenyl ring]-label, 25°C (n = 4) (FMC)
Non-extractable residues after 100 days	23.9-57.7 % after 120 d, [^{14}C- phenyl ring]-label, 20°C (n= 4) (Arysta) 7.7% after 112days, max 94% after 89 days, [^{14}C- phenyl ring]-label, 25°C (n = 4) (FMC)
Relevant metabolites - name and/or code, % of applied (range and maximum)	3-OH-carbofuran (max. 1.32%AR), 3-keto-carbofuran (max. 12.4 %AR). EPCO 31 agreed that 3-OH-carbofuran and 3-keto-carbofuran need to be further assessed as carbofuran metabolites containing the active carbamate moiety.

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

Anaerobic degradation	[^{14}C- phenyl ring]-label, 20°C (Arysta) Mineralisation 2.4-6.1 % after 120 d Non-extractable residues 56.4-62.7% after 120 d Major metabolite : 7-phenol, max level of 62.9 % at 28 d Minor metabolite fractions: M4 ([max. 8.4 % AR after 120d, end of study] was shown to be highly polar and to contain several fractions), M9, M11 and M12.
Soil photolysis	Phenyl ring label, 22.6 ± 0.2°C, Xenon lamp (Arysta) No photodegradation observed [^{14}C- phenyl ring]-label, 11.7-31.7°C, natural light (FMC) Half-live corrected for reactions such as hydrolysis is 87.5 d (winter time) and 30.1 d (summer time)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

Laboratory studies

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								
Sandy loam		5.8	20/40	6.92	-	6.92	13.8	SFO
Silt loam		7.1	20/40	11.61	-	9.39	21.1	SFO
Loam		7.3	20/40	13.04	-	11.46	7.8	SFO
Loam		7.2	20/40	25.99	-	22.54	14.8	SFO
Silt loam		6.1	23/(60% FC)	17.47	-	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			20/40	<1/<1		1**	na	graphical
sandy loam	-	6.3*	20/40	0.27/0.88	-	0.22	1.0	SFO
sandy clay	-	6.9*	20/40	0.51/1.70	-	0.3	1.0	SFO
Geometric mean						0.41		

* in $CaCl_2$

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

** value could be regarded as 0.3 d (since DT_{90} <1)

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			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
sandy 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			20/40	<1/<1		<1**	na	graphical
sandy loam		6.3*	20/40	<1/<1	-	<1**	na	graphical
sandy clay		6.9*	20/40	<1/<1	-	<1**	na	graphical
Geometric mean						<1**		

* in $CaCl_2$
** value could be regarded as 0.3 d (since DT_{90} <1)

	DT_{50lab} (20°C, anaerobic): 7.6 days, 1 soil, r^2 = 0.99318 (Arysta)
	Degradation in the saturated zone: not required
Field studies (state location, range or median with n value)	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)
	DT90f: carbofuran, Netherlands, Spain, Italy, bare soil, 4.4-91 d (n= 5, r^2 = 0.880-0.997) 1st order
Soil accumulation and plateau concentration	No soil accumulation studies available, none required

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Carbofuran ‡

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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					0.432	22	0.96
pH dependence (yes or no)			No				

* in $CaCl_2$

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 $CaCl_2$

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 $CaCl_2$

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

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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 $CaCl_2$

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

Column leaching	Not required
Aged residues leaching	SETAC (FMC) Aged for (d): 30 d Time period (d): 1.5 d Precipitation (mm): 500 mm Leachate: 33.2-78.2 % total residues/radioactivity in leachate 95-98% of the leachate radioactivity is the active substance, 2-5% of the leachate radioactivity is 3-keto-carbofuran and carbofuran-7-phenol. 13.7-49.2 % total residues/radioactivity retained in top 5 cm
Lysimeter/ field leaching studies	Non reliable information available

PEC (soil) (Annex IIIA, point 9.1.3)

Method of calculation	DT_{50} (carbofuran): 27 days Kinetics: 1st order maximum field DT_{50}
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): 600 g/ha

$PEC_{(s)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.800	0.800	-	-
Short term 24h	0.780	0.790	-	-
2d	0.760	0.780		
4d	0.722	0.760		

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Long term 7d 28d 50d 100d	0.668 0.390 0.222 0.061	0.732 0.571 0.451 0.288	-	-

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)	pH 4: hydrolytically stable (FMC, Arysta)
	pH 7, 25 °C: DT50 = 28 - 45.7 d (1st order) (Arysta, FMC) carbofuran-7-phenol: 55.6 % AR (51 d)
	pH 9, 25°C: DT50 = 0.1 d (1st order) (Arysta) carbofuran-phenol or 7-phenol: 98.3% AR (5 d)
Photolytic degradation of active substance and relevant metabolites	Xenon arc lamp with UV filter cut, DT_{50} : 33 days No major metabolite Estimated DT_{50} at 50°N : 108 days (Arysta)
Readily biodegradable (yes/no)	No (5-7% TOD in 5 days) (Arysta)

Degradation in water / sediment

Parent	Distribution (max in water 69.8-94.0% at 0 d. Max. sed 10.7-57.52% after 7-20 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
Pond (Cooper)	6.11	5.3	25	70.07 *	6.8	-	-	-	-	SFO, non linear
River (Rheinsulz)	8.2	7.45	20	9.04	14.8	-	-	-	-	SFO, non linear
Pond (Ormalingen)	8.1	7.08	20	11.64	5.2	-	-	-	-	SFO, non linear
From studies dosed with carbosulfan (carbofuran formed as metabolite of carbosulfan)										
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	-	-	-	-	
Pond (Swarkestone) B	7.77	7.1	20	13.99	9.0	-	-	-	-	SFO, non linear
From studies dosed with benfuracarb (carbofuran formed as metabolite of benfuracarb)										

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

OVP	8.04	8.3	20	13.9-46.3	0.96	8.2-27.2#	0.99	-	-	SFO
SW	7.8	7.9	20	14.8-49.2	0.97	10.8-35.8#	0.99	-	-	SFO

*: normalised to 20°C

**: based on the test systems Cooper, Rheinsulz, Ormalingen

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

#: DT50/90 for dissipation

Carbofuran-7-phenol	Distribution (max in water 5.92-12.0% at 1-20 d. Max. sed 1.89-4.9 % after 7-20 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
Pond (Cooper)	-	-	-	-	-	-	-	-	-	-
River (Rheinsulz)	8.2	7.45	20	1.69	22.0	-	-	-	-	SFO, non linear
Pond (Ormalingen)	~~8.1~~ 7.0	7.08	20	1.86	27.0	-	-	-	-	SFO, non linear
From studies dosed with benfuracarb (carbofuran formed as metabolite of benfuracarb)										
OVP	8.04	8.3	20	20.5-68.1	0.99	-	-	20.5-68.1	0.99	SFO
SW	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						

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 Cooper	6.11	5.3	1.87 %AR after 30 d	32.8 %AR after 30 d	32.8 %AR after 30 d
River (Rheinsulz)	8.2	7.45	19.6% after 102 d	76.8% AR after 56 d	74.3% AR after 102 d
Pond (Ormalingen)	8.1	7.08	7.7% after 102 d	80.0% AR after 56 d	78.4% AR after 102 d
OVP	8.04	8.3	16.7% after 103 d	75.94% after 103 d	75.94% after 103 d
SW	7.8	7.9	13.65% after 103 d	73.81% after 103 d	73.81% after 103 d

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

FOCUSsw step 3	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 to 7 cm Number of applications: 1 Application rate(s): 600 g a.s./ha
Main routes of entry	Drainage, runoff (except 7-phenol-carbofuran)

Parameter	carbofuran	3OHCF	3ketoCF	7-phenolCF
Mw	221.3	237.3 221.3 for MACRO runs*	235.24 221.3 for MACRO runs*	164.2
Water solubility (mg/L, 20°C)	322	6207	4464	1096
Vapour pressure (Pa, 25°C)	8^e-5	3.29e-3**	2.6e-3**	1.32**
DT50 soil (days)	14	0.41	3.01	1
Kom	12.8	31.9	192	598
Koc	22	55	331	1031
1/n	0.96	1	1	0.9
Ffm		1	1	1
Q10	2.58	2.58	2.58	2.58
Plant Uptake	0	0	0	0
Crop washoff	0.146	0.455	0.401	0.234
Water DT50	15.3	1000	1000	9.9
Sediment DT50	1000	1000	1000	1000

*PECs adjusted for MW at end
** Vp data were taken from the dossier of benfuracarb

Scenario	Compound	Max PECsw (µg/L)	Date of max PECsw	Max PECsed (µg/kg)	Date of max PECsed
D3 ((Ditch)	CF	0.0264	02-Feb-93	0.0461	14-Apr-93
D4 ((Pond)	CF	0.1030	30-Dec-85	0.1250	20-Feb-86
D4 ((Stream)	CF	0.0914	16-Dec-85	0.0871	31-Jan-86

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

R1 ((Pond)	CF	0.0000	01-Mar-84	0.0000	01-Mar-84
R1 ((Stream)	CF	0.0000	01-Mar-84	0.0000	01-Mar-84
R3 ((Stream)	CF	0.0000	01-Oct-80	0.0000	01-Oct-80
D3 ((Ditch)	7PCF	0.0000*	29-Jan-93	0.0012*	01-May-93
D4 ((Pond)	7PCF	0.0001*	29-Jan-86	0.0017*	23-Feb-86
D4 ((Stream)	7PCF	0.0002*	01-Jan-85	0.0020*	01-Feb-86
R1 ((Pond)	7PCF	0.0000*	01-Mar-84	0.0000*	01-Mar-84
R1 ((Stream)	7PCF	0.0000*	01-Mar-84	0.0000*	01-Mar-84
R3 ((Stream)	7PCF	0.0000*	01-Oct-80	0.0000*	01-Oct-80
D3 ((Ditch)	3OHCF	0.0008	29-Jan-93	0.0018	19-Apr-93
D4 ((Pond)	3OHCF	0.0041	31-Jan-86	0.0082	27-Mar-86
D4 ((Stream)	3OHCF	0.0024	17-Dec-85	0.0029	31-Jan-86
R1 ((Pond)	3OHCF	0.0000	01-Mar-84	0.0000	01-Mar-84
R1 ((Stream)	3OHCF	0.0000	01-Mar-84	0.0000	01-Mar-84
R3 ((Stream)	3OHCF	0.0000	01-Oct-80	0.0000	01-Oct-80
D3 ((Ditch)	3KCF	0.0026	30-Jan-93	0.0185	01-May-93
D4 ((Pond)	3KCF	0.0079	01-Feb-86	0.0476	01-May-86
D4 ((Stream)	3KCF	0.0044	01-Jan-85	0.0182	30-Jan-86
R1 ((Pond)	3KCF	0.0000	01-Mar-84	0.0000	01-Mar-84
R1 ((Stream)	3KCF	0.0000	01-Mar-84	0.0000	01-Mar-84
R3 ((Stream)	3KCF	0.0000	01-Oct-80	0.0000	01-Oct-80

CF: carbofuran; 7PCF: carbofuran phenol; 3OHCF: 3-Hydroxy-carbofuran; 3KCF: 3-Keto-carbofuran
* Note that for the risk assessment for carbofuran phenol, the meeting PRAPeR 67 recommended the use the parent PEC values (correction for MW and maximum occurrence in W/S systems can be done)

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

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Application rate	
	Application rate: 600 g carbofuran/ha, 1 application, 7 cm soil incorporation sugar beet (application every year) sugar beet (application every 3 years) No. of applications: 1 (incorporation at planting) Time of application: 14 days before emergence

Parameter	carbofuran	3OHCF	3ketoCF	7PCF
Mw	221.3	237.3	235.24	164.2
Water solubility (mg/L, 20°C)	322	6207	4464	1096
Vapour pressure (Pa, 25°C)	8e-5	3.29e-3*	2.6e-3*	1.32*
DT50 soil (days)	14	0.41	3.01	1
Kom	12.8	31.9	192	598
Koc	22	55	331	1031
1/n	0.96	1	1	0.9
Ffm		1	1	1
Q10	2.58	2.58	2.58	2.58
Plant Uptake	0	0	0	0

* Vp data were taken from the dossier of benfuracarb

80th Percentile Annual Average Groundwater FOCUS PEARL PECs (0.600 kg a.s./ha)

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	**1.6643**	0.0437	**0.1176**	0.0028
Hamburg	Sugar beets	**1.5890**	0.0495	**0.2085**	0.0597
Jokioinen	Sugar beets	**1.6238**	0.0391	0.0651	0.0017
Kremsmünster	Sugar beets	**1.2330**	0.0334	**0.1093**	0.0027
Okehampton	Sugar beets	**1.2805**	0.0366	**0.1185**	0.0046
Piacenza	Sugar beets	**2.3195**	0.0738	**0.4252**	**0.1055**
Porto	Sugar beets	0.0366	0.0008	0.0013	0.0000
Sevilla	Sugar beets	**7.2117**	**0.1587**	**0.2120**	0.0063
Thiva	Sugar beets	**0.1936**	0.0054	0.0171	0.0004

80th Percentile Triennial Average Groundwater FOCUS PEARL PECs (0.600 kg a.s./ha)

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	**0.6327**	0.0165	0.0458	0.0011
Hamburg	Sugar beets	**0.5585**	0.0175	0.0733	0.0216
Jokioinen	Sugar beets	**0.5957**	0.0144	0.0224	0.0006

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Kremsmünster	Sugar beets	**0.4143**	0.0111	0.0308	0.0007
Okehampton	Sugar beets	**0.3823**	0.0109	0.0371	0.0013
Piacenza	Sugar beets	**1.0945**	0.0343	**0.1782**	0.0446
Porto	Sugar beets	0.0181	0.0004	0.0006	0.0000
Sevilla	Sugar beets	1.2633	0.0286	0.0481	0.0013
Thiva	Sugar beets	0.0556	0.0016	0.0052	0.0001

80th Percentile Annual Average Groundwater FOCUS PELMO PECs (0.600 kg a.s./ha)

Location	Application Scheme	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)
Châteaudun	Sugar beets	**0.639**	0.017	0.038	0.001
Hamburg	Sugar beets	**0.933**	0.029	**0.114**	0.026
Jokioinen	Sugar beets	**0.762**	0.015	0.022	0.001
Kremsmünster	Sugar beets	**0.600**	0.015	0.030	0.001
Okehampton	Sugar beets	**1.085**	0.030	0.089	0.003
Piacenza	Sugar beets	**1.205**	0.036	**0.178**	0.040
Porto	Sugar beets	0.018	0.000	0.000	0.000
Sevilla	Sugar beets	0.480	0.010	0.010	0.000
Thiva	Sugar beets	0.003	0.000	0.004	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	Not available
Photochemical oxidative degradation in air	DT_{50} of 4.446 hr or 0.371 d derived by the Atkinson method of calculation
Volatilization	from plant surfaces: not required
	from soil: not required

PEC (air)

Method of calculation	Not required

$PEC_{(a)}$

Maximum concentration	Not required

Definition of the Residue (Annex IIA, point 7.3)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Relevant to the environment	**Soil** definition for risk assessment : carbofuran , 3-keto-carbofuran, 3-OH-carbofuran definition for monitoring: carbofuran **Surface water** definition for risk assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol definition for monitoring: carbofuran **Sediment** definition for risk assessment: carbofuran, carbofuran-7-phenol, 3-OH-carbofuran, 3-keto-carbofuran definition for monitoring: carbofuran **Groundwater** Definition for risk assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran definition for monitoring: carbofuran **Air** Definition for risk assessment: carbofuran Definitions for monitoring: 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 relevant for the proposed uses

Classification and proposed labelling (Annex IIA, point 10)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

with regard to fate and behaviour data	Candidate for R53 May cause long-term adverse effects to the aquatic environment

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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	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 ‡				
rat	carbofuran	acute	**LD_{50} = 5.3** – 5.6	-
rat	carbofuran	long-term	NOAEL = 0.1	-
Additional higher tier studies ‡				
AChE activity in brain of *Colinus virginianus* : NOAEL = 0.1 mg a.s./kg b.w.				
Avoidance study with *Anas platyrhynchos* : FAC_{50} = 10 mg a.s./kg feed, the food avoidance concentration is defined as the concentration at which test animals consume equal amounts of treated and untreated feed.				

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

Note : The TER calculations for mammals were performed with a mean NOAEL = 0.71 mg a.s./kg b.w./day. After PRAPeR 68, RMS included its position in the addendum (update May 2009) on the lower NOAEL = 0.1 mg a.s./kg b.w./day

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

Crop and application rate : sugar beet, 1 x 0.600 kg a.s./ha in-furrow

Risk assessment for birds for consumption of granules :

LD_{50}, LC_{50} and NOEC of carbofuran expressed in number of granules for different sizes of birds (based on a weight of 1 granule of 0.87 mg and 0.0437 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}	0.2	0.4	0.8	3.2	8.1
Dietary LC_{50}	0.5	0.9	1.8	7.3	18.3
Long-term NOEC	0.2	0.4	0.7	2.9	7.3

Accidental ingestion of Furadan 5G 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 (i.e. low risk)
Acute – Short-term Exposure					
for individual species data (*)	LD_{50}	LD_{50} 5th percentile = 0.42 mg/kg b.w.	0.2838	0.68	Yes
Dietary – Medium-term Exposure					
Mallard ducklings	LC_{50} (14 day)	1.6 mg/kg b.w./day	0.0570	0.20	Yes
Reproduction – Long-term Exposure					
Mallard duck (24 week study)	NOEC	0.64 mg/kg b.w./day	0.0302	0.27	Yes

Potential ingestion of Furadan 5G 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	0.0196	Yes	0.0062	Yes	0.4971	Yes

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Dietary – Medium-term Exposure							
Realistic worst-case	Small	0.0294	Yes	0.0093	Yes	0.7438	Yes

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

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 %)	7.90	**0.09**	10
	short-term		7.68	**0.21**	10
	long-term		1.44	**0.4**	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 %)	2.14	**0.33**	10
	short-term		2.08	**0.77**	10
	long-term		0.39	**1.64**	10
Yellow wagtail	acute	arthropods (PD = 70 %)	4.16	**0.17**	10
	short-term		3.85	**0.42**	10
	long-term		1.22	**0.52**	10
Blackbird	acute	earthworms (PD = 100 %)	0.24	**2.95**	10
	short-term		0.20	**8.13**	10
	long-term		0.14	**4.50**	10
Skylark	acute	sugar beet seedlings (PD = 33 %), arthropods (PD = 23 %), earthworms (PD = 6 %)	5.85	**0.12**	10
	short-term		5.63	**0.28**	10
	long-term		1.20	**0.54**	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

Risk assessment for mammals for consumption of granules :

LD_{50} and NOAEL of carbofuran expressed in numbers of granules for different sizes of mammals (based on a weight of 1 granule of 0.87 mg and 0.0437 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}	1.82	3.03	6.06	24.24	60.59
Long-term NOAEL	0.24	0.41	0.81	3.25	8.12

Note : The TER calculations for mammals were performed with a mean NOAEL = 0.71 mg a.s./kg b.w./day.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Accidental ingestion of Furadan 5G 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 (i.e. low risk)
Acute – Short-term Exposure					
rat	LD_{50}	5.3 mg/kg b.w.	0.0678	0.049	Yes
Dietary – Medium-term Exposure					
rat	NOAEL (28 d)	5 mg/kg b.w./day	0.0138	0.010	Yes
Reproduction – Long-term Exposure					
rat	NOAEL	0.71 mg/kg b.w./day	0.0073	0.039	Yes

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

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 %)	0.31	17.21	10
	long-term		0.18	**3.90**	5
insectivorous mammal	acute	leafy crop/early arthropods (PD = 100 %)	9.52	**0.56**	10
	long-term		2.80	**0.25**	5
herbivorous mammal	acute	leafy crop/early sugar beet seedlings (PD = 100 %)	2.91	**1.82**	10
	long-term		0.53	**1.33**	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 %)	2.22	**2.38**	10
	long-term		0.73	**0.97**	5
Brown hare	acute	sugar beet seedlings (PD = 40 %)	1.10	**4.81**	10
	long-term		0.20	**3.53**	5

Note : The PD values used in the TER calculations are only for illustrative purposes

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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				
Oncorhynchus mykiss	carbofuran	96 h (semi-static)	Mortality, LC_{50}	0.82 mg a.s./L (nom)
Oncorhynchus mykiss	carbofuran	96 h (semi-static)	Mortality, LC_{50}	0.3625 mg a.s./L (nom)
Lepomis macrochirus	carbofuran	96 h (semi-static)	Mortality, LC_{50}	**0.18 mg a.s./L** (nom)
Oncorhynchus mykiss	carbofuran	28 d fish early life stage	Growth, NOEC	< 0.0087 mg a.s./L (nom)
Cyprinodon variegatus	carbofuran	35 d fish early life stage	Growth, NOEC	**0.006 mg a.s./L** (nom)
Oncorhynchus mykiss	carbofuran	90 d fish early life stage	Growth, NOEC	0.0248 mg a.s./L (nom)
Oncorhynchus mykiss	carbofuran	28 d fish early life stage	Growth, NOEC	0.022 mg a.s./L (nom)
Lepomis macrochirus	7-phenol	96 h (semi-static)	Mortality, LC_{50}	75 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	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)
Aquatic invertebrate				
Daphnia magna	carbofuran	48 h (static)	Mortality, EC_{50}	0.0094 mg a.s./L (nom)
Daphnia magna	carbofuran	48 h (static)	Mortality, EC_{50}	0.0386 mg a.s./L (nom)
Gammarus fasciatus	carbofuran	96 h (static)	Mortality, LC_{50}	0.0028 mg a.s./L (mm)
Hexagenia limbata	carbofuran	96 h (static)	Mortality, LC_{50}	237 mg a.s./L (mm)
Daphnia magna	carbofuran	21 d (semi-static)	Reproduction, NOEC	0.008 mg a.s./L (nom)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Daphnia magna	carbofuran	21 d (flow-through)	Reproduction, NOEC	0.0098 mg a.s./L (mm)
Ceriodaphnia magna	carbofuran	7 d (semi-static)	Reproduction, NOEC	**0.00016 mg a.s./L** (mm)
Daphnia magna	7-phenol	48 h (static)	Mortality, EC_{50}	25 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	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)
Daphnia magna	Furadan 5G	48 h (static)	Mortality, EC_{50}	0.041 mg form/L (mm) (**0.00205 mg a.s./L**)
Sediment dwelling organisms				
Chironomus riparius	carbofuran	28 d (static)	NOEC	**0.004 mg a.s./L** (nom) **0.0032 mg a.s./L** (mm) **0.0022 mg a.s./kg** (nom)
Chironomus riparius	7-phenol	25 d (static)	NOEC	**10 mg/L** (nom) **5.34 mg/L** (mm) **1.36 mg/kg** (nom)
Algae				
Pseudokirchneriella subcapitata	carbofuran	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**6.5 mg a.s./L** (mm) **19 mg a.s./L** (mm)
Pseudokirchneriella subcapitata	7-phenol	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	63 mg/L (nom) > 100 mg/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)
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)
Higher plant				
Not required.				
Microcosm or mesocosm tests				

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Not required.				

[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.

Note : The study with *Ceriodaphnia dubia* and 3-keto-carbofuran is acceptable since the margins of safety in the TER calculations are sufficient (TER > 6203).

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

Crop and application rate : sugar beet, 1 x 0.600 kg a.s./ha in-furrow

Risk assessment for the active substance :

FOCUS Step 1 and 2 TER calculations were deleted since the PEC values were unreliable.

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	0.0264	6818	100
D4	Pond				0.1030	1748	100
D4	Stream				0.0914	1969	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100
D3	Ditch	*Cyprinodon variegatus*	35 d	0.006	0.0264	227	10
D4	Pond				0.1030	58	10
D4	Stream				0.0914	66	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10
D3	Ditch	*Daphnia magna*	48 h	0.00205	0.0264	**78**	100
D4	Pond				0.1030	**20**	100
D4	Stream				0.0914	**22**	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100
D3	Ditch	*Ceriodaphnia dubia*	7 d	0.00016	0.0264	**6.1**	10
D4	Pond				0.1030	**1.6**	10
D4	Stream				0.0914	**1.8**	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Pseudokirchneriella subcapitata*	72 h	6.5	0.0264	246212	10
D4	Pond				0.1030	63107	10
D4	Stream				0.0914	71116	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10
D3	Ditch	*Chironomus riparius*	28 d	0.0032	0.0264	121	10
D4	Pond				0.1030	31	10
D4	Stream				0.0914	35	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

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	0.0461	69	10
D4	Pond				0.1250	26	10
D4	Stream				0.0871	37	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

Risk assessment for the metabolite 3-keto-carbofuran :

FOCUS Step 1 and 2 TER calculations were deleted since the PEC values were unreliable.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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	0.0026	18846	100
D4	Pond				0.0079	6203	100
D4	Stream				0.0044	11136	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100

Risk assessment for the metabolite 3-OH-carbofuran :

FOCUS Step 1 and 2 TER calculations were deleted since the PEC values were unreliable.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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	0.0008	28750	100
D4	Pond				0.0041	5610	100
D4	Stream				0.0024	9583	100
R1	Pond				0.0000	-	100
R1	Stream				0.0000	-	100
R3	Stream				0.0000	-	100

Risk assessment for the metabolite carbofuran phenol (7-phenol) :

FOCUS Step 1, 2 and 3 were deleted since the PEC values were not reliable. The PECsw for the metabolite carobofuran phenol (7-phenol) should be based on the FOCUS Step3 PEC values for carbofuran. The TERs for *C. riparius* would be 51844 and 10880 based on the worst case scenario D4 PECsw of 0.103 µg/L and PECsed of 0.125 µg/kg. .

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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	*Chironomus riparius*	25 d	5.34	0.0000	-	10
D4	Pond				0.0001	53400000	10
D4	Stream				0.0002	26700000	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

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*	25 d	1.36	0.0012	1133333	10
D4	Pond				0.0017	800000	10
D4	Stream				0.0020	680000	10
R1	Pond				0.0000	-	10
R1	Stream				0.0000	-	10
R3	Stream				0.0000	-	10

Bioconcentration				
	carbofuran	Metabolite1	Metabolite2	Metabolite3
$\log P_{O/W}$	1.62 -1.80	-	-	-
Bioconcentration factor (BCF)[1] ‡	11 ± 2.3	-	-	-
Annex VI Trigger for the bioconcentration factor	100	-	-	-
Clearance time (days) (CT_{50})	1.4 ± 0.20	-	-	-
(CT_{90})	4.6 ± 0.67	-	-	-

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Bioconcentration				
Level and nature of residues (%) in organisms after the 14 day depuration phase	4 – 20 % carbofuran	-	-	-

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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)
carbofuran ‡	-	LD_{50} = 0.0357 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 0.600 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.
Carbofuran and its metabolites are transported systemically 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 in sugar beets is acceptable since the exposure to carbofuran in sugar beets is not relevant. Sugar beet is not attractive for pollinating insects : no flower in the production crop; flowers windpollinated.

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

Summary of effects and risk assessment of Carbofuran to non-target terrestrial arthropods (FMC)

Species	Stage	Test substance	Dose (g/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
Typhlodromus pyri	protonymphs	Carbofuran	1.8–18 g a.s./ha	mortality	LD_{50} = 3.65 g a.s./ha HQ = 164	2
Aphidius rhopalosiphi	adults	Carbofuran	1–100 g a.s./ha	mortality	LD_{50} = 2.68 g a.s./ha HQ = 224	2

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Summary of effects and risk assessment of the formulation Furadan 5G to non-target terrestrial arthropods (FMC)

Species	Stage	Test substance	Dose (kg/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
Aleochara bilineata	adults	Furadan 5 G	1-10 kg/ha	mortality	LD_{50} = 3.58 kg/ha HQ = 3	2
Pardosa sp.	adults and sub-adults	Furadan 5 G	3.2-32 kg/ha	mortality	LD_{50} = 2.7 kg/ha HQ = 4	2

Summary of effects and risk assessment of the formulation Diafuran 5G to non-target terrestrial arthropods (Dianica)

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ha)	End point	% effect	Trigger value
Laboratory tests						
Poecilus cupreus	adults	Diafuran 5G, 14 d	600 g a.s./ha, initial	Corrected mortality Food consumption	20 % + 0.8 %	50 % 50 %
Aleochara bilineata	adults	Diafuran 5G, 4 d and 11 d	600 g a.s./ha, initial	Corrected mortality Reproduction	100 % - 100 %	50 % 50 %
Aleochara bilineata	adults	Diafuran 5G, 21 d	600 g a.s./ha, initial	Corrected mortality Parasitism	4.5 % - 60.4 %	50 % 50 %
Pardosa	adults and subadults	Diafuran 5G, 5 d	600 g a.s./ha, initial	Corrected mortality Food consumption	100 % - 100 %	50 % 50 %
Pardosa	adults and subadults	Diafuran 5G, 14 d	600 g a.s./ha, initial	Corrected mortality Food consumption	7.07 % + 5.2 %	50 % 50 %

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

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Summary of effects and risk assessment of the formulation Diafuran 5 G to non-target terrestrial arthropods (FMC)

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ha)	End point	% effect	Trigger value
Extended laboratory tests						
Aleochara bilineata	adults	Curaterr GR 5, 37 d	1000 g a.s./ha, initial	Corrected mortality Parasitism	- 3.4 % - 72.2 %	50 % 50 %
Poecilus cupreus	adults	Curaterr GR 5, 14 d	500 g a.s./ha, initial	Corrected mortality Food consumption	0.0 % - 7.9 %	50 % 50 %
Semi-field tests						
Poecilus cupreus	adults	Curaterr GR 5	500 g a.s./ha, initial	Corrected mortality	68.4 %	50 %
Aleochara bilineata	adults	Curaterr GR 5, 25 d	500 g a.s./ha, initial	Reproduction	- 73.0 %	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

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Field or semi-field tests
A large scale field study (FMC Study No. A2007-6312) 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 Furadan 5G (5% carbofuran) 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. A2007-6312 (designed to investigate the effects of Furadan 5G 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. Recovery occurs for all invertebrate taxa within 2 months after application of 375 g a.s./ha.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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			
Eisenia foetida	Diafuran 5G	acute 14 days	LC_{50} = 4487 mg formulation/kg d.w.soil (**224 mg a.s/kg d.w. soil**)
Eisenia foetida	Diafuran 5G	chronic 8 weeks	NOEC < 16.8 mg formulation/kg d.w.soil (**< 0.84 mg a.s/kg d.w. soil**)
Eisenia foetida	Furadan 5G	acute 14 days	LC_{50} > 1000 mg formulation/kg d.w.soil (**> 50 mg a.s/kg d.w. soil**)
Other soil macro-organisms			
Hypoaspis aculeifer	Furadan 5G	chronic 28 d	NOEC = 200 mg formulation/kg d.w. soil (**10.4 mg a.s./kg d.w. soil**)
Collembola			
Folsomia candida	Furadan 5G	chronic 28 d	NOEC = 4 mg formulation/kg d.w. soil (**0.21 mg a.s./kg d.w. soil**)
Soil micro-organisms			
Nitrogen mineralisation	Diafuran 5G	42 d, unamended soil	-20 % effect at day 42 at 16.0 mg Diafuran 5G/kg d.w. soil (12 kg Diafuran 5G/ha) -40 % effect at day 42 at 32.0 mg Diafuran 5G/kg d.w. soil (24 kg Diafuran 5G/ha) -80 % effect at day 42 at 80.0 mg Diafuran 5G/kg d.w. soil (60 kg Diafuran 5G/ha)
	Diafuran 5G	45 d, amended soil	-25 % effect at day 45 at 16.0 mg Diafuran 5G/kg d.w. soil (12 kg Diafuran 5G/ha) +275 % effect at day 45 at 32.0 mg Diafuran 5G/kg d.w. soil (24 kg Diafuran 5G/ha) +50 % effect at day 45 at 80.0 mg Diafuran 5G/kg d.w. soil (60 kg Diafuran 5G/ha)
Nitrogen mineralisation	Furadan 5G	28 d	+7 % effect at day 28 at 16 mg Furadan 5G/kg d.w. soil (12 kg Furadan 5G/ha) +7 % effect at day 28 at 80 mg Furadan 5G/kg d.w. soil (60 kg Furadan 5G/ha)
Carbon mineralisation	Diafuran 5G	42 d, unamended soil	+38.2 % effect at day 42 at 16.0 mg Diafuran 5G/kg d.w. soil (12 kg Diafuran 5G/ha) +23.5 % effect at day 42 at 32.0 mg Diafuran 5G/kg d.w. soil (24 kg Diafuran 5G/ha) +26.5 % effect at day 42 at 80.0 mg Diafuran 5G/kg d.w. soil (60 kg Diafuran 5G/ha)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Test organism	Test substance	Time scale	End point
	Diafuran 5G	45 d, amended soil	+6.5 % effect at day 45 at 16.0 mg Diafuran 5G/kg d.w. soil (12 kg Diafuran 5G/ha) +25.8 % effect at day 45 at 32.0 mg Diafuran 5G/kg d.w. soil (24 kg Diafuran 5G/ha) +24.2 % effect at day 45 at 80.0 mg Diafuran 5G/kg d.w. soil (60 kg Diafuran 5G/ha)
Carbon mineralisation	Furadan 5G	28 d	-5 % effect at day 28 at 16 mg Furadan 5G/kg d.w. soil (12 kg Furadan 5G/ha) +4 % effect at day 28 at 80 mg Furadan 5G/kg d.w. soil (60 kg Furadan 5G/ha)
Field studies			
Sublethal effects were observed in laboratory studies conducted with benfuracarb (important biomass reduction (biologically and statistically significant) and symptoms were observed at all treatment doses on 100 % of the surviving earthworms, for both the benfuracarb and its formulation) and in the long term toxicity study with carbofuran (NOEC 56 d < 16.8 mg Diafuran 5 G/kg dry soil (0.84 mg a.s./kg dry soil)). The RMS considers that these sublethal effects were evaluated in a valid earthworm field study performed with carbosulfan (Strömel C *et al*, 2002), also addressing the risk of carbofuran. The average actual concentrations in the soil at day 0 were 0.6 mg/kg wet soil and 2.8 mg/kg wet soil, respectively for carbosulfan and carbofuran. 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. In conclusion, the risk of carbofuran to earthworms in sugar beet is addressed.			

Since the log P_{ow} of carbofuran is 1.62 – 1.8, no correction factor 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					
Eisenia foetida	Diafuran 5G	14 d	0.8	280	10
Eisenia foetida	Furadan 5G	14 d	0.8	> 62.5	10
Eisenia foetida	Diafuran 5G	56 d	0.8	< 1.05	5
Other soil macro-organisms					
Folsomia candida	Furadan 5G	28 d	0.8	0.26	5
Hypoaspis aculeifer	Furadan 5G	16 d	0.8	13	5

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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

The notifier was asked to submit data on other non-target organisms (flora and fauna). The RMS agrees with the position paper submitted by the notifier.

The risk to non-target fauna is addressed in other sections of the notifiers submission.
The Terrestrial Guidance Document (SANCO/10329/2002 rev 2 final, 17 October 2002) suggests that “non-target plants” are non-crop plants located outside the treatment area and data are not required where exposure is negligible, e.g. in the case of rodenticides, substances used for wound protection or seed treatment, etc. Furadan 5G is applied, like a seed treatment, directly into the seed furrow and there is, therefore, no drift outside the treated area. Consequently exposure is negligible and, in line with the Guidance Document, no data are required and the risk to non-target plants is acceptable.

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

Test type/organism	Endpoint
Activated sludge	EC_{50} > 10000 mg a.s./L

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

Compartment	
soil	Carbofuran, 3-keto-carbofuran
water	Carbofuran
sediment	Carbofuran, 7-phenol
groundwater	Carbofuran

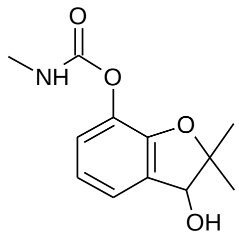
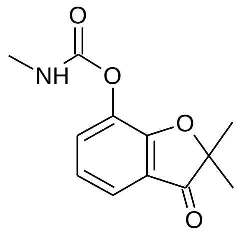
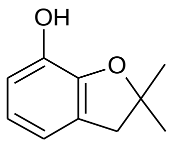
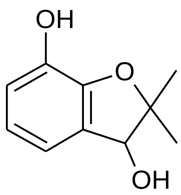
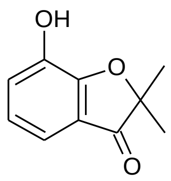
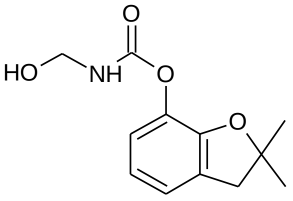
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

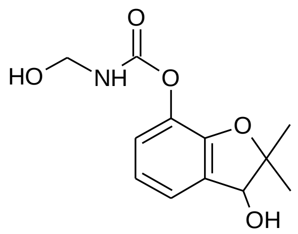
	RMS/peer review proposal
Active substance	N, R50

	RMS/peer review proposal
Preparation	N, R50

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
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-phenol carbofuran-7-phenol	2,2-dimethyl-2,3-dihydro-1-benzofuran-7-ol	
3-OH carbofuran-phenol 3-OH carbofuran-7-phenol	2,2-dimethyl-2,3-dihydro-1-benzofuran-3,7-diol	
3-ketocarbofuran-phenol 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	

LIST OF ABBREVIATIONS

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
d	day
DAR	draft assessment report
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
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
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)
γ-GT	gama glutamyl transferase
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint 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 Database
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
RBC	Red blood cells
RMS	Rapporteur Member State
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
US EPA	United States Environmental Protection Agency

UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year