# Conclusion regarding the peer review of the pesticide risk assessment of the active substance

# carbofuran

## finalised: 28 July 2006

## SUMMARY

Carbofuran is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Belgium being the designated rapporteur Member State submitted the DAR on 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.

A final 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 this report
The conclusion was reached on the basis of the evaluation of the representative uses as insecticide as proposed by the applicant which comprises incorporation into soil (at drilling) to control soil insects where maize, sugar beet or sunflowers will be grew 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 formulated products for the evaluation were Furadan 5G, a granule (GR) and Diafuran 5G, a micrcogranule (MG). Both are registered in some Member States of the EU.

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25

Adequate methods are available to monitor all compounds given in the respective residue definition for food of plant origin, soil and water.

Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least limited 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 or 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 acethylcholinesterase. The overall relevant 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. Furthermore, 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. The classification of Reproduction Toxic Category 3, R62, is proposed. The metabolites 3-OH-carbofuran and 3-keto carbofuran are toxic ($LD_{50}$ of 8 and 107 mg/kg bw, respectively), the hydroxy metabolite is genotoxic as well (Ames test). The dermal absorption value for the granular formulations, Diafuran 5G or Furadan 5G, is 10%. The acceptable daily intake (ADI) and acceptable operator exposure level (AOEL) is 0.001 mg/kg bw/day and the acute reference dose is 0.001 mg/kg bw with the safety factor of 100 applied should be regarded as provisional due to the concerns in relation to possible reproduction effects.

Thus, the estimated exposure should also be considered as provisional. However, if the AOEL is confirmed, the estimated operator exposure according to the US PHED is below the AOEL i.e. 53% if PPE and respiratory protective equipment (RPE) is worn and assuming a maximum work rate of 10 ha/day, see table below. Worker exposure is unlikely to occur, as the formulation is incorporated mechanical means into the soil when sowing. The granular formulation is applied by ground-directed equipment that is nearly dusted free; therefore, the level of bystander exposure to vapour or airborne particles at the time of application is likely to be negligible.

At the time of finalisation of this conclusion, it was noted at the EFSA Evaluation meeting in June 2006 that the new study on spermatogenesis in rats had been provided to the rapporteur and also to the European Chemicals Bureau (ECB) at Ispra, IT for consideration as part of the classification process (March, 2006). In March 2006, the ECB classification meeting proposed that no classification for reproduction was required. EFSA understands from ECB that this conclusion was reached taking into account the results of the new study, which did not confirm the testicular and spermatotoxicity effects in rats reported in published papers. Thus, this position, reached within the ECB process, would support a confirmation of the reference values i.e. ADI, ARfD and AOEL that was provisionally agreed at the mammalian toxicology experts´ meeting (EPCO 33), and a conclusion that no additional safety factor would be required. However it should be noted that the classification proposal has not been formally adopted by a vote within the ECB process nor have the results of the study been considered or peer reviewed within the risk assessment process under Directive 91/414/EEC.

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 were considered applicable to address carbofuran metabolism in plants. Based on all submitted data the metabolic pathway of carbofuran in soil applied uses can be considered as sufficiently investigated. Carbofuran and 3-OH-carbofuran were considered the relevant residues to assess consumer exposure and consumer risk. However, a need to address carbofuran residues in succeeding crops was identified.

Based on the currently proposed residue definition, supervised residue trials in sugar beet, maize and sunflower seed indicated that residues were low and mostly below the respective LOQ.

In livestock animals, carbofuran undergoes an extensive metabolisation. No significant total residues are expected to occur in edible animal matrices taking into account the residue situation for the representative use indicated by the data currently available.

Consumer risk was assessed for carbofuran and 3-OH-carbofuran in the DAR but the assessment was not updated and not agreed on during the peer review process. Based on the initial assessment presented in the DAR the estimated chronic dietary intake of carbofuran and 3-OH-carbofuran is expected to be below the ADI provisionally agreed by EPCO 33. A slight exceedance of the ARfD noted for toddlers consuming maize in the available estimates is primarily caused by the limited sensitivity of the analytical methods applied in the residue trials.

On basis of the laboratory degradation experiments, carbofuran may be from low to high persistent in soil under aerobic conditions. In one of the experiments the metabolite 3-keto-carbofuran exceed the 10 % AR. Carbofuran-7-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.

Only carbofuran-7-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 (FMC) metabolites 3-OH-carborfuran, 3-keto carbofuran and carbofuran-7-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. Carbofuran-7-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 (FMC). 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 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 carbosulfan field studies performed in EU were used by the rapporteur Member State in the risk assessment of carbofuran. The meeting of the experts was not able to determine the reliability of these studies. A position paper from the applicants is available (June 2005) but has not been assessed and peer reviewed. Also the meeting of experts agreed that it is necessary to determine whether the studies from the USA are acceptable for the EU risk assessment.

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

No information on the degradation rate of metabolites is available in the DAR. Rate of degradation in soil should be estimated for the metabolites 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol to complete the FOCUS-GW calculations required.

PEC soil presented in the DAR are based on the worst case EU field half life ($DT_{50}$ = 71.9 d) determined for carbofuran in the carbosulfan field studies. Evaluation meeting agreed that the appropriateness of using this value need to be discussed by the experts meeting. The meeting of experts was not able to conclude on this due to the lack of relevant information for the field studies in the DAR. An addendum from the rapporteur Member State assessing the position paper of the applicants and providing further details on the field studies is awaited. In case dissipation half life of 71.9 d is found to be inappropriate, $PEC_S$ will need to be recalculated.

Carbofuran may be classified as very high mobile compound. A data gap for further batch adsorption/ desorption studies on carbofuran soil metabolites are necessary to complete the FOCUS-GW calculations.

An aged column leaching study shows that carbofuran and its metabolites (3-keto-carbofuran and carbofuran-7-phenol) are mobile and may leach under the conditions of the experiments.

No lysimeter studies were available for carbofuran. One of the applicants (FMC) presented two lysimeter studies not provided in the original dossier (June 2005). These studies have not been assessed and peer reviewed.

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-7-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 41 d. Mineralization was low and bound residue reached a maximum of level of 32.8 % AR. In the neutral or alkaline systems carbofuran dissipated from the water phase with half lives of 5.3-6.9 d and degraded in the whole system with half lives of 7.8 – 11.6 d. The only major metabolite found in the water phase was carbofuran-7-phenol. Only carbofuran reached levels above 10 % AR in the sediment. 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.

The two applicants proposed different approaches to estimate the potential contamination of surface water. None of these approaches follows 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 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.

Available FOCUS GW modelling shows that trigger of 0.1 μg / L was exceeded for four of the eight maize relevant scenarios, four of the nine sugar beet scenarios and one of the two relevant sunflower scenarios. However, this calculation does not take into account the data from the other applicant, which shows that carbofuran may be significantly more persistent in soil. In the case of sugar beet and sunflower the product was assumed to be applied only every three or two years respectively, this limitation is not indicated in the table of representative uses proposed by the applicants. The meeting of the experts identified a new data gap for new 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.

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

An addendum to the fate and behaviour chapter has been provided the 18th of 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 are not adequately referenced. Therefore, studies submitted by the applicant after the DAR was submitted are considered neither evaluated nor peer-reviewed in this conclusion.

Substantial data requirements to address the risk to birds and mammals from uptake of granules, ingestion of treated seedlings and contaminated earthworms were identified in the DAR by the rapporteur Member State. The aquatic risk assessment based on PECsw from drainage resulted in a high acute and chronic risk to aquatic invertebrates. New studies and a refined risk assessment were submitted. The risk to bees for the use in sugar beets is considered to be low because no exposure is expected. Exposure of bees via pollen and nectar is possible for the use in maize and sunflowers. A risk to bees cannot be excluded for the representative uses in maize and sunflowers on the basis of the peer reviewed data. Further studies on the oral toxicity to bees were submitted The risk to non-target arthropods was not sufficiently addressed. The experts´ meeting on ecotoxicology confirmed the data requirement and identified also the need for studies with soil dwelling non-target macro organisms. A high long-term risk to earthworms cannot be excluded from the peer reviewed data. New information was submitted by the applicants. The risk to soil non-target micro-organisms was considered to be low on the basis of data submitted by FMC. A data requirement was set for the applicants to address the risk to other non-target organisms. The risk to biological methods of sewage treatment was assessed as low. An addendum to the chapter on ecotoxicology has been provided on the $18^{th}$ of May 2006. When reported, the information in the addendum has been summarized too briefly to draw any conclusion on its reliability.

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

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## BACKGROUND

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

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

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

- the comments received
- the resulting reporting table (rev. 1-1 of 14 June 2005)
- the consultation report

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
- the evaluation table (<<rev. 2-1 of 19 June 2006)

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

## 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 Acetyl-Choline Esterase (AChE) in the nervous system.

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

The evaluated representative uses as insecticide as proposed by the applicant comprises incorporation into soil (at drilling) to control soil insects where maize, sugar beet or sunflowers will be grew 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.

## 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.
At the moment no FAO specification exists.

The technical materials contain no relevant impurities.

The content of carbofuran in the representative formulations is 50.5 g/kg (pure) and 50.27 g/kg (pure) for Diafuran 5G and Furadan 5G, respectively.
It should be noted that clarification is required with respect to the content of carbofuran in the Diafuran 5G formulation.

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.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of carbofuran in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. carbofuran (sum of carbofuran and 3-OH-carbofuran[3]) in food of plant origin (uses with soil application).
In the case of soil and water the final residue definitions are still under discussion. Depending on further assessment, 3-keto-carbufuran[4] could be included in the residue definition for soil and 3-OH-carbofuran, 3-keto-carbofuran and carbofuran-7-phenol[5] in the definitions for water.

[3] 3-OH-carbofuran: 3-hydroxy-carbofuran; 3-hydroxy-2,3-dihydro-2,2-dimethylbenzofuran-7-yl (dibutylaminothio)methylcarbamate
[4] 3-keto-carbofuran: methyl carbamic acid 2,2-dimethyl-3-oxo-2,3-dihydro-benzofuran-7-yl ester

An analytical method for the determination of residues in air is not required according to SANCO/825/00, due to the application technique (i.e. granular formulation to be incorporated in soil) is such that no relevant exposure is likely to occur). However, a method for the determination of carbofuran is available.
An analytical method for food of animal origin is not required due to the fact that no MRLs are proposed (see 3.4).

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

The discussion in the meeting of experts (EPCO 35, September 2005) on identity, physical and chemical properties and analytical methods was limited to certain properties of carbofuran and one plant protection product, the missing ILV for food of plant origin and to the composition of one plant protection product.

# 2. Mammalian toxicology

Carbofuran was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 33) in September, 2005. The rapporteur Member State has provided an addendum which is dated August but this 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.
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-OH carbofuran which is further conjugated to glucuronic acid and excreted in bile. Enterohepatic recirculation of this metabolite is suggested. 3-OH carbofuran is also hydrolyzed in 3-OH carbofuran-7-phenol[6] or hydroxylated in 3-keto carbofuran, the later being itself

[5] carbofuran-7-phenol: 2,3.dihydro-2,2-diemethyl-7-benzofuranol
[6] 3-OH carbofuran-7-phenol: 2,2-dimethyl-2,3-dihydrobenzofuran-3,7-diol

hydrolyzed in 3-ketocarbofuran-7-phenol[7]. The three metabolites of 3-OH carbofuran are conjugated and excreted in urine mainly.
Carbofuran can also undergo oxidation of its carbamate moiety giving N-OH methylcarbofuran,[8] further hydroxylated in 3-OH-N-OH-methyl carbofuran.[9] 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 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 or 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.

Oral exposure, rat
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/d is proposed.

[7] 3-ketocarbofuran-7-phenol: 7-hydroxy-2,2-dimethylbenzofuran-3(2H)-one
[8] N-OH methylcarbofuran: 2,2-dimethyl-2,3-dihydrobenzofuran-7-yl hydroxymethylcarbamate
[9] 3-OH-N-OH-methyl carbofuran: 3-hydroxy-2,2-dimethyl-2,3-dihydrobenzofuran-7-yl hydroxymethylcarbamate

Oral exposure, dog

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 (Bloch et al,. 1987a) was discussed at the 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, 1996. 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 experts´ meeting. It was confirmed that it 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/d and dose-related inhibition of brain cholinesterase was observed at 100 and 400-mg/kg bw/d. The NOAEL is 25 mg/kg bw/day.

## 2.4 GENOTOXICITY

In the DAR the genotoxic properties of benfuracarb 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. Dianica is requested to submit a new micronucleus test (or to get access to the FMC ones).

In conclusion, the genotoxic potential of carbofuran was discussed at the experts´ meeting and it was concluded that the carbofuran data based for FMC was adequate while Dianica still needs to submit (or get access to an FMC study) an *in vivo* micronucleus test. 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 of 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 as based on decreased body weight and reduced survival of the F1a, F2a and F3a survival at lactation decreased body weight in pups at 50 ppm, the parental NOAEL is also 20 ppm i.e. 1.2 mg/kg bw/day based on body weight gain and food consumption (Schardein, 1990).
The NOAEL from 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 survival at lactation day 4 in pups at 100 ppm (Goldenthal, 1979b).

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 (Pant, 1995), 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 experts' meeting 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. **Therefore, there was a data requirement set for FMC to provide a new study or get access to the Dianica study.** 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 is ongoing (Dianica) but not completed.** The experts agreed to propose the classification of Reproduction Toxic Category 3, **R62**, based on the available data, but final decision is to be made by ECB.
The overall NOAEL for reproduction and parental toxicity is 1.2 mg/kg bw/day.

**EFSA note:** At the time of finalisation of this conclusion, at the EFSA Evaluation meeting in June 2006, it was noted that the new study on spermatogenesis in rats had been provided to the rapporteur and also to ECB for consideration as part of the classification process (March, 2006).
EFSA confirmed that the study has been considered within the ECB process. In March 2006, the ECB classification meeting proposed that no classification for reproduction was required. EFSA understands from ECB that this conclusion was reached taking into account the results of the new study, which did not confirm the testicular and spermatotoxicity effects in rats reported in published

papers. Thus, this position, reached within the ECB process, would support a confirmation of the reference values i.e. ADI, ARfD and AOEL that was provisionally agreed at EPCO 33 (Mammalian toxicology experts´ meeting), and a conclusion that no additional safety factor would be required. However it should be noted that the classification proposal has not been formally adopted by a vote within the ECB process nor have the results of the study been considered or peer reviewed within the risk assessment process under Directive 91/414/EEC.

The teratogenic or developmental effects 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 fetal 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/d, 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 /d. 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).

## 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, 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<br>$LD_{50}$ 8.3 mg/kg bw (**$T^{+}$; R28**).<br>Positive in Ames test and mouse lymphoma tests |
| 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-7-phenol | oral $LD_{50}$ >800 mg/kg bw (**Xn; R22**). |
| carbofuran 7-phenol | oral $LD_{50}$ 1743 mg/kg bw (**Xn; R22**). |

## 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 (Shah; 1987). 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 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 experts´ meeting. The Shah study was performed on rats with carbofuran solubilized in acetone, 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 (Liu and Kim, 2003).

The 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.
However, it should be noted that there is still a data requirement, for formal reasons, for FMC to provide an *in vivo* or *in vitro* dermal absorption study or to get access to the Dianica study.

## 2.11 ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

**EFSA notes:** The reference values should be regarded as provisional for further details see 2.6.

ADI and AOEL

The ADI and AOEL is 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* ADI and AOEL is 0.001 mg/kg bw/day, with the safety factor of 100 applied.**

ARfD

The ARfD is 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

**The *provisional* ARfD is 0.001 mg/kg bw/day, with the safety factor of 100 applied.**

## 2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The estimated operator exposure is made both for the application of Diafuran 5G or Furadan 5G using tractor-mounted equipment. Diafuran G and Furadan 5G are granular formulations, containing 50 g carbofuran/kg, to be applied by mixing granules with the moving soil closing to seed furrow. The maximum application rate is 600 g a.s./ha.

**EFSA note:** The risk assessment should be regarded as provisional until the AOEL is confirmed see chapter 2.6 for further clarifications. The estimated operator exposure based on the provisional AOEL is presented below.

Operator exposure

The *provisional* operator exposure was estimated using the American Pesticide Handlers exposure Database (PHED) as well as the standard models UK-POEM and the German model. The latter models do not have scenarios representative for granular formulations and should therefore only be considered as supplemental. The calculations presented in the DAR are based on the dermal absorption of 10% and the assumption that the treatment is 10 ha/day the total amount handled is 6 kg/day (for sugar beet and maize). In the calculation on the basis of the PHED without respirator, the estimated exposure exceeds the AOEL (206%). However, it should be noted that PPE only refers to gloves. Furthermore, as carbofuran is highly toxic via the inhalatory route, additional respiratory protective equipment is applicable. The estimated exposure is below the AOEL i.e. 53% only if PPE

and respiratory protective equipment (RPE) is worn and the 75th percentile is considered and assuming a maximum work rate of 10 ha/day, see table below.
**EFSA notes:** For consistency in relation to benfuracarb and carbofuran, the body weight of 60 kg for the operator is assumed to in the calculations.

Provisional estimated exposure presented as % of the provisional AOEL (0.001 mg/kg bw/day), according to calculations with the PHED model. The default for body weight of operator is 60 kg and treated area 10 ha/day.

| Model | No PPE | With PPE: | With PPE and RPE: |
|---|---|---|---|
| PHED (75th percentile) 10 ha/day | - | 240% | 53% |

PPE (personal protective equipment): gloves, RPE (respiratory protection equipment)

The UK-POEM and the German model are not appropriate for this representative use and several assumptions are needed. Anyhow, for transparency, calculations are provided. An estimation of operator exposure was performed by the rapporteur Member State using the UK POEM and German Model taking into account the dermal and inhalation exposure during mixing and loading only, excluding application because the use of granular applicators excludes exposure during application. Using the tractor application technique model, and applying protective equipment (gloves) operator exposure is below the AOEL according to the UK and German model, 10% and 24%, respectively.

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 dusted 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.

## 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.

### 3.1.1. PRIMARY CROPS

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[10] (*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 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

[10] 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[11] 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.

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.

[11] 2-hydroxymethyl-3-keto-carbofuran: 2,3-dihydro-2,2-dimethyl-3-oxo-7-benzofuranyl-N-hydroxymethylcarbamate

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.

### 3.1.2. SUCCEEDING AND ROTATIONAL CROPS

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 concluded that there is a need to address residues of carbofuran in succeeding crops.

## 3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

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.

### 3.3. CONSUMER RISK ASSESSMENT

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.

### 3.4. Proposed MRLs

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

Carbofuran fate and behaviour into the environment was discussed in the meeting of experts EPCO 31 (September 2005) on the basis of 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 are not adequately referenced. Therefore, studies submitted by the applicant after the DAR was submitted are considered neither evaluated nor peer-reviewed in this conclusion.

### 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. 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 % AR) were detected but not characterized. Unextractable residue amounted up to 57.7 % AR and mineralization reached a maximum of 32.6 % AR after 120 d.

Another study (FMS, 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). 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-7-phenol.

An additional aerobic soil metabolism study (FMS, Schocken, M. J., 1989) is available. The same metabolites were identified. In this case 3-OH-carbofuran reached a maximum of 0.9 % AR and carbofuran-7-phenol a maximum of 9 % AR at the end of the study (184 d).

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 reaches a maximum of 6.2 % AR at the end of the aerobic phase in this study.

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-7-phenol was identified as major metabolite in this study (max. 62.9 % % AR after 28 d). Another metabolites fraction M4 reached a maximum at he end of the study (max. 8.9 % AR after 120 d) but was shown to contain several compounds. Mineralization was low ($CO_2$ 6.2 % 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-7-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-7-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; FMS, Schocken, M. J., 1989 / $DT_{50\ 10\ °C}$ = 110 d; Dianica, Völk, S., 2002) in soil depending on the study. The meeting of MS experts considered that data package from the applicant FMC could not be considered complete with respect to aerobic soil degradation due to insufficient variability in the properties of soils employed. 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 degradation parameters obtained in the studies performed with benfuracarb (Dianica: Van Noorloos, B., Slangen, P.J., 2002a; Van Noorloos, B., Slangen, P.J., 2002b) and carbosulfan (FMC: Clay, 1980; Markle, 1981a; Taylor, 1983; Baumann and Ferreira, 2001 and Baumann, 2002), where carbofuran appears as metabolite. Addendum with summaries of these studies is not available. Additionally, EFSA notes that some of these studies were considered not acceptable in the DAR of carbosulfan and that neither in the DAR of carbosulfan nor in the DAR or carbofuran the degradation parameters obtained from these studies for carbofuran is provided. Therefore, at this stage the end points from these studies cannot be included in the list of end points.
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) 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 was not able to determine the reliability of these studies. A position paper from the applicants is available (June 2005) but has not been assessed and peer reviewed. Also the meeting of experts agreed that it is necessary to determine whether the studies from the USA sites are acceptable for the EU risk assessment.
No information on the degradation rate of metabolites is available in the DAR. Inspection of the data available (e.g. FMC, Saxena A M *et al* 1994) in the studies performed with carbofuran as parent, indicate that 3-OH-carbofuran may be an intermediate in the formation of 3-keto-carbofuran and therefore low persistent. However, 3-keto carbofuran seems to be relatively high persistent in acidic

soils. Rate of degradation in soil should be estimated for the metabolites 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol to complete the FOCUS-GW calculations required.
PEC soil presented in the DAR are based on the worst case EU field half life ($DT_{50}$ = 71.9 d) determined for carbofuran in the carbosulfan field studies. Evaluation meeting agreed that the appropriateness of using this value need to be discussed by the experts meeting. The meeting of the experts was not able to conclude on this due to the lack of relevant information for the field studies in the DAR. An addendum from the rapporteur Member State assessing the position paper of the applicants and providing further details on the field studies is still awaited. In case dissipation half life of 71.9 d is found to be inappropriate, $PEC_S$ will need to be recalculated.

### 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, necessary to complete the FOCUS-GW calculations, was identified by the meeting of MS experts.
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-7-phenol) are mobile and may leach under the conditions of the experiments.
No lysimeter studies were available for carbofuran in the original dossier. The rapporteur Member State proposed in the DAR a data requirement for a lysimeter study. After the first evaluation meeting (June 2005), one of the applicants (FMC) presented two lysimeter studies. These studies have not been assessed and nor peer reviewed.

## 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-7-phenol[12] was the major hydrolysis products identified. Carbofuran-7-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.

[12] Also called 7-hydroxy-carbofuran in this section of the DAR.

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. Transformation products 3-OH-carbofuran and 3-keto-carbofuran were found both in the water and the sediment phase at low levels (< 0.3 % AR). Mineralization was low ($CO_2$ = 1.81 % AR at the end of the study) and bound residue reached a maximum of level of 32.8 % AR. The rapporteur Member State required in the DAR a new water/sediment study or additional information on 7-phenol metabolite and on the degradation rate of carbofuran. EFSA recalculated the half life ($DT_{50\ whole\ system}$ = 44.6 d) by non-linear regression that passed the $\chi^2$ test with an error level of 6.8 %. Fitting is not very good and it would be necessary to have more data points at longer times to have a reliable half life. However, the available data clearly indicate that a half life must be longer than 30 d for this system. Clarification on metabolite carbofuran-7-phenol seems to be related to the high levels of this metabolite found in the second replicate of the days 20 and 30. These high levels 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 studies under alkaline conditions already show the faster degradation carbofuran and the formation of this metabolite at high levels. Therefore, EFSA does not consider this data requirement essential to finalize the EU risk assessment.

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. The only major metabolite found in the water phase was carbofuran-7-phenol (max. 12.0 % AR after 4 d). Only carbofuran reached levels above 10 % AR in the sediment. Some metabolite fractions (max. 5.9 % AR) 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.

The two applicants proposed different approaches to estimate the potential contamination of surface water. None of these approaches follows 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 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.

Whereas exposure of surface water to the active substance cannot be completely excluded, the meeting of MS experts agreed that exposure to the formulations in its integrity may be excluded when the products are used according the GAPs (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

One of the applicants (Dianica) presented an estimation of the potential for ground water contamination based on the FOCUS GW scheme. The 80$^{th}$ percentile of the annual average concentration in the leachate at 1m depth was calculated for the DIAFURAN 5G representative uses were performed for the relevant scenarios. However, in the case of sugar beet and sunflower the risk assessment was based on applications only every third and second year respectively. This limitation is not indicated in the table of representative uses. Input parameters were based only in the data found in this applicant's dossier. Trigger of 0.1 μg / L was exceeded for four of the eight maize relevant scenarios, four of the nine sugar beet scenarios and one of the two relevant sunflower scenarios. However, this calculation does not take into account the data from the other applicant. These data shows that carbofuran may be significantly more persistent in soil. Therefore, new calculations are needed taking into consideration all available data on this active substance. Applicant FMC provided new FOCUS-GW calculations in June 2005, probably addressing only potential contamination by the parent compound. Addendum with the assessment of this study is not available.

Potential groundwater contamination by the carbofuran metabolites 3-OH-carbofuran and 3-keto-carbofuran (minor soil metabolites containing the toxosphore carbamate) and major soil metabolite carbofuran-7-phenol was not addressed by any of the applicants.

The meeting of the experts identified a new data gap for new 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.

### 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.

## 5.1. RISK TO TERRESTRIAL VERTEBRATES

A risk assessment for birds and mammals was conducted according to SANCO/4145/2000. The rapporteur Member State considered granules of both formulations as comparable and that the risk assessment for uptake of granules was based on the formulation Furadan 5 G (FMC) with a size of 0.6 – 0.85 mm and an average weight of 0.37 mg. The number of granules to reach the acute and dietary $LD_{50}$ dose was calculated to be 0.58 and 1.3 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 sublethal 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 sublethal effects in terms of potential adverse effects in the field. However, the study gives an indication that severe sublethal effects may occur at the proposed GAPs which could lead to an increased mortality in the natural environment.

The risk from consumption of contaminated earthworms was not sufficiently addressed. Cases of secondary poisoning of birds of prey were reported by France. France submitted the reports to the rapporteur Member State. The calculation of the concentration of carbofuran in worms was not done according to SANCO/4145/2000. No addendum was provided by the rapporteur Member State and therefore this point remains open.

Data requirements to address the risk to birds from uptake of granules, treated seedlings and contaminated earthworms and the risk of secondary poisoning of birds of prey were identified by the rapporteur Member State in the DAR for both applicants, FMC and Dianica. A new risk assessment including studies on possible bird kills and secondary poisoning of birds of prey was submitted by FMC in June and July 2005. A new risk assessment on the basis of the data submitted by the applicants for Furadan 5G and Diafuran 5G was presented by the rapporteur Member State in an addendum of May 2006. The risk to birds was assessed as low for the uptake of contaminated earthworms but a high risk was identified for ingestion of granules and treated seedlings for both applicants. The addendum of May 2006 is not peer reviewed.

The reproduction study with mallard duck was assessed by the rapporteur Member State as not acceptable due to several shortcomings. The need for a valid long-term endpoint for birds was discussed in the expert's meeting. The meeting noted that the long-term risk to birds was assessed for similar granular products. It was concluded that there may be a long term risk due to residues in earthworms and hence a valid long-term endpoint has to be established. The meeting suggested conducting the long-term test with mallard duck (*Anas platyrhynchos*) at appropriate dose levels of carbofuran.

The risk to birds and mammals from uptake of contaminated drinking water was assessed as low.

The number of granules to reach the acute $LD_{50}$ and the long-term NOAEL was calculated to be 3 and 0.05 granules for a small mammal of 10 g indicating a potential high acute and long-term risk to mammals. A field study indicated that the application of Furadan 5 G leads to poisoning of small mammals like mice (see above). The risk from uptake of treated seedlings and contaminated earthworms was not sufficiently addressed. Therefore the rapporteur Member State identified in the DAR a requirement for data to address the risk from ingestion of granules, treated seedlings and contaminated earthworms. FMC submitted a new risk assessment for mammals in June/July 2005. Dianica submitted new information in August 2005. In the not peer reviewed addendum of May 2006 the risk from uptake of contaminated earthworms was assessed as low for the use of Furadan 5G and Diafuran 5G. But the risk from uptake of granules and treated seedlings was considered as high for the representative uses of Furadan 5G and Diafuran 5G.

## 5.2. RISK TO AQUATIC ORGANISMS

A data requirement was identified in the DAR for both applicants to calculate the PECsw values with FOCUSsw. The risk assessment which was based on a provisional PECsw value indicated a potential high acute and chronic risk for aquatic invertebrates. A mesocosm study was submitted by FMC. The study was assessed as not being of direct use to refine the risk to aquatic organisms since the test substance was carbosulfan and the substance was applied as a spray while exposure to carbofuran is expected only via drainage for the representative uses. The rapporteur Member State identified a data requirement for both applicants to submit a refined risk assessment for aquatic organisms. The experts´ meeting on fate and behaviour (EPCO 31, September 2005) confirmed that it is unlikely that the formulation would enter surface water. Therefore the meeting agreed that toxicity data with the formulation and aquatic organisms are not required. Since no NOEC value was determined in the fish juvenile growth study submitted by Dianica, the rapporteur Member State identified the need for a new study to establish a reliable long-term NOEC for fish. A new study was submitted in June 2005. The endpoint of this study is given in the addendum of May 2006. No summary or evaluation of the study was included in the addendum.

The experts´ meeting noted that a study on sediment dwelling organism is triggered since the level of applied radioactivity was >10 % in the water/sediment study and the NOEC for daphnids is <0.1 mg/L. Therefore a data gap was identified for both applicants to submit a study with sediment dwelling organisms.

FMC submitted a new aquatic risk assessment in June 2005. The rapporteur Member State provided a new risk assessment in the addendum of May 2006 where the long-term risk to aquatic invertebrates from the use of Furadan 5G was assessed as low.

The peer reviewed first tier risk assessment indicates a high acute and chronic risk for aquatic invertebrates for all representative uses.

### 5.3. RISK TO BEES

Exposure of bees to residues in pollen and nectar of sunflowers and pollen of maize were considered as potential routes of exposure in the assessment of the rapporteur Member State. Since no studies on the oral toxicity of carbofuran to bees were available, the rapporteur Member State set a data requirement for both applicants to submit data on the oral toxicity to bees and a risk assessment for the use in sunflowers and maize. 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.
FMC submitted a study on the acute oral toxicity to bees and a new risk assessment in June/July 2005 and Dianica submitted new data in August 2005. A new risk assessment was presented in the addendum of May 2006. Essential information is missing in the addendum (e.g. study summaries and evaluation of the studies). The addendum is not peer reviewed.

### 5.4. RISK TO OTHER ARTHROPOD SPECIES

Effects of >30% were observed in laboratory studies with *Aleochara bilineata* and *Pardosa sp.* at a dose rate equivalent to the proposed GAP. $LD_{50}$ values from extended lab studies were lower than the proposed use rates. Hence a high risk to non-target arthropods was indicated from the available data for all representative uses. The rapporteur Member State identified the need for further data to address the risk to non-target arthropods. The experts´ meeting confirmed the need for further studies to address the risk to non-target arthropods including effects on soil dwelling macro-organisms (*Folsomia candida* and *Hypoaspis aculeifer*). FMC submitted 5 additional studies with *Aleochara sp*. and carabid beetles in June 2005. Studies with *Folsomia candida* and *Hypoaspis aculeifer* were announced to be submitted. Dianica submitted further data in August 2005. The new data are listed in the addendum of May 2006. The rapporteur Member State concluded that the risk to other non-target arthropod species is not sufficiently addressed for the uses of Furadan 5G and Diafuran 5G. The addendum is not peer reviewed.
Based on the peer reviewed data a high risk to non-target arthropods cannot be excluded.

### 5.5. RISK TO EARTHWORMS

The acute risk to earthworms was assessed as low for all representative uses. However 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 DAR. FMC submitted a position paper and an argumentation for using the earthworm field study with endosulfan 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. The addendum is not peer reviewed.

Based on the peer reviewed data a high long-term risk to earthworms cannot be excluded for all representative uses.

### 5.6. Risk to other soil non-target macro-organisms

The need for data on effects on soil non-target macro-organisms was identified by the EPCO experts´ meeting (see point 5.4. Risk to other arthropod species). A risk assessment was presented in the addendum of May 2005. The long-term risk to soil non-target organisms was assessed as high by the rapporteur Member State for the representative uses of Furadan 5G and Diafuran 5G. The addendum is not peer reviewed.

### 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 all representative uses since the nitrogen level in the treated samples was similar to controls after 28 days.

No studies to address the risk to soil non-target micro-organisms were submitted by Dianica and hence listed as a data requirement in the DAR. A study on soil nitrification and respiration was submitted in June 2006. The effects observed in the study are reported in the addendum of May 2006 to be < ±25 % at concentrations of 0.82 and 4.1 mg carbofuran/kg dry soil. The addendum is not peer reviewed.

### 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 for both applicants. Position papers were submitted by the applicants. 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). The addendum is not peer reviewed.

### 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 1000 mg carbofuran/L. Therefore the risk to biological methods of sewage treatment is considered to be low for all representative uses.

## 6. Residue definitions

**Soil**

Definitions for risk assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol.

Definitions for monitoring: carbofuran, 3-keto-carbofuran (included pending the finalization of the risk to soil dwelling organisms).

**Water**

**Ground water**
Definitions for exposure assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol.
Definitions for monitoring: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol (all metabolites are included pending the finalization of the ground water assessment).

**Surface water**
Definitions for risk assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol.
Definitions for monitoring: carbofuran, 3-keto-carbofuran (included pending the finalization of the surface water assessment).

**Air**
Definitions for risk assessment: carbofuran
Definitions for monitoring: carbofuran

**Food of plant origin**
Definitions for risk assessment: carbofuran and 3-OH carbofuran, expressed as carbofuran (uses with soil application)
Definitions for monitoring: carbofuran and 3-OH carbofuran, expressed as carbofuran (uses with soil application)

**Food of animal origin**
Definitions for risk assessment: 3-OH carbofuran
Definitions for monitoring: not required, however proposed as 3-OH carbofuran if necessary for future uses

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 high persistent ($DT_{50lab}$ = 4.4 – 444 d; $DT_{50field}$ = 1.3 – 125 d) | A high long-term risk to earthworms was identified in a first tier risk assessment. |
| 3-OH-carbofuran | No conclusive data provided, available data indicate that may be low persistent intermediate in the formation of 3-ketocarbofuran | No studies with soil dwelling organisms available. No data required due to the transient nature of the molecule. |
| 3-keto-carbofuran | No conclusive data provided, available data indicate that may be high persistent in acidic soils. | No studies with soil dwelling organisms are available. The risk to soil dwelling organisms needs to be addressed since it contains the active moiety and it is persistent in acidic soils |
| Carbofuran-7-phenol | No conclusive data provided (max of 9 % AR reached after 184 d in one study). | No studies with soil dwelling organisms are available. No studies are required since it does not contain the active moiety and it is formed at low levels in soil. |

**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-GW: trigger exceeded for some scenarios, however new calculations with appropriate input parameters are required. Lysimeter: required by the RMS in the DAR. Two lysimeter studies available not evaluated. | Yes | Yes | Carbofuran is very toxic to aquatic organisms. The risk assessment of the RMS which was based on a provisional PECsw value indicated a potential high acute and chronic risk for aquatic invertebrates |
| 3-OH-carbofuran | No data available | FOCUS-GW: calculation required Lysimeter: required by the RMS in the DAR. Two lysimeter studies available not evaluated. | No data available Data gap (depending on the outcome of the fate assessment) | Relevant Toxic ($LD_{50}$ 8.3 mg/kg bw) It is genotoxic (Ames test) | No data available. The metabolite contains the active moiety. However, the molecule is transient and it appears only at low levels in the water-sediment system and in soil. Only in case that the toxicity of 3-OH-carbofuran is several orders of magnitude higher than the toxicity of carbofuran the risk of the metabolite would not be covered by the risk assessment for the parent carbofuran. |

| 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 | Batch adsorption / desorption studies not available<br>Mobile according aged column leaching experiment | FOCUS-GW: calculation required<br>Lysimeter: required by the RMS in the DAR. Two lysimeter studies available not evaluated. | No data available<br>Data gap<br>(depending on the outcome of the fate assessment) | Relevant<br>Toxic ($LD_{50}$ 107 mg/kg bw)<br>No studies on genotoxicity available | No data available. 3-keto-carbofuran contains the active moiety. It is formed in the water-sediment system at low levels but it is persistent in acidic soils. Therefore the potential risk to aquatic organisms needs to be addressed for vulnerable situations where entry of 3-keto-carbofuran into surface water is possible. |
| Carbofuran-7-phenol | Batch adsorption / desorption studies not available.<br>Mobile according aged column leaching experiment | FOCUS-GW: calculation required<br>Lysimeter: required by the RMS in the DAR. Two lysimeter studies available not evaluated. | No data available<br>Data gap<br>(depending on the outcome of the fate assessment) | Harmful ($LD_{50}$ 1743 mg/kg bw)<br>No studies on genotoxicity available | Carbofuran-7-phenol is markedly less toxic to aquatic organisms compared to carbofuran. No PECsw calculation and no risk assessment was performed. |

**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 a provisional PECsw value indicated a potential high acute and chronic risk for aquatic invertebrates. |
| 3-OH-carbofuran | No data available. The metabolite contains the active moiety. However, the molecule is transient and it appears only at low levels in the water-sediment system and in soil. Therefore it is not likely that the PECsw for 3-OH-carbofuran would exceed the PECsw for carbofuran. Only in case that the toxicity of 3-OH-carbofuran is several orders of magnitude higher than the toxicity of carbofuran the risk of the metabolite would not be covered by the risk assessment for the parent carbofuran. |
| 3-keto-carbofuran | No data available. 3-keto-carbofuran contains the active moiety. It is formed in the water-sediment system at low levels but it is persistent in acidic soils. Therefore the potential risk to aquatic organisms needs to be addressed for vulnerable situations where entry of 3-keto-carbofuran into surface water is possible. |
| Carbofuran-7-phenol (water phase only) | Carbofuran-7-phenol is markedly less toxic to aquatic organisms compared to carbofuran. No PECsw calculation and no risk assessment was performed. However, only in case that the PECsw would be 4 orders of magnitude higher than the PECsw for carbofuran the resulting TERs would be higher than the TERs for 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

- Clarification with respect to the content of carbofuran in the Diafuran 5G formulation (relevant for Dianica, date of submission unknown, data gap identified by the meeting of experts, September 2005; refer to chapter 1).
- Additional ILV data for the method to determine 3-OH-carbofuran in food of plant origin at levels between 0.05 mg/kg and 0.5 mg/kg (relevant for FMC, date of submission unknown, data gap identified by the meeting of experts, September 2005; refer to chapter 1).
- A data requirement/gap was identified in the Dianica dossier for submission of an *in vivo* micronucleus test (or to get access to the FMC study). Data requirement remains for Dianica (refer to point 2.4).
- A data requirement/gap was identified in the FMC dossier for submission of a multigeneration study (or to get access to the Dianica study) (refer to point 2.6).
- A spermatogenesis study was ongoing at the time of experts´ meeting (Dianica). The rapporteur Member State indicated that the study is now available (March, 2006) (Refer to point 2.6).
- A data requirement/gap was identified in the FMC dossier for submission of an *in vitro* or *in vivo* dermal absorption study (or to get access to the Dianica study) (refer to point 2.10).
- A data requirement was identified for Dianica for submission of further metabolism data on the representative uses, since the identity of metabolites was not investigated in the submitted Dianica studies. (relevant for all representative uses evaluated; submission date proposed by the notifier: August 2005; nothing was received by the RMS until February 2006; refer to point 3.1.1).
- A data requirement was identified for Dianica for submission of four residue trials in sunflower for Northern Europe. If residues in these trials should be above LOQ, additional trials would be required for Northern <u>and</u> Southern Europe (relevant for use in sunflower; no submission date proposed by the notifier; refer to point 3.1.1).
- A data requirement was identified for Dianica for submission of additional residue trials on sugar beet for Northern Europe (relevant for use in sugar beet; submission date proposed by the notifier: end of 2006; refer to point 3.1.1). A decision whether additional residue trials are required for FMC for Southern Europe could not be concluded on the basis of the data presented in the DAR.
- Sufficient storage stability data to support the residue trials are necessary for FMC.
- A data requirement was identified for Dianica for submission of additional residue trials in maize in particular for Southern Europe (relevant for use in maize; submission date proposed by the notifier: end of 2006; refer to point 3.1.1).
- A data requirement was identified for FMC for submission of at least four residue trials in maize with a lower LOQ than 0.1 mg/kg. (relevant for use in maize; no submission date proposed by the notifier; refer to point 3.1.1).
- A data requirement was identified in the dossier of both applicants for submission of data addressing residues of carbofuran in succeeding crops. (relevant for all representative uses

evaluated; joint position paper submitted in June 2005; neither evaluated by RMS nor peer reviewed; refer to point 3.1.2).

- A data gap was identified in the FMC dossier for further degradation data in soil under dark aerobic conditions due to the limited range of soil properties covered by the studies submitted (relevant for FMC dossier; submission date proposed by the notifier: no submission date provided; refer to point 4.1.2).
- Rate of degradation in soil should be estimated for the metabolites 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol to complete the FOCUS-GW calculations required (relevant for all representative uses evaluated; submission date proposed by the notifier: Dianica informed in the evaluation table that would summit these data by July 2005 FMC: position paper on carbofuran 7-phenol presented in June 2005, neither evaluated nor peer reviewed ; refer to point 4.1.2).
- Batch adsorption / desorption studies on carbofuran soil metabolites (3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol) may be necessary to complete the FOCUS-GW calculations required (relevant for all representative uses evaluated; submission date proposed by the notifier: Dianica informed in the evaluation table that would summit these data by July 2005; FMC: no date of submission proposed; refer to point 4.1.3).
- Applicants to submit new or available lysimeter studies (relevant for all representative uses evaluated; position paper or studies already submitted by the applicants: FMC in June 2005 and Dianica in July 2005; studies neither evaluated nor peer reviewed; refer to point 4.1.3).
- The rapporteur Member State required in the DAR a new water/sediment study or additional information on 7-phenol metabolite and on the degradation rate of carbofuran for applicant FMC. EFSA does not consider this data requirement essential to finalize the EU risk assessment (relevant for FMC uses, position paper provided by FMC in June 2005 neither evaluated by the rapporteur Member State nor peer reviewed; refer to point 4.2.1).
- $PEC_{SW/SED}$ following FOCUS-SW for carbofuran and metabolites (relevant for all representative uses evaluated; submission date proposed by the notifier: FMC already provided new calculations in June 2005; Dianica informed that would provide new calculations in July 2005; refer to point 4.2.1).
- New FOCUS GW modelling with appropriate input parameters for carbofuran and metabolites 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol (relevant for all representative uses evaluated; submission date proposed by the notifier: no submission date provided (in letter to EFSA FMC informed that new FOCUS groundwater calculations have been submitted, however it is unlikely these calculations reflect the outcome of the meeting of MS experts, the rapporteur Member State confirmed the receipt of FOCUS GW calculations in June 2005 before the experts meeting; neither evaluated nor peer reviewed; refer to point 4.2.2).
- The risk to birds from uptake of granules, treated seedlings and contaminated earthworms needs to be addressed. (relevant for all representative uses; data requirement identified in the DAR; FMC submitted a new risk assessment for birds including studies on possible bird kills and the risk of secondary poisoning of birds of prey; no submission date proposed by Dianica; a new risk assessment was submitted by Arysta for Diafuran 5G; refer to point 5.1).

- A long-term (reproduction) study with birds. (relevant for all representative uses; data gap identified at the EPCO expert's meeting on ecotoxicology in September 2005; data gap open for Dianica and FMC; refer to point 5.1).
- The risk to mammals from ingestion of granules, treated seedlings and contaminated earthworms needs to be addressed (relevant for all representative uses; data requirement identified in the DAR; FMC submitted a new risk assessment for mammals in June/July 2006; Dianica submitted new information in August 2005; refer to point 5.1).
- A fish juvenile growth study (relevant for all uses; data requirement identified in the DAR; new study submitted by Dianica in June 2005; refer to point 5.2).
- A study with sediment dwelling organisms. (relevant for all representative uses; data gap identified in the EPCO experts` meeting on ecotoxicology in September 2005; data gap relevant for all representative uses, no submission date proposed by the applicants; refer to point 5.2).
- A refined risk assessment for aquatic organisms (relevant for all uses; data requirement identified in the DAR; a new risk assessment was submitted by FMC in June 2005, no submission date proposed by Dianica; refer to point 5.2).
- A study on the oral toxicity of carbofuran to bees (relevant for the uses in sunflower and maize; data requirement identified in the DAR; submitted by FMC in June 2005, submitted by Dianica in August 2005; refer to point 5.3).
- A risk assessment for bees (relevant for the uses in sunflower and maize; data requirement identified in the DAR; submitted by FMC in July 2005; submitted by Dianica in August 2005; refer to point 5.3).
- The risk to non-target arthropods including soil dwelling macro-organisms needs to be addressed (relevant for all representative uses; data requirement for non-target arthropods identified in the DAR and confirmed by the EPCO experts` meeting on ecotoxicology in September 2005, the need for studies with soil dwelling macro-organisms was identified in the experts´ meeting; further data were submitted by FMC and Dianca in June, July and August 2005; refer to point 5.4).
- Earthworm field study (relevant for all representative uses; data requirement identified in the DAR; position paper has been submitted by FMC, Dianica proposed to submit a position paper in July 2005, however nothing was received by the rapporteur Member State until February 2006; refer to point 5.5).
- A soil respiration and nitrification study (relevant for all representative uses, data requirement identified in the DAR for Dianica; the study was submitted in June 2006; refer to point 5.7).
- The risk to other non-target organisms needs to be addressed (relevant for all representative uses, data requirement identified in the DAR; FMC submitted a position paper in July 2005; a position paper was submitted by Dianica in August 2005; refer to point 5.8).
- The risk to soil dwelling organisms from the metabolite 3-keto-carbofuran needs to be addressed (relevant for all representative uses; data gap identified by EFSA; no submission date proposed; refer to the table of metabolites).
- The ecotoxicological and pesticidal activity of 3-keto-carbofuran and 3-OH-carbofuran in ground water needs to be addressed depending on the outcome of the fate assessment (relevant

for all representative uses; data gap identified by EFSA; no submission date proposed; refer to tables of metabolites).

- The pesticidal activity of carbofuran-7-phenol needs to be addressed depending on the outcome of the fate assessment (relevant for all representative uses; data gap identified by EFSA; no submission date proposed; refer to tables of metabolites).

## CONCLUSIONS AND RECOMMENDATIONS

**Overall conclusions**

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide as proposed by the applicant which comprises incorporation into soil (at drilling) to control soil insects where maize, sugar beet or sunflowers will be grew 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 formulated products for the evaluation were Furadan 5G, a granule (GR) and Diafuran 5G, a micrcogranule (MG). Both are registered in some Member States of the EU.

Adequate methods are available to monitor all compounds given in the respective residue definition for food of plant origin, soil and water.

Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least limited 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 or 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 acetyl cholinesterase. 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.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. Furthermore, 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. **The classification of Reproduction Toxic Category 3, R62**, is proposed.

The human study (1976) was not considered as scientifically valid. The metabolites 3-OH-carbofuran and 3-keto carbofuran are toxic ($LD_{50}$ of 8 and 107 mg/kg bw, respectively), the hydroxy metabolite is genotoxic as well (Ames test).

The dermal absorption value for the granular formulations, Diafuran 5G or Furadan 5G, is 10% based on the *in vitro* study supported by results from the open literature and that it could be considered as a conservative approach. The acceptable daily intake (ADI) and acceptable operator exposure level (AOEL) is 0.001 mg/kg bw/day and the acute reference dose is 0.001 mg/kg bw with the safety factor of 100 applied should be regarded as provisional due to the concerns in relation to possible reproduction effects.

Thus, the estimated exposure should also be considered as provisional. However, if the AOEL is confirmed, the estimated operator exposure according to the US PHED is below the AOEL i.e. 53% if PPE and respiratory protective equipment (RPE) is worn and assuming a maximum work rate of 10 ha/day, see table below. Worker exposure is unlikely to occur, as the formulation is incorporated mechanical means into the soil when sowing. The granular formulation is applied by ground-directed equipment that is nearly dusted free; therefore, the level of bystander exposure to vapour or airborne particles at the time of application is likely to be negligible.

**EFSA note:** At the time of finalisation of this conclusion, at the EFSA Evaluation meeting in June 2006, it was noted that the new study on spermatogenesis in rats had been provided to the rapporteur and also to ECB for consideration as part of the classification process (March, 2006).

EFSA confirmed that the study has been considered within the ECB process. In March 2006, the ECB classification meeting proposed that no classification for reproduction was required. EFSA understands from ECB that this conclusion was reached taking into account the results of the new study, which did not confirm the testicular and spermatotoxicity effects in rats reported in published papers. Thus, this position, reached within the ECB process, would support a confirmation of the reference values i.e. ADI, ARfD and AOEL that was provisionally agreed at EPCO 33 (Mammalian toxicology experts´ meeting), and a conclusion that no additional safety factor would be required. However it should be noted that the classification proposal has not been formally adopted by a vote within the ECB process nor have the results of the study been considered or peer reviewed within the risk assessment process under Directive 91/414/EEC.

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 were considered applicable to address carbofuran metabolism in plants. Based on all submitted data the metabolic pathway of carbofuran in soil applied uses can be considered as sufficiently investigated. Carbofuran and 3-OH-carbofuran were considered the relevant residues to assess consumer exposure and consumer risk. However, a need to address residues in succeeding crops - resulting from the use of carbofuran - was identified.

Based on the currently proposed residue definition, supervised residue trials in sugar beet, maize and sunflower seed indicated that residues were low and mostly below the respective LOQ.

In livestock animals, carbofuran undergoes an extensive metabolisation. No significant total residues are expected to occur in edible animal matrices taking into account the residue situation for the representative use indicated by the data currently available.
Consumer risk was assessed for carbofuran and 3-OH-carbofuran in the DAR but the assessment was not updated and not agreed on during the peer review process. Based on the initial assessment the estimated chronic dietary intake of carbofuran and 3-OH-carbofuran is expected to be below the ADI provisionally agreed by EPCO 33. A slight exceedance of the ARfD noted for toddlers consuming maize in the available estimates is primarily caused by the limited sensitivity of the analytical methods applied in the residue trials.

On basis of the available laboratory degradation experiments, carbofuran may be from low to high persistent in soil under aerobic conditions ($DT_{50\ lab\ 20\ °C}$ = 9.5- 444 d). In one of the experiments the metabolite 3-keto-carbofuran exceed the 10 % AR. Carbofuran-7-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 (Dianica: Van Noorloos, B., Slangen, P.J., 2002a; Van Noorloos, B., Slangen, P.J., 2002b) and carbosulfan (FMC: Clay, 1980; Markle, 1981a; Taylor, 1983; Baumann and Ferreira, 2001and Baumann, 2002), where carbofuran appears as metabolite. Additionally, EFSA notes that some of these studies were considered not acceptable in the DAR of carbosulfan and that neither in the DAR of carbosulfan nor in the DAR or carbofuran the degradation parameters obtained from these studies for carbofuran is provided. Therefore, at this stage the end points from these studies cannot be included in the list of end points.
Only carbofuran-7-phenol was identified as major metabolite in the validated anaerobic study (max. 62.9 % % AR after 28 d). In this anaerobic study carbofuran is low persistent ($DT_{50\ anaerobic\ 20\ °C}$ = 7.6 d).
In the field studies performed with parent carbofuran in USA (FMC) metabolites 3-OH-carborfuran, 3-keto carbofuran and carbofuran-7-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-7-phenol is not found above the LOD in any of the trials.
Summaries of some field studies performed with carbosulfan (EU, reported in the carbosulfan DAR) as parent compound were provided by one applicant (FMC, Mol, 2002 and Taylor and Houseman, 1982). 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 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 carbosulfan field studies performed in EU were used by the rapporteur Member State in the risk assessment of carbofuran. The meeting of the experts was not able to

determine the reliability of these studies. A position paper from the applicants is available (June 2005) but has not been assessed and peer reviewed. Also the meeting of experts agreed that it is necessary to determine whether the studies from the USA sites are acceptable for the EU risk assessment.

Based on the available information, carbofuran was considered stable to photolysis in soil.
No information on the degradation rate of metabolites is available in the DAR. Rate of degradation in soil should be estimated for the metabolites 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol to complete the FOCUS-GW calculations required.

PEC soil presented in the DAR are based on the worst case EU field half life ($DT_{50}$ = 71.9 d) determined for carbofuran in the carbosulfan field studies. Evaluation meeting agreed that the appropriateness of using this value need to be discussed by the experts meeting. The meeting of experts was not able to conclude on this due to the lack of relevant information for the field studies in the DAR. An addendum from the rapporteur Member State assessing the position paper of the applicants and providing further details on the field studies is still awaited. In case dissipation half life of 71.9 d is found to be inappropriate, $PEC_S$ will need to be recalculated.

Carbofuran may be classified as very high mobile compound ($K_{oc}$ = 17 – 28 mL / g). A data gap for further batch adsorption / desorption studies on carbofuran soil metabolites are necessary to complete the FOCUS-GW calculations.
An aged column leaching study shows that carbofuran and its metabolites (3-keto-carbofuran and carbofuran-7-phenol) are mobile and may leach under the conditions of the experiments.
No lysimeter studies were available for carbofuran in the original dossier. The rapporteur Member State proposed in the DAR a data requirement for a lysimeter study. After the first evaluation meeting (June 2005), one of the applicants (FMC) presented two lysimeter studies. These studies have not been assessed and peer reviewed.
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 and 0.1 d at pH 9. Transformation product carbofuran-7-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 first order half life of approximately 41 d. Transformation products 3-OH-carbofuran and 3-keto-carbofuran were found both in the water and the sediment phase at low levels (< 0.3 % AR). Mineralization was low ($CO_2$ = 1.81 % AR at the end of the study) and bound residue reached a maximum of level of 32.8 % AR. In the neutral or alkaline systems carbofuran dissipated from the water phase with half lives of 5.3-6.9 d and degraded in the whole system with half lives of 7.8 – 11.6 d. The only major metabolite found in the water phase was carbofuran-7-phenol (max. 12.0 % AR after 4 d). Only carbofuran reached levels

above 10 % AR in the sediment. Some metabolite fractions (max. 5.9 % AR) 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.
The two applicants proposed different approaches to estimate the potential contamination of surface water. None of these approaches follows 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 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.
Available FOCUS GW modelling shows that trigger of 0.1 μg / L was exceeded for four of the eight maize relevant scenarios, four of the nine sugar beet scenarios and one of the two relevant sunflower scenarios. However, this calculation does not take into account the data from the other applicant which shows that carbofuran may be significantly more persistent in soil. In the case of sugar beet and sunflower the product was assumed to be applied only every three or two years respectively, this limitation is not indicated in the table of representative uses proposed by the applicants. Therefore, new calculations are needed taking into consideration all available data on this active substance.
The meeting of the experts identified a new data gap for new 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.
Carbofuran is not expected to be prone to long range transport through the air compartment.
An addendum to the fate and behaviour chapter has been provided the 18th of 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 are not adequately referenced. Therefore studies submitted by the applicant after the DAR was submitted are considered neither evaluated nor peer-reviewed in this conclusion.

Substantial data requirements to address the risk to birds and mammals from uptake of granules, ingestion of treated seedlings and contaminated earthworms were identified in the DAR by the rapporteur Member State. The aquatic risk assessment based on PECsw from drainage resulted in a high acute and chronic risk to aquatic invertebrates. New studies and a refined risk assessment were submitted. The risk to bees for the use in sugar beets is considered to be low because no exposure is expected. Exposure of bees via pollen and nectar is possible for the use in maize and sunflowers. A risk to bees cannot be excluded for the representative uses in maize and sunflowers on the basis of the peer reviewed data. Further studies on the oral toxicity to bees were submitted The risk to non-target arthropods was not sufficiently addressed. The experts´ meeting on ecotoxicology confirmed the data requirement and identified also the need for studies with soil dwelling non-target macro organisms. A high long-term risk to earthworms cannot be excluded from the peer reviewed data. New information was submitted by the applicants. The risk to soil non-target micro-organisms was considered to be low on the basis of data submitted by FMC. A data requirement was set for the applicants to address the risk to other non-target organisms. The risk to biological methods of sewage treatment was assessed as low. An addendum to the chapter on ecotoxicology has been provided on the $18^{th}$ of May

2006. When reported, the information in the addendum has been summarized too briefly to draw any conclusion on its reliability.

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

- Appropriate PPE as well as RPE (respiratory protective equipment) is considered in order to have an estimated operator exposure below the provisional AOEL (treated area 10 ha/day, 75$^{th}$ percentile considered), refer to 2.2, 2.6 and 2.12.

## Critical areas of concern

- Highly toxic via oral and inhalatory route, toxic metabolites (3-OH-carbofuran and 3-keto-carbofuran)
- The reference values are provisional due to testicular effects at low doses not completely clarified (study on spematogenesis was ongoing at the time of experts´ meeting). At the time of finalisation of this conclusion, at the EFSA Evaluation meeting in June 2006, it was noted that the new study on spermatogenesis in rats had been provided to the rapporteur and also to ECB for consideration as part of the classification process (March, 2006). EFSA confirmed that the study has been considered within the ECB process. In March 2006, the ECB classification meeting proposed that no classification for reproduction was required. EFSA understands from ECB that this conclusion was reached taking into account the results of the new study, which did not confirm the testicular and spermatotoxicity effects in rats reported in published papers. Thus, this position, reached within the ECB process, would support a confirmation of the reference values i.e. ADI, ARfD and AOEL that was provisionally agreed at EPCO 33 (Mammalian toxicology experts´ meeting), and a conclusion that no additional safety factor would be required. However it should be noted that the classification proposal has not been formally adopted by a vote within the ECB process nor have the results of the study been considered or peer reviewed within the risk assessment process under Directive 91/414/EEC.
- As the AOEL is provisional, pending vote at ECB, the risk assessment for operators is also considered as provisional. Estimated exposure (according to PHED model) based on the provisional AOEL is below the AOEL (53%) only if PPE and RPE is considered.
- No agreed consumer risk assessment available (no updated consumer risk assessment after EPCO 34, provisional toxicological reference values)
- According provisional results there is a potential for groundwater contamination by carbofuran. FOCUS modelling needs to be performed according the representative uses (in particular every year application for sugar beet and sunflower) and employing the adequate input parameters. Potential ground water contamination by carbofuran metabolites (3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol) needs to be addressed.
- Substantial data requirement were identified in the DAR and during the Peer Review for the fate and behaviour section.
- Substantial data requirements were identified in the DAR for almost all groups of organisms in the section on ecotoxicology. The risk was assessed as low for biological methods of sewage

treatment. For all other groups of organisms it was not possible to exclude a high risk on the basis of the peer reviewed data except for bees in sugar beet. The applicants submitted new studies and information to address the data requirements. A final conclusion on the risk to the environment can only be drawn after the evaluation of the new data. An addendum to the chapter on ecotoxicology has been provided on the 18th of May 2006. When reported, the information in the addendum has been summarized too briefly to draw any conclusion on its reliability

# APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

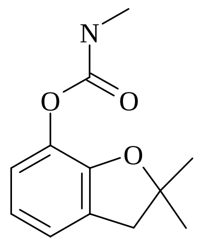
(Abbreviations used in this list are explained in appendix 2)

## Appendix 1.1: 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 | -- |

**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) | *Dianica*: 960 g/kg<br><br>*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 |
| Structural formula ‡ |  |

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

**Physical-chemical properties** (Annex IIA, point 2)

| | |
|---|---|
| Melting point (state purity) ‡ | *Dianica*: melting point 153.1 °C (98.2%)<br><br>*FMC*: melting range 151.2 – 153.7 °C (99.3%) |
| Boiling point (state purity) ‡ | *Dianica*: boiling with partial decomposition at 276 °C (98.2%)<br><br>*FMC*: boiling at 254.1 °C (no decomposition) (99.6%) |
| Temperature of decomposition | *Dianica*: boiling with partial decomposition at 276°C (98.2%)<br><br>*FMC*: boiling at 254.1 °C (no decomposition) (99.6%) |
| Appearance (state purity) ‡ | *Dianica*: white crystalline solid, odourless (purified a.s.)<br><br>*FMC*: off-white powder, aromatic acid-like odour (99.3%) |
| Relative density (state purity) ‡ | *Dianica*: $D_4^{20}$ = 1.228 (98.2%)<br><br>*FMC*: $D_4^{22}$ = 1.290 (99.3%) |
| Surface tension | *Dianica*: 48.9 mN/m at 20.3 °C (90% saturated solution)<br><br>*FMC*: 54.7 mN/m at 20 °C (90% saturated solution) |
| Vapour pressure (in Pa, state temperature) ‡ | *Dianica*: $2.25 \times 10^{-4}$ Pa at 20°C<br><br>*FMC*: $8 \times 10^{-5}$ Pa at 25 °C |
| Henry's law constant (Pa $m^3$ $mol^{-1}$) ‡ | *Dianica*: $1.58 \times 10^{-4}$ $Pa.m^3.mol^{-1}$ at 20 °C<br><br>*FMC*: $5 \times 10^{-5}$ $Pa.m^3.mol^{-1}$ at 25 °C |
| Solubility in water ‡ (g/l or mg/l, state temperature) | *Dianica*: 315 mg/L at 19.5 ± 2.0 °C, no effect of pH<br><br>*FMC*: 322 mg/L at 20.0 ± 0.5 °C, no effect of pH |

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

| | |
|---|---|
| Solubility in organic solvents ‡ (in g/l or mg/l, state temperature) | Dianica:<br>solubility at 20 °C (g/L)<br>n-heptane 0.1<br>xylene 7.8<br>1,2-dichloroethane 106.5<br>methanol 71.0<br>acetone 107.0<br>ethyl acetate 66.9 |
| | FMC:<br>solubility at 20 °C (g/L)<br>n-heptane 0.13<br>xylene 8.0<br>1,2-dichloroethane 91.0<br>methanol 72.8<br>acetone 103.4<br>ethyl acetate 56.1 |
| Partition co-efficient (log POW) ‡ (state pH and temperature) | *Dianica*: 1.8 at 20 °C, no effect of pH<br><br>*FMC*: 1.62 at 22 °C, no effect of pH |
| Hydrolytic stability ($DT_{50}$) ‡ (state pH and temperature) | *Dianica*:<br>pH 4: hydrolytically stable<br>pH 7, 25 °C: $DT_{50}$ = 45.7 d<br>pH 9, 25 °C: $DT_{50}$ = 0.1 d<br><br>*FMC:*<br>pH 7, 25 °C: $DT_{50}$ = 28 d<br>pH 7.5, 25 °C: $DT_{50}$ = 9.1 d<br>pH 8, 25°C: $DT_{50}$ = 2.7 d |
| Dissociation constant ‡ | *Dianica:* no pKa in environmentally relevant pH range<br><br>*FMC*: no pKa in environmentally relevant pH range |
| UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength) | *Dianica*:<br>in neutral methanol:<br>$\lambda_{max}$ 276 nm; ε = 2.80 x $10^3$ $L.mol^{-1}.cm^{-1}$<br>at λ 290 nm : ε = 2.51 x $10^2$ $L.mol^{-1}.cm^{-1}$<br>in acidic methanol:<br>no significant difference in spectrum<br>in alkaline methanol:<br>spectrum differs from that in neutral/acidic conditions ($\lambda_{max}$ 243 and 291 nm) due to |

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

| | |
|---|---|
| | Carbofuran degradation<br><br>*FMC:*<br>in neutral methanol:<br>$\lambda_{max}$ 277 nm; $\varepsilon = 3.28 \times 10^3$ L.mol$^{-1}$.cm$^{-1}$<br>at $\lambda$ 290 nm : $\varepsilon = 500$ L.mol$^{-1}$.cm$^{-1}$<br>in acidic methanol:<br>no significant difference in spectrum<br>in alkaline methanol:<br>spectrum differs from that in neutral/acidic conditions ($\lambda_{max}$ 245 and 292 nm) due to decomposition |
| Photostability ($DT_{50}$) ‡ (aqueous, sunlight, state pH) | *Dianica:*<br>pH 5, 22 °C: $DT_{50} = 33$ d (under Suntest conditions)<br><br>*FMC:*<br>min. $DT_{50} > 126$ d for summertime at latitude 30°, 40° and 50° (calculated assuming $\phi = 1$) |
| Quantum yield of direct phototransformation in water at $\lambda > 290$ nm ‡ | *Dianica*: $\phi$: 0.0015<br><br>*FMC*: direct photolysis is considered to be an insignificant process; no further testing is required |
| Flammability ‡ | *Dianica*: not highly flammable; not auto-flammable<br><br>*FMC*: not highly flammable; not auto-flammable |
| Explosive properties ‡ | *Dianica*: no explosive properties<br><br>*FMC*: no explosive properties |

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

**Summary of uses supported by available data (carbofuran)***

| Crop and/or situation | Member State or Country | Product name | F G or I | Pests or Group of pests controlled | Formulation | | Application | | | | Application rate per treatment | | | PHI (days) | Remarks: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Type | Conc. of a.s. | method kind | growth stage & season | num-ber min max | interval between applications (min) | kg as/hl min max | water l/ha min max | kg as/ha min max | | |
| (a) | | | (b) | (c) | (d-f) | (i) | (f-h) | (j) | (k) | | | | | (l) | (m) |
| Maize ZEAMX | EU | FURADAN 5G - FMC | F | ***Elateridae spp.*** *Scutigerella spp.* *Atomaria linearis* *Aphis spp.* *Blaniulus spp.* *Oscinella frit* *Phyllocnistis spp.* | G | 50 g/kg | Mechanical incorporati on into soil | At drilling | 1 | na | na | na | 0.6 | PHI: not appli-cable as applied at drilling | Granule dropped into seed furrow. Soil then folder over to cover. **[1]** |
| 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 incorporati on into soil | At drilling | 1 | na | na | na | 0.6 | PHI: not appli-cable as applied at drilling | Granule dropped into seed furrow. Soil then folded over to cover. **[1]** |

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

| Crop and/or situation | Member State or Country | Product name | F G or I | Pests or Group of pests controlled | Formulation | | Application | | | | Application rate per treatment | | | PHI (days) | Remarks: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (a) | | | (b) | (c) | Type (d-f) | Conc. of a.s. (i) | method kind (f-h) | growth stage & season (j) | num-ber min max (k) | interval between applications (min) | kg as/hl min max | water l/ha min max | kg as/ha min max | (l) | (m) |
| Maize ZEAMX | EU | DIAFURAN 5G DIANICA | F | *Blaniulus guttulatus* *Atomaria linearis* *Pegomyia betae* *Aphis* *Scutigerella immaculata* *Agriotes spp.* | G | 50 g/kg | Mechanical incorporation into soil | At drilling | 1 | na | na | na | 0.6 | PHI: not appli-cable as applied at drilling | Granule dropped into seed furrow. Soil then folder over to cover. **[1]** |
| Sugar Beet BEAVA | EU | DIAFURAN 5G DIANICA | F | *Oscinella* and *Geomyza* *Scutigerella immaculata* *Agriotes spp.* | G | 50 g/kg | mechanical incorporation into soil | At drilling | 1 | na | na | na | 0.6 | PHI: not appli-cable as applied at drilling | Granule dropped into seed furrow. Soil then folded over to cover. **[1]** |
| Sunflower HELAN | EU | DIAFURAN 5G DIANICA | | *Agriotes spp.* | G | 50 g/kg | mechanical incorporation into soil | At drilling | 1 | na | na | na | 0.6 | PHI: not appli-cable as applied at drilling | Granule dropped into seed furrow. Soil then folded over to cover. **[1]** |

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

[1] The risk assessment has revealed a risk and/or data gap(s) in section 4 and 5.

| | | | | |
|---|---|---|---|---|
| **Remarks:** | * | Uses for which risk assessment could not been concluded due to lack of essential data are marked grey | (h) | Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated |
| | (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) | (i) | g/kg or g/L |
| | (b) | Outdoor or field use (F), glasshouse application (G) or indoor application (I) | (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 |
| | (c) | *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds | | |
| | (d) | *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) | (k) | The minimum and maximum number of application possible under practical conditions of use must be provided |
| | (e) | GCPF Codes - GIFAP Technical Monograph No 2, 1989 | | |
| | (f) | Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench | (l) | PHI - minimum pre-harvest interval |
| | (g) | All abbreviations used must be explained | (m) | Remarks may include: Extent of use/economic importance/restrictions |

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

## Appendix 1.2: Methods of Analysis

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

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

**Analytical methods for residues** (Annex IIA, point 4.2)

| | |
|---|---|
| Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) | *Dianica:*<br>GC-NPD (carbofuran) and HPLC-MSD (3-hydroxy carbofuran); LOQ = 0.01 mg/kg (maize, sunflower, sugarbeet)<br><br>*FMC:*<br>GC-MSD (carbofuran, 3-hydroxy carbofuran); LOQ = 0.05 mg/kg (for each analyte, dry crops, commodities with high fat content)<br>GC-NPD (carbofuran, 3-hydroxy carbofuran); LOQ = 0.05 mg/kg (for each analyte, commodities with high water content, fruits with high acid content)<br>HPLC-PCD with Flu (carbofuran, 3-hydroxy carbofuran);<br>LOQ = 0.05 mg/kg (for each analyte, commodities with high water content) → confirmatory purposes<br><br>*Additional ILV data for 3-hydroxy-carbofuran required* |
| Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) | Not required (not necessary to define residue or propose MRL's) |

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

| | |
|---|---|
| Soil (principle of method and LOQ) | *Dianica:*<br>LC-MS/MS (carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol); LOQ = 0.01 mg/kg<br>(for each analyte)<br>*FMC:*<br>HPLC-PCD with Flu (carbofuran) and GC-MS (dibutylamine); LOQ = 0.005 mg/kg<br>GC-MS (Carbofuran) and HPLC-Flu (dibutylamine); LOQ = 0.007 mg/kg (Carbofuran), 0.01 mg/kg (dibutylamine) |
| Water (principle of method and LOQ) | *Dianica:*<br>HPLC-MS (carbofuran, 3-hydroxy carbofuran, carbofuran-phenol); LOQ = 0.1 µg/L (for each analyte, drinking water, groundwater, surface water)<br>LC-MS/MS (carbofuran, carbofuran-7-phenol); LOQ = 0.1 µg/L (for each analyte, surface water)<br><br>*FMC:*<br>HPLC-PCD with Flu (carbofuran, 3-hydroxy carbofuran); LOQ = 0.1 µg/L (drinking water, surface water)<br>GC-MS (carbofuran); LOQ = 0.05 µg/L (for each analyte, surface water)<br><br>*Depending on the final residue definition for groundwater, additional methodology may be required* |
| Air (principle of method and LOQ) | Not required (the application techniques, i.e. granular formulation to be incorporated in soil) are such that no relevant exposure is likely to occur) |
| Body fluids and tissues (principle of method and LOQ) | *Dianica:*<br>LC-MS/MS (Carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol); LOQ = 50 µg/L (blood, urine), 0.01 mg/kg (tissues)<br>LC-MS/MS (Carbofuran) ; LOQ = 50 µg/L (fluids), 0.1 mg/kg (tissues)<br><br>*FMC:*<br>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 |

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

## Appendix 1.3: 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<br>Hydrolysis of carbamate bond into $CO_2$ |
| Toxicologically significant compounds ‡ (animals, plants and 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 - 2000 mg/kg bw | **Xn; R21** |
| Rat $LC_{50}$ inhalation ‡ | 0.05 mg/L | **$T^+$; R26** |
| Skin irritation ‡ | Non- irritant | |
| Eye irritation ‡ | Non- irritant, but mortality reported (rabbits) | **T; R39/41** |
| Skin sensitization ‡ (test method used and result) | Non- sensitizer (Buehler and M&K) | |

**Short term toxicity** (Annex IIA, point 5.3)

| | |
|---|---|
| Target / critical effect ‡ | Testicular degeneration, clinical signs of neurotoxicity related to AChE inhibition (rat and dogs) |
| Lowest relevant oral NOAEL / NOEL ‡ | 0.1 mg/kg bw/day, 1-year dog<br>and 60 day, rat (published study) |
| Lowest relevant dermal NOAEL / NOEL ‡ | 25 mg/kg bw/day, 21 day rabbit |
| Lowest relevant inhalation NOAEL / NOEL ‡ | No study available |

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

**Genotoxicity** ‡ (Annex IIA, point 5.4)

| | |
|---|---|
| ...................................................................... | Positive results in bacterial tests;<br>Negative in *in vivo* tests |

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

| | |
|---|---|
| Target/critical effect ‡ | Body weight and AChE inhibition |
| Lowest relevant NOAEL / NOEL ‡ | 0.462 mg/kg bw/day, 2 year rat |
| Carcinogenicity ‡ | No carcinogenic potential |

**Reproductive toxicity** (Annex IIA, point 5.6)

| | |
|---|---|
| Reproduction target / critical effect ‡ | Reduced litter parameters in rat multigeneration study<br>Testicular and sperm toxicity (published study, rat) **R62?** |
| Lowest relevant reproductive NOAEL / NOEL ‡ | Parental and reproduction: 1.2 mg/kg bw/day |
| Developmental target / critical effect ‡ | Fetotoxicity and developmental neurotoxicity at maternal toxic doses (rat). |
| Lowest relevant developmental NOAEL / NOEL ‡ | <u>Rat:</u><br>Developmental: 1 mg/kg bw/day<br>Maternal: 0.1 mg/kg bw/day<br><br><u>Rabbit:</u><br>Developmental and maternal: 0.5 mg/kg bw/day |

**Neurotoxicity / Delayed neurotoxicity ‡** (Annex IIA, point 5.7)

| | |
|---|---|
| Delayed neurotoxicity | No delayed neuropathy in hens<br>NOAEL neurotoxicity 0.5 mg/kg bw |
| Subchronic neurotoxicity test | 3.2 mg/kg bw/day, 13-week rat |

**Other toxicological studies ‡** (Annex IIA, point 5.8)

| | |
|---|---|
| Mechanistic study | AChE inhibition: no difference in sensitivity to AChE inhibition with age. |

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

| | |
|---|---|
| Studies on metabolites | 3-OH-carbofuran:<br>$LD_{50}$ oral: 8.3 mg/kg bw **T+, R28**<br>Positive in Ames test strain TA1537 with S9 mix<br>Positive in TK locus in L5178Y mouse lymphoma cells with and w/o S9 mix<br>3-OH-7-phenol:<br>$LD_{50}$ oral: 1654 mg/kg bw **Xn, R22**<br>3 keto-carbofuran:<br>$LD_{50}$ oral: 107 mg/kg bw **T , R25**<br>3-keto-7-phenol:<br>$LD_{50}$ oral: > 800 mg/kg bw **Xn, R22**<br>carbofuran 7-phenol:<br>$LD_{50}$ oral: 1743 mg/kg bw **Xn, R22**<br>negative in Ames test |

**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[1] ‡ | 0.001 mg/kg bw/d | 1-year dog study | 100 |
| AOEL[1] ‡ | 0.001 mg/kg bw/d | 1-year dog study | 100 |
| ARfD[1] ‡ (acute reference dose) | 0.001 mg/kg bw/d | Developmental rat study, maternal toxicity | 100 |

**Dermal absorption** (Annex IIIA, point 7.3)

| | |
|---|---|
| Diafuran 5G and Furadan 5G | 10% based on an *in vitro* study (Dianica) supported by results from the open literature. |

[1] Values and SF are provisional, might be confirmed pending vote of ECB (see 2.6 of the main body).

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

**Acceptable exposure scenarios (including method of calculation)**

| | |
|---|---|
| Operator<br>***Should be considered as provisional until the AOEL is confirmed.*** | Estimated exposures (% of the provisional AOEL) are performed with the PHED model. The maximum application rate is 0.6 kg/ha, work rate 10 ha/day and body weight 60 kg.<br><br>**PPE (gloves)** **PPE+RPE**<br>75th percentile **240%** **53%** |
| Workers | formulation is incorporated into soil by mechanical means during sowing: no exposure |
| Bystanders | formulation is applied by ground directed equipment that is nearly dustfree: no exposure |

**Classification and proposed labelling** (Annex IIA, point 10)

| | | |
|---|---|---|
| with regard to toxicological data | T+; | Very toxic |
| | R21 | Harmful in contact with skin |
| | R26 | Very toxic by inhalation |
| | R28 | Very toxic if swallowed |
| | R39 | Danger of very serious irreversible effects |
| | R41 | Risk of serious damage to eyes |
| | R62? | Possible risk of impaired fertility |
| | | Note: ECB's proposal not to classify for R62 is still to be voted |

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

## Appendix 1.4: Residues

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

| | |
|---|---|
| Plant groups covered | ***FMC***<br>maize (C), potatoes (R), soybeans (P/O) (soil applied carbofuran)<br>Sugar beet (R), rice(C) (soil applied carbosulfan)<br>***DIANICA***<br>Soybean and mungbean (P/O) (soil applied carbofuran),<br>Cabbage (L) (soil applied benfuracarb) |
| Rotational crops | Not submitted, however, the metabolism and behaviour of carbofuran following absorption by the plants via root uptake is known from primary metabolism studies |
| Plant residue definition for monitoring | Carbofuran (Sum of carbofuran and 3–OH-carbofuran expressed as carbofuran). |
| Plant residue definition for risk assessment | Carbofuran (Sum of carbofuran and 3–OH-carbofuran expressed as carbofuran). |
| Conversion factor (monitoring to risk assessment) | None. |

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

| | |
|---|---|
| Animals covered | **FMC**<br>Lactating goats and laying hens (carbofuran)<br>**DIANICA**<br>Laying hens (carbofuran),<br>Lactating goats (benfuracarb) |
| Animal residue definition for monitoring | not peer reviewed and agreed proposal available,<br>EPCO 34 provisional proposal 3-OH-carbofuran |
| Animal residue definition for risk assessment | not peer reviewed and agreed proposal available,<br>EPCO 34 provisional proposal 3-OH-carbofuran |
| Conversion factor (monitoring to risk assessment) | Not applicable. |
| Metabolism in rat and ruminant similar (yes/no) | Yes. |
| Fat soluble residue: (yes/no) | No. |

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

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

| | |
|---|---|
| ...................................................................... | Still to be addressed |

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

| | |
|---|---|
| ...................................................................... | ***FMC***[13]<br>Plant products:<br>No data available on the stability of carbofuran and 3-OH-carbofuran.<br>The carbosulfan content decreased significantly (more than 30 %) within 21 months for green alfalfa, 2 weeks for cabbage, 3 months for corn foliage and 6 months for potatoes.<br>Animal products:<br>No data available on the stability of carbofuran and 3-OH-carbofuran.<br>Residues of carbosulfan and its metabolites couldn't be considered as stable in milk, muscle and liver probably because of the presence of hydrolytic enzymes.<br><br>***DIANICA***<br>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. |

[13] Carbosulfan storage stability to support trials and studies with carbosulfan in the carbofuran dossier

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

***FMC***

| Intakes by livestock ≥ 0.1 mg/kg diet/day: | Ruminant: Yes | Poultry: Yes [14] | Pig: Yes [15] |
|---|---|---|---|
| Muscle | <0.05 | - | - |
| Liver | <0.05 | - | - |
| Kidney | <0.05 | - | - |
| Fat | <0.05 | - | - |
| Milk | <0.025 | - | - |
| Eggs | - | - | - |

***DIANICA***

| Intakes by livestock ≥ 0.1 mg/kg diet/day: | Ruminant: Yes [16] | Poultry: no | Pig: Yes [17] |
|---|---|---|---|
| Muscle | - | - | - |
| Liver | - | - | - |
| Kidney | - | - | - |
| Fat | - | - | - |
| Milk | - | - | - |
| Eggs | - | - | - |

[14] Feeding study not required as the metabolism study in laying hens demonstrated that no significant residues (<0.01 mg/kg) could occur in the eggs and in the edible tissues taking into account the residue levels in potential feedingstuffs obtained at the 1 x dose rate.

[15] 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.

[16] No feeding study was provided and was not required even if significant residues (0.1 mg/kg total diet) occurred in the crops fed to animals (see table B.7.8-1-Volume 3). The metabolism study in lactating goats demonstrated that no significant residues (<0.01 mg/kg) could occur in milk and in edible animal tissues taking into account the residue levels in potential feedingstuffs obtained at the 1 x dose rate.

[17] 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.

**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** | **Provisional MRLs (mg/kg)** | **STMR (mg/kg) (b)** |
|---|---|---|---|---|---|
| **FMC** | | | | | |
| Sugar beet | NE | ***Carbosulfan***<br>**root:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 11 x <0.1, 0.112 mg/kg<br>**Leaves:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 12 x <0.1 mg/kg<br>***Carbofuran***<br>**root:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 5 x <0.1 mg/kg<br>**Leaves:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 5 x <0.1 mg/kg | Samples of leaves/tops and roots at different PHIs up to normal harvest time were analysed for carbosulfan and its metabolites carbofuran and 3-OH-carbofuran. Decay curves are given with last sampling 129 to 173 days after the application.<br>Trials performed in accordance with the critical GAP. | 0.1* | 0.1* |
| | SE | ***Carbosulfan***<br>**root:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 4 x <0.1 mg/kg<br>**Leaves:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 4 x <0.1 mg/kg | | | |

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

| Crop | Northern or Southern Europe | Trials results relevant to the critical GAP (a) | Recommendation/comments | Provisional MRLs (mg/kg) | STMR (mg/kg) (b) |
|---|---|---|---|---|---|
| | | ***Carbofuran***<br>**root:<br>*-carbofuran + 3-OH-carbofuran expressed as carbofuran*: <0.1 mg/kg<br>**Leaves:<br>-carbofuran + 3-OH-carbofuran expressed as carbofuran: <0.1 mg/kg | | | |
| Maize | NE | ***Carbosulfan***<br>**grain:<br>*-carbofuran + 3-OH-carbofuran expressed as carbofuran*: 2 x <0.1 mg/kg<br><br>***Carbofuran***<br>**grain:<br>*-carbofuran + 3-OH-carbofuran expressed as carbofuran*: 5 x <0.1 mg/kg | Samples of plants with cobs (BBCH 18-85) at different PHI's up to normal harvest time and maize grains were analysed for carbosulfan, carbofuran and 3-OH-carbofuran. Decay curves are given with last sampling 160 to 193 days after the application.<br>Trials performed in accordance with the critical GAP. | 0.1* | 0.1* |
| | SE | **Carbosulfan**<br>**grain:<br>-carbofuran + 3-OH-carbofuran expressed as carbofuran equiv: 2 x <0.1 mg/kg<br><br>**Carbofuran** | | 0.1* | 0.1* |

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

| Crop | Northern or Southern Europe | Trials results relevant to the critical GAP (a) | Recommendation/comments | Provisional MRLs (mg/kg) | STMR (mg/kg) (b) |
|---|---|---|---|---|---|
| | | **grain:<br>Application rate: 1.020 and 1.683 kg a.s./ha respectively<br>Results:<br>*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 3 x <0.1 mg/kg | | | |
| ***DIANICA*** | | | | | |
| Sugar beet | NE | **root:<br>*-carbofuran + 3-OH-carbofuran expressed as carbofuran*: <0.02 mg/kg<br>** Top and leaves:<br>*-carbofuran + 3-OH-carbofuran expressed as carbofuran*: <0.02 mg/kg | Trials performed in accordance with the critical GAP. | 0.02* | 0.02* |
| | SE | **root:<br>*-carbofuran + 3-OH-carbofuran expressed as carbofuran*: 4 x <0.02 mg/kg<br>** Top and leaves:<br>*-carbofuran + 3-OH-carbofuran expressed as carbofuran*: 3 x <0.02, 0.034 mg/kg | | | |
| Maize | NE | **grain:<br>*-carbofuran + 3-OH-carbofuran expressed as carbofuran*: 4 x <0.02 mg/kg<br>**Silage:<br>*-carbofuran + 3-OH-carbofuran expressed as* | Trials performed in accordance with the critical GAP. | 0.02* | 0.02* |

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

| Crop | Northern or Southern Europe | Trials results relevant to the critical GAP (a) | Recommendation/comments | Provisional MRLs (mg/kg) | STMR (mg/kg) (b) |
|---|---|---|---|---|---|
| | | *carbofuran*: 3 x <0.02, 0.029 mg/kg | | | |
| | SE | **grain:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 1 x <0.02 mg/kg<br>**Silage:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 0.026 mg/kg | | | |
| Sunflower | NE | The trials are not acceptable | | - | - |
| | SE | **seed:<br>-*carbofuran + 3-OH-carbofuran expressed as carbofuran*: 4 x <0.02 mg/kg | Trials performed in accordance with the critical GAP. | 0.02* | 0.02* |

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

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

**Consumer risk assessment[18] (Annex IIA, point 6.9, Annex IIIA, point 8.8)**

| | |
|---|---|
| ADI | 0.001mg/kg bw/day |
| TMDI (European Diet) (% ADI) | ***FMC***<br>-2.83 % (WHO European diet)<br>-2.29 % (German model)<br>-18.4 % and 38.1 % respectively for children and infants from UK. (Pesticides Safety Directorate Consumer Exposure Model).<br>***DIANICA***<br>-0.85 % (WHO European diet)<br>-0.72 % (German model)<br>-6.4 % and 10.8 % respectively for children and infants from UK. (Pesticides Safety Directorate Consumer Exposure Model). |
| NEDI (% ADI) | - |
| Factors included in NEDI | - |
| ARfD | 0.001 mg/kg bw/day |
| Acute exposure (% ARfD) *)[19] | ***FMC***<br>-Sugar beet: 26.6 % and 81.4 % of ARfD for UK adults and toddlers resp.<br>-Maize grain: 37 % and 102 % of ARfD for UK adults and toddlers resp.<br>***DIANICA***<br>-Sugar beet: 5.33 % and 16.2 % of ARfD for UK adults and toddlers resp.<br>-Maize grain: 7.38 % and 20.41 % of ARfD for UK adults and toddlers resp.<br>-Sunflower seed:5.5 % and 3.28 % of ARfD for UK adults and toddlers resp.<br>-Sunflower seed oil:1.74 % and 5.1 % of ARfD for UK adults and toddlers resp. |

*

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

| Crop/processed crop | Number of studies | Transfer factor | % Transference * |
|---|---|---|---|
| Not required | | | |

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

[18] indicative assessment only, needs to be revised upon receipt of further toxicology and residue data
[19] Need for updated calculation was identified in the expert meeting. New figures submitted by RMS, but without details of calculations. As the results are not comprehensible, they have not been included in the table.

**Proposed MRLs[20] (Annex IIA, point 6.7, Annex IIIA, point 8.6)**

FMC

Expression of the residue: Carbofuran (Carbofuran + 3-OH carbofuran expressed as carbofuran equivalents).

| | |
|---|---|
| Sugar beet | 0.1* |
| Maize | 0.1* |

*) LOQ

DIANICA

Expression of the residue: Carbofuran (Carbofuran + 3-OH carbofuran expressed as carbofuran equivalents).

| | |
|---|---|
| Sugar beet | 0.02* |
| Maize | 0.02* |
| Sunflower seed | 0.02* |

*) LOQ

[20] provisional due to incomplete data base

## Appendix 1.5: 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 d, [$^{14}$C- phenyl ring ]-label, 20°C (n= 4) (Dianica)<br><br>0.7-14.6% after 112-122 d, [$^{14}$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) (Dianica)<br><br>7.7-94% after 112- 89 d, [$^{14}$C- phenyl ring ]-label, 25°C (n = 4) (FMC) |
| Relevant metabolites - name and/or code, % of applied ‡ (range and maximum) | 3-keto Carbofuran: max level of 12.41% at days 181-365, 1 soil, pH 5.7, 25 ºC (FMC)<br>3-OH-carbofuran, max level of 1.32 % AR at day 122 (FMC)<br>carbofuran-7-phenol: max level of 9 % AR at day 184, end of the study (FMC) |

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

| | |
|---|---|
| Anaerobic degradation ‡ | [14C- phenyl ring ]-label, 20°C (Dianica)<br>Mineralisation 2.4-6.1 % after 120 d<br>Non-extractable residues 56.4-62.7% after 120 d<br>Major metabolite: 7-phenol, max level of 62.9 % at 28 d<br>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, 20°C, Xenon lamp (Dianica)<br>No photodegradation observed<br><br>[14C- phenyl ring ]-label, 25°C, natural light (FMC)<br>Half-live corrected for reactions such as hydrolysis is 87.5 d (winter time) and 30.1 d (summer time) |

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

| | |
|---|---|
| Method of calculation | First order (Dianica)<br>First order (FMC) |

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

| | |
|---|---|
| Laboratory studies ‡ (range or median, with n value, with $r^2$ value) | ($DT_{50}$carbofuran (study performed with carbofuran): 15.1, 9.5, 15.8, 19.4 d)<br>($DT_{50}$carbofuran (study performed with benfuracarb): 6.1d, 15 d, 7.6 d, 15 d)<br>**Note: benfuracarb study is not summarized in the carbofuran DAR.**<br><br>$DT_{50lab}$ (normalized to 20°C, pF2.0, aerobic): 175 d ($r^2$ = 0.92), 381d ($r^2$ = 0.98) and 444 d ($r^2$ not reported) ~~4.4-444~~ d, (based on studies with carbofuran as parent - FMC, only values from acceptable studies)<br><br>**Note: carbosulfan studies are not fully summarized neither in the in the carbofuran nor in the carbosulfan DAR.**<br><br>**Overall geometric mean:** 29.28 d |
| | $DT_{90lab}$ (20°C, aerobic): 14.52-1465 d, (based on two studies that were performed with benfuracarb and carbofuran as test substance, some values significantly beyond the duration of the study) |
| | $DT_{50lab}$ (10°C, aerobic): 110 days, 1 soil, $r^2$ = 0.9993 (Dianica) |
| | $DT_{50lab}$ (20°C, anaerobic): 7.6 days, 1 soil, $r^2$ = 0.99318 (Dianica) |
| | Degradation in the saturated zone: not required |
| Field studies ‡ (state location, range or median with n value) | $DT_{50f}$: carbofuran, Netherlands, Spain, Italy, UK, bare soil, 1.3 d -71.9 d (n= 6, $r^2$ =0.88-0.997) 1st order (Field studies were carbosulfan was applied as parent and carbofuran appears as metabolite, FMC)<br>$DT_{50f}$: carbofuran, USA, 5.0 – 121 d (Field studies with carbofuran as parent. Only studies assessed as acceptable and representative of EU conditions by the RMS).<br>**Overall geometric mean:** 20.75 d (no normalization possible with the available data in the summary of the studies). |

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

| | |
|---|---|
| | $DT_{90f}$: carbofuran, Netherlands, Spain, Italy, UK, bare soil, 4.4-237.3 (extrapolated) d ( n= 6, $r^2$ =0.880-0.997) 1st order (Field studies were carbosulfan was applied as parent and carbofuran appears as metabolite, FMC)<br>$DT_{90f}$: carbofuran, USA, 16.5 – 399 d (Field studies with carbofuran as parent. Only studies assessed as acceptable and representative of EU conditions by the RMS). |
| Soil accumulation and plateau concentration ‡ | No soil accumulation studies available. |

**Soil adsorption/desorption** (Annex IIA, point 7.1.2)

| | |
|---|---|
| $K_f$ /$K_{oc}$ ‡<br>$K_d$ ‡<br>pH dependence ‡ (yes / no) (if yes type of dependence) | Koc carbofuran: 17-28 mL/g , (mean 22, $^1/_n$= 0.92-1.01, 4 soils)<br>Kd carbofuran: 0.299-0.549 (mean 0.432, n = 4)<br>No pH dependence (Dianica) |

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

| | |
|---|---|
| Column leaching ‡ | Not required |
| Aged residues leaching ‡ | SETAC (FMC)<br>Aged for (d): 30 d<br>Time period (d): 1.5 d<br>Precipitation (mm): 500 mm<br>Leachate: 33.2-78.2 % total residues/radioactivity in leachate<br>95-98% of the leachate radioactivity is the active substance; 2-5% of the leachate radioactivity is 3-keto-carbofuran and carbofuran-7-phenol.<br>13.7-49.2 % total residues/radioactivity retained in top 5 cm |
| Lysimeter/ field leaching studies ‡ | *Two lysimeter studies have been provided (FMC, June 2005, not evaluated)* |

**PEC (soil)** (Annex IIIA, point 9.1.3)

**Appropriateness of half life assumed is pending confirmation. Values maintained for illustrative purposes.**

**Parent**

| | |
|---|---|
| Method of calculation | $DT_{50}$ (carbofuran): 71.9 days<br><br>Kinetics: 1st order<br>worst case field $DT_{50}$ (worst case FMC study) |

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

| | |
|---|---|
| Application rate | Crop: maize, sugar beet, sunflower<br>0% plant interception: granular application in the sowing bed, soil layer: 5 cm, soil density:1.5 kg/dm$^3$<br>Number of applications: 1<br>Application rate(s): 600 g/ha |

| **PEC**$_{(s)}$ (mg/kg) | Single application Actual | Single application Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|
| Initial | 0.800 | 0.800 | | |
| Short term 24h | 0.792 | 0.796 | | |
| 2d | 0.785 | 0.792 | | |
| 4d | 0.770 | 0.785 | | |
| Long term 7d | 0.748 | 0.774 | | |
| 28d | 0.611 | 0.701 | | |
| 50d | 0.494 | 0.635 | | |
| 100d | 0.305 | 0.513 | | |

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

| | |
|---|---|
| Hydrolysis of active substance and relevant metabolites ($DT_{50}$) ‡<br>(state pH and temperature) | pH 4: hydrolytic stable (FMC, Dianica)<br>pH 7, 25 °C: $DT_{50}$ = 28 - 45.7 d (1$^{st}$ order) (Dianica, FMC)<br>carbofuran-7-phenol: 55.6 % AR (51 d)<br>pH 9, 25°C: $DT_{50}$ = 0.1 d (1$^{st}$ order) (Dianica)<br>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<br>No major metabolite<br>Estimated $DT_{50}$ at 50°N: 108 days (Dianica) |
| Readily biodegradable (yes/no) | No (5-7% TOD in 5 days) (Dianica) |
| Degradation in water/sediment<br>- $DT_{50}$ water ‡<br>- $DT_{90}$ water ‡<br>- $DT_{50}$ whole system ‡<br>- $DT_{90}$ whole system ‡ | “Static” anaerobic conditions (FMC)<br>-<br>-<br>189 days (non linear, $r^2$= 0.96, n= 1) (FMC)<br>- |

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

| | |
|---|---|
| Mineralization | 0.2 %AR (at 365 d, study end, n= 1) |
| Non-extractable residues in sediment | 20.4% AR (at 365 d, study end, n= 1) |
| Distribution in water / sediment systems (active substance) ‡ | Maximum of 54.8 %AR in sediment after 31 days. $DT_{50}$ in sediment not available |
| Distribution in water / sediment systems (metabolites) ‡ | Water:<br>7-phenol: max of 5.7% (365 days, n= 1)<br><br>Sediment:<br>7-phenol: max of 48% (365 days, n= 1) |
| Degradation in water/sediment<br>- $DT_{50}$ water ‡<br>- $DT_{90}$ water ‡<br>- $DT_{50}$ whole system ‡<br>- $DT_{90}$ whole system ‡<br>- $DT_{50}$ whole system ‡<br><br>- $DT_{90}$ whole system ‡ | Aerobic conditions (pH water: 6.11; pH sediment 5.3) (FMC)<br><br>40.9 d (1st order, r2=0.74)<br><br>44.6 (recalculated by EFSA) Error 2 test passed: 6.8 %<br>148.3 (recalculated by EFSA) |
| Mineralization | 1.87 % AR after 30 d (study end) |
| Non-extractable residues in sediment | 32.6 % AR after 30 d (study end) |
| Distribution in water / sediment systems (active substance) ‡ | Maximum of 59.1 %AR in sediment after 20 days. |
| Distribution in water / sediment systems (metabolites) ‡ | No major metabolites found under acidic conditions. |
| Degradation in water/sediment<br><br>- $DT_{50}$ water ‡<br>- $DT_{90}$ water ‡<br>- $DT_{50}$ whole system ‡<br>- $DT_{90}$ whole system ‡ | Aerobic conditions (pH water: 7.0-8.2; pH sediment 7.08-7.45) (Dianica)<br>5.3-6.9 days<br>17.5-22.9 days (1st order, r2= 0.9355-0.9827, n= 2)<br>7.8-11.6 days<br>25.9-38.5 days (1st order, r2= 0.9379-0.9943, n= 2) |
| Mineralization | 7.7-19.6 % AR (at 102 d, study end, n= 2) |
| Non-extractable residues in sediment | 74.3-78.4% AR (at 102 d, study end, n= 2) |
| Distribution in water / sediment systems (active substance) ‡ | Maximum of 10.7-15.8 %AR in sediment after 4-14 days. $DT_{50}$ in sediment 10.7-12.9 days ($DT_{90}$ 35.4-42.8 days, 1st order, r2= 0.9155-0.9906, n= 2) |

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

| | |
|---|---|
| Distribution in water / sediment systems (metabolites) ‡ | Water:<br>Carbofuran-phenol or 7-phenol: max of 10.4-12.0 % (1-4 days, n= 2 [$DT_{50}$ 4.8-7.3 days, 1st order, $r^2$= 0.8104-0.9921, n= 2]<br><br>Sediment:<br>Carbofuran-phenol or 7-phenol: max of 2.9-4.9% (7 days, n= 2). |

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

*The PEC surface water should be revised considering the FOCUS SW recommendations.*

**PEC (sediment)**

*The PEC sediment should be revised considering the FOCUS SW recommendations.*

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

*Calculation shown below were presented by one applicant (Dianica) and maintained for illustrative purposes. Input parameters selected do not reflect all the available information on the active substance.*
*Potential groundwater contamination by the carbofuran metabolites 3-OH-carbofuran (minor metabolite containing the toxosphore carbamate) and major soil metabolites carbofuran-7-phenol and 3-keto-carbofuran need to be addressed.*

| | |
|---|---|
| Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter ) | FOCUS gw scenarios, according to FOCUS guidance.<br>Model(s) used: FOCUS-PELMO (Dianica)<br>Scenarios:<br>Chateaudun, Hamburg, Jokionen, Kremsmünter,Okehampton, Piacenza, Porto , Seville,Thiva<br>Crop: maize, sugar beet, sunflower<br><br>Koc: 18.4 g/ml (22 g/ml should be used)<br>$DT_{50}$: 15 days (20.35 d to be used taking into account all available data) |
| Application rate | Application rate:<br>600 g carbofuran/ha, 1 application, 5 cm soil incorporation<br>maize (application every year)<br>sugar beet (application every 3 years) (in principle application every year is possible according the representative uses GAP table). |

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

| | |
|---|---|
| | sunflower (application every 2 years) (in principle application every year is possible according the representative uses GAP table).<br>No. of applications: 1 (incorporation at planting)<br>Time of application: spring and summer |

**PEC**$_{(gw)}$

| | |
|---|---|
| Maximum concentration | Not provided, not required. |
| Average annual concentration<br>(Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance) | Annual average concentrations (80th percentile) according to FOCUS guidance:<br>carbofuran:<br>0.000 to 0.438 µg/L (more favourable scenarios in Southern Europe)<br><br>(see detailed results in table below) |

| Location | Maize – Percolate concentration carbofuran<br>80th percentile (µg/L) | Sugar beet – Percolate concentration carbofuran<br>80th percentile (µg/L) | sunflower – Percolate concentration carbofuran<br>80th percentile (µg/L) |
|---|---|---|---|
| Chateaudun | 0.033 | 0.115 | Not relevant |
| Hamburg | 0.483 | 0.109 | Not relevant |
| Jokionen | Not relevant | 0.092 | Not relevant |
| Kremsmünster | 0.109 | 0.077 | Not relevant |
| Okehampton | 0.437 | 0.224 | 0.300 |
| Piacenza | 0.350 | 0.331 | Not relevant |
| Porto | 0.000 | 0.001 | Not relevant |
| Seville | 0.000 | 0.016 | 0.000 |
| Thiva | 0.003 | 0.000 | Not relevant |

**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<br>from soil: not required |

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

**PEC (air)**

| | |
|---|---|
| Method of calculation | Not required |

**$PEC_{(a)}$**

| | |
|---|---|
| Maximum concentration | Not required |

**Definition of the Residue** (Annex IIA, point 7.3)

| | |
|---|---|
| Relevant to the environment | **Soil**<br>Definitions for risk assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol.<br>Definitions for monitoring: carbofuran, 3-keto-carbofuran (included pending the finalization of the risk to soil dwelling organisms).<br><br>**Water**<br><br>Ground water<br>Definitions for exposure assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol.<br>Definitions for monitoring: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol (all metabolites are included pending the finalization of the ground water assessment).<br><br>Surface water<br>Definitions for risk assessment: carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol.<br>Definitions for monitoring: carbofuran, 3-keto-carbofuran (included pending the finalization of the surface water assessment).<br><br>**Air**<br>Definitions for risk assessment: carbofuran<br>Definitions for monitoring: carbofuran |

**Monitoring data, if available** (Annex IIA, point 7.4)

| | |
|---|---|
| Soil (indicate location and type of study) | Not available |

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

| | |
|---|---|
| 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) | Monitoring of carbofuran after a field spray application – not relevant for the proposed uses |

**Classification and proposed labelling** (Annex IIA, point 10)

| | |
|---|---|
| with regard to fate and behaviour data | Candidate for<br>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

## Appendix 1.6: Effects on non-target Species

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

| | |
|---|---|
| Acute toxicity to mammals ‡ | $LD_{50}$ (rat) = 5.3 – 5.6 mg a.s./kg b.w. |
| Reproductive toxicity to mammals ‡ | NOAEL (rat) = 0.1 mg a.s./kg b.w./day |
| Acute toxicity to birds ‡ | $LD_{50}$ (*Anas platyrhynchos*, male) = 0.71 mg a.s./kg b.w. |
| Dietary toxicity to birds ‡ | $LC_{50}$ (*Anas platyrhynchos*) = 1.6 mg a.s./kg b.w./day |
| Reproductive toxicity to birds ‡ | No agreed endpoint |

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

| Application rate (kg as/ha) | Crop | Category (*e.g.* insectivorous bird) | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|---|---|
| Not relevant | | | | | |

**$LD_{50}$ and $LC_{50}$ expressed in number of granules for different sizes of birds**

| Time scale | Number of granules for a 15 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 $LD_{50}$ | 0.58 | 2 | 8 | 19 |
| Dietary $LC_{50}$ | 1.3 | 4 | 17 | 43 |

**Calculation of TER's for small birds considering residues of crbofuran in drinking water**

| | |
|---|---|
| Time scale | TER for a 15 g bird |
| Acute exposure | 79 |
| Short term exposure | 178 |

**$LD_{50}$ and NOAEL expressed in number of granules for different sizes of mammals**

| Time scale | Number of granules for a 10 g mammal | Number of granules for a 25 g mammal | Number of granules for a 100 g mammal |
|---|---|---|---|
| Acute oral $LD_{50}$ | 3 | 7 | 29 |
| Developmental rat study Maternal toxicity NOAEL | 0.05 | 0.14 | 0.54 |

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

**Calculation of TER's for small mammals considering residues of Carbofuran in drinking water**

| Time scale | TER for a 10 g mammal |
|---|---|
| Acute exposure | 869 |
| Short term exposure | 16 |

**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 | Endpoint | Toxicity (mg/L) |
|---|---|---|---|---|
| Laboratory tests ‡ | | | | |
| ‡ *Lepomis macrochirus* | Carbofuran | 96 h semi-static | $LC_{50}$ | 0.18 mg a.s./L |
| ‡ *Daphnia magna* | Carbofuran | 48 h static | $EC_{50}$ | 0.0094 mg a.s./L |
| ‡ *Gammarus fasciatus* | Carbofuran | 96 h static | $LC_{50}$ | 0.0028 mg a.s./L |
| ‡ *Selenastrum capricornutum* | Carbofuran | 72 h static | $E_bC_{50}$<br>$E_rC_{50}$ | 6.5 mg a.s./L<br>19 mg a.s./L |
| ‡ *Cyprinodon variegatus* | Carbofuran | 35 d fish early life stage | NOEL | 0.006 mg a.s./L |
| ‡ *Daphnia magna* | Carbofuran | 21 d semi-static | NOEC | 0.008 mg a.s./L |
| ‡ *Ceriodaphnia dubia* | Carbofuran | 7 d semi-static | NOEC | 0.00016 mg a.s./L |

| Microcosm or mesocosm tests |
|---|
| Not available |

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

| Application rate (kg as/ha) | Crop | Organism | Time-scale | Distance (m) | TER | Annex VI Trigger |
|---|---|---|---|---|---|---|
| 0.6 kg a.s./ha | maize, sugarbeet, sunflowers | *Lepomis macrochirus* | acute | - | 1200 | 100 |
| | | *Daphnia magna* | acute | - | 63 | 100 |
| | | *Gammarus fasciatus* | acute | - | 19 | 100 |
| | | *Selenastrum capricornutum* | acute | - | 43333 | 10 |
| | | *Cyprinodon variegatus* | chronic | - | 40 | 10 |
| | | *Daphnia magna* | chronic | - | 53 | 10 |
| | | *Ceriodaphnia dubia* | chronic | - | 1 | 10 |

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

**Bioconcentration**

| | |
|---|---|
| Bioconcentration factor (BCF) ‡ | 3.8 (fillet); 22 (viscera); 12 (whole fish) |
| Annex VI Trigger:for the bioconcentration factor | 100 |
| Clearance time ($CT_{50}$)<br>($CT_{90}$) | 0.5 days<br>– |
| Level of residues (%) in organisms after the 14 day depuration phase | < 5 % (whole fish) |

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

| | |
|---|---|
| Acute oral toxicity ‡ | No data. |
| Acute contact toxicity ‡ | $LD_{50}$ (48 h) = 0.0357 µg a.s./bee |

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

| Application rate (kg as/ha) | Crop | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|---|
| Laboratory tests | | | | |
| 0.6 kg a.s./ha | maize, sugarbeet, sunflowers | contact | Not applicable | Not applicable |

| Field or semi-field tests |
|---|
| Not available |

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

| Species | Stage | Test Substance | Dose | Endpoint | Effect | Annex VI Trigger |
|---|---|---|---|---|---|---|
| Laboratory tests ‡ | | | | | | |
| ‡ *Poecilus cupreus* | adults | Diafuran 5 G | 12 kg/ha | Mortality | 20 % | 30 % |
| ‡ *Aleochara bilineata* | adult female beetles | Diafuran 5 G | 12 kg/ha | Mortality | 100 % | 30 % |
| ‡ *Aleochara bilineata* | adult beetles | Diafuran 5 G | 12 kg/ha | Mortality<br>Reduction in parasitism rate | 4.5 %<br>60.4 % | 30% |

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

| Species | Stage | Test Substance | Dose | Endpoint | Effect | Annex VI Trigger |
|---|---|---|---|---|---|---|
| ‡ *Pardosa sp.* | adults and sub-adults | Diafuran 5 G | 12 kg/ha | Mortality | 100 % | 30 % |
| ‡ *Pardosa sp.* | adults and sub-adults | Diafuran 5 G | 12 kg/ha | Mortality<br>Reduction in food consumption | 13.3 %<br>-5.2 % | 30 % |
| Extended laboratory tests | | | | | | |
| ‡ *Typhlodromus pyri* | protonymphs | Carbofuran | 1.8 – 18 g a.s./ha | $LD_{50}$ | 3.65 g a.s./ha | 50 % |
| ‡ *Aphidius rhopalosiphi* | adults | Carbofuran | 1 – 32 g a.s./ha | $LD_{50}$ | 2.68 g a.s./ha | 50 % |
| ‡ *Aleochara bilineata* | adults | Furadan 5 G | 1 – 10 kg/ha | $LD_{50}$ | 3.58 kg/ha | 50 % |
| ‡ *Pardosa sp.* | adults and subladults | Furadan 5 G | 3.2 – 32 kg/ha | $LD_{50}$ | 2.7 kg/ha | 50 % |

| Field or semi-field tests |
|---|
| Not available |

**Effects on earthworms** (Annex IIA, point 8.4, Annex IIIA, point 10.6)

| | |
|---|---|
| Acute toxicity ‡ | $LC_{50}$ = 4487 mg Diafuran 5 G/kg dry soil<br>$LC_{50}$ > 1000 mg Furadan 5 G/kg dry soil |
| Reproductive toxicity ‡ | NOEC < 16.8 mg Diafuran 5 G/kg dry soil |

**Toxicity/exposure ratios for earthworms (**Annex IIIA, point 10.6)

| Application rate (kg as/ha) | Crop | Time-scale | TER | Annex VI Trigger |
|---|---|---|---|---|
| 0.6 kg a.s./ha | maize, sugarbeet, sunflowers | acute | 280 | 10 |
| | | acute | 62.5 | 10 |
| | | long term | < 1.05 | 5 |

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

**Effects on soil micro-organisms** (Annex IIA, point 8.5, Annex IIIA, point 10.7)

| | |
|---|---|
| Nitrogen mineralization ‡ | No adverse effects of Furadan 5 G at 0.8 (PEC) and 4 (5 x PEC) mg Carbofuran/kg soil after 28 days |
| Carbon mineralization ‡ | No adverse effects of Furadan 5 G at 0.8 (PEC) and 4 (5 x PEC) mg Carbofuran/kg soil after 28 days |

**Classification and proposed labelling** (Annex IIA, point 10)

| | | |
|---|---|---|
| with regard to ecotoxicological data | N, | Dangerous for the environment |
| | R50 / R53 | Very toxic to aquatic organisms / may cause long-term adverse effects in the aquatic environment |

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

## APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

| | |
|---|---|
| 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) |
| GS | growth stage |
| h | hour(s) |
| ha | hectare |
| hL | hectolitre |
| HPLC | high pressure liquid chromatography<br>or high performance liquid chromatography |
| ISO | International Organisation for Standardisation |
| IUPAC | International Union of Pure and Applied Chemistry |
| $K_{oc}$ | 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 |
| PHI | pre-harvest interval |
| $pK_a$ | negative logarithm (to the base 10) of the dissociation constant |
| PPE | personal protective equipment |
| ppm | parts per million ($10^{-6}$) |
| ppp | plant protection product |
| $r^2$ | coefficient of determination |
| RPE | respiratory protective equipment |
| STMR | supervised trials median residue |
| TER | toxicity exposure ratio |
| TMDI | theoretical maximum daily intake |
| UV | ultraviolet |
| WHO | World Health Organisation |
| WG | water dispersible granule |
| yr | year |