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

benfuracarb

finalised: 28 July 2006

SUMMARY

Benfuracarb 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 benfuracarb in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 2 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 sole applicant Otsuka Chemical Co., Ltd. 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 7 March 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 (pre-plantation) to control soil and foliar insects, where brassica will be grown. Benfuracarb can be used as insecticide and nematicide. It should be noted that during the peer review process only the use as insecticide was evaluated.
The representative formulated product for the evaluation was "Oncol 8.6G", a granule (GR), registered in France and Spain.

[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 and surface 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.

Benfuracarb is rapidly and nearly completed absorbed reaching in the rat. The main metabolite of benfuracarb is carbofuran (approximately 30%). The acute inhalatory toxicity is high, whereas the oral toxicity moderate. The toxicity via dermal route was low. It is neither a skin nor an eye irritant nor a skin sensitizer, proposed risk phrases are: T, R23 "Toxic by inhalation" and R22 "Harmful if swallowed" The critical effects are cholinesterase inhibition. Effects on reproduction parameters were observed such as, decreased male fertility, number of live pups and pup weight was decreased, even the entire second generation was lost The appropriate classification for reproduction toxicity could not be agreed and the question should be forwarded to ECB, R62 is high lighted. ECB has concluded R62 but not voted.
The main metabolite of benfuracarb is the active ingredient carbofuran which is more toxic than benfuracarb. The relevant impurity 1,2 dichloroethane, is classified as toxic, Carcinogenic Category 2 (T; R45).
The Acceptable Daily Intake (ADI) and the Acceptable Operator Exposure Level (AOEL) is 0.01 mg/kg bw/day, safety factor 100. The Acute Reference Dose (ARfD) is 0.02 mg/kg bw/day, safety factor 100**.**
The default value of 100% was agreed on for the granular formulation Oncol 8.6 G as no studies were provided. The estimated operator exposure according to the US PHED model is below (86%) the AOEL only if personal protective equipment as well as respiratory equipment is used.

The metabolism, distribution and residue behaviour of benfuracarb was investigated in various crops with different methods of application and at different timings. Based on studies involving a foliar treatment or stem injection a metabolic pathway of benfuracarb in directly treated plants could be established. Currently, benfuracarb, carbofuran and 3-OH-carbofuran were considered the relevant residues to assess consumer exposure and consumer risk. Whether this will be fully applicable to all crops and regardless the mode of application still needs to be confirmed by further data, since the available data on soil applied uses didn't sufficiently identify potentially relevant metabolites for the supported brassica uses. Moreover a need to address residues of carbofuran in succeeding crops following application of benfuracarb was identified.
Based on the currently proposed residue definition, supervised residue trials in cauliflower, broccoli and cabbage indicated that no residues above the respective LOQ are anticipated, however the validity of the results needs to be confirmed by further data. Moreover the residue trial database for brassicas needs to be completed.

With the current knowledge and limited data available and with the provisionally agreed toxicological reference values for carbofuran it is only possible to asses consumer risk preliminary.
Consumer risk has been separately assessed by the rapporteur Member State for benfuracarb residues and for carbofuran and 3-OH-carbofuran residues. The estimated chronic dietary intake of benfuracarb and its metabolites carbofuran and 3-OH-carbofuran was found to be below the ADI of benfuracarb and carbofuran, respectively. A potential acute exposure concern noted for adults and toddlers (up to 370% of carbofuran ARfD) consuming head and flowering brassicas, is primarily caused by the limited sensitivity of the analytical methods applied in the residue trials. In the acute and chronic consumer risk assessment the possible intake of carbofuran through drinking water derived from groundwater was not considered although a significant contribution to the acute and chronic exposure might be expected.

Benfuracarb is rapidly degraded in soil under laboratory dark aerobic conditions yielding carbofuran (maximum 84.6 % AR after 2 d) as major metabolite. This metabolite is low to moderate persistent in soil according the studies presented in the benfuracarb dossier, but may be high persistent according some studies presented by a different applicant in the carbofuran dossier. Relevance of carbofuran data for the assessment of benfuracarb may need further consideration.
Other minor metabolites were detected (maximum sum of them: 34.9 % AR after 0.24 d) that individually did not reached the 10 % AR. Mineralization was high at the end of the study (CO_2 = 27.7 % AR – 66.6 % AR). Amount of unextractable residues reached a maximum = 74.1 % at the end of the study in one of the soils.
Experts meeting agreed that 3-ketocarbofuran and 3-OH-carbofuran (minor carbofuran metabolites containing the carbamate moiety) need to be addressed, as potential benfuracarb soil metabolites, for ground water contamination**.**
The applicant was required to address the degradation of benfuracarb in alkaline soils. A position paper and a new study are available but are still neither evaluated nor peer reviewed.
No soil photolysis study has been provided for benfuracarb. Carbofuran is photolytically stable on soil surface, according the data available in carbofuran dossier.
Degradation of carbofuran seems to be very dependent of the temperature. The rapporteur Member State informed that the applicant had submitted a position paper and a new study to address the degradation of carbofuran at low temperatures but these reports have still not been evaluated and peer reviewed.
Worst case laboratory half lives were used to calculate PEC soil of benfuracarb. Data from a different applicant in carbosulfan dossier show that field worst case half life for carbofuran is 71.9 d in EU sites. Therefore, carbofuran PECs soil were calculated by the rapporteur Member State with this half life. According the conclusion for carbofuran, reliability of this value needs to be further assessed and confirmed.
It was estimated, by the HPLC method, that benfuracarb may be classified as immobile in soil (K_{oc} = 9100 mL / g). Carbofuran may be classified as very high mobile compound (K_{oc} = 17 – 28 mL / g). No data is available with respect the adsorption desorption properties of minor relevant soil metabolites 3-OH-carbofuran and 3-keto-carbofuran.

A lysimeter study is available where two different lysimeters are investigated. Benfuracarb was found at maximum amounts of 0.25 µg / L and carbofuran at maximum amounts of 0.16 µg / L. A new lysimeter study was required by the rapporteur Member State in the DAR. The meeting of MS experts agreed that the new FOCUS GW modelling required can substitute the requirement for a new lysimeter at this stage.

Hydrolysis of benfuracarb is pH dependent with half lives between less than half hour (pH 4) and 26.9 d (pH 9). In the natural water experiment (pH ≈ 7-8) photolysis seems not to contribute significantly to the aqueous degradation of benfuracarb. However, irradiation seems to enhance the degradation of the metabolite carbofuran to carbofuran-7-phenol.

Benfuracarb is not readily biodegradable.

A study with two water sediment systems is available. Both systems are in the alkaline range (pH_{water} 7.8-8.4). Main compounds found in the water phase are benfuracarb and carbofuran (maximum = 58.26 % AR after 2d). Main compounds found in the sediment phase are carbofuran (maximum = 25.31 % after 14 d) and carbofuran-7-phenol (maximum = 13.6 %). The cumulative amounts of CO_2 at the end of the study accounted for 13.6 % AR and 16.7 % AR. Most of the radioactivity was present as bounded residue to the sediment by the end of the study (73.8 % AR – 75.9 % AR).

Benfuracarb dissipates rapidly in water phase with a half life between 6 h to 15 h. Main dissipation process is transformation to carbofuran. Carbofuran dissipates from water phase with half life between 8.2 d to 27.2 d. Main dissipation process is partitioning into sediment. Whole system and sediment phase half lives had not been calculated. A report with the estimation of the whole system half life is available but not evaluated and peer reviewed. Also the half life in the sediment for carbofuran and carbofuran-7-phenol needs to be assessed.

In the carbofuran dossier, 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. 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. These experiments seem to indicate that the degradation of carbofuran may be pH dependent in water sediment systems.

PEC_{SW} of carbofuran has been calculated for a limited number of FOCUS sw scenarios. Calculation of PEC_{SW}, for parent benfuracarb and PEC_{SED} for benfuracarb, carbofuran and carbofuran-7-phenol, need to be performed. Updated FOCUS $PEC_{SW / SED}$ are available but have still not been evaluated and peer reviewed.

PEC gw have been calculated for benfuracarb and carbofuran. Annual average 80th percentiles of benfuracarb were < 0.001 µg / L for all calculated scenarios (7 cabbage spring, 5 cabbage summer). Carbofuran exceed the 0.1 µg / L trigger in 4 of the 7 spring scenarios and in three of the five summer scenarios. In one of the summer scenarios (Hamburg) an 80th percentile annual average of 1.212 µg / L was reached. The applicant was required to address the potential for ground water contamination by the metabolite 3-keto carbofuran. New calculations to address potential groundwater contamination by metabolites 3-OH-carbofuran, carbofuran-7-phenol and 3-keto-carbofuran are available but neither evaluated nor peer reviewed. However, it is noted that these calculations do not take into

consideration the longer half lives observed for carbofuran from the data of the second carbofuran applicant.
Concentrations of benfuracarb in the air compartment are expected to be negligible, due to short persistence in the atmosphere.
An addendum to the fate and behaviour chapter has been provided the 18th of May 2006. 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.

Substantial data requirements to address the risk to birds and mammals from uptake of granules, ingestion of treated seedlings and contaminated earthworms were identified by the rapporteur Member State. Further studies were submitted by the applicant. The aquatic risk assessment based on PECsw from drainage resulted in a high acute and chronic risk to fish and aquatic invertebrates in 2 out of 3 scenarios. Based on the peer-reviewed data a high risk to aquatic organisms cannot be excluded. However the new data need to be evaluated before drawing a final conclusion on the risk to aquatic organisms. The risk to bees from exposure to residues in cabbage was assessed as low since cabbage has no flower in the production crop. The potential risk to bees from residues in flowering weeds should be assessed at Member State level taking into account the agricultural practice (management of weeds in cabbage fields). Data requirements were identified in the DAR to address the risk to ground dwelling arthropods, earthworms, soil non-target micro-organisms and other non-target organisms. New data/information was submitted by the applicant. 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.
The risk to biological methods of sewage treatment was assessed as low for the representative use.

Key words: benfuracarb, peer review, risk assessment, pesticide, insecticide, nematicide

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Benfuracarb 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 benfuracarb, hereafter referred to as the draft assessment report, to the EFSA on 2 August 2004. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the draft assessment report was distributed for consultation on 17 August 2004 to the Member States and the main applicant Otsuka Chemical Co., Ltd 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 7 March 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 16 March 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

Benfuracarb is the ISO common name for ethyl *N*-[2,3-dihydro-2-2-dimethylbenzofuran-7-yloxycarbonyl(methyl)aminothio]-*N*-isopropyl-β-alaniate (IUPAC).

Benfuracarb belongs to the class of benzofuranyl methylcarbamate insecticides such as benfuracarb and carbofuran. It belongs also to the class of carbamate nematicides. Benfuracarb is a systemic insecticide with contact and stomach action. In soil application, benfuracarb is absorbed at root level and moves to the aerial parts of plants to control both soil and foliar pests. The biological activity is based on the transformation into carbofuran inside of the pest. Carbofuran inhibits the Acetyl-Choline Esterase (AChE) in the nervous system.

The representative formulated product for the evaluation was "Oncol 8.6G", a granule (GR), registered in France and Spain.

The evaluated representative uses as insecticide as proposed by the applicant comprises incorporation into soil (pre-plantation) to control soil and foliar insects, where brassica will be grew. Benfuracarb can be used as insecticide and nematicide. It should be noted that during the peer review process only the use as insecticide was evaluated.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of benfuracarb as manufactured should not be less than 930 g/kg.
At the moment no FAO specification exists.

The technical material contains 1,2-dichloroethane (classified as toxic), which has to be regarded as relevant impurity. The maximum content in the technical material should not be higher than 4 g/kg.

The content of benfuracarb in the representative formulation is 90 g/kg (pure).

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 benfuracarb or the respective formulation.

However, no information is available that demonstrate that the content of the relevant impurity 1,2-dichloroethane in the technical material is not increasing in the formulation upon storage.

The main data regarding the identity of benfuracarb 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 benfuracarb in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material. No analytical method is available for the determination of the relevant impurity 1,2-dichloroethane in the formulation.
However, enough data are available to ensure that at least limited quality control measurements of the plant protection product are possible.

With respect to the residue analytical methods for enforcement purposes, adequate methods are available to monitor all compounds given in the respective residue definition, i.e. benfuracarb in food of plant origin; carbofuran (sum of carbofuran and 3-OH-carbofuran[3]) in food of plant origin; benfuracarb and carbofuran in surface water.
Also validated methods for the determination of carbofuran, benfuracarb and 3-OH-carbofuran in blood are available.
The residue definitions for soil and ground water are still under discussion. Depending on further discussion 3-keto-carbofuran[4] could be included in the residue definition for soil and 3-keto-

[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

carbofuran and 3-OH-carbofuran in the definition for ground water. It should be noted that a only a method for the determination of 3-keto-carbofuran in soil would be available, but need to be re-evaluated. For water only methods for the determination of benfuracarb and carbofuran are available.
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 benfuracarb is available.

The methodology used is GC with PN- or MS detection and HPLC 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.
An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2).

The discussion in the meeting of experts (EPCO 35, September 2005) on identity, physical and chemical properties and analytical methods was limited to certain residue analytical methods, the identity and determination of impurities and some clarification with respect to certain physical and chemical properties of benfuracarb.

The assessment of the rapporteur Member State whether or not the "minor revision"[5] of the list of representative uses has any impact on the assessment is still outstanding.

2. Mammalian toxicology

Benfuracarb was discussed at the EPCO experts' meeting for mammalian toxicology (EPCO 33) in September, 2005.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Benfuracarb is rapidly and nearly completely absorbed reaching 42-69% of the dose within 24 h increasing to 69-81% of the dose within 144 h.
Benfuracarb is widely distributed and high levels are found in excretory organs and adrenals. No accumulation occurs after repeated oral exposure.
The main metabolite of benfuracarb is carbofuran. Carbofuran is further metabolized to 3-ketofuran-phenol, 3-hydroxycarbofuran, 3-hydroxycarbofuran-7-phenol and carbofuran phenol. Radioactivity in urine consisted of carbofuran hydrolytic derivatives.
Excretion is high, almost 100% within 7 days, 66-76% of the oral administered dose is excreted within 48 h via urine and 10-12% via faeces.

[5] The amendment is: "Apply the granules homogeneously in the furrow at planting with microgranule applicator (localised application in the plant-hole is not allowed)"

2.2 ACUTE TOXICITY

Overall, the toxic responses are typical for of effects on acetyl cholinesterase activity. The acute inhalatory toxicity is high (LC_{50} 0.3 mg/L) whereas the oral toxicity moderate (LD_{50} 205 mg/kg bw). However, the toxicity via dermal route is low (LD_{50} >2000 mg/kg bw). It is neither a skin or an eye irritant nor a skin sensitizer.

Classification for acute toxicity is needed and the proposed risk phrases are: T, R23 "Toxic by inhalation" and R22 "Harmful if swallowed"

2.3 SHORT TERM TOXICITY

The short term effects of benfuracarb were studied in 10 studies in the rat, mouse and dog for 4 weeks up to 2 years; at doses ranging from 0.6 up to 378 mg/kg bw/day as well as one dermal study in rat. No study on inhalation was submitted.

The critical effects are cholinesterase inhibition. Acetyl cholinesterase (AChE) activity was measured in red blood cells and plasma in the majority of the studies whereas the brain AChE activity was not measured in all studies. Mortality was rarely observed. The critical effects apart from clinical signs of neurotoxicity were hematological changes, thymus and spleen involution, enlarged lymph nodes, hypoplasia of prostate, regressive transformation of adrenal cortex. Some of these effects occurred at doses lower or equal to those producing inhibition of AChE. Dog appeared to be the most sensitive species.

<u>The rat</u>

In rats, increased motor activity, tremor, twitches, body temperature decrease and reduced pain sensitivity, atrophic seminal vesicle, hypoplasia of prostate, transformation of adrenal cortex were apparent at 20 mg/kg bw/day but no effects on AChE were noted.

In the 90-day rat studies, rough hair coat and urine stains appeared together with plasma AChE inhibition from 13 mg/kg bw/day. Brain AChE was not inhibited.

A 1-year rat study was performed in which, at 25 mg/kg bw/day body weight was decreased and statistically significant changes in the clinical chemistry were observed in females. The incidence of cysts in ovaries was also enhanced. In this study, plasma AChE was inhibited at all dose levels, but there was no correlation with clinical signs of neurotoxicity. The NOAEL was 200 ppm i.e. 12 mg/kg bw/day.

<u>The mouse</u>

Contradictory results were seen in the mice studies, brain AChE was inhibited in the 49-day study at 111 mg/kg bw/day without clinical signs of neurotoxicity. However, in the 13-week study, where clinical signs of neurotoxicity were seen, brain AChE was not inhibited at the same dose level. These effects were mainly transient and recovery occurred within 24 h. The NOAEL is around 50 mg/kg bw/day.

The dog

Three studies were evaluated and the doses ranged from 0.625 mg/kg bw/day up to 10 mg/kg bw/day. After 90-day exposure, no clinical signs of cholinesterase inhibition were seen and plasma or RBC AChE was not inhibited. In this study, thymus involution was seen at 2.5 mg/kg bw/day, the NOAEL is thus 0.625 mg/kg bw/day. In the 6-month study, Inhibition of AChE in plasma and RBCs was apparent after administration of 5-mg/kg bw/day as well as hind limb ataxia. In the 1-2 year dog study, clinical signs of neurotoxicity as well as inhibition of plasma cholinesterase were observed from 5 mg/kg bw/day while RBCs- and brain AChE were not significantly affected.

The relevant oral NOAEL was discussed at the experts´ meeting and it was agreed to accept the rapporteur Member State proposal for an overall short term NOAEL of 1 mg/kg bw/day based on the dog studies. The NOAEL is based on the 90-day study (0.625 mg/kg bw/day) and the 6-month and 1-2 year study (2.5 mg/kg bw/day).

Dermal study, rat

In the 28-day dermal rat study, clinical signs of toxicity correlated with plasma cholinesterase inhibition at 25-mg/kg bw/day were noted. The NOAEL for systemic toxicity is 5 mg/kg bw/day and the NOAEL local effect is > 125 mg/kg bw/day.

2.4 GENOTOXICITY

In the DAR the genotoxic properties of benfuracarb were studied in five *in vitro* studies (of which two Ames tests) and three *in vivo* studies. The purity was between 93.4% and 98.4% (as well as pure grade).

In vitro tests

Benfuracarb was tested *in vitro* in the *Salmonella typhimurium* test with and without S9 mix, and in mouse lymphoma cells L5178Y for its ability to induce gene mutations. Negative responses were reported in both tests. Furthermore, benfuracarb did not induce chromosomal aberrations in human peripheral lymphocytes.

In vivo tests

Intraperitoneal injection of benfuracarb at doses ranging from 2.5 to 10 mg/kg bw/day did not induce micronuclei in mice bone marrow. Oral administration of benfuracarb did not produce significant increases in the frequency of micronuclei, but experimental deviations makes the results of one of the three studies not suitable for final evaluation. A rat bone marrow chromosome aberration test gave negative results.

The overall conclusion is that there is no mutagenic or genotoxic potential for benfuracarb.

2.5 LONG TERM TOXICITY

Three long term studies were evaluated, two in the rat (2-year) and one in the mouse (18 month). There was no evidence of carcinogenicity of benfuracarb in either rats or mice. These findings are supported by the absence of genotoxic activity for benfuracarb. The NOAEL is 5.5 mg/kg bw/day in the rat based on clinical signs and inhibition of brain acetylcholine esterase activity.

2.6 REPRODUCTIVE TOXICITY

One multigeneration study in the rat in order to determine the reproductive effects of benfuracarb is presented in the DAR (Schroeder, 1984).

The reproductive effects were discussed at the experts´ meeting. At the highest dose level (400 ppm) statistically significant effects on reproduction parameters were observed such as, decreased male fertility, number of live pups and pup weight was decreased, even the entire second generation was lost. The parental toxicity observed at this dose level was not severe, decreased body weight (around 10%) and increased food consumption (around 20%).

These effects were observed at the lower dose level (100 ppm) as well but to a lesser extent and in this case there are no adverse effects on paternal toxicity and the maternal toxicity observed is reduced body weight by less than 10%. Thus, the parental as well as reproductive including embryotoxic NOAEL is 25 ppm i.e. 1.2 mg/kg bw/day. **The appropriate classification for reproduction toxicity was discussed by the experts but no agreement was reached and the question should be forwarded to ECB.**

EFSA note: Thus, Reproduction toxic category 3 **R62? "Possible risk of impaired fertility"** is high lighted in order to increase transparency. Benfuracarb has been discussed at ECB and R62 was concluded in November 2005, but is not yet voted.

The teratogenic or developmental effects of benfuracarb were studied in one study in one rat and one rabbit study (Schroeder, 1983a and b).

In the rat, one dam in the 10 mg/kg bw/day dose level died at day 12 and one dam died at day 9 in the 40 mg/kg bw/day group, no abortions were registered. At these dose levels the body weight was decreased with 18% and 36%, respectively. At the 40 mg/kg bw/day dose, decreased fetal weight, delayed or incomplete ossification was observed in foetuses. The maternal toxicity observed at this dose level was reduced body weight.

The NOAEL for maternal toxicity for the rat is 2 mg/kg bw/day based on reduced body weight and the NOAEL for developmental toxicity is 10 mg/kg bw/day.

In the rabbit, mortality was also observed at the highest dose levels (10 and 15 mg/kg bw/day), 2 and 3 dams, respectively. Maternal body weight was not affected. At 15 mg/kg bw/day, embryotoxicity was evident such as reduced fetal weights; one dam aborted in the 5 and 10 mg/kg bw/day group.

The NOAEL for maternal toxicity in the rabbit is 15 mg/kg bw/day and the developmental NOAEL is 10 mg/kg bw/day.

2.7 NEUROTOXICITY

Delayed neurotoxicity

An acute toxicity was study performed initially in the hen. The oral LD_{50} is 92 mg/kg bw. A delayed neurotoxicity study was performed in the hen using tri ortho cresyl phosphate (TOCP) as positive control. Signs of acute neurotoxicity were seen at 160 mg/kg bw/day for up to 48-120 hours after dosing. Thereafter, the hens showed no signs of residual or delayed toxicity. No delayed neuromuscular impairment was seen. One hen exhibited mild focal axonal swelling at the lumbo-sacral cord; axonal degeneration was seen in the right sciatic nerve. These lesions were not comparable to lesions produced by TOCP, which were more severe, typically bilateral and usually multiple. Benfuracarb does not induce delayed neurotoxicity in hens.

Short term neurotoxicity study

A 28-day neurotoxicity study was performed in rats. Toxic signs related to inhibition of AChE were observed. There were no treatment related histopathological findings in the nervous system. The NOAEL is 25 ppm i.e. 1.81 mg/kg bw/day based on decreased brain acetyl cholinesterase activity of (30%) at 125 ppm (i.e. 9.4 mg/kg bw/day).

2.8 FURTHER STUDIES

Metabolites

Carbofuran

The main metabolite of benfuracarb is carbofuran, an active substance on its own (rapporteur Member State: Belgium, applicants Dianica and FMC). The studies provided in the dossier and evaluated in the DAR are all from the open literature.

EFSA note: These results from the open literature are not always in accordance on the agreed values confirmed at the experts' meeting when carbofuran was discussed as active substance (EPCO 33). Thus, as carbofuran is a major metabolite in potential food feed, data gaps were identified for the applicant to get access to relevant studies for carbofuran.
The rapporteur Member State informed that the applicant, after the experts´ meeting, has obtained access to the data set for carbofuran provided by Arysta/Dianica.

EFSA note: Below follows the summary on carbofuran and for further information, see the EFSA conclusion report for carbofuran[6]. However, it should be highlighted that there are some data requirements or data gaps for Dianica and that the studies on the metabolites of carbofuran are performed by FMC.

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

[6] Conclusion regarding the peer review of the pesticide risk assessment of the active substance carbofuran, EFSA Scientific Report (2006), 90, 1-88.

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 acetyl cholinesterase. 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 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.

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.

Impurity

The significant impurity (no 7) 1,2 dichlorotehane is present in the toxicological batches before 1995 in the range of 0.5-1.5% while in batches after 1996 0.16-0.27%. 1,2 dichlorotehane is classified (19th ATP) as **Carcinogenic Category 2 R45**, harmful via oral ingestion (**R22**) as well as irritating to eyes, lung and skin (**R36/37/38**). In the range 0.1-20%, the classification is **T; R45**. The level tested in the Ames test, bone marrow *in vivo* was 0.5-1.5% whereas in the *in vitro* tests it was the lower level. The applicant has proposed a maximum limit of 4 g/kg and the acceptability was discussed at the experts meeting. The experts agreed to the proposed limit since the higher level was tested in the Ames test in addition to the fact that benfuracarb was not carcinogenic in neither rat nor mouse.

2.9 MEDICAL DATA

Medical examination of workers participating in the manufacturing process of benfuracarb did not display any adverse signs or symptoms.

2.10 ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) and ACUTE REFERENCE DOSE (ARfD)

ADI

The ADI is based on the NOAELs of 1.2 mg/kg bw /day in the 13-week feeding study in dogs, and the NOAEL of 1.2 mg/kg bw/d in the 2-generation rat study.

The rounded ADI is 0.01 mg/kg bw/day, with the safety factor of 100 applied.

AOEL

The AOEL is based on the overall NOAEL of 1 mg/kg bw/d resulting from the sub chronic feeding studies in dogs, with a safety factor of 100. Correction for oral absorption is not needed.

The AOEL is 0.01 mg/kg bw/day, with the safety factor of 100 applied.

ARfD

The ARfD is based on the NOAEL of 1.81 mg/kg bw/day in the 28-day neurotoxicity study in rat where effects were observed at 125 ppm i.e. 9.4 mg/kg bw/day.

The rounded ARfD is 0.02 mg/kg bw/day, with the safety factor of 100 applied.

2.11 DERMAL ABSORPTION

No studies for the representative formulation Oncol 8.6 G were provided by the applicant. The default value of 100% was agreed by the experts.

2.12 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Oncol 8.6 G is a granular formulation.

Operator exposure

According to the intended uses submitted by the applicant the maximum applied dose is 1 kg a.s./ha. The granules are mixed with the moving soil closing the seed furrow.

The 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 are based on the dermal absorption of 100% and the assumption that the treatment is 20 ha/day the total amount handled is 20 kg/day. The estimated exposure is just the AOEL i.e. 86% only if PPE and respiratory protective equipment (RPE) is worn and the 75th percentile is considered, see table below. Although it should be considered that PPE is solely gloves.

Estimated exposure presented as % of AOEL (0.01 mg/kg bw/day), according to calculations with the PHED model. The default for body weight of operator is 60 kg

Model	**No PPE**	**With PPE:**	**With PPE and RPE:**
PHED (75th percentile)	-	148%	86%
PHED (95th percentile)	-	371%	235%

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 and these are the applied assumptions; tractor mounted hydraulic boom and nozzles model (UK POEM) and the tractor field crops (BBA model) and that the use of granular applicators distributing the granules by drilling reduces operator exposure to loading since no water is needed and eliminates mixing phase as well as application exposure. The work rate is 10 ha/day for tractor-mounted /drawn equipment at for tractor-mounted /drawn equipment and the estimated exposure of the unprotected operator is about 296% and 3400% of the systemic AOEL according to the German and POEM model respectively. Using gloves reduces operator exposure to 14% of AOEL according to the German model and to 34% according to the UK model.

Worker exposure

Oncol 8.6 G is normally used at times when it is not necessary to enter the field shortly after application. The product is incorporated into the soil by mechanical means and the low vapor pressure of benfuracarb makes any exposure very unlikely. It is therefore considered not necessary to determine a particular re-entry period for workers.

Bystander exposure

Considering the use of soil integration and the low vapor pressure of benfuracarb ($2x10^{-7}$ mmHg at 20°C) exposure to vapor is likely to be negligible, and it is accepted that bystander exposure will result primarily from airborne dust via the dermal and inhalation routes. Additionally, it is unlikely that a bystander would be present throughout the whole loading and application operation, and exposure to drifting is, therefore, likely to be considerably lower than the estimated operator exposure value.

3. Residues

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

The representative use for inclusion of benfuracarb in Annex I of 91/414/EEC is a pre-planting granular application to brassicas.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism, distribution and residue behaviour of benfuracarb was investigated in various crops with different methods of application and at different timings.

In a study on cotton, bush beans, and corn plants benfuracarb was applied by either foliar treatment or stem injection. In studies on potatoes and apples benfuracarb was directly sprayed onto potato plants and apple trees, respectively. In terms of the representative use the metabolism studies on cabbage and sugar beets with a treatment at sowing were closest to the proposed GAP for brassicas. However, the identity of metabolites in the study with cabbage was not investigated.

The metabolism study in sugar beets (addendum Sep 2005) with an application rate equal to the proposed rate for brassicas considered leaf and root metabolism. In intermediate root and leaf samples benfuracarb was not found above levels <0.004 mg/kg while carbofuran, 3-OH carbofuran and 3-keto-carbofuran were present in total at a level of 0.05 mg/kg (12% TRR) and 0.2 mg/kg (26% TRR) in theses samples, respectively. Neither benfuracarb nor one of the above mentioned metabolites was found above the LOQ (0.001-0.002 mg/kg) in sugar beet leaves and roots at harvest. EPCO 34 concluded that, although this sugar beet study may have addressed metabolism in brassicas following a soil application of benfuracarb, the study did not sufficiently identify potentially relevant metabolites for the supported brassica uses. A polar fraction T1, in particular the major component of T1 which made up 26% of TRR (0.08 mg/kg) in leaves at harvest, will need to be identified or a new study should be conducted in order to sufficiently identify potentially relevant metabolites for the representative brassica uses.

In the experiment with cotton, bush beans and corn plants following a direct treatment benfuracarb, carbofuran and 3-OH-carbofuran were found to be the major components of the terminal residue (together *ca* 50-95% TRR), with their ratio depending on the PHI but also the amount applied. Data indicate that higher application rates to the same crop seem to slow down metabolic activity and therewith influence the rate of generation of pertinent metabolites. With time, benfuracarb, carbofuran and 3-OH-carbofuran levels decreased, whereas the level of phenol-compounds (carbofuran 7-phenol, 3-hydroxy-7-phenol and 3-keto-7-phenol) seemed to increase, indicating the progress of metabolism. 3-keto-carbofuran was generally present at very low levels.

In the study on apples, again, benfuracarb, carbofuran and 3-OH-carbofuran were found to be the major components, accounting together for *ca* 70% of the total terminal residue in apples, whereof 3-OH carbofuran represented with *ca* 50% by far the greatest part of the TRR in apples.

From metabolism studies with directly treated plants the main metabolic pathway of benfuracarb could be established and consisted primarily of the N-S bond cleavage of the parent compound into carbofuran followed by subsequent hydroxylation on the furane ring to yield 3-OH-carbofuran. Numerous other metabolites were generated from carbofuran by successive hydroxylation or hydrolysis and oxidation steps, amongst them 3-keto-carbofuran and phenolic derivates of carbofuran such as carbofuran 7-phenol, 3-hydroxy-7-phenol and 3-keto-7-phenol (hereafter referred to as carbofuran phenol metabolites), which were further conjugated. Metabolites identified following pre-

emergence application to sugar beets at an early sampling stage indicate that metabolism was similar as in foliar treated crops, even though further information on the identity of a major component (26% TRR) in leaves still needs to be submitted.

The benfuracarb metabolite carbofuran is an active substance itself. It has a higher toxicity than benfuracarb. Also 3-OH-carbofuran and 3-keto-carbofuran are of higher toxicity than benfuracarb. The carbofuran phenol metabolites were tested regarding their acute toxicity and based on that studies considered of lower toxicity than benfuracarb, carbofuran, 3-OH-carbofuran and 3-keto-carbofuran. It is noted that the toxicological information on 3-keto-carbofuran, 3-hydroxy-carbofuran the phenol metabolites carbofuran 7-phenol, 3-hydroxy-7-phenol and 3-keto-7-phenol was gained based on studies provided with the carbofuran dossier by a different notifier (FMC). (Refer to EFSA conclusion on carbofuran)
Considering the level of occurrence and the toxicological relevance of benfuracarb and some of its metabolites it is proposed to include benfuracarb, carbofuran and 3-OH carbofuran in the residue definition for risk assessment purposes for foliar uses. For soil applied uses, such as the representative use on brassicas, the identity of the major component of T1 and its relevance in terms of consumer risk needs to be clarified before the applicability of the above proposed residue definition for risk assessment can be confirmed.
Due to the fact that carbofuran is used as a pesticide itself, for monitoring in general a residue definition consisting of two parts was considered necessary to propose: 1) Benfuracarb to be monitored separately from 2) Carbofuran defined as sum of carbofuran and 3-hydroxy-carbofuran expressed as carbofuran equivalents. In accordance separate MRLs for benfuracarb and carbofuran have been proposed resulting from the uses of benfuracarb in crops (see 3.4). However, whether the proposed compounds would be the most suitable markers to monitor residues arising from benfuracarb soil application would need to be reconsidered, if it turned out that the major compound of T1 were of any relevance for consumer safety.

Residue data under field conditions on cauliflower, broccoli and cabbage from Northern and Southern Europe in accordance with the proposed GAP were submitted. It is noted that the number of trials from Southern-Europe is limited (three trials on Savoy cabbage, no trials on flowering brassica) and that no data have been submitted for leafy brassicas and kohlrabi. Benfuracarb, carbofuran and 3-OH-carbofuran were the residues determined in the trials. However, the used methods of analysis were not completely validated and storage stability data were insufficient. EPCO 34 agreed that a full database of residue trials supporting each representative use, including acceptable associated validation data and storage stability data, would need to be presented. An addendum submitted by the rapporteur Member State in February 2006, partially addressing the issue, was neither peer reviewed nor discussed.
In the trials so far available and evaluated, residues were below the respective LOQ of benfuracarb, carbofuran and 3-OH-carbofuran, respectively. The results allow the consumer risk to be provisionally assessed and MRLs for flowering and head brassicas to be provisionally proposed.

The investigation of effects of industrial or household processing was not triggered for the representative use on brassicas.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Since benfuracarb is degraded very rapidly in soil, the rapporteur Member State considered studies in succeeding crops or a waiting period for planting succeeding crops not necessary. However, benfuracarb is largely degraded to the more toxic carbofuran, which appears also more persistent in soil (refer to 4.1.2). Thus the experts' meeting for residues concluded that there is a need to address residues of carbofuran in succeeding crops following application of benfuracarb.
Shortly prior to the final discussion of benfuracarb in the evaluation meeting the rapporteur Member State indicated its disagreement with the experts' meeting decision. However EFSA still supports the EPCO 34 decision.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

In terms of the representative uses, brassica crops are considered potential feed items. Thus, the dietary burden of livestock animals from residues of concern (i.e. currently proposed as benfuracarb, carbofuran, 3-OH-carbofuran) in brassica crops needs to be estimated to conclude on whether metabolism and feeding studies are required. Based on the currently available residue data for the representative brassica use significant residues in the total diet of livestock animals are not expected. However, since benfuracarb is considered fat-soluble (log pow 4.2) the submitted metabolism study in ruminants is considered useful to indicate whether benfuracarb residues tend to accumulate in fat tissues and subsequently significant residues may occur in edible animal matrices.

In the study lactating goats were orally dosed with benfuracarb radio labelled in the phenyl-ring for 10 consecutive days. Even though the relevant residues on potential feeding stuff are besides benfuracarb also carbofuran and 3-OH- carbofuran, it is noted that the referred to metabolites are not deemed as fat-soluble compounds based on their log pow values and thus their potential to accumulate is considered low. The chosen benfuracarb dose rates correspond to a theoretical overdosing factor of at least 5N and 50N, respectively, with regard to the estimated maximum residues level in the total diet of livestock animals. The majority of the administered radioactivity (94% of total dose) was rapidly excreted. Only a low amount (0.2% of total dose) was excreted with the milk. The TRR in tissues and organs were low and residues did not appear to accumulate in fat tissues. Identification of metabolites in edible tissues was not attempted due to the very low level of the recovered radioactivity.
The metabolic pattern was investigated only in urine and indicated an extensive metabolisation mainly into phenolic metabolites through oxidation and hydrolysis steps. Neither benfuracarb nor its primary metabolite carbofuran were present in urine.

The study is not appropriate to establish a complete picture of the metabolic pathway and pattern in ruminants including edible animal matrices and to conclude on potential relevant metabolites in order to define a residue for risk assessment purposes. However, no significant total residues (<0.01 mg/kg)

are expected to occur in edible animal matrices taking into account the residue situation for the representative use indicated by the data currently available. Thus, no residue definition or MRLs for animal matrices are currently proposed, and no further data on livestock animals are required at this stage.

3.3. CONSUMER RISK ASSESSMENT

The consumer risk assessment cannot be completed due to the uncertainties caused by lacking data identified during the evaluation (relevance of major component of T1 in terms of consumer risk unclear; insufficient residue trial data; provisional toxicological reference values for carbofuran).
With the current knowledge and data available, and with the provisionally agreed toxicological reference values for carbofuran, which are applied also to 3-OH-carbofuran it is only possible to asses consumer risk provisional.

For the sake of transparency the consumer risk assessment provided by the rapporteur Member State is presented below.

To assess consumer risk the rapporteur Member State followed the approach of a separated intake assessment of benfuracarb on one hand and carbofuran plus 3-OH-carbofuran residues on the other hand, applying the toxicological reference values of carbofuran also to 3-OH-carbofuran.
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 provisionally proposed MRLs for flowering and head brassicas. The estimated dietary intake of benfuracarb per se is significantly below (<5%) the benfuracarb ADI of 0.01 mg/kg bw/day for all considered consumer groups. The estimated dietary intake of benfuracarb metabolites carbofuran / 3-OH-carbofuran ranges from 7% to 65% of the provisionally allocated ADI for carbofuran of 0.001 mg/kg bw/day, for the considered consumer groups.
In the acute risk assessment provided in the draft assessment the consumer exposure to benfuracarb and carbofuran (including 3-OH-carbofuran), respectively, was calculated with the UK PSD model and consumption figures for adults and toddler. For cauliflower, broccoli a variability factor of 3 was applied instead of 5. According to these calculations, no exceedance of the ARfD was identified for benfuracarb. For carbofuran and 3-OH-carbofuran the estimates for Brussels sprouts and broccoli were below the ARfD. For cauliflower 150 % and 199% of the ARfD were allocated for adults and toddlers, respectively. For cabbage, the ARfD was exceeded for toddlers (107%), whereas for adults no acute consumer risk was identified (82%).
In the addendum of February 2006 the rapporteur Member State provided a revised acute risk assessment for consumers, based on JMPR FAO/WHO guidelines and consumption figures from the WHO/GEMS Food Database for adults and children. In these calculations, for broccoli and cauliflower the generally agreed variability factor of 5 was applied. As highest residues the respective LOQs for benfuracarb and its relevant metabolites in the supervised residue trials have been applied. According to the rapporteur Member State estimates the acute dietary intake of benfuracarb per se reached at the maximum 20% of the benfuracarb ARfD of 0.02 mg/kg bw/day in the case of children

consuming cauliflower. The estimates of acute dietary intake of carbofuran and 3-OH-carbofuran reached up to 370% of the provisionally allocated ARfD for carbofuran of 0.001 mg/kg bw/day, an exceedance of the ARfD was noted for adults and children consuming head cabbage and cauliflower, and for children consuming broccoli. However, the assessment was neither peer reviewed nor discussed by an experts' meeting. It is noted that the selection of some of the input parameters is not very comprehensible.

Based on the rapporteur Member State assessments a potential acute exposure concern for adults and toddlers consuming head and flowering brassicas is identified, even though this might appear to be a theoretical caused by the limitations of the sensitivity of the analytical methods applied in the residue trials. Considering the high acute toxicity of carbofuran and 3-OH-carbofuran it is advised to attempt a lower LOQ, in particular for 3-OH-carbofuran, in residue trials to be generated in future.

EFSA notes that in groundwater the level of carbofuran is expected to exceed the level of 0.1 µg/L (refer to 4.2.2.); the highest predicted contamination in one of the scenarios gave even 1.2 µg/L. In the consumer risk assessment performed by the rapporteur Member State the possible intake of carbofuran through drinking water derived from groundwater was not considered although a significant contribution to the acute and chronic exposure might be expected.

Even though it might not be of particular relevance for the soil applied brassica use, EFSA notes that the approach of a separated intake assessment for benfuracarb and carbofuran/ 3-OH-carbofuran residues ought to be discussed in general, since a separated assessment does not cover the worst case for the consumer. All three compounds have proven in the available metabolism studies to be simultaneously present as residues on food/feed items (refer to 3.1.1). In acute toxicity studies all three compounds showed the same mode of action and toxicological endpoint, i.e. cholinesterase inhibition, whereas only the potency of the observed effect was different. As the consumer might be exposed to a combination of all three relevant compounds, acute consumer risk to the sum of all three compounds should be assessed by either using the lowest allocated ARfD as a worst case approach or by converting the level of the individual compounds to a common residue before summation. The chronic consumer risk might be assessed in the same manner, even though it is noted that no adequate chronic toxicological data is currently available for 3-OH-carbofuran.

3.4. PROPOSED MRLS

Based on available data the following MRLs are proposed for flowering and head brassicas. The rapporteur Member State considered the proposals as provisional since the data base is incomplete. Whether the trial results are supported by acceptable associated validation data and storage stability data could not be resolved during the evaluation procedure of benfuracarb for Annex I inclusion (see open point 3.8 and data gap 3.4 of the evaluation table). Furthermore no data are available to propose MRLs for leafy brassicas and kohlrabi.

Flowering and head brassicas (provisional):

Benfuracarb 0.05* mg/kg

Carbofuran (sum of carbofuran and 3-hydroxy-carbofuran expressed as carbofuran) 0.1* mg/kg

No Codex Alimentarius Commission (CAC) MRLs are currently in place for benfuracarb or carbofuran on brassicas.

4. Environmental fate and behaviour

Benfuracarb fate and behaviour into the environment was discussed in the meeting of experts EPCO 31 (September 2005) on the basis of the benfuracarb DAR (July 2004) and the benfuracarb Reporting and Evaluation tables.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Metabolism of benfuracarb in soil under dark aerobic conditions at 20 ºC was investigated in two studies with four soils and with ^{14}C benfuracarb labelled at the ring position. The soils were in the range of pH values (5.8-7.1), clay contents (8.2 % - 42.3 %) and organic matter contents (2.3 % - 5.3 %).

In aerobic conditions degradation of benfuracarb in soil rapidly yields **carbofuran**[7] (maximum 84.6 % AR after 2 d). Two other major metabolites were reported in the DAR: **MVIII** (maximum = 16.7 % after one day) and **MVI** (maximum = 16.7 % after one day) that do not correspond to any of the known metabolites of benfuracarb or carbofuran. In the meeting of MS experts, the rapporteur Member State clarified that MVIII and MVII corresponded to the same fraction. Identity of this fraction was investigated in a separated study with identical experimental conditions. In this second study, it was found that this single peak represented three individual compounds one of them tentatively characterized as desmethyl-benfuracarb and two other unknowns. The meeting of experts considered that whereas it can not be completely excluded that some of these metabolites reached the 10 % of applied radioactivity their short half life prevented any further characterization. Therefore, further investigation of the nature of these metabolites was not deemed necessary. Other minor metabolites were detected (maximum sum of them: 34.9 % AR after 0.24 d) that individually did not reached the 10 % AR. However, metabolites at levels between 5 % AR and 10 % AR were not reported. Mineralization was high at the end of the study (CO_2 = 27.7 % AR – 66.6 % AR). Amount of unextractable residues reached a maximum = 74.1 % at the end of the study in one of the soils. No effort to characterize bound residue was reported in the DAR. After the meeting of the experts, the rapporteur Member State confirmed that no detailed characterization of bound residues had been performed in this study.

Additionally, a degradation and metabolism study of carbofuran in four soils under aerobic conditions at 20 ºC is available. 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 > 10 % AR were found. One experiment was repeated at 10 ºC in which metabolite **3-keto-carbofuran**[8] reached a 7.7 % AR at the end of the

[7] carbofuran: 2,3-dihydro-2,2-dimethylbenzofuran-7-yl methylcarbamate
[8] 3-keto-carbofuran: 3-dihydro-2,2-dimethyl-3-oxo-7-benzofuranyl methyl carbamate

study (56 d). Experts meeting agreed that 3-OH-carbofuran (minor carbofuran metabolite containing the carbamate moiety) needs to be addressed, as potential benfuracarb soil metabolite, for ground water contamination**.** However, according the experts meeting the carbofuran metabolite carbofuran-7-phenol does not need to be addressed for benfuracarb.

No soils were investigated in the range of alkaline soils that, according to hydrolysis study, could represent a worst case for chemical degradation. Therefore, the applicant was required to address the degradation of benfuracarb in alkaline soils. A position paper was submitted in April 2005 and a new study was submitted to the rapporteur Member State in August 2005. None of these reports had been evaluated at the time of the experts meeting. The meeting of experts agreed that this new information need to be evaluated in an addendum that was not available at the time of drafting this conclusion. An addendum has been provided on 18 May 2006. 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, the data gap to address the degradation under alkaline soils is maintained.

No anaerobic soil degradation study has been provided.

No soil photolysis study has been provided for benfuracarb, however a soil photolysis study is available for the metabolite carbofuran in the carbofuran dossier that has been used to assess that this metabolite of benfuracarb is photollytically stable on soil surface.

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

Degradation rate of benfuracarb in soil was investigated in the same degradation studies used for the metabolism elucidation.

The available studies indicate that at 20 ºC benfuracarb is very low persistent in soil (DT_{50} = 0.23 d – 0.83 d) and its metabolite carbofuran is low to moderate persistent in soil (DT_{50} = 6.1 d– 19.4 d).

However, degradation of carbofuran seems to be very dependent of the temperature and at 10 ºC is highly persistent (DT_{50} = 110 d). The meeting of experts discussed the impact of this high temperature dependence on the risk assessment. The rapporteur Member State informed that the notifier had submitted a position paper and a new study to address the degradation of carbofuran at low temperatures. The meeting of the experts agreed that this new study needs to be evaluated in an addendum.

Additionally, in the carbofuran dossier there are studies that indicate a potential high persistence of carbofuran in soil ($DT_{50\ lab\ 20ºC}$ = 175 – 444 d). Further clarification on the acceptability of the different carbofuran degradation studies and the reasons for the high differences on the carbofuran half life is expected to be provided by the rapporteur Member State as an addendum to the carbofuran DAR. Relevance of this data for the assessment of benfuracarb may need further consideration when this addendum becomes available.

Unknown metabolites fraction (MVIII-MVI) is very low persistent and transient in nature.

No data on relevant soil metabolites 3-OH-carbofuran and 3-keto-carbofuran are available in the carbofuran dossier.

Worst case laboratory half lives were used to calculate PEC soil of benfuracarb and its metabolite carbofuran. However, data from a different carbofuran notifier show that field worst case half life for carbofuran is 71.9 d in EU sites. Therefore, PECs soil were also calculated by the rapporteur Member State with this half life. According the conclusion for carbofuran, reliability of this value needs to be further assessed and confirmed.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Due to the fast degradation of benfuracarb batch adsorption desorption studies failed to determine a reliable K_{oc}. Nevertheless, by the HPLC method it was estimated that benfuracarb may be classified as immobile in soil (K_{oc} = 9100 mL / g).

A batch adsorption / desorption study is available for carbofuran in four soils. Carbofuran may be classified as very high mobile compound (K_{oc} = 17 – 28 mL / g).

No data available for minor carbofuran relevant soil metabolites 3-OH-carbofuran and 3-keto-carbofuran.

A lysimeter study is available where two different lysimeters are investigated [with application in beets (furrow) and potatoes (spray)]. Both lysimeters were in the acidic range of soils (pH (0-30cm) = 5.1 – 5.4). Annual average amount of radioactivity leaching was in the range 1.3 – 2.5 µg / L. Only few samples were analyzed for individual components. Therefore, it was not possible to calculate annual average concentration for individual components. Benfuracarb was found at maximum amounts of 0.25 µg / L and carbofuran at maximum amounts of 0.16 µg / L. A new lysimeter study was required by the rapporteur Member State in the DAR. The meeting of the experts agreed that the new FOCUS GW modelling required can substitute the requirement for a new lysimeter at this stage.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

In sterile aqueous buffer solutions, hydrolysis of benfuracarb is pH dependent. Half life is less than half hour at pH 4, 1.4 days at pH 7 and 26.9 d at pH 9. Major hydrolysis products were carbofuran and metabolites **MI** (maximum = 36.6 % AR after 30 d at pH = 7), **MIII** (maximum = 13.8 % AR after 23 d at pH 9) and **MIV** (maximum = 10.5 % after 30 d). Desethylbenfuracarb and carbofuran-phenol were identified in a separate study that failed to elucidate the chemical structure of the unknown components MI, MIII and MIV. The meeting of experts agreed that no further investigation of these metabolites was necessary since appear within a range of pHs already investigated in the more relevant water / sediment studies.

The rapporteur Member State stated in the DAR that benfuracarb is readily degradable by direct phototransformation in water. However, the potential contribution of aqueous photolysis to benfuracarb degradation may not be fully established due to the great contribution of hydrolysis at pH (6-7.5) chosen to perform the photolysis sterile study. In the natural water experiment (pH ≈ 7-8)

photolysis seems not to contribute significantly to the aqueous degradation of benfuracarb. However, irradiation seems to enhance the degradation of the metabolite carbofuran to **carbofuran-7-phenol**[9].
Benfuracarb is not readily biodegradable. The substance was found to have a slightly inhibitory effect on microbial activity.
A study with two water sediment systems is available. Both systems are in the alkaline range (pH $_{water}$ 7.8-8.4). Main compounds found in the water phase are benfuracarb and carbofuran (maximum = 58.26 % AR after 2d). Main compounds found in the sediment phase are carbofuran (maximum = 25.31 % after 14 d) and carbofuran-7-phenol (maximum = 13.6 %). The cumulative amounts of CO_2 at the end of the study accounted for 13.6 % AR and 16.7 % AR. Most of the radioactivity was present as bounded residue to the sediment by the end of the study (73.8 % AR – 75.9 % AR).
Benfuracarb dissipates rapidly in water phase with a half life between 6 h to 15 h. Main dissipation process is transformation to carbofuran. Carbofuran dissipates from water phase with half life between 8.2 d to 27.2 d. Main dissipation process is partitioning into sediment. Whole system and sediment phase half lives had not been calculated. Applicant presented a report with the estimation of the whole system half life (H. Willems, 1998). Also, the half life in the sediment for carbofuran and carbofuran-7-phenol needs to be assessed. The rapporteur Member State is expected to provide this evaluation in an addendum.
In the carbofuran dossier, 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. 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. These experiments seem to indicate that the degradation of carbofuran may be pH dependent in water sediment systems.
PEC_{SW} of carbofuran has been calculated for a limited number of FOCUS sw scenarios. Calculations of PEC_{SW} for parent benfuracarb and PEC_{SED} for benfuracarb, carbofuran and carbofuran-7-phenol need to be performed. Updated FOCUS $PEC_{SW\ /\ SED}$ were submitted by the applicant on April 2005. The evaluation of these new calculations by the rapporteur Member State is still not available. An addendum has been provided on 18 May 2006. 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.

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

FOCUS PEARL 1.1.1 PEC gw have been calculated for benfuracarb and carbofuran. Annual average 80th percentile of benfuracarb were < 0.001 µg / L for all calculated scenarios (7 cabbage spring, 5 cabbage summer). Carbofuran exceed the 0.1 µg / L trigger in 4 of the 7 spring scenarios and in three of the five summer scenarios. In one of the summer scenarios (Hamburg) an 80th percentile annual average of 1.212 µg / L was reached. The applicant was required to address the potential for ground water contamination by the benfuracarb metabolite 3-keto carbofuran. The applicant presented new

[9] carbofuran-7-phenol: 2,3.dihydro-2,2-diemthyl-7-benzofuranol.

studies to address potential groundwater contamination by metabolites 3-OH-carbofuran, carbofuran-7-phenol and 3-keto-carbofuran in August 2005. Studies included the determination of the adsorption coefficients and half lives with the corresponding FOCUS GW calculations. The addendum summarising these studies was not available at the time of drafting this conclusion. It is additionally noted that these calculations do not take into consideration the longer half lives observed for carbofuran from the data of the second carbofuran applicant (FMC). An addendum has been provided the 18th of May 2006. 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.

4.3. FATE AND BEHAVIOUR IN AIR

Concentrations of benfuracarb in the air compartment are expected to be negligible, due to short persistence in the atmosphere.

5. Ecotoxicology

Benfuracarb 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. When reported, 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 number of granules to reach the acute and dietary LD_{50} dose was calculated to be 54 and 41 granules for a 15 g bird. To reach a dose equivalent to the reproductive NOEC an amount of 24 granules would be required for a 15 g bird. The need for further information on the acceptance of granules was identified in the DAR to assess the risk from uptake of granules. A study on the acceptance of granules was submitted in April 2005. An addendum was provided by the rapporteur Member State in May 2006. The addendum is not peer reviewed.

The risk from uptake of contaminated drinking water was assessed as low. A data requirement was set in the DAR for the applicant to address the risk from ingestion of treated seedlings. Residue studies and a risk assessment were submitted in August 2005. An addendum was submitted in May 2006. The risk from uptake of contaminated seedlings was considered by the rapporteur Member State as low for benfuracarb but was considered as high for the metabolite carbofuran. However the information provided in the addendum is not peer reviewed.

The risk assessment for secondary poisoning from uptake of contaminated earthworms was based on a study with blackbirds and earthworms treated with benfuracarb. The experts' meeting concluded

that the study was conducted to investigate whether blackbirds would consume contaminated earthworms and whether they would be affected but it was not designed to determine a NOEC in line with the NOECs from dietary studies. It was noted that the exposure period was sufficiently long because the active substance acts as an acute toxin. However, the meeting concluded that the study has certain deficiencies (e.g. birds were not particularly motivated to feed, the relevance of the concentration of benfuracarb to the representative use is not known). An open point was set for the rapporteur Member State to reconsider the study in the light of the discussion at the expert meeting. The risk of secondary poisoning to birds is not finally concluded. Poisoning incidents from uptake of contaminated earthworms were reported by France. A new risk assessment for the uptake of contaminated earthworms was submitted in August 2005. An addendum was submitted in May 2006. The information provided in the addendum is not peer reviewed.
The LC_{50} for the dietary toxicity to mallard duck (*Anas platyrhynchus*) was based on an average food intake for all doses. The meeting did not accept this as food avoidance was observed at all concentrations. Adverse effects were observed at all dose levels and no NOEC could be derived from this particular study. Since the primary concern is the acute risk it was proposed by the meeting to base the first tier risk assessment on the acute endpoint. Ecological parameters, toxicological data or avoidance studies could be used for refinement of the risk assessment.
The reproductive NOEC for birds was discussed in the expert meeting. A statistically significant lower weight of 14 day old survivors was observed in the reproduction study with bobwhite quail (*Colinus virginianus*). Since the difference was only 5% the experts did not reach a conclusion on the ecological relevance of the effect. Therefore a data gap was identified for the applicant to compare the key endpoints on hatchling body weights with historical control data.

The acute risk to mammals from direct uptake of granules was assessed as low as well as the risk from uptake of contaminated drinking water. The long-term risk from uptake of granules was not sufficiently addressed. The rapporteur Member State identified the following data requirements in the DAR: a long-term risk assessment for uptake of granules, the risk from consumption of contaminated earthworms and the risk from ingestion of residues in seedlings. Further data and a new risk assessment were submitted by the applicant in August 2005. An addendum was submitted in May 2006. The information provided in the addendum is not peer reviewed.

5.2. RISK TO AQUATIC ORGANISMS

Since Oncol 10 8.6 G is a granular formulation direct entry into surface is not expected to be a major route of entry. Due to the rapid conversion of benfuracarb to carbofuran the PECsw water values were calculated for carbofuran using (FOCUS Macro) for drainage which was considered to be the most relevant route of entry.
Two out of 3 scenarios resulted in TER values below the relevant Annex VI trigger of 100 and 10 for the acute and chronic risk to fish and aquatic invertebrates. Hence a need for a refined risk assessment was identified in the DAR. The applicant submitted a new juvenile fish growth test and a refined risk assessment for aquatic organism in April 2005. In the addendum of May 2006 two NOEC values

from a juvenile growth test with rainbow trout were mentioned. No study summaries and no risk assessment were provided in the addendum.
The risk of bioaccumulation was assessed as low since the BCF_{ss} for the whole fish was below the trigger of 100.
A rapid shift of benfuracarb and carbofuran to the sediment phase was observed in the water-sediment study but no risk assessment for sediment dwelling organisms was presented. EFSA is of the opinion that the risk to sediment dwelling organisms needs to be addressed and suggests a data gap. In the addendum of May 2006 the rapporteur Member State identified the need for a study with carbofuran and sediment dwelling organisms as a prerequisite to conduct a risk assessment.
An open point was set for the rapporteur Member State to amend the risk assessment taking into account potential changes in the PECsw calculation following from the data requirement on the degradation of benfuracarb under alkaline pH in soil. Data were submitted by the applicant but not evaluated.
No PECsw calculation and no risk assessment were performed for the metabolite carbofuran-7-phenol. The risk from carbofuran-7-phenol is expected to be covered by the risk assessment for carbofuran because of its much lower toxicity (about 4 orders of magnitude). The PECsw for carbofuran-7-phenol would need to be more than 4 orders of magnitude higher than the PECsw for carbofuran to pose a higher risk to aquatic organisms than carbofuran.

Based on the peer-reviewed data a high risk to aquatic organisms cannot be excluded. However, the submitted data need to be evaluated before drawing a final conclusion on the risk to aquatic organisms.

5.3. RISK TO BEES

The exposure of bees was assumed to be negligible since the granules are applied in the sowing bed and cabbage has no flower in the production crop. The expert's meeting agreed that the risk to bees is low for the exposure to residues in cabbage but that there could be a potential exposure of bees foraging on weeds that are present in the field. It was argued by the rapporteur Member State that weeds are controlled and no flowering weeds are present in cabbage fields. Therefore, it is concluded that the risk is considered as low in cabbage fields if no flowering weeds are present. The potential risk to bees foraging on flowering weeds should be assessed at Member State level taking into account the agricultural practice.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The effects of benfuracarb on survival were tested with *Aphidius rhopalosiphi*, *Typhlodromus pyri*, *Coccinella septempunctata*, *Chrysoperla carnea*, *Poecilus cupreus* and *Aleochara bilineata*. The LD_{50} for *A. rhopalosiphi* and *T. pyri* were determined as 43 mL Oncol 20 EC/ha and 42.4 mL Oncol 20 EC/ha. Exposure of ground dwelling arthropods was considered as more relevant because of the suggested use. Tests with the ground dwelling beetles *P. cupreus* and *A. bilineata* and the granular formulation Oncol 8.6 G revealed high mortality rates (59.5%) for *A. bilineata* at the suggested GAP (a dose rate equivalent to 12 kg Oncol 8.6 G/ha). Therefore, a data requirement to address the risk to

ground dwelling non-target arthropods was identified in the DAR. An extended lab study with *A. bilineata* and a new risk assessment was submitted by the applicant in August 2005. In the addendum of May 2006 an endpoint from a study with *Aleochara bilineata* from an extended laboratory test was given. The rapporteur Member State concluded in the addendum that the risk to non-target arthropods is low. However no study summary or evaluation of the study was provided in the addendum.
The new data need to be evaluated before a final conclusion on the risk to non-target arthropods can be drawn.

5.5. RISK TO EARTHWORMS

The TER for the acute risk to earthworms was calculated as 7 based on an endpoint from a study with the formulation Oncol 20 EC. A field study with the formulation Oncol 10 G was submitted but several deficiencies were noted by the rapporteur Member State (e.g. not enough samples were taken and the study does not cover the proposed use rate). An acute study with the active substance and an earthworm field study with appropriate dose levels were identified as data requirements in the DAR. New acute toxicity studies with benfuracarb and the formulation Oncol 8.6 G were submitted in April 2005 together with a new acute risk assessment. The studies were not evaluated by the rapporteur Member State and not peer reviewed. The applicant submitted also a justification why a field study with earthworms is not triggered based on the results of the new toxicity studies. The justification was not evaluated by the rapporteur Member State and is not peer reviewed. In the addendum of May 2006 the acute risk to earthworms from benfuracarb was assessed as low. A reliable study to assess the acute risk to earthworms was not available for carbofuran. A field study was considered necessary to address the long-term risk to earthworms from benfuracarb and its metabolite carbofuran. The addendum of May 2006 is not peer reviewed.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

A study with other soil non-target organisms is not triggered since the DT_{90}(field) for benfuracarb and carbofuran are <100 days. In the addendum of May 2006 the rapporteur Member State suggested a field study to assess the risk to soil macro-organisms. The addendum is not peer reviewed.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The submitted studies were assessed as not acceptable because the soil used in the studies was not representative for European soils, the sand content was too low, no data on its organic carbon content and the microbial biomass were given and formulations different from Oncol 6.8 G were tested. Therefore a data requirement was set by the rapporteur Member State to submit soil nitrification and respiration studies with benfuracarb or carbofuran to address the risk to soil non-target micro-organisms. Studies investigating the effects of carbofuran on soil nitrification and respiration were submitted in April 2005. The rapporteur Member State assessed the risk to soil non-target micro-organisms as low in the addendum of May 2006. The addendum is not peer reviewed.

The risk assessment for soil non-target micro-organisms can only be finalised after evaluation of the new studies.

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

A data requirement was identified in the DAR since no information was provided to address the risk to non-target organisms. Studies on phytotoxic effects with formulations containing benfuracarb were submitted. The studies were listed in the addendum of May 2006. The rapporteur Member State assessed the risk as low. However no study summaries were provided to support the suggested assessment. The addendum is not peer reviewed.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No effects on respiration of activated sewage sludge were observed at the tested dose of 100 mg benfuracarb/L. Therefore it is concluded that the risk from the representative use to biological methods of sewage treatment is low.

6. Residue definitions

Soil

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

Definitions for monitoring: benfuracarb, carbofuran, 3-keto-carbofuran (assessment needs to be finalized).

Water

Ground water

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

Definitions for monitoring: benfuracarb, carbofuran may be confirmed as components of the monitoring residue definition for ground water. Assessment of metabolites 3-keto-carbofuran and 3-OH-carbofuran needs to be finalized.

Surface water

Definitions for risk assessment: benfuracarb (only water phase), carbofuran (water and sediment), Carbofuran-7-phenol (only in sediment).

Definitions for monitoring: benfuracarb (only water phase), carbofuran (water and sediment)

Air

Definitions for risk assessment: benfuracarb, carbofuran.

Definitions for monitoring: benfuracarb, carbofuran.

Food of plant origin

Definitions for risk assessment: benfuracarb, carbofuran and 3-hydroxy-carbofuran;
confirmed for foliar uses, however, full applicability for soil applied uses to be demonstrated by further data

Definitions for monitoring: two definitions necessary: 1) benfuracarb; 2) carbofuran (sum of carbofuran and 3-hydroxy-carbofuran expressed as carbofuran)

Food of animal origin

Definitions for risk assessment: not proposed due to limited data, however the study demonstrates that no bioaccumulation occurs

Definitions for monitoring: not required for representative use

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
Benfuracarb	Very low persistent (DT_{50} = 0.23 – 0.83 d)	The first tier risk assessment indicates a high acute risk to earthworms. Further studies are required to finalise the risk assessment.
Carbofuran	Low to moderate persistent (DT_{50} = 6.1 – 19.4 d) A high temperature dependence was apparent in the available study at 10 ºC (DT_{50} = 110 d). Some studies in the dossier of carbofuran show that it may be high persistent in soil (DT_{50} > 100 d). Relevance of this information to the assessment of carbofuran as metabolite of benfuracarb may need further consideration.	The risk form carbofuran was not assessed in the DAR for benfuracarb. The first tier risk assessment conducted in the DAR for carbofuran indicated a high long-term risk to earthworms.
3-keto-carbofuran (only at low temperatures 10 ºC).	Half life not available, contains the carbamate moiety. Appears as metabolite of benfuracarb in the study performed at 10 ºC. It is a carbofuran metabolite.	No studies with soil dwelling organisms available. The risk to soil dwelling organisms needs to be addressed since it contains the active moiety and it is persistent in acidic soils
3-OH-carbofuran	Half life not available. Minor carbofuran metabolite that contains the carbamate moiety. Needs to be addressed for benfuracarb.	No studies with soil dwelling organisms available. No data required due to the transient nature of the molecule.

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 activity	Ecotoxicological activity
Benfuracarb	Estimated to be immobile	FOCUS: No Lysimeter: Yes (individual samples, annual average concentration not available)	Yes	Yes	Benfuracarb is very toxic to fish and aquatic invertebrates (the toxicity is similar to carbofuran). Due to the rapid conversion to carbofuran the aquatic risk assessment is based on the PECsw for carbofuran.
Carbofuran	Very high mobile (K_{oc} = 17–28 mL/g)	FOCUS: Yes, trigger 0.1 µg / L exceeded for 4 of 7 scenarios, trigger 0.75 µg / L exceeded for 1 of 7 scenarios.[10] Lysimeter: Yes (individual samples, annual average concentration not available)	Yes	More toxic than benfuracarb (30 times) Very toxic by oral and inhalatory exposure Toxic towards reproduction	A potential high risk for fish and aquatic invertebrates was identified in the risk assessment for surface water on the basis of the peer reviewed data. However, new data were submitted but not evaluated by the RMS.

[10] Carbofuran longer half lives from the second carbofuran notifier were not considered in this calculation. New calculation required taking into consideration carbofuran end points.

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 activity	Ecotoxicological activity
3-keto-carbofuran	To be assessed. Data gap	To be assessed. Data gap	No data available Data gap (depending on the outcome of the fate assessment)	More toxic than benfuracarb (3-fold) Toxic via oral exposure	No data available Data gap (depending on the outcome of the fate assessment)
3-OH-carbofuran	To be assessed. Data gap	To be assessed. Data gap	No data available Data gap (depending on the outcome of the fate assessment)	More toxic than benfuracarb (10 times) Very toxic via oral exposure	No data available Data gap (depending on the outcome of the fate assessment)

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Benfuracarb (only water phase)	Benfuracarb is very toxic to fish and aquatic invertebrates (the toxicity is similar to carbofuran). Due to the rapid conversion to carbofuran the aquatic risk assessment is based on the PEC_{SW} for carbofuran.
Carbofuran (water and sediment)	A potential high risk for fish and aquatic invertebrates was identified on the basis of the peer reviewed data. However, new data were submitted but not evaluated by the RMS.

Compound (name and/or code)	**Ecotoxicology**
Carbofuran-7-phenol (only in sediment)	Carbofuran-7-phenol is markedly less toxic to aquatic organisms compared to benfuracarb and carbofuran. No PECsw calculation and no risk assessment was performed. However, only in case that the PEC_{SW} would be 4 orders of magnitude higher than the PEC_{SW} for carbofuran the resulting TERs would be higher than the TERs for carbofuran.

Air

Compound (name and/or code)	**Toxicology**
Benfuracarb	Toxic inhalatory exposure LC_{50} 0.3 mg/L (T; R23)
Carbofuran	Very toxic via inhalatory exposure L C_{50} 0.05 mg/L (T^{+}; R26)

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

- Analytical method for the determination of the relevant impurity 1,2-dichloroethane in the formulation (date of submission unknown, data gap identified by the meeting of experts; refer to chapter 1)
- Depending on the final residue definitions for soil and ground water, it could be necessary to require further data.
- The applicant to provide the relevant studies (or a letter of access to) on the metabolite carbofuran. According to the rapporteur Member State, the applicant has access to the carbofuran dossier of Dianica (refer to chapter 2.8)
- The sugar beet metabolism study did not sufficiently identify potentially relevant metabolites for the supported brassica uses. A fraction T1 (if material still available from the original study), will need to be identified or a new study should be conducted in order to sufficiently identify potentially relevant metabolites (relevant for all representative uses; date of submission unknown; data gap identified by the meeting of experts; refer to point 3.1.1).
- A complete residue trial database including associated validation data with a sufficient sensitivity i.e. a sufficiently low LOQ, need to be presented (relevant for all representative uses; date of submission unknown; data gap identified by the meeting of experts; refer to point 3.1.1).
- Applicant to submit the full set of storage stability data for all relevant matrices in the section of residues (relevant for all representative uses; date of submission unknown; data gap identified by the meeting of experts; refer to point 3.1.1).
- Applicant to address residues of carbofuran in succeeding crops following application of benfuracarb (relevant for all representative uses; date of submission unknown; data gap identified by the meeting of experts; refer to point 3.1.2).
- Applicant to address the degradation of benfuracarb in alkaline soils (relevant for all representative uses; study submitted in August 2005, neither evaluated nor peer reviewed; refer to point 4.1.1).
- Applicant to provide $PEC_{SW/SED}$ for benfuracarb and for carbofuran as metabolite to benfuracarb (relevant for all representative uses; study submitted in October 2004 and updated on April 2005, neither evaluated nor peer reviewed; refer to point 4.2.1).
- Applicant to provide FOCUS PEC_{GW} of benfuracarb metabolites 3-OH-carbofuran and 3-ketocarbofuran and of metabolite carbofuran with input parameters resulting from carbofuran assessment and list of end points (relevant for all representative uses; study submitted in August 2005, neither evaluated nor peer reviewed; refer to point 4.2.2).
- A study on the acceptance of granules by birds (relevant for all representative uses; data requirement identified in the DAR; study was submitted in April 2005; refer to point 5.1).
- Reproductive NOEC for birds - a comparison of the key endpoints on hatchling body weights with historical control data is required (relevant for all representative uses; data gap identified in the EPCO experts' meeting in September 2005; no submission date proposed by the applicant; refer to point 5.1).

- Risk assessment for birds from uptake of treated seedlings (relevant for all representative uses; data requirement identified in the DAR; residue studies and a risk assessment were submitted in August 2005; refer to point 5.1).
- Risk assessment for birds from uptake of contaminated earthworms. (relevant for all representative uses; data requirement identified in the evaluation meeting of March 2005; risk assessment submitted in August 2005; refer to point 5.1).
- Long-term risk assessment for mammals from uptake of granules (relevant for all representative uses; data requirement identified in the DAR; new risk assessment submitted in August 2005; refer to point 5.1).
- Risk assessment for mammals from uptake of contaminated earthworms (relevant for all representative uses; data requirement identified in the DAR; risk assessment submitted in August 2005; refer to point 5.1).
- Risk assessment for mammals from uptake of residues in seedlings (relevant for all representative uses; data requirement identified in the DAR; risk assessment submitted in August 2005; refer to point 5.1).
- Submission of a study with fish to establish a reliable NOEC value (relevant for all representative uses; data requirement identified in the DAR; a juvenile growth test with fish was submitted in April 2005; refer to point 5.2).
- The risk to sediment dwelling organisms needs to be addressed (relevant for all representative uses; data gap identified by the EFSA; no submission date proposed; refer to point 5.2).
- A refined risk assessment for aquatic organisms (relevant for all representative uses; data requirement identified in the DAR; a juvenile growth test with fish was submitted in April 2005; refer to point 5.2).
- The risk to ground dwelling non-target arthropods needs to be addressed. (relevant for all representative uses; data requirement identified in the DAR; an extended lab study with *Aleochara bilineata* and a new risk assessment were submitted in August 2005; refer to point 5.4).
- Acute toxicity study with benfuracarb and earthworms (relevant for all representative uses; data requirement identified in the DAR; acute toxicity studies with benfuracarb and with the formulation Oncol 6.8 G were submitted in April 2005; refer to point 5.5).
- A field study with earthworms at appropriate dose rates (relevant for all representative uses; data requirement identified in the DAR; a justification that an earthworm field study is not triggered was submitted in April 2005; refer to point 5.5).
- Soil nitrification study with benfuracarb or carbofuran (relevant for all representative uses; data requirement identified in the DAR; soil nitrification study with carbofuran was submitted in April 2005; refer to point 5.7).
- Soil respiration study with benfuracarb or carbofuran (relevant for all representative uses; data requirement identified in the DAR; soil respiration study with carbofuran was submitted in April 2005; refer to point 5.7).

- Information on the risk to other non-target organisms (relevant for all representative uses; data requirement identified in the DAR; studies on phytotoxic effects were submitted in April 2005; refer to point 5.8).
- Data on the ecotoxicological and pesticidal activity of 3-keto-carbofuran and 3-OH-carbofuran in ground water are needed (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 (pre-plantation) to control soil and foliar insects, where brassica will be grew. Benfuracarb can be used as insecticide and nematicide. It should be noted that during the peer review process only the use as insecticide was evaluated.
The representative formulated product for the evaluation was "Oncol 8.6G", a granule (GR), registered in France and Spain.

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

Benfuracarb is rapidly and nearly completely absorbed reaching in the rat. The main metabolite of benfuracarb is carbofuran (approximately 30%). The acute inhalatory toxicity is high (LC_{50} 0.3 mg/L) whereas the oral toxicity moderate (LD_{50} 205 mg/kg bw). However, the toxicity via dermal route was low (LD_{50} >2000 mg/kg bw). It is neither a skin nor an eye irritant nor a skin sensitizer, proposed risk phrases are: T, R23 “Toxic by inhalation” and R22 “Harmful if swallowed” The critical effects are cholinesterase inhibition. And the dog was the most sensitive species. The relevant short term NOAEL is 1 mg/kg bw/day. It is not mutagenic, genotoxic or carcinogenic. The long term NOAEL is 5.5 mg/kg bw/day in the rat based on clinical signs and inhibition of brain acetylcholine esterase activity.
Effects on reproduction parameters were observed such as, decreased male fertility, number of live pups and pup weight was decreased, even the entire second generation was lost The parental toxicity observed at this dose level was not severe, decreased body weight (around 10%) and increased food consumption (around 20%).The parental as well as reproductive including embryotoxic NOAEL is 25 ppm i.e. 1.2 mg/kg bw/day. The appropriate classification for reproduction toxicity could not be

agreed and the question should be forwarded to ECB, R62 is high lighted. ECB has concluded R62 but not voted.

The main metabolite of benfuracarb is the active ingredient carbofuran which is more toxic than benfuracarb. The relevant impurity 1,2 dichlorotehane, proposed maximum limit 4 g/kg, is classified as toxic, Carcinogenic Category 2 (T; R45).

The Acceptable Daily Intake (ADI) is 0.01 mg/kg bw/day, based on the NOAELs of 1.2 mg/kg bw /day in the 13-week feeding study in dogs, and the NOAEL of 1.2 mg/kg bw/d in the 2-generation rat study mean 1 mg/kg bw/d, with the safety factor of 100 applied

The Acceptable Operator Exposure Level (AOEL) is 0.01 mg/kg bw/day based on the overall NOAEL of 1 mg/kg bw/d dogs, with a safety factor of 100.

The Acute Reference Dose (ARfD) is 0.02 mg/kg bw/day based on the NOAEL of 1.81 mg/kg bw/day in the 28-day neurotoxicity study in rat, with the safety factor of 100 applied**.**

The default value of 100% was agreed on for the granular formulation Oncol 8.6 G no studies were provided by the applicant.

The estimated operator exposure according to the US PHED model is below the AOEL (86%) if personal protective equipment as well as respiratory equipment is used.

The metabolism, distribution and residue behaviour of benfuracarb was investigated in various crops with different methods of application and at different timings.

In studies on cabbage and sugar beet, uptake and distribution of residues was investigated following an application of benfuracarb to the soil. The identity of metabolites was not investigated in the study with cabbage. Although the metabolism study in sugar beet may have addressed metabolism in brassicas, the study did not sufficiently identify potentially relevant metabolites for the supported brassica uses, and thus further data are necessary to fully conclude on the plant metabolism in terms of soil applied uses.

Following a direct application to cotton plants, bush beans, corn plants, potatoes and apples, benfuracarb, carbofuran and 3-OH-carbofuran were the major components of the terminal residue in these crops. In the course of time the level of phenol metabolites, i.e. carbofuran 7-phenol, 3-hydroxy-7-phenol and 3-keto-7-phenol tended to increase. It could be concluded that the degradation of benfuracarb in plants having received a foliar treatment consisted primarily of the N-S bond cleavage of the parent compound into carbofuran followed by hydroxylation or hydrolysis and oxidation steps to yield 3-OH-carbofuran and phenol metabolites of carbofuran, which were further conjugated.

Benfuracarb, carbofuran and 3-OH-carbofuran were considered the relevant residues to assess consumer exposure and consumer risk. The unrestricted applicability of this residue definition to all uses, including the soil applied brassica use will need to be confirmed.

Furthermore, even though benfuracarb is degraded very rapidly in soil, the experts' meeting for residues concluded that there is a need to also address residues of carbofuran in succeeding crops following application of benfuracarb.

In residue trials under field conditions benfuracarb, carbofuran and 3-OH-carbofuran were analysed for in cauliflower, broccoli and cabbage and residues were found to be below the respective LOQ,

however the validity of the results needs to be confirmed by further data. Moreover the residue trial database for brassicas needs to be completed.
From a study with lactating goats it was concluded that benfuracarb and its metabolites are unlikely to accumulate in edible animal tissues and no significant total residues are expected to occur when brassicas are fed to livestock.
With the current knowledge and limited data available and with the provisionally agreed toxicological reference values for carbofuran it is only possible to asses consumer risk preliminary.
Consumer risk has been separately assessed by the rapporteur Member State for benfuracarb residues and for carbofuran and 3-OH-carbofuran residues. The estimated chronic dietary intake of benfuracarb and its metabolites carbofuran and 3-OH-carbofuran was found to be below the ADI of benfuracarb and carbofuran, respectively. A potential acute exposure concern noted for adults and toddlers (up to 370% of carbofuran ARfD) consuming head and flowering brassicas, is primarily caused by the limited sensitivity of the analytical methods applied in the residue trials.

Benfuracarb is rapidly degraded in soil (DT_{50} = 0.23 d – 0.83 d) under laboratory dark aerobic conditions yielding carbofuran (maximum 84.6 % AR after 2 d) as major metabolite. This metabolite is low to moderate persistent in soil (DT_{50} = 6.1 d– 19.4 d) according the studies presented in the benfuracarb dossier, but may be high persistent according some studies presented by a different applicant in the carbofuran dossier ($DT_{50\ lab\ 20^{o}C}$ = 175 – 444 d). Relevance of carbofuran data for the assessment of benfuracarb may need further consideration when the rapporteur Member State addendum for carbofuran becomes available.
Another major residue fraction (maximum = 16.7 % after one day) was identified. In a separated study, it was found that this peak represented three individual compounds one of them tentatively characterized as desmethyl-benfuracarb. The meeting of experts considered the rapid disappearance of this fraction and agreed that further investigation was not deemed necessary. Other minor metabolites were detected (maximum sum of them: 34.9 % AR after 0.24 d) that individually did not reached the 10 % AR. Mineralization was high at the end of the study (CO_2 = 27.7 % AR – 66.6 % AR). Amount of unextractable residues reached a maximum = 74.1 % at the end of the study in one of the soils. After the meeting of the MS experts, the rapporteur Member State confirmed that no detailed characterization of bound residues had been performed in this study.
Experts meeting agreed that 3-ketocarbofuran and 3-OH-carbofuran (minor carbofuran metabolites containing the carbamate moiety) need to be addressed, as potential benfuracarb soil metabolites, for ground water contamination**.**
The applicant was required to address the degradation of benfuracarb in alkaline soils. A position paper and a new study are available but are still not evaluated or peer reviewed.
No soil photolysis study has been provided for benfuracarb; however a soil photolysis study is available for the metabolite carbofuran in the corresponding dossier. This metabolite is photollytically stable on soil surface.
Degradation of carbofuran seems to be very dependent of the temperature. The rapporteur Member State informed that the applicant had submitted a position paper and a new study to address the

degradation of carbofuran at low temperatures but these reports have still not been evaluated and peer reviewed.

Worst case laboratory half lives were used to calculate PEC soil of benfuracarb. Data from a different applicant in carbofuran dossier show that field worst case half life for carbofuran is 71.9 d in EU sites. Therefore, carbofuran PECs soil were calculated by the rapporteur Member State with this half life. According the conclusion for carbofuran, reliability of this value needs to be further assessed and confirmed.

It was estimated, by the HPLC method, that benfuracarb may be classified as immobile in soil (K_{oc} = 9100 mL / g). Carbofuran may be classified as very high mobile compound (K_{oc} = 17 – 28 mL / g). No data is available with respect the adsorption desorption properties of minor soil metabolites 3-OH-carbofuran and 3-keto-carbofuran.

A lysimeter study is available where two different lysimeters are investigated [with application in beets (furrow) and potatoes (spray)]. Only few samples were analyzed and it was not possible to calculate annual average concentration for individual components. Benfuracarb was found at maximum amounts of 0.25 µg / L and carbofuran at maximum amounts of 0.16 µg / L. A new lysimeter study was required by the rapporteur Member State in the DAR. The meeting of MS experts agreed that the new FOCUS GW modelling required can substitute the requirement for a new lysimeter at this stage.

Hydrolysis of benfuracarb is pH dependent with half lives between less than half hour (pH 4) and 26.9 d (pH 9). The potential contribution of aqueous photolysis to benfuracarb degradation may not be fully established due to the great contribution of hydrolysis at pH (6-7.5) chosen to perform the photolysis sterile study. In the natural water experiment (pH ≈ 7-8) photolysis seems not to contribute significantly to the aqueous degradation of benfuracarb. However, irradiation seems to enhance the degradation of the metabolite carbofuran to carbofuran-7-phenol.

Benfuracarb is not readily biodegradable. The substance was found to have a slightly inhibitory effect on microbial activity.

A study with two water sediment systems is available. Both systems are in the alkaline range (pH_{water} 7.8-8.4). Main compounds found in the water phase are benfuracarb and carbofuran (maximum = 58.26 % AR after 2d). Main compounds found in the sediment phase are carbofuran (maximum = 25.31 % after 14 d) and carbofuran-7-phenol (maximum = 13.6 %). The cumulative amounts of CO_2 at the end of the study accounted for 13.6 % AR and 16.7 % AR. Most of the radioactivity was present as bounded residue to the sediment by the end of the study (73.8 % AR – 75.9 % AR).

Benfuracarb dissipates rapidly in water phase with a half life between 6 h to 15 h. Main dissipation process is transformation to carbofuran. Carbofuran dissipates from water phase with half life between 8.2 d to 27.2 d. Main dissipation process is partitioning into sediment. Whole system and sediment phase half lives had not been calculated. A report with the estimation of the whole system half life is available but not evaluated and peer reviewed. Also the half life in the sediment for carbofuran and carbofuran-7-phenol need to be assessed.

In the carbofuran dossier, 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. 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. These experiments seem to indicate that the degradation of carbofuran may be pH dependent in water sediment systems.

PEC_{SW} of carbofuran has been calculated for a limited number of FOCUS sw scenarios. Calculation of PEC_{SW}, for parent benfuracarb and PEC_{SED} for benfuracarb, carbofuran and carbofuran-7-phenol, need to be performed. Updated FOCUS $PEC_{SW / SED}$ are available but have still not been evaluated and peer reviewed.

PEC gw have been calculated for benfuracarb and carbofuran. Annual average 80th percentiles of benfuracarb were < 0.001 µg / L for all calculated scenarios (7 cabbage spring, 5 cabbage summer). Carbofuran exceed the 0.1 µg / L trigger in 4 of the 7 spring scenarios and in three of the five summer scenarios. In one of the summer scenarios (Hamburg) an 80th percentile annual average of 1.212 µg / L was reached. The applicant was required to address the potential for ground water contamination by the metabolite 3-keto carbofuran. New calculations to address potential groundwater contamination by metabolites 3-OH-carbofuran, carbofuran-7-phenol and 3-keto-carbofuran are available but neither evaluated nor peer reviewed. However, it is noted that these calculations do not take into consideration the longer half lives observed for carbofuran from the data of the second carbofuran applicant.

Concentrations of benfuracarb in the air compartment are expected to be negligible, due to short persistence in the atmosphere.

An addendum to the fate and behaviour chapter has been provided the 18th of May 2006. 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.

Substantial data requirements to address the risk to birds and mammals from uptake of granules, ingestion of treated seedlings and contaminated earthworms were identified by the rapporteur Member State. Further studies were submitted by the applicant. The aquatic risk assessment based on PECsw from drainage resulted in a high acute and chronic risk to fish and aquatic invertebrates in 2 out of 3 scenarios. Based on the peer-reviewed data a high risk to aquatic organisms cannot be excluded. However the new data need to be evaluated before drawing a final conclusion on the risk to aquatic organisms. The risk to bees from exposure to residues in cabbage was assessed as low since cabbage has no flower in the production crop. The potential risk to bees from residues in flowering weeds should be assessed at Member State level taking into account the agricultural practice (management of weeds in cabbage fields). Data requirements were identified in the DAR to address the risk to ground dwelling arthropods, earthworms, soil non-target micro-organisms and other non-target organisms. New data/information was submitted by the applicant. 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.

The risk to biological methods of sewage treatment was assessed as low for the representative use.

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

- Personal as well as respiratory protective equipment is needed for operators (20 ha/day is considered), see 2.12
- The potential risk to bees from residues in flowering volunteer plants should be assessed at Member State level taking into account the agricultural practice (management of weeds in cabbage fields) (refer to point 5.3).

Critical areas of concern

- It is highly toxic via inhalatory exposure. There is reproduction toxic effects observed in the rat and rabbit, ECB has concluded on R62 but not voted.
- The major metabolite carbofuran (30% in rat metabolism studies) is more toxic than benfuracarb (approximately 30 times).
- The estimated operator exposure according to the US PHED model is below (86%) the AOEL only if personal protective equipment as well as respiratory equipment is considered.
- The relevant impurity 1,2 dichloroethane, proposed maximum limit 4 g/kg, is classified as toxic, Carcinogenic Category 2 (T; R45).
- The consumer risk assessment needs to be confirmed pending the results of the outstanding studies (data gaps). A preliminary assessment indicates a potential acute exposure concern for carbofuran residues (resulting from the use of benfuracarb) for adults and toddlers by applying the LOQ achieved in the currently available residue trials in the consumer intake estimates. However, residues of the metabolite carbofuran in groundwater contributing to the total consumer exposure via drinking water have to be considered.
- Potential for groundwater contamination under vulnerable situations by benfuracarb metabolite carbofuran. Potential groundwater contamination by other metabolites not fully addressed.
- 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 and for bees. For all other groups of organisms it was not possible to exclude a high risk on the basis of the peer reviewed data. The applicant 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 18 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

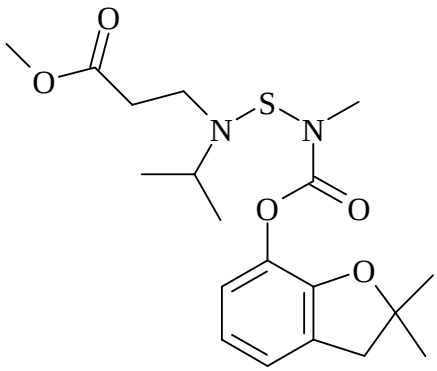
Active substance (ISO Common Name) ‡	Benfuracarb
Function (e.g. fungicide)	Insecticide, nematicide

Rapporteur Member State	Belgium
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	Ethyl N-[2,3-dihydro-2,2-dimethylbenzofuran-7-yloxycarbonyl(methyl)aminothio]-N-isopropyl-β-alaninate
Chemical name (CA) ‡	Eethyl *N*-[[[[(2,3-dihydro-2,2-dimethyl-7-benzofuranyl)oxy]carbonyl]methylamino] thio]-*N*-(1-methylethyl)-β-alaninate
CIPAC No ‡	501
CAS No ‡	82560-54-1
EEC No (EINECS or ELINCS) ‡	Not assigned
FAO Specification ‡ (including year of publication)	Not available
Minimum purity of the active substance as manufactured ‡ (g/kg)	930 g/kg (commercial plant)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	1,2-dichloroethane (EDC) - max. 4 g/kg
Molecular formula ‡	$C_{20}H_{30}N_2O_5S$
Molecular mass ‡	410.5

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

Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	No freezing point/freezing range can be determined (98.1%)
Boiling point (state purity) ‡	No boiling point below 190 °C (98.7%)
Temperature of decomposition	Thermal decomposition above 200 °C (98.7%)
Appearance (state purity) ‡	Pale yellow, slightly viscous oil; no characteristic odour (98.7%)
Relative density (state purity) ‡	D_4^{20} = 1.15 (98.7%)
Surface tension	52.4 mN/m at 20 °C (90% saturated solution)
Vapour pressure (in Pa, state temperature) ‡	4.2 x 10^{-6} Pa at 25 °C
Henry's law constant (Pa m^3 mol^{-1}) ‡	2.1x 10^{-4} $Pa.m^3.mol^{-1}$ at 20 - 25 °C
Solubility in water ‡ (g/L or mg/L, state temperature)	pH 4, 20 °C: ca 8 mg/L (no accurate measurement due to hydrolytical instability)
	pH 7, 20 °C: 8.4 mg/L
	pH 10, 20 °C: 8.4 mg/L
Solubility in organic solvents ‡ (in g/L or mg/L, state temperature)	Solubility at 20 °C (g/L) hexane > 1000 xylene > 1000 dichloromethane > 1000 ethanol > 1000 acetone > 1000 ethyl acetate > 1000
Partition co-efficient (log POW) ‡ (state pH and temperature)	<u>Determined value :</u> pH ≈ 6.3, 25 °C: 4.22 no effect of pH <u>calculated values :</u> 4.37 (ClogP software) 4.06 (EPISUITE model, version 3.11)

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

Hydrolytic stability (DT50) ‡ (state pH and temperature)	pH 4, 20 °C : DT_{50} < 0.5 hr
	pH 7, 20 °C : DT_{50} = 1.4 d
	pH 9, 20 °C : DT_{50} = 26.9 d
Dissociation constant ‡	Not applicable (no dissociation in water)
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	<u>In neutral methanol:</u> λ_{max} 277.5 - 281.5 nm; ε = 3.36 x 10^3 $L.mol^{-1}.cm^{-1}$ at λ 290 nm : ε = 6.14 x 10^2 $L.mol^{-1}.cm^{-1}$ <u>in acidic and basic methanol:</u> no significant difference in spectra
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	Purified water (pH ≈ 6-7.5, 25 °C): DT_{50} = 31.5 hrs
Quantum yield of direct phototransformation in water at λ > 290 nm ‡	ϕ = 0.106
Flammability ‡	Flash point = 154.5 °C auto-ignition temperature = 370 °C
Explosive properties ‡	No explosive properties

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

List of representative uses evaluated*

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)	number min max (k)	interval between applications (min)	kg as/hl min max	water L/ha min max	kg as/ha min max	(l)	(m)
Brassicas	EU-Member States	ONCOL 8.6G	F	*Plutella xylostella* and *Brevicoryne brassicae* (= cabbage root fly)	GR	86 g/kg	**	pre-plantation	1	Not applicable	Not applicable	Not applicable	1.0	Not applicable	** Apply the granules on the planting row with micro granule applicator [1]

[1] The risk assessment has revealed a data gap(s) and/or a risk (exceedance of relevant threshold) in sections 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)	All abbreviations used must be explained	(l)	PHI - minimum pre-harvest interval
	(g)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(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)	CIPAC Method 501/TC/(M)/3: HPLC-UV (ISTD)
Impurities in technical as (principle of method)	HPLC-UV 1,2-dichloroethane by GC-MS
Plant protection product (principle of method)	HPLC-UV; CIPAC Method 501/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)	GC-NPD, conf. by LC-MS (benfuracarb, carbofuran, 3-hydroxy carbofuran) LOQ = 0.05 mg/kg (benfuracarb, 3-hydroxy carbofuran, (for each analyte), 0.01 mg/kg (carbofuran) (brassicas)
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required (no-MRLs proposed)
Soil (principle of method and LOQ)	LC-MS/MS (carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol); LOQ = 0.01 mg/kg *Depending on the final residue definition for soil, additional methodology may be required.*
Water (principle of method and LOQ)	GC-MS (benfuracarb) and LC-MS/MS (carbofuran, carbofuran-7-phenol); LOQ = 0.1 µg/L (surface water; for each analyte) *Depending on the final residue definition for ground water, additional methodology may be required.*
Air (principle of method and LOQ)	Not required (vapour pressure is very low and 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)	LC-MS/MS (carbofuran); LOQ = 50 µg/L (fluids), 0.1 mg/kg (tissues)

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 ‡	Relatively rapid, 70-81% based on levels in urine within 144 h (rats, 6.7 or 40 mg/kg bw)
Distribution ‡	Large, highest level in excretory organs and carcass
Potential for accumulation ‡	No evidence of accumulation
Rate and extent of excretion ‡	Extensively excreted, 70-80% in urines; 13-26% in faeces within 48h
Metabolism in animals ‡	Extensive; Benfuracarb breaks down to carbofuran, which is further hydroxylated/oxidated into 3-ketofuran-7-phenol, 3-hydroxycarbofuran, 3-hydroxycarbofuran-7-phenol, carbofuran phenol
Toxicologically significant compounds ‡ (animals, plants and environment)	Benfuracarb and metabolites with the carbamate moiety, such as carbofuran

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	205 mg/kg bw	**Xn; R22**
Rat LD_{50} dermal ‡	>2000 mg/kg bw	
Rat LC_{50} inhalation ‡	0.344 mg/L	**T; R23**
Skin irritation ‡	Non- irritant	
Eye irritation ‡	Non- irritant	
Skin sensitization ‡ (test method used and result)	Non- sensitizer (M&K test)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Clinical signs of neurotoxicity, inhibition of acetyl cholinesterase, thymus involution (dogs)
Lowest relevant oral NOAEL / NOEL ‡	Overall: 1 mg/kg bw/d (13-week ; 6 month and 12-24 month dog)
Lowest relevant dermal NOAEL / NOEL ‡	5 mg/kg bw/d (28 day, rat)
Lowest relevant inhalation NOAEL / NOEL ‡	Not relevant

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

Genotoxicity ‡ (Annex IIA, point 5.4)

……	Negative *in vitro* and *in vivo*

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

Target/critical effect ‡	Clinical signs of neurotoxicity, acetylcholinesterase inhibition (rat)
Lowest relevant NOAEL / NOEL ‡	5.5 mg/kg bw/day, 104 week, rat
Carcinogenicity ‡	No carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Reduced pregnancy rate and male fertility indices, reduced pup survival **R62?**
Lowest relevant reproductive NOAEL / NOEL ‡	Parental, reproductive and embryotoxic: 1.2 mg/kg bw/day
Developmental target / critical effect ‡	Delayed or incomplete ossification and delayed fetal weight (rat). Reduced fetal weight and abortions (rabbit)
Lowest relevant developmental NOAEL / NOEL ‡	Rabbit: Developmental: 10 mg/kg bw/day Maternal : 15 mg/kg bw/day Rat: Developmental: 10 mg/kg bw/day Maternal : 2 mg/kg bw/day

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

Delayed neurotoxicity	No delayed neuropathy in hens LD50 92 mg/kg bw
Short term toxicity	1.81 mg/kg bw/day, 28 day rat

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

Other toxicological studies ‡ (Annex IIA, point 5.8)

Metabolites

The information presented on carbofuran and other metabolites was agreed on in the context of the assessment of the active substance carbofuran. Further details are given in the EFSA conclusion on carbofuran.

Carbofuran[11] Acute toxicity	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 (carbofuran)	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 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
Genotoxicity (carbofuran)	Positive results in bacterial tests; Negative in *in vivo* tests
Long term toxicity and carcinogenicity (carbofuran)	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

[11] It should be noted that the applicant for benfuracarb has access to the carbofuran dossier from Dianica.

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

Reproductive toxicity (carbofuran)	Reproduction target / critical effect Reduced litter parameters in rat multigeneration study 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 Rat: Developmental: 1 mg/kg bw/day Maternal: 0.1 mg/kg bw/day Rabbit: Developmental and maternal: 0.5 mg/kg bw/day
Neurotoxicity / delayed neurotoxicity (carbofuran)	Delayed neurotoxicity No delayed neuropathy in hens NOAEL neurotoxicity 0.5 mg/kg bw Subchronic neurotoxicity test 3.2 mg/kg bw/day, 13-week rat
Other toxicological studies (carbofuran)	Mechanistic study AChE inhibition: no difference in sensitivity to AChE inhibition with age.
ADI[12] (carbofuran)	0.001 mg/kg bw/d (1-year dog study, SF: 100)
AOEL[12] (carbofuran)	0.001 mg/kg bw/d (1-year dog study, SF: 100)
ARfD[12] (carbofuran)	0.001 mg/kg bw/d (Developmental rat study, maternal toxicity, SF: 100)
3-OH-carbofuran:	LD_{50} oral: 8.3 mg/kg bw Positive in Ames test strain TA1537 with S9 mix Positive in TK locus in L5178Y mouse lymphoma cells with and w/o S9 mix **T+, R28**
3-OH-7-phenol:	LD_{50} oral: 1654 mg/kg bw **Xn, R22**
3-keto-7-phenol:	LD_{50} oral: > 800 mg/kg bw **Xn, R22**

[12] Values and SF are provisional, might be confirmed pending vote of ECB

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

Carbofuran 7-phenol:	LD_{50} oral: 1743 mg/kg bw negative in Ames test **Xn, R22**

Medical data ‡ (Annex IIA, point 5.9)

……..	Medical examination of workers participating in the manufacturing process of benfuracarb did not display any adverse signs or symptoms.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/day	Overall NOAEL in dogs, 2 generation rat studies	100
AOEL ‡	0.01 mg/kg bw/day	Overall NOAEL in dogs, 2 generation rat studies	100
ARfD ‡ (acute reference dose)	0.02 mg/kg bw/day	28 day, rat neurotoxicity study	100

Dermal absorption (Annex IIIA, point 7.3)

Oncol 8.6G	No studies are available. Default value of 100% based on physical chemical properties applied.

Acceptable exposure scenarios (including method of calculation)

Operator	Estimated exposure (% of the AOEL) is performed with the PHED model. The maximum application rate is 1 kg/ha, work rate 20 ha/day and body weight 60 kg.		
		PPE (gloves)	PPE+RPE
	75^{th} percentile	148%	86%
	95^{th} percentile	371%	235%
Workers	Soil incorporation: no worker exposure		
Bystanders	Soil incorporation : no exposure		

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T; Toxic R22 Harmful if swallowed R23 Toxic by inhalation R62? Possible risk of impaired fertility (category 3) **EFSA note:** Benfuracarb has been discussed at ECB and R62 was concluded in November, 2005, but is not yet 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	Cotton, bush beans, maize, potatoes, apples (foliar application) cabbage, sugar beet (soil application)
Rotational crops	No data available
Plant residue definition for monitoring	-Benfuracarb, -Carbofuran (sum of Carbofuran + 3-OH-carbofuran expressed as carbofuran equivalents). (these residue definitions will be re-considered after evaluation of the metabolism studies provided).
Plant residue definition for risk assessment	-Benfuracarb, carbofuran and 3-OH-carbofuran. (these residue definitions will be re-considered after evaluation of the metabolism studies provided).
Conversion factor (monitoring to risk assessment)	To be reconsidered after confirmation of residue definitions.

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

Animals covered	Lactating goats
Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor (monitoring to risk assessment)	-
Metabolism in rat and ruminant similar (yes/no)	Yes.
Fat soluble residue: (yes/no)	Yes.

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

	Benfuracarb is degraded very rapidly (DT_{90} value is 3 days max. in laboratory studies). Residues in succeeding crops still to be addressed in terms of soil metabolites of benfuracarb

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

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

No raw data were provided *New data required*

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: Yes*	Poultry: no	Pig: No
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-	-	-
Eggs	-	-	-

*: No ruminant feeding study was provided and was not required even if the first criterion to require a feeding study was fulfilled (significant residues ≥ 0.1 mg/kg of total diet – occurred in the crops fed to animals). In fact, the metabolism study in lactating goats demonstrated that no significant residues (<0.01 mg/kg) could occur in milk and edible tissues taking into account the residue levels in the potential feedingstuffs obtained at the 1 x dose rate.

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

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

Crop	Northern or Southern Region	Trials results relevant to the critical GAP (a)	Recommendation / comments	MRL	STMR (b)
Cauliflower	NE	*Benfuracarb :* <0.05, <0.05, <0.05, <0.04, <0.04, <0.04, <0.04 mg/kg *Carbofuran + 3-OH-carbofuran expressed as carbofuran equivalents:* <0.06, <0.06, <0.06, <0.06, <0.06, <0.06, <0.06 mg/kg.	Trials performed in accordance with the critical GAP.	*Benfuracarb*: 0.05* *Carbofuran + 3-OH-carbofuran expressed as carbofuran*: 0.1*.	*Benfuracarb*: 0.05* *Carbofuran + 3-OH-carbofuran expressed as carbofuran*: 0.1*.
	SE	No trial provided.			
Broccoli	NE	*Benfuracarb :* <0.05 mg/kg *Carbofuran + 3-OH-carbofuran expressed as carbofuran equivalents:* <0.06 mg/kg.		-	-
	SE	No trial provided.			
Head cabbage	NE	Findings : *Benfuracarb :* <0.05, <0.04, <0.04, <0.04, <0.04 mg/kg *Carbofuran + 3-OH-carbofuran expressed as carbofuran equivalents:* <0.06, <0.06, <0.06, <0.06, <0.06 mg/kg.		*Benfuracarb*: 0.05* *Carbofuran + 3-OH-carbofuran expressed as carbofuran*: 0.1*.	*Benfuracarb*: 0.05* *Carbofuran +3-OH-carbofuran expressed as carbofuran*: 0.1*.
	SE	*Benfuracarb :* <0.05, <0.05, <0.05 mg/kg *Carbofuran + 3-OH-carbofuran expressed as carbofuran equivalents:* <0.06, <0.06, <0.06 mg/kg.			
No residue data base provided for leafy brassica and kohlrabi. Remarks : -The data base set is incomplete both for the flowering brassica and head cabbage. -Provisional MRLs are proposed for flowering brassica and head brassica (according to EU guidance doc.7525/VI/95-rev.7-Table 4)					

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

(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 (Annex IIA, point 6.9, Annex IIIA, point 8.8)

a)Benfuracarb

ADI	0.01mg/kg bw/day
TMDI (% ADI)	0.35 % (WHO European diet) 0.76 % (German model) 1.39 % and 3.25 % respectively for children and infants from UK. (Pesticides Safety Directorate Consumer Exposure Model).
IEDI (European Diet) (% ADI)	-
Factors included in NEDI	-
ARfD	0.02 mg/kg bw/day
Acute exposure (% ARfD)	UK PSD model: Adults / toddlers Cauliflower [1)]: 6.2 % / 8.3 % Broccoli [1)]: 1.8 % / 4.0 % Cabbage : 3.4 % / 4.4 % Brussels sprouts : 1.1 % / 2.0 %
	New IESTI calculations provided by RMS in Addendum Feb. 2006 (not peer reviewed) WHO IESTI model: Adults / children Cauliflower: 10 % / 20 % Broccoli: 4% / 10 % Cabbages, head: 5% / 10 % Brussels sprouts: 2% / 3 %

[1)] Calculation was performed with variability factor of 3 instead of 5.

b)Carbofuran + 3-OH-carbofuran expressed as carbofuran equivalents

ADI	0.001 mg/kg bw/day
TMDI (% ADI)[4)]	7.0 % (WHO European diet) 15.3 % (German model) 27.8 % and 64.9 % respectively for children and infants from UK. (Pesticides Safety Directorate Consumer Exposure Model).
IEDI ((European Diet) (% ADI)	-
Factors included in NEDI	-
ARfD	0.001mg/kg bw/day

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

Acute exposure (% ARfD)[4)]

	UK PSD model:	
	Adults	Toddlers
Cauliflower [1)] :	148.6 %	198.6 %
Broccoli [1)]:	43.5 %	96.7 %
Cabbage :	81.7 %	106.8 %
Brussels sprouts :	27.3 %	47.5 %
New IESTI calculations provided by RMS in Addendum Feb. 2006 (not peer reviewed)		
	WHO IESTI model:	
	Adults	children
Cauliflower :	250 %	370 %
Broccoli:	90%	310% [2)] /330 % [3)]
Cabbages, head:	120%	280 %
Brussels sprouts:	40%	80 %

[1)] Calculation was performed with variability factor of 3 instead of 5.
[2)] Calculated with large portion USA and unit weight data from Japan
[3)] Calculated with large portion from USA and unit weight data from USA
[4)] Carbofuran residues in groundwater used as drinking water were not considered.

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

Not required.

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

Expression of the residue	**Crops**	**MRLs (mg/kg)**
Benfuracarb	Flowering and head brassica	0.05*
Carbofuran (Carbofuran + 3-OH-carbofuran expressed as Carbofuran equivalents)		0.1*
These are provisional MRLs as the databases covering Northern and Southern EU are incomplete for both flowering and head brassica. No MRL can be proposed for leafy brassica and kohlrabi as no residue trials have been presented.		

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

Appendix 1.5: Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	27.7-66.6% % after 120 d, [^{14}C-ring]-label (n= 4)
Non-extractable residues after 100 days ‡	37.6-74.1% after 120 d, [^{14}C-ring]-label (n= 4)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	Carbofuran: max level of 84.6 % at *2* d [^{14}C-ring]-label (n= 4) Metabolite M VIII: max level of 16.7 % at 1 d, [^{14}C-ring]-label (n= 4). This single peak represented 3 individual metabolites (A = desmethyl-benfuracarb ?, B = not determined, C = reaction product between carbofuran and a natural soil compound) *Degradation under alkaline soils needs to be addressed.*

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

Mineralization after 100 days ‡	26.9-66.3% after 120 d, [^{14}C-ring]-label (n= 4)
Non-extractable residues after 100 days ‡	23.9-57.7% after 120 d, [^{14}C-ring]-label (n= 4)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	*EPCO 31 agreed that 3-OH-carbofuran and 3-keto-carbofuran need to be further assessed as carbofuran metabolites containing the active carbamate moiety.*

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

Anaerobic degradation ‡	Benfuracarb: not required Carbofuran: Mineralisation 2.4-6.1 % after 120 d Non-extractable residues 56.4-62.7% after 120 d Major metabolite: 7-phenol, max level of 62.9 % at 28 d Minor metabolites: M4 (was shown to be highly polar and to contain several fractions), M9, M11 and M12. [^{14}C-ring]-label

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

Soil photolysis ‡	Benfuracarb: no data available. Carbofuran: photolytically stable on soil surface. No photodegradation product.

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

Method of calculation	Laboratory: first order kinetics *Degradation under alkaline soils needs to be addressed.*
Laboratory studies ‡ (range or median, with n value, with r^2 value)	Benfuracarb: DT_{50lab} (20°C, aerobic): 0.23-0.83 d, mean 0.52 d (n= 4, r^2 = 0.824-0.998) Carbofuran: DT_{50lab} (20°C, aerobic): 6.1-19.4 d, mean 12.94 d (n= 8, r^2 = 0.9524-0.999) (based on two studies that were performed with benfuracarb and carbofuran as test substance) Longer DT_{50} (175 – 444 d) are obtained in the studies submitted by another notifier of the carbofuran dossier. Further clarification on the high differences observed form different sources has been required during the peer review of carbofuran DAR. Overall geometric mean carbofuran DT_{50}: 29.28 d
	Benfuracarb: DT_{90lab} (20°C, aerobic): 0.78-2.8 d, mean 1.76 d (n= 4, r^2 = 0.824-0.998) Carbofuran: DT_{90lab} (20°C, aerobic): 20-64.7 d, mean 42.95 d (n= 8, r^2 = 0.9524-0.999) (based on two studies that were performed with benfuracarb and carbofuran as test substance). Much longer DT_{90} may be expected form the studies provided by the other carbofuran applicant.
	Benfuracarb: not required Carbofuran: DT_{50lab} (10°C, aerobic): 110 d (n= 1, r^2 = 0.9993) Clarification on the effect of temperature on the rate of degradation required.
	Benfuracarb: not required Carbofuran: DT_{50lab} (20°C, anaerobic): 7.6 d (n= 1, r^2 = 0.99318)

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

	degradation in the saturated zone: not required
Field studies ‡ (state location, range or median with n value)	DT_{50f}: not required for benfuracarb. Field dissipation studies from a different applicant are available in the carbofuran dossier. Carbofuran field DT_{50} = 71.9 d (employed for PEC soil calculation in carbofuran and carbosulfan dossiers)
	DT_{90f}: not required for benfuracarb. Data from a different applicant available in the carbofuran dossier.
Soil accumulation and plateau concentration ‡	Not required

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡	Benfuracarb: log K_{oc} = 3.96; K_{oc} = 9.1 * 10^3 (by HPLC method) Koc carbofuran: 17-28 mL/g , (mean 22, $^1/_n$= 0.92-1.01, 4 soils) Kd carbofuran: 0.299-0.549 (0.432, n = 4) No data available for minor carbofuran soil metabolites 3-OH-carbofuran and 3-keto-carbofuran.
pH dependence ‡ (yes / no) (if yes type of dependence)	No pH dependence

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

Column leaching ‡	No data available
Aged residues leaching ‡	No data available
Lysimeter/ field leaching studies ‡	BBA guideline, outdoor lysimeter study performed in Hamburg, Germany. The soil was a light sandy loam Crop : 1st year, beets; 2nd year, potato, 3rd year, wheat Lysimeter 1: 1st year, furrow appl. of 1290 g a.s./ha Lysimeter 2 : 1st year, furrow appl. of 1290 g a.s./ha 2nd year, spray appl. of 411 g a.s./ha Precipitation (mm): 1012 mm/year Time period (d): 1200 d

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

	Mean annual concentration in the leachate: 1.3-2.5 µg a.s. equivalent /L Benfuracarb and carbofuran transiently leached at level above 0.1 µg/L. Due to the short number of samples it is not possible to calculate annual average concentrations. Radioactivity mainly in upper soil layer, due to the mode of application, the radioactivity is not distributed homogeneously

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	DT_{50} (benfuracarb): 0.83 days Kinetics: 1st order worst case lab DT_{50}
Application rate	Crop: brassicas 0% plant interception: granular application in the sowing bed, soil layer: 5 cm, soil density : 1.5 kg/dm^3 Number of applications: 1 Application rate(s): 1000 g a.s./ha

$PEC_{(s)}$ (mg/kg)	Single application Actual (mg/kg soil)	Single application Time weighted average (mg/kg soil)	Multiple application Actual (mg/kg soil)	Multiple application Time weighted average (mg/kg soil)
Initial	1.333	1.333	-	-
Short term 24h	0.578	0.904	-	-
2d	0.250	0.648		
4d	0.047	0.385		
Long term 7d	0.004	0.227	-	-
28d	> 0.001	0.057		
50d	> 0.001	0.031		
100d	> 0.001	0.015		

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

Metabolite

Method of calculation	DT_{50} (carbofuran): 71.9 days Kinetics: 1st order worst case field DT_{50} (EU sites worst case FMC study)
Application rate	Crop: brassicas 0% plant interception: granular application in the sowing bed, soil layer: 5 cm, soil density :1.5 kg/dm^3 Number of applications: 1 Application rate(s): 540 g/ha (assumed carbofuran is formed at a maximum of 100% of the applied dose, molecular mass of benfuracarb is 410.5; molecular mass of carbofuran is 221.3)

$PEC_{(s)}$ (mg/kg)	Single application Actual (mg/kg soil)	Single application Time weighted average (mg/kg soil)	Multiple application Actual (mg/kg soil)	Multiple application Time weighted average (mg/kg soil)
Initial	0.720	0.720	-	-
Short term 24h	0.713	0.717	-	-
2d	0.706	0.713		
4d	0.693	0.706		
Long term 7d	0.673	0.696	-	-
28d	0.550	0.631		
50d	0.445	0.571		
100d	0.275	0.462		

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	pH 4: 20°C DT_{50} <0.5 hr (1st order) carbofuran: 100 %AR (0.5 hr) Carbofuran: pH 5: hydrolytically stable

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

	pH 7: 20°C DT_{50} 1.4 d (1st order) carbofuran: max 73.9% AR (15 d) Metabolite MI: 36.6% AR (30 d) carbofuran : pH 7, 25°C : DT_{50} = 45.7 d (1st order) carbofuran-phenol or 7-phenol: 55.6 % AR (51 d)
	pH 9: 20°C DT_{50} 26.9 d (1st order) carbofuran: max 16.6 %AR (30 d) 3 unknown (groups of) metabolites : M I (up to 28.2% after 30 d) (possibly desethyl benfuracarb and carbofuran-phenol) M III (max. 13.8% after 23 d, unstable under lab cond.) M IV (observed only after 30 d at 10.5%, artefact) desethyl benfuracarb and carbofuran-phenol present at pH 7 and 9 carbofuran: pH 9, 25°C : DT_{50} = 0.1 d (1st order) carbofuran-phenol or 7-phenol : 98.3% AR (5 d)
Photolytic degradation of active substance and relevant metabolites ‡	Xenon light source with UV filter, continuous irradiation DT_{50} 15.6 days (irradiated, river water) DT_{50} 4.7 days (dark, river water) DT_{50} 15.3 hr (irradiated, purified water) DT_{50} 30.4 hr (dark, purified water) The potential contribution of aqueous photolysis to benfuracarb degradation may not be fully established due to the great contribution of hydrolysis at pH (6-7.5) chosen to perform the photolysis sterile study. Major degradates river water: carbofuran (27.6% after 20 d) and carbofuran-phenol (19.7% after 20 d) in irradiated samples; carbofuran (91.7% after 20 d) in dark controls purified water: carbofuran (93.6% after 72 hrs in irradiated samples; 80.1% after 72 hrs in dark controls)

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

	carbofuran: Xenon arc lamp with UV filter cut, DT_{50} : 33 days No major metabolite Estimated DT_{50} at 50°N : 108 days
Readily biodegradable (yes/no)	Not readily biodegradable
Degradation in water/sediment - DT_{50} water ‡	DT_{50} (benfuracarb, water): not available due to rapid dissipation to sediment and conversion to carbofuran
- DT_{90} water ‡	
- DT_{50} whole system ‡	DT_{50} (benfuracarb, whole system): 6-15 h (kinetics not given, n= 2)
- DT_{90} whole system ‡	DT_{90} (benfuracarb, whole system): 3-5 d (n= 2)
Mineralization	17-25 % AR (at 59-103 d, study end, n= 2)
Non-extractable residues	70-80% AR (at 59-103 d, study end, n= 2)
Distribution in water / sediment systems (active substance) ‡	Carbofuran: max of 25-20 % AR at day 14-2 DT_{50} (carbofuran, whole system): 8.2-27.2 d (1^{st} order, r^2= 0.9948-0.9901, n= 2) DT_{90} (carbofuran, whole system): 10.8-35.8 d (1^{st} order, r^2= 0.9948-0.9901, n= 2) Carbofuran-7-phenol: max of 14% AR at day 14 (in one test system). *Degradation data for the metabolite may need to be required.*
Distribution in water / sediment systems (metabolites) ‡	Carbofuran: max of 46-58 % AR at day 6-2
Degradation in water/sediment - DT_{50} water ‡	DT_{50} (carbofuran, water): not available due to rapid dissipation to sediment (estimated to be between 8.2 and 27.2 d)
- DT_{50} whole system ‡	No data available, *data required*
- DT_{90} whole system ‡	No data available, *data required*

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

Calculation of PEC_{SW} for parent benfuracarb and PEC_{SED} for benfuracarb, carbofuran and carbofuran-7-phenol has been required.

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

Parent

Method of calculation	Focus-Macro calculation (application every year) DT_{50} (carbofuran): 19.4 days Kinetics: 1st order worst case lab DT_{50} Koc carbofuran: 22 mL/g, $^1/_n$= 0.92-1.01 DT_{50} (carbofuran, sediment): 27.2 days Kinetics: 1st order worst case w/s DT_{50} carbofuran is not present in the water phase
Application rate	Crop: brassicas 0% plant interception: granular application in the sowing bed, Number of applications: 1 Application rate(s): 540 g/ha (assumed carbofuran is formed at a maximum of 100% of the applied dose, molecular mass of benfuracarb is 410.5; molecular mass of carbofuran is 221.3)
Main routes of entry	Drainage (D3, D4 and D6 Focus scenarios)

$PEC_{(sw)}$

Crop	**Focus scenario**	**Scenarios characteristics**	**Max drain flow concentration (µg/L) carbofuran**	**Background level (µg/L) carbofuran**
Cabbage	D3 (mainly present in Northern Belgium, Netherlands)	747 mm/year, sand drained at 1.75 m with 76 m spacing	0.195 µg/L	0.195 µg/L
Cabbage	D4 (mainly present in UK, Germany, Poland, Denmark, Italy, Belgium, Netherlands)	659 mm/year, loam over sandy loam drained at 1.2m with 100 m spacing	4.18 µg/L	1.5 µg/L
Cabbage	D6 (mainly present in Mediterranean countries)	683 mm/year, clay loam over clay drained at 1 m with 8m spacing	38.7µg/L	5 µg/L

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

PEC (sediment)

Data required.

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

Results need to be revised with the mean carbofuran half life taking into consideration all the available data (overall geometric mean for carbofuran : 29.28 d). Potential groundwater contamination by metabolite 3-OH-carbofuran and 3-keto-carbofuran needs to be addressed.

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS-PEARL version 1.1.1 Scenarios: Chateaudun, Hamburg, Jokioinen, Kremsmünster, Porto, Sevilla, Thiva Crop: cabbage Mean DT_{50} (lab, benfuracarb): 0.44 d (normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). Mean K_{foc} (benfuracarb): 9100 mL/g, Kom = 5278 mL/g, $^1/_n$= 0.9 (default). Mean DT_{50} (lab, carbofuran): 11.5 d (normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). Mean K_{foc} (carbofuran): 22 mL/g, Kom = 12.8 mL/g, $^1/_n$= 0.96 (default).
Application rate	Application rate: 1000 g a.s./ha. No. of applications: 1 (incorporation at 1.5 cm, at planting) Time of application: spring and summer

$PEC_{(gw)}$

Maximum concentration	-
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Annual average concentrations (80th percentile) according to FOCUS guidance: benfuracarb: 0.000 µg/L (for all the scenarios) carbofuran: 0.168 to 1.212, median : 0.248 µg/L for North European scenarios 0.002 to 0.071, median : 0.009 µg/L for South European scenarios (see detailed results in table below)

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

PEC(gw) - FOCUS modelling results

Focus scenario		Annual average concentrations (80th percentile) (µg/L)	
Crop	location	Benfuracarb	Carbofuran
Cabbage (spring)	Chateaudun	0.000	0.214
	Hamburg	0.000	0.248
	Jokioinen	0.000	0.208
	Kremsmünster	0.000	0.249
	Porto	0.000	0.002
	Sevilla	0.000	0.009
	Thiva	0.000	0.052
Cabbage (summer)	Chateaudun	0.000	0.168
	Hamburg	0.000	1.212
	Kremsmünster	0.000	0.642
	Porto	0.000	0.071
	Sevilla	0.000	0.002

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

Direct photolysis in air ‡	No data available, not required
Quantum yield of direct phototransformation	No data available, not required
Photochemical oxidative degradation in air ‡	Atkinson method : overall OH rate constant K_{OH} = 1.589 x 10^{-10} cm^3/molecule.sec → estimated lifetime in atmosphere = 3.5 hr or 0.15 d (using global OH-concentration of 5.0 x 10^5 OH radicals/cm^3)
Volatilization ‡	From plant surfaces: Not required from soil: Not required

PEC (air)

Method of calculation	Not required

$PEC_{(a)}$

Maximum concentration	Not required

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

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	**Soil** Definitions for risk assessment: benfuracarb, carbofuran, 3-OH-carbofuran, 3-keto-carbofuran. Definitions for monitoring: benfuracarb, carbofuran, 3-keto-carbofuran (assessment needs to be finalized). **Water** **Ground water** Definitions for exposure assessment: benfuracarb, carbofuran, 3-OH-carbofuran, 3-keto-carbofuran. Definitions for monitoring: benfuracarb, carbofuran may be confirmed as components of the monitoring residue definition for ground water. Assessment of metabolites 3-keto-carbofuran and 3-OH-carbofuran needs to be finalized. **Surface water** Definitions for risk assessment: benfuracarb (only water phase), carbofuran (water and sediment), Carbofuran-7-phenol (only in sediment), Definitions for monitoring: benfuracarb (only water phase), carbofuran (water and sediment) **Air** Definitions for risk assessment: benfuracarb, carbofuran. Definitions for monitoring: benfuracarb, carbofuran.

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

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R 53 May cause long-term adverse effect 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 of Benfuracarb on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Acute toxicity to mammals ‡ Reproductive toxicity to mammals ‡	LD_{50} (rat) = 205 mg a.s./kg b.w. NOAEL (rat) = 1.2 mg a.s./kg b.w./day
Acute toxicity to birds ‡	LD_{50} (*Anas platyrhynchos*) = 19.8 mg a.s./kg b.w.
Dietary toxicity to birds ‡	LC_{50} (*Anas platyrhynchos*) = 15 mg a.s./kg b.w./day
Reproductive toxicity to birds ‡	NOEC (*Colinus virginianus*) = 8.93 mg a.s./kg b.w./day

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

Acute toxicity to mammals ‡ Reproductive toxicity to mammals ‡	LD_{50} (rat) = 5.3 – 5.6 mg Carbofuran/kg b.w. NOAEL (rat) = 0.1 mg Carbofuran/kg b.w./day
Acute toxicity to birds ‡	LD_{50} (*Anas platyrhynchos*) = 0.76 mg Carbofuran/kg b.w.
Dietary toxicity to birds ‡	LC_{50} (*Anas platyrhynchos*) = 10 mg Carbofuran/kg b.w./day
Reproductive toxicity to birds ‡	Not available.

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}, LC_{50} and NOEC of Benfuracarb 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}	54	180	720	1800
Dietary LC_{50}	41	136	545	1364
Reproductive NOEC	24	81	325	812

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

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

Time scale	TER for a 15 g bird
Acute exposure	84
Short term exposure	1111

LD_{50} and NOAEL of Benfuracarb 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}	373	932	3727
Two generation NOAEL	2	5	22

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
Long 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*	Benfuracarb	96 h semi-static	LC_{50}	0.017 mg a.s./L
‡ *Daphnia magna*	Benfuracarb	48 h static	EC_{50}	0.0099 mg a.s./L
‡ *Selenastrum capricornutum*	Benfuracarb	72 h static	EC_{50}	> 2.2 mg a.s./L
‡ *Chironomus riparius*	Benfuracarb	28 d static	EC_{50} NOEC	0.0041 mg a.s./L 0.001 mg a.s./L
‡ *Lepomis macrochirus*	Carbofuran	96 h semi-static	**LC_{50}**	**0.18 mg carbofuran/L**
‡ *Oncorhynchus mykiss*	Carbofuran	28 d fish juvenile growth test	**NOEC**	**< 0.0087 mg carbofuran/L**
‡ *Daphnia magna*	Carbofuran	48 h static	**EC_{50}**	**0.0094 mg carbofuran/L**
‡ *Daphnia magna*	Carbofuran	21 d semi-static	**NOEC**	**0.008 mg carbofuran/L**

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/L)
Laboratory tests ‡				
‡ *Selenastrum capricornutum*	Carbofuran	72 h static	**E_bC_{50}** **E_rC_{50}**	**6.5 mg carbofuran/L** **19 mg carbofuran/L**
‡ *Lepomis macrochirus*	7-phenol	96 h semi-static	LC_{50}	75 mg 7-phenol/L
‡ *Daphnia magna*	7-phenol	48 h static	EC_{50}	25 mg 7-phenol/L
‡ *Selenastrum capricornutum*	7-phenol	72 h static	E_bC_{50} E_rC_{50}	63 mg 7-phenol/L > 100 mg 7-phenol/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
1 kg a.s./ha	Cabbage Scenario D3	*Lepomis macrochirus*	acute	-	923	100
		Daphnia magna	acute	-	482	100
		Selenastrum capricornutum	acute	-	33333	10
		Oncorhynchus mykiss	chronic	-	< 45	10
		Daphnia magna	chronic	-	41	10
1 kg a.s./ha	Cabbage Scenario D4	*Lepomis macrochirus*	acute	-	43	100
		Daphnia magna	acute	-	2.2	100
		Selenastrum capricornutum	acute	-	1555	10
		Oncorhynchus mykiss	chronic	-	< 5.8	10
		Daphnia magna	chronic	-	5.3	10
1 kg a.s./ha	Cabbage Scenario D5	*Lepomis macrochirus*	acute	-	4.7	100
		Daphnia magna	acute	-	0.24	100
		Selenastrum capricornutum	acute	-	168	10
		Oncorhynchus mykiss	chronic	-	< 1.7	10
		Daphnia magna	chronic	-	1.6	10

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

Bioconcentration

Bioconcentration factor (BCF) ‡	48 (fillet); 172 (viscera); 90 (whole fish)
Annex VI Trigger: for the bioconcentration factor	100
Clearance time (CT_{50})	CT_{50} (1) = 0.44 days; CT_{50} (2) = 10 days (biphasic depuration curve)
(CT_{90})	CT_{90} (1) = 1.46 days; CT_{90} (2) = 33.2 days (biphasic depuration curve)
Level of residues (%) in organisms after the 14 day depuration phase	< 0.5 % after 12 days (whole fish)

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

Acute oral toxicity ‡	LD_{50} (48 h) = 0.92 µg a.s./bee
Acute contact toxicity ‡	LD_{50} (96 h) = 0.19 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				
1 kg a.s./ha	brassicas	contact	Not applicable	Not applicable
1 kg a.s./ha	brassicas	oral	Not applicable	Not applicable

The calculated hazard quotients are not relevant for granule incorporation use.

Field or semi-field tests
Not required.

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests ‡						
‡ *Coccinella septempunctata*	larvae	Oncol 20 EC	0.5 mL/ 100 mL water	mortality	100 %	30 %

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

Species	Stage	Test Substance	Dose (kg as/ha)	Endpoint	Effect	Annex VI Trigger
Extended lab tests						
‡ *Aphidius rhopalosiphi*	adult females	Oncol 20 EC	3.2 – 320 mL/ha	LD_{50} (48 h)	43 mL/ha	
‡ *Typhlodromus pyri*	protonymphs	Oncol 20 EC	16 – 100 mL/ha	LD_{50} (7 d)	42.4 mL/ha	
‡ *Chrysoperla carnea*	larvae	Oncol 20 EC	0.01-1.0 L/ha	LD_{50} (20 d)	24 mL/ha	
‡ *Poecilus cupreus*	adult beetles	Oncol 8.6 G	12 kg/ha	mortality	0 %	50 %
‡ *Aleochara bilineata*	adult beetles	Oncol 8.6 G	12 kg/ha	Mortality Reduction in hatching rate	59.5 % 57.6 %	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} (*Eisenia foetida*, 14 d) = 46.58 mg Oncol 20 EC/kg substrate
Reproductive toxicity ‡	Not required.

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
1 kg a.s./ha	Brassicas	acute	7	10

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

Nitrogen mineralization ‡	Not available.
Carbon mineralization ‡	Not available.

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N,	Dangerous to the environment
	R50/53	Very toxic to aquatic organisms, 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 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 or high performance liquid chromatography
IEDI	international estimated daily intake
IESTI	international estimated short term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
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