## CONCLUSION ON PESTICIDE PEER REVIEW

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

**European Food Safety Authority**[2]

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## SUMMARY

Carbetamide is one of the 79 substances of the third stage part A of the review programme covered by Commission Regulation (EC) No 1490/2002[3], as amended by Commission Regulation (EC) No 1095/2007[4]. In accordance with the Regulation, at the request of the Commission of the European Communities (hereafter referred to as 'the Commission'), the EFSA organised a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by France, being the designated rapporteur Member State (RMS). The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of carbetamide in Annex I to Council Directive 91/414/EEC.

Following the Commission Decision of 05 December 2008 (2008/934/EC)[5] concerning the non-inclusion of carbetamide in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Feinchemie Schwebda GmbH made a resubmission application for the inclusion of carbetamide in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[6]. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, France, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 12 February 2010.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 16 February 2010. The EFSA collated and forwarded all comments received to the Commission on 02 April 2010.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission requested the EFSA to conduct a focused peer review in the area of mammalian toxicology and deliver its conclusions on carbetamide.

1 On request from the European Commission, Question No EFSA-Q-2010-00840, issued on 22 November 2010.
2 Correspondence: praper@efsa.europa.eu
3 OJ L224, 21.08.2002, p.25
4 OJ L 246, 21.9.2007, p. 19
5 OJ L 333, 11.12.2008, p. 11
6 OJ L 15, 18.01.2008, p.5

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The conclusions laid down in this report were reached on the basis of the evaluation of the representative use of carbetamide as a herbicide on winter oilseed rape as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

No critical areas of concern were identified in the area of physical-chemical properties. Two data gaps were identified for spectra and a specific chiral method for the active substance in the formulation.

No critical areas of concern or data gaps were identified in the area of mammalian toxicology.

Based on the metabolism study conducted on rapeseed, the residue for monitoring and risk assessment was defined as carbetamide (sum R/S isomers). Additional information is required in order to address the residues in following crops in the case of crop failure. No critical areas of concern were identified in the residue section. The consumer risk assessment was finalised and no chronic or acute concern was identified.

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at the EU level for the representative use assessed. The potential for groundwater exposure from the representative use by carbetamide and the groundwater relevant metabolite (*RS*) carbetamide-COOH above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by 5 out of the 6 pertinent FOCUS groundwater scenarios. Under the vulnerable conditions represented by just the Piacenza FOCUS groundwater scenario, groundwater exposure at concentrations above 0.1 µg/L cannot be excluded. For the typical situation where oilseed rape is grown in rotation with other crops, the 80$^{th}$ percentile annual average recharge concentrations leaving the top 1m soil layer were predicted to be up to 0.215 µg carbetamide/L and 0.260 µg (*RS*) carbetamide-COOH/L at the Piacenza scenario[7].

No critical areas of concern were identified for the environmental risk assessment. Risk mitigation measures equivalent to a 5m no-spray buffer zone are required to identify a low risk for non-target plants following the representative use of carbetamide. Application of run-off mitigation measures (e.g. 10m buffer strips) would be required to identify a low risk to aquatic organisms in agricultural landscapes similar to the R3 stream scenario. It was recommended to not apply carbetamide on drained soils in agricultural landscapes comparable to the FOCUS D2 scenarion, as a low risk was not identifyed for the representative use. Based on the recommended mitigation measure the risk to non-target organisms was assessed as low.

**KEY WORDS**

Carbetamide, peer review, risk assessment, pesticide, herbicide

[7] though anaerobic top soil conditions would be necessary for (*RS*) carbetamide-COOH to be formed and these would not typically be present under the conditions of the FOCUS groundwater scenarios (including Piacenza) that represent freely draining topsoil conditions.

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## BACKGROUND

### Legislative framework

Commission Regulation (EC) No 1490/2002[8], as amended by Commission Regulation (EC) No 1095/2007[9] lays down the detailed rules for the implementation of the third stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure for organising, upon request of the Commission of the European Communities (hereafter referred to as 'the Commission'), a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the designated rapporteur Member State.

Commission Regulation (EC) No 33/2008[10] lays down the detailed rules for the application of Council Directive 91/414/EEC for a regular and accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of Council Directive 91/414/EEC but which were not included in Annex I. This regulates for the EFSA the procedure for organising the consultation of Member States and the applicant for comments on the Additional Report provided by the designated RMS, and upon request of the Commission the organisation of a peer review and/or delivery of its conclusions on the active substance.

### Peer review conducted in accordance with Commission Regulation (EC) No 1490/2002

Carbetamide is one of the 79 substances of the third stage part A of the review programme covered by Commission Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007. In accordance with the Regulation, at the request of the Commission, the EFSA organised a peer review of the DAR provided by the designated rapporteur Member State, France, which was received by the EFSA on 20 February 2006 (France, 2006).

The peer review was initiated on 30 June 2006 by dispatching the DAR to Member States and the applicant Feinchemie Schwebda GmbH for consultation and comments. In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table.

The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of carbetamide in Annex I to Council Directive 91/414/EEC.

### Peer review conducted in accordance with Commission Regulation (EC) No 33/2008

Following the Commission Decision of 05 December 2008 (2008/934/EC)[11] concerning the non-inclusion of carbetamide in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Feinchemie Schwebda GmbH made a resubmission application for the inclusion of carbetamide in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18, France, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report (France 2010a) was received by the EFSA on 12 February 2010.

In accordance with Article 19, the EFSA distributed the Additional Report to Member States and the applicant for comments on 16 February 2010. In addition, the EFSA conducted a public consultation

[8] OJ L224, 21.08.2002, p.25
[9] OJ L246, 21.9.2007, p.19
[10] OJ L 15, 18.01.2008, p.
[11] OJ L 333, 11.12.2008, p.11

on the Additional Report. The EFSA collated and forwarded all comments received to the Commission on 02 April 2010. At the same time, the collated comments were forwarded to the RMS, who compiled a merged Reporting Table for the comments on the DAR and Additional Report. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response was evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 05 May 2010 the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on carbetamide within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information was required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 02 June 2010. The applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that the EFSA should organise a consultation with Member State experts in the area of mammalian toxicology, and that further information should be requested from the applicant in the areas of physical-chemical properties, residues and fate and behaviour.

The outcome of the telephone conference, together with EFSA's further consideration of the comments, is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in consultation with Member State experts, and the additional information to be submitted by the applicant, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in October/November 2010.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative use as a herbicide on winter oilseed rape as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2010) comprises the following documents:

- the comments received on the DAR and the Additional Report,
- the Reporting Table (revision 1-1; 02 June 2010)
- the Evaluation Table (22 November 2010)
- the report(s) of the scientific consultation with Member State experts (where relevant).

Given the importance of the DAR and the Additional Report including its addendum (compiled version of October 2010 containing all individually submitted addenda, France, 2010b) and the Peer Review Report, both documents are considered respectively as background documents A and B to this

conclusion.

## THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Carbetamide is the ISO common name for (*R*)-1-(ethylcarbamoyl)ethyl carbanilate (IUPAC).

The representative formulated product for the evaluation was 'FSG01002H' a water dispersible granule (WG) containing 600 g/kg carbetamide.

The representative use evaluated comprises outdoor foliar spraying against annual grasses and some broad-leaved weeds in oilseed rape. Full details of the GAP can be found in the list of end points in Appendix A.

## CONCLUSIONS OF THE EVALUATION

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

The minimum purity of the active substance as manufactured is 950 g/kg. The minimum purity given in the FAO specification is 930 g/kg. This FAO specification was done under the old procedure and is therefore applicable to all sources of carbetamide. No relevant impurities were identified in carbetamide.

The main data regarding the identity of carbetamide and its physical and chemical properties are given in Appendix A. Data gaps were identified for spectra and a specific chiral method for the active substance in the formulation.

Chiral methods are not required for the residues (see sections 3 and 4).

Carbetamide can be analysed in plants, soil and water by LC-MS/MS. (*R,S)*Carbetamide-COOH can also be analysed by LC-MS/MS in surface and ground water, although the residue definition for surface water is carbetamide only. Carbetamide in air can be analysed by LC-DAD. A method for products of animal origin is not required as a residue definition is not set and no MRLs are proposed. A method of analysis for body fluids and tissues is not required as carbetamide is not classified as toxic or very toxic.

### 2. Mammalian toxicity

Carbetamide was discussed in the PRAPeR 81 expert meeting. The technical specification is supported by the batches used in the toxicological studies. The impurities are not considered relevant from the toxicological point of view.

In mammals, carbetamide is of low acute toxicity after oral administration in rats and of moderate oral acute toxicity after oral administration in mice. Hence carbetamide has been shown to be harmful if swallowed (R22). This are based on mice data which shows higher sensitivity than rats. Carbetamide is of low acute dermal toxicity. There is no available data on acute inhalation; a study is not required (the vapour pressure does not trigger the performance of a study).

Carbetamide is not skin or eye irritating nor a skin sensitizer (Maximisation test). Carbetamide is extensively and rapidly absorbed and excreted after oral administration; oral absorption is >80 %.

The main target organs after short-term repeated oral administration were the liver (rats and dogs) and thyroid (dogs) seen as increases in organ weights. In rats the liver weight change was associated with centrolobular hypertrophy. Additional effects observed in the dog were the following; neurological signs manifested as unsteadiness, drowsiness and tremor and haemosiderin deposition in hepatic Kupffer cells sometimes correlated with decreases in red blood cell count (RBC). The relevant short-term NOAEL (No Observed Adverse Effect Level) is 12.5 mg/kg bw/day based on the 13 week rat study.

At resubmission a full set of new genotoxicity studies with known purity of the active substance was provided. No genotoxic potential of the substance has been observed in the *in vitro* and *in vivo* genotoxicity studies.

After long-term repeated exposure in rats and mice, carbetamide induced the same toxic effects as observed in the short-term studies. The relevant NOAEL for chronic toxicity was 6 mg/kg bw/day based on the 2 year rat study. Hepatocellular carcinoma and adenoma and thyroid follicular adenoma were seen in B6C3F1 mice at the high dose (exceeding MTD), however this mouse strain is known to be particularly sensitive to the induction of hepatocellular tumours. Proliferative or hypertrophic lesions in the liver, pituitary gland and the thyroid were seen at the two highest doses in mice. A mechanism study performed on B6C3F1 mice showed carbetamide to be an inducer of a variety of hepatic cytochrome P450 enzymes, which could support the proposed mechanism of hepatocarcinogenicity. In the high dose (exceeding MTD) several rare tumours including carcinomas occurred in different tissues (brain astrocytoma, liver cholangiocarcinoma and adrenal phaeochromocytoma) in mice and rats, the tumour incidences were all above the available historical control ranges. In addition the tumours were not sex-specific. Based on these data carbetamide is considered to be a non-genotoxic carcinogen and the risk phrase R40 "Limited evidence of a carcinogenic effect" is proposed. The NOAELs for carcinogenicity in rats and mice were 6 mg/kg bw/day and 21 mg/kg bw/day, respectively.

In the two-generation study in rats, no adverse effects in fertility or reproductive parameters were observed. A NOAEL for parental toxicity was not identified as increased liver weight was observed at the lowest dose level tested being the LOAEL (65 mg/kg bw/d). The NOAEL for offspring and reproductive effects was 208 mg/kg bw/day based on decreased body weigh gain, liver enlargement, hepatocyte hypertrophy and longer gestational times in some females. In the developmental study in rats severe abnormalities including complex malformations (associating elongated genital tubercle, imperforate anus, vestigial/absent tail and cardiovascular malformations) were observed in doses with no marked maternal toxicity during the dosing period: a slight reduction in maternal body weigh gain was observed after dosing (during late gestation) and it was considered unlikely to be the cause of the observed malformations. The maternal and developmental NOAELs were 450 mg/kg bw/day (rats). In the developmental study in rabbit teratogenicity such as skeletal abnormalities, delayed ossifications and post-implantation losses were observed at doses that caused minimal maternal toxicity (i.e slight reduction in maternal body weigh gain). Maternal and developmental NOAELs were 40 mg/kg bw/day. The majority of experts in the PRAPeR 81 meeting agreed to propose the risk phrase R63 "Possible risk of harm to the unborn child".

Since carbetamide is currently proposed to be classified with R63 and R40, and in the absence of further data, the metabolite *(R,S)*Carbetamide-COOH is considered to be relevant if it is found in groundwater at higher levels than 0.1 µg/L (see section 4).

The agreed Acceptable Daily Intake (ADI) is 0.06 mg/kg bw/day and the agreed Acceptable Operator Exposure Level (AOEL) is 0.12 mg/kg bw/day based on the long-term rat study and the 90-day rat study, respectively. The agreed Acute Reference Dose (ARfD) of 0.3 mg/kg bw was set based on the short-term studies in dogs (90 day and 1 year). All reference values were derived by using a safety factor of 100. The relevant dermal absorption values for FSG01002H are 0.2% for the concentrate and 9.4% for the dilution

The estimated operator exposure is below the AOEL (87.8%) without using personal protective equipment (PPE) based on the German model. Worker and bystander exposure estimates were below the AOEL.

## 3. Residues

Two plant metabolism studies conducted on oilseed rape and using $^{14}$C-carbetamide labelled on the phenyl ring were provided. The earlier study conducted in 1984 was however considered as not acceptable and the conclusion reached on the plant metabolism are based on the second study performed in 2007. This study was carried out in compliance with the supported GAP, the treatment taking place at the 4-6 leaves stage, with an application rate of 2100 g a.s./ha (1.2N).

Carbetamide was progressively metabolised in plant, its proportions decreasing in leaves from 90% TRR 18 days after application to 8% TRR at harvest. Several other metabolites were detected in leaves, all accounting for less than 3% TRR. In mature grains, carbetamide was the only compound indentified, accounting for 13% TRR (0.04 mg/kg), with most of the radioactivity being recovered as bound residues (60% TRR). Based on this study the residue for monitoring and risk assessment was defined as carbetamide (as a sum of R/S isomers).

A sufficient number of supervised residue trials was submitted to derive a MRL for rapeseeds. Samples from trials in Southern Europe were however analysed using different analytical methods achieving unsuitable LOQs of 0.04 to 0.10 mg/kg. Nevertheless and having regard to the no-residue situation in seeds, additional trials in Southern Europe using a more accurate method were not required. These residue data are supported by the storage stability study showing carbetamide residues as stable up to 14 months in water and oil containing matrices, when stored at -22/-25°C. Processing studies were not provided and are not required. Limited information was submitted concerning the residues in rotational crops since the $DT_{90}$ was initially estimated to be less than 100 days in soil. However and considering that the $DT_{90}$ was calculated to be above 100 days in two types of soil (see section 4), EFSA is of the opinion that additional data are required to address the possible residue levels in conditions simulating a crop failure.

A cow metabolism study was submitted although the predicted intakes by animals were calculated to be far below 0.10 mg/kg DM. This study was however regarded as not appropriate since no characterisation of the residues was conducted in any matrices.

No chronic or acute concern was identified, the highest TMDI and IESTI being only 0.1% of the ADI and less than 0.05% of the ARfD, when calculated using the EFSA PRIMo rev2 model. Having regard to the low residue levels in rapeseed and the low consumer intakes, information on the isomeric composition of the residues is not relevant for the representative use.

## 4. Environmental fate and behaviour

At the time of application carbetamide is present as the R stereoisomer. Satisfactory information was provided to conclude that it would be expected that residues in environmental matrices would remain as carbetamide (i.e. just the R stereoisomer). For the identified anaerobic soil transformation product carbetamide-COOH, satisfactory information was provided to conclude that it would be expected that residues in environmental matrices would be racemic (i.e. *(RS)*Carbetamide-COOH).

In soil laboratory incubations under aerobic conditions in the dark, carbetamide exhibited low to moderate persistence, forming no metabolites that would trigger further assessment (<5% applied radioactivity (AR) the lowest exposure assessment trigger value, that originates from the guidance document on relevant metabolites; European Commission, 2003). Mineralisation of the phenyl ring 14C radiolabel to carbon dioxide accounted for 45 - 65 % AR after 92 days. The formation of unextractable residues (not extracted by acetone followed by acidified methanol) for this radiolabel accounted for 26 - 51 % AR after 92 days. In anaerobic soil incubations carbetamide exhibited moderate persistence forming the major (>10% AR) metabolite *(RS)*Carbetamide-COOH (maximum 37%AR) which under these conditions also exhibited moderate persistence. In aerobic soil incubations (RS) carbetamide-COOH exhibited low persistence. Carbetamide exhibited high mobility in soil. (RS) carbetamide -COOH exhibited very high soil mobility. It was concluded that the adsorption of carbetamide was not pH dependent and the very low adsorption of *(RS)*Carbetamide-COOH meant pH dependence did not need to be explicitly considered in leaching assessments.

In laboratory incubations in dark aerobic natural sediment water systems, carbetamide exhibited moderate to medium persistence, forming no major metabolites. The unextractable sediment fraction (not extracted by acetone followed by methanol/water) was a sink for the phenyl ring 14C radiolabel, accounting for 26 – 30 % AR at study end (100 days). Mineralisation of this radiolabel accounted for 20 - 29 % AR at the end of the study. The necessary surface water and sediment exposure assessments (Predicted environmental concentrations (PEC)) were carried out for the metabolite (RS) carbetamide-COOH, using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 1.1 of the steps 1-2 in

FOCUS calculator). For the active substance carbetamide, appropriate step 3 (FOCUS, 2001) and some step 4 calculations were available[12]. The step 4 calculation (provided for just the R3 stream scenario) appropriately followed the FOCUS (FOCUS, 2007) guidance and combined no-spray buffer zones with vegetative buffer strips of up to 10m (reducing drift by 80.6%, solute flux in run-off by 60 %, and eroded sediment flux reduced by 85%). Risk managers and others may wish to note that whilst run-off mitigation is included in the step 4 calculations available, the FOCUS (FOCUS, 2007) report acknowledges that for substances with KFoc < 2000 mL/g (i.e. carbetamide), the general applicability and effectiveness of run-off mitigation measures had been less clearly demonstrated in the available scientific literature, than for more strongly adsorbed compounds.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (FOCUS, 2000) scenarios and the model PEARL 3.3.3 and PELMO 3.3.2[13] for the active substance carbetamide and its major anaerobic soil metabolite *(RS)*Carbetamide-COOH. The potential for groundwater exposure from the representative uses by carbetamide and *(RS)*Carbetamide-COOH above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by 5 out of the 6 pertinent FOCUS groundwater scenarios pertinent for winter oilseed rape. In geoclimatic situations represented by just the Piacenza scenario 80th percentile annual average recharge concentrations leaving the top 1m soil layer were predicted to be up to 0.215 µg carbetamide/L and 0.260 µg *(RS)*Carbetamide-COOH/L[14] for the more usual situation where oil seed rape is grown in rotation (one in three year simulated). In the situation where this crop was grown every year these concentrations were predicted to be up to 0.526 µg carbetamide/L and 0.623 µg *(RS)*Carbetamide-COOH/L.

The PEC in soil, surface water, sediment, and groundwater covering the representative uses assessed can be found in Appendix A of this conclusion.

## 5. Ecotoxicology

The test material applied in exotoxicological testing was considered to be in compliance with the technical specification of carbetamide and only the relevant R stereoisomer of carbetamide was considered in the ecotoxicological testing (see also section 4). The risk assessment was based on the following documents: European Commission (2002 a,b,c), SETAC (2001), EFSA (2009).

The risk from dietary uptake of carbetamide and the risk from consumption of contaminated drinking water were assessed as low to birds and mammals. The risk from secondary poisoning was not assessed for birds and mammals (logPow < 3). The acute risk to birds from the formulation was additionally assessed as low.

Carbetamide was assessed as harmful to aquatic organisms, based on acute toxicity data for the technical substance. Based on data available the formulation appears to be 30-fold more toxic (acute and chronic) to fish than the active substance. The formulation should be classified as toxic to aquatic organisms. The active substance and the formulation was however equally toxic to invertebrates and algae. The acute and chronic toxicity to fish is driving the aquatic risk assessment, in addition to the chronic toxicity endpoint for *Daphnia*. Based on FOCUSsw step 3 calculations and the toxicity data for the active substance, a low risk was identified in 5 out of 6 full scenarios. No mitigation measures were identified to address the chronic risk for *Daphnia* in the remaining D2 drainage scenario. A low risk was identified in 4 out of 6 full FOCUSsw step 3 scenarios, based on toxicity data of the

[12] Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2007) and Walker equation coefficient of 0.7 with the exception of the step 4 calculations where a Q10 of 2.2 had been used.
[13] Simulations complied with EFSA (EFSA, 2004) and were available where the agreed Q10 of 2.58 (following EFSA, 2007) was utilised and Walker equation coefficient of 0.7 was utilised.
[14] Note for (*RS*) carbetamide-COOH to be present in the soil column in significant amounts anaerobic topsoil conditions would be necessary and such conditions would not generally be expected under the freely draining soil hydrology conditions represented by the FOCUS groundwater scenarios that only account for soil water movement through the top 1.2-2.6m of the soil column.

formulation. In the remaining two scenarios, the chronic risk was only addressed at FOCUSsw Step 4 including a 10m buffer strips for the R3 scenario. As for the risk assessment performed for the active substance, the risk to aquatic organisms was not addressed in the D2 drainage scenario, based on toxicity of the formulation. Following the DAR it is recommended not to apply carbetamide on drained soils comparable to geoclimatic conditions of the D2 scenarios. During the peer review a chronic toxicity study with Daphnia with a slightly lower toxicity endpoint than that originally submitted in the dossier was identified, and a data gap was agreed. EFSA does not consider that the inclusion of the slightly lower endpoint for Daphnia would change the outcome of the aquatic risk assessment. Toxicological data were provided for the metabolite *(R,S)*Carbetamide-COOH, which proved to be less toxic than the parent to fish, invertebrates and algae. The risk to sediment dwellers was assessed as low for carbetamide based on the low acute toxicity to Daphnia. Additionally, the risk to sediment dwellers was assessed as low for *(R,S)*Carbetamide-COOH, based on a *Chironomus* study. Carbetamide was not considered to have potential for bioaccumulation (logPow=1.78).

Risk mitigation equivalent to a 5m no-spray buffer zone was required to identify a low risk to non-target plants following the representative use of carbetamide.

The risk to bees, non-target arthropods, earthworms, soil-living macro- and micro-organisms and biological method for waste water treatment was assessed as low based on the representative use and the data available.

## 6. Overview of the risk assessment of compounds listed in residue definitions triggering the assessment of effects data for the environmental compartments

### 6.1. Soil

| Compound (name and/or code) | Persistence | Ecotoxicology |
|---|---|---|
| carbetamide | low to moderate persistence<br><br>Single first order $DT_{50}$ 4-29 days (20°C, pF2 soil moisture) | The risk to soil-living organisms was assessed as low |
| (*RS*) carbetamide-COOH | low persistence<br><br>Single first order $DT_{50}$ 1-2 days (20°C, pF2 soil moisture) | The risk to soil-living organisms was assessed as low |

### 6.2. Ground water

| Compound (name and/or code) | Mobility in soil | >0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter) | Pesticidal activity | Toxicological relevance | Ecotoxicological activity |
|---|---|---|---|---|---|
| carbetamide | High mobility $K_{Foc}$ 59-118 mL/g | At 1 (Piacenza, 0.215µg/L) out of 6 scenarios | Yes | Yes | Yes |
| (*RS*) carbetamide-COOH | Very high mobility $K_{doc}$ 1-12.9 mL/g | At 1 (Piacenza, 0.26µg/L) out of 6 scenarios | No | Yes.<br><br>Based on the toxicological properties of the parent compound the metabolite is toxicologically relevant. | No |

### 6.3. Surface water and sediment

| Compound (name and/or code) | Ecotoxicology |
|---|---|
| carbetamide | Carbetamide was assessed as harmful to aquatic organisms. A low risk was identified for a majority of scenarios at FOCUSsw step 3: |
| (*RS*) carbetamide-COOH | The risk to aquatic organisms was assessed as low. |

### 6.4. Air

| Compound (name and/or code) | Toxicology |
|---|---|
| carbetamide | No data available – not required |

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

- IR, NMR, MS spectra of material of known purity (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)
- A chiral method for the active substance in the formulation (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)
- Information on the residues in succeeding crops in case of crop failure (relevant for the representative use evaluated; submission date proposed by the applicant: unknown; see section 3).
- The chronic toxicity study available for *Daphnia* with a slightly lower toxicity endpoint than originally submitted should be provided for the aquatic risk assessment (relevant for the representative use evaluated; submission date proposed by the applicant: unknown; see section 5).

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

- Risk mitigation equivalent to a 5m no-spray buffer zone was required to identify a low risk to non-target plants following the representative use of carbetamide.
- Application of run-off mitigation (e.g. 10m buffer strips) would be required to identify a low risk to aquatic organisms in agricultural landscapes similar to the R3 stream scenario.
- In order to protect aquatic invertebrates from chronic effects, it was recommended to not apply carbetamide on drained soils in agricultural landscapes comparable to the FOCUS D2 scenarios.

## ISSUES THAT COULD NOT BE FINALISED

- none

## CRITICAL AREAS OF CONCERN

- none

## REFERENCES

France, 2006. Draft Assessment Report (DAR) on the active substance carbetamide. prepared by the rapporteur Member State France in the framework of Directive 91/414/EEC, February 2006

France, 2010a. Additional Report to the Draft Assessment Report on the active substance carbetamide prepared by the rapporteur Member State France in the framework of Commission Regulation (EC) No 33/2008, February 2010.

France, 2010b. Final Addendum to the Additional Report on carbetamide, compiled by EFSA, October 2010.

EFSA (European Food Safety Authority), 2010. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance carbetamide.

Guidance documents[15]:

European Commission, 2003. Guidance document on assessment of the relevance of metabolites in groundwater of substances regulated under council directive 91/414/EEC. SANCO/221/2000-rev 10-final, 25 February 2003.

European Commission, 2002b. Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002 rev.2 final, 17 October 2002.

European Commission, 2002c. Guidance Document on Aquatic Ecotoxicology Under Council Directive 91/414/EEC. SANCO/3268/2001 rev 4 (final), 17 October 2002.

European Commission, 2002a. Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC. SANCO/4145/2002; 25 September 2002.

FOCUS, 2001. "FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC". Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2. 245 pp.

FOCUS, 2007. "Landscape And Mitigation Factors In Aquatic Risk Assessment. Volume 1. Extended Summary and Recommendations". Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment, EC Document Reference SANCO/10422/2005 v2.0. 169 pp.

FOCUS, 2000. "FOCUS Groundwater Scenarios in the EU review of active substances". Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference SANCO/321/2000-rev.2. 202 pp, as updated by the Generic Guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002

EFSA, 2007. Scientific Opinion of the Panel on Plant Protection Products and their Residues on a request from EFSA related to the default *Q*10 value used to describe the temperature effect on transformation rates of pesticides in soil. The EFSA Journal (2007) 622, 1-32

EFSA, 2004. Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models comparability and the consistency of this risk assessment of groundwater contamination. The EFSA Journal (2004) 93, 1-20

EFSA 2009. Guidance Document on Risk Assessment for Birds and Mammals on request of EFSA. EFSA Journal 2009; 7(12):1438

SETAC (Society of Environmental Toxicology and Chemistry), 2001. Guidance Document on Regulatory Testing and Risk Assessment procedures for Plant Protection Products with Non-Target Arthropods. ESCORT 2.

[15] For further guidance documents see http://ec.europa.eu/food/plant/protection/resources/publications_en.htm#council (EC) or http://www.oecd.org/document/59/0,3343,en_2649_34383_1916347_1_1_1_1,00.html (OECD)

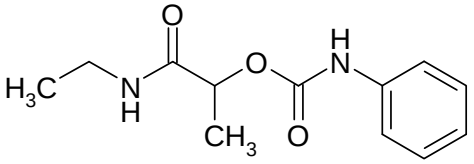
# APPENDICES

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

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

| | |
|---|---|
| Active substance (ISO Common Name) | Carbetamide |
| Function (*e.g.* fungicide) | Herbicide |
| Rapporteur Member State | France |

**Identity** (Annex IIA, point 1)

| | |
|---|---|
| Chemical name (IUPAC) | (*R*)-1-(Ethylcarbamoyl)ethyl carbanilate |
| Chemical name (CA) | (*R*)-N-Ethyl-2-[[(phenylamino)carbonyl]oxy]-propanamide |
| CIPAC No | 95 |
| CAS No | 16118-49-3 |
| EEC No (EINECS or ELINCS) | 240-286-6 |
| FAO Specification (including year of publication) | 930 g/kg (1988)<br>Water and volatile impurities Max : 10 g/kg<br>Acetone insolubles Max : 5 g/kg |
| Minimum purity of the active substance as Manufactured (g/kg) | 950 g/kg |
| Identity of relevant impurities (of toxicological, environmental and/or other significance) in the Active substance as manufactured (g/kg) | None |
| Molecular formula | $C_{12}H_{16}N_2O_3$ |
| Molecular mass | **236.27 g/mol** |
| Structural formula |  |

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

| | |
|---|---|
| Melting point (state purity) ‡ | 108.7 – 110.6°C (Purified 99.5%) |
| Boiling point (state purity) ‡ | To be determined 235-240°C (98.8%) |
| Temperature of decomposition (state purity) | To be determined none up to 400 °C (98.8%) |
| Appearance (state purity) ‡ | Colourless powder (purity 99.5%) |
| | |
| Vapour pressure (state temperature, state purity) ‡ | 3 $10^{-7}$ Pa at 20°C (99.7%) |
| Henry's law constant ‡ | 1.93 .$10^{-8}$ at 20°C |
| Solubility in water (state temperature, state purity and pH) ‡ | pH 5 : 3.05 g/l at 23°C (97.8%)<br>pH 7 : 3.27 g/l at 23°C (97.8%)<br>pH 9 : 3.67 g/l at 23°C (97.8%) |
| | |
| Solubility in organic solvents ‡ (state temperature, state purity) | Solubity was determined at 20°C (97.2%) :<br>Acetone: > 250 g/L<br>Dichloroethane: > 250 g/L<br>Ethyl acetate: > 250 g/L<br>n- Heptane: = 0.026 g/L<br>Methanol: > 250 g/L<br>p-Xylene: = 2.4 g/L |
| Surface tension ‡ (state concentration and temperature, state purity) | 68.6 mN/m at 20°C and 1 g/L (98.8%) |
| Partition co-efficient ‡ (state temperature, pH and purity) | Buffered at 20°C (97%):<br>pH 4: log Pow: 1.76<br>pH 7: log Pow: 1.78<br>pH 9: log Pow: 1.76 |
| | |
| Dissociation constant (state purity) ‡ | pKa : approximately 11.3 at 20°C (99.5%) |
| UV/VIS absorption (max.) incl. ε ‡ (state purity, pH) | ε = 104.49 l.mol-1.cm-1 at 205.8 nm<br>ε = 104.30 l.mol-1.cm-1 at 234.8 nm<br>ε < 10 at λ >295 nm |
| Flammability ‡ (state purity) | Not highly inflammable (97.2%) |
| Explosive properties ‡ (state purity) | None |
| Oxidising properties ‡ (state purity) | None |

*List of uses supported by available data*

| Crop and/ or situation (a) | Product name | F G or I (b) | Pests or Group of pests controlled (c) | Formulation ** | | Application | | | | Application rate per treatment | | | PHI (days) (l) | Remarks (m) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Type (d-f) | Conc. of ai (i) | method kind (f-h) | growth stage & season (j) | number min-max (k) | interval between applications | kg ai/hL min-max | Water L/ha min-max | kg ai/ha min-max | | |
| N/S Europe: Winter oilseed rape | FSG01 002H | **F** | Annual grasses and some broad-leaved weeds | WG | **600** | Tractor mounted sprayer | Post emergence from autumn up to end of dormant period (till BBCH 14-16) | 1 | n.r. | 0.90 | 200–400 | 1.8 | n.r. | |

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI - minimum pre-harvest interval

## Methods of analysis

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

| | |
|---|---|
| Technical a.s. (principle of the method) | HPLC / UV |
| Impurities in technical a.s. (principle of method) | HPLC / UV |
| Plant protection product (principle of method) | HPLC / UV for determination of sum R+S isomer in PPP Open for a specific chiral method |

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

**Residue definitions for monitoring purposes**

| | | |
|---|---|---|
| Food of plant origin | | Carbetamide (sum of isomers R+S) |
| Food of animal origin | | none |
| Soil | | Carbetamide (sum of isomers R+S) |
| Water | surface | Carbetamide (sum of isomers R+S) |
| | drinking/ground | Carbetamide (sum of isomers R+S)<br>Carbetamide-COOH (sum of isomers R+S) |
| Air | | Carbetamide (sum of isomers R+S) |

**Monitoring/Enforcement methods**

| | |
|---|---|
| Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes) | Carbetamide :<br>LC/MS-MS<br>LOQ = 0.02 mg/kg (chicory plant, chicory root, rape seed) (ILV provided) |
| Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes) | No data given ; no data required as no residue definition is set |
| Soil (analytical technique and LOQ) | Carbetamide :<br>LC/MS-MS<br>LOQ = 0.02 mg/kg |
| Water (analytical technique and LOQ) | Carbetamide :<br>LC/MS/MS<br>LOQ = 0.05 µg/l (surface and drinking water)<br>Carbetamide COOH:<br>LC/MS/MS<br>LOQ = 0.05 µg/l (surface and drinking water) |

| | |
|---|---|
| Air (analytical technique and LOQ) | Carbetamide :<br>LC/DAD<br>LOQ = 0.4 µg/m$^3$ |
| Body fluids and tissues (analytical technique and LOQ) | No data given ; no data required as carbetamide is not classified as “toxic or highly toxic” |

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

| | |
|---|---|
| With regard to physical/chemical data | None |

*Impact on Human and Animal Health*

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

| | |
|---|---|
| Rate and extent of oral absorption ‡ | Rat: rapid and extensive (>80%) within 24 h.<br>Dog: $T_{max}$ 0.5-4 hours |
| Distribution ‡ | Rat: Poorly distributed.<br>Organ with higher amount: Liver (at 96 h and 21 days) |
| Potential for accumulation ‡ | Rat: None |
| Rate and extent of excretion ‡ | Rat: Rapid elimination via urine ( 81%), faeces (12%) within 24 hours after dosing. |
| Metabolism in animals ‡ | Rat: Degradation of the carbamate moiety and para-hydroxylation |
| Toxicologically relevant compounds ‡ (animals and plants) | Parent |
| Toxicologically relevant compounds ‡ (environment) | Parent<br>Carbetamide-COOH |

**Acute toxicity (Annex IIA, point 5.2)**

| | | |
|---|---|---|
| $LD_{50}$ oral ‡ | Rat: $LD_{50}$ > 2000 mg/kg (combined sexes)<br>Mice: $LD_{50}$ = 1,718 mg/kg bw (combined sexes) | R22 |
| Rat $LD_{50}$ dermal ‡ | > 2,000 mg/kg bw | - |
| Rat $LC_{50}$ inhalation ‡ | No study required (vapour pressure of carbetamide at 20°C is $3.10^{-7}$ Pa) | - |
| Skin irritation ‡ | Non irritant | - |
| Eye irritation ‡ | Non irritant | - |
| Skin sensitisation ‡ | Non sensitizer (M&K) | - |

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

| | |
|---|---|
| Target / critical effect | Rats: slight hematotoxicity (anemia), liver (centrolobular hypertrophy).<br>Dogs: slight neurologic toxicity, slight hematotoxicity (anemia), liver (increased weight), thyroids (follicular epithelium hypertrophy). Inhibition of Ach-E. |
| Lowest relevant oral NOAEL / NOEL | 12.5 mg/kg/day; 13 week rat<br>30 mg/kg bw/day ;90 day and 1 year |
| Lowest relevant dermal NOAEL / NOEL | No study |
| Lowest relevant inhalation NOAEL / NOEL | **No study** |

| | |
|---|---|
| **Genotoxicity** (Annex IIA, point 5.4) | No genotoxic potential |

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

| | | |
|---|---|---|
| Target/critical effect | Rats: slight hematotoxicity (anemia in females), liver (centrolobular hypertrophy), thyroids (follicular epithelial hypertrophy).<br>Mice: liver (centrolobular hypertrophy and neoplasms), thyroids (follicular epithelial hypertrophy and neoplasms in females), adrenals (phaeochromocytomas in females) | |
| Lowest relevant NOAEL / NOEL chronic toxicity | 6 mg/kg bw/day (2-year oral study in rats)<br>21 mg/kg bw/day (2-year oral study in mice) | |
| Carcinogenicity | In mice: liver (hepatocellular tumors, cholangiocarcinoma), thyroids (adenomas) and adrenals (phaeochromocytomas in females).<br>In rat: brain (astrocytoma) | R40 |

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

**Reproduction toxicity**

| | | |
|---|---|---|
| Reproduction target / critical effect ‡ | Parental : increases liver weight<br>Reproductive : longer gestational times<br>Offspring :decreased body weigh gain, liver enlargement, hepatocyte hypertrophy | |
| Relevant parental NOAEL ‡ | No NOAEL identified. LOAEL = 65 mg/kg bw/day | |
| Relevant reproductive NOAEL ‡ | 208 mg/kg bw/day | |
| Relevant offspring NOAEL ‡ | 208 mg/kg bw/day | |

**Developmental toxicity**

| | | |
|---|---|---|
| Developmental target / critical effect ‡ | Rats: Abortions, higher incidence of post-implantation loss, signs of fetal immaturity, complex malformations without marked maternal toxicity (slight reduction in maternal body weigh gain)<br>Rabbit: benign fetal abnormalities without | R63 |

| | | |
|---|---|---|
| | marked maternal toxicity (slight reduction in maternal body weigh gain) | |
| Relevant maternal NOAEL ‡ | 450 mg/kg bw/day (rat)<br>40 mg/kg bw/day (rabbits) | |
| Relevant developmental NOAEL ‡ | 450 mg/kg bw/day (rat)<br>40 mg/kg bw/day (rabbits) | |

**Neurotoxicity (Annex IIA, point 5.7)**

| | | |
|---|---|---|
| Acute neurotoxicity ‡ | NOAEL = 5000 mg/kg (Hens) | |
| Repeated neurotoxicity ‡ | No data | |
| Delayed neurotoxicity ‡ | No data | |

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

Mechanism studies ‡

| |
|---|
| Mecanistic study: carbetamide is an inducer of a variety of hepatic cytochrome P450 enzymes. |

**Medical data** (Annex IIA, point 5.9)

| |
|---|
| Manufacturing plant employee medical surveillance data discloses no exposure-related health effects. |

| **Summary** (Annex IIA, point 5.10) | Value | Study | Safety factor |
|---|---|---|---|
| ADI | 0.06 mg/kg bw/d | 2-year rat | 100 |
| AOEL | 0.12 mg/kg bw/d | 90-day rat | 100 |
| ARfD | 0.3 mg/kg bw | 1-year and 90-d dog | 100 |

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

Formulation FSG01002H

| |
|---|
| Concentrate (WG 600 g/kg): 0.2%<br>Spray dilution (WG 3.75 g/L): 9.4%<br><br>(*In vitro* human data from a comparative *in vitro* human/rat study) |

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

| | | | |
|---|---|---|---|
| Operator | Acceptable with BBA model | | |
| | | POEM (50 ha) | BBA (20 ha) |

| | | | |
|---|---|---|---|
| | No PPE | 812.5% | 87.8 |
| | Gloves (Mixing, loading and application) | 385.9 | |
| Workers | 6 % unprotected. | | |
| Bystanders | 1.3% of AOEL. | | |

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

| | RMS/peer review proposal |
|---|---|
| Substance classified (carbetamide) | Xn (Harmfull)<br>R22: Harmful if swallowed<br>Carc. Cat.3 R40: Limited evidence of a carcinogenic effect<br>Repr. Cat.3 R 63: Possible risk of harm to the unborn child |

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

| | |
|---|---|
| Plant groups covered | Pulse/Oilseeds (Oilseed rape) |
| Rotational crops | Limited data provided (information to cover the residues in case of crop failure required) |
| Metabolism in rotational crops similar to metabolism in primary crops? | Not applicable. |
| Processed commodities | Not provided and not required |
| Residue pattern in processed commodities similar to residue pattern in raw commodities? | Not applicable. |
| Plant residue definition for monitoring | Carbetamide |
| Plant residue definition for risk assessment | Carbetamide |
| Conversion factor (monitoring to risk assessment) | No |

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

| | |
|---|---|
| Animals covered | Lactating cow (not required) |
| Time needed to reach a plateau concentration in milk and eggs | Not applicable |
| Animal residue definition for monitoring | Not required |
| Animal residue definition for risk assessment | Not required |
| Conversion factor (monitoring to risk assessment) | Not applicable |
| Metabolism in rat and ruminant similar (yes/no) | Not applicable |
| Fat soluble residue: (yes/no) | Not investigated |

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

| |
|---|
| None expected ($DT_{90}$ <100 days)<br>Crop failure scenario not investigated |

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

| |
|---|
| Carbetamide residues stable up to 14 months when stored froze at -22°/-25°C, in water (chicory leaves and roots, alfalfa) and oil (rape seeds) containing matrices. |

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

| | **Ruminant:** | **Poultry:** | **Pig:** |
|---|---|---|---|
| | Conditions of requirement of feeding studies | | |
| Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level) | No | No | No |
| Potential for accumulation (yes/no): | n/a | n/a | n/a |
| Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no) | n/a | n/a | n/a |
| | Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant)<br>Residue levels in matrices : Mean (max) mg/kg | | |
| Muscle | n/a | n/a | n/a |
| Liver | n/a | n/a | n/a |
| Kidney | n/a | n/a | n/a |
| Fat | n/a | n/a | n/a |
| Milk | n/a | | |
| Eggs | | n/a | |

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

| Crop | Northern or Mediterranean Region, field or glasshouse, and any other useful information | **Trials results relevant to the representative uses** (a) | **Recommendation/comments** | **MRL** estimated from trials according to the representative use | **HR** (c) | **STMR** (b) |
|---|---|---|---|---|---|---|
| **Oilseed rape** | North | 6x <0.02; 2x <0.025; 3x <0.10 | No further data required in southern EU having regard to the no residue situation. | 0.1 | <0.1 | <0.02 |
| | South | <0.04; <0.07; <0.08; <0.10 | | | | |

(a) Numbers of trials in which particular residue levels were reported
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

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

| | |
|---|---|
| ADI | 0.06 mg/kg bw/day |
| TMDI (% ADI) according to EFSA PRIMo rev2 model | Highest TMDI: 0.1% ADI (WHO cluster diet E) |
| TMDI (% ADI) according to national (to be specified) diets | none |
| IEDI (WHO European Diet) (% ADI) | none |
| NEDI (specify diet) (% ADI) | none |
| Factors included in IEDI and NEDI | none |
| ARfD | 0.3 mg/kg bw |
| IESTI (% ARfD) according to EFSA PRIMo rev2 model | Highest IESTI: <0.05% ARfD (Rape seed) |
| NESTI (% ARfD) according to national (to be specified) large portion consumption data | none |
| Factors included in IESTI and NESTI | none |

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

| Crop/ process/ processed product | Number of studies | Processing factors | | Amount transferred (%) (Optional) |
|---|---|---|---|---|
| | | Transfer factor | Yield factor | |
| None (not required) | | | | |

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

| | |
|---|---|
| Oil seed rape | 0.1 mg/kg |

When the MRL is proposed at the LOQ, this should be annotated by an asterisk (*) after the figure.

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

| | |
|---|---|
| Mineralization after 100 days ‡ | 45-65 % after 92 d, [$^{14}$C-Carbetamide]-label<br>n[16]= 2<br>2 concentrations (1 and 10 ppm), 25°C |
| Non-extractable residues after 100 days ‡ | Max 35-51 % after 14-29 d,<br>26-41 % after 92 d<br>n = 2, 2 concentrations (1 and 10 ppm), 25°C |
| Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum) | None (metabolites < 5% each) |

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

Anaerobic degradation ‡

| | |
|---|---|
| Mineralization after 100 days | 0.6 % after 120 d, [$^{14}$C-Carbetamide]-label (n= 1) |
| Non-extractable residues after 100 days | 28.8-30.9 % after 120 d, [$^{14}$C-Carbetamide]-label (n= 1) |
| Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum) | (*RS*) Carbetamid-COOH (n= 1)<br>In soil extract :<br>Maximum of 16.5-15.1 % at 50 d (mean = 15.8 %)<br>Range 0.6% (3 days) – 16.5-15.1 % (50 days)<br>In water phase :<br>Maximum of 19.4-23.3% at 50 d (mean = 21.4 %)<br>Range 0.7% (1 day) – 23.3-19.4% (50 days)<br>In whole system:<br>Maximum of 37.2 % at 50 days |

Soil photolysis ‡

| | |
|---|---|
| Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum) | No photodegradation |

[16] n corresponds to the number of soils.

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

Laboratory studies ‡

| Carbetamide | | | Aerobic conditions | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Soil type | X [17] | pH | t. °C / % MWHC | $DT_{50}$ /$DT_{90}$ (d) | $DT_{50}$ (d) 20 °C [18]pF2/10kPa | | $DT_{50}$ (d) 20 °C [19]pF2/10kPa | | St. ($r^2$) | $\chi^2$ | Method of calculation |
| Speyer 2.1 - Sand | | 6.2 | 20°C / 45% | 22.21 / 73.8 | 22.21 | | 22.21 | | 0.990 | 5.5 | SFO |
| Speyer 2.2 - Loamy sand | | 5.6 | 20°C / 45% | 12.10 / 40.2 | 12.10 | | 12.10 | | 0.996 | 3.6 | SFO |
| Speyer 2.3 -Sandy loam | | 5.7 | 20°C / 45% | 32.89 / 109.3 | 28.90 | | 28.90 | | 0.988 | 4.9 | SFO |
| Speyer 3A -Sandy loam | | 6.5 | 20°C / 45% | 4.18 / 13.9 | 4.02 | | 4.02 | | 0.994 | 5.8 | SFO |
| Speyer 5M - Sandy loam | | 6.9 | 20°C / 45% | 10.80 / 35.9 | 8.99 | | 8.99 | | 0.996 | 4.1 | SFO |
| Speyer 6S - Clay loam | | 7.0 | 20°C / 45% | 20.60 / 68.4 | 14.88 | | 14.88 | | 0.986 | 6.9 | SFO |
| BBA2.3 - Sandy loam | | 6.5 | 20°C / - | 40.2 / 133.5 | 40.2 | | 40.2 | | - | 4.8 | - |
| BBA2.2 - Loamy sand | | 6.1 | 20°C / - | 15.7 / 52.3 | 15.7 | | 15.7 | | - | 5.6 | - |
| Emerainville - Clay loam 1ppm | | 7.0 | 25°C / 75% FC | 4.93 / 16.4 | 5.64 | 6.30 * | 6.11 | 6.83 * | 0.989 | 10.8 | SFO |
| Emerianville - Clay loam 10 ppm | | 7.0 | 25°C / 75% FC | 6.15 / 20.4 | 7.03 | | 7.63 | | 0.984 | 12.5 | SFO |
| Le Mort - Silty clay loam 1ppm | | 7.6 | 25°C / 75% FC | 3.36 / 11.2 | 4.28 | 5.22 * | 4.64 | 5.65 * | 0.987 | 13.2 | SFO |
| Le Mort - Silty clay loam 10 ppm | | 7.6 | 25°C / 75% FC | 4.99 / 16.6 | 6.36 | | 6.89 | | 0.988 | 11.9 | SFO |
| Geometric mean/median (n=10) | | | | | 12.41/13.49 | | 12.61/13.49 | | | | |

* geometric mean of both values

[17] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.
[18] A Q10 value of 2.2 is used for normalisation
[19] A Q10 value of 2.58 is used for normalisation

| (*RS*) Carbetamide-COOH | Aerobic conditions | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Soil type | X [20] | pH | t. °C / % MWHC | $DT_{50}$ /$DT_{90}$ (d) | $DT_{50}$ (d) 20 °C pF2/10kPa | St. ($r^2$) | $\chi^2$ | Method of calculation |
| Loamy sand | | 5.80 ($CaCl_2$) | 20/19.08 | 1.3/4.3 | 1.3/4.3 | 0.925 | 21.4 | SFO |
| Sandy loam | | 7.00 ($CaCl_2$) | 20/15.75 | 2.2/7.4 | 2.2/7.4 | 0.968 | 4.1 | SFO |
| Sandy loam | | 7.26 ($CaCl_2$) | 20/11.08 | 1.1/3.6 | 1.1/3.6 | 0.988 | 5.1 | SFO |
| Geometric mean/median | | | - | 1.5/1.3 | 1.5/1.3 | - | | 1.5/1.3 |

| Carbetamide | Anaerobic conditions (total system: soil and water phase) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Soil type | X [21] | pH | t. °C / % MWHC | $DT_{50}$ /$DT_{90}$ (d) | $DT_{50}$ (d) 20 °C [22]pF2/10kPa | St. ($r^2$) | $\chi^2$ | Method of calculation |
| Loamy sand | | 7.1 ($CaCl_2$) | 20 | 22.6/75.1 | - | 0.987 | 3.3 | SFO |
| Geometric mean/median | | | | | | | | |

| (*RS*) Carbetamide-COOH | Anaerobic conditions (total system: soil and water phase) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Soil type | X [23] | pH | t. °C / % MWHC | $DT_{50}$ /$DT_{90}$ (d) | $DT_{50}$ (d) 20 °C pF2/10kPa | St. ($r^2$) | $\chi^2$ | FFM (%) [24] | Method of calculation |
| Loamy sand | | 7.1 ($CaCl_2$) | 20 | 47.9/159.3 | - | 0.945 | 19.8 | 66 | SFO |
| Geometric mean/median | | | | | | | | | |

Field studies ‡ : indicative study

| | |
|---|---|
| pH dependence ‡ (yes / no) (if yes type of dependence) | no |
| Soil accumulation and plateau concentration ‡ | No data, not required |

[20] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.
[21] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.
[22] A Q10 value of 2.2 is used for normalisation at 20 °C
[23] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.
[24] Fraction of formation from parent

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

| Carbetamide ‡ | | | | | | | |
|---|---|---|---|---|---|---|---|
| Soil Type | OC % | Soil pH | Kd (mL/g) | Koc (mL/g) | Kf (mL/g) | Kfoc (mL/g) | 1/n |
| Loamy sand | 1.12 | 7.25 | - | - | 0.67 | 59.8 | 1.00 |
| Loam | 1.59 | 7.4 | - | - | 1.86 | 117.0 | 0.89 |
| Sandy loam | 3.06 | 6.8 | - | - | 1.82 | 59.5 | 0.88 |
| Clay loam | 0.99 | 7.8 | - | - | 1.17 | 118.2 | 0.93 |
| Arithmetic mean/median | | | | | | 88.6 | 0.93 |
| pH dependence, Yes or No | | | No | | | | |

| (*RS*) Carbetamide-COOH ‡ | | | | | | | |
|---|---|---|---|---|---|---|---|
| Soil Type | OC % | Soil pH | Kd (mL/g) | Koc (mL/g) | Kf (mL/g) | Kfoc (mL/g) | 1/n |
| Loamy sand | 2.21 | 5.7 ($CaCl_2$) | 0.09 | 4.1 | - | - | - |
| Sandy loam | 0.93 | 6.5 ($CaCl_2$) | 0.12 | 12.9 | - | - | - |
| Clay loam | 2.02 | 7.1 ($CaCl_2$) | 0.02 | 1.0 | - | - | - |
| Arithmetic mean/median | | | 0.08/0.09 | 6.0/4.1 | - | - | - |
| pH dependence, Yes or No | | | No | | | | |

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

| | |
|---|---|
| Column leaching ‡ | No study : not required |
| Aged residues leaching ‡ | No study : not required |
| Lysimeter/ field leaching studies ‡ | Lysimeter studies : no data, not required<br>Field leaching studies :<br>Location: Switzerland<br>Soil properties: clay loam, pH = 8.0, OC= 2.6%, MWHC = no data<br>Dates of application : 15 November 1989<br>Crop : oilseed rape |

| |
|---|
| Interception estimated: no data<br>Number of applications: 1 year, 1 application per year<br>Duration : November 1989 to August 1990<br>Application rate: 2 kg/ha/year<br>Average annual rainfall (mm): 720<br>Carbetamide levels in soil water lower than detection limits in all samples taken at 90 cm depth (<0.04 - <0.19 µg/L) and 130 cm depth (<0.02 - <0.17 µg/L).<br>This entry relates to a non radiolabelled field leaching study and the sample volumes in the suction cup samples were small as recharge to the depth of the suction samplers was limited. |

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

| | |
|---|---|
| Carbetamide<br>Method of calculation | $DT_{50}$ (d): 40.2 days<br>Kinetics: SFO<br>Field or Lab: representative worst case from laboratory studies. |
| Application data | Crop: winter oilseed rape<br>Depth of soil layer: 5 cm<br>Soil bulk density: 1.5 g/cm$^3$<br>40 % plant interception: Post-emergence<br>Number of applications: 1<br>Interval (d): -<br>Application rate(s): 1800 a.s./ha |

| **PEC$_{(s)}$** (mg/kg) | | Single application Actual | Single application Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|---|
| Initial | | 1.4400 | - | - | |
| Short term | 24h | 1.4153 | 1.4276 | - | - |
| | 2d | 1.3911 | 1.4154 | - | - |
| | 4d | 1.3438 | 1.3913 | - | - |
| Long term | 7d | 1.2759 | 1.3563 | - | - |
| | 28d | 0.8875 | 1.1416 | - | - |
| | 50d | 0.6068 | 0.9641 | - | - |
| | 100d | 0.2557 | 0.6852 | - | - |
| Plateau concentration | | Not required | | | |

| | |
|---|---|
| (*RS*) Carbetamide-COOH<br>Method of calculation | $DT_{50}$ (d): 2.2 days<br>Kinetics: SFO<br>Field or Lab: representative worst case from laboratory studies. |
| Application data | Crop: winter oilseed rape<br>Depth of soil layer: 5 cm<br>Soil bulk density: 1.5 g/cm$^3$<br>40 % plant interception: Post-emergence<br>Number of applications: 1<br>Interval (d): -<br>Maximum occurrence in soil: 37.2 %<br>Application rate(s): 1800 a.s./ha |

| **$PEC_{(s)}$** (mg/kg) | Single application Actual | Single application Time weighted average | Multiple application Actual | Multiple application Time weighted average |
|---|---|---|---|---|
| Initial | 0.474 | - | - | - |
| Plateau concentration | Not required | | | |

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

| | |
|---|---|
| Hydrolytic degradation of the active substance and metabolites > 10 % ‡ | pH 3: stable (6% or 15% degraded after 1 month at 25°C or 35°C, respectively)<br>Main metabolite : 12913RP (<5% at 25°C) |
| | pH 6: stable (10% or 26% degraded after 1 month at 25°C or 35°C, respectively)<br>Main metabolite : 10810RP (<10% at 25°C) |
| | pH 9 : 21 d at 25 °C and 7 days at 35°C (1$^{st}$ order, $r^2$=x)<br>Main metabolite 10810 RP and aniline (16% and 40%, respectively, at 25°C) |
| Photolytic degradation of active substance and metabolites above 10 % ‡ | No light absorption at λ > 290 nm |
| Quantum yield of direct phototransformation in water at Σ > 290 nm | No light absorption at λ > 290 nm |
| Readily biodegradable ‡ (yes/no) | No |

**Degradation in water / sediment**

| Parent | Distribution (eg max in water 99.58-96.30% after 0 d. Max. sed 31.7-33.2 % after 14 d) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Water / sediment system | pH water phase | pH sed | t. °C | $DT_{50}$-$DT_{90}$ whole sys. | $\chi^2$ | $DT_{50}$-$DT_{90}$ water | $\chi^2$ | $DT_{50}$- $DT_{90}$ sed | $\chi^2$ | Method of calculation |
| River Roding | 7.90 | 7.7 | 20 | 33.6/1017 FOMC | 2.95 | 8.0/94.5 DFOP | 7.99 | 150/499 SFO | 6.72 | Whole system, water and sediment: level-I |
| Manningtree | 6.19 | 6.2 | 20 | 81.0/3650 FOMC | 1.48 | 12.8/141 HS | 3.91 | 424/1409 SFO | 0.69 | Whole system, water and sediment: level-I |
| Geometric mean/median | | | | 58.8[25]/- | | - | | - | | - |

| Mineralization and non extractable residues | | | | | |
|---|---|---|---|---|---|
| Water / sediment system | pH water phase | pH sed | Mineralization x % after n d. (end of the study). | Non-extractable residues in sed. max x % after 120 d | Non-extractable residues in sed. max x % after 120 d (end of the study) |
| River Roding | 7.90 | 7.7 | 29.18% after 100 d | 30.01% after 100 d | 30.01% after 100 d |
| Manningtree | 6.19 | 6.2 | 19.87% after 100 d | 25.65% after 100 d | 25.65% after 100 d |

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

Carbetamide

Parameters used in FOCUSsw step 1 and 2

Version control no. of FOCUS calculator: STEPS 1-2 in FOCUS 1.1

Molecular weight (g/mol): 236.3

Water solubility (mg/L): 3670

$K_{OC}/K_{OM}$ (L/kg): 88.6 / 51.39

$DT_{50}$ soil (d): 12.6 days (Lab, SFO) – Q10 = 2.58

$DT_{50}$ soil (d): 12.4 days (Lab, SFO) – Q10 = 2.20

$DT_{50}$ water/sediment system (d): 58.8

$DT_{50}$ water (d): 58.8

[25] *This mean corresponds to the geomean of SFO DT50 values (44.8 and 77.3 days) since it is accepted that the back DT50 values calculated from FOMC kinetic model (306 and 1099 days) are considered as too conservative for the risk assessment.*

| | |
|---|---|
| | $DT_{50}$ sediment (d): 1000<br>Minimal crop cover (%): 20 |
| Parameters used in FOCUSsw step 3 (if performed) | FOCUS software: SWASH FOCUS version 1.1.<br>Vapour pressure: $3x10^{-7}$ Pa<br>Kom/Koc: 88.6 / 51.39<br>1/n: 0.925 |
| Application rate | Crop: winter oilseed rape<br>Crop interception: interception depending on growth stage<br>Number of applications: 1<br>Interval (d): -<br>Application rate(s): 1.800 kg as/ha<br>Application window: - |
| (*RS*) Carbetamide-COOH<br>Parameters used in FOCUSsw step 1 and 2 | Version control no. of FOCUS calculator: STEPS 1-2 in FOCUS 1.1<br>Molecular weight (g/mol): 209.2<br>Water solubility (mg/L): 412000<br>KOC/KOM (L/kg): 6.0 / -<br>Maximal occurrence in soil (%): 39.8 [26]<br>Maximal occurrence in water/sediment studies (%): 5.9<br>DT50 soil (d): 1.5 days (Lab, SFO)<br>DT50 water/sediment system (d): 1000<br>DT50 water (d): 1000<br>DT50 sediment (d): 1000<br>Minimal crop cover (%): 20 |

[26] *Maximum occurrence of 37.2 % should be used for the risk assessment. Results reported below are calculated from the value of 39.8 %. It is considered as a worst case. So, the PECsw values are not presented with the adequate parameters since that did not change the conclusion.*

| Carbetamide | | | | | |
|---|---|---|---|---|---|
| FOCUS STEP 1 Scenario | Day after overall maximum | $PEC_{SW}$ (µg/L) | | $PEC_{SED}$ (µg/kg) | |
| | | Actual | TWA | Actual | TWA |
| | 0 h | 553.16 | | 482.83 | |
| (*RS*) Carbetamide-COOH | | | | | |
| FOCUS STEP 1 Scenario | Day after overall maximum | $PEC_{SW}$ (µg/L) | | $PEC_{SED}$ (µg/kg) | |
| | | Actual | TWA | Actual | TWA |
| | 0 h | 210.60 | | 12.58 | |
| | 24 h | 210.45 | 210.52 | 12.63 | 12.61 |
| | 2 d | 210.30 | 210.45 | 12.62 | 12.61 |
| | 4 d | 210.01 | 210.30 | 12.60 | 12.61 |
| | 7 d | 209.57 | 210.08 | 12.57 | 12.60 |
| | 14 d | 208.56 | 209.58 | 12.51 | 12.57 |
| | 21d | 207.55 | 209.07 | 12.45 | 12.54 |
| | 28 d | 206.55 | 208.56 | 12.39 | 12.51 |
| | 42 d | 204.55 | 207.56 | 12.27 | 12.45 |

| Carbetamide | | | | | |
|---|---|---|---|---|---|
| FOCUS STEP 2 Scenario | Day after overall maximum | $PEC_{SW}$ (µg/L) | | $PEC_{SED}$ (µg/kg) | |
| | | Actual | TWA | Actual | TWA |
| Northern EU | 0 h | 143.86 | | 126.92 | |
| Southern EU | 0 h | 118.02 | | 104.05 | |
| (*RS*) Carbetamide-COOH | | | | | |
| FOCUS STEP 2 Scenario | Day after overall maximum | $PEC_{SW}$ (µg/L) | | $PEC_{SED}$ (µg/kg) | |
| | | Actual | TWA | Actual | TWA |
| Northern EU | 0 h | 10.77 | | 0.65 | |
| | 24 h | 10.76 | 10.76 | 0.65 | 0.65 |
| | 2 d | 10.75 | 10.76 | 0.64 | 0.65 |
| | 4 d | 10.74 | 10.75 | 0.64 | 0.64 |
| | 7 d | 10.71 | 10.74 | 0.64 | 0.64 |
| | 14 d | 10.66 | 10.71 | 0.64 | 0.64 |
| | 21d | 10.61 | 10.69 | 0.64 | 0.64 |
| | 28 d | 10.56 | 10.66 | 0.63 | 0.64 |

| Carbetamide | | | | | |
|---|---|---|---|---|---|
| FOCUS STEP 2 Scenario | Day after overall maximum | $PEC_{SW}$ (µg/L) | | $PEC_{SED}$ (µg/kg) | |
| | | Actual | TWA | Actual | TWA |
| | 42 d | 10.46 | 10.61 | 0.63 | 0.64 |
| Southern EU | 0 h | 8.79 | | 0.53 | |

| FOCUS STEP 3 Scenario | Water body | Q10 value | Day after overall maximum | $PEC_{SW}$ (µg/L) | | $PEC_{SED}$ (µg/kg) | |
|---|---|---|---|---|---|---|---|
| | | | | Actual | TWA | Actual | TWA |
| D2 ditch, drainage | | 2.58 | 0 h | 146.367 | | 80.151 | |
| | | | 24 h | 55.769 | 99.204 | 79.040 | 79.754 |
| | | | 2 d | 45.337 | 86.857 | 78.209 | 79.519 |
| | | | 4 d | 38.114 | 74.528 | 77.177 | 79.372 |
| | | | 7 d | 67.735 | 69.144 | 74.911 | 79.069 |
| | | | 14 d | 55.550 | 62.333 | 69.853 | 78.520 |
| | | | 21d | 55.767 | 59.647 | 68.187 | 77.361 |
| | | | 28 d | 53.182 | 57.211 | 66.006 | 75.899 |
| | | | 42 d | 21.939 | 49.936 | 61.010 | 73.208 |
| | | 2.20 | 0 d | 139.718 | | 71.522 | |
| D2 stream, drainage | | 2.58 | 0 h | 91.356 | | 46.764 | |
| | | | 24 h | 23.709 | 56.259 | 46.020 | 46.430 |
| | | | 2 d | 12.524 | 49.663 | 45.569 | 46.232 |
| | | | 4 d | 15.080 | 41.778 | 45.044 | 46.145 |
| | | | 7 d | 45.986 | 38.138 | 43.749 | 45.480 |
| | | | 14 d | 28.734 | 33.883 | 40.664 | 45.412 |
| | | | 21 d | 31.636 | 33.272 | 39.963 | 44.621 |
| | | | 28 d | 31.620 | 31.457 | 38.857 | 43.799 |
| | | | 42 d | 12.791 | 27.285 | 36.048 | 42.432 |
| | | 2.2 | 0 d | 87.210 | | 41.276 | |
| D3 ditch, spray drift | | 2.58 | 0 h | 11.460 | | 2.790 | |
| D4 pond, drainage | | 2.58 | 0 h | 3.644 | | 8.509 | |
| | | | 24 h | 3.640 | 3.644 | 8.509 | 8.509 |
| | | | 2 d | 3.629 | 6.642 | 8.509 | 8.509 |
| | | | 4 d | 3.593 | 3.638 | 8.506 | 8.509 |

| FOCUS STEP 3 Scenario | Water body | Q10 value | Day after overall maximum | $PEC_{SW}$ (µg/L) | | $PEC_{SED}$ (µg/kg) | |
|---|---|---|---|---|---|---|---|
| | | | | Actual | TWA | Actual | TWA |
| | | | 7 d | 3.523 | 3.626 | 8.500 | 8.508 |
| | | | 14 d | 3.343 | 3.588 | 8.477 | 8.506 |
| | | | 21 d | 3.167 | 3.532 | 8.441 | 8.502 |
| | | | 28 d | 3.186 | 3.467 | 8.394 | 8.947 |
| | | | 42 d | 3.010 | 3.367 | - | 8.483 |
| D4 stream, spray drift | | 2.58 | 0 h | 9.871 | | 3.291 | |
| D5 pond, drainage | | 2.58 | 0 h | 2.227 | | 5.333 | |
| D5 stream, spray drift | | 2.58 | 0 h | 10.649 | | 2.260 | |
| R1 pond, spray drift | | 2.58 | 0 h | 0.394 | | 0.581 | |
| R1 stream, spray drift | | 2.58 | 0 h | 7.547 | | 0.668 | |
| R3 stream, runoff | | 2.58 | 0 h | 42.808 | | 8.534 | |
| | | | 24 h | 16.387 | 28.352 | 5.550 | 6.664 |
| | | | 2 d | 0.032 | 17.720 | 3.640 | 5.908 |
| | | | 4 d | 0.007 | 8.868 | 2.632 | 4.615 |
| | | | 7 d | 0.003 | 5.212 | 2.132 | 3.722 |
| | | | 14 d | 0.001 | 2.817 | 1.522 | 2.772 |
| | | | 21 d | 0.001 | 1.879 | 1.254 | 2.314 |
| | | | 28 d | 0.001 | 1.409 | 1.112 | 2.038 |
| | | | 42 d | 0.006 | 0.947 | 0.910 | 1.695 |
| | | 2.20 | 0 d | 41.846 | | 8.352 | |

| FOCUS STEP 4 Scenario | Water body | Q10 value | Day after overall maximum | $PEC_{SW}$ (µg/L) | | $PEC_{SED}$ (µg/kg) | |
|---|---|---|---|---|---|---|---|
| | | | | Actual | TWA | Actual | TWA |
| R3, Stream, runoff Width of vegetated buffer zone = 10 m | | 2.2 | 0 h | 19.071 | | 3.793 | |

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

| | |
|---|---|
| Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter ) | For FOCUS gw modelling, values used –<br>Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance.<br>Model(s) used: PELMO version 3.3.2 & PEARL version 3.3.3<br>Scenarios (list of names):<br>Châteaudun, Hamburg, Kremsmünster, Okehampton, Piacenza, Porto<br>Crop: winter oilseed rape<br><br>Parent and metabolite *:<br>Geometric mean parent $DT_{50lab}$ = 11.2 d (n = 12, normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58).<br>$K_{OC}$: 88.6, arithmetic mean, $^1/_n$= 0.925.<br>Metabolites: (*RS*) Carbetamide-COOH<br>Geometric mean metabolite $DT_{50lab}$ = 1.5 d<br>$K_{OC}$: 6.0, arithmetic mean, $^1/_n$= 1.0 (default value).<br>Kinetic formation fraction of (*RS*) Carbetamide-COOH from carbetamide 0.66<br><br>Parent only **:<br>Geometric mean parent $DT_{50lab}$ = 12.6 d (n = 10, normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58).<br>$K_{OC}$: 88.6, arithmetic mean, $^1/_n$= 0.925. |
| Application rate | Application rate: 1.800 kg/ha.<br>No. of applications: 1<br>Time of application (month or season):<br>Châteaudun : 08th September<br>Hamburg : 03rd September<br>Kremsmünster : 03rd September<br>Okehampton : 15th August<br>Piacenza : 06th October<br>Porto : 08th September |

**PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m) _ application every year**

| | | | | |
|---|---|---|---|---|
| PELMO 3.3.2l / winter oilseed rape | Q10 value | 2.58 | 2.58 | 2.58 |
| | Scenario | Parent * (µg/L) | Metabolite * (µg/L) | Parent only ** (µg/L) |
| | Chateaudun | <0.001 | 0.004 | < 0.001 |
| | Hamburg | 0.007 | **0.312** | 0.019 |
| | Kremsmunster | 0.002 | 0.070 | 0.005 |
| | Okehampton | 0.003 | 0.046 | 0.009 |
| | Piacenza | **0.232** | **0.623** | **0.372** |
| | Porto | <0.001 | 0.010 | < 0.0001 |
| PEARL 3.3.3. / winter oilseed rape | Q10 value | 2.58 | 2.58 | 2.58 |
| | Scenario | Parent * (µg/L) | Metabolite * (µg/L) | Parent only ** (µg/L) |
| | Chateaudun | <0.001 | 0.007 | 0.0013 |
| | Hamburg | 0.020 | **0.156** | 0.0472 |
| | Kremsmunster | 0.017 | 0.037 | 0.0377 |
| | Okehampton | 0.013 | 0.025 | 0.0310 |
| | Piacenza | **0.347** | **0.268** | **0.5265** |
| | Porto | <0.001 | 0.008 | < 0.0001 |

**PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m) _ application every three years**

| | | | | |
|---|---|---|---|---|
| PELMO 3.3.2l / winter oilseed rape | Q10 value | 2.58 | 2.58 | 2.58 |
| | Scenario | Parent * (µg/L) | Metabolite * (µg/L) | Parent only ** (µg/L) |
| | Chateaudun | <0.001 | 0.002 | < 0.001 |
| | Hamburg | 0.001 | 0.085 | 0.0030 |
| | Kremsmunster | 0.001 | 0.027 | 0.0010 |
| | Okehampton | 0.001 | 0.014 | 0.0030 |
| | Piacenza | 0.072 | **0.260** | **0.1050** |
| | Porto | <0.001 | 0.004 | < 0.0001 |
| PEARL 3.3.3. / winter oilseed rape | Q10 value | 2.58 | 2.58 | 2.58 |
| | Scenario | Parent * (µg/L) | Metabolite * (µg/L) | Parent only ** (µg/L) |
| | Chateaudun | <0.001 | 0.003 | 0.0006 |
| | Hamburg | 0.008 | 0.061 | 0.0176 |
| | Kremsmunster | 0.002 | 0.012 | 0.0057 |
| | Okehampton | 0.004 | 0.011 | 0.0106 |
| | Piacenza | **0.143** | **0.132** | **0.2152** |
| | Porto | <0.001 | 0.002 | < 0.0001 |

**$PEC_{(gw)}$** From lysimeter / field studies : no data, no required

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

| | |
|---|---|
| Direct photolysis in air ‡ | Not studied - no data requested |
| Quantum yield of direct phototransformation | Not studied - no data requested as no significant absorption > 290 nm |
| Photochemical oxidative degradation in air ‡ | $DT_{50}$ of 2.151 hours derived by the Atkinson model. OH (12h) concentration assumed = 1.5E6 $OH/cm^3$ |
| Volatilisation ‡ | from plant surfaces (BBA guideline): 9% within 24 hours |
| | from soil surfaces (BBA guideline): 3 % within 24 hours |
| Metabolites | None |

## PEC (air)

| | |
|---|---|
| Method of calculation | - |

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

| | |
|---|---|
| Maximum concentration | Not calculated, negligible concentrations expected in air |

**Residues requiring further assessment**

| | |
|---|---|
| Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology) or for which a groundwater exposure assessment is triggered. | Soil: Carbetamide, (*RS*) Carbetamide-COOH<br>Surface Water: Carbetamide, (*RS*) Carbetamide-COOH<br>Sediment: Carbetamide, (*RS*) Carbetamide-COOH<br>Ground water: Carbetamide, (*RS*) Carbetamide-COOH<br>Air: Carbetamide |

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

| | |
|---|---|
| Soil (indicate location and type of study) | No data, not required |
| Surface water (indicate location and type of study) | No data, not required |
| Ground water (indicate location and type of study) | No data, not required |
| Air (indicate location and type of study) | No data, not required |

**Points pertinent to the classification and proposed labelling with regard to fate and behaviour data**

| |
|---|
| Candidate for R53 |

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

| Species | Test substance | Time scale | End point (mg/kg bw/day) | End point (mg/kg feed) |
|---|---|---|---|---|
| Birds ‡ | | | | |
| *Bobwhite quail* | a.s. | Acute | > 2000 | |
| *Japanese quail* | Preparation FSG 01002 H | Acute | > 1200 (a.s.) | |
| *Japanese quail* | a.s. | Short-term | > 1044 | |
| *Japanese quail* | a.s. | Long-term | Reproduction : 169<br>Adults: 341 | |
| Mammals ‡ | | | | |
| *rat* | a.s. | Acute | > 2000 | |
| *mice* | a.s. | Acute | 1718 | |
| *rat* | Preparation FSG 01002 H | Acute | > 1200 (a.s.) | |
| *Rat* | a.s. | Long-term, 104-week oral | 7 | |
| *Mice* | a.s. | Long-term, 104-week oral | 21 | |
| *rat* | a.s. | Long-term, two generation oral | 208 (reproduction) | |
| Additional higher tier studies ‡ | | | | |
| | | | | |

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

Crop and application rate

| Indicator species/Category | Time scale | ETE | TER | Annex VI Trigger |
|---|---|---|---|---|
| Tier 1 (Birds) | | | | |
| Medium herbivorous | Acute | 119.02 | > 10.08* | 10 |
| insectivorous | Acute | 97.34 | > 12.33 | 10 |
| Medium herbivorous | Short-term | 54.72 | > 19.08 | 10 |
| insectivorous | Short-term | 54.29 | > 19.23 | 10 |
| Medium herbivorous | Long-term | 29.00 | 11.76 | 5 |
| insectivorous | Long-term | 54.29 | 6.28 | 5 |
| Tier 1 (Mammals) | | | | |
| Medium herbivorous | Acute | 43.85 | 39.18 | 10 |
| Medium herbivorous | Long-term | 10.65 | 19.53 | 5 |

* Based on the formulation (FSG 01002) endpoint.

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

| Group | Test substance | Time-scale (Test type) | End point | Toxicity[1] (mg/L) |
|---|---|---|---|---|
| Laboratory tests ‡ | | | | |
| Fish | | | | |
| *Onchorhynchus mykiss* | a.s. | 96 hr (static) | Mortality, $EC_{50}$ | > 100 (nom) |
| *Cyprinus carpio* | a.s. | 96 hr (static) | Mortality, $EC_{50}$ | > 100 (nom) |
| *Onchorhynchus mykiss* | a.s. | 21 d (static) | Growth NOEC | > 100 (nom) |
| *Onchorhynchus mykiss* | Preparation | 96 hr (static) | Mortality, $EC_{50}$ | 5.7 (form)<br>3.4 (a.s.) (nom) |
| *Onchorhynchus mykiss* | Preparation | 28 d (semi-static) | Growth NOEC | 5.7 (form)<br>3.4 (a.s.)<br>(nom) |
| *Onchorhynchus mykiss* | Metabolite (*RS*) carbetamide-COOH | 96 hr (flow-through) | Mortality, $EC_{50}$ | > 100 (nom) |
| Aquatic invertebrate | | | | |
| *Daphnia magna* | a.s. | 48 h (static) | Mortality, $EC_{50}$ | 81 (nom) |
| *Daphnia magna* | a.s. | 21 d (static) | Reproduction, NOEC | 1 (parental) (nom) |
| *Daphnia magna* | Preparation | 48 h (static) | Mortality, $EC_{50}$ | > 100 (form)<br>> 59.1 (a.s.) (nom) |
| *Daphnia magna* | Preparation | 21 d (static) | Reproduction, NOEC | 1710 (form)<br>1.03 (a.s.) (parental) (nom) |
| *Daphnia magna* | Metabolite (*RS*) carbetamide-COOH | 48 h (static) | Mortality, $EC_{50}$ | > 100 (a.s.) (nom) |
| Sediment dwelling organisms | | | | |
| *Chironomus riparius* | Metabolite (*RS*) carbetamide-COOH | 28 d (static) | NOEC | 640 (a.s.) (nom) |
| Algae | | | | |
| *Scenedesmus subspicatus* | a.s. | 72 h (static) | Biomass: $E_bC_{50}$<br>Growth rate: $E_rC_{50}$ | 158 (nom)<br>305 |
| *Navicula pelliculosa* | a.s. | 72 h (static) | Biomass: $E_bC_{50}$<br>Growth rate: $E_rC_{50}$ | 128 (nom)<br>212 |

| Group | Test substance | Time-scale (Test type) | End point | Toxicity[1] (mg/L) |
|---|---|---|---|---|
| *Navicula pelliculosa* | Preparation | 72 h (static) | Biomass: $E_bC_{50}$<br><br>Growth rate: $E_rC_{50}$ | 99 (form)<br>59.4 (a.s.) (nom)<br>108 (form)<br>64.8 (a.s) |
| *Scenedesmus subspicatus* | Metabolite (*RS*) carbetamide-COOH | 72 h (static) | Biomass: $E_bC_{50}$<br>Growth rate: $E_rC_{50}$ | > 100 (nom)<br>> 100 |
| Higher plant | | | | |
| *Lemna minor* | a.s. | 7 d (static) | Fronds, $EbC_{50}$<br>$ErC_{50}$ | 629 (nom)<br>301 |
| *Lemna gibba* | Metabolite (*RS*) carbetamide-COOH | 14 d (static) | Fronds, $EbC_{50}$<br>$ErC_{50}$ | 110.8 (nom)<br>460.5 |
| Microcosm or mesocosm tests | | | | |
| Indicate if not required | | | | |

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

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

**FOCUS Step1**

Winter oilseed rape, 1.8 kg a.s./ha

| Test substance | Organism | Toxicity end point (µg/L) | Time scale | $PEC_i$ | $PEC_{twa}$ | TER | Annex VI Trigger[1] |
|---|---|---|---|---|---|---|---|
| a.s. | Fish | 96h LC50 = > 100000 | Acute | 553.16 | | > 180.8 | 100 |
| a.s. | Fish | NOEC = 32000 | Chronic | 553.16 | | 57.85 | 10 |
| a.s. | Aquatic invertebrates | 48h EC50 = 81000 | Acute | 553.16 | | 146.4 | 100 |
| a.s. | Aquatic invertebrates | NOEC = 1000 | Chronic | 553.16 | | 1.8 | 10 |
| a.s. | Algae | EbC50 = 128000 | Chronic | 553.16 | | 231.4 | 10 |
| a.s. | Higher plants[2] | ErC50 = 301000 | Chronic | 553.16 | | 544.2 | 10 |
| Metabolite (*RS*) carbetamide-COOH | Fish | 96h LC50 > 100000 | Acute | 210.6 | | > 474.8 | 100 |

| Test substance | Organism | Toxicity end point (µg/L) | Time scale | $PEC_i$ | $PEC_{twa}$ | TER | Annex VI Trigger[1] |
|---|---|---|---|---|---|---|---|
| Metabolite (*RS*) carbetamide-COOH | Aquatic invertebrates | 48h EC50 > 100000 | Acute | 210.6 | | > 474.8 | 100 |
| Metabolite (*RS*) carbetamide-COOH | Algae | EbC50 > 100000 | Chronic | 210.6 | | > 474.8 | 10 |
| Metabolite (*RS*) carbetamide-COOH | Higher plants[2] | ErC50 = 110800 | Chronic | 210.6 | | 526.1 | 10 |
| Metabolite (*RS*) carbetamide-COOH | Sediment dwelling organisms | 28d NOEC = | Chronic | 12.58 ($PEC_{sed}$) | | 50874 | 10 |
| Product | Fish | 96h LC50 = 3400 | Acute | 553.16 | | 6.15 | 100 |
| Product | Fish | NOEC = 3400 | Chronic | 553.16 | | 6.15 | 10 |
| Product | Aquatic invertebrates | 48h EC50 = 59100 | Acute | 553.16 | | 106.8 | 100 |
| Product | Aquatic invertebrates | NOEC = 1030 | Chronic | 553.16 | | 1.86 | 10 |
| Product | Algae | EbC50 = 59400 | Chronic | 553.16 | | 107.4 | 10 |

[1]If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

**FOCUS Step 2**

Winter oilseed rape, 1.8 kg a.s./ha (until BBCH 14-16), Northern Europe and Southern Europe

| Test substance | N/S[1] | Organism | Toxicity end point (µg/L) | Time scale | PECmax | TER | Annex VI Trigger[2] |
|---|---|---|---|---|---|---|---|
| a.s. | N | Aquatic invertebrates | 1000 | Chronic | 146.55 | **6.82** | 10 |
| a.s. | S | Aquatic invertebrates | 1000 | Chronic | 120.17 | **8.32** | 10 |
| Product | N | Fish | 3400 | Acute | 146.55 | **23.2** | 100 |
| Product | S | Fish | 3400 | Acute | 120.17 | **28.3** | 100 |
| Product | N | Fish | 3400 | Chronic | 146.55 | 23.2 | 10 |
| Product | S | Fish | 3400 | Chronic | 120.17 | 28.3 | 10 |
| Product | N | Aquatic invertebrates | 1030 | Chronic | 146.55 | **7.03** | 10 |
| Product | S | Aquatic invertebrates | 1030 | Chronic | 120.17 | **8.6** | 10 |

[1] Northern or Southern

[2] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

**Refined aquatic risk assessment using higher tier FOCUS modelling.**

**FOCUS Step 3**

Winter oilseed rape, 1.8 kg a.s./ha

| Test substance | Scenario | Water body type | Test organism[1] | Time scale | Toxicity end point (µg/L) | $PEC_{sw, max}$ | TER | Annex VI trigger[2] |
|---|---|---|---|---|---|---|---|---|
| a.s. | Drainage (D2) | ditch | Aquatic invertebrates | Chronic | 1000 | 146.367 | **6.8** | 10 |
| | | stream | Aquatic invertebrates | Chronic | 1000 | 91.356 | 10.95 | 10 |
| | Drainage (D3) | ditch | Aquatic invertebrates | Chronic | 1000 | 11.460 | 87.3 | 10 |
| | Drainage (D4) | pond | Aquatic invertebrates | Chronic | 1000 | 3.644 | 274.4 | 10 |
| | | stream | Aquatic invertebrates | Chronic | 1000 | 9.871 | 101.3 | 10 |
| | Drainage (D5) | pond | Aquatic invertebrates | Chronic | 1000 | 2.227 | 449.03 | 10 |
| | | stream | Aquatic invertebrates | Chronic | 1000 | 10.649 | 93.9 | 10 |
| | Run-off (R1) | pond | Aquatic invertebrates | Chronic | 1000 | 0.394 | 2532 | 10 |
| | Run-off (R1) | stream | Aquatic invertebrates | Chronic | 1000 | 7.547 | 132.5 | 10 |
| | Run-off (R3) | stream | Aquatic invertebrates | Chronic | 1000 | 42.808 | 23.4 | 10 |
| Product | Drainage (D2) | ditch | Fish | Acute | 3400 | 146.367 | **23.2** | 100 |
| | | stream | Fish | Acute | 3400 | 91.356 | **37.2** | 100 |
| | Drainage (D3) | ditch | Fish | Acute | 3400 | 11.460 | 297 | 100 |
| | Drainage (D4) | pond | Fish | Acute | 3400 | 3.644 | 933 | 100 |
| | | stream | Fish | Acute | 3400 | 9.871 | 344 | 100 |
| | Drainage (D5) | pond | Fish | Acute | 3400 | 2.227 | 1527 | 100 |
| | | stream | Fish | Acute | 3400 | 10.649 | 319 | 100 |
| | Run-off (R1) | pond | Fish | Acute | 3400 | 0.394 | 8629 | 100 |
| | Run-off (R1) | stream | Fish | Acute | 3400 | 7.547 | 450 | 100 |
| | Run-off (R3) | stream | Fish | Acute | 3400 | 42.808 | **79.4** | 100 |
| Product | Drainage (D2) | ditch | Fish | Chronic | 3400 | 146.367 | **23.2** | 10 |
| | | stream | Fish | Chronic | 3400 | 91.356 | **37.2** | 10 |

| Test substance | Scenario | Water body type | Test organism[1] | Time scale | Toxicity end point (µg/L) | $PEC_{sw, max}$ | TER | Annex VI trigger[2] |
|---|---|---|---|---|---|---|---|---|
| | Drainage (D3) | ditch | Fish | Chronic | 3400 | 11.460 | 297 | 10 |
| | Drainage (D4) | pond | Fish | Chronic | 3400 | 3.644 | 933 | 10 |
| | | stream | Fish | Chronic | 3400 | 9.871 | 344 | 10 |
| | Drainage (D5) | pond | Fish | Chronic | 3400 | 2.227 | 1527 | 10 |
| | | stream | Fish | Chronic | 3400 | 10.649 | 319 | 10 |
| | Run-off (R1) | pond | Fish | Chronic | 3400 | 0.394 | 8629 | 10 |
| | Run-off (R1) | stream | Fish | Chronic | 3400 | 7.547 | 450 | 10 |
| | Run-off (R3) | stream | Fish | Chronic | 3400 | 42.808 | **79.4** | 10 |
| Product | Drainage (D2) | ditch | Aquatic invertebrates | Chronic | 1030 | 146.367 | **7.03** | 10 |
| | | stream | Aquatic invertebrates | Chronic | 1030 | 91.356 | 11.3 | 10 |
| | Drainage (D3) | ditch | Aquatic invertebrates | Chronic | 1030 | 11.460 | 89.9 | 10 |
| | Drainage (D4) | pond | Aquatic invertebrates | Chronic | 1030 | 3.644 | 282 | 10 |
| | | stream | Aquatic invertebrates | Chronic | 1030 | 9.871 | 104 | 10 |
| | Drainage (D5) | pond | Aquatic invertebrates | Chronic | 1030 | 2.227 | 462 | 10 |
| | | stream | Aquatic invertebrates | Chronic | 1030 | 10.649 | 96.7 | 10 |
| | Run-off (R1) | pond | Aquatic invertebrates | Chronic | 1030 | 0.394 | 2614 | 10 |
| | Run-off (R1) | stream | Aquatic invertebrates | Chronic | 1030 | 7.547 | 136 | 10 |
| | Run-off (R3) | stream | Aquatic invertebrates | Chronic | 1030 | 42.808 | 24 | 10 |

[1] include critical groups which fail at Step 2.

[2] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

**FOCUS Step 4**

Crop and application rate

| Scenario | Water body type | Test organism | Time scale | Toxicity end point (µg/L) | Buffer zone distance | $PEC_{sw, max}$ | TER | Annex VI trigger[1] |
|---|---|---|---|---|---|---|---|---|
| Run-off (R3) | stream | Aquatic invertebrates | Chronic | 1030 | 10 m | 19.071 | 52.4 | 10 |

[1] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

A FOCUS Step 4 calculations were conducted for run-off scenario. Appropriate risk mitigation measures (buffer strip of 10 m, restriction on drained soils) should be taken into account to reduce possible impacts.

| **Bioconcentration** | |
|---|---|
| | Active substance |
| $logP_{O/W}$ | 1.78 |
| Bioconcentration factor (BCF)[1] ‡ | - |
| Annex VI Trigger for the bioconcentration factor | - |
| Clearance time (days) ($CT_{50}$) | - |
| ($CT_{90}$) | - |
| Level and nature of residues (%) in organisms after the 14 day depuration phase | - |

[1] only required if log $P_{O/W}$ >3.

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

| Test substance | Acute oral toxicity ($LD_{50}$ µg/bee) | Acute contact toxicity ($LD_{50}$ µg/bee) |
|---|---|---|
| a.s. ‡ | - | - |
| Preparation[1] | > 63.22 (a.s.) | > 100 (a.s.) |
| Field or semi-field tests | | |
| Indicate if not required | | |

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

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

Crop and application rate

| Test substance | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|
| Preparation | Contact | < 18 | 50 |

| Test substance | Route | Hazard quotient | Annex VI Trigger |
|---|---|---|---|
| Preparation | oral | < 28.5 | 50 |

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

Laboratory tests with standard sensitive species

| Species | Test Substance | End point | Effect ($LR_{50}$ g/ha[1]) |
|---|---|---|---|
| *Typhlodromus pyri* ‡ | FSG 01002H | Mortality | > 3015 (a.s.) |
| *Aphidius rhopalosiphi* ‡ | FSG 01002H | Mortality | > 3015 (a.s.) |

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Crop and application rate

| Test substance | Species | Effect ($LR_{50}$ g/ha) | HQ in-field | HQ off-field[1] | Trigger |
|---|---|---|---|---|---|
| FSG 01002H | *Typhlodromus pyri* | > 3015 (a.s.) | < 0.597 | < 0.016 (1 m) | 2 |
| FSG 01002H | *Aphidius rhopalosiphi* | > 3015 (a.s.) | < 0.597 | < 0.016 (1 m) | 2 |

[1] indicate distance assumed to calculate the drift rate

| Field or semi-field tests |
|---|
| Indicate if not required |

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

| Test organism | Test substance | Time scale | End point[1] |
|---|---|---|---|
| Earthworms | | | |
| *Eisenia foetida* | a.s. ‡ | Acute 14 days | $LC_{50}$ = 660 mg a.s./kg d.w.soil |
| *Eisenia foetida* | Preparation | Acute | $LC_{50}$ > 591 mg a.s./kg d.w.soil |
| *Eisenia foetida* | Metabolite (*RS*) carbetamide-COOH | Acute | $LC_{50}$ > 1000 mg a.s./kg d.w.soil |
| Soil micro-organisms | | | |
| Nitrogen mineralisation | preparation | 56 days | 42.3 % effect at day 28 and 17.2 % effect at day 56 at 34.3 mg./kg d.w.soil (eq. 20.01 mg a.s/kg dry soil) |
| Nitrogen mineralisation | Metabolite (*RS*) carbetamide-COOH | 28 days | < 25 % effect at 20 mg/kg d.w. soil |
| Carbon mineralisation | preparation | 28 days | < 25 % effect at day 28 at 34.3 mg./kg d.w.soil (eq. 20.01 mg a.s/kg dry soil) |

| Test organism | Test substance | Time scale | End point[1] |
|---|---|---|---|
| Carbon mineralisation | Metabolite (*RS*) carbetamide-COOH | 42 days | < 25 % effect at 20 mg/kg d.w. soil |
| Field studies[2] | | | |
| Indicate if not required | | | |

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. $LC_{50corr}$)
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

**Toxicity/exposure ratios for soil organisms**

Crop and application rate

| Test organism | Test substance | Time scale | Soil PECmax | TER | Trigger |
|---|---|---|---|---|---|
| Earthworms | | | | | |
| *Eisenia foetida* | a.s. ‡ | Acute | 1.44 | 458 | 10 |
| *Eisenia foetida* | Preparation | Acute | 1.44 | > 410 | 10 |
| | Metabolite (*RS*) carbetamide-COOH | Acute | 0.507 | > 986 | 10 |
| Other soil macro-organisms | | | | | |

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

Preliminary screening data

| |
|---|
| Not required for herbicides as $ER_{50}$ tests should be provided |

Laboratory dose response tests

| Most sensitive species | Test substance | $ER_{50}$ (g /ha) vegetative vigour | $ER_{50}$ (g /ha)[2] emergence | Exposure[1] (g a.s./ha)[2] | TER | Trigger |
|---|---|---|---|---|---|---|
| *Poa annua* | carbetamide | 200 (phytotoxicity) | - | 49.86 (1 m)<br>10.26 (5 m) | **4.01**<br>19.49 | 5 |
| *Avena sativa* | Preparation | 1280 (a.s.) | > 3000 | 49.86 (1 m)<br>10.26 (5 m) | 25.67<br>124.76 | 5 |
| *Poa annua* | metabolite (*RS*) carbetamide-COOH | 4870 (phytotoxicity) | - | | -[2] | |

[1] based on Ganzelmeier drift data
[2] covered by the parent risk assessment

Additional studies (e.g. semi-field or field studies)

| |
|---|
| |

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

| Test type/organism | end point |
|---|---|

| | |
|---|---|
| Activated sludge | 3-hour EC50 = 1106 mg/L (eq. 635.6 mg a.s./L) |

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

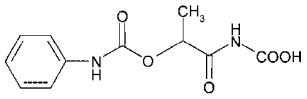
| Compartment | |
|---|---|
| soil | Parent (carbetamide) |
| water | Parent (carbetamide) |
| sediment | Parent (carbetamide) |

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

| | RMS/peer review proposal |
|---|---|
| Active substance | R52/53 |

| | RMS/peer review proposal |
|---|---|
| Preparation | N R51/53 |

## APPENDIX B – USED COMPOUND CODE(S)

| Code/Trivial name* | Chemical name | Structural formula |
|---|---|---|
| **(*RS*) carbetamide-COOH** | (*RS*) 2-phenylcarbamoyl-propionic acid |  |

* The metabolite name in bold is the name used in the conclusion.

## ABBREVIATIONS

| | |
|---|---|
| 1/n | slope of Freundlich isotherm |
| ε | decadic molar extinction coefficient |
| °C | degree Celsius (centigrade) |
| µg | microgram |
| µm | micrometer (micron) |
| a.s. | active substance |
| AChE | acetylcholinesterase |
| ADE | actual dermal exposure |
| ADI | acceptable daily intake |
| AF | assessment factor |
| AOEL | acceptable operator exposure level |
| AP | alkaline phosphatase |
| AR | applied radioactivity |
| ARfD | acute reference dose |
| AST | aspartate aminotransferase (SGOT) |
| AV | avoidance factor |
| BCF | bioconcentration factor |
| BUN | blood urea nitrogen |
| bw | body weight |
| CAS | Chemical Abstract Service |
| CFU | colony forming units |
| ChE | cholinesterase |
| CI | confidence interval |
| CIPAC | Collaborative International Pesticide Analytical Council Limited |
| CL | confidence limits |
| d | day |
| DAA | days after application |
| DAR | draft assessment report |
| DAT | days after treatment |
| DM | dry matter |
| $DT_{50}$ | period required for 50 percent disappearance (define method of estimation) |
| $DT_{90}$ | period required for 90 percent disappearance (define method of estimation) |
| dw | dry weight |
| $EbC_{50}$ | effective concentration (biomass) |
| $EC_{50}$ | effective concentration |
| ECHA | European Chemical Agency |
| EEC | European Economic Community |
| EINECS | European Inventory of Existing Commercial Chemical Substances |
| ELINCS | European List of New Chemical Substances |
| EMDI | estimated maximum daily intake |
| $ER_{50}$ | emergence rate/effective rate, median |
| $ErC_{50}$ | effective concentration (growth rate) |
| EU | European Union |
| EUROPOEM | European Predictive Operator Exposure Model |
| f(twa) | time weighted average factor |
| FAO | Food and Agriculture Organisation of the United Nations |
| FIR | Food intake rate |
| FOB | functional observation battery |
| FOCUS | Forum for the Co-ordination of Pesticide Fate Models and their Use |
| g | gram |
| GAP | good agricultural practice |
| GC | gas chromatography |
| GCPF | Global Crop Protection Federation (formerly known as GIFAP) |

| | |
|---|---|
| GGT | gamma glutamyl transferase |
| GM | geometric mean |
| GS | growth stage |
| GSH | glutathion |
| h | hour(s) |
| ha | hectare |
| Hb | haemoglobin |
| Hct | haematocrit |
| hL | hectolitre |
| HPLC | high pressure liquid chromatography or high performance liquid chromatography |
| HPLC-MS | high pressure liquid chromatography – mass spectrometry |
| HQ | hazard quotient |
| IEDI | international estimated daily intake |
| IESTI | international estimated short-term intake |
| ISO | International Organisation for Standardisation |
| IUPAC | International Union of Pure and Applied Chemistry |
| JMPR | Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues) |
| $K_{doc}$ | organic carbon linear adsorption coefficient |
| kg | kilogram |
| $K_{Foc}$ | Freundlich organic carbon adsorption coefficient |
| L | litre |
| LC | liquid chromatography |
| $LC_{50}$ | lethal concentration, median |
| LC-MS | liquid chromatography-mass spectrometry |
| LC-MS-MS | liquid chromatography with tandem mass spectrometry |
| $LD_{50}$ | lethal dose, median; dosis letalis media |
| LDH | lactate dehydrogenase |
| LOAEL | lowest observable adverse effect level |
| LOD | limit of detection |
| LOQ | limit of quantification (determination) |
| m | metre |
| M/L | mixing and loading |
| MAF | multiple application factor |
| MCH | mean corpuscular haemoglobin |
| MCHC | mean corpuscular haemoglobin concentration |
| MCV | mean corpuscular volume |
| mg | milligram |
| mL | millilitre |
| mm | millimetre |
| MRL | maximum residue limit or level |
| MS | mass spectrometry |
| MSDS | material safety data sheet |
| MTD | maximum tolerated dose |
| MWHC | maximum water holding capacity |
| NESTI | national estimated short-term intake |
| ng | nanogram |
| NOAEC | no observed adverse effect concentration |
| NOAEL | no observed adverse effect level |
| NOEC | no observed effect concentration |
| NOEL | no observed effect level |
| OM | organic matter content |
| Pa | Pascal |

| | |
|---|---|
| PD | proportion of different food types |
| PEC | predicted environmental concentration |
| $PEC_{air}$ | predicted environmental concentration in air |
| $PEC_{gw}$ | predicted environmental concentration in ground water |
| $PEC_{sed}$ | predicted environmental concentration in sediment |
| $PEC_{soil}$ | predicted environmental concentration in soil |
| $PEC_{sw}$ | predicted environmental concentration in surface water |
| pH | pH-value |
| PHED | pesticide handler's exposure data |
| PHI | pre-harvest interval |
| PIE | potential inhalation exposure |
| $pK_a$ | negative logarithm (to the base 10) of the dissociation constant |
| $P_{ow}$ | partition coefficient between *n*-octanol and water |
| PPE | personal protective equipment |
| ppm | parts per million ($10^{-6}$) |
| ppp | plant protection product |
| PT | proportion of diet obtained in the treated area |
| PTT | partial thromboplastin time |
| QSAR | quantitative structure-activity relationship |
| $r^2$ | coefficient of determination |
| RPE | respiratory protective equipment |
| RUD | residue per unit dose |
| SC | suspension concentrate |
| SD | standard deviation |
| SFO | single first-order |
| SSD | species sensitivity distribution |
| STMR | supervised trials median residue |
| $t_{1/2}$ | half-life (define method of estimation) |
| TER | toxicity exposure ratio |
| $TER_A$ | toxicity exposure ratio for acute exposure |
| $TER_{LT}$ | toxicity exposure ratio following chronic exposure |
| $TER_{ST}$ | toxicity exposure ratio following repeated exposure |
| TK | technical concentrate |
| TLV | threshold limit value |
| TMDI | theoretical maximum daily intake |
| TRR | total radioactive residue |
| TSH | thyroid stimulating hormone (thyrotropin) |
| TWA | time weighted average |
| UDS | unscheduled DNA synthesis |
| UV | ultraviolet |
| W/S | water/sediment |
| w/v | weight per volume |
| w/w | weight per weight |
| WBC | white blood cell |
| WG | water dispersible granule |
| WHO | World Health Organisation |
| wk | week |
| yr | year |