CONCLUSION ON PESTICIDE PEER REVIEW

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

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Carboxin is one of the 84 substances of the third stage part B 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 the United Kingdom, 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 carboxin in Annex I to Council Directive 91/414/EEC.

Following the Commission Decision of 5 December 2008 (2008/934/EC)[5] concerning the non-inclusion of carboxin in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Chemtura Europe Ltd made a resubmission application for the inclusion of carboxin 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, the United Kingdom, 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 4 December 2009.

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 8 December 2009. The EFSA collated and forwarded all comments received to the Commission on 22 January 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 carboxin.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of carboxin as a fungicide on cereals as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

1 On request from the European Commission, Question No EFSA-Q-2010-00132, issued on 11 October 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

Suggested citation: European Food Safety Authority; Conclusion on the peer review of the pesticide risk assessment of the active substance carboxin. EFSA Journal 2010;8(10):1857. [65 pp.] doi:10.2903/j.efsa.2010.1857. Available online: www.efsa.europa.eu/efsajournal.htm

Data gaps are identified in the section identity and analytical methods. A critical area of concern is identified for the technical specification.

For mammalian toxicology, a critical area of concern is identified, as based on the available information the batches tested in the mammalian toxicology section could not be considered toxicologically equivalent to the currently proposed technical specification (which was not agreed by the physical-chemical section). As classification with R40 (carcinogen category 3) is proposed for carboxin, the groundwater metabolites are considered toxicologically relevant. It is noted that the sulfone metabolite of carboxin is the active substance oxycarboxin, which is relevant being an active substance with pesticidal activity.

For residues no critical areas of concern are identified. However, the risk assessment cannot be finalised as there is a data gap identified for rotational crops.

The data available on fate and behaviour in the environment are essentially sufficient to carry out the required environmental exposure assessments at EU level for the representative uses assessed. The potential for groundwater exposure by several metabolites is predicted to be high over a wide range of geoclimatic conditions represented by the FOCUS groundwater scenarios. It should be noted that one of these metabolites (oxycarboxin) is a pesticide active substance (fungicide). As all metabolites are considered toxicologically relevant, a critical area of concern has been identified.

A data gap remains to address the long-term risk to granivorous birds and mammals, and herbivorous mammals for the representative uses of carboxin as a seed treatment. This has been considered to be a critical area of concern. In addition, a data gap is identified to address the risk to birds and mammals from the representative formulation. For all other groups of non-target organisms the risk was assessed as low without the need for further refinements or risk mitigation measures.

KEY WORDS

Carboxin, peer review, risk assessment, pesticide, fungicide

TABLE OF CONTENTS

BACKGROUND

Legislative framework

Commission Regulation (EC) No 1490/2002[7], as amended by Commission Regulation (EC) No 1095/2007[8] 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[9] 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(s) 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

Carboxin is one of the 84 substances of the third stage part B 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 (The United Kingdom, 2006) provided by the designated rapporteur Member State, the United Kingdom, which was received by the EFSA on 5 April 2006.

The peer review was initiated on 24 July 2006 by dispatching the DAR to Member States and the applicant Chemtura Europe Ltd (formerly Crompton Europe Limited) for consultation and comments. In addition, the EFSA conducted a public consultation on the DAR.

The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of carboxin 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 5 December 2008 (2008/934/EC)[10] concerning the non-inclusion of carboxin in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Chemtura Europe Ltd made a resubmission application for the inclusion of carboxin 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 particular with regard to the following: the metabolism of carboxin in mammals and its genotoxic risk to humans; soil metabolite identification; the risk to groundwater and refined ecotoxicology risk assessment.

In accordance with Article 18, the United Kingdom, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report (The United Kingdom, 2009). The Additional Report was received by the EFSA on 4 December 2009.

[7] OJ L224, 21.08.2002, p.25
[8] OJ L246, 21.9.2007, p.19
[9] OJ L 15, 18.01.2008, p.5
[10] OJ L 333, 11.12.2008, p.11

In accordance with Article 19, the EFSA distributed the Additional Report to Member States and the applicant for comments on 8 December 2009. In addition, the EFSA conducted a public consultation on the Additional Report. The EFSA collated and forwarded all comments received to the Commission on 22 January 2010. At the same time, the collated comments were forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were 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 22 February 2010, the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on carboxin within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were 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 23 February 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 mammalian toxicology, environmental fate and behaviour and ecotoxicology.

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 August 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 uses as a fungicide on cereals, 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 (EFSA, 2010), 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 comprises the following documents:

- the comments received,
- the Reporting Table (revision 1-1; 24 February 2010),
- the Evaluation Table (22 September 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 July 2010 containing all individually submitted addenda) (The United Kingdom, 2010) 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

Carboxin is the ISO common name for 5,6-dihydro-2-methyl-1,4-oxathiine-3-carboxanilide (IUPAC).

The representative formulated product for the evaluation was 'Vitavax 200FF', a flowable concentrate for seed treatment (FS), containing 200 g/L carboxin and 200 g/L thiram, registered under different trade names in Europe.

The representative uses evaluated comprises seed treatment to control soil and seed borne diseases in cereals (wheat, barley, oats, rye and triticale). Full details of the representative uses 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 carboxin technical material is 970 g/kg. No FAO specification exists.

Data gaps are identified for a new 5-batch analysis with specific analytical methods, and a new technical specification for the impurities.

Beside the specification, the assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of carboxin or the respective formulation. The main data regarding the identity of carboxin and its physical and chemical properties are given in Appendix A.

Analytical methods are available for the determination of carboxin and the impurities in the technical material and for the determination of the active substance in the representative formulation. Adequate analytical methods are available for the determination of the compounds in the residue definition for monitoring in food of plant origin. Methods for food of animal origin are not relevant as no MRL is proposed. There are HPLC-MS/MS methods available for the determination of carboxin, carboxin sulfoxide, oxycarboxin (carboxin sulfone), P/V-54 and P/V-55 in soil, however a data gap has been identified for a method for the determination of metabolite M6, plus validation data generated on different soil types. In water, carboxin, carboxin sulfoxide and oxycarboxin (carboxin sulfone) can be monitored by HPLC-MS/MS, however data gaps have been identified for analytical methods for the metabolites M6, P/V-54 and P/V-55 in surface and ground water, and additionally for M9 in ground water, as well as validation data generated on surface water. Carboxin residues in air can be monitored by HPLC-MS/MS. Analytical methods for the determination of residues in body fluids and tissues are not required as carboxin is not classified as toxic or highly toxic.

2. Mammalian toxicity

Carboxin toxicity in mammals was discussed at the PRAPeR expert meeting 76 held in June 2010.

After the experts' meeting the RMS submitted an addendum assessing the composition of batches tested in the mammalian toxicology data package. Based on the available information the batches cannot be considered toxicologically equivalent to the currently proposed technical specification (which was not accepted by the physical-chemical section).

In mammals, carboxin is of low acute oral, dermal and inhalational toxicity; it is not a skin or eye irritant, however it is a skin sensitiser (R43 "**May cause sensitization by skin contact**" is proposed). The target organ for repeated administration in rodents is the kidney (with lesions of the renal tubules, chronic nephritis and progressive nephropathy); in addition, fibrous osteodystrophy of the femur and parathyroid hyperplasia occur in chronic toxicity studies. The relevant No Observed Adverse Effect Levels (NOAELs) for short and long-term toxicity are 5.5 mg/kg bw/day and 0.82 mg/kg bw/day, respectively. The majority of the experts agreed to propose classification R40 ("**Limited evidence of a carcinogenic effect**") based on hepatocellular carcinomas in male rats; there was also an increased

incidence of lung adenomas in male mice. However, the evidence for carcinogenicity was considered to be equivocal. The issue of classification with R40 for carcinogenic effects should be flagged to the European Chemicals Agency (EChA) by the RMS. In genotoxicity studies carboxin showed some positive results *in vitro*, equivocal and negative results in *in vivo* bone marrow chromosome aberration assays in rats, and negative results in an *in vivo* unscheduled DNA synthesis (UDS) assay. Overall, it was considered that carboxin does not have genotoxic potential relevant to humans. Carboxin was neither a reproductive nor a developmental toxicant in a rat multi-generation study: the relevant parental, offspring and reproductive NOAELs in rats are 1 mg/kg bw/day, 10 mg/kg bw/day, and 20 mg/kg bw/day, respectively. In a developmental study the maternal and developmental NOAEL in rabbits is set at 75 mg/kg bw/day; in rats, the maternal and developmental NOAELs are established at 10 mg/kg bw/day and 90 mg/kg bw/day, respectively. Carboxin did not show any neurotoxic potential.

The Acceptable Daily Intake (ADI) is 0.008 mg/kg bw/day, based on the 2-year rat study with a safety factor of 100. Based on the toxicological profile of carboxin, it was not considered necessary to set an Acute Reference Dose (ARfD). The Acceptable Operator Exposure Level (AOEL) is 0.055 mg/kg bw/day, based on the 90-day study in rats with a safety factor of 100. The exposure assessment for operators treating seed (both French and UK version of the SeedTropex model) indicates levels below the AOEL (80 % with French version, 98 % with UK version of the model), with the use of gloves for all operations, except bagging (French version) and with the use of coveralls and gloves (UK version of the model). For sowing seed activities (loading and sowing treated seeds) the estimated exposure is 29 % of the AOEL (when no personal protective equipment (PPE) is worn). No re-entry scenario is foreseen for seed treatment. Bystander exposure is unlikely, however, considering forklift operators, who may be present but are not directly involved in the treatment process, the estimated exposure is < 3% of the AOEL. Similarly, bystander exposure is unlikely during loading/sowing of treated seed (in any case it will not exceed the exposure of 29 % of AOEL of operators during sowing seed activities).

No assessment of the toxicological relevance of the groundwater metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone) was summarised in the Additional Report; the toxicological assessment of the relevance of groundwater metabolite M9 could not be assessed due to the lack of data. As for metabolites P/V-54 and P/V-55, based on the available data (acute oral LD_{50} greater than 3500 mg/kg bw; negative in a battery of *in vitro* genotoxicity studies; 13-week dietary toxicity NOAEL in rats 480 ppm - highest dose tested), P/V-54 was initially proposed as toxicologically non-relevant, and based on structural similarity with P/V-54, metabolite P/V-55 was also considered as toxicologically non-relevant. However, based on the proposal for classification of the parent compound as Cat 3 R40, the groundwater metabolites should be regarded as toxicologically relevant, with the exception of oxycarboxin (carboxin sulfone), which is relevant being an active substance with pesticidal activity.

3. Residues

The metabolism of carboxin was investigated in a wheat seed treatment study; two major components were identified in the grain and straw as carboxin sulfoxide and oxycarboxin (carboxin sulfone), accounting for 9 % of the total radioactivity in the grain, and 53 % of the total radioactivity in the straw (no parent carboxin was detected in the grain or straw). On the basis of this metabolism study it was concluded that the residue definition for risk assessment and monitoring is carboxin plus its metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone), expressed as carboxin. A case was presented for the non-submission of a rotational crop metabolism study. However, the case was considered unsatisfactory as the DT_{90} for residues is much greater than 100 days. A data gap has therefore been identified for a rotational crop metabolism study. The need for animal metabolism studies was not triggered, as intakes are low. Sufficient residue trials were supplied for the north and south of Europe; all residues were < 0.03 mg/kg. Residues were shown to be stable in freezer storage for up to 18 months in forage and grain, and 24 months in straw. The need for processing studies was not triggered.

The consumer risk assessment using the EFSA PRIMo rev 2 gave intakes of less than 5 % of the ADI. An acute reference dose was not set. However, due to the data gap identified for rotational crops the consumer risk assessment cannot be finalised at this stage.

4. Environmental fate and behaviour

In soil laboratory incubations under aerobic conditions in the dark, carboxin exhibits very low to low persistence, forming five major (>10 % applied radioactivity (AR)) soil metabolites, namely carboxin sulfoxide, oxycarboxin (carboxin sulfone), P/V-54, P/V-55 and M6. Another soil metabolite, M9 that reached 9.9 % AR, triggers the necessary evaluations for groundwater contamination. The rate of mineralisation to carbon dioxide was a significant sink; it varied between 21.3 - 55.3 % AR after 118 - 120 days. Formation of unextractable residues was also relatively significant, accounting for 11.8 - 32.7 % AR after 118 - 120 days. Under anaerobic conditions, the degradation of carboxin was significantly reduced compared to the aerobic conditions. The soil metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone) were formed along with some other unquantified metabolites, however further assessment of these metabolites were not considered necessary, since long-term exposure of carboxin to anaerobic conditions, and hence formation of anaerobic metabolites at significant levels in the environment, was considered to be unlikely. In a soil photolysis study, carboxin degraded rapidly, and carboxin sulfoxide and a tricyclic compound were identified. However, further assessment of these metabolites was not considered necessary, since carboxin is used exclusively as a seed treatment and thus it will not be exposed to light, and photolytic products detected under laboratory conditions will not be formed in the environment. Regarding the persistence of the aerobic soil metabolites the following classification can be applied: carboxin sulfoxide - low to very high persistence, oxycarboxin (carboxin sulfone) - low to moderate persistence, P/V-54 - medium to high persistence, P/V-55 - moderate persistence, M6 - low persistence, and M9 - low to medium persistence. It should be highlighted that for the metabolite P/V-55 only one, and for the metabolite P/V-54 only two reliable soil DT_{50} values were available for the subsequent PEC (predicted environmental concentrations) calculations. Therefore a data gap has been identified for additional soil DT_{50} values for these metabolites. It is noted however that the available DT_{50} values, obtained using peak-down single first-order (SFO) kinetics, might be considered as worst case for a simple first-tier exposure assessment. Dissipation of carboxin and its soil metabolites was investigated in four field trials in the EU. Reliable field DT_{50} values could however be derived only for the parent carboxin and for the metabolite carboxin sulfoxide. These field trials confirmed the fast disappearance of carboxin from the soil compartment. Carboxin exhibited high to medium mobility, while carboxin sulfoxide exhibited high mobility, and oxycarboxin (carboxin sulfone) exhibited very high to high mobility in soil. Metabolites P/V-54 and P/V-55 exhibited very high mobility in soil, but no experimental data for mobility were available for the M6 and M9 metabolites. There was a slight indication that the adsorption of carboxin, carboxin sulfoxide and P/V-55 might be pH dependent, however strong and clear correlations could not be established. PECsoil for carboxin was calculated based on the worst-case non-normalized field DT_{50}. For the metabolites, initial PECsoil values were calculated based on the initial PECsoil of carboxin. It should be noted that in the PECsoil calculations for three metabolites (oxycarboxin (carboxin sulfone), P/V-54 and P/V-55) the maximum observed residues from the field studies, the results of which were uncertain, were considered. If the results from the laboratory studies had been used, the PECsoil for P/V-54 and P/V-55 would be lower, but for oxycarboxin (carboxin sulfone) it would be significantly higher. However, considering the apparent large margin of safety in the risk assessment for soil-dwelling organisms (see section 5), it was considered that updated calculations are not necessary.

Carboxin is stable to hydrolysis, but in an aqueous photolysis study carboxin exhibited fast degradation, forming two major metabolites. The further assessment of these metabolites was not considered necessary since carboxin is used exclusively as a seed treatment. However, further consideration of this route of degradation would be necessary if exposure of the water bodies (e.g. via spray drift) was possible. In laboratory incubations in aerobic natural water-sediment systems, carboxin gradually partitioned to the sediment and exhibited moderate persistence (whole system SFO DT_{50} 11 - 24 days), forming the major metabolite carboxin sulfoxide. Several minor metabolites were

also formed and an unidentified component (Rt 2.0 min) reached 10 % AR in the water phase in one of the systems at the beginning of the incubations. Mineralisation to carbon dioxide accounted for 24 – 40 % AR, while residues not extracted from the sediment represented 33 – 40 % AR at the end of the study. It should be noted that due to some shortcomings in the methodology of the water-sediment study, the results should be considered with some caution and the formation of other metabolites (or the same ones at higher amounts) could not be excluded if a more appropriate methodology were used. However, considering the use pattern and the properties of carboxin (especially the fast degradation in soil), the exposure of natural water bodies to carboxin is considered to be minimal. Hence, no further data are deemed necessary. Further consideration of the degradation of carboxin in water-sediment systems would however be necessary if direct exposure of the water bodies (e.g. spray drift) was possible. The necessary surface water and sediment exposure assessments (PECsw, PECsed) were appropriately carried out using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 1.1 of the steps 1-2 in FOCUS calculator) for carboxin and its metabolites, including M9. Moreover, step 3 modelling was run and the results confirmed that PECsw/sed were higher in step 1 and 2 models.

The necessary groundwater exposure assessments were carried out using FOCUS (FOCUS, 2000) scenarios and models (PELMO 3.3.2 and PEARL 3.3.3[11]). The potential for groundwater exposure from the representative uses by carboxin or the metabolite M6 above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by the relevant FOCUS groundwater scenarios. However, there is a considerable potential for groundwater contamination by all the other metabolites (carboxin sulfoxide, oxycarboxin (carboxin sulfone), P/V-54, P/V-55 and M9). The predicted concentrations for metabolite M9 was < 0.1 µg/L only for the Porto groundwater scenario when applications to spring cereals were simulated, and was always above this trigger for winter cereals. For metabolite P/V-54, the parametric drinking water limit is exceeded for all groundwater scenarios for both winter and spring cereals. The metabolite P/V-55 exceeded the parametric drinking water limit for all groundwater scenarios when applications to winter cereals were modelled (and also for some scenarios when spring cereals were modelled). Carboxin sulfoxide and oxycarboxin (carboxin sulfone) exceeded the trigger of 0.1 µg/L in case of some scenarios when applications to winter cereals were modelled, while no groundwater concentrations were predicted > 0.1 µg/L for applications to spring cereals. It should be noted that oxycarboxin (carboxin sulfone) is a pesticide active substance (fungicide) therefore is a relevant metabolite. Considering that all these metabolites are considered toxicologically relevant (see section 2), combined with the fact that the predicted groundwater concentrations of P/V-54, P/V-55 and M9 exceed 0.1µg/L for more than half of the FOCUS scenarios, the high leaching potential of these metabolites has been regarded as a critical area of concern. It should be noted that the simulations were done by the RMS and that the degradation kinetics were also re-evaluated using the recommendations of the FOCUS kinetic guidance (FOCUS, 2006). The applicant did not agree with the approaches followed by the RMS and considered these results as absolute worst-cases (see also Evaluation Table section 4 and Addendum 1 Vol3 B.8 of the Additional Report (The United Kingdom, 2010)). This addendum includes the assessment of a position paper[12] submitted by the applicant. Considering the whole data set available, and the uncertainties that arose during the derivation of realistic degradation parameters for the secondary metabolites (which may come from the relatively poor data set for these metabolites), EFSA agrees with the RMS that these simulations are regarded as realistic worst case. It should also be noted that, although no detailed evaluation is available, it was considered possible to refine the groundwater modelling input parameters of Koc and 1/n for M9 in the manner described by the applicant in this position paper. As a consequence, it might be possible that by using the refined input parameters, potentially more groundwater scenarios would display maximum PECgw < 0.1 µg/L for the proposed applications to winter or spring cereals. However, it should be indicated that there is an uncertainty over this conclusion, as key supporting documentation for the position paper containing the required details of simulations had not been provided by the applicant.

[11] Simulations correctly utilised the agreed Q10 of 2.58 (EFSA 2007) and Walker equation coefficient of 0.7
[12] U. Wanner and J. Nag, 2009; Chemtura Study Number 2009-030

Carboxin has a low potential for volatilization with an estimated atmospheric half-life shorter than 2 days. Therefore, long-range transport through the atmosphere is not expected.

The PEC in soil, surface water, sediment and groundwater, covering the representative uses assessed, can be found in Appendix A of this conclusion. It is noted however that all the PEC calculations are based on the assumption that 220 kg seeds are sown in one hectare and the application rate of 132 g/ha is based on that scenario. This might be a representative value, however depending on environmental and agronomical conditions, the weight of the sowed seeds, and consequently the liquid used for seed dressing that includes carboxin can significantly differ across Europe.

5. Ecotoxicology

A data gap remains to assess the compliance of the ecotoxicological test batches with the technical specification of carboxin.

The acute, short-term and long-term risk to herbivorous birds was assessed as low, as was the acute risk to granivorous birds at tier I following the SANCO/4145 guidance document for birds and mammals (European Commission, 2002). The short-term TER for granivorous birds was below the Annex VI trigger at tier 1. However, it was considered that the acute risk to birds from a single feeding bout of treated seed was likely to be higher than the short-term risk, and the acute TER was above the Annex VI trigger. Furthermore, the short-term dietary studies were carried out at 5000 ppm with no effects and it was considered unlikely that studies would be available at higher concentrations. Since there were no effects on either species (mallard duck (*Anas platyrhynchos*) and bobwhite quail (*Colinus virginianus*)) at this concentration, and the acute risk was assessed as low, the short-term risk was considered to be low. The long-term risk to granivorous birds failed to meet the Annex VI trigger at tier 1. Additional information was provided by the applicant and evaluated in Addendum 2 dated June 2010 (The United Kingdom, 2010). A new study on residue decline in seed and seedlings was taken into consideration, as the decline rate was lower. The refined risk assessment provided by the applicant was not considered satisfactory due to the lack of data to support the selection of relevant focal species (including expected breeding season). The RMS did undertake a phase specific long-term risk assessment for skylark (*Alauda arvensis*) following the new guidance document for birds and mammals (EFSA, 2009), which failed to identify a low risk. Based on the data available it was not possible to address the long-term risk to granivorous birds for the representative uses as a seed treatment, and a data gap is identified. It is recommended that wood pigeon (*Columba palumbus*) should be included as one of the relevant focal species for further refinements. The risk to birds from secondary poisoning, carboxin metabolites, and exposure via cereal shoots grown from treated seeds was assessed as low.

Whereas the acute risk to granivorous and herbivorous mammals and the risk from secondary poisoning was assessed as low, a long-term risk to granivorous and herbivorous mammals following short-term exposure from the representative uses could not be ruled out. Additional information was provided by the applicant (evaluated in Addendum 2 dated June 2010; The United Kingdom, 2010). The refinement based on measured residue decline in seed and seedlings was insufficient to address the long-term risk to granivorous and herbivorous mammals. Further refinements following the outline of the new guidance document for birds and mammals (EFSA, 2009) were not considered satisfactory, as data to support the choice of relevant focal species (including relevant breeding season) were missing. A data gap remained to address the long-term risk to granivorous and herbivorous mammals for the representative uses of carboxin as a seed treatment.

Overall, a potential high long-term risk to granivorous birds and mammals, and herbivorous mammals could not be excluded based on the data available. The risk to birds and mammals from the representative formulation was not assessed in the DAR or the Additional Report, and therefore a data gap is identified.

Carboxin was considered to be very toxic to aquatic organisms, based on algae toxicity data. The acute and chronic risk to aquatic organisms was assessed as low for the representative uses of carboxin,

based on FOCUSsw step 2 exposure estimates. The acute risk from the metabolites oxycarboxin (carboxin sulfone), carboxin sulfoxide and P/V-54 was assessed as low, based on experimental data and $FOCUS_{sw}$ step 1 PEC values. P/V-55 showed no activity against biological systems and therefore the risk was considered low. The TER for M6 and M9 also exceeded the Annex VI trigger values, assuming ten times higher toxicity of the metabolites compared to the toxicity of carboxin and using $FOCUS_{sw}$ step 2 PEC values. The chronic risk from all the metabolites was also considered as low, based on estimated toxicity or lack of biological activity. For carboxin sulfoxide the long-term risk assessment was considered as low based on a conservative exposure and effects assumption. It is noted that FOCUS Step 3 modelling was submitted by the applicant for this metabolite as additional information to confirm a low risk in the long-term risk assessment for aquatic organisms. However, as the study was not considered necessary for the risk assessment, it was not evaluated, and thus not peer reviewed (see Additional Report, B.9.2.7.1b; The United Kingdom, 2009). The risk from carboxin and its relevant metabolites expected to be present in groundwater at levels above 0.1 µg/L was assessed as low. The risk from carboxin to sediment-dwelling invertebrates was assessed as low. Overall, the risk to aquatic organisms was assessed as low for the representative uses of carboxin as a seed treatment.

No direct exposure to bees from the treated seeds themselves was anticipated. A potential risk from dust exposure was not considered in the DAR or the Additional Report. EFSA, however, is of the opinion that the potential risk from dust exposure would be low, as the hazard quotient (HQ) would meet the Annex VI trigger for a worst-case situation of dust concentration similar to the representative use rate (132 g a.s./ha). The risk to honeybees from aphid honeydew produced from treated cereals was assessed as low. At the proposed rates of use the acute and chronic risk from carboxin and its metabolites to earthworms was assessed as low. A potential increase in soil concentration of oxycarboxin (carboxin sulfone) (see section 4) was not considered to change the conclusion of low risk, given the high margin of safety. Carboxin and its metabolite oxycarboxin (carboxin sulfone) are not persistent in soil (DT_{90} < 100 days) and are of limited toxicity to soil non-target macro-organisms, arthropods, earthworms and soil microbial processes. At the proposed rates of use the risk from all relevant metabolites (including carboxin sulfoxide, P/V-54, P/V-55 and M6) to soil-dwelling organisms was considered to be low.

Based on the data available the risk to non-target arthropods, non-target soil micro-organisms, biological treatment of waste water, and non-target plants was assessed as low.

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

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
carboxin	Very low to low persistence Single first-order DT_{50} 0.06-1.68 days[a] (20°C, pF2 soil moisture) Field studies (EU): Single first-order DT_{50} 0.3-11 days[b] (not normalized values)	The risk to soil-dwelling organisms was considered as low.
carboxin sulfoxide	Low to very high persistence Single first-order (peak-down) DT_{50} 9.1-53 days[a], (20°C, pF2 soil moisture) Double first-order in parallel slow phase DT_{50} 260-1431[a,c] days (20°C, pF2 soil moisture) Field studies (EU): Single first-order DT_{50} 25-117 days (not normalized values)	The risk to soil-dwelling organisms was considered as low.
oxycarboxin (carboxin sulfone)	Low to moderate persistence Single first-order DT_{50} 8.8-26.6 days (20°C, pF2 soil moisture)	The risk to soil-dwelling organisms was considered as low.
P/V-54	Medium to high persistence[d] Single first-order (peak-down) DT_{50} 77.4-113 days (20°C, pF2 soil moisture)	The risk to soil-dwelling organisms was considered as low.
P/V-55	Moderate persistence[e] Single first-order (peak-down) DT_{50} 18.6 days (20°C, pF2 soil moisture)	The risk to soil-dwelling organisms was considered as low.

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
M6	Low persistence[f] estimated DT_{50} < 2 days based on that DT_{90} < 4 days	The risk to soil-dwelling organisms was considered as low.

(a): two DT_{50} values were derived from each soil (two experiments with two different label positions); the values indicated here refer to the individual experiments
(b): 3 values out of the 4 are < 2 days, 1 value is 11 days
(c): the rate of decline of the slow phase is not significantly different from 0, therefore the value of 1431 days is uncertain
(d): only two reliable values are available (n=2)
(e): only one reliable value is available (n=1)
(f): to be considered as a rough classification that is based on only estimated degradation parameters

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
carboxin	High to medium mobility K_{Foc} 123 – 213 mL/g	No	Yes	Yes	Very toxic to aquatic organisms. Risk to aquatic organisms considered as low.
carboxin sulfoxide	High mobility K_{Foc} 70 – 126 mL/g	Yes (FOCUS); trigger 0.1 µg/L exceeded for 2 of 9 scenarios for winter cereals	No	Yes (based on the proposed classification of carboxin as Cat 3 R40, to be confirmed by EChA).	Risk to aquatic organisms considered as low.
oxycarboxin (carboxin sulfone)	Very high to high mobility K_{Foc} 33 – 139 mL/g	Yes (FOCUS); trigger 0.1 µg/L exceeded for 3 of 9 scenarios for winter cereals.	Yes	Yes (it is an active substance with pesticidal activity)	Risk to aquatic organisms considered as low.
P/V-54	Very high mobility K_{Foc} 11 – 31 mL/g	Yes (FOCUS); trigger 0.75 µg/L exceeded for all scenarios for winter+spring cereals	No	Yes (based on the proposed classification of carboxin as Cat 3 R40, to be confirmed by EChA). Available data showed acute oral LD_{50} greater than 3500 mg/kg bw; negative in a battery of *in vitro* genotoxicity studies; 13-week dietary toxicity study in rats: NOAEL 480 ppm - highest dose tested.	Risk to aquatic organisms considered as low.

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
P/V-55	Very high mobility K_{Foc} 5 – 18 mL/g	Yes (FOCUS); - trigger 0.1 µg/L exceeded for all scenarios, trigger 0.75 µg/L exceeded for 2 of 9 scenarios for winter cereals - trigger 0.1 µg/L exceeded for 4 of 6 scenarios for spring cereals	No	Yes (based on the proposed classification of carboxin as Cat 3 R40, to be confirmed by EChA).	Risk to aquatic organisms considered as low.
M6	No experimental data are available	No[a]	No	No data, not needed	Risk to aquatic organisms considered as low.
M9	No experimental data are available	Yes (FOCUS)[a]; - trigger 0.1 µg/L exceeded for all scenarios, trigger 0.75 µg/L exceeded for 7 of 9 scenarios for winter cereals - trigger 0.1µg/L exceeded for 5 of 6 scenarios for spring cereals	No	Yes (based on the proposed classification of carboxin as Cat 3 R40, to be confirmed by EChA).	Risk to aquatic organisms considered as low.

a): Due to lack of experimental K_{oc}/K_{Foc} data, the default of 10 mL/g was used in the modelling

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
carboxin	Very toxic to aquatic organisms. The risk was considered as low for the representative uses.
carboxin sulfoxide	Harmful to aquatic organisms. The risk was considered as low for the representative uses.
oxycarboxin (carboxin sulfone)	Very toxic to aquatic organisms. The risk was considered as low for the representative uses.
P/V-54	The risk was considered as low for the representative uses.
P/V-55	The risk was considered as low for the representative uses.
M6	The risk was considered as low for the representative uses.

6.4. Air

Compound (name and/or code)	Toxicology
carboxin	Not acutely toxic via inhalation.

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

- New 5-batch analysis with specific analytical methods (relevant for the representative uses evaluated; submission date proposed by the applicant: unknown; see section 1).
- New technical specification for the impurities (relevant for the representative uses evaluated; submission date proposed by the applicant: unknown; see section 1).
- Analytical method for the determination of metabolite M6 in soil and validation data generated on different soil types (relevant for the representative uses evaluated; submission date proposed by the applicant: unknown; see sections 1 and 4).
- Analytical methods for the determination of metabolites M6, P/V-54 and P/V-55 in ground and surface water, and for the determination of metabolite M9 in ground water, and validation data generated on surface water (relevant for the representative uses evaluated; submission date proposed by the applicant: unknown; see sections 1 and 4).
- Rotational crop metabolism study (relevant for the representative uses evaluated; submission date proposed by the applicant: unknown; see section 3).
- Additional soil DT_{50} values (to be used for a potentially refined PECgw modelling) to be generated for the soil metabolites P/V-54 and P/V-55 (relevant for the representative uses evaluated; identified by EFSA during the resubmission; submission date proposed by the applicant: unknown; see section 4).
- Assessment of the compliance of the ecotoxicological test material with the technical specification of carboxin (relevant for the representative uses evaluated; submission date proposed by the applicant: unknown; see section 5).
- The long-term risk to granivorous birds should be addressed. It is recommended that wood pigeon (*Columba palumbus*) should be included as one of the relevant focal species for further refinements (relevant for the representative uses evaluated; submission date proposed by the applicant: unknown; see section 5).
- The long-term risk to granivorous and herbivorous mammals should be addressed (relevant for the representative uses evaluated; submission date proposed by the applicant: unknown; see section 5).
- The risk to birds and mammals from the representative formulation should be addressed (relevant for the representative uses 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

- The use of personal protective equipment is necessary to reduce exposure levels to below the AOEL for operators.
- All the PEC calculations are based on the assumption that 220 kg seed are sown in one hectare and the application rate of 132 g a.s./ha is based on that scenario. Where more seeds need to be sown (depending on environmental and agronomical conditions), higher amounts of carboxin might be introduced to the environment.

ISSUES THAT COULD NOT BE FINALISED

- The consumer risk assessment cannot be finalised as there is a data gap for rotational crops. A case was presented for the non-submission of a rotational crop metabolism study. However, the case was considered unsatisfactory as the DT_{90} for residues is much greater than 100 days.

- A data gap was set for additional soil DT_{50} values for the soil metabolites P/V-54 and P/V-55. If these further data indicate higher persistence, all the PEC calculations for these metabolites would need to be repeated with the new results.

- An assessment of the compliance of the ecotoxicological test material with the technical specification of carboxin is outstanding.

- An assessment of the risk to birds and mammals from the representative formulation is outstanding.

CRITICAL AREAS OF CONCERN

- The batches tested in the mammalian toxicology section are not compliant with the currently proposed technical specification. Furthermore, there is a data gap for a new proposed technical specification for the impurities and for new 5-batch data.

- Based on the proposed classification of carboxin as carcinogenic Cat 3 R40 the metabolites are considered as toxicologically relevant in the context of the groundwater relevance assessment. This constitutes a critical area of concern for P/V-54, P/V-55 and M9, as for these metabolites the predicted groundwater concentrations exceed 0.1µg/L for more than half of the FOCUS groundwater scenarios.

- A potential high long-term risk to granivorous birds and mammals, and herbivorous mammals could not be excluded based on the data available.

REFERENCES

ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).

EFSA (European Food Safety Authority), 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. EFSA Journal 2007; 622, 1-32.

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

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 carboxin.

European Commission, 2002. Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC. SANCO/4145/2000.

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.

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.

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 (2006). "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration" Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0, 434 pp

The United Kingdom, 2006. Draft Assessment Report (DAR) on the active substance carboxin prepared by the rapporteur Member State the United Kingdom in the framework of Directive 91/414/EEC, March 2006.

The United Kingdom, 2009. Additional Report to the Draft Assessment Report on the active substance carboxin prepared by the rapporteur Member State the United Kingdom in the framework of Commission Regulation (EC) No 33/2008, December 2009.

The United Kingdom, 2010. Final Addendum to the Draft Assessment Report and Additional Report on carboxin, compiled by EFSA, July 2010.

APPENDICES

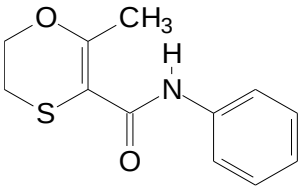
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name) ‡	carboxin
Function (*e.g.* fungicide)	fungicide

Rapporteur Member State	UK
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	5,6-dihydro-2-methyl-1,4-oxathiine-3-carboxanilide
Chemical name (CA) ‡	5,6-dihydro-2-methyl-*N*-phenyl-1,4-oxathiin-3-carboxamide
CIPAC No ‡	273
CAS No ‡	5234-68-4
EC No (EINECS or ELINCS) ‡	226-031-1
FAO Specification (including year of publication) ‡	Not listed.
Minimum purity of the active substance as manufactured ‡	970 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Open
Molecular formula ‡	$C_{12}H_{13}NO_2S$
Molecular mass ‡	235.303 g/mol
Structural formula ‡	

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

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	91-92°C (99.9%)
Boiling point (state purity) ‡	Not measured, decomposes above 210°C (99.9%)
Temperature of decomposition (state purity)	-
Appearance (state purity) ‡	Pure - White solid (99.9%) Technical – Pale yellow solid (97%)
Vapour pressure (state temperature, state purity) ‡	2 x 10^{-5} Pa at 25 °C (99.9%)
Henry's law constant ‡	3.2 x 10^{-5} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	0.148g/l at pH5 and 20°C 0.134g/L at pH7 and 20°C 0.138g/L at pH9 and 20°C (99.9%)
Solubility in organic solvents ‡ (state temperature, state purity)	acetone 221.2g/L at 20°C 1,2-dichloroethane 262.8g/L at 20°C dichloromethane 414.8g/L at 20°C ethyl acetate 107.7g/L at 20°C heptane 1.118g/L at 20°C methanol 89.33g/L at 20°C n-octanol 20.74g/L at 20°C toluene 52.52g/L at 20°C xylene 33.75g/L at 20°C (97%)
Surface tension ‡ (state concentration and temperature, state purity)	61.2 mN/m at 20°C (90 % saturated solution) (98.2 %)
Partition co-efficient ‡ (state temperature, pH and purity)	Log Pow = 2.3 Range of pHs was not looked due to the pKa being < 0.5 and the solubility in water not altering with pH. (99.9%)
Dissociation constant (state purity) ‡	pKa = <0.5 (99.3%)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	UV absorb 205 nm (ε = 17443 l mol^{-1} cm^{-1}) UV absorb 295 nm (ε = 6585.4 l mol^{-1} cm^{-1}) (99.9%)
Flammability ‡ (state purity)	Non-flammable (98.2%)
Explosive properties ‡ (state purity)	Non-explosive (98.2%)

Oxidising properties ‡ (state purity)	Non-oxidising (98.2%)

Summary of representative uses evaluated (carboxin)*

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
					Type	Conc. of as	method kind	growth stage & season	number min max	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max		
(a)			(b)	(c)	(d-f)	(i)	(f-h)	(j)	(k)					(l)	(m)
Small grain cereals: Wheat Barley Oats Rye Triticale	EU (Region North and South)	Vitavax 200FF	F	Soil and seed borne diseases	FS	carboxin 200 g/L + thiram 200 g/L	Seed treatment	Seed before planting (BBCH growth stage 00)	1	Not applicable	3 L/ton seed = 600 g carboxin/ton seed + 600 g thiram/ton seed. At a seed rate of 220 kg/ha, the application rate is 0.66 litres/ha (equivalent to 132 g carboxin/ha + 132 g thiram/ha)			Not applicable	[I] [II] [III] [IV]

[I] The batches tested in the mammalian toxicology section are not compliant with the proposed specification. In addition, there is a data gap for a new technical specification for the impurities and for new 5-batch data, and an assessment of the compliance of the ecotoxicological test material with the technical specification of carboxin is outstanding.
[II] The potential for groundwater exposure by the metabolites P/V-54, P/V-55 and M9 above the parametric drinking water limit of 0.1µg/L is high over a wide range of geoclimatic conditions represented by FOCUS groundwater scenarios. For metabolite P/V-54 the parametric drinking water limit as well as the trigger of 0.75 µg/L is exceeded for all of the groundwater scenarios.
[III]A potential high long-term risk to granivorous birds and mammals, and herbivorous mammals could not be excluded based on the data available. An assessment of the risk to birds and mammals from the representative formulation is outstanding.
[IV]The consumer risk assessment cannot be finalised as there is a data gap for rotational crops.

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV
Impurities in technical as (analytical technique)	HPLC-UV
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Carboxin plus its metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone)[14] expressed as carboxin.
Food of animal origin		Not required as positive residues of carboxin not expected in products of animal origin.
Soil		Carboxin, carboxin sulfoxide, oxycarboxin (carboxin sulfone), M6, P/V-54 and P/V-55.
Water	surface	Carboxin and carboxin sulfoxide (through direct formation in water) and oxycarboxin (carboxin sulfone) (via soil). In addition, the soil metabolites, M6, P/V-54 and P/V-55 could theoretically reach water via run-off and drainage.
	drinking/ground	Carboxin, carboxin sulfoxide, oxycarboxin (carboxin sulfone), M6, M9, P/V-54 and P/V-55. FOCUS modelling for all these metabolites showed that M9, P/V-54 and P/V-55 had the potential to exceed 0.1 μg/L.
Air		Carboxin

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Carboxin (and its metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone)) residues were determined by HPLC/MS/MS, with a LOQ of 0.01 mg/kg for each individual component (wheat forage, straw, grain and ILV wheat straw).

[14] In the applicant's dossier, DAR, AR, reporting table and evaluation table this compound is usually referred to as carboxin sulfone

Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	No methods of analysis for animal products were submitted or required, as positive residues in animal products are unlikely to occur, due to residues of carboxin in cereal grain and straw being below 0.1mg/kg total diet (and below the limit of determination).
Soil (analytical technique and LOQ)	Carboxin (and its metabolites carboxin sulfoxide, oxycarboxin (carboxin sulfone), P/V-54 and P/V-55) residues were determined by HPLC/MS/MS, with a LOQ of 0.005 mg/kg for each individual component. Method for the determination of M6 is currently not available – Data gap
Water (analytical technique and LOQ)	Carboxin (and its metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone)) residues were determined by HPLC-MS/MS, with a LOQ of 0.1 μg/l for each individual component. Methods for the determination of M6, P/V-54, P/V-55 and M9 are currently not available – Data gap
Air (analytical technique and LOQ)	Carboxin residues were determined by HPLC/MS/MS, with a LOQ of 2 $\mu g/m^3$.
Body fluids and tissues (analytical technique and LOQ)	Not required as carboxin is not classified as acutely toxic or very toxic.

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

	RMS/peer review proposal
Active substance	None required.

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	At least 60 % of the administered low dose levels were excreted in urine within 12 hours and 75% within 24 hours.
Distribution ‡	Widely distributed based on the residue levels at termination.
Potential for accumulation ‡	Minimal, based on the residue levels at termination.
Rate and extent of excretion ‡	Rapid and extensive elimination with 77-82 % in urine and 6-11% in faeces within 72 hours.
Metabolism in animals ‡	Oxidation to carboxin sulfoxide followed by *p*-hydroxylation of the phenyl ring to yield para-hydroxylated carboxin. Hydrolysis of the amide bond of para-hydroxylated carboxin followed by N-acetylation yields 4-acetamidophenol, some of which undergoes conjugation to form 4-acetamidophenol glucuronide.
Toxicologically relevant compounds ‡ (animals and plants)	Parent and metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone).
Toxicologically relevant compounds ‡ (environment)	Based on the proposed classification of carboxin as Carc Cat 3 R40, the groundwater metabolites were regarded as relevant. Oxycarboxin (sulfone metabolite of carboxin) is considered relevant being an active substance with pesticidal activity.

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	2588 mg/kg bw for male rats.	
Rat LD_{50} dermal ‡	>4000 mg/kg bw for both sexes.	
Rat LC_{50} inhalation ‡	>4.7 mg/L for both sexes (4 hour exposure at the highest attainable concentration).	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Slight irritant. Not classifiable according to EC criteria.	
Skin sensitisation ‡	Positive in a M & K test	R43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Kidneys/lesions of the renal tubules, chronic nephritis & progressive nephropathy.	
Relevant oral NOAEL ‡	5.5 mg/kg bw/day for male rats.	
Relevant dermal NOAEL ‡	30 mg/kg bw/day for male rats.	
Relevant inhalation NOAEL ‡	Not applicable	

Genotoxicity ‡ (Annex IIA, point 5.4)

a) In vitro studies	a) Positive results in the chromosome aberration test in the presence of metabolic activation and positive in the unscheduled DNA repair test (both with batch 956).	
b) In vivo studies	b) Equivocal results in one bone marrow test, and negative results in the second bone marrow test (no analytical data for both batches). Negative in rat *in vivo* UDS assay.	

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

Target/critical effect ‡	Kidney: lesions of the renal tubules, chronic nephritis & progressive nephropathy. Bone/Parathyroids: Fibrous osteodystrophy of the femur/parathyroid hyperplasia	
Relevant NOAEL ‡	0.82 mg/kg bw/day for male rats.	
Carcinogenicity ‡	CAT: 3 carcinogen. An increased incidence of hepatocellular carcinoma in male rats and an increased incidence (and early onset) of lung adenoma in male mice.	R40

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No reproductive effects were observed at the highest dose used.	
Relevant parental NOAEL ‡	1.0 mg/kg bw/day for both sexes	
Relevant reproductive NOAEL ‡	20 and 30 mg/kg bw/day for males and females, respectively.	
Relevant offspring NOAEL ‡	10.0 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Reduced foetal weight in rats	
Relevant maternal NOAEL ‡	10 mg/kg bw/day in rats 75 mg/kg bw/day in rabbits	
Relevant developmental NOAEL ‡	90 mg/kg bw/day in rats 75 mg/kg bw/day in rabbits	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Not applicable	
Repeated neurotoxicity ‡	Not applicable	
Delayed neurotoxicity ‡	Not applicable	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No studies submitted.
Studies performed on metabolites or impurities ‡	P/V-54 (a soil metabolite) was negative in a battery of *in vitro* genotoxicity studies. Acute oral study on P/V-54: the acute oral LD_{50} value of P/V-54 was greater than 3500 mg/kg bw. P/V-54: A 13-week dietary toxicity study in rats: A NOAEL of 480 ppm was determined (highest dose tested).

Medical data ‡ (Annex IIA, point 5.9)

No reports relating to clinical cases or poisoning incidents.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.008 mg/kg bw/day	2-year rat study	100
AOEL ‡	0.055 mg/kg bw/day	90-day rat study	100
ARfD ‡	Not allocated, not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

'Vitavax 200FF' (flowable concentrate formulation containing 200 g/l carboxin and 200 g/l thiram).	i) 3.3% for the concentrate ii) 5% for the 1:1 aqueous dilution

Exposure scenarios (Annex IIIA, point 7.2)

Operator	**Operators treating seed** – The French version of the SeedTropex model (70^{th} percentile values) predicts levels of exposure for operators treating seeds with 'Vitavax 200FF' that are below the AOEL (80%) for operators wearing gloves for all

	tasks, except bagging. The UK version of this exposure model also suggests that levels of exposure will be below the AOEL (98 %) with the use of coveralls and gloves during the calibration, mixing/loading and cleaning tasks, and coveralls during bagging. **Operators sowing seed -** predicted exposures for operators loading and sowing seed treated with 'Vitavax 200FF' are below the AOEL (29 % of the AOEL where no PPE is worn).
Workers	'Vitavax 200FF' is only used for treating seeds prior to sowing. No re-entry scenario is given.
Bystanders	Predicted exposures for persons, who may be present but are not directly involved in the treatment process, are below the AOEL (< 3% of the AOEL). It is unlikely that bystander exposure will occur during loading/sowing of seed treated with 'Vitavax 200FF'.

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

	RMS and PRAPeR proposal
Carboxin	i) CAT 3 carcinogen: Limited evidence of a carcinogenic effect (R40). ii) May cause sensitisation by skin contact (R43)

Residues

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

Plant groups covered	Wheat
Rotational crops	Open
Metabolism in rotational crops similar to metabolism in primary crops?	Open
Processed commodities	No data were submitted or required, due to residues in cereal grains at harvest being below the limit of determination (0.03 mg/kg).
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not required.
Plant residue definition for monitoring	Carboxin plus its metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone) expressed as carboxin.
Plant residue definition for risk assessment	Carboxin plus its metabolites carboxin sulfoxide and oxycarboxin (carboxin sulfone) expressed as carboxin.
Conversion factor (monitoring to risk assessment)	None.

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

Animals covered	No data were submitted or required as positive residues in animal products are unlikely to occur, due to residues in cereal grain and straw unlikely to occur at or above the trigger value for such studies of 0.1 mg/kg total diet (residues of carboxin in cereal grain and straw were below the limit of determination of 0.03 mg/kg).
Time needed to reach a plateau concentration in milk and eggs	Not required.
Animal residue definition for monitoring	Not required.
Animal residue definition for risk assessment	Not required.
Conversion factor (monitoring to risk assessment)	Not required.
Metabolism in rat and ruminant similar (yes/no)	Not required.
Fat soluble residue: (yes/no)	Not required.

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

Open

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

Freezer stability study showed that residues of carboxin and its sulfoxide and sulfone metabolites are stable for up to 18 months in wheat forage and grain, and for up to 24 months in straw.

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) Potential for accumulation (yes/no): Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No data were submitted or required on animal feeding studies as positive residues in animal products are unlikely to occur at or above the trigger value for such studies of 0.1 mg/kg total diet (residues of carboxin in cereal grain and straw were below the limit of determination of 0.03 mg/kg).		
Muscle			
Liver			
Kidney			
Fat			
Milk			
Eggs			

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (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)
Cereal grain	NEU SEU	11 x <0.03 13 x <0.03		0.03	0.03	0.03

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

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

ADI	0.008 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	The total intake is < 5 % of the ADI using the EFSA PRIMo model rev 2.
TMDI (% ADI) according to national (to be specified) diets	-
IEDI (WHO European Diet) (% ADI)	-
NEDI (specify diet) (% ADI)	-
Factors included in IEDI and NEDI	-
ARfD	None
IESTI (% ARfD)	-
NESTI (% ARfD) according to national (to be specified) large portion consumption data	-
Factors included in IESTI and NESTI	-

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	
No data were submitted or required, due to residues in cereal grains at harvest being below the limit of determination (0.03 mg/kg).				

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

Cereal grains	0.03 mg/kg*

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

Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	30.3-55.3% of AR after 120d, [^{14}C-oxathiine]-carboxin (n=3) 27.4% of AR after 118d, [^{14}C-oxathiine]-carboxin (n=1) 28.7-44.3% of AR after 120d, [^{14}C-UL-phenyl]-carboxin (n=2) 21.3% of AR after 118d, [^{14}C-UL-phenyl]-carboxin (n=1)
Non-extractable residues after 100 days ‡	24.7-27.6% of AR after 120d, [^{14}C-oxathiine]-carboxin (n=3) 11.76% of AR after 118d, , [^{14}C-oxathiine]-carboxin (n=1) 28.9-32.7% of AR after 120d, [^{14}C-UL-phenyl]-carboxin (n=2) 24.90% of AR after 118d, [^{14}C-UL-phenyl]-carboxin (n=1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range of the maximum)	**Carboxin sulfoxide**, 59.5-78.2% at 1-7d, [^{14}C-oxathiine]-carboxin (n=4) Carboxin sulfoxide, 49.7-65.9% at 1-7d, [^{14}C-UL-phenyl]-carboxin (n=4) **Oxycarboxin** (carboxin sulfone), 4.8-17.0% at 14-61d, [^{14}C-oxathiine]-carboxin (n=4) Oxycarboxin (carboxin sulfone), 5.4-14.2% at 14-118d, [^{14}C-UL-phenyl]-carboxin (n=4) **M6** (2-[(2-anilino-2-oxoacetyl)thio]ethyl acetate), 6.1-10.1% at 0-0.16d, [^{14}C-oxathiine]-carboxin (n=3) M6 (2-[(2-anilino-2-oxoacetyl)thio]ethyl acetate), 5.9-9.3% at 0-1d, [^{14}C-UL-phenyl]-carboxin (n=3) **M9** (hydrated carboxin sulfoxide), 3.2-6.9% at 7d, [^{14}C-oxathiine]-carboxin (n=3) M9 (hydrated carboxin sulfoxide), 5.9-9.9% at 4-14d, [^{14}C-UL-phenyl]-carboxin (n=3) **P/V-54** (oxathiine amide sulfoxide), 3.8-27.4% at 28-60d, [^{14}C-oxathiine]-carboxin (n=3) **P/V-55** (oxathiine amide sulfone), 0.7-14.5% at 28-60d, [^{14}C-oxathiine]-carboxin (n=3)

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

Anaerobic degradation ‡

Mineralization after 100 days	0.8% of AR after 60d, [^{14}C-oxathiin]-carboxin (n=1) 0.4% of AR after 60 d, [^{14}C-UL-phenyl]-carboxin

	(n=1) No study of mineralization in sterile soil was submitted or considered necessary by the Rapporteur.
Non-extractable residues after 100 days	20.8% of AR after 60d, [^{14}C-oxathiin]-carboxin (n=1) 31.7% of AR after 60d, [^{14}C-UL-phenyl]-carboxin (n=1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None, however see note below: Carboxin is used as a seed treatment and degrades extremely rapidly under aerobic conditions. It is considered that the compound will not be exposed to anaerobic conditions, and hence significant levels of anaerobic metabolites of carboxin will not be formed in the environment. However, where anaerobic conditions do occur, the potential formation of different metabolites to those formed via aerobic degradation, should be considered.

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None Note: Carboxin is used as a seed treatment and is not expected to be exposed to light following applications according to the GAP. Therefore photolysis is not expected to be a major route of dissipation in the field for the representative uses.

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

Laboratory studies ‡

Carboxin	Aerobic conditions							
Soil type	pH	t. °C / % MWHC		DT_{50} /DT_{90} (d)		DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Spra 11, oxathiine	7.6	20	40	0.65	2.16	0.51	17.6	SFO
Spra 11, phenyl*	7.6	20	40	0.54*	1.79*	0.42*	28.7	SFO
Senozan, oxathiine	6.8	20	40	0.08	0.27	0.06	2.1	SFO
Senozan, phenyl	6.8	20	40	0.13	0.43	0.10	1.3	SFO
Castor, oxathiine	7.4	20	40	0.52	1.73	0.47	20.3	SFO
Castor, phenyl	7.4	20	40	0.39	1.29	0.36	18.0	SFO
Sandy loam, oxathiine	6.8	25	75% of 1/3 bar	1.12	3.72	1.68	3.3	SFO
Sandy loam, phenyl	6.8	25	75% of 1/3 bar	1.05	3.49	1.58	8.1	SFO
Stolpe, oxathiine	5.88	20	44	0.07	0.23	0.07	7.5	SFO
Stolpe, phenyl	5.88	20	44	0.08	0.27	0.07	9.0	SFO
Geometric mean Median				0.30/ 1.0 0.45/ 1.49		0.28 0.41	-	

* excluded from mean calculation due to poor kinetic fit

Note: two additional DT_{50} values (0.4 d and 1.1 d) are available originating from a supplementary route of degradation study, however these values were not used in the further assessments.

Carboxin sulfoxide	Aerobic conditions								
Soil type	pH	t. °C / % MWHC		DT_{50}/ DT_{90} (d)		Peak occur-ence*	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Spra 11, oxathiine	7.6	20	40	23.1	76.7	78.2	18.1	7.6	SFO – peak down
Spra 11, phenyl	7.6	20	40	38.5	127.9	62.5	30.1	4.7	SFO – peak down
Senozan, oxathiine	6.8	20	40	11.2	37.1	59.5	9.1	7.0	SFO – peak down
Senozan, phenyl	6.8	20	40	13.1	43.4	49.7	10.7	4.1	SFO – peak down
Castor, oxathiine	7.4	20	40	57.8	191.8	74.6	52.5	2.6	SFO – peak down
Castor, phenyl	7.4	20	40	53.3	177.0	64.9	48.4	3.1	SFO – peak down

Carboxin sulfoxide	Aerobic conditions								
Soil type	pH	t. °C / % MWHC		DT_{50}/ DT_{90} (d)		Peak occur-ence*	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Stolpe, oxathiine	5.88	20	44	9.48 – fast; 1552 - slow	31.5 – fast; 5153 - slow	65.0	8.8 – fast 1431 - slow**	2.6	DFOP
Stolpe, phenyl	5.88	20	44	4.43 – fast; 280 - slow	14.7 – fast; 929.6 - slow	65.9	4.1 – fast 260 - slow	4.5	DFOP
Geometric mean Median				19.0/ 63.0 – fast; 60.3/ 200 - slow 21.0/ 69.6 – fast; 42.7/ 142 - slow			16.3 – fast 51.6 - slow 16.6 – fast 36.9 - slow		

*Peak occurrence quoted instead of formation fraction as formation fractions are not calculated in peak down kinetic evaluations.
** rate of degradation do not significantly different from 0.

Oxycarboxin (carboxin sulfone)	Aerobic conditions								
Soil type	pH	t. °C / % MWHC		DT_{50}/ DT_{90} (d)		Peak occur-ence	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Spra 11, phenyl	7.6	20	40	10.2	33.9	*	8.8	2.6	SFO
Senozan, phenyl	6.8	20	40	25.6	85.0	*	25.6	3.7	SFO
Castor, phenyl	7.4	20	40	28.1	93.3	*	26.6	4.4	SFO
Geometric mean Median				19.4/ 64.5 25.6/ 85.0			18.1 25.6	-	

*not applicable because oxycarboxin (carboxin sulfone) was applied as parent in the degradation study
Note: two additional DT_{50} values (4.5 d and 60.2 d) are available those were originating from a study where the parent carboxin was applied. These values however, were not used in the further assessments.

P/V-54	Aerobic conditions								
Soil type	pH	t. °C / % MWHC		DT_{50}/ DT_{90} (d)		Peak occur-ence*	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Spra 11, oxathiine	7.6	20	40	99.0	328.7	27.4	77.4	3.0	SFO – peak down

P/V-54	Aerobic conditions							
Soil type	pH	t. °C / % MWHC		DT_{50}/ DT_{90} (d)		Peak occur-ence*	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Senozan, oxathiine	6.8	20	40	139	461.5	19.6	113	3.3	SFO – peak down
Geometric mean Median				117/ 390 119/ 395			93.5† 95.2		

*Peak occurrence quoted instead of formation fraction as formation fractions are not calculated in peak down kinetic evaluations.
†A corrected geometric mean value of 93.5 should be used in FOCUS modelling

P/V-55	Aerobic conditions								
Soil type	pH	t. °C / % MWHC		DT_{50}/ DT_{90} (d)		Peak occur-ence*	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Senozan, oxathiine	6.8	20	40	22.8	75.7	14.5	18.6	3.3	SFO – peak down
mean/median				n.a.			n.a.		

*Peak occurrence quoted instead of formation fraction as formation fractions are not calculated in peak down kinetic evaluations.

M6	Aerobic conditions								
Soil type	pH	t. °C / % MWHC		DT_{50}/ DT_{90} (d)		Peak occur-ence	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Spra 11, oxathiine	7.6	20	40	Unable to calculate due to transient nature, however, in all cases M6 was undetectable within 4 days.		6.9			
Spra 11, phenyl	7.6	20	40			7.7			
Senozan, oxathiine	6.8	20	40			6.1			
Senozan, phenyl	6.8	20	40			5.9			
Castor, oxathiine	7.4	20	40			10.1			
Castor, phenyl	7.4	20	40			9.3			
Estimate				<2	<4.0				

M9	Aerobic conditions								
Soil type	pH	t. °C / % MWHC		DT_{50}/ DT_{90} (d)		Peak occur-ence*	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Spra 11, phenyl	7.6	20	40	49.5	164	6.1	38.7	11.4	SFO – peak down
Senozan, oxathiine	6.8	20	40	12.0	39.7	6.9	9.74	20.2	SFO – peak down
Senozan, phenyl	6.8	20	40	12.0	39.7	9.9	9.74	3.0	SFO – peak down
Castor, phenyl	7.4	20	40	69.3	230	5.9	63.0	4.5	SFO – peak down
Geometric mean Median				34.5/ 114.5 49.5/ 164			28.7 38.7		

*Peak occurrence quoted instead of formation fraction as formation fractions are not calculated in peak down kinetic evaluations.

Field studies ‡

Carboxin	Aerobic conditions							
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	pH ($CaCl_2$)	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Clay loam, bare	UK	7.4	30	1.35	4.5	0.807	n.d.	SFO
Clay, bare	UK	6.6	30	11	37	0.865	n.d.	SFO
Silt loam, bare	Germany	7.5	30	0.27	0.9	0.899	n.d.	SFO
Silt loam, bare	Italy	7.5	30	0.6	2.0	0.968	n.d.	SFO
Arithmetic mean Geometric mean Median				3.3 1.2 1.0	11.1 4.2 3.3			

n.d. not determined

Carboxin sulfoxide	Aerobic conditions							
Soil type	Location	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation
Clay loam, bare	UK	7.4	30	56.9	189	0.961	n.d.	SFO
Clay, bare	UK	6.6	30	117	388	0.859	n.d.	SFO
Silt loam, bare	Germany	7.5	30	24.5	81.5	0.845	n.d.	SFO
Silt loam, bare	Italy	7.5	30	62	207	0.773	n.d.	SFO

Carboxin sulfoxide	Aerobic conditions							
Soil type	Location	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation
Arithmetic mean				65.1	216			
Geometric mean				56.4	188			
Median				59.5	198			

pH dependence ‡ (yes / no) (if yes type of dependence)	No pH dependence was observed for degradation of carboxin or its metabolites in field studies.
Soil accumulation and plateau concentration ‡	An accumulation phase was included in the dissipation study. However, the interim dissipation results indicated no cause for concern regarding accumulation of carboxin, carboxin sulfoxide or oxycarboxin (carboxin sulfone).

Laboratory studies ‡

Carboxin	Anaerobic conditions†						
Soil type	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)		DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam, oxathiin	6.8	25	103	342	n.d.	0.924	SFO
Sandy loam, phenyl	6.8	25	146	484	n.d.	0.83	SFO
Geometric mean/median							

† As carboxin is used as a seed treatment and degrades extremely rapidly under aerobic conditions, it is considered that the compound will not be exposed to anaerobic conditions and hence significant levels of anaerobic metabolites of carboxin will not be formed in the environment.

Carboxin sulfoxide	Anaerobic conditions†							
Soil type	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)		f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam, oxathiin	6.8	25	23.2	77.1	*	n.d.	1.00	SFO
Sandy loam, phenyl	6.8	25	19.6	65.1	*	n.d.	0.996	SFO
Geometric mean/median		6.8						

*No formation fraction since carboxin sulfoxide was as parent in study.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Carboxin ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand, Bethany, USA	0.9	4.5	1.11	124	1.92	213	0.79
Clay loam, Castor, UK	2.2	7.5	1.78	81	2.71	123	0.81
Loam, Senozan, Fance	1.2	5.9	1.10	92	1.61	134	0.81
Clay, Spra-II, Spain	1.2	7.7	1.03	86	1.56	130	0.82
Sandy loam, Stolpe, Germany	1.2	5.9	1.37	114	1.95	162	0.79
Arithmetic mean					1.95	152	0.81
pH dependence, Yes or No			no (no clear correlation)				

Carboxin sulfoxide ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sand, LUFA, Germany	0.48	6.0			0.44	92	1.1
Sandy loam. Les Evouettes, Switzerland	1.2	4.8			1.5	126	0.78
Clay-Clay loam, Itingen, Switzerland	2.8	6.9			1.9	70	0.57
Arithmetic mean					1.28	96	0.82
pH dependence (yes or no)			no (no clear correlation)				

Oxycarboxin (carboxin sulfone) ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Clay, Mississippi, USA	1.8	6.6			1.1	62	0.932
Sand, Maryland, USA	0.23	6.0			0.1	47	0.785
Sandy loam, Connecticut, USA	2.3	6.6			0.8	33	0.845
Silt loam, Maryland, USA	0.99	6.7			0.3	34	0.923
Clay, Maryland, USA	2.78	5.9			1.636	58.8	0.9235
Sand, Maryland, USA	0.52	6.5			0.264	50.6	0.8784
Loam, Mississippi, USA	0.70	7.6			0.687	98.7	0.8077
Sandy loam, California, USA	0.29	6.5			0.403	138.9	0.6825
Arithmetic mean					0.66	65.4	0.847
pH dependence, Yes or No			no				

P/V-54 (oxathiine amide sulfoxide) ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand, CT, USA	0.75	4.6	0.09	12	0.08	11	1.02
Clay loam, France	1.02	7.6	0.32	30	0.30	30	1.01
Loam, UK	0.90	5.9	0.29	32	0.28	31	1.03
Arithmetic mean					0.22	24	1.02
pH dependence, Yes or No			no				

P/V-55 (oxathiine amide sulfone) ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand, CT, USA	0.75	4.6	0.08	11	0.04	5	1.09
Clay loam, France	1.02	7.6	0.16	15	0.19	18	0.89
Loam, UK	0.90	5.9	0.13	14	0.15	17	0.85
Arithmetic mean					0.13	13	0.94
pH dependence, Yes or No			no (no clear correlation)				

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

Column leaching ‡	No study submitted and none considered necessary.
Aged residues leaching ‡	No study submitted and none considered necessary.
Lysimeter/ field leaching studies ‡	No study submitted and none considered necessary.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent	DT_{50} (d): 11 days (representative longest field dissipation)
Method of calculation	Kinetics: SFO

Application data	Crop: winter cereals Depth of soil layer: 5cm Soil bulk density: 1.5g/cm^3 % plant interception: Seed treatment therefore no crop interception assumed Number of applications: 1 Interval (d): n.a. Application rate(s): 132 g as/ha

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.176		n.a.	
Short term 24h	0.165	0.171	n.a.	n.a.
2d	0.155	0.165	n.a.	n.a.
4d	0.137	0.156	n.a.	n.a.
Long term 7d	0.113	0.142	n.a.	n.a.
28d	0.030	0.083	n.a.	n.a.
50d	0.008	0.053	n.a.	n.a.
100d	0.000	0.028	n.a.	n.a.
Plateau concentration	n.a.			

Metabolite	Representative worse case field/laboratory	Conversion factor	Single application initial **PEC$_{(s)}$** (mg/kg)
carboxin sulfoxide	Field	0.927[1]	0.163
oxycarboxin (carboxin sulfone)	Field	0.080[1,3]	0.014
P/V-54	Field	0.251[1,3]	0.044
P/V-55	Field	0.127[1,3]	0.022
M9	Laboratory	0.113[2]	0.030
M6	Laboratory	0.115[2]	0.028

[1]Conversion factor determined using the peak formation of each metabolite seen in the field study compared with the theoretical maximum concentration of carboxin in the soil.
[2]Conversion factor determined using the maximum observed laboratory formation fraction corrected for difference of molecular weight between metabolite and carboxin.
[3]the maximum observed residues are uncertain due to some shortcomings of the field studies

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	Carboxin was hydrolytically stable at environmentally relevant pH values (pH 4, 7 and 9).
	The hydrolytic stability of carboxin sulfoxide is pH dependent. At pH 4 and 7 carboxin sulfoxide is stable to hydrolysis. At pH 10, the calculated half-life (using non-linear regression) of carboxin sulfoxide is 4.92 days at 22ºC.
	The hydrolytic stability of oxycarboxin (carboxin sulfone) is pH dependent. At pH 5 oxycarboxin (carboxin sulfone) is stable to hydrolysis. The hydrolysis half-life of oxycarboxin (carboxin sulfone) at pH 7 and 9, (using non-linear regression) was 9.8 days and 3.4 hours.
Photolytic degradation of active substance and metabolites above 10 % ‡	Carboxin DT_{50} 2.64 hours (r^2=0.903, first-order, non-linear regression). Xenon lamp, light intensity of 600 W/m^2 for 8 hour light 16 hour dark cycle. Global irradiation of 670 W/m^2 Metabolites: oxo-(phenyl amino)acetic acid (55% AR) and carboxin sulfoxide (20.4% AR)
Quantum yield of direct phototransformation in water at Σ > 290 nm	4.00 x 10^{-3} mol/Einstein $^{-1}$
Readily biodegradable ‡ (yes/no)	Carboxin is not readily biodegradable

Degradation in water / sediment

Carboxin	Distribution in ditch system, max in aqueous phase 74% at week 0, max in sediment phase 27% at week 2. Distribution in river system, max in aqueous phase 74% at week 0, max in sediment phase 10% at weeks 2 and 4.

Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys. (days)		St. (r^2)	DT_{50}-DT_{90} water (days)		St. (r^2)	DT_{50}- DT_{90} sediment (days)		St. (r^2)	Method of calc.
Ditch system	8.7	7.2	20	23.5	78.1	0.968	12.6	41.7	0.972	68.8	228.5	0.972	SFO
River system	7.9	7.4	20	11.0	36.5	0.978	14.7	49.0	0.963	8.7	29.0	0.963	SFO
Arithmetic mean/median Geometric mean				17.3 16.1	57.3		13.7 13.6	45.3		38.8 24.5	128.7		

Carboxin sulfoxide	Distribution in ditch system, max in aqueous phase 11% at week 2, max in sediment phase 4% at week 4. Distribution in river system, max in aqueous phase 19% at week 4, max in sediment phase 6% at week 2.												
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys. (days)		St. (r^2)	DT_{50}-DT_{90} water (days)		r^2	DT_{50}- DT_{90} sediment (days)		St. (r^2)	Method of calc.
Ditch system	8.7	7.2	20	33.2	110.5	0.968	7.4	24.7	0.972	11.7	38.8	0.972	SFO
River system	7.9	7.4	20	22.1	73.4	0.978	23.8	79.0	0.963	4.4	14.5	0.963	SFO
Arithmetic mean/median Geometric mean				27.7 27.1	91.9		15.6 13.3	51.9		8.1 7.2	26.6		

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 n d	Non-extractable residues in sed. max x % after n d (end of the study)
Ditch system	8.7	7.2	23.7% of AR at 13 weeks	40.2% of AR at 13 weeks	40.2% of AR at 13 weeks
River system	7.9	7.4	40.1% of AR at 13 weeks	33.4% of AR at 13 weeks	33.4% of AR at 13 weeks

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

Carboxin Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 235.3 Water solubility (mg/L): 147.0 at 20ºC K_{FOC} (L/kg): 152 DT_{50} soil (d): 0.28 (mean laboratory rate normalised to 20°C and pF 2. In accordance with FOCUS SFO) DT_{50} water/sediment system (d): 16.1 (geomean whole system value from 2 sediment water studies) DT_{50} water (d): 13.6 (geomean from 2 sediment water studies) DT_{50} sediment (d): 24.5 (geomean from 2 sediment water studies) Crop interception (%): no interception
Parameters used in FOCUSsw step 3 (if performed)	Vapour pressure: 1.0 x 10^{-10} Pa at 25ºC 1/n: 0.81 See table below for metabolite properties.
Application rate	Crop: seed treatment therefore bare soil Crop interception: 0% Number of applications: 1 Interval (d): n.a

Application rate(s): 132 g as/ha

PEC_{sw} and PEC_{sed} of the active substance carboxin at the recommended dose rate of 0.132 kg a.s./ha calculated using FOCUS step 1 software

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	37.80		55.61	
	24 h	36.01	36.90	54.74	55.17
	2 d	34.49	36.08	52.43	54.37
	4 d	31.65	34.56	48.10	52.30
	7 d	27.81	32.47	42.28	49.23
	14 d	20.58	28.24	31.28	42.86
	21 d	15.22	24.75	23.14	37.58
	28 d	11.26	21.85	17.12	33.18
	42 d	6.16	17.39	9.37	26.40

Initial PEC_{sw} and PEC_{sed} of the carboxin metabolites at the recommended dose rate of 0.132 kg carboxin /ha calculated using FOCUS step 1 software

Winter cereals (Oct-Feb) north Europe		
Metabolite	Maximum surface water concentration (µg/l)	Maximum sediment concentration (µg/ kg)
carboxin sulfoxide	32.97	31.27
oxycarboxin (carboxin sulfone)	7.82	5.11
P/V-54	8.70	2.09
P/V-55	5.10	0.66
M6	4.98	35.22
M9	4.92	34.78

NB. Maximum metabolite PEC values are the same as those originally reported in Sections B.8.6.1 and B.8.6.2 in Volume 3 of the carboxin DAR.

PEC_{sw} and PEC_{sed} of the active substance carboxin at the recommended dose rate of 0.132 kg a.s./ha calculated using FOCUS step 2 software

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	1.21		1.23	
	24 h	1.02	1.12	1.17	1.20
	2 d	0.97	1.06	1.12	1.17
	4 d	0.88	0.99	1.02	1.12
	7 d	0.72	0.90	0.89	1.05
	14 d	0.52	0.76	0.64	0.90
	21 d	0.37	0.65	0.46	0.78
	28 d	0.27	0.57	0.33	0.68
	42 d	0.14	0.44	0.17	0.54
Southern EU	North Europe, winter cereal application presented only, since this combination generates the highest concentrations of carboxin and metabolites in water.				

Initial PEC_{sw} and PEC_{sed} of the carboxin metabolites at the recommended dose rate of 0.132 kg carboxin /ha calculated using FOCUS step 2 software

Winter cereals (Oct-Feb) north Europe		
Metabolite	Maximum surface water concentration (µg/l)	Maximum sediment concentration (µg/ kg)
carboxin sulfoxide	15.72	14.99
oxycarboxin (carboxin sulfone)	3.35	2.19
P/V-54	4.22	1.01
P/V-55	2.19	0.29
M6	0.62	4.40
M9	2.23	15.79

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
Step 3 modelling was run and the results confirmed that PECsw/sed were higher in step 1 and 2 models.						

Carboxin metabolite parameters used in FOCUS Steps 1 and 2 and FOCUS Groundwater						
Properties	carboxin sulfoxide	oxycarboxin (carboxin sulfone)	P/V-54	P/V-55	M6	M9
Molecular mass (g mol^{-1})	251.3	267.3	175.2	191.2	267.29	269.3
Water solubility (mg/L)	587.7[(1)]	1400	4.296×10^5 [(1)]	2.438×10^4 [(1)]	2.797×10^4	1000[(2)]
K_{Foc} (ml/g) (arithmetic mean) [(4)]	96	65.4	24	13	10/10000 [(3)]	10/10000 [(3)]
Freundlich exponent (arithmetic mean)	0.82	0.847	1.02	0.94	default[(5)]	default[(5)]
DT_{50} at 20°C and pF 2 (days)	16.25/ 51.55[(6)]	18.13	93.53[(12)]	18.57	<2	28.74
Max. amount in soil (%)	78.2	17.0	27.4	14.5	10.1	9.9
Max. amount in water/sediment (%)	30	0.00001[(7)]	0.00001[(7)]	0.00001[(7)]	0.00001[(7)]	0.00001[(7)]
Degradation DT_{50} water (days)	13.3	1000[(11)]	1000[(11)]	1000[(11)]	1000[(11)]	1000[(11)]
Degradation DT_{50} sediment (days)	7.2	1000[(11)]	1000[(11)]	1000[(11)]	1000[(11)]	1000[(11)]
Dissipation DT_{50} water/sediment system (days)	27.1	1000[(11)]	1000[(11)]	1000[(11)]	1000[(11)]	1000[(11)]
Formation Fraction (Groundwater modelling only)	0.9	1.0[(8)]	0.5[(9)]	-[(10)]	-[(10)]	-[(10)]

[(1)]estimated from EPI Win version 3.10;
[(2)]simple default value selected for M9 water solubility (will not influence the PEC values derived)
[(3)] realistic worst-case default selected according to the Aquatic Guidance Document; Kfoc value of 10,000 ml/g was assumed as worse case for sediment and 10.0 ml/g was assumed as worse case for surface water and groundwater
[(4)]for modelling with FOCUS PEARL Kfom estimated by dividing Kfoc by 1.724.
[(5)] A default value of 1.0 was selected as a realistic worst case.
[(6)] 1 soil was kinetically modelled with DFOP kinetics, therefore two geomeans calculated, one with slow phase DT_{50} and one with fast phase. In surface water modelling slow phase DT_{50} used for calculation of carboxin sulfoxide PEC. In groundwater modelling slow phase geomean DT_{50} value used for calculation of carboxin sulfoxide PEC and oxycarboxin (carboxin sulfone) PEC. Fast phase geomean DT_{50} values used for calculation of P/V-54 PEC.
[(7)]default value of 0.00001% used in surface water modelling since the metabolites were not detected in water/sediment studies
[(8)] Formation fraction from carboxin sulfoxide with slow phase geomean carboxin sulfoxide DT_{50}
[(9)] Formation fraction from carboxin sulfoxide with fast phase geomean carboxin sulfoxide DT_{50}.
[(10)] No formation fraction required as individual modelling performed, and therefore maximum formation (peak occurance) used.

(11) worst-case estimate of 1000 days used since metabolites were not detected in water/sediment studies.
(12) geomean of 2 values from which the higher value is 113 days that might be used in PEC calculations.

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 – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PELMO v 3.3.2 and PEARL v 3.3.3 Scenarios (list of names): Chateaudun, Hamburg, Jokioinen, Kremsmunster, Okehampton, Piacenza, Porto, Sevilla, Thiva Crop: winter cereal Mean parent DT_{50lab} 0.28 days (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). K_{OC}: parent, mean 152, $^{1}/_{n}$= 0.81. See table above for metabolite properties.
Application rate	Application rate: 132 g/ha. No. of applications: 1 Time of application (month or season): winter

FOCUS PELMO estimation of groundwater PEC values for carboxin and its soil metabolites following application to winter wheat

Location	80th percentile concentration in groundwater [µg/l]						
	carboxin	carboxin sulfoxide	oxycarboxin (carboxin sulfone)	M9	P/V-54	M6	P/V-55
Chateaudun	<0.001	<0.001	<0.001	0.661	4.820	<0.001	0.134
Hamburg	<0.001	0.012	0.027	1.825	6.429	0.006	0.669
Jokioinen	<0.001	<0.001	<0.001	1.885	6.679	0.005	0.483
Kremsmunster	<0.001	0.004	0.010	0.863	4.674	0.003	0.262
Okehampton	<0.001	0.018	0.048	1.312	5.017	0.001	0.579
Piacenza	<0.001	0.069	0.147	1.278	4.438	0.014	0.651
Porto	<0.001	<0.001	<0.001	0.798	2.220	0.001	0.167
Sevilla	<0.001	<0.001	<0.001	0.388	1.703	< 0.001	0.085
Thiva	<0.001	<0.001	<0.001	0.676	4.106	0.001	0.166

FOCUS PEARL estimation of groundwater PEC values for carboxin and its soil metabolites following application to winter wheat

Location	80th percentile concentration in groundwater [µg/l]						
	carboxin	carboxin sulfoxide	oxycarboxin (carboxin sulfone)	M9	P/V-54	M6	P/V-55
Chateaudun	<0.001	0.003	0.007	0.856	4.934	<0.001	0.362
Hamburg	<0.001	0.085	0.140	1.657	6.113	0.006	0.981
Jokioinen	<0.001	0.002	0.008	1.556	6.384	0.003	0.920
Kremsmunster	<0.001	0.051	0.084	0.903	4.125	0.002	0.496
Okehampton	<0.001	0.119	0.156	1.199	4.496	0.001	0.730
Piacenza	<0.001	0.217	0.257	0.997	3.798	0.006	0.623
Porto	<0.001	<0.001	<0.001	0.604	1.897	<0.001	0.323
Sevilla	<0.001	<0.001	<0.001	0.541	2.803	<0.001	0.251
Thiva	<0.001	0.003	0.010	0.883	4.292	0.002	0.442

FOCUS PELMO estimation of groundwater PEC values for carboxin and its soil metabolites following application to spring wheat

Location	80th percentile concentration in groundwater [µg/l]						
	carboxin	carboxin sulfoxide	oxycarboxin (carboxin sulfone)	M9	P/V-54	M6	P/V-55
Chateaudun	<0.001	<0.001	<0.001	0.101	2.746	<0.001	0.009
Hamburg	<0.001	0.001	0.004	0.363	4.978	<0.001	0.091
Jokioinen	<0.001	<0.001	<0.001	0.498	5.908	<0.001	0.079
Kremsmunster	<0.001	<0.001	<0.001	0.312	4.238	<0.001	0.053
Okehampton	<0.001	0.001	0.002	0.348	3.921	<0.001	0.095
Porto	<0.001	<0.001	<0.001	0.083	1.271	<0.001	0.004

FOCUS PEARL estimation of groundwater PEC values for carboxin and its soil metabolites following application to spring wheat

Location	80th percentile concentration in groundwater [µg/l]						
	carboxin	carboxin sulfoxide	oxycarboxin (carboxin sulfone)	M9	P/V-54	M6	P/V-55
Chateaudun	<0.001	<0.001	<0.001	0.194	3.495	<0.001	0.046
Hamburg	<0.001	0.038	0.061	0.619	5.644	<0.001	0.241
Jokioinen	<0.001	<0.001	0.021	0.566	5.392	<0.001	0.197
Kremsmunster	<0.001	0.029	0.050	0.443	4.076	<0.001	0.182
Okehampton	<0.001	0.038	0.065	0.416	3.574	<0.001	0.180
Porto	<0.001	<0.001	<0.001	0.094	1.181	<0.001	0.019

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

Direct photolysis in air ‡	Not studied – not required.
Quantum yield of direct phototransformation	Not studied – not required.
Photochemical oxidative degradation in air ‡	1.9 hours based on a rate constant of 202.5 x 10^{-12} cm^3 $molecule^{-1}$ sec^{-1} and an OH radical concentration of 5 x 10^5 molecules cm^{-3}
Volatilisation ‡	Not studied – not required.
Metabolites	None

PEC (air)

Method of calculation	Expert judgement based on that the vapour pressure of carboxin is 2.0 x 10^{-5} Pa at 25°C and the Henry's law constant is 3.2 x 10^{-10} atm.m^3/mole at 25°C. These values demonstrate low volatility of carboxin and a low tendency to partition from water to air.

$PEC_{(a)}$

Maximum concentration	Assumed to be negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	**Soil**: carboxin, carboxin sulfoxide, oxycarboxin (carboxin sulfone), M6, P/V-54 and P/V-55 **Surface water**: carboxin, carboxin sulfoxide, oxycarboxin (carboxin sulfone), M6, P/V-54 and P/V-55 **Ground water**: carboxin, carboxin sulfoxide, oxycarboxin (carboxin sulfone), M6, M9, P/V-54 and P/V-55 **Air**: carboxin

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

Soil (indicate location and type of study)	None submitted
Surface water (indicate location and type of study)	None submitted
Ground water (indicate location and type of study)	None submitted

Air (indicate location and type of study)	None submitted

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

Candidate for R53.

Ecotoxicology

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 *Colinus virginianus*	carboxin	Acute	>2150	
Mallard *Anas platyrhynchos*	oxycarboxin (carboxin sulfone)	Acute	1250	
Bobwhite quail *Colinus virginianus*	carboxin	Short-term	>985[#]	5000
Bobwhite quail *Colinus virginianus*	oxycarboxin (carboxin sulfone)	Short-term	>2195	>10000
Bobwhite quail *Colinus virginianus*	carboxin	Long-term	83	1000
Mammals				
Rat	carboxin	Acute	2588	
Rat	carboxin	Long-term	20	400
Additional higher tier studies: No further relevant studies submitted.				
[#]Converted to daily dose using mean bw of 37.065 g and average food consumption of 7.3 g. Daily dose = 5000*7.3/37.065 = 985 mg a.s./kg bw/day.				

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

Winter cereals, 132 g carboxin/ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Granivorous bird	Acute	228	14.48	10
Granivorous bird	Short-term	228	>4.32[1]	10
Granivorous bird	Long-term	228	**0.36**[2]	5
Large herbivorous bird	Acute	10.1	326.4	10
Large herbivorous bird	Short-term	10.1	97.4	10
Large herbivorous bird	Long-term	4.3	19.5	5
Tier 1 (Mammals)				
Granivorous mammal	Acute	138	18.75	10
Granivorous mammal	Long-term	138	**0.14**[3]	5
Small herbivorous mammal	Acute	32.0	81.0	10
Small herbivorous mammal	Long-term	13.4	**1.5**[3]	5

[1] TER_{ST} considered to be covered sufficiently by the acute assessment.

[2] Further consideration required for exposure of breeding granivorous birds (see Addendum 2of June 2010; The United Kingdom, 2010)
[3] Further consideration required for exposure of breeding granivorous/herbivorous mammals (see Addendum 2 of June 2010; The United Kingdom, 2010)

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 (mg/L)
Laboratory tests				
Fish				
Oncorhynchus mykiss	carboxin	96 hr (flow-through)	Mortality, LC_{50}	2.3($_{mm}$)
Cyprinus carpio	carboxin	21 d (semi-static)	Growth NOEC	0.32($_{nom}$)
Oncorhynchus mykiss	carboxin sulfoxide	96 hr (static)	Mortality, LC_{50}	>25($_{nom}$)
Oncorhynchus mykiss	oxycarboxin (carboxin sulfone)	96 hr (static)	Mortality, LC_{50}	19.9($_{nom}$)
Oncorhynchus mykiss	P/V - 54	96 hr (static)	Mortality, LC_{50}	>100($_{nom}$)
Aquatic invertebrate				
Daphnia magna	carboxin	48 h (flow-through)	Mortality, EC_{50}	>57($_{mm}$)
Daphnia magna	carboxin	17 d (static)	Reproduction, NOEC	0.32($_{nom}$)
Daphnia magna	carboxin sulfoxide	48 h (static)	Mortality, EC_{50}	>25($_{nom}$)
Daphnia magna	oxycarboxin (carboxin sulfone)	48 h (static)	Mortality, EC_{50}	69.1($_{nom}$)
Daphnia magna	P/V - 54	48 h (static)	Mortality, EC_{50}	>100($_{nom}$)
Sediment-dwelling organisms: No studies submitted.				
Algae				
Pseudokirchneriella subcapitata	carboxin	72 h (static)	Growth rate: E_rC_{50}	0.48($_{mm}$)
Pseudokirchneriella subcapitata	carboxin sulfoxide	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>25($_{nom}$) >25($_{nom}$)
Pseudokirchneriella subcapitata	oxycarboxin (carboxin sulfone)	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.46($_{mm}$) 2.76($_{mm}$)
Pseudokirchneriella subcapitata	P/V - 54	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>100($_{nom}$) >100($_{nom}$)

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg/L)
Microcosm or mesocosm tests: No studies submitted.				

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

FOCUS Step1

Winter cereals, 132 g carboxin/ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i[1]	TER	Annex VI Trigger[1]
carboxin	Fish	2.3	Acute	0.0378	**61**	100
carboxin	Fish	0.32	Chronic	0.0378	**8.5**	10
carboxin	Aquatic invertebrates	57	Acute	0.0378	1508	100
carboxin	Aquatic invertebrates	0.32	Chronic	0.0378	**8.5**	10
carboxin	Algae	0.48	Short-term Chronic	0.0378	13	10
carboxin sulfoxide	Fish	>25	Acute	0.0330	> 758	100
carboxin sulfoxide	Aquatic invertebrates	>25	Acute	0.0330	> 758	100
carboxin sulfoxide	Algae	>25	Short-term Chronic	0.0330	> 758	10
oxycarboxin (carboxin sulfone)	Fish	19.9	Acute	0.0078	2545	100
oxycarboxin (carboxin sulfone)	Aquatic invertebrates	69.1	Acute	0.0078	8836	100
oxycarboxin (carboxin sulfone)	Algae	0.46	Short-term Chronic	0.0078	59	10
P/V-54	Fish	>100	Acute	0.0087	>11494	100
P/V-54	Aquatic invertebrates	>100	Acute	0.0087	>11494	100
P/V-54	Algae	>100	Short-term Chronic	0.0087	>11494	10

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i[1]	TER	Annex VI Trigger[1]
M6	Fish	0.23[2]	Acute	0.00498	**46**	100
M6	Aquatic invertebrates	5.7[2]	Acute	0.00498	1145	100
M6	Algae	0.048[2]	Short-term Chronic	0.00498	10	10
M9	Fish	0.23[2]	Acute	0.0049	**47**	100
M9	Aquatic invertebrates	5.7[2]	Acute	0.0049	1159	100
M9	Algae	0.048[2]	Short-term Chronic	0.0049	10	10

[1]The maximum initial PEC_{SW} for the a.s. and the metabolites resulting from drainflow/run-off only.
[2] No toxicity data were submitted, so the toxicity was estimated assuming ten times higher toxicity of the metabolite compared to the toxicity of carboxin.

FOCUS Step 2

Winter cereals, 132 g carboxin/ha, Northern Europe

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	TER	Annex VI Trigger[1]
carboxin	Fish	2.3	Acute	0.0012	1901	100
carboxin	Fish	0.32	Chronic	0.0012	264	10
carboxin	Aquatic invertebrates	57	Acute	0.0012	47107	100
carboxin	Aquatic invertebrates	0.32	Chronic	0.0012	264	10
carboxin	Algae	0.48	Short-term Chronic	0.0012	397	10
carboxin sulfoxide	Fish	> 25	Acute	0.0157	>1590	100
carboxin sulfoxide	Aquatic invertebrates	> 25	Acute	0.0157	>1590	100
carboxin sulfoxide	Algae	> 25	Short-term Chronic	0.0157	>1590	10
oxycarboxin (carboxin sulfone)	Fish	19.9	Acute	0.0034	5940	100
oxycarboxin (carboxin sulfone)	Aquatic invertebrates	69.1	Acute	0.0034	20627	100
oxycarboxin (carboxin sulfone)	Algae	0.46	Short-term Chronic	0.0034	137	10
P/V-54	Fish	> 100	Acute	0.0042	>23697	100
P/V-54	Aquatic invertebrates	> 100	Acute	0.0042	>23697	100
P/V-54	Algae	> 100	Short-term Chronic	0.0042	>23697	10
M6	Fish	0.23[2]	Acute	0.00062	371	100
M6	Aquatic invertebrates	5.7[2]	Acute	0.00062	9194	100
M6	Algae	0.048[2]	Short-term Chronic	0.00062	77	10
M9	Fish	0.23[2]	Acute	0.0022	103	100
M9	Aquatic invertebrates	5.7[2]	Acute	0.0022	2556	100
M9	Algae	0.048[2]	Short-term Chronic	0.0022	22	10

[1]The maximum initial PEC_{SW} for the a.s. and the metabolites resulting from drainflow/run-off only.
[2] No toxicity data were submitted, so the toxicity was estimated assuming ten times higher toxicity of the metabolite compared to the toxicity of carboxin.

Bioconcentration	
	carboxin
$logP_{O/W}$	2.3[1]

[1] log $P_{O/W}$ <3 for the active substance, therefore no assessment is required. The log $P_{O/W}$ for the metabolites are also likely to be below 3 (see section B.9.2.4.6)

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)
carboxin	>100	>100
oxycarboxin (carboxin sulfone)		181.29
Field or semi-field tests: No studies submitted		

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

Due to the use of carboxin only as a seed treatment the standard hazard quotient calculation and triggers are not considered applicable. An assessment of risks from systemic transport of carboxin into flowers and foliage has been conducted (section B.9.4.3) and the risk is considered to be low.

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

Laboratory tests with standard sensitive species
Further laboratory and extended laboratory studies

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect	Trigger value
Folsomia candida (Collembola)	Adults and juveniles	Artificial soil treated with 'Vitavax 200FF'[2]	1000, 500, 250, 125 and 62.5 mg formn/kg d.w. soil	Mortality Reproduction	0 0	30%[1]
Aleochara bilineata (rove beetle)	Adults and juveniles	Sand containing seeds treated with 'Vitavax 200FF'[2]	776 mg carboxin/kg seed and 770 mg thiram/kg seed	Mortality Reproduction	0 -21.5%	30%[1]
Poecilus cupreus (predatory ground beetle)	Adults	Sand containing seeds treated with 'Vitavax 200FF'[2]	776 mg carboxin/kg seed and 770 mg thiram/kg seed	Mortality Food consumption	0 0	30%[1]

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect	Trigger value
Folsomia candida (Collembola)	Adults and juveniles	Artificial soil treated with oxycarboxin (carboxin sulfone)	1000, 500, 250, 125 and 62.5 mg/kg d.w. soil	Mortality Reproduction	0 Significant reduction at 1000 mg/kg d.w. soil	30%[1]

[1] Due to the use being a seed treatment a standard ESCORT 2 risk assessment was not conducted. The 50% trigger for ESCORT 1 and Annex VI is therefore applied.
[2] 'Vitavax 200FF' is a FS formulation for seed treatment containing two active substances; 200 g carboxin/L and 200 g thiram/L.

Field or semi-field tests: No studies submitted

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 fetida	carboxin	Acute 14 days	LC_{50} >250 mg a.s./kg d.w.soil[1]
Eisenia fetida	oxycarboxin (carboxin sulfone)	Chronic 8 weeks	NOEC 50 mg a.s./kg d.w.soil[1]
Eisenia fetida	'Vitavax 200FF'	Acute	LC_{50} >87 mg formulation/kg d.w.soil[1]
Other soil macro-organisms – see data on *Folsomia candida* in previous section			
Soil micro-organisms			
Nitrogen mineralisation	carboxin		No significant effect at day 28 at 0.880 mg a.s./kg d.w.soil (660 g a.s/ha)
Carbon mineralisation	a.s. ‡		No significant effect at day 28 at 0.880 mg a.s./kg d.w.soil (660 g a.s/ha)
Field studies – no studies were submitted			

[1] end point has been divided by 2 as log Pow is > 2.0 (log Pow = 2.3)

Toxicity/exposure ratios for soil organisms

Cereals, 132 g carboxin/ha

Test organism	Test substance	Time scale	Soil PEC[1]	TER	Trigger
Earthworms					
Eisenia fetida	carboxin	Acute	0.176	>1420	10
Eisenia fetida	Preparation	Acute	0.176	>85	10

Test organism	Test substance	Time scale	Soil PEC[1]	TER	Trigger
Eisenia fetida	oxycarboxin (carboxin sulfone)	Chronic	0.014	>3571	5

[1] The maximum initial PEC_{SOIL} for the a.s. and oxycarboxin (carboxin sulfone) was used.

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

Preliminary screening data

Not required as carboxin does not have herbicidal properties and is a seed treatment.

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

Test type/organism	end point
Activated sludge	up to 16.3% inhibition at 1000 mg/L[1]

[1]not considered of ecotoxicological relevance at concentrations resulting from the representative use of carboxin.

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

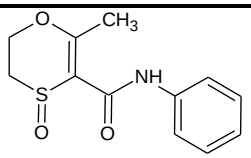
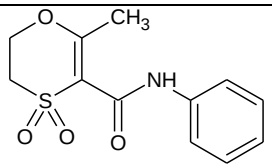
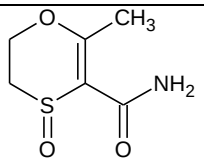
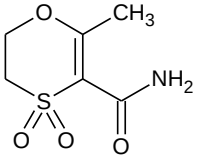
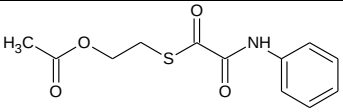
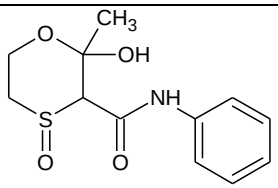
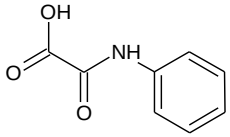
Compartment	
soil	carboxin, oxycarboxin (carboxin sulfone), carboxin sulfoxide, M6
water	carboxin, oxycarboxin (carboxin sulfone), carboxin sulfoxide, M6
groundwater	carboxin, oxycarboxin (carboxin sulfone), carboxin sulfoxide, M6, M9

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

	RMS/peer review proposal
Active substance	R50 Very toxic to aquatic organisms R53 May cause long-term adverse effects in the aquatic environment ('N' symbol)

	RMS/peer review proposal
Preparation	R50 Very toxic to aquatic organisms R53 May cause long-term adverse effects in the aquatic environment ('N' symbol)

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name*	Structural formula*
carboxin sulfoxide	2-methyl-*N*-phenyl-5,6-dihydro-1,4-oxathiine-3-carboxamide 4-oxide	
oxycarboxin (carboxin sulfone)	5,6-dihydro-2-methyl-1,4-oxathiine-3-carboxanilide 4,4-dioxide	
P/V-54	2-methyl-5,6-dihydro-1,4-oxathiine-3-carboxamide 4-oxide	
P/V-55	2-methyl-5,6-dihydro-1,4-oxathiine-3-carboxamide 4,4-dioxide	
M6	2-{[anilino(oxo)acetyl]sulfanyl}ethyl acetate	
M9	(2*RS*)-2-hydroxy-2-methyl-*N*-phenyl-1,4-oxathiane-3-carboxamide 4-oxide	
oxo-(phenyl amino)acetic acid	oxo(phenylamino)acetic acid	

* ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).

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)
ETE	estimated theoretical exposure
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
FS	flowable concentrate for seed treatment
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
HPLC-MS-MS	high pressure liquid chromatography with tandem mass spectrometry
HPLC-UV	high pressure liquid chromatography with ultraviolet detector
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ILV	inter laboratory validation
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
NEU	northern Europe
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
SEU	southern Europe
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
WHO	World Health Organisation
wk	week
yr	year