CONCLUSION ON PESTICIDE PEER REVIEW

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

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SUMMARY

Commission Regulation (EC) No 737/2007[3] (hereinafter referred to as 'the Regulation') lays down the procedure for the renewal of the inclusion of a first group of active substances in Annex I to Council Directive 91/414/EEC and establishes the list of those substances. Spiroxamine is one of the first group of active substances listed in the Regulation.

In accordance with Article 6 of the Regulation, the notifier Bayer CropScience submitted a dossier on spiroxamine to Germany and Hungary being the designated rapporteur Member State (RMS), and co-rapporteur Member State, respectively. In accordance with Article 10 of the Regulation, Germany prepared an Assessment Report in consultation with Hungary which was submitted to the EFSA and the Commission of the European Communities (hereafter referred to as 'the Commission'). The Assessment Report was received by the EFSA on 17 September 2009.

In accordance with Article 11 of the Regulation, the EFSA distributed the Assessment Report to Member States and the notifier for comments on 21 September 2009. The EFSA collated and forwarded all comments received to the Commission on 23 October 2009.

In accordance with Article 12, following consideration of the Assessment Report and the comments received, the Commission requested the EFSA to arrange an expert consultation on the Assessment Report as appropriate and deliver its conclusions on spiroxamine.

The conclusions presented in this report were reached on the basis of the evaluation of the representative uses of spiroxamine as a fungicide on grapes, wheat, triticale, rye, barley and oats as proposed by the notifier. Full details of the representative uses can be found in Appendix A to this report.

The preferential metabolism/degradation of each enantiomer in plants, animals and the environment, and the possible impact on the toxicity, the worker and consumer risk assessment, and on the environment were not investigated in the studies submitted in the dossier and should be addressed.

For the section on physical-chemical properties no critical areas of concern were identified. Data gaps were identified for quality control data to support the specification, for a final report of the validation for two impurities for the level of ethoxylation of formulants and ILV data for products of animal origin.

1 On request from the European Commission, Question No EFSA-Q-2010-00012, issued on 01 September 2010

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3 OJ L169, 29.06.2007, p.10

Suggested citation: European Food Safety Authority; Conclusion on the peer review of the pesticide risk assessment of the active substance spiroxamine. EFSA Journal 2010;8(10)1719. [102 pp.]. doi:10.2903/j.efsa.2010 1719. Available online: www.efsa.europa.eu

A data gap was identified for the toxicological profile of the metabolites found in fruit residues consisting of 4-*tert*-butyl-cyclohexanol and its derivatives, and aminodiol. A data gap was identified for the diastereomer ratio found in plant residues to which workers are exposed. Worker exposure to "Prosper EC 500" after 3 applications in grapes exceeds the AOEL even when the use of personal protective equipment (PPE) is considered and applying a 50% decrease in residues between each application (7 days interval).

Metabolism in plant was investigated on cereals (wheat) and on fruit crops (grape and banana). For monitoring, the residue in plant was defined as the parent spiroxamine. For risk assessment, two separate residue definitions were proposed for cereals and for fruit crops. However for fruits, this definition has to be considered provisional, pending additional information on the toxicity of the group B and C metabolites. In animal, the residue was defined as metabolite M06 for monitoring and two separate definitions were proposed for risk assessment, for ruminant and poultry. There was no consumer risk assessment possible for grapes. For cereals, no acute or chronic concern was identified, the TMDI and IESTI being below the ADI and the ARfD values.

The data available on environmental fate and behaviour are essentially sufficient to carry out the required environmental exposure assessments at EU level for the representative uses, with the notable exceptions that the potential for groundwater contamination by metabolite M03 (KWG 4168-N-oxide)is not finalised. Another data gap was also identified to address potential preferential enantio-selective degradation in the aquatic environment.

The acute and short-term risk for birds was assessed as low for the representative uses. After the necessary refinement the long-term risk for birds was considered low. The acute and long-term risk for mammals was assessed as low after the adequate refinement for the representative uses. High risk was identified for aquatic organisms even with risk mitigation measures.

The risk for non-target arthropods in the off-field area in grapes use was assessed as low. However, a high risk was initially identified in the in-field area. Taking into account all available information (extended and field studies) the PRAPeR 75 meeting concluded that the risk for the in-field areas can be assessed as low for the use in grapes. The risk to nin target arthropos in the in-field and off-field area from the use in cereals was assessed as low.

The risk for bees, earthworms and other non-target soil-macro-organisms, soil micro-organism and biological methods for sewage treatment was assessed as low

KEY WORDS

spiroxamine, peer review, risk assessment, pesticide, fungicide

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BACKGROUND

Commission Regulation (EC) No 737/2007[4] (hereinafter referred to as 'the Regulation') lays down the procedure for the renewal of the inclusion of a first group of active substances in Annex I to Council Directive 91/414/EEC and establishes the list of those substances. Spiroxamine is one of the first group of active substances listed in the Regulation.

In accordance with Article 6 of the Regulation, the notifier Bayer CropScience submitted a dossier on Spiroxamine to Germany and Hungary being the designated rapporteur Member State (RMS), and co-rapporteur Member State, respectively. In accordance with Article 10 of the Regulation, Germany prepared an Assessment Report in consultation with Hungary which was submitted to the EFSA and the Commission of the European Communities (hereafter referred to as 'the Commission'). The Assessment Report was received by the EFSA on 17 September 2009

In accordance with Article 11 of the Regulation, the EFSA distributed the Assessment Report to Member States and the notifier for comments on 21 September 2009. A 30 day period was provided for commenting. In addition, the EFSA conducted a public consultation on the Assessment Report. The EFSA collated and forwarded all comments received to the Commission on 23 October 2009. At the same time, the collated comments were forwarded to the RMS for compilation in the format of a Reporting Table. The notifier was invited to respond to the comments in column 3 of the Reporting Table. The RMS also provided a response to the comments in column 3.

In accordance with Article 12, following consideration of the Assessment Report and the comments received, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 23 November 2009 the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on spiroxamine. The need for expert consultation was considered in a telephone conference between the EFSA, the RMS, the co-RMS and the Commission on 30 November 2009. On the basis of the comments received, the notifier'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 areas of mammalian toxicology, residues, 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, 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 May 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 in agriculture and viticulture as proposed by the notifier. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the peer review report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The peer review report comprises the following documents:

[4] OJ L169, 29.06.2007, p.10

- the comments received,
- the Reporting Table (revision 1.1, 26. November 2009)
- the Evaluation Table (24 June 2010),
- the report(s) of the scientific consultation with Member State experts (where relevant).

Given the importance of the Assessment Report including its addendum (compiled version of May 2010 containing all individually submitted addenda) 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

Spiroxamine is the ISO common name for 8-*tert*-butyl-1,4-dioxaspiro[4.5]decan-2-ylmethyl(ethyl)(propyl)amine (IUPAC).

The representative formulated products for the evaluation were 'Hoggar, Prosper, Prosper 500 EC' which is a 500 g/L emulsifiable concentrate (EC) and 'Input' and 'Helix' an EC formulation containing 160 g/L prothioconazole and 300 g/L spiroxamine.

The representative uses evaluated comprise outdoor foliar spraying against fungal diseases in grapes with the 'Hoggar' formulation and in wheat, triticale, rye, barley and oats with the 'Input' formulation. Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

It must be noted that spiroxamine has diastereo isomers, but the possible preferential metabolism/degradation of each enantiomer in animals, plants and the environment was not investigated in the studies submitted in the dossier and was therefore not considered during the peer review. Moreover, the analytical methods used in the studies reported through all sections were not stereo-selective, and all values mentioned as "spiroxamine" have to be considered as "sum of diastereo isomers". The possible impact of each individual enantiomer on the toxicity, the worker and consumer risk assessment and the environment was not evaluated. Data gaps (applicable for sections 2, 3, 4 and 5) were therefore identified to address the impact on the risk assessment of the isomeric composition of the substance.

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

The minimum purity of spiroxamine as manufactured should not be less than 950g/kg. The proposed ratio of the diastereo isomers and the maximum content of impurities is not supported by the available data. A data gap has been identified for quality control data and the final amended report for the validation for two impurities. On the basis of the available information spiroxamine does not contain any relevant impurities. There is currently no FAO specification for spiroxamine.

The main data regarding the identity of spiroxamine and its physical and chemical properties are given in Appendix A.

For the formulations the proposed tank mixes were not considered. A data gap was identified for the level of ethoxylation of some of the formulants. For the mixed formulation with prothioconazole it should be noted that no methods of analysis were provided for prothioconazole or its relevant impurity prothioconazole-desthio.

Residues of spiroxamine in plants can be analysed by a LC-MS/MS method. In products of animal origin spiroxamine carboxylic acid can be analysed by a LC-MS/MS method but a data gap has been identified for ILV data. Soil is analysed for spiroxamine using a LC-MS/Ms method, water by GC-MS and air by GC-NPD. A method for body fluids and tissues is not necessary as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

Spiroxamine was discussed at the PRAPeR Expert Meeting on mammalian toxicology (PRAPeR 73) in March 2010. The proposed technical specification is supported by the toxicological assessment.

Oral absorption is rapid but limited, spiroxamine is extensively metabolised as no parent compound was present either in urine or in faeces.

Moderate acute toxicity is observed when spiroxamine is administered by the oral, dermal or inhalation routes, it is severely irritant to skin and may cause sensitisation by skin contact.

The target organ and critical of spiroxamine are the liver and irritant effects on the mucosal epithelium of the oesophagus and fore-stomach. Additionally, eye cataracts were observed in dogs. The relevant short-term and long term NOAEL is 2.5 mg/kg bw/day from the 1-year dog study. No genotoxic or carcinogenic potential was observed. Fertility and overall reproductive performance were not impaired, but malformations (cleft palate) were observed in rats above the concurrent and historical control data at dose levels also inducing maternal toxicity, leading to a proposal for classification with R63 "Possible risk of harm to the unborn child". This proposal was not supported by one Member State. No specific neurotoxic effects were found in acute and repeated-dose neurotoxicity studies, but an acute NOAEL of 10 mg/kg bw/day was obtained from the acute neurotoxicity study.

The metabolites found in plant residues were grouped according to their chemical structure in three groups (A, B and C); for metabolites included into Group A (spiroxamine-related structure) their toxicity is covered by the reference values of the parent. For the two other groups (4-tert-butyl cyclohexan-ol-related and aminodiol-related structures), no conclusion could be drawn on their toxicological profile and a data gap was identified on this issue.

The relevance of potential groundwater metabolites is based on the classification of the parent compound as harmful for the development (R63 "possible risk of harm to the unborn child") as proposed during the peer review.

The acceptable daily intake (ADI) of spiroxamine is 0.025 mg/kg bw/day, applying an assessment factor of 100 to the NOAEL from the 1-year dog study. The acceptable operator exposure level (AOEL) is 0.015 mg/kg bw/day derived from the same study and applying an additional correction factor of 60% for limited oral absorption. The acute reference dose (ARfD) is 0.1 mg/kg bw derived from the acute neurotoxicity study in rat, with a safety factor of 100.

Operator, worker and bystander risk assessments were re-calculated by the rapporteur Member State after the expert meeting using the agreed AOEL. The estimated operator exposure to the formulation "Prosper EC 500" (for grapes) is below the AOEL according to the German model if personal protective equipment (PPE) is worn when handling the product (gloves during mixing and loading, and gloves, standard protective garment, sturdy footwear, hood and visor during application). The estimated exposure to spiroxamine from the formulations "Helix" and "Input" EC 460" (for cereals) is below the AOEL according to the German model if PPE are used (gloves during mixing and loading, gloves, standard protective garment and sturdy footwear during application).

The exposure to bystanders and residents is below the AOEL

Worker exposure to spiroxamine after applications of "Helix" or"Input" EC 460" (in cereals) is below the AOEL without considering the use of PPE. Worker exposure to "Prosper EC 500" (in grapes) exceeds the AOEL (124.7% of the AOEL) when considering the use of PPE after three applications and considering a 50% decrease in residues between each application (7 days interval). A data gap was identified for the diastereomer ratio found in plant residues to which workers are exposed. If a conservative worst case approach is considered, that the toxicity is increased four times due to the change in the diastereomer ratio to which workers are exposed, then the use of PPE should be recommended to workers entering the crops treated with spiroxamine.

3. Residues

Spiroxamine was discussed in the PRAPeR TC 29 expert teleconference in March 2010.

Metabolism in plant was investigated in two plant groups, on cereals (wheat) and on fruit crops (grape and banana) using foliar applications of ^{14}C-spiroxamine, either labelled on the cyclohexyl or the dioxalane moiety.

In the two plant groups, spiroxamine was seen to be the major component of the residues accounting in mature crops for 3-25% TRR in wheat grain and wheat straw and 25-60% TRR in grape and banana. Therefore, the parent was considered as an adequate maker for the residues in plants and the residue for monitoring was defined as spiroxamine. Significant differences were however observed in the metabolism of spiroxamine in the two plant groups. In cereals, the metabolism proceeds mainly by oxidation and desalkylation at the amine group and by hydroxylation at the *tert*-butyl group, leading to metabolites retaining the global structure of the parent (group A metabolites), the N-oxide metabolite (M03) being the main one. In fruits, the cleavage of the parent molecule at the dioxalane moiety results in the two following classes of metabolites; the group B metabolites containing the *tert*-butyl cyclohexanol moiety (metabolites M13, M14 and their sugar conjugates) and the group C metabolites containing the aminodiol structure (metabolite M28) and its derivatives (M29, M30). At harvest in fruit, group B and group C metabolites were globally observed in similar proportions to the parent. Analytical methods were developed by the notifier where residues are quantified after hydrolysis as *tert*-butylcyclohexanol (M15) or as aminodiol (M28). Re-analyses of the radiolabelled samples have shown these methods able to consider 73% of the TRR in straw when quantified as *tert*-butyl cyclohexanone and 79% of the TRR in grape when quantified as aminodiol. Based on this information, the two following residue definitions were proposed for the risk assessment:

- **Cereals** Sum spiroxamine and metabolites containing the *tert*-butylcyclohexanone moiety, expressed as spiroxamine,
- **Fruit crops:** Sum spiroxamine and metabolites containing the N-ethyl-N-propyl-1,2-dihydroxy-3-amino-propane moiety, expressed as spiroxamine.

However, the residue definition for risk assessment in fruit crops has to be considered provisional since the PRAPeR 73 meeting on toxicology was unable to conclude on the toxicity of the group B and C metabolites (see section 2). The metabolic profile observed in the rotational crops studies was similar to that observed in cereals. The main routes involve the desalkylation of the parent compound yielding the metabolites M01 and M02, and the oxidation of the *tert*-butyl group leading to hydroxy and carboxylic acid derivatives, especially present as hexose conjugates. Consequently, the residue definition proposed for cereals and relying on the *tert*-butylcyclohexanone moiety is also appropriate to cover the residues in rotational crops.

A sufficient number of supervised residue trials were submitted to derive MRLs for cereals and grapes. Most of the samples were analysed in parallel for spiroxamine and for the total residues, as aminodiol (grape) or as *tert*-butylcyclohexanone (barley). These results were used to derive conversion factors for the risk assessment. To demonstrate the stability of the residues under frozen conditions, barley samples were spiked with spiroxamine and the N-oxide metabolite (M03), and grape and banana samples were spiked with spiroxamine and aminodiol (M28). Recoveries were shown to be acceptable up to *c.a.* 18 months. However, analyses were performed using common moiety methods and a possible degradation to the metabolites covered by these analytical methods cannot be excluded. Therefore, a new stability study where samples are specifically analysed for spiroxamine was identified as a data gap. No standard hydrolysis study simulating pasteurisation, baking and sterilisation was provided and the nature of the residues in processed commodities was not sufficiently investigated to propose a residue definition. Since there are clear indications from the processing studies on grape that the parent is almost totally degraded to metabolites covered by the aminodiol analytical method, standard hydrolysis studies are required to address the nature of the residues in processed commodities.

Animal metabolism studies on goat and poultry were performed with the ^{14}C-cyclohexyl label only. However, since only one metabolite resulting from the cleavage of the parent structure was found in very low proportions (0.4% TRR), a new study with an additional labelling was considered not necessary. The metabolism was more extensive in goat, where the parent was almost totally absent, the main metabolite being the carboxylic acid metabolite (M06, 10-53% TRR), its glucoronide conjugate (M19, 8-33%TRR) and the hydroxy carboxylic acid metabolite (M07). In poultry, parent spiroxamine remains present in significant proportions in all matrices (up to 77% TRR in fat). The metabolism proceeds via desalkylation of the amino group, yielding the metabolites M01 and M02 (up to 21%

TRR in liver) and by oxidation to the carboxylic acid metabolite (M06), accounting for 37% TRR in muscle and eggs. Based on these studies, the residue definition for monitoring was limited to the carboxylic acid metabolite (M06) only and two different definitions were proposed for risk assessment:

- **Ruminants and pigs**: Sum spiroxamine carboxylic acid (M06), its glucoronide conjugate (M19) and hydroxy acid spiroxamine (M07), expressed as spiroxamine
- **Poultry**: Sum spiroxamine, desethyl-spiroxamine (M01), despropyl-spiroxamine (M02) and -carboxylic acid (M06) expressed as spiroxamine

Conversion factors for the risk assessment were derived for the different animal matrices, based on the respective proportions at which the compounds were detected in the metabolism studies. MRLs were derived for ruminant products from the feeding study, where samples were analysed for the M06 metabolite. Conversely, the samples from the poultry feeding study were analysed using a *tert*-butyl-cyclohexanone moiety method considering spiroxamine, metabolites M01 and M02 but not the metabolite M06. This study was therefore considered as not appropriate to derive MRLs for poultry products. However, with regard to the poultry intake calculated for the representative uses and the overall residue levels observed in the feeding and metabolism studies, it was concluded that residues are not expected to be present in significant levels in poultry matrices and no MRLs were proposed. If additional uses lead to an increase in the intake by poultry, the submission of a new feeding study where samples are analysed according to the residue definition for monitoring should be reconsidered.

Since no toxicological endpoints were defined for the group B and C metabolites and considering they represent a significant part of the residues in fruit crops, it was not possible to conduct a consumer risk assessment for grape. Therefore, the risk assessment was limited to the cereals only. No chronic or acute concerns were identified, the TMDI and IESTI calculated using the EFSA PRIMo model, being only 10% of the ADI (DK child) and 5% of the ARfD (bovine edible offal). The impact of a possible change in the diastereomer ratios was not taken into account, but of no concern on the overall consumer risk assessment, as the highest intake was calculated to be less than 10% of the ADI.

4. Environmental fate and behaviour

Spiroxamine was discussed in the PRAPeR 74 meeting in March 2010. The regulatory dossier provides no information on the behaviour of each individual spiroxamine enantiomer in the aquatic environment. It is not known if one isomer is degraded more quickly than the other or if any other conversion may occur in the water/sediment systems investigated. Consequently a data gap was identified.

Under laboratory conditions none of the metabolites account for more than 10% of the applied radioactivity (AR) at any time during the soil metabolism studies. The metabolites M01 (KWG 4168-desethyl), M02 (KWG 4168 – despropyl) and M03 (KWG 4168—N-oxide) account for more than 5% AR in at least two sequential measurements during the studies and therefore need to be further assessed for potential groundwater contamination (European Commission, 2003). The ultimate degradation product was carbon dioxide which accounted for 22 - 45% of the applied radioactivity after 100 days. Reliable degradation data were available from only 1 soil because of the lack of information of the goodness of fit of the kinetic analysis for the other 5 additional soils. As a consequence, the risk assessment was based on the results of eighteen field dissipation trials conducted in Northern and Southern Europe. The studies have been re-evaluated to determine the first order non-normalised degradation rates of spiroxamine to be used in the calculations for the predicted environmental concentrations in soil (PEC_{soil} modelling). At the PRAPeR 74 meeting new PEC_{soil} values including accumulation and plateau concentration calculations were required based on the trial site where the pattern of decline would result in the highest calculated accumulation. The RMS provided the new PEC_{soil} assessment in the Addendum dated 6 April 2010 (Germany 2010). However, the EFSA considered the approach used by the RMS not in line with the recommendations provided during the meeting and therefore the new values could not be considered valid. In response to EFSA seeking clarifications, the RMS provided in a position paper (available in the final addendum,

Germany 2010) additional PEC_{soil} calculations for all the field trials available. The EFSA confirms that these new values are acceptable and can be used for the risk assessment for terrestrial organisms. The dissipation of spiroxamine in soils under field conditions showed that the active substance formed two major metabolites KWG 4168-desethyl (M01) and KWG 4168-despropyl (M02), which exhibit moderate persistence. Degradation experiments in soil under the influence of light showed that photolysis contributed to the overall degradation of spiroxamine in soil. A total of eight degradation products were observed in the soil extracts but each of them accounted for less than 10% of the applied radioactivity. Spiroxamine and its metabolites M01 (KWG 4168-desethyl) and M02 (KWG 4168-despropyl) are immobile to low mobile in soil. The metabolite M03 (KWG 4168-N-oxide) exhibits low to medium soil mobility. There was no evidence of pH dependence of adsorption for any of these compounds.

In aerobic natural sediment water systems (laboratory incubations) spiroxamine dissipated relatively rapidly from the water phase via partitioning to the sediment. Two major metabolites were detected in the water phase of the systems: M03 (KWG 4168-N-oxide) representing max 11.3% AR, and M06 (KWG 4168-acid) at max 25.6% AR. The final degradation product CO_2 was observed at rates between 7 and 27% AR. A new kinetic evaluation (Level PI) of data from the two water sediment systems "Hönninger Weiher" and "Stilwell" to derive modelling endpoints was performed by the RMS after the meeting of experts PRAPeR 74 (Addendum 6 April 2010). Although the EFSA considers the new assessment not fully acceptable (refer to new open point 4.51 of the Evaluation Table) no new surface water assessment is required. The RMS performed new PEC_{sw} and PEC_{sed} calculations on the basis of the re-calculated geometric mean fieldDT_{50} in soil of 45.0 days and according to the GAP proposed for the uses in cereals (winter and spring) and for use in vine (vine late only). The FOCUS SW procedure (FOCUS, 2001; FOCUS, 2007) was followed up to step 4. Twenty meters non-spray buffer zones to reduce spray drift inputs were simulated. PEC_{SW} values for the metabolites M01, M02 and M06 were calculated up to step 2 of the FOCUS scheme. In a worst case approach the metabolite M03 was considered in the aquatic risk assessment to the same amount as the parent spiroxamine according to 100% formation (Step 2 max PEC_{sw}= 13.48 µg/L).

The groundwater contamination assessment agreed follows the PPR panel opinions (EFSA 2004; EFSA, 2007), and addresses the potential groundwater contamination by spiroxamine plus metabolites M01 and M02, using FOCUS PELMO (3.2.2) and FOCUS PEARL (3.3.3) (FOCUS, 2000). The results of the simulation indicate that 80th percentile annual average concentrations of spiroxamine and the metabolites M01 and M02 would be well below the parametric drinking water limit of 0.1 µg/L over the 20 years simulation period. For metabolite M03 a data gap was identifies at the PRAPeR 74 meeting for a groundwater exposure assessment with a better justified soil DT_{50} than that currently provided (refer to expert consultation 4.2 of the Report of PRAPeR 74).

The PEC in soil, surface water, sediment and groundwater, as agreed by the peer review for the representative uses assessed, can be found in Appendix A of this conclusion.

5. Ecotoxicology

Spiroxamine has been discussed in the PRAPeR 75 expert meeting in March 2010.

The acute and short-term risk to birds was assessed as low for direct dietary exposure for the representative uses evaluated. Higher tier refinements were required to address the long-term risk to birds for the representative uses. For both uses the refined risk assessment was based on the increase of the chronic endpoint (NOEC) from 2.02 mg a.s./kg_{bw}/day to 5.40 mg a.s./kg_{bw}/day and on the multiple adverse effects in the highest dose tested. The risk assessment for birds for the use in grapes was refined based on the use of three field studies to determine the residues (RUD) in insects and to calculate the f_{twa}. In addition, the notifier submitted different field studies to determine the focal bird species and the diets of birds in vineyards (one study in Italy and three studies in France). The risk assessment for birds for the use in cereals was refined, based on the use of four field studies to

determine the residue (RUD) in insects and to calculate the f_{twa}. The notifier submitted an additional five field studies to determine the focal bird species and its diet in cereal crops in Germany, Poland, Italy three in France and one in Spain. The refinement procedure proposed by the notifier was considered valid for the representative uses. This was included in Annex B.9.1. of the Re-Assessment Report for the Annex –I renewal (Germany 2010). After refinement the TER_{lt} values were above the Annex VI trigger values for the representative uses. The risk for earthworm-eating birds initially was assessed as high for the use in grapes. A refined risk assessment was presented in the AR and considered acceptable. The risk for fish-eating birds was assessed as low. The risk from the uptake via drinking water was assessed as low.

For small herbivorous mammals the acute and long-term TER values in first tier risk assessment for the use in grapes and the acute and long-term TER values for cereals did not meet the Annex VI trigger values. The notifier submitted higher tier studies in order to address the high acute and reproductive risk for mammals. One field study to determine the focal mammal species and its diet in vineyards and one study in cereals were presented in the Re-Assessment Report. The proposed refinement of the acute risk assessment included the refinement of the RUD, and the multiple application factor (MAF) and the wood mouse as focal species. The refinement of the chronic risk assessment was based on an increase of the relevant chronic endpoint (NOEL) from 9.19 mg as/kg bw/d to 22.2mg as/kg bw/d , refinement of RUD, MAF and proportion of diet obtained from the treated area (PT). The refinement for both the acute and chronic risk were considered valid (Annex B.9.3. of the Re-Assessment Report for the Annex –I renewal). The acute and long-term TER values estimated after the refinement were above the Annex VI trigger values, indicating that the acute and chronic risk to mammals was assessed as low. The risk to mammals from the uptake via drinking water and from the secondary poisoning was assessed as low for the representative uses in mammals.

Spiroxamine is very toxic to the aquatic organisms. Acute and long-term effects on algae were driving the aquatic risk assessment. No full FOCUS step 3 scenarios resulted in TERs above the Annex VI trigger values for aquatic organisms. The TER values estimated with risk mitigation measures such as a non-spray-buffer zone of 20 m (FOCUS step 4), were below the Annex VI trigger value for all the scenarios, except the R1, indicating a high risk for the aquatic organisms for the use in grapes. Furthermore, the TER values estimated with a 20 m non-spray buffer zone were below the trigger value, (except in D5, for spring application and D4 and R1 for winter application), indicating a high risk for the use in cereals. A mesocosm study was available with Spiroxamine EC 500, to address the risk to invertebrates and aquatic plants. A NOAEAC for the mesocosm was set up to 9.3 µg a.s./L. In order to cover for the remaining level of uncertainty mainly caused by a heterogeneous growth pattern in filamentous algae in the ponds, the assessment factor should be 5. However, this proposal is valid only for spring application with a maximum of 3 applications per year and an interval of > 7 days. A TER trigger of 5 was met based on worst case exposure and risk mitigation measures (e.g. non-spray buffer zone of 5 m) for only an early use in grapes. As conclusion for the use of the Spiroxamine in grapes and cereals a high risk was identified with risk mitigations up to 20 m non-spray buffer zone. The risk for spiroxamine metabolites M01, M03 and M06 was assessed as low. The risk for the metabolite M02 needs to be further addressed and a data gap was identified. The exposure patterns and consequent risk assessment to aquatic organisms needs to be characterised further, in relation to the impact that the potentially varying enantiomer ratios of spiroxamine may have on the risks assessed and the extent of risk mitigation required. A data gap was identified.

The oral and contact Hazard Quotients (HQ) were well below the Annex VI trigger values, indicating a low risk for bees, based on the data available in the assessment report.

The in-field HQ estimated for the two standard species *Typhlodromus pyri* and *Aphidius rhopalosiphi* were above the Annex VI trigger value, indicating a high risk for the use in grapes. However, the off-field HQ for both standard species was below the trigger value, indicating a low risk for the off-field area. Further extended laboratory studies with the formulation with A. *rhopalosiphi* on additional ground/leaf-dwelling arthropods like *Bembidion tetracolum*, *Pardosa* spp, *Chrisoperla carnea*, and *Cocinella septempunctata* were presented in the AR. Five field studies were submitted with the *T.*

pyri. The PRAPeR 75 expert meeting agreed to use a weight-of-evidence approach (based on Escort 2) to refine the in-field risk: HQ in-field not far above the trigger. Additional species show low effects, so the standard species are confirmed to be sensitive. Field studies indicate only limited effects. Dissipation is fast so recolonisation may occur. Therefore, the risk within in-field areas is acceptable for the use in grapes. For the use in cereals a few extended laboratories studies were submitted with A. *rophalosiphi, T. pyri, C. septempuncatata* and with *Aleochara bilneata.* The results indicated that the effects were lower than the trigger of 50% indicated in the ESCORT II. Therefore, the risk for the in-field and off-field areas for the use in cereals was assessed as low.

New PECs were estimated by EFSA and therefore new TERs values were calculated. The TERs values were estimated to be above the Annex VI trigger value. The risk for earthworms and other non-target soil-macro-organisms, was assessed as low. The risk to soil micro-organisms and biological methods for sewage treatment was assessed as low.

The impact of a possible change in the diastereomer ratios was not taken into account, a concern on the overall environmental risk assessment was observed, as the toxicity endpoint could be decreased by a factor of 4, and the outcome of the risk assessment would change for non target species.

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
spiroxamine	moderate to medium persistent field$DT_{50\ norm\ 20\ °C,\ pF\ 2}$ = 24.2-88.0 d ($DT_{50\ lab}$ = 22 d at 20°C and 55% MWHC) (based on aerobic degradation study with 1 soil; data available for other 5 soils but not fully peer reviewed because of the lack of further information on the goodness of fit of kinetic analysis)	The risk from Spiroxamine for earthworms was assessed as low.
KWG 4168-desethyl (M01) (major metabolite in the field dissipation studies)	moderate persistent field$DT_{50\ norm\ 20\ °C,\ pF\ 2}$ = 17.0-54.7 d	The risk of M01 for earthworms was assessed as low.
KWG 4168-despropyl (M02) (major metabolite in the field dissipation studies)	moderate persistent field$DT_{50\ norm\ 20\ °C,\ pF\ 2}$ = 17.0-52.5 d	The risk of M02 for earthworms was assessed as low.

6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
spiroxamine	low to immobile (K_{Foc} = 659 – 6417 mL/g)	FOCUS PEARL 3.3.3 and FOCUS PELMO 3.2.2: no	No	Yes	Very toxic for the aquatic organisms and the risk for aquatic organisms was assessed high.

KWG 4168-desethyl (M01)	low to immobile (K_{Foc} = 1237 – 10510 mL/g)	FOCUS PEARL 3.3.3 and FOCUS PELMO 3.2.2: no	No	Reference values of the parent apply to this metabolite Relevance rely on the proposed classification of the parent as R63	Very toxic for the aquatic organisms and the risk for aquatic organisms was assessed as low.
KWG 4168-despropyl (M02)	low to immobile (K_{Foc} = 916 – 8993 mL/g)	FOCUS PEARL 3.3.3 and FOCUS PELMO 3.2.2: no	No	Reference values of the parent apply to this metabolite Relevance rely on the proposed classification of the parent as R63	No data available, data gap proposed.
KWG 4168-N-oxide (M03)	medium to low (K_{Foc} = 350 – 1640 mL/g)	no data, data required	No	Rat oral LD_{50} ~707 mg/kg bw (Xn; R22) No genotoxic potential *in vitro* Reference values of the parent apply to this metabolite Relevance rely on the proposed classification of the parent as R63	Very toxic for the aquatic organisms and the risk for aquatic organisms was assessed as low.

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
spiroxamine	Very toxic for the aquatic organisms and unacceptable risk for aquatic organisms.
KWG 4168-desethyl (M01) (from soil, via runoff and drainage)	Very toxic for the aquatic organisms and the risk for aquatic organisms was assessed as low.
KWG 4168-despropyl (M02) (from soil, via runoff and drainage)	**No data available.**
4168-N-oxide (M03)	Very toxic for the aquatic organisms and the risk for aquatic organisms was assessed as low.
KWG 4168-acid (M06)	Very toxic for the aquatic organisms and the risk for aquatic organisms was assessed as low.

6.4. Air

Compound (name and/or code)	Toxicology
spiroxamine	Rat LC_{50} inhalation = 2 mg/L air (4-h exposure, nose-only); Xn, R20 “Harmful by inhalation”

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

- Quality control data to support the specification (relevant for all representative uses evaluated, submission date proposed by the notifier: unknown; see section 1)
- Level of ethoxylation of formulants (relevant for all representative uses ; submission date proposed by the notifier: unknown; see section 1)
- The amended study report for two impurities (relevant for all representative uses evaluated ; submission date proposed by the notifier: unknown; see section 1)
- ILV data for products of animal origin (relevant for all representative uses ; submission date proposed by the notifier: unknown; see section 1)
- Toxicological information on plant metabolites of group B (tert-butyl-cyclohexanol group) and group C (aminodiol group) is missing. (relevant for use in grapes; submission date proposed by the notifier: unknown; see section 2 and 3)
- Spiroxamine consists of diasteromer isomers. The preferential metabolism/degradation of each isomer in plants and animals and their possible impact on the toxicity, on the worker and consumer risk assessment need to be addressed (relevant for the representative uses evaluated; no submission date proposed; refer to point 2 and 3).
- A storage stability study where samples are analysed for the parent compound spiroxamine is required (relevant for the representative uses evaluated; submission date proposed by the notifier: unknown, see section 3).
- A standard hydrolysis study simulating pasteurisation, baking and sterilisation is required (relevant for all the representative uses evaluated; submission date proposed by the notifier: unknown, see sections 3).
- The exposure patterns and consequent risk assessment to aquatic organisms needs to be characterised further, in relation to the impact that the potentially varying enantiomer ratios of spiroxamine may have on the risks assessed and the extent of risk mitigation required (relevant for all the representative uses evaluated; submission date proposed by the notifier: unknown, see sections 4 and 5)
- The groundwater exposure assessment for metabolite KWG 4168-N-oxide (M03) with a better justified soil DT_{50} than that currently provided (relevant for all the representative uses evaluated; submission date proposed by the notifier: unknown, see section 4)
- Information on the assumed equilibrium between metabolite M03 and spiroxamine (this data gap can be considered superseded if a groundwater assessment for M03 with a better justified soil DT_{50} than that currently provided will be available; relevant for all the representative uses evaluated; submission date proposed by the notifier: unknown, see section 4)
- The risk of the M02 metabolite for the aquatic organism needs to be addressed(relevant for all representative uses evaluated; submission date proposed by the notifier: unknown ; see section 5)

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

- Operator exposure is below the AOEL if personal protective equipment is worn (gloves during mixing and loading, and gloves, standard protective garment, sturdy footwear, hood and visor during application for cereals; and for grapes, gloves during mixing and loading, and gloves, standard protective garment and sturdy footwear during application) (see section 2).

ISSUES THAT COULD NOT BE FINALISED

- The preferential metabolism/degradation of each enantiomer in plants, animals and the environment, and the possible impact on the toxicity, the worker and consumer risk assessment, and on the environment were not investigated in the studies submitted in the dossier. This needs to be addressed.

- The consumer risk assessment for grapes could not be concluded since no toxicological endpoints were defined for the group B and group C metabolites and which represent a significant part of the residues in fruit crops and probably in processed commodities.

- The groundwater exposure assessment for metabolite KWG 4168-N-oxide (M03) has not been addressed.

CRITICAL AREAS OF CONCERN

- High risk was identified even with the use of risk mitigation measure of a non-spray buffer zone of 20 m (except in D5, for Spring cereals application and D4 and R1 for winter cereals application, and R1 for the grapes use) for aquatic organisms.

- The impact of a possible change in the diastereomer ratios was not taken into account, a concern on the overall environmental risk assessment was observed, as the toxicity endpoint could be decreased by a factor of 4, and the outcome of the risk assessment would change for non target species.

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

APPENDICES

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

Appendix III: Listing of end points

Appendix III.1: Chapter 1 (identity, physical and chemical properties, details of uses, further information, classification and labelling)

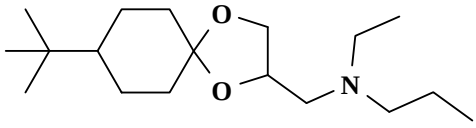
Active substance (ISO Common Name) ‡	Spiroxamine
Function (*e.g.* fungicide)	fungicide

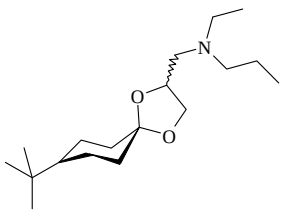
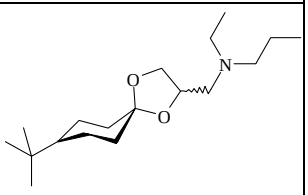
Rapporteur Member State	Federal Republic of Germany
Co-rapporteur Member State	Hungary

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	8-*tert*-butyl-1,4-dioxaspiro[4.5]decan-2-ylmethyl(ethyl)(propyl)amine (ISO) *N*-{[8-(1,1-dimethylethyl)-1,4-dioxaspiro[4.5]dec-2-yl]methyl}-*N*-ethylpropan-1-amine (ACD software)
Chemical name (CA) ‡	1,4-Dioxaspiro[4.5]decane-2-methanamine, 8-(1,1-dimethylethyl)-N-ethyl-N-propyl-
CIPAC No ‡	572
CAS No ‡	118134-30-8 (unstated stereochemistry)
EC No (EINECS or ELINCS) ‡	none
FAO Specification (including year of publication) ‡	none
Minimum purity of the active substance as manufactured ‡	950 g/kg Open for the ratio range for diasteromers.
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	none
Molecular formula ‡	$C_{18}H_{35}NO_2$
Molecular mass ‡	297.5 g/mol

Structural formula ‡



	
diastereomer "cis" KWG 4168 A equatorial/axial (ea) configuration	diastereomer "trans" KWG 4168 B equatorial/equatorial (ee) configuration

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	< - 170 °C °C (> 98. 6 %)
Boiling point (state purity) ‡	Not applicable
Temperature of decomposition (state purity)	Starts at 120 °C (99 %)
Appearance (state purity) ‡	Faintly yellowish liquid (98.7 %) Light brown oily liquid (technical material)
Vapour pressure (state temperature, state purity) ‡	Diastereomer A 4.0×10^{-3} Pa at 20 °C (98.6 %) Diastereomer B 6×10^{-3} Pa at 20 °C (99.3 %)
Henry's law constant ‡	Diastereomer A 2.5×10^{-3} Pa m^3 mol^{-1} Diastereomer B 5.0×10^{-3} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	pH 3: >200 g/L at 20 °C (pH) (99 %) Diastereomer A pH 5: 470 mg/L at 20 °C (pH) (99 %) pH 9: 14 mg/L at 20 °C (pH) (99 %) Diastereomer B pH 5: 340 mg/L at 20 °C (pH) (99 %) pH 9: 10 mg/L at 20 °C (pH) (99 %)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20 °C in g/L (99 %) *n*-hexane > 200 g/L at 20 °C toluene > 200 g/L at 20 °C dichloromethane > 200 g/L at 20 °C 2-propanol > 200 g/L at 20 °C 1-octanol > 200 g/L at 20 °C PEG > 200 g/L at 20 °C PEG + ethanol > 200 g/L at 20 °C acetone > 200 g/L at 20 °C dimethylformamide > 200 g/L at 20 °C ethylacetate > 200 g/L at 20 °C acetonitril > 200 g/L at 20 °C
Surface tension ‡ (state concentration and temperature, state purity)	Concentration [mg/L] / surface tension [mN/m] 2 / 57 20 / 53 200 / 47 at 20 °C (pH 7)
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ at 20 °C diastereomer A pH 5 1.28 pH 7 2.79 pH 9 4.88 diastereomer B pH 5 1.41 pH 7 2.98 pH 9 5.08

Dissociation constant (state purity) ‡	pK_a = 6.9 (99 %) in water pK_a = 7.9 (99 %) in water /40 % 2-propanol
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	The UV-Spectrum shows no maximum of absorbance in the range of 200 nm – 400 nm for both isomers. ε at 290 nm: < 10
Flammability ‡ (state purity)	147 °C (flash point) (97.2 %)
Explosive properties ‡ (state purity)	None (A 14) (97.2 %)
Oxidising properties ‡ (state purity)	None (A 21) (97.0 %)

1) Summary of representative uses evaluated (*name of active substance or the respective variant*) Spiroxamine 500 g/L*

Crop and/ or situation (a)	Member State or Country	Product Name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	Growth stage & season (j)	number min/max (k)	interval between applications (min)	g as/hL min-max (l)	water L/ha min-max	g as/ha min-max (l)		
Grape	France	HOGGAR PROSPER	F	Powdery mildew (*Uncinula necator)*	EC	500 g/L	spraying	BBCH 13 - 85	1 - 3	10 - 12	75 - 200	150 - 400	300	35	Not supported by available data (1) (2)
Grape	Italy	PROSPER 500 EC	F	Powdery mildew (*Uncinula necator)*	EC	500 g/L	spraying	BBCH 13 - 19 79 - 85	1 - 2 2 - 3	7 10 - 14	20 30 - 40	1000 1000	1 - 2 x 200 2 – 3 x 300 - 400	table 14 wine 35	Not supported by available data (1) (2)

(1): The consumer risk assessment could not be conduced for grape, pending additional information on the toxicity of the group B and group C metabolites.
(2) Worker exposure with PPE exceeds the AOEL when the three applications are taken into account and considering a 50% decrease in residues between each application (7 days interval)

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

2) Summary of representative uses evaluated (*name of active substance or the respective variant*)*Prothioconazole + Spiroxamine EC 460 (160 + 300) g/L

Crop and/ or situation (a)	Member State or Country	Product Name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI** (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/max (k)	interval between applications (min)	g as/hL min - max (l)	water L/ha min-max	g as/ha min-max (l)		
Wheat & Triticale	EU - N EU - S	Input, Helix	F	Foliar & ear diseases	EC	160 + 300 g/L	Field crop sprayer	BBCH 30 to BBCH 69	2	14 to 21 days	50-100 (Prothio.) + 93,75-187,5 (Spirox.)	200 - 400	200 + 375		** depending on national request: either PHI in days or growth stage at the latest application
Rye	EU - N EU - S	Input, Helix	F	Foliar & ear diseases	EC	160 + 300 g/L	Field crop sprayer	BBCH 30 to BBCH 61 – 69#	2	14 to 21 days	50-100 (Prothio.) + 93,75-187,5 (Spirox.)	200 - 400	200 + 375		# may vary according to national conditions
Barley & Oat	EU - N EU - S	Input, Helix	F	Foliar & ear diseases	EC	160 + 300 g/L	Field crop sprayer	BBCH 30 to BBCH 61	2	14 to 21 days	50-100 (Prothio.) + 93,75-187,5 (Spirox.)	200 - 400	200 + 375		

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

Appendix III.2: Chapter 2 (methods of analysis)

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

Technical as (analytical technique)	GC-FID
Impurities in technical as (analytical technique)	GC-FID
Plant protection product (analytical technique)	GC-FID

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		spiroxamine
Food of animal origin		spiroxamine carboxylic acid, expressed as spiroxamine
Soil		spiroxamine
Water	surface	spiroxamine
	drinking/ground	spiroxamine
Air		spiroxamine

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	spiroxamine LC-MS/MS 0.01 mg/kg (wheat flour, lemon, cucumber) confirmation by second MS/MS transition, ILV included LC-MS/MS 0.05 mg/kg (barley grain, tomato, rape seed, banana pulp, orange fruit, hops) confirmation by second MS/MS transition, no ILV LC-MS/MS 0.05 mg/kg (barley grain, tomato, banana pulp, hops) confirmation by second MS/MS transition, ILV
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	spiroxamine carboxylic acid LC-MS/MS 0.02 mg/kg (bovine: muscle, liver, kidney, fat) 0.01 mg/kg (milk) for fat only for confirmatory purposes GC-MSD 0.02 mg/kg (fat, eggs) confirmation by GC-MSD of a silylated derivative sufficiently validated ILV for all matrices are missing
Soil (analytical technique and LOQ)	spiroxamine LC-MS/MS 0.001 mg/kg GC-MSD 0.01 mg/kg
Water (analytical technique and LOQ)	spiroxamine GC-MS 0.01 µg/L (drinking water, surface water) confirmation by second gas chromatographic column of different polarity

Air (analytical technique and LOQ)	spiroxamine GC-NPD 7.7 µg/m³ (35 °C, 80 % rH)
Body fluids and tissues (analytical technique and LOQ)	not required, not classified as T/T^{+}

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

	RMS/peer review proposal
Active substance	none

Appendix III.3: Chapter 3 (impact on human and animal health)

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

Rate and extent of oral absorption ‡	Rapid, about 60 % within 48 h, based on urinary excretion
Distribution ‡	Wide, highest residues in liver, thymus, adrenals (high dose: fat)
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	> 80 % within 48 h (urine: > 60 %, faeces: > 20 %)
Metabolism in animals ‡	Extensively metabolised (oxidation, sulphate conjugation, dealkylation)
Toxicologically relevant compounds ‡ (animals and plants)	Spiroxamine
Toxicologically relevant compounds ‡ (environment)	Spiroxamine and metabolites

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	~ 500 mg/kg bw	R22
Rat LD_{50} dermal ‡	1068 mg/kg bw	R21
Rat LC_{50} inhalation ‡	2 mg/L air; slight pulmonary irritation (4-h exposure, nose-only)	R20
Skin irritation ‡	Severe irritant	R38
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Sensitiser (M&K; Buehler)	R43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Oral: Liver (histological findings, wt ↑, clinical chemistry), clinical signs, effects on mucosal epithelium of oesophagus and fore-stomach; additionally in dogs: eye (cataracts) Dermal: skin irritation By inhalation: irritation of the respiratory tract	
Relevant oral NOAEL ‡	28-day, rat: 3.4 mg/kg bw/day 90-day, rat: 1.9 mg/kg bw/day 90-day, dog: 15.1 mg/kg bw/day 1-year, dog: 2.5 mg/kg bw/day 90-day, mouse: 25 mg/kg bw/day	
Relevant dermal NOAEL ‡	21-day, rabbit: local effects: 0.2 mg/kg bw/day systemic effects: 5 mg/kg bw/day highest dose tested)	
Relevant inhalation NOAEL ‡	28-day, rat: 14.3 mg/m³ air (6-h exposure, nose only, 3.9 mg/kg bw/day)	

Genotoxicity ‡ (Annex IIA, point 5.4)

	No genotoxic potential	

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

Target/critical effect ‡	Both species: acanthosis & hyperkeratosis of oesophagus mucosa; bw ↓; Additionally in rats: hyperplasia of urinary bladder; mortality ↑; uterus (masses, distension) Additionally in mice: ovaries (cyst); acanthosis & hyperkeratosis of tail; acanthosis of auricles; liver (histological changes)	
Relevant NOAEL ‡	2-year, rat: 4.2 mg/kg bw/day 18-month, mouse: 4.5 mg/kg bw/day	
Carcinogenicity ‡	No evidence for carcinogenicity	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Adult: bw and feed intake ↓; APTT ↑ Reproduction and fertility: no evidence for impairment of fertility and reproduction Offspring: bw gain ↓, delayed development	
Relevant parental NOAEL ‡	5.5 mg/kg bw/day	
Relevant reproductive NOAEL ‡	21 mg/kg bw/day	
Relevant offspring NOAEL ‡	5.5 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Maternal: Rat: bw gain and feed intake ↓ Rat, dermal: bw gain ↓ Rabbit: bw gain and feed intake ↓, clinical signs, mortality Developmental: Rat: delayed ossification, wt ↓, cleft palate Rat, dermal: wavy ribs Rabbit: wt ↓, spontaneous skeletal malformations slightly ↑ (hydrocephalus internus + caudal displacement of ears, chicken breast)	R63
Relevant maternal NOAEL ‡	Rat: 30 mg/kg bw/day Rat, dermal: 20 mg/kg bw/day / <5 mg/kg bw/day (systemic / local effects) Rabbit: 20 mg/kg bw/day	

Relevant developmental NOAEL ‡	Rat: 30 mg/kg bw/day Rat, dermal: 20 mg/kg bw/day Rabbit: 20 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Signs of acute toxicity related to general toxicity of spiroxamine NOAEL: 10 mg/kg bw/day	
Repeated neurotoxicity ‡	No evidence for neurotoxicity up to 50 mg/kg bw/day, systemic toxicity (bw ↓, clinical chemistry findings, histological findings in the oesophagus) NOAEL: 2.4 mg/kg bw/day	
Delayed neurotoxicity ‡	No data – not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Lung function was depressed upon inhalatory exposure in rats and mice; tolerated air concentrations were 450 mg/m³ or 16 mg/m³, respectively Spiroxamine did not inhibit aromatase or steroidogenesis *in vitro*

Studies performed on metabolites or impurities ‡	
Metabolite KWG 4168 N-oxide (M03)	Rat LD_{50} oral: ~707 mg/kg bw (f) **R22** No genotoxic potential *in vitro* 28-day, rat: bw ↓, liver (slight enzyme induction), hyperkeratosis in oesophagus and fore stomach, urinary bladder (hyperplasia); NOAEL: 12.9 mg/kg bw/day 90-day, rat: bw ↓, liver (clinical chemistry, enzyme induction), hyperkeratosis in oesophagus and fore stomach; NOAEL: 8.8 mg/kg bw/day
Impurity AE 1344320	Rat oral: 2000 < LD_{50} < 5000 mg/kg bw Skin & eye irritant **R38-41** Ames test: negative
Impurity AE 1344300	Rat oral: 500 < LD_{50} < 710 mg/kg bw (M) 212 < LD_{50} < 500 mg/kg bw (F) **R22** Rat LC_{50} inhalative (4-h exp., nose only, vapour): ~13825/16303 mg/m³ air (M/F) **R20** Skin and eye corrosive **R35-41** Skin sensitisation: non-sensitiser (M&K) Ames test: negative
Impurity AE 2077192	Rat LD_{50} oral: > 2000 mg/kg bw Ames test: negative
Impurity AE 2074422	Ames test: negative
Impurity AE 1344301	Ames test: negative
Impurity AE 2078647	Rat oral: 300 < LD_{50} < 500 mg/kg bw **R22** Ames test: negative

Medical data ‡ (Annex IIA, point 5.9)

No adverse effects in manufacturing personnel reported.

Clinical cases/case reports were submitted, correlation between spiroxamine and the observed symptoms is unclear, besides findings of skin and eye irritation from splashes with spiroxamine-containing products.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.025 mg/kg bw/day	1 year, dog	100
AOEL sys.‡	0.015 mg/kg bw/day	1 year, dog	overall 167 100 + 60*
ARfD ‡	0.1 mg/kg bw	Acute neurotoxicity, rat	100

*correction for limited oral absorption

Dermal absorption ‡ (Annex IIIA, point 7.3)

Spiroxamine (a.s.)	100 % (default) considering physico-chemical properties (molecular mass: 297.5; log P_{ow}: 1.28-5.08)
Impulse EC 500, KWG 4168 500 EC	15 % for the concentrate (applied dose appr. 5 mg/cm^2) and 35 % or 40 % for the dilutions (applied dose appr. 0.02 mg/cm^2 or 0.008 mg/cm^2, respectively) based on *in vitro* human skin (supported by human *in vivo*)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	**Spiroxamine EC 500** (application rate 0.4 kg spiroxamine/ha) German model — % of AOEL *High crop tractor mounted equipment* Without PPE — 1517.3 With PPE (gloves – M&L + applic., protective garment, sturdy footwear, hood & visor – applic.) — 73.4 *High crop hand held sprayer* Without PPE — 1800.4 With PPE (gloves – M&L + applic., protective garment, sturdy footwear, hood & visor – applic.) — 49.4 UK POEM Not calculated **Prothioconazole & spiroxamine EC 460** (application rate 0.375 kg spiroxamine/ha) *Field crop tractor mounted equipment* German model — % of AOEL Without PPE — 841.1 With PPE (gloves – M&L + applic., protective garment, and sturdy footwear – applic.) — 44.8 UK POEM — % of AOEL Without PPE — 4125.0* With PPE (gloves – M&L + applic.) — 615.0*
Workers	**Spiroxamine EC 500** — % of AOEL Without PPE — 2488.7* With PPE (gloves, long sleeved shirt & long trousers) — 124.7* **Prothioconazole & spiroxamine EC 460** Without PPE — 75% of AOEL

Bystanders	**Spiroxamine EC 500** % of AOEL Bystanders max. 22.1 % Residents max. 57.5*% (children, after three applications using a drift value of 1.02 %) **Prothioconazole & spiroxamine EC 460** % of AOEL Bystanders max. 4.8 % Residents max. 52.3*% (children, after two applications using a drift value of 0.24 %)

*values agreed during the written procedure according to the agreed AOEL and re-calculation of the residential exposure considering three/two applications scenario as applicable, as reported in the final addendum.

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

	RMS/peer review proposal
Substance classified (Spiroxamine)	Directive 67/548/EEC: Xn - Harmful R20/21/22 - Harmful by inhalation, in contact with skin and if swallowed R38 - Irritating to skin R43 - May cause sensitisation by skin contact Additional proposal by RMS: R63 - Possible risk of harm to the unborn child (Cat. 3)

Appendix III.4: Chapter 4 (residues)

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

Plant groups covered	Fruits (grapes, banana), cereals (wheat)
Rotational crops	Cereals (wheat), leafy crops (Swiss chard, turnip leaves) and root crops (turnip root)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	No standard hydrolysis study was provided (data gap) and the nature of the residues in processed commodities in not sufficiently investigated
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Spiroxamine (parent only)
Plant residue definition for risk assessment	**Cereals and rotational crops:** Sum of spiroxamine and metabolites containing the tert.-butylcyclohexanone moiety, expressed as spiroxamine **Fruits:** Sum of spiroxamine and metabolites containing the N-ethyl-N-propyl-1,2-dihydroxy-3-amino-propane moiety, expressed as spiroxamine (provisional)
Conversion factor (monitoring to risk assessment)	Cereal grain: 4.3 (1/0.23) Cereal straw: 5.9 (1/0.17) Grapes: 2.0 (1/0.50) (provisional) Banana: 1.7 (1/0.61)(provisional)

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

Animals covered	Laying hen, lactating goat
Time needed to reach a plateau concentration in milk and eggs	2 days (milk) Not applicable (eggs; no residues)
Animal residue definition for monitoring	Spiroxamine carboxylic acid (M06), expressed as spiroxamine
Animal residue definition for risk assessment	**Ruminants:** spiroxamine carboxylic acid (M06), its glucuronide conjugate (M19) and -hydroxy acid (M07),expressed as spiroxamine **Poultry:** spiroxamine (parent), -desethyl (M01) -despropyl (M02) and -carboxylic acid (M06) expressed as spiroxamine
Conversion factor (monitoring to risk assessment)	Ruminant/pig muscle: 1.4 Ruminant/pig liver: 2.8 Ruminant/pig kidney: 3.8 Ruminant/pig fat: 1.8 Milk: 1.2 Poultry liver: 7.6 Poultry muscle: 2.0 Poultry fat: 53.5

	Poultry egg: 1.9
Metabolism in rat and ruminant similar (yes/no)	Yes (but major ruminant metabolite M07 was not found in rat excreta. Toxicologists suggest, that reference values for spiroxamine are applicable to M07)
Fat soluble residue: (yes/no)	No

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

Residues in rotational crops negligible

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

When stored frozen at c.a. -18/-20°C: Spiroxamine, N-oxide (M03) and incurred residues Cereals (forage, straw, grain): ≥516-566 days Spiroxamine and aminodiol Grapes : ≥529-585 d (grapes, raisins, juice) Banana: ≥21 months But samples were analysed using common moiety methods and possible degradation of spiroxamine to metabolites covered by these methods can not be excluded (data gap). However stability of spiroxamine confirmed in banana over 21 months in one study were samples were effectively analysed as spiroxamine

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)	2.81/6.95 mg/kg DM (dairy/beef cattle)	0.12 mg/kg DM	0.14 mg/kg DM
Potential for accumulation (yes/no):	no	no	no
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	yes	no	yes
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (Max) mg/kg		
Muscle	0.05 (0.057) (20 mg/kg DM)	<0.02# (all dose levels)	
Liver	0.16 (0.177) (6 mg/kg DM)	<0.05# (all dose levels)	
Kidney	0.10 (0.106) (6 mg/kg DM)	Not analysed	
Fat	0.09 (0.154) (20 mg/kg DM)	<0.05# (all dose levels)	
Milk	0.02 (0.025) (6 mg/kg DM)		
Eggs		<0.02# (all dose levels)	

#: Poultry samples were not analysed according residue definition for monitoring as spiroxamine-carboxylic acid (M06), but using a common moiety method taking into account spiroxamine, spiroxamine-desethyl (M01), spiroxamine-despropyl (M02). This study is not appropriate du derived MRLs for poultry products.

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) according to the residue definition for monitoring (spiroxamine only).

Crop	Northern/ Southern Region	Trials results relevant to the representative uses (a)	Recommendation/ Comments	MRL estimated from trials according to representative use	HR (c)	STMR (b)
Rye, triticale, wheat (Grain)	Northern	2x <0.01, 0.02, 0.03, 10x <0.05		0.05*	0.05	0.05
	Southern	3x <0.01, 0.01, 4x <0.05		0.05*	0.05	0.03
Rye, triticale, wheat (Straw)	Northern	0.24, 0.31, 0.39, 0.40, 0.47, 0.50, 2x 0.69, 0.70, 2x 1.1, 1.2		n.a.	1.2	0.60
	Southern	0.31, 0.36, 0.45, 0.51, 0.55, 0.65, 0.71, 2.0		n.a.	2.0	0.53
Barley, oats (Grain)	Northern	<0.01, 0.01, 2x 0.02, 10x <0.05		0.05*	0.05	0.05
	Southern	3x 0.01, 0.02, 4x <0.05		0.05*	0.05	0.04
Barley, oats (Straw)	Northern	0.06, 0.09, 0.12, 0.23, 0.36, 0.41, 0.47, 0.49, 2x 0.54, 0.57, 2x 0.59, 0.61		n.a.	0.61	0.48
	Southern	0.07, 0.10, 0.32, 0.44, 0.55, 0.70, 0.73, 0.77		n.a.	0.77	0.50
Grapes (wine)	Northern	0.06, 2x 0.10, 2x 0.12, 0.13, 0.15, 2x 0.17, 2x 0.20, 0.22, 0.33	R_{max}: 0.36; R_{ber}: 0.40	0.5	0.33	0.15
	Southern	*2x* <0.05, 0.07, 0.09, 0.10, 0.14, 0.17, 0.20	R_{max}: 0.29; R_{ber}: 0.33	0.5	0.20	0.10
Grape (table)	Southern	0.09, 2x 0.13, 0.19, 0.20, 0.21, 0.24, 0.31	R_{max}: 0.41; R_{ber}: 0.47	0.5	0.31	0.20
Note: The use on banana is not considered as a representative use for the annex I inclusion under directive 91/414/EEC. Values below are informative only.						
Banana	EU and Non-EU	Whole fruits: 0.07, 0.09, 0.28, 0.33, 0.34, 2x 0.35, 0.40, 0.40, 0.44, 0.80, 0.82, 0.91, 0.97, 1.2, 2.0 (Underlined: EU trials, Martinique)	R_{max}: 1.85 R_{ber}: 1.78	2 (import tolerance)	2.0	0.40

(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
n.a. not applicable

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) according to the residue definition for risk assessment

Cereals: sum spiroxamine and metabolites containing the *tert*-butylcyclohexanone moiety, expressed as spiroxamine

Fruits: sum spiroxamine and metabolites containing the N-ethyl-N-propyl-1,2-dihydroxy-3-amino-propane moiety, expressed as spiroxamine

[Values in italics and square brackets are calculated from parent values using a conversion factor of 2.0 for grape,4.3 for cereal grain and 5.9 for cereal straw , see B.7.6]

Crop	Northern Southern Region	Trials results relevant to the representative uses (a)	Recommendation /comments	MRL	HR (mg/kg) (c)	STMR (mg/kg) (b)
Rye, triticale and wheat (grain)	Northern	*[2x <0.04]*, 9x <0.05, *[0.09], [0.13], [8x <0.22]*		n.a.	0.22	0.05
	Southern	*[3x <0.04], [0.04], [4x <0.22)]*		n.a.	0.22	0.13
Rye, triticale and wheat (straw)	Northern	*1.3, 1.4, [1.4], [1.8], [2.3], [2.4], 2.4, 2.7, [2.8], [2.9], [3x 4.1], 2x 5.4, [2x 6.5], [7.1], 7.6*		n.a.	7.6	2.9
	Southern	*[1.8], [2.1], [2.7], [3.0], [3.2], [3.8], [4.2], [11.8]*		n.a.	11.8	3.1
Barley, oats (grain)	Northern	*[<0.04], [0.04],2x <0.05, 2x 0.05, 0.07, [2x 0.09], 0.10, 0.11, [8x <0.22)]*		n.a.	0.22	0.10
	Southern	*[3x 0.04], [0.09], [4x <0.22]*		n.a.	0.22	0.15
Barley, oats (Straw)	Northern	*[0.35], [0.53], 0.66, [0.71], 1.2, 1.3, [1.4], [2.1], [2.4], [2.8], [2.9], [3.2(2)], [3.4], [2x 3.5)], [3.6], 3.8, 5.2*		n.a.	3.6	2.8
	Southern	*[0.41], [0.59], [1.9], [2.6], [3.2], [4.1], [4.3], [4.5]*		n.a.	2.9	4.5
Grapes (wine)	Northern	*0.16, 0.22, 0.29, 0.34, 0.38, 2x 0.40, 0.41, 0.42, 0.46, 0.48, 0.52, 0.56, 0.63*		n.a.	0.63	0.41
	Southern	*0.07, 0.08, 2x 0.09, 0.13, 3x 0.26, 0.27, 2x 0.28, 0.29, 0.31, 0.32, 0.43, 0.55*		n.a.	0.55	0.27
Grapes (table)	Southern	0.05, 0.15, 0.16(3), 0.18, 2x 0.19, 0.27, 2x 0.30, 2x 0.31, 0.32, 0.33, 0.46, 0.47, 0.55, 0.57, 0.67, 0.69, 0.73, 1.1		n.a.	1.1	0.31
Note: The use on banana is not considered as a representative use for the annex I inclusion under directive 91/414/EEC. Values below are informative only.						
Banana	Non-EU	Pulp: 2x 0.06, 2x 0.08, 0.11, 0.12	(import tolerance)		0.12	0.08

(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

n.a. not applicable

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

Only cereals and ruminant products are taken into account in the consumer risk assessment. Fruit crops are not considered, pending conclusion on the toxicity of group B and group C metabolites.

ADI	0.025 mg/kg
TMDI (% ADI) according to EFSA PRIMo model	Max. 10% ADI (DK child) (using MRLs and proposed conversion factors)
TMDI (% ADI) according to national (to be specified) diets	-
IEDI (% ADI) according to EFSA PRIMO model)	Max. 6% ADI (DK child);
NEDI (specify diet) (% ADI)	-
Factors included in IEDI and NEDI	STMRs for cereal grains based on the total residue.
ARfD	0.1 mg/kg
IESTI (% ARfD) according to EFSA PRIMO Model rev.	5% bovine liver, 3~~.2~~ % wheat flour (fruit crops not considered)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	-
Factors included in IESTI and NESTI	MRLs and proposed conversion factors

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[a]	Yield factor	
Wheat grain – not relevant due to low residues	-	-	-	-
Barley grain – not relevant due to low residues	2			
Pearl barley, brewer´s malt, malt culms, brewer´s grain, brewer´s yeast, beer		<1	-	-
Grapes (total residues)				
Must	8	0.49	-	-
Wine after bottling	9	0.61	-	-
Young wine	3	0.49	-	-
Juice	1	0.71	-	-
Raisins	1	4.0	-	-

[a]: Transfer factor calculated as total residue in processed commodity / total residue in RAC (total residue according to residue definition for risk assessment). Transfer factors for grape have to be considered provisional pending conclusion on the toxicity of group B and group C metabolites.

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

Wheat, rye, triticale	0.05*mg//kg
Barley, oats	0.05*mg/kg
Grapes (table)	0.5 mg/kg (provisional) [a]
Grapes (wine)	0.5 mg/kg (provisional) [a]
Ruminant muscle Ruminant liver Ruminant kidney Ruminant fat Milk	0.05 mg/kg 0.2 mg/kg 0.2 mg/kg 0.05 mg/kg 0.02* mg/kg

[a]: consumer risk assessment cannot be performed for uses on grapes and banana due to insufficient characterisation of the toxicological properties of the group B and group C metabolites.
When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

Appendix III.5: Chapter 5 (fate and behaviour in the environment)

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

Mineralisation after 100 days ‡	22-45 % AR after 100 d, [^{14}C-cycloheyl]-label (n[1] = 5) 41 % AR after 120 d, [1,3-dioxolane-4-^{14}C]-label (n = 1)
Non-extractable residues after 100 days ‡	17-23 % AR after 100 d, [^{14}C-cycloheyl]-label (n[2] = 5) 33 % AR after 120 d, [1,3-dioxolane-4-^{14}C]-label (n = 1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	KWG 4168-desethyl (M01) Lab.: 1-8.8 % AR at 0-60 d (n = 6) Field: > 10 % KWG 4168-despropyl (M02) Lab.: 1-9.2 % AR at 0-60 d (n = 6) Field: > 10 % KWG 4168-N-oxide (M03) Lab.: 1-7.9 % AR at 0-181 d (n = 6) Field: not investigated

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

Anaerobic degradation ‡	
Mineralisation after 100 days	The anaerobic degradation of spiroxamine was only investigated in a water/sediment study. The degradation under anaerobic conditions showed, that no additional metabolites were formed compared with those occurring under aerobic conditions.
Non-extractable residues after 100 days	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	
Soil photolysis ‡	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Degradation experiments in soil under the influence of light showed, that photolysis contributed to the overall degradation, but that no new metabolites were formed. The formation of metabolites found were all far less than 10 %

[1] n corresponds to the number of soils.
[2] n corresponds to the number of soils.

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

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X[3]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
silt loam	-	8.1	20 °C / 40 % MWHC	*	-		
sandy loam	-	6.5	20 °C / 40 % MWHC	*	-		
sandy loam	-	7.1	20 °C / 48 % MWHC	*	-		
loamy sand	-	6.3	20 °C / 40 % MWHC	*	-		
loam	-	8.7	20 °C / 15 % MWHC (75 % of 1/3 bar)	*	-		
silt loam	-	7.0	20 °C / 55 % MWHC	22.1 / 73**	-	Chi^2: 13.2	1st order
Geometric mean/median							

* data available but not fully validated because of the lacking of information on the goodness of fit (visual and statistical assessment) of the kinetic analysis.
** calculated (DT_{90} = DT_{50}*3.32)
Data

Metabolites	Aerobic conditions: no laboratory studies performed, because all metabolites were approximately 7-9 % of the applied radioactivity							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Geometric mean/median								

In the following two separate tables are presented, one with field values for persistence and the other one with field values for use in modelling.

[3] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

Field studies (best fit, not normalised)‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X1	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (chi2)	DT_{50} (d) (SFO) non-norm.	Method of calculation
Northern Europe									
silt loam (bare soil)	Höfchen, DE, 30122/1		6.5	0-10	13.3	186.2	8.9	56.1**	FOMC
loam (vegetation)	Laacher Hof, DE, 30124/8		6.8	0-10	37.2	176.0	8.5	59.8+	DFOP
sandy loam (vegetation)	Thurston, UK, 30262/7		7.5	0-10	6.8	466.2	13.4	79.7+	FOMC
loamy sand (vegetation)	Pakenham, UK, 30263/5		7.3	0-10	2.9*	228.3*	16.8	68.8**	FOMC
silt loam (bare soil)	Höfchen, DE, 40006/8		6.4	0-10	50.0	316.1	5.9	95.2++	FOMC
sandy loam (bare soil)	Laacher Hof, DE, 40007/6		6.6	0-10	17.0	159.4	10.6	48.0**	FOMC
sandy loam (bare soil)	An der Scheune, DE, 40008/4		5.9	0-10	10.6	1796	10.0	123.8+	FOMC
silt loam (bare soil)	Swisttal-Hohn, DE, 40009/2		6.7	0-10	8.2	81.8	6.2	24.6**	FOMC
clay loam / silt loam (bare soil)	Albig, DE, 40010/6		7.8	0-10	6.2	65.7	7.6	19.8**	FOMC
sandy loam (spring barley)	Thurston, UK, 40097/1		7.4	0-10	1.6	127.5	5.5	145.3+ 1)	DFOP
sandy loam (spring barley)	Thurston, UK, 40100/5		7.4	0-10	7.8	378.0	6.5		DFOP
sandy loam (spring barley)	Pakenham, UK, 40099/8		7.0	0-10	9.3	207.9	7.8	113.8+ 1)	DFOP
sandy loam (spring barley)	Pakenham, UK, 40101/3		7.0	0-10	11.8	255.5	9.3		DFOP
silt loam (spring wheat)	Touffreville, FR, 40193/5		7.2	0-10	5.9	48.3	4.2	14.5**	FOMC
Southern Europe									
silty loamy sand (wine)	Laudun, FR, 50135/2		7.7	0-10	1.6	72.9	10.6	22.0**	FOMC
weak loamy sand (bare soil)	Nogarole Rocca, IT, 50136/0		7.7	0-10	4.0	42.9	3.6	22.7+	DFOP

Field studies (best fit, not normalised)‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X1	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (chi2)	DT_{50} (d) (SFO) non-norm.	Method of calculation
silty loamy sand (bare soil)	Laudun, FR, 40198/6		7.7	0-10	7.4 *	158.1 *	18.0	75.3^{+}	DFOP
silt loam (wine)	Filetto, IT, 40424/1		7.6	0-10	71.5	237.7	17.2	71.5	SFO
Geometric mean/median					8.9 / 8.0	153 / 176		57.0 / 69.4	

* = not included in the geometric mean and median calculations due to poor fitting
** = Back-calculated from FOMC (DT_{90} / 3.32)
+ = slow-phase DFOP; ++ = slow-phase HS
[1)] = calculated as replicates

Field studies (normalised data for use in modelling)‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X1	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (chi2)	DT_{50} (d) Norm.	Method of calculation
Northern Europe									
silt loam (bare soil)	Höfchen, DE, 30122/1		6.5	0-10	-	-	11.3	36.5^{+}	SFO
loam (vegetation)	Laacher Hof, DE, 30124/8		6.8	0-10	-	-	7.0	38.7^{+}	SFO
sandy loam (vegetation)	Thurston, UK, 30262/7		7.5	0-10	-	-	6.8	54.2^{+}	SFO
loamy sand (vegetation)	Pakenham, UK, 30263/5		7.3	0-10	-	-	8.9	51.7^{+}	SFO
silt loam (bare soil)	Höfchen, DE, 40006/8		6.4	0-10	-	-	5.2	68.6^{+}	SFO
sandy loam (bare soil)	Laacher Hof, DE, 40007/6		6.6	0-10	-	-	9.8	29.9^{+}	SFO
sandy loam (bare soil)	An der Scheune, DE, 40008/4		5.9	0-10	-	-	9.1	70.0^{+}	SFO
silt loam (bare soil)	Swisttal-Hohn, DE, 40009/2		6.7	0-10	-	-	8.2	39.4^{+}	SFO
clay loam / silt loam (bare soil)	Albig, DE, 40010/6		7.8	0-10	-	-	7.4	36.7^{+}	SFO

Field studies (normalised data for use in modelling)‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X1	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (chi2)	DT_{50} (d) Norm.	Method of calculation
sandy loam (spring barley)	Thurston, UK, 40097/1		7.4	0-10	-	-	5.8	88.0[+ 1)]	SFO
sandy loam (spring barley)	Thurston, UK, 40100/5		7.4	0-10	-	-	6.5		SFO
sandy loam (spring barley)	Pakenham, UK, 40099/8		7.0	0-10	-	-	7.8	53.1[+ 1)]	SFO
sandy loam (spring barley)	Pakenham, UK, 40101/3		7.0	0-10	-	-	9.2		SFO
silt loam (spring wheat)	Touffreville, FR, 40193/5		7.2	0-10	-	-	3.6	24.2[+]	SFO
Southern Europe									
silty loamy sand (wine)	Laudun, FR, 50135/2		7.7	0-10	-	-	6.3	36.1+	SFO
weak loamy sand (bare soil)	Nogarole Rocca, IT, 50136/0		7.7	0-10	-	-	4.6	25.4+	SFO
silty loamy sand (bare soil)	Laudun, FR, 40198/6		7.7	0-10	-	-	18.5	72.2[+]	SFO
silt loam (wine)	Filetto, IT, 40424/1		7.6	0-10	-	-	14.3	46.5[+]	SFO
Geometric mean/median					-	-		45.0 / 43.0	

+ = slow-phase DFOP;
[1)] = calculated as replicates

Metabolite KWG 4557 (M01)

	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	f.f.	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation
Northern Europe									
silt loam (bare soil)	Höfchen, DE, 30122/1	0.268	6.5	0-10	12.1*	40.2*	33.8	9.8*	SFO
loam (vegetation)	Laacher Hof, DE, 30124/8	0.434	6.8	0-10	30.5	101.2	13.6	19.6	SFO
sandy loam (vegetation)	Thurston, UK, 30262/7	0.338	7.5	0-10	51.2	170.2	5.5	35.3	SFO
loamy sand (vegetation)	Pakenham, UK, 30263/5	0.262	7.3	0-10	66.6	221.1	16.2	47.6*	SFO
silt loam (bare soil)	Höfchen, DE,	0.236	6.4	0-10	38.6	128.1	22.7	32.9	SFO

Metabolite KWG 4557 (M01)					Aerobic conditions				
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	f.f.	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation
	40006/8								
sandy loam (bare soil)	Laacher Hof, DE, 40007/6	0.133	6.6	0-10	90.8	301.7	15.9	54.0	SFO
sandy loam (bare soil)	An der Scheune, DE, 40008/4	0.105	5.9	0-10	385.6*	1280*	12.3	142.6*	SFO
silt loam (bare soil)	Swisttal-Hohn, DE, 40009/2	0.263	6.7	0-10	35.5	117.9	21.3	29.6	SFO
clay loam / silt loam (bare soil)	Albig, DE, 40010/6	0.175	7.8	0-10	56.3	186.9	20.0	44.8	SFO
sandy loam (spring barley)	Thurston, UK, 40097/1	0.239	7.4	0-10	78.6	261.1	10.5	47.7	SFO
sandy loam (spring barley)	Pakenham, UK, 40099/8	0.261	7.0	0-10	77.1	256.2	7.6	36.0	SFO
sandy loam (spring barley)	Thurston, UK, 40100/5	0.266	7.4	0-10	90.7	301.3	17.0	54.7	SFO
sandy loam (spring barley)	Pakenham, UK, 40101/3	0.202	7.0	0-10	96.7	321.1	12.2	45.3	SFO
silt loam (spring wheat)	Touffreville, FR, 40193/5	0.122	7.2	0-10	25.3	84.2	24.4	17.0	SFO
Southern Europe									
silty loamy sand (wine)	Laudun, FR, 50135/2	0.147	7.7	0-10	35.3	117.3	24.2	19.8	SFO
weak loamy sand (bare soil)	Nogarole Rocca, IT, 50136/0	0.152	7.7	0-10	65.1	216.2	11.5	69.9*	SFO
silty loamy sand (bare soil)	Laudun, FR, 40198/6	ND	7.7	0-10	ND	ND	-	-	-
silt loam (wine)	Filetto, IT, 40424/1	ND	7.6	0-10	ND	ND	-	-	-
Arithmetic mean / median		0.23 / 0.24							
Geometric mean/median					54.9 / 60.7			33.9 / 35.7	

ND = Not determined
* = not included in the geometric mean or median calculation due to poor fits

Metabolite KWG 4669 (M02)					Aerobic conditions				
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	f.f.	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation

Metabolite KWG 4669 (M02)					Aerobic conditions				
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	f.f.	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation
Northern Europe									
silt loam (bare soil)	Höfchen, DE, 30122/1	0.450	6.5	0-10	14.0*	46.6*	29.8	11.0*	SFO
loam (vegetation)	Laacher Hof, DE, 30124/8	0.417	6.8	0-10	28.6	95.1	14.1	18.6	SFO
sandy loam (vegetation)	Thurston, UK, 30262/7	0.356	7.5	0-10	58.4	194.1	7.2	39.9	SFO
loamy sand (vegetation)	Pakenham, UK, 30263/5	0.302	7.3	0-10	74.7	248.1	16.3	53.0*	SFO
silt loam (bare soil)	Höfchen, DE, 40006/8	0.261	6.4	0-10	32.9	109.2	20.3	29.5	SFO
sandy loam (bare soil)	Laacher Hof, DE, 40007/6	0.134	6.6	0-10	76.1	252.7	17.0	47.6	SFO
sandy loam (bare soil)	An der Scheune, DE, 40008/4	0.099	5.9	0-10	247.1 *	820.8*	17.4	96.4*	SFO
silt loam (bare soil)	Swisttal-Hohn, DE, 40009/2	0.250	6.7	0-10	42.1	140.0	19.8	34.3	SFO
clay loam / silt loam (bare soil)	Albig, DE, 40010/6	0.179	7.8	0-10	61.6	204.5	14.2	49.8	SFO
sandy loam (spring barley)	Thurston, UK, 40097/1	0.286	7.4	0-10	81.1	269.6	12.8	49.7	SFO
sandy loam (spring barley)	Pakenham, UK, 40099/8	0.288	7.0	0-10	78.2	259.7	5.9	36.5	SFO
sandy loam (spring barley)	Thurston, UK, 40100/5	0.307	7.4	0-10	86.7	288.1	17.3	52.5	SFO
sandy loam (spring barley)	Pakenham, UK, 40101/3	0.230	7.0	0-10	95.7	318.0	9.7	44.7	SFO
silt loam (spring wheat)	Touffreville, FR, 40193/5	0.135	7.2	0-10	24.9	82.8	28.6	17.0	SFO
Southern Europe									
silty loamy sand (wine)	Laudun, FR, 50135/2		7.7	0-10	36.4	121.0	22.4	20.6	SFO
weak loamy sand (bare soil)	Nogarole Rocca, IT, 50136/0		7.7	0-10	22.6	75.1	4.6	24.4	SFO
Geometric mean/median					51.3 / 60.0			33.4 /36.5	

ND = Not determined (not enough data points)
* = not included in the geometric mean or median calculation due to poor fits

pH dependence ‡ (yes / no) (if yes type of dependence)	no
Soil accumulation and plateau concentration ‡	See PECsoil calculations.

Laboratory studies ‡

Parent	Anaerobic conditions: no specific study performed						
Soil type	X[4]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Geometric mean/median							

Metabolites	Anaerobic conditions: no specific study performed							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Geometric mean/median								

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
loamy sand	1.8	7.0			12.78	710	0.7851
silt loam	2.4	6.0			44.98	1874	0.8310
silty clay	0.64	7.6			41.07	6417	0.8854
loamy sand	0.3	7.7			7.25	2415	0.8333
sand	0.7	5.9			4.61	659	0.7682
sand	0.2	6.7			8.552	[4276]*	1.063
sandy loam	0.45	5.8			14.47	[3216]*	1.055
sandy loam	1.12	6.7			15.09	[1347]*	1.025
loam	0.97	7.8			381.7	[39346]*	1.024
silty clay	1.05	5.1			892.6	[85008]*	1.013
Arithmetic mean/median						2415 / 1874	0.8206 / 0.8324

[4] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

pH dependence, Yes or No	No. Due to the basic properties (amine) of spiroxamine, a significant absorption was observed in all soils. The pH range of natural soils used in agriculture is expected to have only a very minor influence because spiroxamine was also relatively stable in hydrolysis experiments conducted at different pH values.

* U.S. soil not considered for calculating the mean (worst case approach)

Metabolite KWG 4557 -desethyl (M01)‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
sand	0.32	7.0 / 6.3			3.96	1237.0	0.8668
sandy loam	1.12	6.7 / 6.7			16.27	1452.7	0.8131
loam	0.97	8.7 / 7.8			58.81	6062.6	0.8621
silty clay loam	1.49	6.1 / 5.5			156.6	10510.5	0.8518
Arithmetic mean/median						4816/ 3757.65	0.8485
pH dependence (yes or no)			no				

Metabolite KWG 4168-despropyl (M02)‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
sand	0.32	7.0 / 6.3			2.93	916.7	0.8764
sandy loam	1.12	6.7 / 6.7			12.79	1141.6	0.8271
loam	0.97	8.7 / 7.8			54.39	5608.8	0.9222
silty clay loam	1.49	6.1 / 5.5			134.0	8993.6	0.8855
Arithmetic mean/median						4165 / 3375	0.8778 / 0.881
pH dependence (yes or no)			no				

Metabolite KWG-N-oxide (M03)‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
sand	0.32	7.0 / 6.3			1.77	552.3	0.9388
sandy loam	1.12	6.7 / 6.7			3.93	350.5	0.8714
loam	0.97	8.7 / 7.8			15.9	1640.9	0.8898
silty clay loam	1.49	6.1 / 5.5			370.9	24893*.	0.8348
Arithmetic mean/median						848 / 552	0.884 / 0.881
pH dependence (yes or no)			no				

* outlier, not considered for calculating the mean

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

Column leaching ‡	no study performed
Aged residues leaching ‡	Aged for (d): 30 and 62 d Time period (d): 2 d Eluation (mm): 393 mm
	aged for 30 to 32 d (n = 5): Analysis of soil residues post ageing (soil residues pre-leaching): 42-69 % active substance, 1.1-7.4 % M1, 0.7-5.2 % M2, 1.1-2.3 % M3 non extractable residues: > 15.7-27 %, total residues/radioactivity retained in upper segment: 73.3 – 95.8 % aged for 60 to 62 d (n = 3): Analysis of soil residues post ageing (soil residues pre-leaching): 26-55 % active substance, 7.3-8.5 % M1, 4.7-5.8 % M2, 1.7-2.0 % M3 non extractable residues: > 18-25 %, total residues/radioactivity retained in upper segment: 58 – 83 %
	Leachate: 0.2-0.5 % total residues/radioactivity in leachate 0.004-0.03 % active substance, 0.028 -0.029 % M3
Lysimeter/ field leaching studies ‡	not study performed

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	Worst case kinetic (checked for all the field DT50 values) for use in vine and cereals: DT_{50} (d)/DT_{90} (d): 71.5/237.7 days SFO (field dissipation trial Filetto 40424/1)
Application data	Crop: vines Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 50 %/50 %/60 % plant interception: Number of applications: 3 Interval (d): 10 Application rate(s): 3 * 300 g as/ha
Application data	Crop: cereals Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm3 70 % plant interception: Number of applications: 2 Interval (d): 14 Application rate(s): 2 * 375 g as/ha

Crop vines

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial				0.506	
Short term	24 h			0.501	0.504
	2 d			0.497	0.501
	4 d			0.487	0.497
Long term	7 d			0.473	0.490
	28 d			0.386	0.445
	50 d			0.312	0.410
	100 d			0.192	0.342
Plateau concentration (calculated by the reporting RMS)		0.522 mg/kg PECaccu after infinite years (0.5063 mg/kg (PECini) + 0.0152 mg/kg (PECplateau))			

Crop cereals

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial				0.281	-
Short term	24 h			0.278	0.280
	2 d			0.276	0.278
	4 d			0.270	0.276
Long term	7 d			0.263	0.272
	28 d			0.214	0.246
	50 d			0.173	0.223
	100 d			0.107	0.184
Plateau concentration (calculated by the reporting RMS)		0.283 mg/kg PECaccu after infinite years (0.281 mg/kg (PECini) + 0.002 mg/kg (PECplateau))			

Metabolite M01		Recalculation (worst case approach)			
Method of calculation		Molecular weight relative to the parent: 0.91 DT_{50} (d): no degradation considered			
Application data		crop: vines: Application rate assumed: 165.9 g/ha cumulative annual value (assumed crop interception of 50%/50%/60%, molar ratio, maximum formation of 43.4 % of the applied dose).			
PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial				0.221	
Short term	24 h			-	-
	2 d			-	-
	4 d			-	-
Long term	7 d			-	-
	28 d			-	-
	50 d			-	-
	100 d			-	-
Plateau conc. (calc. by the RMS)		0.0437 mg/kg after infinite years assuming a worst case DT_{50} of 90.7 d			
Metabolite M01		Recalculation (worst case approach)			

Method of calculation		Molecular weight relative to the parent: 0.91 DT_{50} (d): -no degradation considered			
Application data		crop: cereals: Application rate assumed: 88.9 g/ha cumulative annual value (assumed crop interception of 70%/70%, molar ratio, maximum formation of 43.4 % of the applied dose).			
$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial				0.118	
Short term	24 h			-	-
	2 d			-	-
	4 d			-	-
Long term	7 d			-	-
	28 d			-	-
	50 d			-	-
	100 d			-	-
Plateau concentration (calc. by the reporting RMS)		0.0245 mg/kg after infinite years assuming a worst case DT_{50} of 90.7 d			
-Metabolite M02 Method of calculation		Recalculation (worst case approach) Molecular weight relative to the parent: 0.86 DT_{50} (d): no degradation considered			
Application data		crop: vines: Application rate assumed: 162.5 g/ha cumulative annual value (assumed crop interception of 50%/50%/60%, molar ratio, maximum formation of 45.0 % of the applied dose).			
$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial				0.217	
Short term	24 h			-	-
	2 d			-	-
	4 d			-	-
Long term	7 d			-	-
	28 d			-	-
	50 d			-	-
	100 d			-	-
Plateau concentration		0.0274 mg/kg after infinite			

(calculated by the reporting RMS)	years assuming a worst case DT_{50} of 85 d

Metabolite M02	Recalculation (worst case approach)
Method of calculation	Molecular weight relative to the parent: 0.86 DT_{50} (d): no degradation considered
Application data	crop: cereals: Application rate assumed: 87.1 g/ha cumulative annual value (assumed crop interception of 70%/70%, molar ratio, maximum formation of 45 % of the applied dose)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial				0.116	
Short term	24 h			-	-
	2 d			-	-
	4 d			-	-
Long term	7 d			-	-
	28 d			-	-
	50 d			-	-

Plateau concentration (calculated by the reporting RMS)	0.0148 mg/kg after infinite years assuming a worst case DT_{50} of 85 d

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	Stable in buffer at pH 4, pH 7 and pH 9, except traces of isomer B being hydrolysed at pH 4. Expected DT_{50}>1 year. EPA incubation experiment: pH 4 50 °C: Spiroxamine was stable
	pH 7 50 °C: Spiroxamine was stable
	pH 9 50 °C: approx. 4 % was hydrolysed during 30 days of incubation at 25 °C, yielding small amounts of KWG 4168-desethyl, KWG 4168-despropyl and KWG 4168-N-oxide.
Photolytic degradation of active substance and metabolites above 10 % ‡	Experimental photolytic half-life of Spiroxamine in sterile aqueous buffered solution at 25 °C: 50.5 d Conversion to a predicted environmental half-life at the worst case site (solar conditions at Phoenix/USA): 236 d The main degradation products were KWG 4168-desethyl, KWG 4168-despropyl), KWG 4168 – hydroxy and KWG 4168 - N-oxide and each of them accounted far less than 10 % of the applied radioactivity.

Quantum yield of direct phototransformation in water at Σ > 290 nm	ϕ = 0.00064
Readily biodegradable ‡ (yes/no)	No data submitted, substance considered not ready biodegradable.

Degradation in water / sediment

Parent	Distribution (e.g. max in water 75.5 % after 6 h. Max. sed. 60 % after 2 d)									
Water / sediment system	pH water phase	pH sed.	t °C	DT_{50} - DT_{90} whole sys. (d)	St. (chi^2)	DT_{50} - DT_{90} water (d)	St. (chi^2)	DT_{50} - DT_{90} sed. (d)	St. (chi^2)	Method of calculation
Hönninger Weiher	7.2	6.2	20	346**	13.4	0.6 – 2.0 *	6.6	310 – 1028 *	2.9	SFO/ Level PI
Stillwell	8.5	7.8	20	247 – 820 **	7.8	1.3 – 4.3 *	7.3	-	-	SFO/ Level PI
Anglerweiher	7.1	7.2	20	16.4 – 54.3	12.6	0.8	10.5	39.3	17.3	SFO/ Level PI
Hönninger Weiher	7.2	5.5	20	51.6 – 171	18.4	0.7	11.7	152.9	13.1	SFO/ Level PI
Geometric mean/median				66.2 / 71.6		0.8		23		

* DisT50 / DisT90 (Level PI evaluation)
** SFO kinetics derived from slow Phase DFOP

Metabolite M01	Distribution (< 10 % in the system)									
Water / sediment system	pH water phase	pH sed.	t. °C	DT_{50} - DT_{90} whole sys.	St. (chi^2)	DT_{50} - DT_{90} water	r^2	DT_{50} - DT_{90} sed.	St. (r^2)	Method of calculation
endpoint from anaerobic study not relevant for modelling: conservative defaults are recommended for modelling										
Metabolite M02	Distribution (< 10 % in the system)									
Water / sediment system	pH water phase	pH sed.	t. °C	DT_{50} - DT_{90} whole sys.	St. (chi^2)	DT_{50} - DT_{90} water	r^2	DT_{50} - DT_{90} sed.	St. (r^2)	Method of calculation
endpoint from anaerobic study not relevant for modelling: conservative defaults are recommended for modelling										
Metabolite M03	Distribution (max in water 11.3 % at day 0. Max. sed. 1.5 % after 30 d)									
Water / sediment system	pH water phase	pH sed.	t. °C	DT_{50} - DT_{90} whole sys.	St. (chi^2)	DT_{50} - DT_{90} water	r^2	DT_{50} - DT_{90} sed.	St. (r^2)	Method of calculation
no kinetic evaluation performed: conservative defaults are recommended for modelling										

Metabolite M06	Distribution (max in water 25.6 % after 14 d. Max. sed. 8.9 % after 118 d)									
Water / sediment system	pH water phase	pH sed.	t. °C	DT_{50} - DT_{90} whole sys.	St. (chi^2)	DT_{50} - DT_{90} water	r^2	DT_{50} - DT_{90} sed.	St. (r^2)	Method of calculation
Anglerweiher	7.1	6.6	20	42.5 – 141	18.4	-	-	-	-	SFO
Hönninger Weiher	7.2	5.2	20	ND		-	-	-	-	
Geometric mean/median										

Mineralisation and non extractable residues					
Water / sediment system	pH water phase	pH sed.	Mineralisation 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)
Anglerweiher	7.1	6.6	27 %	33.2 (end)	33.2 (118 d)
Hönninger Weiher	7.2	5.2	7.6 %	40.7 (end)	40.7 (118 d)
Stillwell	8.5	7.8	17 %	65.8-69.5 % (day 56)	46.2-51.6 % (100.d)
Hönninger Weiher	7.2	6.2	7 %	48.6 % (14 d)	44 % (100 d)

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

Parent Parameters used in $FOCUS_{sw}$ step 1 and 2	Version control no. of FOCUS calculator: Molecular weight (g/mol): 297.5 Water solubility (mg/L): 470 K_{OC}/K_{OM} (L/kg): 2415 / 1400 DT_{50} soil (d): Calculations Notifier: 30.3 days (geometric mean, field n=18) Re-calculations RMS: with the geometric mean DT50 in soil of 45.0 d derived from the slow phase of DFOP kinetics observed in the 18 field dissipation studies, showed only minor changes to the original values provided by the notifier (concentrations in surface water after use of spiroxamine in cereals and vine is mainly affected by spray drift entries). DT_{50} water/sediment system (d): - DT_{50} water (d): 3.1 (geom. mean) of level P-II DegT50) DT_{50} sediment (d): 1000 (worst case) Maximum occurrence observed in sediment (%): 50.7 (this represents not the worst case, which was determined to 60.1 % (dioxane labelled)
Parent Parameters used in $FOCUS_{sw}$ step 3 and step 4	Version control no.'s of FOCUS software: SWASH 2.1 Vapour pressure: 0.00972 Pa K_{om}/K_{oc}: 2415 / 1400 1/n: (Freundlich exponent general or for soil, susp. solids

	or sediment respectively) 0.82
Metabolite M01 (KWG 4168-desethyl) Parameters used in $FOCUS_{sw}$ step 1 and 2	Molecular weight: 269.4 Water solubility (mg/L): 14.8 Soil or water metabolite: soil K_{oc}/K_{om} (L/kg): 4816 / 2794 DT_{50} soil (d): 33.9 days days (geometric mean, field n=16) In accordance with FOCUS SFO DT_{50} water/sediment system (d): - DT_{50} water (d): 1000 (worst case) DT_{50} sediment (d): 1000 (worst case) Maximum occurrence observed (% molar basis with respect to the parent) Water: 0.0001: soil: 8.8 %
Metabolite M02 (KWG 4168-despropyl) Parameters used in $FOCUS_{sw}$ step 1 and 2	Molecular weight: 255.4 Water solubility (mg/L): 46.6 Soil or water metabolite: soil K_{oc}/K_{om} (L/kg): 4165 / 2416 DT_{50} soil (d): 33.4 days days (geometric mean, field n=16) In accordance with FOCUS SFO DT_{50} water/sediment system (d): - DT_{50} water (d): 1000 (worst case) DT_{50} sediment (d): 1000 (worst case) Maximum occurrence observed (% molar basis with respect to the parent) Water: 0.0001: soil: 5.8 %
Metabolite M03 (KWG 4168-N-oxide) Parameters used in $FOCUS_{sw}$ step 1 and 2	In a worst case approach the metabolite M03 was considered in aquatic risk assessment to the same amount as the parent spiroxamine according to 100% formation (Step 2 PECsw for spiroxamine = 13.48 µg/L).
Metabolite M06 (KWG 4168-acid) Parameters used in $FOCUS_{sw}$ step 1 and 2	Molecular weight: 327.5 Water solubility (mg/L):1000 Soil or water metabolite: water K_{oc}/K_{om} (L/kg): 0.0001 DT_{50} water/sediment system (d): - DT_{50} water (d): 1000 (worst case) DT_{50} sediment (d): 1000 (worst case) Maximum occurrence observed (% molar basis with respect to the parent) Water: 31.3 soil: 0.0001
Main routes of entry	drift, run-off
Application rate	Crop: vines, variation 1

	Crop interception: 40 /50 /60 Number of applications: 3 Interval (d): 10 Application rate(s): 3 * 300 g as/ha Application window: BBCH 13-85
Application rate	Crop: vines, variation 2 Crop interception: 50 /50 Number of applications: 2 Interval (d): 7 Application rate(s): 2 * 200 g as/ha Application window: BBCH 13-19
Application rate	Crop: vines, variation 3 Crop interception: 85 / 85 /85 Number of applications: 3 Interval (d): 10 Application rate(s): 3 * 400 g as/ha Application window: BBCH 79-85
Application rate	Crop: vines, variation 4 Crop interception: 50 / 50 / 85 / 85 /85 Number of applications: 2 + 3 Interval (d): 10 / 10 Application rate(s): 2 * 200 + 3 * 400 g as/ha Application window: BBCH 13-19 and BBCH 79-85
Application rate	Crop: cereals, variation 1 Crop interception: 50 /50 Number of applications: 2 Interval (d): 14 Application rate(s): 2 * 375 g as/ha Application window: BBCH 30
Application rate	Crop: cereals, variation 2 Crop interception: 70 /70 Number of applications: 2 Interval (d): 14 Application rate(s): 2 * 375 g as/ha Application window: BBCH 30-69 (wheat, rye triticale) BBCH 30-61 (barley)

FOCUS STEP 1 simulations were generally not performed.

Crop	Compound	FOCUS STEP 2 $PEC_{sw, max}$ (µg/L)	
		1 x 300 g as/ha	3 x 300 g as/ha
Vines , variation 1 South Europe	Spiroxamine	5.71	13.48
	KWG 4168-desethyl (M01)	0.24	0.59
	KWG 4168-despropyl (M02)	0.17	0.42
	KWG 4168-acid (M06)	0.93	2.61
		FOCUS STEP 2 $PEC_{sed, max}$ (µg/kg)	
		1 x 300 g as/ha	3 x 300 g as/ha
	Spiroxamine	136.62	323.63
	KWG 4168-desethyl (M01)	11.44	28.36
	KWG 4168-despropyl (M02)	6.99	17.29
	KWG 4168-acid (M06)	0.00	0.00
Vines early, variation 2 South Europe		FOCUS STEP 2 $PEC_{sw, max}$ (µg/L)	
		1 x 200 g as/ha	2 x 200 g as/ha
	Spiroxamine	3.80	6.93
	KWG 4168-desethyl (M01)	0.16	0.30
	KWG 4168-despropyl (M02)	0.11	0.21
	KWG 4168-acid (M06)	0.62	1.14
		FOCUS STEP 2 $PEC_{sed, max}$ (µg/kg)	
		1 x 200 g as/ha	2 x 200 g as/ha
	Spiroxamine	91.08	166.16
	KWG 4168-desethyl (M01)	7.62	14.23
	KWG 4168-despropyl (M02)	4.66	8.69
	KWG 4168-acid (M06)	0.00	0.00
Vines late, variation 3 South Europe		FOCUS STEP 2 $PEC_{sw, max}$ (µg/L)	
		1 x 400 g as/ha	3 x 400 g as/ha
	Spiroxamine	10.70	11.03
	KWG 4168-desethyl (M01)	0.12	0.29
	KWG 4168-despropyl (M02)	0.08	0.21
	KWG 4168-acid (M06)	3.69	9.44
		FOCUS STEP 2 $PEC_{sed, max}$ (µg/kg)	
		1 x 400 g as/ha	3 x 400 g as/ha
	Spiroxamine	107.72	222.43
	KWG 4168-desethyl (M01)	5.72	14.18
	KWG 4168-despropyl (M02)	3.50	8.64
	KWG 4168-acid (M06)	0.00	0.00

Vines variation 4 early + late South Europe	Compound	FOCUS STEP 2 $PEC_{sw, max}$ (µg/L)	
		1 x 400 g as/ha	5 x 400 g as/ha
	Spiroxamine	10.70	17.86
	KWG 4168-desethyl (M01)	0.20	0.69
	KWG 4168-despropyl (M02)	0.14	0.48
	KWG 4168-acid (M06)	3.69	15.03
		FOCUS STEP 2 $PEC_{sed, max}$ (µg/kg)	
		1 x 400 g as/ha	5 x 400 g as/ha
	Spiroxamine	149.47	424.11
	KWG 4168-desethyl (M01)	9.53	33.00
	KWG 4168-despropyl (M02)	5.83	20.07
	KWG 4168-acid (M06)	0.00	0.00
cereals, variation 1* North Europe		FOCUS STEP 2 $PEC_{sw, max}$ (µg/L)	
		1 x 375 g as/ha	2 x 375 g as/ha
	Spiroxamine	3.45	5.49
	KWG 4168-desethyl (M01)	0.12	0.22
	KWG 4168-despropyl (M02)	0.09	0.15
	KWG 4168-acid (M06)	1.19	2.09
		FOCUS STEP 2 $PEC_{sed, max}$ (µg/kg)	
		1 x 375 g as/ha	2 x 375 g as/ha
	Spiroxamine	79.76	130.74
	KWG 4168-desethyl (M01)	5.96	10.43
	KWG 4168-despropyl (M02)	3.64	6.36
	KWG 4168-acid (M06)	0.00	0.00
cereals, variation 1* Sourth Europe	Compound	FOCUS STEP 2 $PEC_{sw, max}$ (µg/L)	
		1 x 375 g as/ha	2 x 375 g as/ha
	Spiroxamine	6.07	10.15
	KWG 4168-desethyl (M01)	0.25	0.43
	KWG 4168-despropyl (M02)	0.17	0.31
	KWG 4168-acid (M06)	1.19	2.09
		FOCUS STEP 2 $PEC_{sed, max}$ (µg/kg)	
		1 x 375 g as/ha	2 x 375 g as/ha
	Spiroxamine	145	243.33
	KWG 4168-desethyl (M01)	11.91	20.86
	KWG 4168-despropyl (M02)	7.28	12.73
	KWG 4168-acid (M06)	0.00	0.00

* Simulations with variation 2 are not reported since they do not represent worst case conditions

FOCUS STEP 3 Vines , variation 1	Scenario	Water body	$PEC_{sw, max}$ (µg/L)	
			1 x 300 g as/ha	3 x 300g as/ha
	D6 (Thiva)	Ditch	5.090	4.654
	R1 (Weiherbach)	Pond	0.182	0.177
	R1 (Weiherbach)	Stream	3.671	3.194
	R2 (Porto)	Stream	5.018	4.277
	R3 (Bologna)	Stream	5.275	4.515
	R4 (Roujan)	Stream	3.684	3.141
			$PEC_{sed, max}$ (µg/kg)	
			1 x 300 g as/ha	3 x 300g as/ha
	D6 (Thiva)	Ditch	5.125	15.109
	R1 (Weiherbach)	Pond	0.636	1.17
	R1 (Weiherbach)	Stream	0.585	1.941
	R2 (Porto)	Stream	1.133	2.56
	R3 (Bologna)	Stream	1.216	2.224
	R4 (Roujan)	Stream	2.318	2.564

FOCUS STEP 3 Vines early, variation 2			$PEC_{sw, max}$ (µg/L)	
			1 x 200 g as/ha	3 x 200 g as/ha
	D6 (Thiva)	Ditch	1.126	1.044
	R1 (Weiherbach)	Pond	0.038	0.037
	R1 (Weiherbach)	Stream	0.808	0.732
	R2 (Porto)	Stream	1.104	1.000
	R3 (Bologna)	Stream	1.161	1.056
	R4 (Roujan)	Stream	0.811	0.734
			$PEC_{sed, max}$ (µg/kg)	
			1 x 200 g as/ha	2 x 200g as/ha
	D6 (Thiva)	Ditch	1.184	2.740
	R1 (Weiherbach)	Pond	0.148	0.215
	R1 (Weiherbach)	Stream	0.344	0.664
	R2 (Porto)	Stream	0.676	1.452
	R3 (Bologna)	Stream	0.270	0.459
	R4 (Roujan)	Stream	1.449	1.447

FOCUS STEP 3 Vines late, variation 3	Scenario	Water body	$PEC_{sw, max}$ (µg/L)	
			1 x 400 g as/ha	3 x 400 g as/ha
	D6 (Thiva)	Ditch	6.834	6.052
	R1 (Weiherbach)	Pond	0.243	0.212
	R1 (Weiherbach)	Stream	4.875	4.272
	R2 (Porto)	Stream	6.720	5.728
	R3 (Bologna)	Stream	7.066	6.026
	R4 (Roujan)	Stream	5.011	4.272
			$PEC_{sed, max}$ (µg/kg)	
			1 x 400 g as/ha	3 x 400 g as/ha
	D6 (Thiva)	Ditch	10.088	17.682
	R1 (Weiherbach)	Pond	0.622	1.142
	R1 (Weiherbach)	Stream	0.467	1.078
	R2 (Porto)	Stream	0.757	1.404
	R3 (Bologna)	Stream	1.823	5.814
	R4 (Roujan)	Stream	0.784	1.476
FOCUS STEP 3 Vines late, variation 4 (only multiple applications)			$PEC_{sw, max}$ (µg/L)	
			2 x 200 g as/ha + 3 x 400 g as/ha	
	D6 (Thiva)	Ditch		5.968
	R1 (Weiherbach)	Pond		0.237
	R1 (Weiherbach)	Stream		4.112
	R2 (Porto)	Stream		5.489
	R3 (Bologna)	Stream		5.799
	R4 (Roujan)	Stream		4.111
			$PEC_{sed, max}$ (µg/kg)	
			2 x 200 g as/ha + 3 x 400 g as/ha	
	D6 (Thiva)	Ditch		23.279
	R1 (Weiherbach)	Pond		1.693
	R1 (Weiherbach)	Stream		2.358
	R2 (Porto)	Stream		3.495
	R3 (Bologna)	Stream		4.378
	R4 (Roujan)	Stream		4.054

		Water body	1 x 375 g as/ha			2 x 375 g as/ha		
			$PEC_{sw, max}$ [µg/L]	$PEC_{sed, max}$ [µg/kg]	$TWA_{sw, 21 d}$ [µg/L]	$PEC_{sw, max}$ [µg/L]	$PEC_{sed, max}$ [µg/kg]	$TWA_{sw, 21 d}$ [µg/L]
FOCUS STEP 3 spring cereals	D1 (Lanna)	ditch	2.392	5.621	0.648	2.309	8.013	0.868
		stream	2.092	1.253	0.085	1.810	1.667	0.143
	D3 (Vredepeel)	ditch	2.364	1.514	0.106	2.072	2.412	0.209
	D4 (Skousbo)	pond	0.081	0.222	0.020	0.071	0.329	0.028
		stream	2.040	0.408	0.026	1.768	0.595	0.046
	D5 (La Jaillière)	pond	0.081	0.308	0.029	0.076	0.427	0.036
		stream	2.001	0.093	0.006	1.783	0.169	0.013
	R4 (Roujan)	stream	1.563	6.488	0.139	1.353	6.624	0.144
FOCUS STEP 3 winter cereals	D1 (Lanna)	ditch	2.392	5.621	0.648	2.309	8.013	0.868
		stream	2.092	1.253	0.085	1.810	1.667	0.143
	D2 (Brimstone)	ditch	2.395	5.524	0.468	2.116	7.350	0.713
		stream	2.131	4.924	0.397	1.842	4.282	0.358
	D3 (Vredepeel)	ditch	2.364	1.572	0.110	2.069	2.198	0.192
	D4 (Skousbo)	pond	0.081	0.270	0.025	0.072	0.387	0.030
		stream	2.013	0.283	0.018	1.766	0.512	0.039
	D5 (La Jaillière)	pond	0.081	0.344	0.033	0.083	0.524	0.043
		stream	1.903	0.059	0.004	1.793	0.162	0.011
	D6 (Thiva)	ditch	2.332	0.674	0.045	2.076	2.691	0.214
	R1 (Weiherbach)	pond	0.081	0.479	0.031	0.103	1.072	0.056
		stream	1.557	3.422	0.033	1.346	8.947	0.103
	R3 (Bologna)	stream	2.187	3.159	0.029	1.902	6.801	0.085
	R4 (Roujan)	stream	1.557	3.947	0.097	1.726	9.594	0.250

FOCUS STEP 4 Vines, variation 1						
			$PEC_{sw, max}$ (µg/L)			
			5 m buffer zone		10 m buffer zone	
	Scenario	Water body	1 x 300 g as/ha	3 x 300 g as/ha	1 x 300 g as/ha	3 x 300 g as/ha
	D6 (Thiva)	Ditch	3.076	2.790	1.113	0.993
	R1 (Weiherbach)	Pond	a)	a)	0.116	0.112
	R1 (Weiherbach)	Stream	2.675	2.317	0.968	0.828
	R2 (Porto)	Stream	3.656	3.103	1.323	1.108
	R3 (Bologna)	Stream	3.843	3.276	1.391	1.170
	R4 (Roujan)	Stream	2.684	2.279	0.971	0.814
			$PEC_{sed, max}$ (µg/kg)			
			5 m buffer zone		10 m buffer zone	
	Scenario	Water body	1 x 300 g as/ha	3 x 300 g as/ha	1 x 300 g as/ha	3 x 300 g as/ha
	D6 (Thiva)	Ditch	3.145	9.366	1.171	3.558
	R1 (Weiherbach)	Pond	a)	a)	0.415	0.748
	R1 (Weiherbach)	Stream	0.556	1.802	0.181	0.586
	R2 (Porto)	Stream	1.083	2.452	0.224	0.505
	R3 (Bologna)	Stream	0.888	1.809	0.323	0.611
	R4 (Roujan)	Stream	2.254	2.426	0.701	0.762
			20 m buffer zone			
			$PEC_{sw, max}$ (µg/L)		$PEC_{sed, max}$ (µg/kg)	
	Scenario	Water body	1 x 300 g as/ha	3 x 300 g as/ha	1 x 300 g as/ha	3 x 300 g as/ha
	D6 (Thiva)	Ditch	0.390	0.342	0.421	1.306
	R1 (Weiherbach)	Pond	0.058	0.056	0.216	0.390
	R1 (Weiherbach)	Stream	0.339	0.286	0.084	0.264
	R2 (Porto)	Stream	0.463	0.383	0.085	0.191
	R3 (Bologna)	Stream	0.487	0.404	0.114	0.257
	R4 (Roujan)	Stream	0.340	0.281	0.327	0.348

a) not provided by the applicant

FOCUS STEP 4 Vines early, variation 2			$PEC_{sw, max}$ (µg/L)			
			5 m buffer zone		10 m buffer zone	
	Scenario	Water body	1 x 200 g as/ha	2 x 200 g as/ha	1 x 200 g as/ha	2 x 200 g as/ha
	D6 (Thiva)	Ditch	0.671	0.611	0.236	0.207
	R1 (Weiherbach)	Pond	a)	a)	0.024	0.023
	R1 (Weiherbach)	Stream	0.583	0.523	0.205	0.178
	R2 (Porto)	Stream	0.797	0.714	0.280	0.243
	R3 (Bologna)	Stream	0.838	0.754	0.295	0.256
	R4 (Roujan)	Stream	0.606	0.609	0.275	0.276
			$PEC_{sed, max}$ (µg/kg)			
			5 m buffer zone		10 m buffer zone	
	Scenario	Water body	1 x 200 g as/ha	2 x 200 g as/ha	1 x 200 g as/ha	2 x 200 g as/ha
	D6 (Thiva)	Ditch	0.715	1.648	0.257	0.588
	R1 (Weiherbach)	Pond	a)	a)	0.094	0.133
	R1 (Weiherbach)	Stream	0.337	0.648	0.104	0.198
	R2 (Porto)	Stream	0.662	1.426	0.123	0.268
	R3 (Bologna)	Stream	0.195	0.330	0.069	0.115
	R4 (Roujan)	Stream	1.433	1.432	0.423	0.423
			20 m buffer zone			
			$PEC_{sw, max}$ (µg/L)		$PEC_{sed, max}$ (µg/kg)	
			1 x 200 g as/ha	2 x 200 g as/ha	1 x 200 g as/ha	2 x 200 g as/ha
	D6 (Thiva)	Ditch	0.080	0.068	0.090	0.202
	R1 (Weiherbach)	Pond	0.012	0.011	0.050	0.066
	R1 (Weiherbach)	Stream	0.070	0.091	0.049	0.093
	R2 (Porto)	Stream	0.095	0.080	0.046	0.101
	R3 (Bologna)	Stream	0.100	0.084	0.024	0.039
	R4 (Roujan)	Stream	0.144	0.144	0.198	0.198

FOCUS STEP 4 Vines late, variation 3			$PEC_{sw, max}$ (µg/L)			
			5 m buffer zone		10 m buffer zone	
	Scenario	Water body	1 x 400 g as/ha	3 x 400 g as/ha	1 x 400 g as/ha	3 x 400 g as/ha
	D6 (Thiva)	Ditch	4.130	3.632	1.495	1.295
	R1 (Weiherbach)	Pond	a)	a)	0.155	0.134
	R1 (Weiherbach)	Stream	3.550	3.098	1.285	1.107
	R2 (Porto)	Stream	4.894	4.154	1.771	1.484
	R3 (Bologna)	Stream	5.146	4.371	1.862	1.561
	R4 (Roujan)	Stream	3.649	3.098	1.320	1.106
			$PEC_{sed, max}$ (µg/kg)			
			5 m buffer zone		10 m buffer zone	
	Scenario	Water body	1 x 400 g as/ha	3 x 400 g as/ha	1 x 400 g as/ha	3 x 400 g as/ha
	D6 (Thiva)	Ditch	6.227	10.982	2.343	4.190
	R1 (Weiherbach)	Pond	a)	a)	0.404	0.745
	R1 (Weiherbach)	Stream	0.387	0.821	0.133	0.292
	R2 (Porto)	Stream	0.644	1.352	0.194	0.302
	R3 (Bologna)	Stream	1.331	5.531	0.484	1.439
	R4 (Roujan)	Stream	0.571	1.319	0.207	0.513
			20 m buffer zone			
			$PEC_{sw, max}$ (µg/L)		$PEC_{sed, max}$ (µg/kg)	
			1 x 400 g as/ha	3 x 400 g as/ha	1 x 400 g as/ha	3 x 400 g as/ha
	D6 (Thiva)	Ditch	0.523	0.447	0.850	1.544
	R1 (Weiherbach)	Pond	0.078	0.067	0.209	0.389
	R1 (Weiherbach)	Stream	0.450	0.382	0.054	0.109
	R2 (Porto)	Stream	0.620	0.513	0.075	0.111
	R3 (Bologna)	Stream	0.652	0.540	0.171	0.619
	R4 (Roujan)	Stream	0.462	0.382	0.073	0.237

FOCUS STEP 4, Vines early + late (only multiple applications)	Scenario	Water body	$PEC_{sw, max}$ (µg/L)		
			5 m	10 m	20 m
	D6 (Thiva)	Ditch	3.583	1.278	0.441
	R1 (Weiherbach)	Pond	a)	0.150	0.074
	R1 (Weiherbach)	Stream	2.983	1.066	0.369
	R2 (Porto)	Stream	3.982	1.424	0.492
	R3 (Bologna)	Stream	4.207	1.504	0.520
	R4 (Roujan)	Stream	2.982	1.066	0.369
			$PEC_{sed, max}$ (µg/kg)		
			5 m	10 m	20 m
	D6 (Thiva)	Ditch	14.493	5.555	2.060
	R1 (Weiherbach)	Pond	a)	1.091	0.569
	R1 (Weiherbach)	Stream	1.991	0.656	0.275
	R2 (Porto)	Stream	3.271	0.712	0.268
	R3 (Bologna)	Stream	4.055	1.408	0.627
	R4 (Roujan)	Stream	3.914	0.951	0.402

No TWA reported for FOCUS STEP 2 simulations

rop	Scenario	TWAC 21 (µg/L) in water*		
		vines, variation 1 1 x 300 g as/ha	vines, variation 1 3 x 300 g as/ha	vines, variation 3 1 x 400 g as/ha
FOCUS STEP 3	D6 (ditch)	0.457	1.503	0.964
	R1 (pond)	0.063	0.081	0.059
	R1 (stream)	0.035	0.071	0.031
	R2 (stream)	0.030	0.056	0.041
	R3 (stream)	0.078	0.152	0.118
	R4 (stream)	0.092	0.128	0.050

no TWA 21 d reported for variation 2 as it does not represent worst case conditions

Due to big number of scenarios only worst case combinations are reported on level FOCUS STEP 4

Scenario	Day	$PEC_{act, sw}$ (µg/L)	$TWAC_{sw}$ (µg/L)	$PEC_{act, sed}$ (µg/kg)	$TWAC_{sed}$ (µg/kg)
FOCUS STEP 4, vines, variation 1		Single application 1 x 300 g as/ha to vines at 5 m buffer zone			
D6 (ditch)	21	0.021	0.275	1.830	2.511
R1 (stream)	21	< 0.001	0.029	0.430	0.485
R2 (stream)	21	< 0.001	0.023	0.941	1.002
R3 (stream)	21	< 0.001	0.057	0.429	0.610
R4 (stream)	21	< 0.001	0.086	1.530	1.812
FOCUS STEP 4, vines, variation 1		Multiple application 3 x 300 g as/ha to vines at 5 m buffer zone			
D6 (ditch)	21	0.056	0.897	5.897	7.951

Scenario	Day	$PEC_{act, sw}$ (µg/L)	$TWAC_{sw}$ (µg/L)	$PEC_{act, sed}$ (µg/kg)	$TWAC_{sed}$ (µg/kg)
R1 (stream)	21	< 0.001	0.063	1.236	1.462
R2 (stream)	21	< 0.001	0.044	2.260	2.287
R3 (stream)	21	0.001	0.110	1.582	1.689
R4 (stream)	21	< 0.001	0.112	1.735	2.017
FOCUS STEP 4, vines, variation 1		Single application 1 x 300 g as/ha to vines at 10 m buffer zone			
D6 (ditch)	21	0.008	0.098	0.722	0.964
R1 (pond)	21	0.011	0.040	0.324	0.396
R1 (stream)	21	< 0.001	0.011	0.131	0.153
R2 (stream)	21	< 0.001	0.009	0.184	0.202
R3 (stream)	21	< 0.001	0.021	0.171	0.234
R4 (stream)	21	< 0.001	0.037	0.425	0.537
FOCUS STEP 4, vines, variation 1		Multiple application 3 x 300 g as/ha to vines at 10 m buffer zone			
D6 (ditch)	21	0.021	0.316	2.309	3.062
R1 (pond)	21	0.006	0.051	0.570	0.711
R1 (stream)	21	< 0.001	0.026	0.371	0.460
R2 (stream)	21	< 0.001	0.017	0.467	0.463
R3 (stream)	21	< 0.001	0.039	0.567	0.536
R4 (stream)	21	< 0.001	0.046	0.504	0.613

Scenario	Day	$PEC_{act, sw}$ (µg/L)	$TWAC_{sw}$ (µg/L)	$PEC_{act, sed}$ (µg/kg)	$TWAC_{sed}$ (µg/kg)
FOCUS STEP 4, vines, variation 1		Single application 1 x 300 g as/ha to vines at 20 m buffer zone			
D6 (ditch)	21	0.003	0.034	0.275	0.357
R1 (pond)	21	0.005	0.020	0.171	0.207
R1 (stream)	21	< 0.001	0.005	0.061	0.071
R2 (stream)	21	< 0.001	0.003	0.069	0.076
R3 (stream)	21	< 0.001	0.007	0.066	0.087
R4 (stream)	21	< 0.001	0.018	0.198	0.252
FOCUS STEP 4, vines, variation 3		Multiple application 3 x 300 g as/ha to vines at 20 m buffer zone			
D6 (ditch)	21	0.007	0.108	0.876	1.140
R1 (pond)	21	0.003	0.025	0.301	0.372
R1 (stream)	21	< 0.001	0.012	0.168	0.209
R2 (stream)	21	< 0.001	0.007	0.174	0.174
R3 (stream)	21	< 0.001	0.014	0.181	0.232
R4 (stream)	21	< 0.001	0.021	0.227	0.279
FOCUS STEP 4, vines, variation 3		Single application 1 x 400 g as/ha to vines late at 5 m buffer zone			
D6 (ditch)	21	0.036	0.579	3.459	4.974
R1 (pond)	21	< 0.001	0.024	0.249	0.309
R1 (stream)	21	< 0.001	0.031	0.444	0.613
R2 (stream)	21	< 0.001	0.086	0.620	1.058
R3 (stream)	21	< 0.001	0.036	0.286	0.398
R4 (stream)	21	< 0.001	0.021	0.227	0.279
FOCUS STEP 4, vines, variation 3		Single application 1 x 400 g as/ha to vines late at 10 m buffer zone			
D6 (ditch)	21	0.013	0.207	1.371	1.917
R1 (pond)	21	0.004	0.037	0.290	0.372
R1 (stream)	21	< 0.001	0.009	0.085	0.109

R2 (stream)	21	< 0.001	0.012	0.127	0.156
R3 (stream)	21	< 0.001	0.031	0.248	0.345
R4 (stream)	21	< 0.001	0.013	0.114	0.152
FOCUS STEP 4, vines, variation 3		Single application 1 x 400 g as/ha to vines late at 20 m buffer zone			
D6 (ditch)	21	0.005	0.072	0.525	0.713
R1 (pond)	21	0.002	0.019	0.154	0.194
R1 (stream)	21	< 0.001	0.003	0.036	0.044
R2 (stream)	21	< 0.001	0.004	0.051	0.062
R3 (stream)	21	< 0.001	0.011	0.096	0.137
R4 (stream)	21	< 0.001	0.005	0.044	0.056

	Water body	1 x 375 g as/ha			2 x 375 g as/ha		
		$PEC_{sw, max}$ [µg/L]	$PEC_{sed, max}$ [µg/kg]	$TWA_{sw, 21 d}$ [µg/L]	$PEC_{sw, max}$ [µg/L]	$PEC_{sed, max}$ [µg/kg]	$TWA_{sw, 21 d}$ [µg/kg]
FOCUS STEP 4, Spring cereals, 5 m buffer zone							
D1 (Lanna)	ditch	0.647	1.623	0.170	0.593	2.234	0.220
	stream	0.763	0.462	0.031	0.639	0.614	0.050
D3 (Vredepeel)	ditch	0.640	0.417	0.029	0.537	0.659	0.054
D4 (Skousbo)	pond	0.070	0.193	0.017	0.061	0.286	0.024
	stream	0.744	0.150	0.010	0.624	0.217	0.016
D5 (La Jaillière)	pond	0.070	0.268	0.025	0.065	0.370	0.031
	stream	0.730	0.034	0.002	0.629	0.061	0.004
R4 (Roujan)	stream	0.908	6.419	0.130	0.911	6.595	0.135
FOCUS STEP 4, Winter cereals, 5 m buffer zone							
D1 (Lanna)	ditch	0.647	1.623	0.170	0.593	2.234	0.220
	stream	0.763	0.462	0.031	0.639	0.614	0.050
D2 (Brimstone)	ditch	0.648	1.569	0.125	0.548	2.074	0.183
	stream	0.777	1.864	0.144	0.650	1.568	0.126
D3 (Vredepeel)	ditch	0.640	0.433	0.030	0.536	0.602	0.050
D4 (Skousbo)	pond	0.070	0.236	0.022	0.062	0.336	0.026
	stream	0.734	0.103	0.007	0.623	0.186	0.014
D5 (La Jaillière)	pond	0.070	0.300	0.029	0.071	0.455	0.037
	stream	0.694	0.022	0.001	0.633	0.058	0.004
D6 (Thiva)	ditch	0.631	0.184	0.012	0.538	0.726	0.055
R1 Weiherbach)	pond	0.070	0.449	0.027	0.102	1.036	0.054
	stream	0.568	3.386	0.033	1.258	8.887	0.098
R3 (Bologna)	stream	0.798	3.025	0.023	1.228	6.482	0.064
R4 (Roujan)	stream	0.698	3.907	0.097	1.726	9.502	0.247

	Time after max. peak [days]	PECsw [µg/L]	TWAsw [µg/L]	PECsed [µg/kg]	TWAsed [µg/kg]	PECsw [µg/L]	TWAsw [µg/L]	PECsed [µg/kg]	TWAsed [µg/kg]
spring cereals	FOCUS STEP 4 5 m buffer	D1 (Lanna), ditch single application				D1 (Lanna), stream single application			
Initial	0	0.647	-	1.623	-	0.763	-	0.462	-
Short-term	1	0.524	0.582	1.620	1.623	0.211	0.561	0.449	0.460
	2	0.427	0.527	1.612	1.622	0.008	0.316	0.431	0.454
	4	0.290	0.440	1.582	1.619	0.001	0.159	0.399	0.439
Long-term	7	0.175	0.349	1.514	1.610	< 0.001	0.091	0.359	0.418
	14	0.073	0.231	1.348	1.570	< 0.001	0.046	0.292	0.375
	21	0.033	0.170	1.215	1.514	< 0.001	0.031	0.249	0.342
	28	0.020	0.134	1.112	1.455	< 0.001	0.023	0.219	0.316
	42	0.011	0.094	0.967	1.346	< 0.001	0.016	0.180	0.278
	50	0.008	0.081	0.907	1.291	< 0.001	0.013	0.165	0.261
	100	0.002	0.043	0.694	1.059	< 0.001	0.007	0.118	0.200
spring cereals	FOCUS STEP 4 5 m buffer	D3 (Vredepeel), ditch single application				D4 (Skousbo) pond, single application			
Initial	0	0.640	-	0.417	-	0.070	-	0.193	-
Short-term	1	0.250	0.460	0.406	0.415	0.058	0.064	0.193	0.193
	2	0.025	0.285	0.390	0.411	0.047	0.058	0.192	0.193
	4	0.001	0.146	0.362	0.399	0.032	0.048	0.188	0.193
Long-term	7	0.001	0.084	0.328	0.381	0.018	0.038	0.180	0.191
	14	< 0.001	0.042	0.269	0.344	0.005	0.024	0.160	0.186
	21	< 0.001	0.029	0.231	0.315	0.002	0.017	0.143	0.180
	28	< 0.001	0.022	0.204	0.292	0.001	0.013	0.130	0.172
	42	< 0.001	0.014	0.169	0.258	< 0.001	0.009	0.111	0.159
	50	< 0.001	0.012	0.155	0.243	< 0.001	0.008	0.103	0.152
	100	< 0.001	0.006	0.111	0.187	< 0.001	0.004	0.077	0.122
spring cereals	FOCUS STEP 4 5 m buffer	D4 (Skousbo), stream single application				D5 (La Jailliere) pond, single application			
Initial	0	0.744	-	0.150	-	0.070	-	0.268	-

Short-term	1	< 0.001	0.198	0.145	0.148	0.063	0.066	0.268	0.268
	2	< 0.001	0.099	0.140	0.146	0.056	0.063	0.266	0.268
	4	< 0.001	0.050	0.131	0.141	0.045	0.057	0.262	0.267
Long-term	7	< 0.001	0.028	0.119	0.135	0.030	0.048	0.253	0.266
	14	< 0.001	0.014	0.099	0.122	0.011	0.034	0.229	0.261
	21	< 0.001	0.010	0.085	0.113	0.005	0.025	0.207	0.253
	28	< 0.001	0.007	0.075	0.105	0.003	0.020	0.189	0.245
	42	< 0.001	0.005	0.062	0.093	< 0.001	0.014	0.161	0.228
	50	< 0.001	0.004	0.057	0.087	< 0.001	0.012	0.150	0.219
	100	< 0.001	0.002	0.040	0.067	< 0.001	0.006	0.108	0.177

spring cereals	FOCUS STEP 4 5 m buffer	D5 (La Jailliere), stream single application				R4 (Roujan), stream multiple application			
Initial	0	0.730	-	0.034	-	0.911	-	6.595	-
Short-term	1	< 0.001	0.046	0.033	0.033	0.891	0.855	6.583	6.590
	2	< 0.001	0.023	0.032	0.033	0.267	0.735	6.572	6.585
	4	< 0.001	0.012	0.031	0.032	0.002	0.381	6.551	6.574
Long-term	7	< 0.001	0.007	0.029	0.031	0.681	0.280	6.519	6.559
	14	< 0.001	0.003	0.025	0.029	0.001	0.202	6.499	6.527
	21	< 0.001	0.002	0.022	0.027	< 0.001	0.135	6.433	6.509
	28	< 0.001	0.002	0.019	0.025	< 0.001	0.105	6.372	6.488
	42	< 0.001	0.001	0.016	0.023	< 0.001	0.070	6.261	6.478
	50	< 0.001	0.001	0.015	0.022	< 0.001	0.059	6.203	6.461
	100	< 0.001	< 0.001	0.010	0.017	< 0.001	0.030		6.337
winter cereals	FOCUS STEP 4 5 m buffer	D4 (Skousbo) stream, single application				D5 (La Jailliere), pond multiple application			
Initial	0	0.734	-	0.103	-	0.071	-	0.455	-
Short-term	1	< 0.001	0.137	0.100	0.102	0.064	0.067	0.454	0.455
	2	< 0.001	0.069	0.097	0.101	0.058	0.064	0.452	0.455
	4	< 0.001	0.034	0.091	0.098	0.047	0.058	0.445	0.454

Long-term	7	< 0.001	0.020	0.084	0.094	0.035	0.051	0.430	0.452
	14	< 0.001	0.010	0.070	0.085	0.015	0.037	0.390	0.443
	21	< 0.001	0.007	0.061	0.079	0.007	0.037	0.354	0.431
	28	< 0.001	0.005	0.054	0.074	0.004	0.034	0.324	0.417
	42	< 0.001	0.003	0.045	0.065	0.002	0.025	0.278	0.389
	50	< 0.001	0.003	0.041	0.062	0.001	0.021	0.259	0.375
	100	< 0.001	0.001	0.029	0.048	< 0.001	0.011	0.190	0.307
	Time after max. peak [days]	PEC_{sw} [µg/L]	TWA_{sw} [µg/L]	PEC_{sed} [µg/kg]	TWA_{sed} [µg/kg]	PEC_{sw} [µg/L]	TWA_{sw} [µg/L]	PEC_{sed} [µg/kg]	TWA_{sed} [µg/kg]
winter cereals	FOCUS STEP 4 5 m buffer	D1 (Lanna), ditch single application				D1 (Lanna), stream single application			
Initial	0	0.647	-	1.623	-	0.763	-	0.462	-
Short-term	1	0.524	0.582	1.620	1.623	0.211	0.561	0.449	0.460
	2	0.427	0.527	1.612	1.622	0.008	0.316	0.431	0.454
	4	0.290	0.440	1.582	1.619	0.001	0.159	0.399	0.439
Long-term	7	0.175	0.349	1.514	1.610	< 0.001	0.091	0.359	0.418
	14	0.073	0.231	1.348	1.570	< 0.001	0.046	0.292	0.375
	21	0.033	0.170	1.215	1.514	< 0.001	0.031	0.249	0.342
	28	0.020	0.134	1.112	1.455	< 0.001	0.023	0.219	0.316
	42	0.011	0.094	0.967	1.346	< 0.001	0.016	0.180	0.278
	50	0.008	0.081	0.907	1.291	< 0.001	0.013	0.165	0.261
	100	0.004	0.043	0.701	1.059	< 0.001	0.007	0.118	0.200
winter cereals	FOCUS STEP 4 5 m buffer	D2 (Brimstone), ditch single application				D2 (Brimstone), stream single application			
Initial	0	0.648	-	1.569	-	0.777	-	1.864	-
Short-term	1	0.530	0.586	1.494	1.552	0.636	0.703	1.768	1.843
	2	0.437	0.533	1.428	1.533	0.524	0.640	1.681	1.819
	4	0.304	0.449	1.314	1.493	0.365	0.539	1.533	1.769

Long-term	7	0.003	0.359	1.175	1.433	< 0.001	0.428	1.357	1.692
	14	0.006	0.182	0.995	1.304	< 0.001	0.214	1.101	1.526
	21	0.016	0.125	0.909	1.205	0.011	0.144	0.992	1.392
	28	0.014	0.098	0.842	1.134	0.013	0.111	0.918	1.296
	42	0.008	0.069	0.740	1.031	0.008	0.078	0.810	1.165
	50	0.007	0.059	0.696	0.986	0.007	0.067	0.762	1.109
	100	0.002	0.031	0.526	0.801	0.003	0.035	0.578	0.893
winter cereals	FOCUS STEP 4 5 m buffer	D3 (Vredepeel), ditch single application				D4 (Skousbo) pond, single application			
Initial	0	0.640	-	0.433	-	0.070	-	0.236	-
Short-term	1	0.264	0.473	0.422	0.431	0.062	0.066	0.235	0.236
	2	0.027	0.296	0.406	0.427	0.054	0.062	0.234	0.235
	4	0.001	0.151	0.377	0.415	0.039	0.054	0.230	0.235
Long-term	7	0.001	0.087	0.340	0.396	0.024	0.044	0.222	0.234
	14	< 0.001	0.044	0.279	0.357	0.009	0.030	0.201	0.229
	21	< 0.001	0.030	0.239	0.327	0.004	0.022	0.181	0.222
	28	< 0.001	0.022	0.210	0.303	0.002	0.017	0.164	0.214
	42	< 0.001	0.015	0.174	0.267	< 0.001	0.012	0.140	0.199
	50	< 0.001	0.013	0.160	0.251	< 0.001	0.010	0.130	0.191
	100	< 0.001	0.006	0.114	0.193	< 0.001	0.005	0.095	0.154

	Time after max. peak [days]	PEC_{sw} [µg/L]	TWA_{sw} [µg/L]	PEC_{sed} [µg/kg]	TWA_{sed} [µg/kg]	PEC_{sw} [µg/L]	TWA_{sw} [µg/L]	PEC_{sed} [µg/kg]	TWA_{sed} [µg/kg]
winter cereals	FOCUS STEP 4 5 m buffer	D5 (La Jailliere), stream single application				D6 (Thiva), ditch single application			
Initial	0	0.694	-	0.022	-	0.631	-	0.184	-
Short-term	1	< 0.001	0.030	0.021	0.021	0.009	0.243	0.179	0.183
	2	< 0.001	0.015	0.021	0.021	< 0.001	0.123	0.173	0.180
	4	< 0.001	0.007	0.020	0.021	< 0.001	0.061	0.161	0.175

Long-term	7	< 0.001	0.004	0.018	0.020	< 0.001	0.035	0.148	0.167
	14	< 0.001	0.002	0.016	0.019	< 0.001	0.018	0.124	0.152
	21	< 0.001	0.001	0.014	0.017	< 0.001	0.012	0.108	0.140
	28	< 0.001	0.001	0.013	0.016	< 0.001	0.009	0.097	0.131
	42	< 0.001	< 0.001	0.011	0.015	< 0.001	0.006	0.082	0.117
	50	< 0.001	< 0.001	0.010	0.014	< 0.001	0.005	0.076	0.111
	100	< 0.001	< 0.001	0.007	0.011	< 0.001	0.003	0.055	0.088
winter cereals	FOCUS STEP 4 5 m buffer	R1 (Weiherbach), pond multiple application				R1 (Weiherbach), stream multiple application			
Initial	0	0.102	-	1.036	-	1.258	-	8.887	-
Short-term	1	0.090	0.096	1.034	1.035	< 0.001	0.667	8.828	8.868
	2	0.077	0.091	1.031	1.035	< 0.001	0.334	8.770	8.842
	4	0.056	0.080	1.019	1.034	0.004	0.167	8.663	8.787
Long-term	7	0.035	0.066	0.993	1.030	< 0.001	0.163	8.525	8.710
	14	0.014	0.063	0.925	1.015	0.038	0.125	8.263	8.556
	21	0.007	0.054	0.872	0.992	< 0.001	0.098	8.057	8.428
	28	0.026	0.052	0.826	0.985	< 0.001	0.078	8.024	8.345
	42	0.004	0.044	0.776	0.980	< 0.001	0.062	8.009	8.201
	50	0.003	0.040	0.742	0.966	< 0.001	0.054	7.818	8.157
	100	0.005	0.025	0.697	0.865	< 0.001	0.031	7.746	7.935
winter cereals	FOCUS STEP 4 5 m buffer	R3 (Bologna), stream multiple application				R4 (Roujan), stream multiple application			
Initial	0	1.228	-	6.482	-	1.726	-	9.502	-
Short-term	1	0.233	1.040	6.409	6.464	1.632	1.567	9.320	9.446
	2	0.004	0.549	6.333	6.433	0.490	1.366	9.148	9.372
	4	0.003	0.276	6.199	6.364	0.003	0.707	8.851	9.248
Long-term	7	0.002	0.159	6.034	6.268	1.226	0.543	8.496	9.071
	14	0.001	0.096	5.753	6.160	0.002	0.370	7.919	8.906
	21	< 0.001	0.064	5.557	6.112	0.001	0.247	7.541	8.635
	28	0.001	0.066	6.035	6.058	< 0.001	0.189	7.264	8.392
	42	0.001	0.056	6.088	6.000	< 0.001	0.126	6.854	8.007
	50	< 0.001	0.052	5.859	5.997	< 0.001	0.106	6.663	7.832
	100	< 0.001	0.028	5.224	5.735	< 0.001	0.054	6.380	7.097

PEC ground water (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUSgw modelling, values used - Modelling using FOCUS model(s), with appropriate $FOCUS_{gw}$ scenarios, according to FOCUS guidance. Model(s) used: (with version control no.(s)) FOCUS PELMO 3.2.2 and FOCUS PEARL 3.3.3 Crop: cereals, vines Parent: DT_{50} soil (d): 60.5 days (geometric mean, Lab. n=4)** K_{OC}: arithmetic mean 2415, $^1/_n$ = 0.82. Metabolite KWG 4168-desethyl (M01): Geometric mean $DT_{50field}$ 33.9 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). average formation fraction: 23%*** K_{OC}: arithmetic mean 4816, $^1/_n$ = 0.85. Metabolite KWG 4168-despropyl (M02): Geometric mean $DT_{50field}$ 33.4 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). average formation fraction: 25 %*** K_{OC}: arithmetic mean 4165, $^1/_n$ = 0.88. **Metabolite KWG 4168-N-oxide (M03): no PECgw available, data required** no lysimeter studies performed
	** due to the worst case character no updated recalculation was performed on the basis of the re-evaluated endpoint for modelling 45.0 d derived from the slow phase of DFOP kinetics (filed studes, n=18) *** although the average formation fractions were determined to 23% and 25% for metabolite M01 and M02, respectively the PECgw calculations were performed using average formations fractions of 22% and 23% for metabolite M01 and M02, respectively. It is not expected that minor changes would have a serious impact on the outcome of the PECgw calculations for metabolite M01 and M02.

Application rate	Crop: vines, variation 1 Crop interception: 50 /50 /60 Number of applications: 3 Interval (d): 10 Application rate(s): 3 * 300 g as/ha Application window: BBCH 13-85 Application dates: 07-Sep, 17-Sep, 27-Sep
Application rate	Crop: vines, variation 2 Crop interception: 50 /50 Number of applications: 2 Interval (d): 7 Application rate(s): 2 * 200 g as/ha Application window: BBCH 13-19 Application dates: 11-Apr, 18-Apr
Application rate	Crop: vines, variation 3 Crop interception: 85 / 85 /85 Number of applications: 3 Interval (d): 10 Application rate(s): 3 * 400 g as/ha Application window: BBCH 79-85 Application dates: 07-Sep, 17-Sep, 27-Sep
Application rate	Crop: vines, variation 4 Crop interception: 50 / 50 / 85 / 85 /85 Number of applications: 2 + 3 Interval (d): 10 / 10 Application rate(s): 2 * 200 + 3 * 400 g as/ha Application window: BBCH 13-19 and BBCH 79-85 Application dates: 11-Apr, 18-Apr, 07-Sep, 17-Sep, 27-Sep
Application rate	Crop: cereals, variation 1 Crop interception: 70 / 70 Number of applications: 2 Interval (d): 14 Application rate(s): 2 * 375 g as/ha Application window: BBCH 30 Application dates: 01-Apr, 15-Apr

Application rate	Crop: cereals, variation 2 Crop interception: 70 /70 Number of applications: 2 Interval (d): 14 Application rate(s): 2 * 375 g as/ha Application window: BBCH 30-69 (wheat, rye triticale) BBCH 30-61 (barley) Application dates: 10-Apr, 24-Apr

PEC_{gw} - FOCUS modelling results (80^{th} percentile annual average concentration at 1 m)

	Parent (µg/L)	Metabolite (µg/L)	
FOCUS PELMO and FOCUS PEARL vines, all variations		KWG 4168-desethyl (M01)	KWG 4168-despropy (M02)
	<0.0001	<0.0001	<0.0001
	<0.0001	<0.0001	<0.0001
	<0.0001	<0.0001	<0.0001
	<0.0001	<0.0001	<0.0001
	<0.0001	<0.0001	<0.0001
	<0.0001	<0.0001	<0.0001
	<0.0001	<0.0001	<0.0001

PEC_{gw} - FOCUS modelling results (80^{th} percentile annual average concentration at 1 m)

	Scenario	Parent (µg/L)	Metabolite (µg/L)	
FOCUS PELMO and FOCUS PEARL cereals, all variations			KWG 4168-desethyl (M01)	KWG 4168-despropyl (M02)
	Chateaudun	< 0.001	< 0.001	< 0.001
	Hamburg	< 0.001	< 0.001	< 0.001
	Jokioinen	< 0.001	< 0.001	< 0.001
	Kremsmunster	< 0.001	< 0.001	< 0.001
	Okehampton	< 0.001	< 0.001	< 0.001
	Piacenza	< 0.001	< 0.001	< 0.001
	Porto	< 0.001	< 0.001	< 0.001
	Sevilla	< 0.001	< 0.001	< 0.001
	Thiva	< 0.001	< 0.001	< 0.001

$PEC_{(gw)}$ From lysimeter / field studies no studies performed

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

Direct photolysis in air ‡	The chemical lifetime of spiroxamine in the troposphere according to the procedure described by Atkinson was in the range of one to three hours, with respect to the OH-radical reaction only. On account of the relatively short chemical lifetime of spiroxamine in the air it is not to be expected that the active ingredient can be transported in gaseous phase over large distances or can accumulate in the air.
Quantum yield of direct phototransformation	The quantum yield of direct photo-degradation of spiroxamine was determined according to the ECETOC-method. The quantum yield was calculated to be only 0.00064. Direct photodegradation in water contributes to the overall elimination of spiroxamine in the environment to a very low extent, only.
Photochemical oxidative degradation in air ‡	DT_{50}air < 3 h (12-hr day; $1.5*10^6$ OH/cm^3) The chemical stability of Spiroxamine in air is predominantly determined by hydrogen abstractions caused by OH-radicals. It is to be expected that the attack at the different parts of the Spiroxamine molecule results in the formation of various primary radicals leading to secondary oxidation products, which can be eliminated from the air by wet and/or dry deposition.
Volatilisation ‡	The total vapour pressure of Spiroxamine was calculated as 9.7 x 10-3 Pa 20 °C. The volatilisation rate from a simulated winter wheat field, including soil, with different weather scenarios was on average 24 % within the measuring period of 24 hours.
Metabolites	None

PEC_{air}

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	negligible for long range transport, short range transport via volatilisation / deposition should be considred in risk assessment at member state level.

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: spiroxamine, KWG 4168-desethyl (M01), KWG 4168-despropyl (M02) * Surface water: spiroxamine, KWG 4168 acid (M06) KWG 4168-N-oxide (M03)

Sediment: spiroxamine Ground water: spiroxamine, KWG 4168-desethyl (M01), KWG 4168-despropyl (M02), KWG 4168-N-oxide (M03) Air: spiroxamine

* KWG 4168-N-oxide (M03) was found in laboratory degradation studies < 10% but 2*>5 % AR and was not investigated in the field degradation studies. RMS performed a risk assessment for soil organisms (earthworms) for KWG 4168-N-oxide (M03).

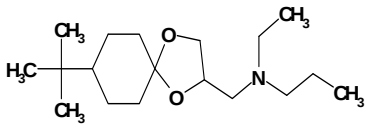
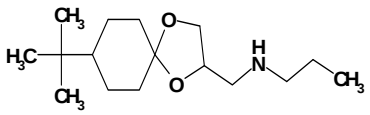
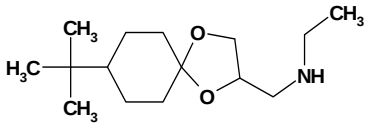
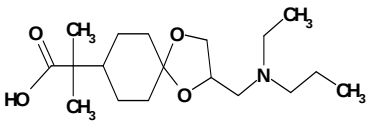
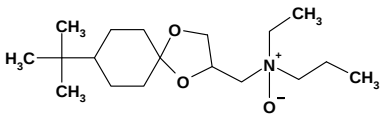
Monitoring data, if available (Annex IIA, point 7.4)

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

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

Prerequisite for chronic categories are met.

Appendix 1 - Compound code(s) used in the list of endpoints

Code/Trivial name	Structural formula
Spiroxamine Spiroxamine (parent substance)	
KWG 4168 - desethyl (code: M01)	
KWG 4168 - despropyl (code: M02)	
KWG 4168 – acid (code: M06)	
KWG 4168-N-oxid (code:M03)	

Appendix III.6: Chapter 6 (effects on non-target species)

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

Species	Test substance	Time scale	Endpoint (mg/kg bw/day)	Endpoint (mg/kg feed)
Birds ‡				
Colinus virginianus	Spiroxamine	Acute	LD_{50} = 565	---
Colinus virginianus	Spiroxamine EC500 (491.4 g ai/L)	Acute	LD_{50} = 971 product LD_{50} = 477 as	---
Colinus virginianus	Spiroxamine	Short-term	LDD_{50} > 358	LC_{50} >5000
Anas platyrhynchos	Spiroxamine	Short-term	LDD_{50} = 874	LC_{50} >5000
Colinus virginianus	Spiroxamine	Long-term	NOEL = 2.02 NOAEL = 5.4	NOEC = 29.3 NOAEC = 78.6
Anas platyrhynchos	Spiroxamine	Long-term	NOEL = 10.6	NOEC = 78.6
Mammals ‡				
rat	Spiroxamine	Acute	LD_{50}>500<560 (f)	---
mouse	Spiroxamine	Acute	LD_{50} ~ 460 (m)	---
rat	Spiroxamine EC 500	Acute	LD_{50} ~1000 (m) LD_{50} >200<1000 (f)	---
rat	Prothioconazole & Spiroxamine EC 460	Acute	LD_{50} = 750	---
rat	Spiroxamine	Long-term	NOEL = 9.19	NOEC = 80
rat	Spiroxamine	Long-term	NOEL = 22.2	NOEC = 300
Additional higher tier studies ‡				

[1] NOEL of 2.02 mg/kg bw/d was used for the TIER-1 assessment, whereas the NOAEL of 5.40 mg/kg bw/d was used in the refined risk assessment

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

Crop and application rate

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds) – European use pattern in grapes				
Insectivorous birds (10 g)	Acute	16.2	29.4	10
Insectivorous birds (10 g)	Short-term	9.05	>40	10
Insectivorous birds (10 g)	Long-term	9.05	0.22	5
Tier 1 (Birds) – specific countries use pattern in grapes				
Insectivorous birds (10 g)	Acute	21.6	22.1	10
Insectivorous birds (10 g)	Short-term	12.1	>30	10
Insectivorous birds (10 g)	Long-term	12.1	0.17	5
Tier 1 (Birds) – application in cereals (early)				
Large herbivorous birds (3000 g)	Acute	28.1	20	10
Large herbivorous birds (3000 g)	Short-term	17.6	>20	10
Large herbivorous birds (3000 g)	Long-term	9.305	0.2	5
Insectivorous birds (10 g)	Acute	20.280	28	10
Insectivorous birds (10 g)	Short-term	11.310	>32	10
Insectivorous birds (10 g)	Long-term	11.310	0.2	5
Tier 1– uptake via drinking water (Birds) - application in grapes				
insectivorous bird	Acute	0.004	500,000	10
Tier 1 – secondary poisoning (Birds) – application in grapes				
Earthworm-eating bird	Long-term (European use /specific countries use)	1.14 / 0.96	4.7 / 5.6	5
Fish-eating bird	Long-term (European use /specific countries use pattern)	0.027 / 0.018	197 / 307	5
Tier 1 – secondary poisoning (Birds) - application in cereals				
Earthworm-eating bird	Long-term	0.625	8.6	5
Fish-eating bird	Long-term	0.0158	341	5

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Higher tier refinement (Birds) - European use pattern in grapes				
Great tit (19 g) Black redstart (16.5 g) Linnet (15.3 g) Woodlark (28.5 g)	Long-term	0.18 0.59 0.80/0.64/0.48 0.50	30.4[1] 9.2 6.7/8.4/11.2[3] 10.8	5
Higher tier refinement (Birds) - specific countries use pattern in grapes				
Great tit (19 g) Black redstart (16.5 g) Linnet (15.3 g) Woodlark (28.5 g)	Long-term	0.24 0.79 0.64 0.63	22.8[1] 6.9[2] 8.4[3] 8.5[4]	5
Higher tier refinement (Birds) – application in cereals (early)				
Large herbivorous birds (goose)	Long-term	0.306	18 [5]	5
omnivorous birds (quail, 100 g)	Long-term	0.656	8.23 [6]	5
omnivorous birds (lark, 37.2 g)	Long-term	0.624	8.65 [7]	5
insectivorous birds (yellow wagtail, 17 g)	Long-term	0.47	11.5 [8]	5
Tier 1 (Mammals) - European use pattern				
Small herbivorous mammals	Acute	53.2	8.6	10
Small herbivorous mammals	Long-term	10.2	0.90	5
Tier 1 (Mammals) – specific countries use pattern				
Small herbivorous mammals	Acute	70.9	6.5	10
Small herbivorous mammals	Long-term	13.6	0.67	5
Tier 1 (Mammals) – application in cereals (early)				
Small herbivorous mammals	Acute	88.8	8.6	10
Small herbivorous mammals	Long-term	29.4	0.3	5
Insectivorous mammals	Acute	3.31	139	10
Insectivorous mammals	Long-term	1.21	7.6	5
Tier 1– uptake via drinking water (Mammals) – application in grapes				
insectivorous bird	Acute	0.003	153,333	10
Tier 1 – secondary poisoning (Mammals) - application in grapes				
Earthworm-eating mammals	Long-term (European use /specific countries use)	1.453 / 1.225	15.3 / 18.1	5

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Fish-eating mammals	Long-term (European use /specific countries use)	0.017 / 0.011	1306 / 2036	5
Tier 1 – secondary poisoning (Mammals) - application in cereals				
Earthworm-eating mammals	Long-term	0.568	27.9	5
Fish-eating mammals	Long-term	0.00891	2492	5
Higher tier refinement (Mammals)				
Small herbivorous mammals	Acute	16.26	28 [9]	10
Small herbivorous mammals	Long-term	3.473	6.5 [10]	5

[1] refinements used: DT_{50} (insects) = 3.38 d, FIR/bw = 0.85, MAF×TWA = 0.48 (21 d interval), PT = 0.05

[2] refinements used: RUD = 17, DT_{50} (insects) = 3.38 d, FIR/bw = 0.86, MAF×TWA = 0.48 (21 d interval), PT = 0.28

[3] refinements used: DT_{50} (weed seeds) = 4.0 d, FIR/bw = 0.31, MAF×TWA = 0.55 (21 d interval) PT = 0.78, Intercept. = 50-70 %

[4] refinements used: DT_{50} (insects) = 3.38 d, DT_{50} (weed seeds) = 4 d, FIR/bw (invertebrates) = 0.76, FIR/bw (seeds) = 0.25, MAF×TWA = 0.48 (invertebrates; 21 d interval), MAF×TWA = 0.55 (seeds; 21 d interval), PT = 0.86, PD (invertebrates) = 92.1 %, PD (seeds) = 7.9 %, Intercept. (weed seeds) = 50-70 %

[5] refinements used: FIR/bw = 0.44, residues = 11.7 mg/kg, f_{twa} = 0.332, PT = 0.18

[6] refinements used: FIR/bw = 0.93 (plant) / 0.37 (arthropods), RUD = 5.1 (arthropods), residues = 11.7 (plant) mg/kg, f_{twa} = 0.332 (plant) / 0.21 (arthropods), PT = 0.65, PD = 0.25 (plants) / 0.75 (arthropods)

[7] refinements used: FIR/bw = 1.06 (plants) / 0.23 (seeds) / 0.7 (arthropods), RUD = 5.1 (arthropods), residues = 11.7 (plants and seeds) mg/kg, f_{twa} = 0.332 (plant and seeds) / 0.21 (arthropods), PT = 0.5 (plants and seeds) / 0.5 (arthropods)

[8] refinements used: FIR/bw = 0.88, f_{twa} = 0.21, PT = 0.4, PD = 0.5

[9] refinements used: residues = 11.7 mg/kg (plants)

[10] refinements used: residues = 11.7 mg/kg (plants), PT = 0.64, f_{twa} = 0.3302

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)	Endpoint	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Danio rerio	Spiroxamine	96 h (static)	Mortality, LC_{50}	2.41 $_{nom}$
Danio rerio	Spiroxamine	230 d (flow-through)	FLC, Mortality F1-ELS, NOEC/EC_{10}	0.002 $_{nom}$
Oncorynchus mykiss	Spiroxamine	93 d (flow-through)	ELS, EC_0	0.014 $_{based\ on\ nom\ NOEC\ values}$
Oncorynchus mykiss	Spiroxamine EC 500	96 h (static)	Mortality, LC_{50}	5.62 as $_{mm}$ 11.5 prepar.
Oncorynchus mykiss	Prothioconazole & Spiroxamine EC 460	96 h (static)	Mortality, LC_{50}	6.57 preparation $_{nom}$
Aquatic invertebrate				
Daphnia magna	Spiroxamine	48 h (flow-through)	Immobilisation, EC_{50}	3.0 $_{mm}$
Daphnia magna	Spiroxamine	21 d (flow-through)	Reproduction, NOEC	0.034 $_{nom}$
Daphnia magna	Spiroxamine EC 500	48 h (static)	Immobilisation, EC_{50}	5.1 as $_{nom}$ 10.3 prep
Daphnia magna	Prothioconazole & Spiroxamine EC 460	48 h (static)	Immobilisation, EC_{50}	6.3 preparation $_{mm}$
Daphnia magna	Metabolite KWG 4168-N-oxide (M03)	48 h (static)	Immobilisation, EC_{50}	> 100 $_{nom}$
Sediment dwelling organisms				
Chironomus riparius	Spiroxamine	28 d (static) spiked water	NOEC	5.6 $_{nom}$
Chironomus riparius	Spiroxamine EC 500	28 d (static), spiked water	NOEC	≥ 0.0025 as $_{mm}$
Algae				
Skeletonema costatum	^{14}C-Spiroxamine	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.0013 as $_{nom}^2$ 0.0063 as $_{nom}^2$
Desmodesmus subspicatus	Spiroxamine	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.0032 $_{nom}^2$ 0.012
Desmodesmus subspicatus	Spiroxamine EC 500	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50} Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.0059 as $_{nom}$ 0.0143 0.012 prep 0.029

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg/L)
Pseudokirchneriella subcapitata	Prothioconazole & Spiroxamine EC 460		Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.015 prep $_{nom}$ 0.16
Desmodesmus subspicatus	Metabolite KWG 4168-N-oxide (M03)	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	9.98 $_{nom}$ 31.68
Desmodesmus subspicatus	Metabolite KWG 4168-desethyl (M01)	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.133 $_{nom}$ 0.737
Desmodesmus subspicatus	Metabolite KWG 4168-acid (M06)	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	>3.2 $_{nom}$ >3.2 $_{nom}$
Higher plant				
Lemna gibba	Spiroxamine	7 d (static)	Fronds, Yield EC_{50} Growth rate: E_rC_{50}	3.02 $_{mm}$ 6.78
	Prothioconazole & Spiroxamine EC 460	7 d (static)	Fronds, E_bC_{50}	0.039 prep $_{nom}$ 0.057
Mesocosm tests: Preparation Spiroxamine EC 500, 3 applications, 7 day interval, 84 d after treatment, static: Effects on phytoplankton, zooplankton, macrophytes: NOAEAC(3 x) 9.3 µg as/L $_{nom\ (measured\ initial)}$, only for use in spring with 3 applications with 7 day interval. NOEC (3x) 1.0 µg as/L $_{nom\ (measured\ initial)}$				

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

[2] nominal = measured initial concentration

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

FOCUS Step 2

1) Spiroxamine EC 500:

European use pattern: Vines, grapes, 1-3 x 300 g as/ha, BBCH 13-85,
Specific countries use pattern: Grapes, early, 1-2 x 200 g as/ha, BBCH 13-19, and Grapes late, BBCH 79-85, 2-3 x 300-400 g as/ha. Maximum $PEC_{sw\ max}$ value for 3 x 300 g as/ha, European use pattern

Test substance	N/S[1]	Organism[2]	Toxicity endpoint (mg/L)	Time scale	PEC[3] max (µg/L)	TER	Annex VI Trigger[4]
Spiroxamine	S	Fish	2.41	Acute	13.48	179	100
Spiroxamine	S	Fish	0.002	Chronic	13.48	0.15	10
Spiroxamine	S	Aquatic invertebrates	3.0	Acute	13.48	223	100
Spiroxamine	S	Aquatic invertebrates	0.034	Chronic	13.48	2.5	10
Spiroxamine	S	Algae (marine diatom)	0.0013	Chronic	13.48	0.1	10
Spiroxamine	S	Higher plants[5]	3.02	Chronic	13.48	224	10

Test substance	N/S[1]	Organism[2]	Toxicity endpoint (mg/L)	Time scale	PEC[3] max (µg/L)	TER	Annex VI Trigger[4]
Spiroxamine	S	Sediment-dwelling organisms[6], water spiked	5.6	Chronic	13.48	415	10
Metabolite KWG 4168-N-oxide (M03)	S	Algae	9.98	Chronic	13.48 [7]	740	10
Metabolite KWG 4168-desethyl (M01)	S	Algae	0.133	Chronic	0.59	225	10
Metabolite KWG 4168-acid (M06)	S	Algae	3.2	Chronic	9.44	339	10
Spiroxamine E C 500	S	Algae	0.0059 as	Chronic	13.48 as	0.4	10
Spiroxamine EC 500	S	Mesocosm	0.001 as	Chronic	13.48 as	0.07	2

2) Prothioconazole & Spiroxamine EC 460:
Cereals, 2 x 200 g Prothioconazole/ha and 375 g Spiroxamine/ha, BBCH 30-69
Maximum PECsw max value for 1 x 375 g as/ha,

Test substance	N/S[1]	Organism[2]	Toxicity endpoint (mg/L)	Time scale	PEC[3] max (µg/L)	TER	Annex VI Trigger[4]
Spiroxamine	S	Fish	2.41	Acute	10.15	237	100
Spiroxamine	S	Fish	0.002	Chronic	10.15	0.2	10
Spiroxamine	S	Aquatic invertebrates	3.0	Acute	10.15	296	100
Spiroxamine	S	Aquatic invertebrates	0.034	Chronic	10.15	3.3	10
Spiroxamine	S	Algae	0.0013	Chronic	10.15	0.13	10
Spiroxamine	S	Higher plants[5]	3.02	Chronic	10.15	298	10
Spiroxamine	S	Sediment-dwelling organisms[6], water spiked	5.6	Chronic	10.15	552	10
Spiroxamine (as Spiroxamine EC 500)	S	Mesocosm	0.001 as	Chronic	10.15 as	0.1	2
Metabolite KWG 4168-N-oxide (M03)	S	Algae	9.98	Chronic	10.15 [7]	983	10
Metabolite KWG 4168-desethyl (M01)	S	Algae	0.133	Chronic	0.43	309	10

Test substance	N/S[1]	Organism[2]	Toxicity endpoint (mg/L)	Time scale	PEC[3] max (µg/L)	TER	Annex VI Trigger[4]
Metabolite KWG 4168-acid (M06)	S	Algae	3.2	Chronic	2.09	1531	10
Prothioconazole & Spiroxamine EC 460	S	Algae	0.015 preparation	Chronic	11.5 [8] preparation	1.3	10

[1] indicate whether Northern or Southern
[2] include critical groups which fail at Step 1.
[3] indicate whether maximum or twa values have been used.
[4] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.
[5] only required for herbicides
[6] consider the need for PEC_{sw} and PEC_{sed} and indicate which has been used
[7] PEC value for parent compound was selected as worst case
8 PEC value for the preparation EC 460 is calculated based on drift only

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

1) Spiroxamine EC 500:
European use pattern: Vines, grapes, 1-3 x 300 g as/ha, BBCH 13-85; Specific countries use pattern: Grapes, early, 1-2 x 200 g as/ha, BBCH 13-19, and Grapes late, BBCH 79-85, 2-3 x 300-400 g as/ha. Maximum PECsw max value used

Scenario[1,2,3]	$PEC_{sw,max}$[4*] [µg as/L]	Fish prolonged	Invertebrates prolonged	Algae (marine diatom)	Mesocosm (Spiroxamine EC 500)	Annex VI trigger[5] (Trigger for mesocosm)
		Danio rerio EC_{10} = 2,0 µg as/L	*Daphnia magna* NOEC = 34 µg as/L	*Skeletonema costatum* EbC_{50} = 1.3µg as/L	NOEC = 1.0 µg as/L	
European use pattern						
D6 /ditch	5,09	0,4	6,7	0.3	0.2	10 (2)
R1 /pond	0,182	11	187	7.1	5.5	10 (2)
R1 /stream	3,671	0,5	9,3	0.4	0.3	10 (2)
R2 /stream	5,018	0,4	6,8	0.3	0.2	10 (2)
R3 /stream	5,275	0,4	6,4	0.2	0.2	10 (2)
R4 /stream	3,684	0,5	9,2	0.4	0.3	10 (2)
Specific countries use pattern						
D6 /ditch	6,834	0,3	5	0.2	0.1	10 (2)
R1 /pond	0,243	8,2	140	5.3	4.1	10 (2)
R1 /stream	4,875	0,4	7	0.3	0.2	10 (2)
R2 /stream	6,72	0,3	5,1	0.2	0.1	10 (2)
R3 /s tream	7,066	0,3	4,8	0.2	0.1	10 (2)
R4 /stream	5,011	0,4	6,8	0.3	0.2	10 (2)

2) Prothioconazole & Spiroxamine EC 460:
Cereals, 2 x 200 g Prothioconazole/ha and 375 g Spiroxamine/ha, BBCH 30-69

Scenario[1,2,3]	$PEC_{sw,max}$[4*] [µg as/L]	Fish prolonged	Invertebrates prolonged	Algae (marine diatom)	Mesocosm (Spiroxamine EC 500)	Annex VI trigger[5] (Trigger for mesocosm)
		Danio rerio	*Daphnia magna*	*Skeletonema costatum*		
		EC_{10} = 2,0 µg as/L	NOEC = 34 µg as/L	EbC_{50} = 1.3µg as/L	NOEC = 1.0 µg as/L	
D1 /ditch	2,392	0.8	14	0.5	0.4	10 (2)
D1 /stream	2,092	1.0	16	0.6	0.5	10 (2)
D2 /ditch	2,395	0.8	14	0.5	0.4	10 (2)
D2 /stream	2.131	0.9	16	0.6	0.5	10 (2)
D3 /ditch	2.355	0.8	14	0.6	0.4	10 (2)
D4 /pond	0,081	24.6	419	16.0	12.3	10 (2)
D4 /stream	2.045	1.0	17	0.6	0.5	10(2)
D5 /pond	0.081	24.6	419	16.0	12.3	10 (2)
D5 /stream	2.206	0.9	15	0.6	0.5	10(2)
D6 /ditch	2.382	0.8	14	0.5	0.4	10 (2)
R1 /pond	0.115	17.4	296	11.3	8.7	10 (2)
R1 /stream	1.554	1.3	22	0.8	0.6	10 (2)
R3 /stream	2,187*	0.9	16	0.6	0.5	10 (2)
R4 /stream	1,557*	1.3	22	0.8	0.6	10 (2)

[1] drainage (D1 - D6) and run-off (R1 - R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.
[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

* Due to only minor effects of recalculation of DT_{50} on the PEC values in single applications, PEC values for multiple application were not recalculation and therefore still based on the notifier's DT_{50}

FOCUS Step 4

1) Spiroxamine EC 500:
European use pattern: Vines, grapes, 1-3 x 300 g as/ha, BBCH 13-85,
Specific countries use pattern: Grapes, early, 1-2 x 200 g as/ha, BBCH 13-19, and Grapes late, BBCH 79-85, 2-3 x 300-400 g as/ha.
Maximum PECsw max value for 1 x 400 g as/ha, Specific countries use pattern
(related to the EC_{10} of 2.0 µg as/L)

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (µg/L)	Buffer zone distance	PEC_{sw}[4] max	TER	Annex VI trigger[5]
D6	ditch	Fish	Chronic	0.002	20 m	0.523	3.8	10
R1	pond	Fish	Chronic	0.002	20 m	0.078	26	10

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (µg/L)	Buffer zone distance	PEC_{sw}[4] max	TER	Annex VI trigger[5]
R1-R4	stream	Fish	Chronic	0.002	20 m	0.450-0.652	3.1-4.4	10

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (µg/L)	Buffer zone distance	PEC_{sw}[4] max	TER	Annex VI trigger[5]
D6	ditch	Algae	Chronic	1.3	20 m	0.523	2.5	10
R1	pond	Algae	Chronic	1.3	20 m	0.078	16.6	10
R1-	stream	Algae	Chronic		20 m	0.450-	2.9	10
R2	Stream	Algae	Chronic	1.3	20 m	0.62	2	10
R3	Stream	Algae	Chronic	1.3	20 m	0.652.	2	10
R4	Stream	Algae	Chronic	1.3	20 m	0.462	2.8	10

2) Prothioconazole & Spiroxamine EC 460:
Cereals, 2 x 200 g Prothioconazole/ha and 375 g Spiroxamine/ha, BBCH 30-69
Maximum PECsw max of value used (1 x or 2x application).
(related to the EC_{10} (fish chronic of 2.0 µg as/L)

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (mg/L)	Buffer zone distance	PEC_{sw}[4] max	TER	Annex VI trigger[5]
spring cereals								
D1	ditch	Fish	Chronic	0.002	20 m	0.177	11.3	10
D1	stream	Fish	Chronic	0.002	20 m	0.197	10.2	10
D3	ditch	Fish	Chronic	0.002	20 m	0.176	11.4	10
D4	pond	Fish	Chronic	0.002	20 m	0.034	58.8	10
D4	stream	Fish	Chronic	0.002	20 m	0.184	10.9	10
D5	pond	Fish	Chronic	0.002	20 m	0.034	58.8	10
D5	stream	Fish	Chronic	0.002	20 m	0.183	10.9	10
R4	stream	Fish	Chronic	0.002	20 m	0.381	5.2	10
Winter cereals								
D1	ditch	Fish	Chronic	0.002	20 m	0.178	11.2	10
D1	stream	Fish	Chronic	0.002	20 m	0.21	9.5	10
D2	ditch	Fish	Chronic	0.002	20 m	0.178	11.2	10
D2	stream	Fish	Chronic	0.002	20 m	0.214	9.3	10

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (mg/L)	Buffer zone distance	PEC_{sw}[4] max	TER	Annex VI trigger[5]
D3	ditch	Fish	Chronic	0.002	20 m	0.175	11.4	10
D4	pond	Fish	Chronic	0.002	20 m	0.034	58.8	10
D4	stream	Fish	Chronic	0.002	20 m	0.205		10
D5	pond	Fish	Chronic	0.002	20 m	0.034	58.8	10
D5	stream	Fish	Chronic	0.002	20 m	0.221		10
D6	ditch	Fish	Chronic	0.002	20 m	0.177	11.3	10
R1	pond	Fish	Chronic	0.002	20 m	0.034	58.8	10
R1	stream	Fish	Chronic	0.002	20 m	0.299*	6.7	10
R3	stream	Fish	Chronic	0.002	20 m	0.294*	6.8	10
R4	stream	Fish	Chronic	0.002	20 m	0.412*	4.9	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 3.

[4] indicate whether PEC_{sw}, or PEC_{sed} and whether maximum or twa values used
[5] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

* Due to only minor effects of recalculation of DT_{50} on the PEC values in single applications, PEC values for multiple application were not recalculation and therefore still based on the notifier's DT_{50}

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (mg/L)	Buffer zone distance	PEC_{sw}[4] max	TER	Annex VI trigger[5]
spring cereals								
D1	ditch	Algae	Chronic	0.0013	20 m	0.177	[7.3]	10
D1	stream	Algae	Chronic	0.0013	20 m	0.197	6.5	10
D3	ditch	Algae	Chronic	0.0013	20 m	0.176	7.3	10
D4	pond	Algae	Chronic	0.0013	20 m	0.034	38	10
D4	stream	Algae	Chronic	0.0013	20 m	0.184	7	10
D5	pond	Algae	Chronic	0.0013	20 m	0.034	38	10
D5	stream	Algae	Chronic	0.0013	20 m	0.183	7	10
R4	stream	Algae	Chronic	0.0013	20 m	0.381	3.4	10

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity endpoint (mg/L)	Buffer zone distance	PEC_{sw}[4] max	TER	Annex VI trigger[5]
Winter cereals		Algae		0.0013				
D1	ditch	Algae	Chronic	0.0013	20 m	0.178	7.3	10
D1	stream	Algae	Chronic	0.0013	20 m	0.21	6.1	10
D2	ditch	Algae	Chronic	0.0013	20 m	0.178	7.3	10
D2	stream	Algae	Chronic	0.0013	20 m	0.214	6	10
D3	ditch	Algae	Chronic	0.0013	20 m	0.175	7.4	10
D4	pond	Algae	Chronic	0.0013	20 m	0.034	38	10
D4	stream	Algae	Chronic	0.0013	20 m	0.205	6.3	10
D5	pond	Algae	Chronic	0.0013	20 m	0.034	5.8	10
D5	stream	Algae	Chronic	0.0013	20 m	0.221	7.3	10
D6	ditch	Algae	Chronic	0.0013	20 m	0.177	7.3	10
R1	pond	Algae	Chronic	0.0013	20 m	0.034	38	10
R1	stream	Algae	Chronic	0.0013	20 m	0.299*	4.3	10
R3	stream	Algae	Chronic	0.0013	20 m	0.294*	4.4	10
R4	stream	Algae	Chronic	0.0013	20 m	0.412*	3.1	10

Bioconcentration

	Spiroxamine	Metabolites
log $P_{O/W}$	diastereomer A: ph 7 2.79, pH 9 4.88 diastereomer B: ph 7 2.98, pH 9 5.08	M01 < 3 (estim.) M02 < 3 (estim.) M03 < 2 (estim.) M06 1.1 (estim.)
Bioconcentration factor (BCF)[1] ‡ whole fish	87* ^{14}C	not relevant
Annex VI Trigger for the bioconcentration factor	100	
Clearance time (days) (CT_{50})	0.55 days (at 20 µg as/L)/ 0.78 days (at 200 µg as/L)for whole fish	
(CT_{90})	-	
Level and nature of residues (%) in organisms after the 14 day depuration phase	Level at steady state: 1.64 mg/kg ^{14}C (at 20 µg as/L) 13.4 mg/kg ^{14}C (at 200 µg as/L) 94 % / 99 % of the mean measured plateau radioactivity was depurated from whole fish	

[1] only required if log $P_{O/W}$ > 3.
* based on total ^{14}C or on specific compounds

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)
Spiroxamine tech. (Bell, 1994) **	*> 100*	*4.2*
*Spiroxamine EC 500 (Bell, 1994)***	*> 12.5**	*30**
Spiroxamine EC 500 (Kleiner, 1997)	77*	> 200*
Spiroxamine EC 460 + Prothioconazol (Barth , 2001)	346*	420*
Field or semi-field tests		
Under practical conditions according to BBA Guideline VI, 23-1 (1991) no negative effects on honey bee colonies, bee brood and behaviour could be observed when a 500 g/L-Spiroxamine EC formulation was applied during bee flight in bee attractive crops at rates of 1.5 and 3.0 L /ha, respectively.		

* LD_{50} expressed in units of µg preparation/bee
** data in italic letters already discussed in line with the first Annex I inclusion

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

800 g product/ha (~ 400 g as/ha), grapes, cereals

Test substance	Route	Hazard quotient	Annex VI Trigger
Spiroxamine tech. (Bell, 1994)	~~Contact~~ oral	*< 4*	50
	contact	*95*	50
Spiroxamine EC 500 (Bell, 1994)	oral	*< 64*	50
	contact	*27*	50
Spiroxamine EC 500 (Kleiner, 1997)	oral	10	50
	contact	< 4	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	Endpoint	Effect (LR_{50} g as/ha[1]) / (LR_{50} L product/ha[1])
Typhlodromus pyri ‡	Spiroxamine EC500	Mortality	240 g as/ha
Aphidius rhopalosiphi ‡	Spiroxamine EC500	Mortality	80.1 g as/ha[1]

[1] for preparations indicate whether endpoint is expressed in units of as or preparation

Crop and application rate: Spiroxamine EC500 - grapes and 400 g as/ha, three applications

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
Spiroxamine EC500	*Typhlodromus pyri*	240	2.9	0.26	2

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
Spiroxamine EC500	*Aphidius rhopalosiphi*	80.1	8.6	0.79	2

[1]indicate distance assumed to calculate the drift rate

Further laboratory and extended laboratory studies ‡ Spiroxamine EC 500

Species	Life stage	Test substance, substrate and duration	Dose (g as/ha)[1,2]	Endpoint	% effect[3]	Trigger value
Aphidius rhopalosiphi	--	Barley plants, 48 h	100 173 300 520 900	Corrected mortality, reproduction	Mortality / reproduction 0 / 37.5 3.3 / -43.1 0 / 18.1 0 / 19 3.3 / 5.2	50 %
Coccinella septempunctata	larvae	Glass plates, 12 d preimaginal mortality; 3 weeks	90 375 750 1500	Corrected mortality, reproduction, hatching	Mortality / reproduction / hatching 9 / 10 / 4 -6 / 1 / 3 -3 / 5 / 1 56 / not assessed / not assessed	50 %
Chrysoperla carnea	larvae	Glass plates; mortality: 7 days fecundity: 4 weeks	250 400 640 1000 1600	Corrected mortality, reproduction, hatching	Mortality / reproduction /hatching 0 / n.a. / n.a. 0 / n.a. / n.a. 0 / n.a. / n.a. 0 / 9 / 7 9 / -4 / 2	50 %
Pardosa spp.	adults	Quarz sand, 18 days	2 x 750	Corrected mortality, effect on feeding rate	Mortality / feeding rate 80 / 6	50 %
Pardosa spp.	adults	Silty sand soil, 18 days	2 x 737	Corrected mortality, effect on feeding rate	Mortality / feeding rate 0 / -6	50 %

Species	Life stage	Test substance, substrate and duration	Dose (g as/ha)[1,2]	Endpoint	% effect[3]	Trigger value
Bembidion tetracolum.	4 - 8 weeks old	Quarz sand, 35 days	2 x 375 2 x 750 2 x 1500	Corrected mortality, effect on feeding rate	Mortality / feeding rate 6 / 0 45/-75 100 / 100	50 %
Bembidion tetracolum.	4 - 8 weeks old	Loamy sand soil, 35 days	2 x 750 2 x 1500	Corrected mortality, effect on feeding rate	Mortality / feeding rate 3.3 / 16 6.6 / 16	50 %

[1] indicate whether initial or aged residues
[2] for preparations indicate whether dose is expressed in units of as or preparation
[3] positive percentages relate to adverse effects

Further laboratory and extended laboratory studies Prothioconazole & Spiroxamine EC 460

Species	Life stage	Test substance, substrate and duration	Dose (L product/ ha)[1,2]	Endpoint	% effect[3]	Trigger value
Aphidius rhopalosiphi	adults	Maize plants, 14 days	2.5 L/ha 1.25 L/ha	Corrected mortality /reproduction	Mortality / reproduction 100 / - 0 / -3	50 %
Aphidius rhopalosiphi	adults	Maize plants, aged residues, 14 days for each exposure	2 x 1.25 L/ha (21 d interval)	Corrected mortality /reproduction	Mortality / reproduction DAT 0: 0 / 3 DAT 7: 0 / 9	50 %
Aphidius rhopalosiphi	< 48 h	Barley plants, aged residues, 48 h for each mortality test	3 x 1.25 L/ha (14 d interval)	Corrected mortality /reproduction	Mortality / reproduction DAT 0: 0 / 13.4 DAT 7: 3.4 / -10.6	50 %
Typhlodromus pyri	proto-nymphs	Bean leaves, 14 days	2.5 L/ha 1.25 L/ha	Corrected mortality /reproduction	Mortality / reproduction 6.3 / 6.5 2.1 / 0	50 %
Typhlodromus pyri	proto-nymphs	Maize plants, aged residues, 14 days	2 x 1.25 L/ha,	Corrected mortality /reproduction	Mortality / reproduction DAT 0: 0 / 0 DAT 7: 2 / 1.4	50 %

Species	Life stage	Test substance, substrate and duration	Dose (L product/ ha)[1,2]	Endpoint	% effect[3]	Trigger value
Coccinella semptempunctata	4 days old larvae	Bean leaves, pre-imaginal mortality: 12 - 19 days fecundity: 2 weeks	control 0.012 0.058 0.266 1.250 2.875	Corrected mortality / fertile eggs/female/day / hatching rate	Mortality / fertile eggs/female/day / hatching rate -- / 16.6 / 78.1 21.4 / 11.1 / 70.9 25.0 / 9.1 / 71.7 21.4 / 44.4 / 71.6 10.7 7 19.4 / 66.3 25.0 / 19.9 / 74.4	50 %
Aleochara bilineata	adults	Sandy soil (LUFA 2.1), 70 days	Control 0.175 0.340 0.661 1.286 2.500	parasitation rate / effect on reproduction	parasitation rate / reproduction 37.9 / -- 36.6 / 3.4 34.0 / 10.2 36.2 / 4.4 33.6 / 11.3 34.4 / 9.2	50 %

[1] indicate whether initial or aged residues
[2] for preparations indicate whether dose is expressed in units of as or preparation
[3] positive percentages relate to adverse effects

Field or semi-field tests[1]: Spiroxamine EC500
Semi field test: *A. rhopalosiphi* 750 g as/ha; pupae; emergence: 3 % effect; mortality 9.7 % effect Field test: *T. pyri*, 216, 426, 550, 667, 754, 889 mL product/ha: 1 week after 6th treatment: 5 % Field test: *T. pyri*, 302, 283, 756, 762, 735, 769 mL product/ha: 4 weeks after 6th treatment: 59 % (H&T) Field test: *T. pyri*, 300, 721, 738, 732 mL product/ha: 4 weeks after 4th treatment: 12 % (H&T) Field test: *T. pyri*, 330, 550, 660, 880 mL product/ha: 4 days after 2rd treatment: 31 %; 18 days after 3rd treatment: 25 % Field test: *T. pyri*, sum: 300, 610, 740, 890 mL product/ha:10 days after 3rd treatment: 24.2 %, 28 d after 4th treatment: 8.3 *Amblyseius aberrans*: 3 x 600; 4 weeks after 3rd treatment: 18.5 (H&T)

[1] In studies where the abundances of the populations before treatment were evaluated the effect values were corrected according to Henderson-Tilton (H&T) due to high variation of abundance between treated and control areas. Otherwise Abbott's correction was used.

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	Endpoint[1] (as = Spiroxamine)
Earthworms			
Eisenia fetida	Spiroxamine ‡	Acute 14 days	$LC_{50\ corr}$ > 500 mg as/kg d.w.soil
Eisenia fetida	Prothioconazole & Spiroxamine EC 460	Acute 14 days	$LC_{50\ corr}$ > 500 mg preparation/kg d.w.soil (> 148.6 mg as/kg d.w.soil)
Eisenia fetida	Spiroxamine EC 500	Chronic, 56 d	NOEC ≥ 3750 g as/ha (≥ 5.0 mg as/kg d.w.soil)[3]

Test organism	Test substance	Time scale	Endpoint[1] (as = Spiroxamine)
Eisenia fetida	Prothioconazole & Spiroxamine EC 460	Chronic, 56 d	NOEC = 32 mg preparation/kg d.w.soil (9.51 mg as/kg d.w.soil)
Eisenia fetida	Metabolite KWG 4168-desethyl (M01)	Chronic, 56 d	NOEC 100 mg met/kg d.w.soil
Eisenia fetida	Metabolite KWG 4168-N-oxide (M03)	Chronic, 56 d	NOEC 100 mg met/kg d.w.soil
Other soil macro-organisms			
Collembola			
Folsomia candida	Spiroxamine ‡	Chronic, 28 d	NOEC 32 mg as/kg d.w.soil
Folsomia candida	Prothioconazole & Spiroxamine EC 460	Chronic, 28 d	NOEC 10 mg preparation/kg d.w.soil NOEC 2.92 mg as/kg d.w.soil
Folsomia candida	Metabolite KWG 4168-desethyl (M01)	Chronic, 28 d	NOEC 316 mg metabolite/kg d.w.soil
Folsomia candida	Metabolite KWG 4168-despropyl (M02)	Chronic, 28 d	NOEC 316 mg metabolite/kg d.w.soil
Soil micro-organisms			
Nitrogen mineralisation	Spiroxamine EC 500	28 d	< 25 % effect at day 28 at 0.75 kg as/ha
	Spiroxamine EC 500	56 d	< 25 % effect at day 28 at 7.5 kg as/ha
	KWG 4168 -desethyl (metabolite 1)	28 d	< 25 % effect at day 28 at 3.75 kg as/ha
Carbon mineralisation	Spiroxamine EC 500	28 d	< 25 % effect at day 28 at 0.75 and 7.5 kg as/ha
Field studies[2]			
Litter bag - Spiroxamine EC 500: 57.54 g/ha (= 28.8 g as/ha) applied, simulating a plateau concentration of nom. 19.2 µg as/kg soil; additional application of 450 g as/ha; (10 days after compound application spring barley was sown and litter bags containing wheat straw buried); >88 % degradation in control after 173 days (trigger is 60 %), wheat straw degradation in treated plots (rel. to control): after 29 days: 104.6 % after 92 days: 97.8 %, after 173 days: 99.5 %			

[1] indicate where endpoint has been corrected due to log $P_{o/w}$ > 2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above and earthworm field studies
[3] considering a soil density of 1.5 g/cm³ and a depth of 5 cm

Toxicity/exposure ratios for soil organisms

1) Spiroxamine EC 500:
European use pattern: Vines, grapes, 1-3 x 300 g as/ha, BBCH 13-85; Specific countries use pattern: Grapes, early, 1-2 x 200 g as/ha, BBCH 13-19, and Grapes late, BBCH 79-85, 2-3 x 300-400 g as/ha.
Maximum PEC_{soil} of all uses in grapes: European use pattern, 3 x 300 g as/ha
2) Prothioconazole & Spiroxamine EC 460:
Cereals, 2 x 200 g Prothioconazole/ha and 375 g Spiroxamine/ha, BBCH 30-69
maximum PEC_{soil} value after application of 2 x 375 g as/ha spiroxamine to cereals
Allover maximum $PEC_{soil\ initial}$ of Spiroxamine-metabolites: PEC from use in vines, European use pattern

Test organism	Test substance	Time scale	Soil PEC [2]	TER	Trigger
Earthworms					

Test organism	Test substance	Time scale	Soil PEC [2]	TER	Trigger
Eisenia fetida	Spiroxamine ‡	Acute	0.522 mg as/kg	> 957	10
Eisenia fetida	Prothioconazole & Spiroxamine EC 460	Acute	0.283 mg as/kg	>525	10
Eisenia fetida	Spiroxamine EC 500	Chronic	0.522 mg as/kg	≥ 10	5
Eisenia fetida	Prothioconazole & Spiroxamine EC 460	Chronic	0.283 mg as/kg	33	5
Eisenia fetida	Metabolite KWG 4168-desethyl (M01)	Chronic	0.221 mg/kg	452	5
Eisenia fetida	Metabolite KWG 4168-N-oxide (M03)	Chronic	0.042 mg/kg	2381	5
Other soil macro-organisms					
Collembola	Spiroxamine ‡	Chronic	0.522 mg as/kg	61	5
Collembola	Prothioconazole & Spiroxamine EC 460	Chronic	0.283 mg as/kg	10	5
Collembola	Metabolite KWG 4168-desethyl (M01)	Chronic	0.221 mg/kg	1430	5
Collembola	Metabolite KWG 4168-despropyl (M02)	Chronic	0.217 mg/kg	1456	5

[1] to be completed where first Tier triggers are breached
[2] PECsoil including accumulation (PEC_{ini} + $PEC_{plateau}$)

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

Preliminary screening data

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

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha)[2] emergence	Exposure[1] (g/ha)[2]	TER	Trigger
Abutilon theophrasti Amanthus retroflexus	Spiroxamine EC 500	--	> 400	74.52 g as/ha	> 5.4	5
Soy bean	Prothioconazole & Spiroxamine EC 160 + 300	--	> 1.25	0.057 L/ha	> 21.9	5

[1] exposure has been estimated based on Ganzelmeier drift data
[2] for preparations indicate whether dose is expressed in units of as or preparation

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

Due to low effects not required.

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

Test type/organism	Endpoint
Respiration inhibition test / activated sludge, Spiroxamine	EC_{50} 191 mg/L

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

Compartment	
soil	Parent (Spiroxamine)
water	Parent (Spiroxamine) *
sediment	Parent (Spiroxamine)
groundwater	Parent (Spiroxamine)

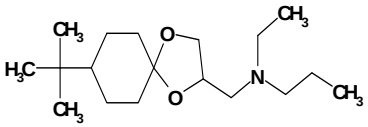
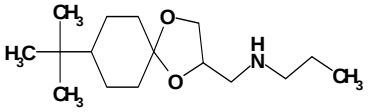
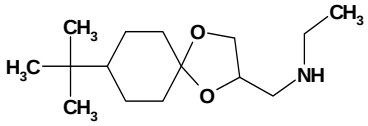
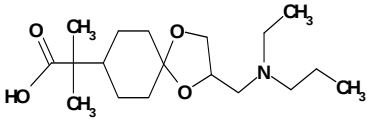
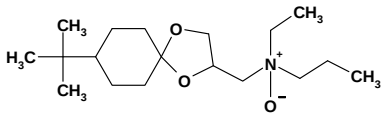
* Metabolite M06 is tentatively regarded as relevant unless therelevant algae study is submitted and demonstrates non-relevance.

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

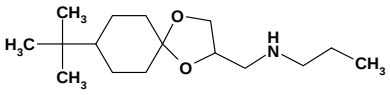
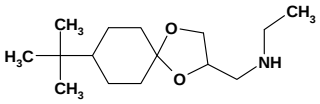
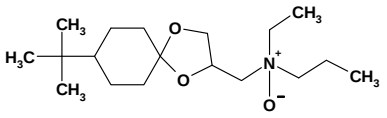
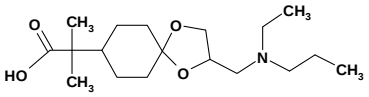
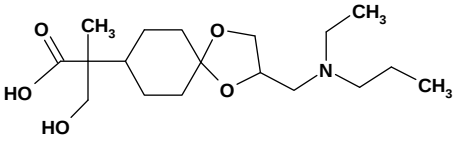
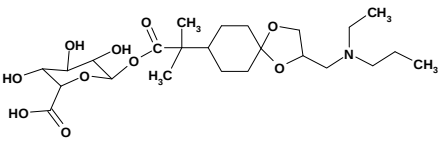
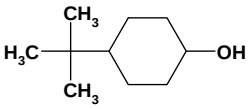
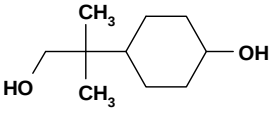
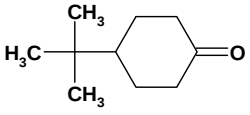
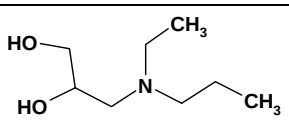
	RMS/peer review proposal
Active substance	Spiroxamine: Acute Category 1, Chronic Category 1 Label: environment, GSH 09

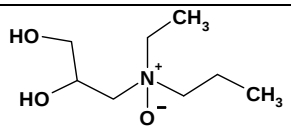
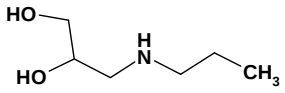
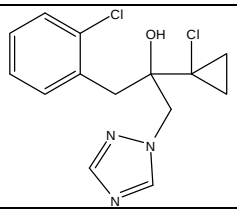
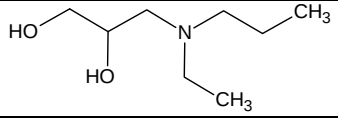
	RMS/peer review proposal
Preparation	Spiroxamine EC 500: Acute Category 1, Chronic Category 1 Label: environment, GSH 09 Prothioconazole & Spiroxamine EC 460: Acute Category 1, Chronic Category 1 Label: environment, GSH 09

Appendix 1 - Compound code(s) used in the list of endpoints

Code/Trivial name	Structural formula	Chemical name
Spiroxamine (KWG 4168) Spiroxamine (parent substance)		Spiroxamine (KWG 4168) Spiroxamine (parent substance)
KWG 4168 - desethyl (code: M01)		KWG 4168 - desethyl (code: M01)
KWG 4168 - despropyl (code: M02)		KWG 4168 - despropyl (code: M02)
KWG 4168 – acid (code: M06)		KWG 4168 – acid (code: M06)
KWG 4168-N-oxid (code:M03)		KWG 4168-N-oxid (code:M03)

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name	Structural formula
Spiroxamine-desethyl KWG 4168-desethyl M01 (Group A metabolite)	N-[(8-tert-butyl-1,4-dioxaspiro[4.5]dec-2-yl) methyl]propan-1-amine	
Spiroxamine-despropyl KWG 4168-despropyl M02 (Group A metabolite)	N-[(8-tert-butyl-1,4-dioxaspiro[4.5]dec-2-yl) methyl]ethanamine	
Spiroxamine-N-oxide KWG 4168-N-oxide M03 (Group A metabolite)	[(8-tert-butyl-1,4-dioxaspiro[4.5]dec-2-yl)methyl]ethyl(propyl)amine oxide	
Spiroxamine-carboxylic acid KWG 4168-acid M06 (Group A metabolite)	2-(2-{[ethyl(propyl)amino]methyl}-1,4-dioxaspiro[4.5]dec-8-yl)-2-methylpropanoic acid	
Spiroxamine-hydroxy acid M07 (Group A metabolite)	2-(2-{[ethyl(propyl)amino]methyl}-1,4-dioxaspiro[4.5]dec-8-yl)-3-hydroxy-2-methylpropanoic acid	
Spiroxamine-acid glucuronide (M19) (Group A metabolite)	2-(2-{[ethyl(propyl)nitroryl] methyl}-1,4-dioxaspiro[4.5]dec-8-yl)-2-methylpropyl hexopyranoside	
tert-butyl-cyclohexanol Spiroxamine-cyclohexanol M13 (Group B metabolite)	4-tert-butylcyclohexanol	
Spiroxamine-diol M14 (Group B metabolite)	4-(1-hydroxy-2-methylpropan-2-yl)cyclohexanol	
tert-butyl-cyclohexanone Spiroxamine-ketone M15 (Group B metabolite)	4-(1-hydroxy-2-methylpropan-2-yl)cyclohexanol	
M28 Aminodiol (Group C metabolite)	3-[ethyl(propyl)amino]propane-1,2-diol	

Aminodiol-N-oxide M29 (Group C metabolite)	3-[ethyl(propyl)nitroryl]propane-1,2-diol	
Desethyl-aminodiol M30 (Group C metabolite)	3-(propylamino)propane-1,2-diol	
Prothiocionazole-desthio	2-(1-chlorocycloproyl)1-(2-chlorophenyl)-3-(1,2,4-triazol-1-yl)-propan-2-ol	
-	N-ethyl-N-propyl-1,2-dihydroxy-3-amino-propane	

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

ABBREVIATIONS

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

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

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