CONCLUSION ON PESTICIDE PEER REVIEW

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

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ABSTRACT

The conclusions of the European Food Safety Authority (EFSA) following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State the United Kingdom, for the pesticide active substance spinetoram are reported. The context of the peer review was that required by Commission Regulation (EU) No 188/2011. The conclusions were reached on the basis of the evaluation of the representative uses of spinetoram as an insecticide on grapes. The reliable endpoints concluded as being appropriate for use in regulatory risk assessment, derived from the available studies and literature in the dossier peer reviewed, are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified.

KEY WORDS

spinetoram, peer review, risk assessment, pesticide, insecticide

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SUMMARY

Spinetoram is a new active substance for which in accordance with Article 6(2) of Council Directive 91/414/EEC the United Kingdom (hereinafter referred to as the 'RMS') received an application from Dow AgroSciences for approval. Complying with Article 6(3) of Directive 91/414/EEC, the completeness of the dossier was checked by the RMS. The European Commission recognised in principle the completeness of the dossier by Commission Decision 2008/740/EC of 12 September 2008.

The RMS provided its initial evaluation of the dossier on spinetoram in the Draft Assessment Report (DAR), which was received by the EFSA on 23 February 2012. The peer review was initiated on 3 April 2012 by dispatching the DAR for consultation of the Member States and the applicant Dow AgroSciences.

Following consideration of the comments received on the DAR, it was concluded that EFSA should conduct an expert consultation in the areas of mammalian toxicology and ecotoxicology and EFSA should adopt a conclusion on whether spinetoram can be expected to meet the conditions provided for in Article 5 of Directive 91/414/EEC, in accordance with Article 8 of Commission Regulation (EU) No 188/2011.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of spinetoram as an insecticide on grapes, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

A general data gap and issue not finalised was identified for data to prove that the stereochemistry of the metabolites (including where metabolites are possible isomers derived from both factors of the active substance) tested in the toxicological and ecotoxicological studies was identical to the stereochemistry of the metabolites identified in the metabolism/degradation studies in animals, plants and the environment.

In the area of identity, physical/chemical/technical properties and methods of analysis a data gap was identified for confirmatory method/data for residue analysis in high oil content and dry matrices of plant origin.

In the area of mammalian toxicology, no data gaps and no areas of concern were identified. The worker risk assessment is pending on whether the stereochemistry of the residues relevant to worker exposure can be considered identical to that of the composite characterised by the toxicological reference values allocated to XDE-175.

In the area of residues no areas of concern were identified. The consumer risk assessment is pending on whether the stereochemistry of the residues relevant to consumer exposure can be considered identical to that of the composite characterised by the toxicological reference values allocated to XDE-175.

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessment at EU level for the representative use assessed. For the representative use, the potential for groundwater exposure above the parametric drinking water limit of 0.1 µg/L was assessed as low for spinetoram and its relevant metabolites.

A number of data gaps were identified in the section of ecotoxicology in the area of aquatic organisms and a critical area of concern for non-target arthropods. Risk mitigation measures are recommended to be applied in order to mitigate the risk to aquatic organisms and bees. The environmental risk assessment is pending on further data to prove that the stereochemistry of the metabolites (including where metabolites are possible isomers derived from both factors of the active substance) tested in the ecotoxicological studies was identical to the stereochemistry of the metabolites identified in the metabolism/degradation studies in the environment.

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BACKGROUND

In accordance with Article 80(1)(a) of Regulation (EC) No 1107/2009,[3] Council Directive 91/414/EEC[4] continues to apply with respect to the procedure and conditions for approval for active substances for which a decision recognising in principle the completeness of the dossier was adopted in accordance with Article 6(3) of that Directive before 14 June 2011.

Commission Regulation (EU) No 188/2011[5] (hereinafter referred to as 'the Regulation') lays down the detailed rules for the implementation of Council Directive 91/414/EEC as regards the procedure for the assessment of active substances which were not on the market on 26 July 1993. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant for comments on the initial evaluation in the Draft Assessment Report (DAR) provided by the rapporteur Member State (RMS), and the organisation of an expert consultation, where appropriate.

In accordance with Article 8 of the Regulation, EFSA is required to adopt a conclusion on whether the active substance is expected to meet the conditions provided for in Article 5 of Directive 91/414/EEC within 4 months from the end of the period provided for the submission of written comments, subject to an extension of 2 months where an expert consultation is necessary, and a further extension of upto 8 months where additional information is required to be submitted by the applicant in accordance with Article 8(3).

In accordance with Article 6(2) of Council Directive 91/414/EEC the United Kingdom (hereinafter referred to as the 'RMS') received an application from Dow AgroSciences for approval of the active substance spinetoram. Complying with Article 6(3) of Directive 91/414/EEC, the completeness of the dossier was checked by the RMS. The European Commission recognised in principle the completeness of the dossier by Commission Decision 2008/740/EC of 12 September 2008.[6]

The RMS provided its initial evaluation of the dossier on spinetoram in the Draft Assessment Report (DAR), which was received by the EFSA on 23 February 2012 (United Kingdom, 2012). The peer review was initiated on 3 April 2012 by dispatching the DAR to Member States and the applicant Dow AgroSciences for consultation and comments.

In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 8(3) of the Regulation were considered in a telephone conference between the EFSA, the RMS, and the European Commission on 20 July 2012. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof it was concluded that additional information should be requested from the applicant and the EFSA should organise an expert consultation in the areas of mammalian toxicology and ecotoxicology.

[3] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ No L 309, 24.11.2009, p. 1-50.
[4] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1-32, as last amended.
[5] Commission Regulation (EU) No 188/2011 of 25 February 2011 laying down detailed rules for the implementation of Council Directive 91/414/EEC as regards the procedure for the assessment of active substances which were not on the market 2 years after the date of notification of that Directive. OJ No L 53, 26.2.2011, p. 51-55.
[6] Commission Decision 2008/740/EC: Commission Decision of 12 September 2008 recognising in principle the completeness of the dossier submitted for detailed examination in view of the possible inclusion of spinetoram in Annex I to Council Directive 91/414/EEC (notified under document number C(2008) 4965). OJ No L 249, 18.9.2008, p. 21–22.

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 an expert consultation, and the additional information to be submitted by the applicant, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert consultation where this 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 April 2013.

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 an insecticide on grapes as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2013) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the DAR,
- the Reporting Table (20 July 2012),
- the Evaluation Table (2 May 2013),
- the reports of the scientific consultation with Member State experts (where relevant),
- the comments received on the assessment of the additional information (where relevant),
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its addendum (compiled version of March 2013 containing all individually submitted addenda (United Kingdom, 2013)) 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

Spinetoram (XDE-175) is the ISO common name for the mixture of 50–90% (2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranosyloxy)-13-[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methylpyran-2-yloxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro-14-methyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecine-7,15-dione (XDE-175-J major factor) and 50–10% (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-2-(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranosyloxy)-13-[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methylpyran-2-yloxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecine-7,15-dione (XDE-175-L minor factor).

The representative formulated product for the evaluation was 'GF-1587' a suspension concentrate (SC) containing 120 g/L spinetoram.

The representative uses evaluated comprise field spraying against *Polychrosis (Lobesia) botrana* on grapes. Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

The molecules of both factors of spinetoram contain multiple chiral centers. The methods of analysis used to generate regulatory studies for the risk assessment did not resolve enantiomers. Therefore results indicated from these studies may be for mixture of isomers and not necessarily the individual compounds as specified in Appendix B. The possible impact of racemisation of the active substance factors and the metabolites on the toxicity, the consumer risk assessment and the environment was not specifically addressed. Therefore a general data gap was identified for data to prove that the stereochemistry of the metabolites (including where metabolites are possible isomers derived from both factors of the active substance) tested in the toxicological and ecotoxicological studies was identical to the stereochemistry of the metabolites identified in the metabolism/degradation studies in animals, plants and the environment.

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

The following guidance documents were followed in the production of this conclusion: SANCO/3030/99 rev. 4 (European Commission, 2000) and SANCO/825/00 rev. 8.1 (European Commission, 2010).

The minimum purity of spinetoram as manufactured is 830 g/kg (based on pilot scale production), with a specified content of XDE-175-J factor in the range 70-90% (581-810 g/kg) and a specified content of XDE-175-L factor in the range 10-30% (83-270 g/kg). At the moment no FAO specification exists.

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

Adequate analytical methods are available for the determination of spinetoram in technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

Residues of spinetoram in food and feed of plant origin can be monitored by LC-MS/MS with LOQs of 0.02 mg/kg (0.01 mg/kg for each of the two factors). A data gap was identified for a confirmatory method/data for high oil content and dry matrices. Considering the representative uses evaluated methods for monitoring in food of animal origin are not required. However a method (LC-MS/MS) for analysis of spinetoram residues (both factors of the active substance and some metabolites) in muscle,

liver, kidney, fat and milk was validated at LOQ of 0.01 mg/kg for each individual component but it should be noted that confirmatory data were provided only for milk and muscle. Appropriate LC-MS/MS methods exist to enforce the residue definitions for monitoring purposes in soil, water and air. A method for residues in body fluids and tissues is not required as the active substance is not classified as toxic or very toxic. However a LC-MS/MS based method was validated for residues in body fluids (urine and blood) but confirmatory data were not presented.

2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000 rev. 10 - final (European Commission, 2003), SANCO/222/2000 rev. 7 (European Commission, 2004) and SANCO/10597/2003 – rev. 8.1 (European Commission, 2009).

Many of the toxicological studies were performed with a compound of 83% purity. Most of the impurities are spinosyns, and have a similar structure to spinetoram (i.e. are high molecular weight macrolides). The impurities are not considered to be of greater toxicological concern than spinetoram, and it can be considered that the batches used in the toxicological studies are representative of the technical specification. Therefore, the NOAELs do not have to be corrected for the lower purity of the active substance in the tested material.

The metabolism of the 2 active factors XDE-175-J and XDE-175-L was evaluated separately in a series of ADME studies. Both were rapidly absorbed and eliminated mainly via faeces during the first 24 hours, but the biliary excretion was not quantified. Comparison of plasma AUCs after oral or intravenous administration of 10 mg/kg bw indicated that a minimum of 26-29% of XDE-175-J and 39-57% of XDE-175-L were systematically available. The major metabolic pathway for each factor was via glutathione conjugation of the parent, and glutathione conjugation of metabolites arising from N-demethylation and O-deethylation of each factor, as well as hydroxylation of parent XDE-175-J.

With regard to the acute toxicity, each of the required studies has been conducted with 2 different ratios of J and L factors (75J:25L and 85J:15L). Both were of low acute toxicity (by oral, dermal and inhalation routes) and are not classified as skin or eye irritants. Based on a positive result in the local lymph node assay with 75J:25L, the classification[7] as Skin sensitiser, category 1, H317 'May cause an allergic skin reaction', is proposed for spinetoram.

Most of the short term toxicity studies with XDE-175 were performed with the ratio 75:25 for the factors J and L respectively. Cytoplasmic vacuolation was observed in several tissues/organs in rats, mice and dogs (particularly in parenchymal cells and macrophages). Considering that it may be a degenerative change, this effect has been taken into account during the derivation of the NOAELs for the different studies where it was observed. For 75J:25L and 85J:15L the relevant short term NOAEL in rats are 11 mg/kg bw per day and 9 mg/kg bw per day respectively (based on 90-day studies). In mice, the relevant short term NOAEL is 9 mg/kg bw per day. In the 90-day dog study, a LOAEL 5.7 mg/kg bw per day has been identified based on macrophage vacuolation in several organs/tissues of males at the low dose level. In the 1-year dog study, the NOAEL is 2.5 mg/kg bw per day based on moderate bilateral arteritis in the epididymides of one male and very slight to slight arteritis in several organs of one female. Based on the observations of bone marrow toxicity and arteritis in dogs, the classification[7] as Category 2 Specific Target Organ Toxicant (STOT-RE) and H373 'May cause damage to organ through prolonged or repeated exposure' is proposed for spinetoram. No genotoxic or carcinogenic properties were shown in the available studies, with a long term NOAEL of 10.8 mg/kg bw per day for rats and 18.8 mg/kg bw per day for mice. Based on the finding of dystocia in the multigeneration rat study, the classification[7] as Reproductive Toxicant Category 2, H361f 'Suspected of damaging fertility', is proposed for spinetoram, with a parental and reproductive NOAEL of 10

[7] It should be noted that classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals.

mg/kg bw per day, and a NOAEL for the offspring of 75 mg/kg bw per day. Adverse pup effects at 75 mg/kg bw per day were considered to be related to dystocia (i.e. evidence of reproductive toxicity) rather than specific offspring toxicity. No developmental toxicity was observed in rats or rabbits. No neurotoxic effects were shown after acute or repeated exposure of rats. Several metabolites (N-demethyl-175-J, N-formyl-175-J and L) were shown to have a low acute oral toxicity (LD_{50} = 3129 or >5000 mg/kg bw) and were not mutagenic in Ames tests.

The Acceptable Daily Intake (ADI) is 0.025 mg/kg bw per day, based on the 1-year dog study. The Acute Reference Dose (ARfD) is 0.1 mg/kg bw based on the rat multigeneration study. The Acceptable Operator Exposure Level (AOEL) is 0.0065 based on the 1-year dog study, applying a correction of 26% for oral absorption. All reference values were derived with the use of an uncertainty factor (UF) of 100.

For the representative use in grapes, the application by broadcast air assisted or hand-held sprayers were considered. Based on the German model and EUROPOEM data set for application to vines, levels of exposure below the AOEL have been identified for operators. Estimates of bystander exposure from spray drift were all below the AOEL. For the worker exposure estimates, a first tier exposure assessment was not calculated but field studies were presented for the derivation of specific factors applicable to harvesting of grapes (DFR and TC). This gave a predicted exposure of 15% of the AOEL. Considering the limitations of the analytical method used for the DFR decline study, the worst case assumption of no decline in residue would result in a predicted exposure of ~30% of the AOEL after 3 applications.

It is noted that the worker exposure estimates have not taken into account the possibility of multiple isomers in the residues they will be exposed to. Therefore the risk assessment cannot be concluded for the workers pending on whether the stereochemistry of the residues relevant to their exposure can be considered identical to that of the composite characterised by the toxicological reference values allocated to XDE-175.

3. Residues

The assessment in the residue section below is based on the guidance documents listed in the document 1607/VI/97 rev. 2 (European Commission, 1999), and the JMPR recommendations on livestock burden calculations stated in the 2004 and 2007 JMPR reports (JMPR, 2004, 2007).

Metabolism was investigated in fruit crops (apples), leafy crops (lettuce), and in root and tuber crops (turnips) after foliar application of the two factors XDE-175-J (as a mixture of 3 forms) and XDE–175-L (as a mixture of 2 forms), all radio labelled in the macrolide portion of the molecules. The fate of the pyran-derivative part of the molecule was not investigated but a case was made that this portion of the molecule would be present in low proportions (<5% TTR) and would be expected to degrade completely to small carbon units incorporated into natural plant constituents.

Metabolism of XDE–175 was similar in the three crop groups investigated. No or little translocation into the treated crops was observed and residues were mostly recovered from crop surfaces. XDE-175-J was the predominant component of the residue at harvest in apples, lettuce and turnips (35 –69% of TRR). XDE-175-L was also present, but in lower proportions. The major metabolites identified were N-demethyl-175-J and N-formyl-175-J. To a lesser extent, N-demethyl-175-L and N-formyl-175-L were present. The formation of conjugated residues in plants was low. Among the two XDE–175 factors, XDE-175-L (the minor factor of the active substance) tended to be metabolised faster than XDE-175-J. As it regards enantiomers of the metabolites, a general data gap was identified to demonstrate that the stereochemistry of compounds tested in the toxicological (and ecotoxicological) studies was basically identical to the stereochemistry of residues identified in the metabolism/degradation studies in animals, plants and the environment.

The assessment of residues in rotational crops is not required for permanent crops such as grape vines. The effects of processing on the nature of residues was investigated in a standard hydrolysis study

simulating industrial and household processing with XDE-175-J, XDE-175-L and the metabolites N-demethyl-175-J and N-formyl-175-J. Results indicated that there was some degradation (7-11%) to the C17-pseudyaglycone-175-J/ -175-L, respectively, but this proportion was not considered of concern in consumer risk assessments.

The residue definition for risk assessment was set as 'Spinetoram (sum of XDE-175-J, XDE-175-L), metabolites N-demethyl-175-J and N-formyl-175-J, expressed as spinetoram'. For monitoring, a residue definition as 'Spinetoram (sum of XDE-175-J, XDE-175-L) only' was proposed.

Livestock metabolism was investigated with parent compound in goat and hens. XDE-175 was barely metabolised and was by far the predominant residue in animal products. The studies do not address the metabolism and residue levels of the plant metabolites (N-demethyl-175-J and N-formyl-175-J) in animal commodities to which livestock could be significantly exposed through the diet. However, livestock studies are not required to support the representative use in grapes, and reconsideration of the issue and setting of a residue definition in livestock is required for future uses with relevance to livestock exposure.

Residue trials in grapes are available and supported by storage stability data and analytical methods.

An MRL of 0.5 mg/kg was proposed for grapes.

The consumer risk assessment performed with the EFSA Pesticides Residues Intake Model (PRIMo) indicated that the maximum chronic exposure (IEDI) for table and wine grapes is less than 1% of the ADI for spinetoram. In an acute consumer risk assessment the calculated maximum exposure was 27% of the ARfD for table grapes.

The consumer risk assessment is pending further whether the stereochemistry of the residues relevant to consumer exposure can be considered identical to that of the composite characterised by the toxicological reference values allocated to XDE-175.

4. Environmental fate and behaviour

In soil laboratory incubations under aerobic conditions in the dark, XDE-175-J and XDE-175-L exhibited low to medium persistence and low to moderate persistence, respectively. The major metabolites (>10 % applied radioactivity (AR)), N-demethyl-175-J (max 69.7 % AR, exhibited moderate to high persistence), N-demethyl-N-nitroso-175-J (max 19.6 % AR, exhibited medium to high persistance), N-demethyl-175-L (max 43.8% AR, exhibited low to medium persistence), N-demethyl-N-nitroso-175-L (max 13.6 % AR, exhibited moderate to medium persistence), N-succinyl-L (max 16.3 % AR, exhibited high persistence) and the minor non-transient metabolite (<10 % AR) N-succinyl-J (max 8.9 % AR, exhibited very high persistence) were formed. Mineralisation of macrolide ring system label to carbon dioxide accounted for 0.4-19.1 % AR after 125-127 days for XDE-175-J and 1.1-23.7 % AR after 123-127 days for XDE-175-L. The formation of unextractable residues (not extracted by three times 70 mL methanol: 0.1N NaOH (90:10)) for this radiolabel accounted for 4.6-26.5 % AR after 125-127 days for XDE-175-J and 10.8-35.6 % AR after 123-127 days for XDE-175-L. Satisfactory anaerobic degradation studies were not supplied for XDE-175-J and XDE-175-L. The representative use assessed at EU level is grapes. Anaerobic conditions are not expected in grape vines and therefore the lack of sufficient anaerobic studies was considered acceptable. Member States should be aware that if other representative uses will be applied for in the future anaerobic studies may be needed. In a laboratory photodegradation study on soil, photolysis was observed when comparing the dark and the irradiated conditions. In the irradiated samples, XDE-175-J and XDE-175-L exhibited medium persistence and moderate persistence, respectively. The persistence in the photodegradation study was in the same range as the persistence in the soil laboratory incubations under aerobic conditions in the dark. Novel photolysis products compared to the aerobic incubations were not formed. XDE-175-J and XDE-175-L exhibited low to slight mobility and low mobility to immobility, respectively. The metabolites N-demethyl-175-J and N-demethyl-175-L exhibited low to slight mobility. Mobility studies according to OECD Guideline for the Testing of Chemicals No. 106 were

not available for the metabolites N-demethyl-N-nitroso-175-J, N-demethyl-N-nitroso-175-L, N-succinyl-L and N-succinyl-J. Estimated Koc values showed low to slight mobility for these metabolites. In satisfactory field dissipation studies carried out in Southern and Northern France, Germany and Spain (spray application made in May/June to bare soil, 600 g as/ha) XDE-175-J exhibited very low to moderate persistence and XDE-175-L exhibited very low to low persistence. The metabolites N-demethyl-N-nitroso-175-J, N-demethyl-N-nitroso-175-L, N-succinyl-L and N-succinyl-J were not found in concentrations ≥ 1.8 % under field conditions. The majority of residues were observed to be in the upper 10 cm, with some observed in the 10-20 cm layer. In general residues that were observed in the 10-20 cm layer were < LOQ, however in some occasions (usually early in the study) residues were observed > LOQ in this layer. Lack of detection would not be expected to be due to leaching. The metabolites N-demethyl-N-nitroso-175-J, N-demethyl-N-nitroso-175-L, N-succinyl-L and N-succinyl-J were not considered as relevant under field conditions and PEC values were not calculated. Field study DT_{50} values were accepted as being reasonable estimates of degradation and were normalised to FOCUS reference conditions (20 ^{o}C and pF2 soil moisture) using the time step normalisation procedure in accordance with FOCUS (2006) kinetics guidance.
In laboratory incubations in dark aerobic natural sediment water systems, XDE-175-J and XDE-175-L readily partitioned to the sediment where they exhibited high persistence. The unextractable sediment fraction (not extracted by 65:27:8 methanol:NaCl:1 NaOH) was a minor sink for the macrolide ring system ^{14}C radiolabel, accounting for 0.2-0.5 % AR at the study end (107 days). The rate of decline of XDE-175-J and XDE-175-L in a laboratory sterile aqueous photolysis experiment was faster relative to the decline that occurred in the aerobic water incubations. In the sterile aqueous photolysis study the metabolite N-demethyl-175-L was found above 10 % AR (12.8 % AR). In a sterile aqueous buffer study the metabolites N-demethyl-175-J and 13,14-beta-dihydro-C17-pseudoaglycone-175-L were found above 10 % AR (27.8 % AR and 23.3 % AR, respectively). An aquatic field dissipation study was also included in the assessment, low persistence were seen in the water phase for both XDE-175-J and XDE-175-L. The sediment samples in this study displayed concentrations < LOD for all analytes both before application and at the study termination. The necessary surface water and sediment exposure assessment (Predicted environmental concentrations (PEC)) calculations were carried out for the metabolites, using the FOCUS (FOCUS, 2001) steps 1, 2, 3 and 4 approach, N-demethyl-175-J, N-demethyl-175-L and 13,14-beta-dihydro-C17-pseudoaglycone-175-L. For the metabolite 13,14-beta-dihydro-C17-pseudoaglycone-175-L step 3 and step 4 values were presented based on the maximum parent step 3 and step 4 values and then adjusted for molecular mass and maximum occurrence. For the active substances, XDE-175-J and XDE-175-L, appropriate steps 1, 2, 3 (FOCUS, 2001) and 4 calculations were available[8]. The steps 1-2 were calculated using version 1.1 FOCUS calculator, step 3 was calculated using SWASH interface version 3.1, TOXSWA version 2.1.1, MACRO version 4.3, PRZM version 3.21.b and step 4 was calculated using SWAN tool version 1.1.4. The step 4 calculations were divided into a 'step 4.1' (field studies were used for soil degradation rate and the long phase DT_{50} water from the aquatic field dissipation study), a step 4.2 (inclusion of a buffer zone to mitigate spray drift) and a 4.3 (run-off mitigation by a vegetative buffer strip in addition to the spray drift buffer zone). The 'step 4.1', 'step 4.2 and 'step 4.3' calculations appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray drift buffer zones of 25 m being implemented for the D6 drainage scenario (representing a 94.5 % spray drift reduction). Combined no-spray buffer zones of 30m (representing a 79.5 – 95 % spray drift reduction) with vegetative buffer strips of up to 20 m (reducing solute flux by 80% and erosion flux by 95%) were implemented for the run-off scenarios. The SWAN tool was appropriately used to implement these mitigation measures in the simulations. The actual application rate used for the individual parent factors assumed that 90 % of total XDE-175 was XDE-175-J and that 30 % was XDE-175-L. Corrected application rates were therefore 3 x 32.4 g as/ha for XDE-175-J and 3 x 10.8 g as/ha for XDE-175-L. The surface water PEC values for total XDE-175 were calculated by multiplying the XDE-175-J PEC by 85/90 and the XDE-175-L PEC by 15/30, and summing the two resulting PEC values. The ratio of 85J:15L was considered to be a realistic conservative parent factor.

[8] All simulations at steps 3 and 4 correctly utilised the agreed Q10 of 2.58 (following EFSA PPR, 2007) and Walker equation coefficient of 0.7.

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (FOCUS, 2009) scenarios and the model FOCUS PEARL 4.4.4[9] for the active substances XDE-175-J and XDE-175-L and the metabolites N-demethyl-175-J and N-demethyl-175-L. The potential for groundwater exposure from the representative uses by the active substances and the metabolites above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by the 7 pertinent FOCUS groundwater scenarios. In the groundwater exposure assessment a plant uptake factor of 0.5 was used for both the parents and the metabolites. Neither the parents nor the metabolites were demonstrated to be systemic and therefore a plant uptake factor of 0 should have been used according to the FOCUS (2000) recommendations. However, due to the predicted low levels in groundwater these calculations were considered acceptable for the representative uses applied for. Member States should be aware that a new groundwater exposure assessment based on the correct plant uptake factor for the parent and for the metabolites could be necessary in case other representative uses will be applied for in the future and if the systemicity of the compounds from soil has not been shown.

The possible stereochemistry of the metabolites (including where metabolites are possible isomers derived from both factors of the active substance) is not considered to be an issue for groundwater. The reason for this is that the parents (XDE-175-J, XDE-175-L) and the metabolites (N-demethyl-175-J, N-demethyl-175-L) showed a high adsorption. It is very likely that possible isomers will exhibit comparable mobility as the parents and the assessed metabolites. Therefore even though degradation rates of individual isomers might differ from those that are available for sum of isomers, the groundwater levels for potential isomers are expected to be similarly low as those currently presented for sum of isomers.

5. Ecotoxicology

For the environmental risk assessments the following documents were considered: European Commission 2002a, 2002b, 2002c and SETAC (2001).

The environmental risk assessment is pending on further data to prove that the stereochemistry of the metabolites (including where metabolites are possible isomers derived from both factors of the active substance) tested in the ecotoxicological studies was identical to the stereochemistry of the metabolites identified in the metabolism/degradation studies in the environment.

A low risk to birds and mammals via dietary exposure, consumption of contaminated water and from bioaccumulation in earthworms and fish was concluded for the representative use of spinetoram in grapes.

Toxicity data for the technical active substance (a mixture of XDE-175-J and XDE-175-L), the representative formulation ('GF-1587') and the relevant metabolites (N-demethyl-175-J and N-demethyl-175-L) were available for aquatic organisms (see Appendix A). The risk assessment using FOCUS step 3 exposure estimations indicated high risk for crustaceans (*Daphnia magna*) and sediment-dwelling organisms (*Chironomus riparius*) for the technical active substance and for the metabolite N-demethyl-175-J. Therefore the exposure assessments were refined considering mitigation measures (spray drift and runoff mitigation) at FOCUS step 4. Furthermore a higher tier laboratory study mimicking a realistic exposure pattern of the water layer was available for daphnids (21-day chronic study). In this static study, 4 applications of the active substance with 5-days interval were made and the concentrations of the test water between the applications were not maintained. The endpoint (21-day NOEC) derived from this study was considerably higher than the endpoints originating from similar studies where the concentrations of the water were maintained. This endpoint and the related risk assessments (using FOCUS step 4 exposure estimations) were discussed at the Pesticides Peer Review Meeting 100. The experts at the meeting agreed with the available higher tier risk assessments including the use of the endpoint from the higher tier laboratory study. As a result of the higher tier risk assessments, a low risk to aquatic organisms was concluded for situations represented by some

[9] Simulations correctly utilised the agreed Q10 of 2.58 (following EFSA PPR, 2007) and Walker equation coefficient of 0.7.

FOCUS surface water scenarios when risk mitigation measures were considered (no-spray buffer zone or no-spray buffer zone in combination with vegetative buffer strip). However, high risk was concluded for situations represented by the R4 and D6 FOCUS surface water scenarios even if risk mitigation measures (run-off mitigation in addition to the spray drift buffer zone) were considered. Therefore a data gap was identified for further risk assessments for aquatic organisms for situations represented by the R4 and D6 FOCUS surface water scenarios. Toxicity data for the aquatic metabolite 13,14-beta-dihydro-C17-pseudoaglycone-175-L were not available, however a low risk was concluded to aquatic organisms on the basis of a qualitative risk assessment presented in the DAR.

First tier risk assessments (HQ approach) for the active substance and the representative formulation indicated high risk for honey bees. Therefore higher tier studies (foliage residue contact test and tunnel test) were taken into consideration. The results of the foliage residue contact laboratory test indicated that mortality is not expected when bees are exposed to dry residues (aged residues) on over sprayed foliage. However, increased mortality was observed in the tunnel test after bees could forage on flowering *Phacelia* that was over sprayed (1 x 36 g a.s./ha) in the previous evening (after the foraging activity of the bees). The increase in mortality in this treatment group was considered to be temporary and moderate (on average ca. 4 to 2 folds increase compared to the control for the first and the second day after the treatment, respectively). The average mortality calculated for the full 7-day post-treatment period of this treatment group was the same as in the control. In another treatment group of the tunnel test a daytime spray application was performed to the flowering *Phacelia* when bees were actively foraging. A clear and statistically significant increase in bee mortality was observed in this treatment group for the first few days after the application. Considering these data, a high risk can be concluded for bees if the spray application is performed in the presence of bees (e.g. foraging on plants between the rows of grapevine or feeding on honey dew). It was also suggested by the available data that the risk to bees could be mitigated if bees are not present at the time and shortly after the spray application. It is further noted that mitigation measures like evening application or the removal of beehives before application might not be effective for wild bees (e.g. bumble bees, solitary bees living in or close to the treated field).

The risk to non-target arthropods was discussed at the Pesticides Peer Review Meeting 100. On the basis of a risk assessment with the standard tier 1 indicator species a high in-field and off-field risk to non-target arthropods was indicated for the representative use on grapes. A number of higher tier studies (extended laboratory and field test) were available that demonstrated a potential for in-field population recovery of several taxonomic groups of arthropods. However, no recovery by the end of a field study (4 months after the application) was demonstrated for *Lathridiidae* beetles. This was raised as a concern for other (non-tested) taxonomic groups that are potentially impacted by the application of spinetoram. Therefore the experts at the meeting concluded that there was a need to further address the in-field recovery of non-target arthropods (within a year of the last application). Furthermore, it was agreed that the risk assessment must include a consideration of the sensitivity of non-target *Lepidoptera* species. Therefore the experts agreed to identify a data gap to further consider the risk to non-target arthropods.

A low risk was concluded for earthworms and other soil macroorganisms, soil microorganisms, non-target terrestrial plants and organisms involved in biological methods for sewage treatment on the basis of the available data and assessments.

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
XDE-175-J	low to medium persistence Single first-order DT_{50lab} 5.0-86.9 days (20°C and 55 % MWHC) EU field trials DT_{50} 2.49 days (single first-order) and DT_{50} 0.48-59.3 (biphasic kinetics)	A low risk was concluded for soil organisms.
XDE-175-L	low to moderate persistence Single first-order DT_{50lab} 5.1-48.3 days (20°C and 55 % MWHC) EU field trials DT_{50} 2.02 days (single first-order) and DT_{50} 0.15-2.38 (biphasic kinetics)	
N-demethyl-175-J	moderate to high persistence Single first-order DT_{50lab} 19.6-330 days (20°C and 55 % MWHC) EU field trials DT_{50} 20.5-98.9 days (single first-order, peak down)	A low risk was concluded for soil organisms.

N-demethyl-175-L	low to medium persistence Single first-order DT_{50lab} 3.1-95.0 days (20°C and 55 % MWHC) EU field trials DT_{50} 1.70-2.46 days (single first-order, peak down)	A low risk was concluded for soil organisms.

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**
XDE-175-J	low to slight mobility (K_{Foc} = 1263-6257 mL/g)	No	Yes for the mixture of J and L factors	Yes for the mixture of J and L factors	Yes for the mixture of J and L factors
XDE-175-L	low mobility to immobile (K_{Foc} = 999-7779 mL/g)	No	Yes for the mixture of J and L factors	Yes for the mixture of J and L factors	Yes for the mixture of J and L factors
N-demethyl-175-J	low to slight mobility (K_{Foc} = 1257-3733 mL/g)	No	Yes	- oral LD_{50} = 3129 mg/kg bw - Ames test negative	Similar toxicity as the parent to a number of non-target organisms
N-demethyl-175-L	low to slight mobility (K_{Foc} = 1249-4364 mL/g)	No	Yes	No data available	Similar toxicity as the parent to a number of non-target organisms

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
XDE-175-J	A data gap for some European situations was identified.
XDE-175-L	A data gap for some European situations was identified.
N-demethyl-175-J	A data gap for some European situations was identified.
N-demethyl-175-L	The risk to aquatic organisms was assessed as low.
13,14-beta-dihydro-C17-pseudoaglycone-175-L	The risk to aquatic organisms was assessed as low.

6.4. Air

Compound (name and/or code)	Toxicology
XDE-175-J	Inhalation LC_{50} > 5 mg/L (nose-only) for the mixture of J and L factors
XDE-175-L	Inhalation LC_{50} > 5 mg/L (nose-only) for the mixture of J and L factors

7. List of studies to be generated, still ongoing or available but not peer reviewed.

This is a complete list of the data gaps identified during the peer review process, including those areas where a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 7 of Directive 91/414/EEC concerning information on potentially harmful effects).

- Data to prove that the stereochemistry of the metabolites (including where metabolites are possible isomers derived from both factors of the active substance) tested in the toxicological and ecotoxicological studies was identical to the stereochemistry of the metabolites identified in the metabolism/degradation studies in animals, plants and the environment (relevant for representative use evaluated; submission date proposed by the applicant: unknown).

- Confirmatory method/data for residue analysis in high oil content and dry matrices of plant origin (relevant for representative use evaluated; submission date proposed by the applicant: unknown; see section 1).

- Further risk assessments are necessary for aquatic organisms for situations represented by D6 and R4 FOCUS surface water scenarios (relevant for representative use in grapes for situations represented by D6 and R4 FOCUS surface water scenarios; submission date proposed by the applicant: unknown; see section 5).

- Further risk assessments are necessary for non-target arthropods with special consideration to in-field recovery and sensitivity of non-target *Lepidoptera* species (relevant for representative use evaluated; submission date proposed by the applicant: unknown; see section 5).

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

- Spray drift mitigation equivalent to 30 metres no-spray buffer zone was used to demonstrate low risk for aquatic organisms for European situations represented by R2 FOCUS surface water scenario. Spray drift mitigation equivalent to using 30 metres non-spray buffer zone and additionally runoff mitigation equivalent to using 20 metres vegetative buffer strip was used to demonstrate low risk for aquatic organisms for European situations represented by R1 and R3 FOCUS surface water scenarios. Therefore application of spray drift and run-off mitigation measures should be considered for some European situations in order to mitigate the risk of spinetoram to aquatic organisms.

- In order to mitigate the risk to bees, spinetoram should only be applied when bees are not present in or in the vicinity of the crop.

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

1. The risk assessment for the workers, consumers and the environment is pending on further data to prove that the stereochemistry of the metabolites (including where metabolites are possible isomers derived from both factors of the active substance) tested in the toxicological and ecotoxicological studies was identical to the stereochemistry of the metabolites identified in the metabolism/degradation studies in animals, plants and the environment.

9.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

2. In-field recovery of non-target arthropods was not sufficiently demonstrated.

9.3. Overview of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 8, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

Representative use		**Grapes**
Operator risk	Risk identified	
	Assessment not finalised	
Worker risk	Risk identified	
	Assessment not finalised	X[1]
Bystander risk	Risk identified	
	Assessment not finalised	
Consumer risk	Risk identified	
	Assessment not finalised	X[1]
Risk to wild non target terrestrial vertebrates	Risk identified	
	Assessment not finalised	X[1]
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified	X[2]
	Assessment not finalised	X[1]
Risk to aquatic organisms	Risk identified	2 out of 5 FOCUS SW scenarios
	Assessment not finalised	X[1]
Groundwater exposure active substance	Legal parametric value breached	
	Assessment not finalised	

Groundwater exposure metabolites	Legal parametric value breached	
	Parametric value of 10µg/L[(a)] breached	
	Assessment not finalised	
Comments/Remarks		

The superscript numbers in this table relate to the numbered points indicated in sections 9.1 and 9.2. Where there is no superscript number see sections 2 to 6 for further information.
(a): Value for non-relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

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APPENDICES

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

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

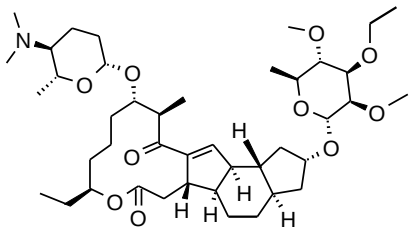
Active substance (ISO Common Name) ‡	Spinetoram [Spinetoram is a mixture of two main components, 50-90 % 3′-*O*-ethyl, 5,6-dihydro spinosyn J (XDE-175-J-major factor) and 50-10 % 3′-*O*-ethyl-spinosyn L (XDE-175-L minor factor)] [N.B. Throughout this evaluation document the manufacturer's development code number (XDE-175) has been used as at the start of the evaluation the common name had not been agreed]
Function (*e.g.* fungicide)	Insecticide
Rapporteur Member State	UK
Co-rapporteur Member State	Not applicable

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	XDE-175-J (Major factor) (2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*, 16b*R*)-2-(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranosyloxy)-13-[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methylpyran-2-yloxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro-14-methyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecine-7,15-dione XDE 175-L (Minor factor) (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-2-(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranosyloxy)-13-[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methylpyran-2-yloxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecine-7,15-dione
Chemical name (CA) ‡	XDE-175-J (Major factor) 1*H*-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-O-ethyl-2,4-di-O methyl-a-L-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro 14-methyl-, (2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*, 16a*S*,16b*R*) XDE-175-L (Minor factor) 1*H*-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione, 2-

	[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-a-L-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-, (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)
CIPAC No ‡	802
CAS No ‡	XDE-175-J: 187166-40-1 XDE-175-L: 187166-15-0 XDE-175 (Spinetoram): 935545-74-7
EC No (EINECS or ELINCS) ‡	Not available
FAO Specification (including year of publication) ‡	Not available
Minimum purity of the active substance as manufactured ‡	830 g/kg (pilot-scale production) Tolerance limits (g/kg) XDE-175-J = 581-810 XDE-175-L = 83-270 Tolerance limits (% ratio) XDE-175-J = 70-90 XDE-175-L = 10-30
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	XDE-175-J: $C_{42}H_{69}NO_{10}$ XDE-175-L: $C_{43}H_{69}NO_{10}$
Molecular mass ‡	XDE-175-J: 748.02 XDE-175-L: 760.03

Structural formula ‡



XDE-175-J

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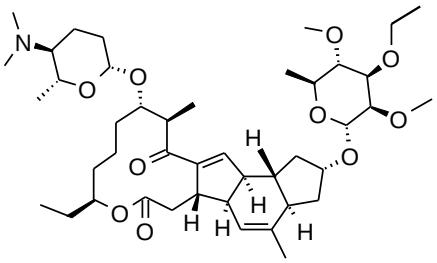


XDE-175-L

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	XDE-175-J: 143.4 °C (99.0 % pure) XDE-175-L: 70.8 °C (99.1 % pure)
Boiling point (state purity) ‡	decomposes before boiling
Temperature of decomposition (state purity)	XDE-175-J: 297.8 °C (99.0 % pure) XDE-175-L: 290.7 °C (99.1 % pure)
Appearance (state purity) ‡	XDE-175: off-white solid (85.8 % tech) XDE-175-J: white powder (99.0 % pure) XDE-175-L: white-yellow crystals (99.1 % pure)
Vapour pressure (state temperature, state purity) ‡	XDE-175-J (99.0 % pure): 5.3×10^{-5} Pa at 20 °C 6.0×10^{-5} Pa at 25 °C XDE-175-L (99.1 % pure): 2.1×10^{-5} Pa at 20 °C 4.2×10^{-5} Pa at 25 °C
Henry's law constant ‡	XDE-175-J: 4.0×10^{-3} Pa.m^3/mol unbuffered 9.4×10^{-5} Pa.m^3/mol at pH 5 3.5×10^{-3} Pa.m^3/mol at pH 7 6.3×10^{-3} Pa.m^3/mol at pH 10 XDE-175-L: 5.0×10^{-4} Pa.m^3/mol unbuffered 9.8×10^{-3} Pa.m^3/mol at pH 5 3.4×10^{-4} Pa.m^3/mol at pH 7 2.3×10^{-2} Pa.m^3/mol at pH 10
Solubility in water (state temperature, state purity and pH) ‡	XDE-175-J (99.0 % pure at 20 °C): Purified water 10.0 mg/L pH 5 buffer solution 423 mg/L pH 7 buffer solution 11.3 mg/L pH 10 buffer solution 6.27 mg/L XDE-175-L (99.1 % pure at 20 °C): Purified water 31.9 mg/L pH 5 buffer solution 1.63 g/L pH 7 buffer solution 46.7 mg/L pH 9 buffer solution 1.98 mg/L pH 10 buffer solution 0.71 mg/L
Solubility in organic solvents ‡ (state temperature, state purity)	XDE-175 (85.6 % tech at 20 °C) Methanol >250 g/L Acetone >250 g/L Xylene >250 g/L 1,2-dichloroethane >250 g/L Ethyl acetate >250 g/L n-heptane 61.0 g/L n-octanol 132 g/L
Surface tension ‡ (state concentration and temperature, state purity)	XDE-175 (85.8 % tech at 20 °C): 54.0 mN/m (90 % saturated solution)

Partition co-efficient ‡ (state temperature, pH and purity)	XDE-175-J (99.0 % pure at 20 °C): Log Kow = 2.44 at pH 5 Log Kow = 4.09 at pH 7 Log Kow = 4.22 at pH 9 XDE-175-L (99.1 % pure at 20 °C): Log Kow = 2.94 at pH 5 Log Kow = 4.49 at pH 7 Log Kow = 4.82 at pH 9
Dissociation constant (state purity) ‡	XDE-175-J (99.0 % pure): pK_a = 7.86 ± 0.04 at 25 °C XDE-175-L (99.1 % pure): pK_a = 7.59 ± 0.06 at 25 °C
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	XDE-175-J (97.6 % pure): Neutral solution (pH 7.57) Absorption maxima = 245 nm Extinction coefficient = 12200 L/(mol.cm) Acidic solution (pH 1.04) Absorption maxima = 247 nm Extinction coefficient = 12400 L/(mol.cm) Basic solution (pH 12.57) Absorption maxima = 247 nm Extinction coefficient = 12400 L/(mol.cm) XDE-175-L (96.1 % pure): Neutral solution (pH 7.75) Absorption maxima = 243 nm Extinction coefficient = 11100 L/(mol.cm) Acidic solution (pH 1.05) Absorption maxima = 202 and 245 nm Extinction coefficient = 9800 and 11400 L/(mol.cm) Basic solution (pH 12.66) Absorption maxima = 244 nm Extinction coefficient = 11200 L/(mol.cm)
Flammability ‡ (state purity)	Not flammable (XDE-175, 85.8 % tech) No self-ignition below 400 °C (XDE-175, 85.8 % tech)
Explosive properties ‡ (state purity)	Not explosive (XDE-175, 85.8 % tech)
Oxidising properties ‡ (state purity)	Not oxidising (XDE-175, 85.8 % tech)

Summary of representative uses evaluated (spinetoram)*

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)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha (l)		
Grapes (wine and table)	NEU and SEU	GF-1587	F	Polychrosis (Lobesia) botrana	SC	120 g/L	Power-operated hydraulic or air-assisted sprayer	From BBCH 71 through the year	1-3	10 days	0.0024 -0.036	100-1500	0.036	7	

* 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

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV (250 nm)
Impurities in technical as (analytical technique)	HPLC-UV (250 nm) GC-FID
Plant protection product (analytical technique)	HPLC-UV (250 nm)

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		XDE-175 (sum of XDE-175-J and XDE-175-L)
Food of animal origin		Residue definition not agreed
Soil		XDE-175 (sum of XDE-175-J and XDE-175-L) and the N-demethyl-175-J and N-demethyl-175-L metabolites
Water	surface	XDE-175 (sum of XDE-175-J and XDE-175-L) and the N-demethyl-175-J and N-demethyl-175-L metabolites
	drinking/ground	XDE-175 (sum of XDE-175-J and XDE-175-L) and the N-demethyl-175-J and N-demethyl-175-L metabolites
Air		XDE-175 (sum of XDE-175-J and XDE-175-L)

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	LC-MS/MS (acidic, wet, dry and oily crops) LOQ = 0.02 mg/kg (XDE-175; 0.01 mg/kg individually for XDE-175-J and XDE-175-L) (Acceptable ILV) Confirmatory method/data for oily and dry crops is required. DFG-S19 (apple, orange and grape)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	LC-MS/MS (tissues and milk) LOQ = 0.02 mg/kg (XDE-175; 0.01 mg/kg individually for XDE-175-J and XDE-175-L) (Acceptable ILV, confirmatory data provided only for milk and muscle)
Soil (analytical technique and LOQ)	LC-MS/MS (soil and sediment) LOQ = 0.005 mg/kg for each analyte (XDE-175-J, XDE-175-L, N-demethyl-175-J and N-demethyl-175-L)
Water (analytical technique and LOQ)	LC-MS/MS (drinking, ground and surface water) LOQ = 0.03 µg/L for each analyte (XDE-175-J, XDE-175-L, N-demethyl-175-J and N-demethyl-175-L)
Air (analytical technique and LOQ)	LC-MS/MS (ambient and elevated temperature and humidity) LOQ = 0.5 µg/m^3 (XDE-175)

Body fluids and tissues (analytical technique and LOQ)	LC-MS/MS (urine and blood) LOQ = 0.02 mg/kg (XDE-175; 0.01 mg/kg individually for XDE-175-J and XDE-175-L) (confirmatory data not provided)

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

	RMS/peer review proposal
Active substance	None

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	26-29% (XDE-175-J), 39-57% (XDE-175-L) based on comparison of plasma AUCs following oral and IV dosing (measure of bioavailability for all organs except liver). 80-90% based on % dose excreted in urine following oral dosing plus % dose excreted in faeces following IV dosing (measure of bioavailability for liver).
Distribution ‡	At plasma Cmax, highest concentrations in GI tract, lymph nodes, liver, lungs, adrenals, spleen. At 7 days post dose, highest concentrations were consistently in fat and kidneys (XDE-175-J) and fat and lymph nodes (XDE-175-L).
Potential for accumulation ‡	Potential for slow accumulation of low amounts based on occurrence of lysosomal vacuoles (probably consisting of lipid bound XDE-175/metabolites) in repeat dose studies.
Rate and extent of excretion ‡	85% excreted in faeces (evidence for significant biliary excretion); majority excreted in first 24h
Metabolism in animals ‡	Highly metabolised (at least 60% dose metabolised). Main pathways: glutathione conjugation of parent and of N-demethyl and 0-deethyl metabolites, hydroxylation of parent XDE-175-J.
Toxicologically relevant compounds ‡ (animals and plants)	Spinetoram and metabolites
Toxicologically relevant compounds ‡ (environment)	Spinetoram

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	>5000 mg/kg bw (75J:25L and 85J:15L)	
Rat LD_{50} dermal ‡	>5000 mg/kg bw (75J:25L and 85J:15L)	
Rat LC_{50} inhalation ‡	>5 mg/L (75J:25L and 85J:15L) (nose-only)	
Skin irritation ‡	No irritation (75J:25L) Slight reversible irritation (85J:15L)	
Eye irritation ‡	Slight reversible irritation (75J:25L and 85J:15L)	
Skin sensitisation ‡	Sensitiser (weak) in LLNA (75J:25L) Non-sensitiser in LLNA (85J:15L)	(R43) H317

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Cytoplasmic vacuolation, in several tissues/organs (rats, mice, dogs) Macrophage aggregates, in several tissues/organs (rats, mice) Arteritis, in several tissues; bone marrow necrosis (dogs)	
Relevant oral NOAEL ‡	<u>For 75J:25L</u> 90-day rat: 11 mg/kg bw per day* 90-day mouse: 9 mg/kg bw per day* 90-day dog: LOAEL= 5.7 mg/kg bw per day 1-year dog: 2.5 mg/kg bw per day <u>For 85J:15L</u> 90-day rat: 9 mg/kg bw per day	(R48/22) STOT-RE H 373
Relevant dermal NOAEL ‡	28-day rat: 1000 mg/kg bw/day (75J:25L).	
Relevant inhalation NOAEL ‡	No data available, none required	

* NOAEL for this study in the DAR is slightly different because it was corrected for purity. No correction for purity is however necessary.

Genotoxicity ‡ (Annex IIA, point 5.4)

Not genotoxic *in vitro* (75J:25L, 85J:15L) or *in vivo* (75J:25L)	

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

Target/critical effect ‡	Cell vacuolation in thyroid, retinal degeneration at dose above LOAEL (rat) Stomach lesions, macrophage aggregations in lung, vacuolation in epididymidal cells (mouse)	
Relevant NOAEL ‡	10.8 mg/kg bw per day (2-yr rat, 75J:25L) 18.8 mg/kg bw per day (18-month mouse, 75J:25L)	
Carcinogenicity ‡	XDE-175 (75J:25L) is unlikely to pose a carcinogenic risk to humans	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Dystocia, increased post implantation loss, reduced litter size or pup survival in the presence of maternal toxicity. Effects in pups regarded as being related to dystocia, rather than specific developmental effects.	
Relevant parental NOAEL ‡	10 mg/kg bw per day (75J:25L)	

Relevant reproductive NOAEL ‡	10 mg/kg bw per day (75J:25L)	(R62) H361f
Relevant offspring NOAEL ‡	75 mg/kg bw per day (75J:25L)	

Developmental toxicity

Developmental target / critical effect ‡	No adverse effects	
Relevant maternal NOAEL ‡	Rat: 100 mg/kg bw per day (75J:25L) Rabbit: 12 mg/kg bw per day (75J:25L)*	
Relevant developmental NOAEL ‡	Rat: 300 mg/kg bw per day (75J:25L) Rabbit: 72 mg/kg bw per day (75J:25L)*	

* NOAELs for this study in the DAR are slightly different because they were corrected for purity. No correction for purity is however necessary.

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Not neurotoxic, rat (75J:25L) NOAEL 2000 mg /kg bw	
Repeated neurotoxicity ‡	Not neurotoxic, 1-year rat (75J:25L) NOAEL 36.7 mg/kg bw per day	
Delayed neurotoxicity ‡	No data available, not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data available, not required
Studies performed on metabolites or impurities ‡	**N-demethyl-175-J** Rat oral LD_{50}: 3129 mg/kg bw Ames negative **N-formyl-175-J** Rat oral LD_{50}: >5000 mg/kg bw Ames negative **N-formyl -175-L** Rat oral LD_{50}: >5000 mg/kg bw Ames negative

Medical data ‡ (Annex IIA, point 5.9)

No information available

Summary (Annex IIA, point 5.10)	Value (in mg/kg bw per day, or mg/kg bw)	Study	Safety factor
ADI ‡	0.025	1-year dog	100
AOEL (short-term systemic)‡	0.0065	1-year dog	100 (26% oral absorption)
ARfD ‡	0.1	Multigeneration rat	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (GF-1587 11% SC)	For the concentrate: 0.2% For a 0.3 g a.s./l dilution: 5% For a 0.024 or 0.036 g a.s./l dilution: 11%

Exposure scenarios (Annex IIIA, point 7.2)

Operator	The exposure estimates with UK POEM are above the AOEL (178 to 357% of AOEL) with or without the use of personal protective equipment, for broadcast air spraying and hand-held use. The exposure estimates with the German model are 82 and 41% of the AOEL without the use of personal protective equipment, respectively for air assisted spraying and hand-held use. The exposure estimate according to EUROPOEM, for air-assisted spraying, is 83% of the AOEL without the use of personal protective equipment.
Workers	Re-entry exposure for workers performing cultivation and harvesting tasks in treated grapevines was predicted using the EUROPOEM II re-entry model and specific transfer co-efficient and dislodgeable foliar residue data for vines. This gave a predicted exposure of 15% of the AOEL. There is a possibility that the analytical method used for the DFR decline study did not detect toxicologically significant metabolites, but if these data are discounted, predicted exposure after 3 treatments is still ~30% of the AOEL.
Bystanders/residents	Predicted bystander exposure to drifting spray was 17% (Lloyd & Cross) or 14-45% (Rautmann) of the AOEL for air-assisted sprayers. Exposure to volatilised XDE-175 was predicted to be 8% of the AOEL using surrogate data. Exposure due to spray drift fallout onto adjacent property was predicted to be 2% of the AOEL for air-assisted sprayers.

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

	RMS/ Pesticides Peer Review meeting proposal
Substance classified (spinetoram)	R43 , R48/22, Repr. Cat 3 R62 (under Directive 67/548/EEC) H317, STOT-RE H373, Repr. 2 H361f (under Regulation 1272/2008)

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

Plant groups covered	Fruiting (apple), leafy (lettuce) and root and tuber (turnip) [foliar treatment]
Rotational crops	None
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable
Processed commodities	pH 4, 90°C, 20 minutes; pH 5, 100°C, 60 minutes; pH 6, 120°C, 20 minutes
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	XDE-175 (sum of XDE-175-J and XDE-175-L)
Plant residue definition for risk assessment	XDE-175 (sum of XDE-175-J and XDE-175-L) and the N-demethyl-175-J and N-formyl-175-J metabolites, expressed as XDE-175
Conversion factor (monitoring to risk assessment)	None proposed

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

Animals covered	Laying hen and lactating goat
Time needed to reach a plateau concentration in milk and eggs	Eggs: not reached within 7 days Milk: 4 days
Animal residue definition for monitoring	no definition agreed upon during peer review
Animal residue definition for risk assessment	no definition agreed upon during peer review
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes Log Pow > 3 at pH 7 and 9 for XDE-175-J and XDE-175-L. Highest tissue residues measured in fat for goat and hen.

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

Not required. Grapes are a permanent crop.

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

XDE-175-J, XDE-175-L, N-demethyl-175-J and N-formyl-175-J stable for up to 372 days in wheat grain, soybean, orange, lettuce and sugar beet.

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

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

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Grapes (table and wine)	SEU (field)	Risk assessment: 11 x <0.04, 0.051, 0.057, 0.063, 0.065, 0.095, 0.134, 0.153, 0.36, 0.418 Enforcement: 10 x <0.02, 0.021, 0.03, 0.037, 0.043, 0.045, 0.075, 0.114, 0.12, 0.27, 0.33	HR from SEU trials MRL proposal based on R(max) of 0.272 from SEU trials	n/a 0.3	0.418 n/a	n/a n/a
Grapes (table and wine)	NEU (field)	Risk assessment: <0.04, 0.04, 0.041, 0.043, 0.048, 0.052, 0.054, 0.105 Enforcement: <0.02, 0.02, 0.021, 0.023, 0.028, 2 x 0.032, 0.076	STMR from NEU trials n/a	n/a n/a	n/a n/a	0.046 n/a

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

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

ADI	0.025 mg/kg bw per day
TMDI (% ADI) for WHO Cluster Diet B according to EFSA Primo model	n/a – see IEDI
NEDI (% ADI) according to national (to be specified) diets	2 % (UK Vegetarian)
IEDI (European Diet) (% ADI)	0.8 % (FR all population)
Factors included in IEDI and NEDI	-
ARfD	0.1 mg/kg bw
IESTI (% ARfD)	27 % (DE child – Table grapes)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	25 % (UK toddler – Table grapes)
Factors included in IESTI and NESTI	-

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Commodity	Transfer factor	
Grapes (wine making)	2 (PHI 7 days)	Juice Pomace Young wine Bottled wine	1.0 <1.3 1.0 1.0	--
Grapes (wine making)	2 (PHI 0 days)	Juice Pomace Young wine Bottled wine	1.0 <2.6 <0.74 <0.74	--
Grapes (raisin production)	1 (PHI 7 days)	Raisins	1.0	--
Grapes (raisin production)	1 (PHI 0 days)	Raisins	1.6	--

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

Grapes: 0.5 mg/kg

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

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

Mineralization after 100 days ‡	20 °C: 0.4 – 19.1 % AR after 125 - 127 d, all labels, XDE-175-J (n[10]= 8) 1.1 – 23.7 % AR after 123 - 127 d, all labels, XDE-175-L (n = 8) 0.3 % AR after 120 d, all labels, XDE-175-J, sterile conditions (n = 1) 0.8 % AR after 120 d, all labels, XDE-175-L, sterile conditions (n = 1) 10 °C: 0.6 % AR after 127 d, all labels, XDE-175-J (n = 1) 1.5 % AR after 127 d, all labels, XDE-175-L (n = 1)
Non-extractable residues after 100 days ‡	20 °C: 4.6 – 26.5 % AR after 125 – 127 d, all labels, XDE-175-J (n = 8) 10.8 – 35.6 % AR after 123 - 127 d, all labels, XDE-175-L (n = 8) 5.6 % AR after 120 d, all labels, XDE-175-J, sterile conditions (n = 1) 4.3 % AR after 120 d, all labels, XDE-175-L, sterile conditions (n = 1) 10 °C: 8.9 % AR after 127 d, all labels, XDE-175-J (n = 1) 13.6 % AR after 127 d, all labels, XDE-175-L (n = 1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	20 °C: N-demethyl-175-J – 30.6 – 69.7 % AR at 14 - 125 d (n= 8) N-demethyl-N-nitroso-175-J [11]– 1.7 – 19.6 %AR at 57 - 127 d (n= 4) N-succinyl-J[11] – 1.0 – 8.9 % AR at 14 - 127 d (n= 4) N-demethyl-175-L – 14.0 – 43.8 % AR at 3 - 98 d (n= 8) N-demethyl-N-nitroso-175-L[11] – 3.5 – 13.6 %AR at 3 - 70 d (n= 4) N-succinyl-L[11]– 1.9 – 16.3 % AR at 21 - 127 d (n= 4) All labels 10 °C: N-demethyl-175-J – 61.3 % AR at 127 d (n= 1) N-demethyl-N-nitroso-175-J[11] – 21.0 %AR at 71 d (n= 1) N-succinyl-J[11] –9.6 % AR at 99 d (n= 1) N-demethyl-175-L – 34.8 % AR at 127 d (n= 1) N-demethyl-N-nitroso-175-L[11]– 16.3 %AR at 56 d (n= 1) N-succinyl-L[11] – 7.7 % AR at 98 d (n= 1) All labels

[10] n corresponds to the number of soils.
[11] These metabolites were not considered as relevant under field conditions and PEC values were not calculated.

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

Anaerobic degradation ‡	
Mineralization after 100 days	No acceptable study supplied.
Non-extractable residues after 100 days	No acceptable study supplied.
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No acceptable study supplied.
Soil photolysis ‡	
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None

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

Laboratory studies ‡

Parent – XDE-175-J	Aerobic conditions						
Soil type (USDA)	% OC	pH (H_2O)	t. °C / % FC (% pF2)	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (χ 2)	Method of calculation
Site I - sandy loam soil	0.8	7.9	20 °C/ 1/3 bar (70 %)	8.07/ 26.81	6.3	8.0	SFO
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	141/ 72881*	-‡	1.9	FOMC – to be used for triggering
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	126/ 420*	86.9	7.0	SFO – to be used for modelling
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	9.1/ 41.9	-‡	5.3	FOMC – to be used for triggering
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	10.4/ 34.4	8.8	13.7	SFO – to be used for modelling
Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)	11.1/ 64.7	-‡	3.6	FOMC – to be used for triggering
Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)	14.4/ 46.7	9.8	13.6	SFO – to be used for modelling
Site I - sandy loam soil	0.8	7.9	10 °C/ 1/3 bar (70 %)	20.8/ 69.2	6.3‡	5.8	SFO
Commerce - Loam	0.6	7.5	25 °C/ 75 % 1/3 bar (47 %§)	23.3/ 77.3	21.5	5.1	SFO†
Fayette – Silt loam	1.1	7.4	25 °C/ 75 % 1/3 bar (69 %§)	29/ 95	35.1	7.3	SFO†
Kimberlina/ Nord – Sandy loam	0.7	8.1	25 °C/ 75 % 1/3 bar (61 %§)	23/ 75	25.5	10.6	SFO†
Slagle - Loam	0.5	5.8	25 °C/ 75 % 1/3 bar (26 %§)	8.15/ 27.1	5.0	12.0	SFO†
Geometric mean for use in modelling			-	-	16.1	-	-

* DT value extrapolated beyond study duration

§ Reported as a percentage of standard FOCUS field capacity values for the relevant USDA soil type as moisture contents at field capacity were not reported in the study

† Values acceptable for modelling only

‡ Value not included in geometric mean calculation for use in modelling

NB. The RMS considered that it is not appropriate to normalise non-SFO DT_{50} and DT_{90} values (see discussion above).

Parent – XDE-175-L	Aerobic conditions						
Soil type (USDA)	% OC	pH (water)	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (χ2)	Method of calculation
Site I - sandy loam soil	0.8	7.9	20 °C/ 1/3 bar (70 %)	6.6/ 22.1	5.1	8.0	SFO
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	47.7/ 1615*	-‡	4.0	FOMC – to be used for triggering
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	70.0/ 232*	48.3	10.4	SFO – to be used for modelling
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	7.05/ 32.9	-‡	9.0	FOMC – to be used for triggering
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	7.89/ 26.2	6.7	14.4	SFO – to be used for modelling
Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)	8.40/ 75.1	-‡ (22.6)††	11.3	FOMC
Site I - sandy loam soil	0.8	7.9	10 °C/ 1/3 bar (70 %)	16.2/ 53.8	4.9‡	6.8	SFO
Commerce - Loam	0.6	7.5	25 °C/ 75 % 1/3 bar (47 %§)	17/ 58	15.7	12.5	SFO†
Fayette – Silt loam	1.1	7.4	25 °C/ 75 % 1/3 bar (69 %§)	15/ 49	18.2	16.0	SFO†
Kimberlina/ Nord – Sandy loam	0.7	8.1	25 °C/ 75 % 1/3 bar (61 %§)	17/ 57	18.9	19.0	SFO†
Slagle - Loam	0.5	5.8	25 °C/ 75 % 1/3 bar (26 %§)	3/ 11	1.8	16.4	SFO†
Geometric mean for use in modelling			-	-	11.8	-	-

* DT value extrapolated beyond study duration

§ Reported as a percentage of standard FOCUS field capacity values for the relevant USDA soil type as moisture contents at field capacity were not reported in the study

† Values acceptable for modelling only

†† Value acceptable for modelling shown in brackets – calculated from non-normalised FOMC DT90 divided by 3.32

‡ Value not in geometric mean calculation, which is for use in modelling

NB. The RMS considered that it is not appropriate to normalise non-SFO DT_{50} and DT_{90} values (see discussion above).

N-demethyl-175-J	Aerobic conditions							
Soil type	% OC	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. kdp/ kf	DT_{50} (d) 20°C pF2/10kPa	St. (χ2)	Method of calculation
Site I - sandy loam soil	0.8	7.9	20 °C/ 1/3 bar (70 %)	136/ 452*	0.58	106.1	7.7	Parent SFO followed by SFO
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	-	-	-	-	NC
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	-	-	-	-	NC
Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)	-	-	-	-	NC
Site I - sandy loam soil	0.8	7.9	10 °C/ 1/3 bar (70 %)	-	-	-	-	NC
Commerce - Loam	0.6	7.5	25 °C/ 75 % 1/3 bar (47 %§)	257/ 853*	0.88	237	3.0	SFO†
Fayette – Silt loam	1.1	7.4	25 °C/ 75 % 1/3 bar (69 %§)	273/ 907*	0.94	330	7.1	SFO†
Kimberlina/ Nord – Sandy loam	0.7	8.1	25 °C/ 75 % 1/3 bar (61 %§)	156/ 519*	0.83	173	14.3	SFO†
Slagle - Loam	0.5	5.8	25 °C/ 75 % 1/3 bar (26 %§)	32/ 106	0.87	19.6	17.1	SFO†
Geometric mean for use in modelling			-	-	-#	123	-	-

* DT value extrapolated beyond study duration

NC = not calculated – metabolite concentrations still increasing at study termination

§ Reported as a percentage of standard FOCUS field capacity values for the relevant USDA soil type as moisture contents at field capacity were not reported in the study

† Values acceptable for modelling only

Maximum formation fraction of 0.94 used in modelling

N-demethyl-175-L	Aerobic conditions							
Soil type	% OC	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. kdp/ kf	DT_{50} (d) 20°C pF2/10kPa	St. (χ2)	Method of calculation
Site I - sandy loam soil	0.8	7.9	20 °C/ 1/3 bar (70 %)	59.9/ 199*	0.44	46.7	12.1	Parent SFO followed by SFO
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	-	-	-	-	NC

Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	102/ 340*	0.19	86.4‡	5.4	Parent FOMC followed by SFO
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	112/ 373*	0.48	95.0	6.5	Parent SFO followed by SFO
Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)			-		NC
Site I - sandy loam soil	0.8	7.9	10 °C/ 1/3 bar (70 %)	115/ 382*	0.44	34.7‡	8.3	Parent SFO followed by SFO
Commerce - Loam	0.6	7.5	25 °C/ 75 % 1/3 bar (47 %§)	88/ 291	0.65	81.4	23.9	SFO†
Fayette – Silt loam	1.1	7.4	25 °C/ 75 % 1/3 bar (69 %§)	18/ 59	1.0	21.8‡	27.8	SFO††
Kimberlina/ Nord – Sandy loam	0.7	8.1	25 °C/ 75 % 1/3 bar (61 %§)	29/ 97	0.85	32.2‡	32.7	SFO††
Slagle - Loam	0.5	5.8	25 °C/ 75 % 1/3 bar (26 %§)	5/ 18	0.31	3.1‡	22.4	SFO††
Geometric mean for use in modelling			-	-	-#	71.2	-	-

* DT value extrapolated beyond study duration

NC = not calculated – metabolite concentrations still increasing at study termination

§ Reported as a percentage of standard FOCUS field capacity values for the relevant USDA soil type as moisture contents at field capacity were not reported in the study

† Values acceptable for modelling only

†† Values not acceptable for modelling or triggering due to unacceptable fit

‡ Value not in geometric mean calculation, which is for use in modelling

Maximum formation fraction of 0.65 used in modelling

N-demethyl-N-nitroso-175-J	Aerobic conditions							
Soil type	% OC	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. kdp/ kf	DT_{50}/ DT_{90} (d) 20°C pF2/10kPa	St. (χ2)	Method of calculation
Site I - sandy loam soil	0.8	7.9	20 °C/ 1/3 bar (70 %)	281*/932*	-	219/ 727	3.1	SFO peak down
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	-	-	-	-	NC
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	-	-	-	-	NC

Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)	114*/378*	-	77.5/ 257	13.6	SFO peak down
Site I - sandy loam soil	0.8	7.9	10 °C/ 1/3 bar (70 %)	-	-	-	-	NC
Maximum DT_{50} for use in modelling (since data for only two soils is available)			-	-	-	219	-	-

* DT value extrapolated beyond study termination

NC = not calculated – metabolite concentrations still increasing at study termination or concentrations too low

N-demethyl-N-nitroso-175-L	Aerobic conditions							
Soil type	% OC	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. kdp/ kf	DT_{50} (d) 20°C pF2/10kPa	St. (χ2)	Method of calculation
Site I - sandy loam soil	0.8	7.9	20 °C/ 1/3 bar (70 %)	95*/315*	-	74.1/ 246	18.9	SFO peak down
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	-	-	-	-	NC
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	-	-	-	-	NC
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	-	-	-	-	NC
Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)	55.3*/184*	-	37.6/ 125†	22.9	SFO peak down
Site I - sandy loam soil	0.8	7.9	10 °C/ 1/3 bar (70 %)	85*/ 283*	-	25.7/ 85.4	6.3	SFO peak down
Maximum DT50 for use in modelling (since data for only two soils is available)			-	-	-	74.1	-	-

* DT value extrapolated beyond study termination

NC = not calculated – metabolite concentrations still increasing at study termination or concentrations too low

†Values not acceptable for modelling or triggering due to unacceptable fit

N-succinyl-J	Aerobic conditions							
Soil type	% OC	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. kdp/ kf	DT_{50} (d) 20°C pF2/10kPa	St. (χ2)	Method of calculation
Site I - sandy loam soil	0.8	7.9	20 °C/ 1/3 bar (70 %)	756*/2510*	-	590/1958	6.3	SFO peak down
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	-	-	-	-	NC

Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	-	-	-	-	NC
Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)	-	-	-	-	NC
Site I - sandy loam soil	0.8	7.9	10 °C/ 1/3 bar (70 %)	-	-	-	-	NC
Maximum DT50 for use in modelling (since data for only two soils is available)			-	-	-	590	-	-

* DT value extrapolated beyond study termination

NC = not calculated – metabolite concentrations still increasing at study termination or concentrations too low

N-succinyl-L	Aerobic conditions							
Soil type	% OC	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. kdp/ kf	DT_{50} (d) 20°C pF2/10kPa	St. (χ2)	Method of calculation
Site I - sandy loam soil	0.8	7.9	20 °C/ 1/3 bar (70 %)	140*/464*	-	109/ 362	9.1	SFO peak down
Speyer LUFA 2.2 – loamy sand soil	1.8	6.0	20 °C/ 1/3 bar (59 %)	-	-	-	-	NC
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	-	-	-	-	NC
Little Shelford – sandy loam soil	1.2	7.8	20 °C/ 1/3 bar (79 %)	-	-	-	-	NC
Speyer LUFA 3A – sandy clay loam	1.3	7.8	20 °C/ 1/3 bar (58 %)	-	-	-	-	NC
Site I - sandy loam soil	0.8	7.9	10 °C/ 1/3 bar (70 %)	-	-	-	-	NC
Maximum DT50 for use in modelling (since data for only two soils is available)			-	-	-	109	-	-

* DT value extrapolated beyond study termination

NC = not calculated – metabolite concentrations still increasing at study termination or concentrations too low

†Values not acceptable for modelling or triggering due to unacceptable fit

Field studies ‡

Parent – XDE-175-J	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	% OC	pH (H_2O)	Depth (cm)	DT_{50} (d) Norm	DT_{90}(d) Norm	St. (χ2)	DT_{50} (d; modelling)#	Method of calculation
Loam	Elne, France (S)	1.77	6.9	0 - 20	0.032	1.58	19.9	0.48	FOMC
Silt loam	Meistratzheim, France (N)	1.45	7.8	0 - 20	2.49	8.27	8.3	2.49	SFO

Sand	Dollern, Germany	2.87	6.8	0 - 20	0.289	197	26.8	59.3	FOMC
Silty clay loam	Alpera, Spain	1.79	7.9	0 - 20	1.64	25.7	17.1	7.74	FOMC
Geometric mean								4.84	
Parent – XDE-175-L	Aerobic conditions								
Soil type	Location	% OC	pH	Depth (cm)	DT_{50} (d) Norm	DT_{90} (d) Norm	St. ($\chi 2$)	DT_{50} (d; modelling)	Method of calculation
Loam	Elne, France (S)	1.77	6.9	0 - 20	0.066	0.510	22.8	0.15	FOMC
Silt loam	Meistratzheim, France (N)	1.45	7.8	0 - 20	2.02	6.72	28.3	2.02	SFO
Sand	Dollern, Germany	2.87	6.8	0 - 20	0.051	1.43	8.8	0.43	FOMC
Silty clay loam	Alpera, Spain	1.79	7.9	0 - 20	0.93	7.91	13.9	2.38	FOMC
Geometric mean								0.75	

Metabolite – N-demethyl-175-J	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	Max observed (% w/w)	pH (H_2O)	Depth (cm)	DT_{50} (d) Norm	DT_{90}(d) Norm	St. ($\chi 2$)	DT_{50} (d; modelling)	Method of calculation
Loam	Elne, France (S)	15.8	6.9	0 - 20	28.2	93.6	31.1	28.2	Peak-down SFO
Silt loam	Meistratzheim, France (N)	30.9	7.8	0 - 20	20.5	68.2	34.1	20.5§	Peak-down SFO
Sand	Dollern, Germany	17.2	6.8	0 - 20	98.9	328	29.0	98.9	Peak-down SFO
Silty clay loam	Alpera, Spain	18.5	7.9	0 - 20	65.9	219	24.5	65.9	Peak-down SFO
Geometric mean								56.9	
Metabolite – N-demethyl-175-L	Aerobic conditions								
Soil type	Location	Max observed (% w/w)	pH	Depth (cm)	DT_{50} (d) Norm	DT_{90} (d) Norm	St. ($\chi 2$)	DT_{50} (d; modelling)	Method of calculation
Loam	Elne, France (S)	2.5	6.9	0 - 20					NC*
Silt loam	Meistratzheim, France (N)	16.9	7.8	0 - 20	1.70	5.65	26.8	1.70	Peak down – SFO

Sand	Dollern, Germany	2.3	6.8	0 - 20	2.46	8.17	18.1	2.46	Peak down – SFO
Silty clay loam	Alpera, Spain	6.0	7.9	0 - 20					NC*
Geometric mean†								2.08†	

* NC = not calculated – too few data points

§ Value excluded from geomean calculation

† Maximum values used in PEC calculations/ modelling as a worst case as only two DT50 values available.

DT_{50} calculated from back calculated FOMC kinetics

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	No study submitted and soil accumulation not required to be addressed since field dissipation study DT_{90} values did not exceed 1 year.

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	X[12]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
No acceptable study submitted							

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

XDE-175-J ‡							
Soil Type (USDA)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Flint Hall, Herts., UK – Clay loam	2.9	7.8	61	2108	41	1409	0.891
Pidemont, Italy - Loam	1.2	6.3	35	2952	41	3399	1.071
Hanhofen, Germany – Loamy sand	1.8	6.0	35	1931	30	1694	0.956
Altluâheim, Germany – Sandy clay loam	1.3	7.8	39	2967	29	2227	0.924
Longwoods Quarry, Linolnshire, UK – Loamy sand	0.8	7.9	29	3650	21	2590	0.871
Okabe-chow, Japan – Sandy loam	3.0	5.7	44	1470	39	1291	0.973
Little Shelford, Cambridgeshire, UK – Sandy loam	1.6	7.6	66	4134	57	3591	0.971
Oakville, USA – Loamy Sand	0.8	6.7	14	1800	10.1	1263	0.83
Kimberlina/ Nord, USA – Sandy Loam	0.7	8.1	38	5490	43.8	6257	1.11
Slagle, USA - Loam	0.5	5.8	12	2344	8.6	1720	0.89
Arithmetic mean					32	2544	0.949
pH dependence, Yes or No			No				

XDE-175-L ‡							
Soil Type (USDA)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Flint Hall, Herts., UK – Clay loam	2.9	7.8	107	3697	92	3184	0.974
Pidemont, Italy - Loam	1.2	6.3	109	9087	22	1837	0.716
Hanhofen, Germany – Loamy sand	1.8	6.0	54	3002	46	2550	1.006
Altluâheim, Germany – Sandy clay loam	1.3	7.8	63	4836	15	1133	0.712
Longwoods Quarry, Linolnshire, UK – Loamy sand	0.8	7.9	43	5343	18	2214	0.815
Okabe-chow, Japan – Sandy loam	3.0	5.7	74	2471	30	999	0.820
Little Shelford, Cambridgeshire, UK – Sandy loam	1.6	7.6	116	7227	124	7779	1.017
Oakville, USA – Loamy Sand	0.8	6.7	31	3936	-	-	-
Kimberlina/ Nord, USA – Sandy Loam	0.7	8.1	92	13185	-	-	-
Slagle, USA - Loam	0.5	5.8	24	4816	-	-	-
Arithmetic mean/median					50	2814	0.866
pH dependence, Yes or No			No				

N-demethyl-175-J ‡							
Soil Type (USDA)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Flint Hall, Herts., UK – Clay loam	2.9	7.8	67	2303	48	1671	0.914
Pidemont, Italy - Loam	1.2	6.3	46	3847	26	2203	0.866
Hanhofen, Germany – Loamy sand	1.8	6.0	48	2662	38	2119	0.937
Altluâheim, Germany – Sandy clay loam	1.3	7.8	43	3338	31	2353	0.895
Longwoods Quarry, Linolnshire, UK – Loamy sand	0.8	7.9	36	4460	28	3444	0.914
Okabe-chow, Japan – Sandy loam	3.0	5.7	51	1684	38	1257	0.914
Little Shelford, Cambridgeshire, UK – Sandy loam	1.6	7.6	86	5369	60	3733	0.906
Oakville, USA – Loamy Sand	0.8	6.7	16	2062	-	-	-
Kimberlina/ Nord, USA – Sandy Loam	0.7	8.1	32	4642	-	-	-
Slagle, USA - Loam	0.5	5.8	8	1631	-	-	-
Arithmetic mean/median					38	2397	0.907
pH dependence (yes or no)			No				

N-demethyl-175-L ‡							
Soil Type (USDA)	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Flint Hall, Herts., UK – Clay loam	2.9	7.8	112	3859	68	2332	0.928
Pidemont, Italy - Loam	1.2	6.3	77	6457	19	1589	0.732
Hanhofen, Germany – Loamy sand	1.8	6.0	72	3991	25	1362	0.788
Altluâheim, Germany – Sandy clay loam	1.3	7.8	59	4549	22	1721	0.800
Longwoods Quarry, Linolnshire, UK – Loamy sand	0.8	7.9	48	5960	35	4364	0.949
Okabe-chow, Japan – Sandy loam	3.0	5.7	78	2588	37	1249	0.856
Little Shelford, Cambridgeshire, UK – Sandy loam	1.6	7.6	128	7976	68	4258	0.893
Oakville, USA – Loamy Sand	0.8	6.7	34	4270	-	-	-
Kimberlina/ Nord, USA – Sandy Loam	0.7	8.1	81	11559	-	-	-
Slagle, USA - Loam	0.5	5.8	19	3718	-	-	-
Arithmetic mean/median					39	2411	0.849
pH dependence (yes or no)			No				

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

Column leaching ‡	No study submitted – none required.
Aged residues leaching ‡	No study submitted – none required.
Lysimeter/ field leaching studies ‡	No study submitted – none required.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent – XDE-175-J	DT_{50} (d): 141 d (DT_{90} of 72881 d)
Method of calculation	Kinetics: FOMC (α = 0.264 and β = 10.60)
	Field or Lab: representative worst case from lab studies.
Application data	Crop: Vines
	Depth of soil layer: 5cm
	Soil bulk density: 1.5g/cm^3
	% plant interception: 0 % (worst case value; application to vines at GS 71 indicates 85 %)
	Number of applications: 3
	Interval (d): 7 d
	Application rate(s): 3 x 30.6 g as/ha (assumes 85 % of XDE-175 is XDE-175-J)

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		-		0.109	
Short term	24h	-	-	0.107	0.108
	2d	-	-	0.106	0.107
	4d	-	-	0.103	0.106
Long term	7d	-	-	0.099	0.104
	28d	-	-	0.084	0.094
	50d	-	-	0.075	0.087
	100d	-	-	0.065	0.079
Plateau concentration		Not calculated. Field dissipation studies indicate that soil accumulation is not required to be addressed.			

Parent – XDE-175-L	DT_{50} (d): 47.7 d (DT_{90} of 1615 d)
Method of calculation	Kinetics: FOMC (α = 0.495 and β = 15.61)
	Field or Lab: representative worst case from lab studies.
Application data	Crop: Vines
	Depth of soil layer: 5cm
	Soil bulk density: 1.5g/cm^3
	% plant interception: 0 % (worst case value; application to vines at GS 71 indicates 85 %)
	Number of applications: 3
	Interval (d): 7 d
	Application rate(s): 3 x 5.4 g as/ha (assumes 15 % of XDE-175 is XDE-175-L)

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		-		0.0184	
Short term	24h	-	-	0.0180	0.0182
	2d	-	-	0.0176	0.0180
	4d	-	-	0.0169	0.0176
Long term	7d	-	-	0.0160	0.0171
	28d	-	-	0.0121	0.0147
	50d	-	-	0.0101	0.0134
	100d	-	-	0.0078	0.0113
Plateau concentration		Not calculated. Field dissipation studies indicate that soil accumulation is not required to be addressed.			

Parent – Total XDE-175 Method of calculation	PEC values for XDE-175-J and XDE-175-L were summed. Therefore a ratio of 85J:15L* is assumed for an application of 3 x 36 g as/ ha.
Application data	-

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		-		0.127	
Short term	24h	-	-	0.125	0.126
	2d	-	-	0.124	0.125
	4d	-	-	0.120	0.124
Long term	7d	-	-	0.115	0.121
	28d	-	-	0.096	0.109
	50d	-	-	0.085	0.100
	100d	-	-	0.073	0.090
Plateau concentration		Not calculated. Field dissipation studies indicate that soil accumulation is not required to be addressed.			

*The ratio of the two factors in the active substance commonly varies from 75J:25L to 85J:15L. Ecotox data have only been supplied for the total active substance XDE-175 and therefore the PECs for the individual factors are only relevant for calculating the PEC for total XDE-175. Therefore as a worst case for the PECsoil calculation, the factor with the longest DT_{50} was assumed to be present in its maximum concentration in the active substance ratio, and since DT_{50} values are longer for XDE-175-J than XDE-175-L a ratio of 85J: 15L was assumed for the calculation as a worst case.

Maximum PEC_{soil} values for XDE-175-J, XDE-175-L and their major N-demethyl metabolites in a 5cm soil layer following application to vines according to the proposed critical GAP

compound	Molecular weight	Maximum Occurrence (% AR)	Max PECsoil (mg/ kg)
XDE-175-J	748	-	0.109
XDE-175-L	760	-	0.0184
N-demethyl-175-J	734	69.7	0.0746
N-demethyl-175-L	746	43.8	0.0079

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 5: XDE-175-J stable at 25 °C XDE-175-L stable at 25 °C
	pH 7: XDE-175-J stable at 25 °C XDE-175-L stable at 25 °C
	pH 9: XDE-175-J slow degradation at 25 °C* XDE-175-L: DT_{50} = 156 d at 25 °C (SFO; r^2=0.928) N-demethyl-175-J: max 6.7 %AR (30 d) N-demethyl-175-L: max 11.9 %AR (30 d)

Photolytic degradation of active substance and metabolites above 10 % ‡	<u>Sterile aqueous buffer solution – pH 7 (Direct phototransformation).</u> XDE-175-J: DT_{50} = 0.375 d (9 hr; xenon lamp filtered to remove λ < 290 nm); estimated DT_{50} at 40°N summer sun = 0.5 d (12 hr) MW813: 11 %AR (7 d); estimated DT_{50} at 40°N summer sun = 6.8 days† (peak down SFO) N-demethyl-175-J: 8.0 % AR (0.7 d); no estimated DT_{50} – max concentration < 10 % AR. XDE-175-L: DT_{50} = 0.170 d (4.1 hr; xenon lamp filtered to remove λ < 290 nm); estimated DT_{50} at 40°N summer sun = 0.3 d (7.3 hr) N-demethyl-175-L: 12.8 %AR (0.17 d); estimated DT_{50} at 40°N summer sun = 0.4 days (10 hr; SFO) <u>Sterile natural water, Iowa, USA - pH 8.5</u> XDE-175-J: DT_{50} = 0.13 d (3.1 hr; xenon lamp filtered to remove λ < 290 nm); estimated DT_{50} at 40°N summer sun = 0.25 d (6 hr) N-demethyl-175-J: 27.8 % AR (0.33 d); estimated DT_{50} at 40°N summer sun = 0.97 days (23.3 hr; peak down SFO). XDE-175-L: DT_{50} = 0.07 d (1.7 hr; xenon lamp filtered to remove λ < 290 nm); estimated DT_{50} at 40°N summer sun = 0.12 d (2.9 hr) 13,14-beta-dihydro-C17-pseudoaglycone-175-L: 23.3 % AR (0.33 d); estimated DT_{50} at 40°N summer sun = 1.36 days (peak down SFO) N-demethyl-175-L: 9.8 %AR (0.13 d); no estimated DT_{50} – max concentration < 10 % AR.
Quantum yield of direct phototransformation in water at Σ > 290 nm	XDE-175-J: 4.2×10^{-2} XDE-175-L: 6.6×10^{-2}
Readily biodegradable ‡ (yes/no)	Not readily biodegradable.

* Actual degradation rate and DT_{50} was not calculated because 91.9 % AR remained as parent at study termination

† the RMS considers that the value should be treated with caution; only three data points in curve fit.

Degradation in water / sediment studies

Parent – XDE-175-J	Distribution - Max in water = 80.9 % AR after 0 d, Swiss lake system (mean; n=2). Max. in sediment = 81.5 % AR after 63 d, Alto Garda system (mean; n=2).									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys. (d)	St. (χ^2)	†DT_{50}-DT_{90} water (d)	St. (χ^2)	†DT_{50}-DT_{90} sed (d)	St. (χ^2)	Method of calculation
Swiss Lake, Derbyshire, England – sand*	7.1	6.9	20	187/ 622	6.5	5.0/ 58.1 3.4 DT_{50} fast phase 45.0 DT_{50} slow phase	14.0	134/ 444	2.7	SFO whole system; DFOP water phase; SFO peak down sediment phase
Alto Garda, Brescia, Italy – sandy loam	8.1	8.1	20	315/ 1047	3.6	5.0/ 22.0	11.7	206/ 685	5.0	SFO whole system; FOMC water phase; SFO peak down sediment phase
Geometric mean/median				243/ 807		5.0/ 35.8		166/ 551		
Parent – XDE-175-L	Distribution - Max in water = 73.6 % AR after 0 d, Swiss lake system (mean; n=2). Max. in sediment = 82.4 % AR after 35 d, Alto Garda system (mean; n=2).									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	†DT_{50}-DT_{90} water	St. (χ^2)	†DT_{50}-DT_{90} sed	St. (χ^2)	Method of calculation
Swiss Lake, Derbyshire, England – sand	7.1	6.9	20	315/ 1047	6.5	5.0/ 29.0	8.7	NC	-	SFO whole system; FOMC water phase.
Alto Garda, Brescia, Italy – sandy loam	8.1	8.1	20	292/ 971	3.4	5.6/ 18.5	11.4	227/ 754	2.9	SFO whole system; SFO water phase; SFO peak down sediment phase
Geometric mean/median				303/ 1008		5.3/ 23.2		227/ 754		

* Water phase value calculated by DFOP kinetics, hence an overall DT50 and DT90 as well as DT50 values for the fast and slow phases are reported.
NC – not calculated, insufficient decline phase.
† Water and sediment phase DT50 values represent dissipation not degradation as they do not remove partitioning processes

N-demethyl-XDE-175-J	Distribution - Max in water = 8.4 % AR after 7 d, Swiss lake system (n=1). Max. in sediment = 19.9 % AR after 107 d, Swiss lake system (mean; n=2).									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	†DT_{50}-DT_{90} water	χ^2	†DT_{50}-DT_{90} sed	St. (χ^2)	Method of calculation
Swiss Lake, Derbyshire, England – sand	7.1	6.9	20	NC	-	74‡/ 245‡	24.7	NC	-	Peak down SFO
Alto Garda, Brescia, Italy – sandy loam	8.1	8.1	20	NC	-	NC	-	NC	-	NA
Geometric mean/median				-		-		-		

NC – not calculated, insufficient decline phase.
† Water and sediment phase DT50 values represent dissipation not degradation as they do not remove partitioning processes
‡ Calculated values not considered acceptable by RMS

N-demethyl-XDE-175-L	Distribution - Max in water = 9.2 % AR after 3 d, Swiss lake system (mean; n=2). Max. in sediment = 12.7 % AR after 107 d, Alto Garda system (mean; n=2).									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	†DT_{50}-DT_{90} water	χ^2	†DT_{50}-DT_{90} sed	St. (χ^2)	Method of calculation
Swiss Lake, Derbyshire, England – sand	7.1	6.9	20	NC	-	18‡/ 60‡	22.5	NC	-	Peak down SFO
Alto Garda, Brescia, Italy – sandy loam	8.1	8.1	20	NC	-	NC	-	NC	-	NA
Geometric mean/median				-		-		-		

NC – not calculated, insufficient decline phase.
† Water and sediment phase DT50 values represent dissipation not degradation as they do not remove partitioning processes
‡ Calculated values not considered acceptable by RMS

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Swiss Lake, Derbyshire, England – sand - XDE-175-J	7.1	6.9	0.3 % AR (mean; n=2; 107d)	3.5 % AR (n=1; 91d)	4.6 % AR (mean; n=2; 107d)

Alto Garda, Brescia, Italy – sandy loam – XDE-175-J	8.1	8.1	0.2 % AR (mean; n=2; 107d)	8.6 % AR (mean; n=2; 91d)	6.8 % AR (n=1; 107d)
Swiss Lake, Derbyshire, England – sand - XDE-175-L	7.1	6.9	0.3 % AR (mean; n=2; 107d)	4.6 % AR (mean; n=2; 107d)	4.6 % AR (mean; n=2; 107d)
Alto Garda, Brescia, Italy – sandy loam – XDE-175-L	8.1	8.1	0.5 % AR (mean; n=2; 107d)	8.2 % AR (mean; n=2; 91d & 107d)	8.2 % AR (mean; n=2; 107d)

Aquatic Field Dissipation Study

Parent – Total XDE-175-J	Distribution – XDE-175-J max in water = 1.275 µg/ L after 0.5 d at Indiana site (station 2 – shallow end). Max. sed < LOD (0.0015 µg/ g) at all time-points and locations. XDE-175-L max in water = 0.305 µg/ L after 0.5 d at Indiana site (station 2 –shallow end). Max. sed < LOD (0.0015 µg/ g) at all time-points and locations.									
Location	Latitude	Depth of water body (m)	pH water	pH sed	t. (°C depth measured cm)*	Hourly solar radiation (kJm^{-2}; range and experiment total)	Light Extinction depth (cm)	DT_{50}- DT_{90} water (hr) (long phase DT_{50})	St. (χ^2)	Method of calculation
Tifton, Georgia, USA	31.5 °N	0.5 – 1.0	7.8	7.8	30.4 – 33.5 (47.5 cm)	0 – 3383 (17587)	48 cm	0.920 hr/ 68.6 hr (0.04d/ 2.9d) Long phase = 33.5 hr† Short phase = 0.35 hr††	14.3	DFOP (box model)
Seymour, Indiana, USA	39 °N	0.5 – 1.0	8.5	7.8	27.2 – 28.5 (48 cm)	0 – 3249 (26044)	18 cm	0.511 hr/ 55.1 hr (0.02d/ 2.3d) Long phase = 29.5 hr† Short phase = 0.23 hr††	14.8	DFOP (box model)

Median						0.716 hr/ 61.9 hr (0.03d/ 2.6d)		

* For both sites maximum surface water temperatures were approximately 35 – 37 °C. Approximate values quoted as values read from graph.
† Long phase DT50 to be used in parent modelling
†† Short phase DT50 to be used in metabolite modelling

Metabolite – N-demethyl-175	Distribution – XDE-175-J max in water = 1.066 µg/ L after 0.5 d at Indiana site (station 2 – shallow end). Max. sed < LOD (0.0015 µg/ g) at all time-points and locations. XDE-175-L max in water = 0.205 µg/ L after 0.5 d at Indiana site (station 2 – shallow end). Max. sed < LOD (0.0015 µg/ g) at all time-points and locations.									
Location	Latitude	Depth of water body (m)	pH water	pH sed	t. (°C depth measured cm)*	Hourly solar radiation (kJm^{-2}; range and experiment total)	Light Extinction depth (cm)	DT_{50}- DT_{90} water (hr)	St. (χ^2)	Method of calculation
Tifton, Georgia, USA	31.5 °N	0.5 – 1.0	7.8	7.8	30.4 – 33.5 (47.5 cm)	0 – 3383 (17587)	48	54.0/ 180 (2.3d/ 7.5d)	13.5	Box model. Parent DFOP – metab SFO
Seymour, Indiana, USA	39 °N	0.5 – 1.0	8.5	7.8	27.2 – 28.5 (48 cm)	0 – 3249 (26044)	18	15.2/ 50.5 (0.63d/ 2.1d)	21.7	Box model. Parent DFOP – metab SFO
Median								1.5d/ 4.8d		

* For both sites maximum surface water temperatures were approximately 35 – 37 °C. Approximate values quoted as values read from graph.

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

Parent XDE-175 Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: 1.1. Molecular weight (g/mol): XDE-175-J – 748 XDE-175-L – 760 Water solubility (mg/L): XDE-175-J – 11.3 XDE-175-L – 46.7 K_{OC} (L/kg) : XDE-175-J – 2544.1 (mean) XDE-175-L – 2813.7 (mean) DT_{50} soil (d): XDE-175-J – 16.1 days (Lab geomean) XDE-175-L - 11.8 days (Lab geomean) DT_{50} water/sediment system (d): XDE-175-J – 315 d (worst case; n=2) XDE-175-L – 315d (worst case; n=2) DT_{50} water (d): XDE-175-J - 1000 d (default worst case) XDE-175-L – 1000 d (default worst-case) DT_{50} sediment (d): XDE-175-J - 315 d (whole system worst case; n=2) XDE-175-L – 315 d (whole system worst case; n=2) Crop interception (%): full canopy
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: SWASH vers. 2.1., FOCUS MACRO vers. 4.3b., FOCUS PRZM vers., 3.21.b, TOXSWA vers. 2.1.1. Vapour pressure: XDE-175-J – 5.3 x 10-5 Pa XDE-175-L – 2.1 x 10-5 Pa K_{OC} (L/kg) : XDE-175-J – 2544.1 (mean) XDE-175-L – 2813.7 (mean) 1/n: XDE-175-J – 0.95 (mean) XDE-175-L -0.87 (mean) Drift loading for each drift event : XDE-175-J – ditch - 0.1676 mg/m^2; pond - 0.0198 mg/m^2; stream - 0.1669 mg/m^2 XDE-175-L – ditch - 0.0559 mg/m^2; pond - 0.0066 mg/m^2; stream - 0.05568 mg/m^2
XDE-175 Parameters used in FOCUSsw step 4	DT_{50} soil (d): XDE-175-J – 4.84 days (field geomean) XDE-175-L – 0.75 days (field geomean) DT_{50} water (d): XDE-175-J – 1.40 d (worst case –aqueous dissipation study – DFOP long phase) XDE-175-L – 1.40 d (worst case –aqueous dissipation study – DFOP long phase) DT_{50} sediment (d):

	XDE-175-J - 315 d (lab - whole system worst case; n=2) XDE-175-L – 315 d (lab -whole system worst case; n=2) Vapour pressure: XDE-175-J – 0 Pa XDE-175-L – 0 Pa K_{OC} (L/kg): XDE-175-J – 2544.1 (mean) XDE-175-L –2813.7 (mean) 1/n: XDE-175-J – 0.95 (mean) XDE-175-L – 0.87 (mean) Corrected Drift loading at step 4.2 & 4.3 for each drift event due to 30 m buffer zone : XDE-175-J – ditch - 0.0069 mg/m^2; pond - 0.0041 mg/m^2; stream - 0.0083 mg/m^2 XDE-175-L – ditch - 0.0023 mg/m^2; pond - 0.0014 mg/m^2; stream - 0.0028 mg/m^2 Run-off mitigation at Step 4.3 (in addition to spray drift mitigation): A 20 m vegetative buffer strip was assumed and the following corrections performed: Fractional reduction in run-off volume: 0.80 Fractional reduction in run-off flux: 0.80 Fractional reduction in erosion mass: 0.95 Fractional reduction in erosion flux: 0.95
Application rate	Crop: vines, late applications Crop interception: Calculated by FOCUS models Number of applications: *3* Interval (d): *7* Application rate(s): *3 x 36 g as*/ha total XDE-175 (85J: 15L) XDE-175-J – 3 x 32.4 g as/ ha XDE-175-L – 3 x 10.8 g as/ ha Application window: 50 days prior to harvest; 44 day window.
Main routes of entry	Spray drift.
N-demethyl-XDE-175-J, N-demethyl-XDE-175-L and 13,14-beta-dihydro-C17-pseudoaglycone-175-L Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): N-demethyl-XDE-175-J – 734 N-demethyl-XDE-175-L – 746 13,14-beta-dihydro-C17-pseudoaglycone-175-L - 621 Water solubility (mg/L): N-demethyl-XDE-175-J – 1330 N-demethyl-XDE-175-L – 149 13,14-beta-dihydro-C17-pseudoaglycone-175-L - 46.7 (assumed same as parent) Soil or water metabolite: N-demethyl-XDE-175-J – soil and water N-demethyl-XDE-175-L – soil and water 13,14-beta-dihydro-C17-pseudoaglycone-175-L - water Koc (L/kg): †N-demethyl-XDE-175-J – 2397.1 (mean) †N-demethyl-XDE-175-L – 2410.7 (mean) 13,14-beta-dihydro-C17-pseudoaglycone-175-L – 2813.7

(assumed same as parent)
DT_{50} soil (d):
N-demethyl-XDE-175-J – 123 d (lab geomean)
N-demethyl-XDE-175-L – 71.2 d (lab geomean)
13,14-beta-dihydro-C17-pseudoaglycone-175-L – 1000 d (FOCUS default)

DT50 water/sediment system (d):
N-demethyl-XDE-175-J – 1000 d (default worst case)
N-demethyl-XDE-175-L - 1000 d (default worst case)
13,14-beta-dihydro-C17-pseudoaglycone-175-L - 1000 d (default worst case)

DT_{50} water (d):
N-demethyl-XDE-175-J – 1000 d (default worst case)
N-demethyl-XDE-175-L - 1000 d (default worst case)
13,14-beta-dihydro-C17-pseudoaglycone-175-L - 1000 d (default worst case)

DT_{50} sediment (d):
N-demethyl-XDE-175-J – 1000 d (default worst case)
N-demethyl-XDE-175-L - 1000 d (default worst case)
13,14-beta-dihydro-C17-pseudoaglycone-175-L - 1000 d (default worst case)

Crop interception (%): full canopy

Maximum occurrence observed (% molar basis with respect to the parent):
Soil:
N-demethyl-XDE-175-J – 100 % (assumed worse case)
N-demethyl-XDE-175-L - 100 % (assumed worse case)
13,14-beta-dihydro-C17-pseudoaglycone-175-L - 1×10^{-20} %

Water/ sediment:
N-demethyl-XDE-175-J – 100 % (assumed worse case)
N-demethyl-XDE-175-L - 100 % (assumed worse case)
13,14-beta-dihydro-C17-pseudoaglycone-175-L– 23 %

N-demethyl-XDE-175-J and N-demethyl-XDE-175-L Parameters used in FOCUSsw step 3	Vapour pressure: N-demethyl-XDE-175-J – 5.6 x 10^{-5} Pa N-demethyl-XDE-175-L – 2.1 x 10^{-5} Pa (assumed same as parent) Koc (L/kg) : N-demethyl-XDE-175-J – 2397.1 (mean) N-demethyl-XDE-175-L – 2410.7 (mean) 1/n: N-demethyl-XDE-175-J – 0.91 N-demethyl-XDE-175-L – 0.85 Formation fraction in soil (k_{dp}/k_f): N-demethyl-XDE-175-J – 1.0 N-demethyl-XDE-175-L – 1.0 NB. A maximum occurrence was used for immediate formation following spray drift inputs due to photolysis of parent: Max occurrence due to aqueous photolysis (and assumed drift loading for each individual event): N-demethyl-XDE-175-J – 27.8 % (ditch - 0.0457 mg/m^2; pond - 0.0054 mg/m^2; stream - 0.0455 mg/m^2) N-demethyl-XDE-175-L – 9.8 % (ditch - 0.0054 mg/m^2; pond - 0.0006 mg/m^2; stream - 0.0054 mg/m^2)

N-demethyl-XDE-175-J and N-demethyl-XDE-175-L Parameters used in FOCUSsw step 4	DT_{50} soil (d): N-demethyl-XDE-175-J – 56.9 days (field geomean) N-demethyl-XDE-175-L – 2.46 days (field geomean) DT_{50} water (d): N-demethyl-XDE-175-J – 2.3 d (worst case –aqueous dissipation study) N-demethyl-XDE-175-L – 2.3 d (worst case –aqueous dissipation study) DT_{50} sediment (d): XDE-175-J - 1000 d (default worst case) XDE-175-L – 1000 d (default worst case) Vapour pressure: N-demethyl-XDE-175-J – 0 Pa (assumed same as parent) N-demethyl-XDE-175-L – 0 Pa (assumed same as parent) Formation fraction in soil (k_{dp}/k_f): N-demethyl-XDE-175-J – 0.50 (worst case - field studies)* N-demethyl-XDE-175-L – 0.65 (worst case - lab studies) Koc (L/kg) : N-demethyl-XDE-175-J – 2397.1 (mean) N-demethyl-XDE-175-L – 2410.7 (mean) 1/n: N-demethyl-XDE-175-J – 0.91 N-demethyl-XDE-175-L – 0.85 Corrected Drift loading at Step 4.2 & 4.3 for each individual event due to 30 m buffer zone and immediate aqueous photolysis of parent: N-demethyl-XDE-175-J – ditch - 0.0019 mg/m^2; pond - 0.0011 mg/m^2; stream - 0.0023 mg/m^2 N-demethyl-XDE-175-L – ditch - 0.00022 mg/m^2; pond - 0.000013 mg/m^2; stream - 0.00027 mg/m^2 Run-off mitigation at Step 4.3 (in addition to spray drift mitigation): A 20 m vegetative buffer strip was assumed and the following corrections performed: Fractional reduction in run-off volume: 0.80 Fractional reduction in run-off flux: 0.80 Fractional reduction in erosion mass: 0.95 Fractional reduction in erosion flux: 0.95
Application rate	Crop: vines, late applications Crop interception: Calculated by FOCUS models Number of applications: *3* Interval (d): *7* Application rate(s): *3 x 36 g as*/ha total XDE-175 (85J: 15L) XDE-175-J – 3 x 32.4 g as/ ha XDE-175-L – 3 x 10.8 g as/ ha Application window: 50 days prior to harvest; 44 day window.
Main routes of entry	Spray drift. Run-off for some scenario/ compound combinations. Run-off or drainflow for N-demethyl-175-J at Step 4.

*At Step 4 the formation fraction for N-demethyl-XDE-175-J was deduced by comparing mean DT50 values for XDE-175-J and N-demethyl-175-J to the patterns of formation and decline observed in field studies and

amending formation fractions until peak metabolite concentrations were exceeded in all tests. Therefore, the RMS considers that the selection represents a realistic worst case. See Volume 3 Section B.8.1.3.1 – study c for full discussion. The worst case formation fraction derived from lab studies was utilised for N-demethyl-175-L. NB. At Steps 1 & 2 PECs for the 13,14-beta-dihydro-C17-pseudoaglycone-175-L metabolite were calculated using the FOCUS Step 1 & 2 tool and assuming worst case default values (all DT50 values were assumed as 1000 d) or the input parameters for the parent L factor (Koc, water solubility). Because it was not observed in soil, a formation from the XDE-175-L parent factor of 1 x 10^{-20} % AR was input by the Applicant as a surrogate zero value, because the model does not accept an input value of 0 %. For step 3 onwards PECs for the 13,14-beta-dihydro-C17-pseudoaglycone-175-L metabolite were calculated based on parent XDE-175-L PEC values and correcting for maximum formation and molecular mass.

Step 1 Maximum PECsw and PECsed as calculated in the RMS modelling

Scenario	Compartment	Maximum PECsw (µg / L) or PECsed (µg / kg d.w.)		
		XDE-175	N-demethyl-	13,14-beta-dihydro-C17-pseudoaglycone-175-L
XDE-175-J	Surface water	9.98	10.13	-
	Sediment	202.3	196.1	-
XDE-175-L	Surface Water	3.14	3.37	0.16
	Sediment	68.94	65.46	0.96
Total XDE-175	Surface Water	11.00	-	-
	Sediment†	225.5	-	-

Step 2 Maximum PECsw and PECsed values as calculated in the RMS modelling

Scenario	Compartment	Maximum PECsw (µg / L) or PECsed (µg / kg d.w.)		
		XDE-175-	N-demethyl-	13,14-beta-dihydro-C17-pseudoaglycone-175-L
NE – XDE-175-J	Surface water	1.19 (0.87)	1.19 (0.85)	-
	Sediment	19.89 (8.13)	22.67 (8.39)	-
SE – XDE-175-J	Surface Water	1.19 (0.87)	1.34 (0.85)	-
	Sediment	23.49 (9.71)	27.79 (10.17)	-
NE – XDE-175-L	Surface water	0.39 (0.29)	0.40 (0.28)	0.07 (0.03)
	Sediment	6.44 (2.71)	7.42 (2.78)	0.82 (0.32)
SE – XDE-175-L	Surface Water	0.39 (0.29)	0.44 (0.28)	0.07 (0.03)
	Sediment	7.50 (3.21)	9.06 (3.37)	0.82 (0.32)
NE – Total XDE-175	Surface water	1.32 (0.97)	1.32 (0.94)	-
	Sediment†	22.01 (9.03)	25.12 (9.31)	-
SE – Total XDE-175	Surface Water	1.32 (0.97)	1.49 (0.94)	-
	Sediment†	25.94 (10.78)	30.78 (11.29)	-

NB. Values in brackets represent PECs following a single application

Step 3 maximum PECsw (µg/ L) and PECsed (µg/ kg) for XDE-175, the individual parent factors and metabolites from FOCUS SW modelling

Scenario	**Water Body**	**Compound**					
		XDE-175-J	**XDE-175-L**	**Total XDE-175**	**N-demethyl-175-J**	**N-demethyl-175-L**	**13,14-beta-dihydro-C17-pseudoaglycone-175-L†**
D6	ditch –sw	0.784	0.248	0.864	0.209	0.0235	0.0466
	ditch - sed	2.905	1.34	3.414	0.931	0.147	-
R1	pond – sw	0.0488	0.0153	0.0537	0.0139	0.00153	0.0029
	pond – sed	0.414	0.198	0.490	0.174	0.0359	-
R1	stream – sw	0.407	0.135	0.452	0.111	0.0148	0.0253

	stream – sed	0.105	0.0475	0.123	0.0493	0.0239	-
R2	stream – sw	0.545	0.181	0.605	0.148	0.0175	0.0340
	stream – sed	0.105	0.0444	0.121	0.346	0.243	-
R3	stream – sw	0.573	0.191	0.637	0.156	0.0187	0.0359
	stream - sed	1.097	0.544	1.308	0.228	0.158	-
R4	stream – sw	0.407	0.135	0.451	0.201 (run-off)	0.0438 (run-off)	0.0254
	stream - sed	0.274	0.0833	0.300	0.349	0.144	-

NB. Peak concentrations arise due to drift inputs unless otherwise stated.
†13,14-beta-dihydro-C17-pseudoaglycone-175-L metabolite PECs were calculated assuming the maximum occurrence (23 %) and correcting for molecular mass, from maximum XDE-175-L concentrations (621/760).

Step 4.1 maximum PECsw (µg/ L) and PECsed (µg/ kg) for XDE-175, the individual parent factors and metabolites from FOCUS SW modelling

Scenario	Water Body	Compound					
		XDE-175-J	XDE-175-L	Total XDE-175‡	N-demethyl-175-J	N-demethyl-175-L	13,14-beta-dihydro-C17-pseudoaglycone-175-L†
D6	ditch –sw	0.576	0.190	0.639	0.164	0.0189	0.0357
	ditch - sed	1.020	0.487	1.207	0.449	0.0728	-
R1	pond – sw	0.0246	0.00805	0.0273	0.00756	0.00082	0.0015
	pond – sed	0.0721	0.0375	0.0868	0.00705	0.00554	-
R1	stream – sw	0.407	0.135	0.452	0.111	0.0131	0.0254
	stream – sed	0.103	0.0463	0.120	0.0363	0.00501	-
R2	stream – sw	0.545	0.181	0.605	0.148	0.0175	0.0340
	stream – sed	0.0687	0.0304	0.0801	0.176	0.00331	-
R3	stream – sw	0.573	0.191	0.637	0.156	0.0184	0.0359
	stream - sed	0.883	0.212	0.940	0.241	0.146	-
R4	stream – sw	0.407	0.135	0.452	0.111	0.0131	0.0254
	stream - sed	0.149	0.0478	0.165	0.161	0.0144	-

NB. Peak concentrations arise due to drift inputs unless otherwise stated.
†13,14-beta-dihydro-C17-pseudoaglycone-175-L metabolite PECs were calculated assuming the maximum occurrence (23 %) and correcting for molecular mass, from maximum XDE-175-L concentrations (621/760).

Step 4.2 (25m buffer zone D6, 30 m buffer zone R scenarios) maximum PECsw (µg/ L) and PECsed (µg/ kg) for XDE-175, the individual parent factors and metabolites from FOCUS SW modelling

Scenario	Water Body	Compound					
		XDE-175-J	XDE-175-L	Total XDE-175	N-demethyl-175-J	N-demethyl-175-L	13,14-beta-dihydro-C17-pseudoaglycone-175-L†
D6	ditch –sw	0.0301	0.00986	0.0334	0.0195 (drainflow)	0.000761	0.0019

	ditch - sed	-	-	-	-	-	-
R1	pond – sw	0.00509	0.00170	0.0057	0.00172 (run-off)	0.000176	0.0003
	pond – sed	0.0154	0.00844	0.0188	0.0100	0.00127	-
R1	stream – sw	0.0202	0.00677	0.0225	0.0404 (run-off)	0.000649	0.0013
	stream – sed	0.00843	0.00252	0.0092	0.0288	0.000579	-
R2	stream – sw	0.0271	0.00908	0.0301	0.0156 (run-off)	0.000871	0.0017
	stream – sed	0.0120	0.00164	0.0122	0.172	0.000428	-
R3	stream – sw	0.104 (run-off)	0.00955	0.103	0.0384 (run-off)	0.00476 (run-off)	0.0018
	stream - sed	0.810	0.169	0.850	0.217	0.142	-
R4	stream – sw	0.165 (run-off)	0.00677	0.159	0.0786 (run-off)	0.00620 (run-off)	0.0013
	stream - sed	0.142	0.0119	0.140	0.152	0.0102	-

NB. Peak concentrations arise due to drift inputs unless otherwise stated.
†13,14-beta-dihydro-C17-pseudoaglycone-175-L metabolite PECs were calculated assuming the maximum occurrence (23 %) and correcting for molecular mass, from maximum XDE-175-L concentrations (621/760).

Step 4.3 (30 m no spray buffer zone and 20 vegetated buffer strip except D6 with 25m nospray buffer) maximum PECsw (µg/ L) and PECsed (µg/ kg) for XDE-175, the individual parent factors and metabolites from FOCUS SW modelling

Scenario	Water Body	Compound						
		XDE-175-J	XDE-175-L	Total XDE-175	Accumulated Total XDE-175	N-demethyl-175-J	N-demethyl-175-L	13,14-beta-dihydro-C17-pseudoaglycone-175-L†
D6	ditch –sw	0.0301	0.00986	0.0334	-	0.0195 (drainflow)	0.000761	0.0019
	ditch - sed	-	-	-	-	-	-	-
R1	pond – sw	0.00509	0.00170	0.0057	-	0.00154	0.000176	0.0003
	pond – sed	0.0154	0.00844	0.0188	0.0340 (0.0069)	0.00740	0.00127	-
R1	stream – sw	0.0202	0.00677	0.0225	-	0.00936 (run-off)	0.000649	0.0013
	stream – sed	0.00530	0.00252	0.0063	0.0114 (0.0024)	0.00559	0.000269	-
R2	stream – sw	0.0271	0.00908	0.0301	-	0.00749 (run-off)	0.000871	0.0017
	stream – sed	0.00354	0.00164	0.0042	0.0076 (0.0014)	0.129	0.000178	-
R3	stream – sw	0.0285	0.00955	0.0317	-	0.00911 (run-off)	0.00113 (run-off)	0.0018
	stream - sed	0.0770	0.0125	0.0790	0.1430 (0.0286)	0.0225	0.00904	-

R4	stream – sw	0.0383 (run-off)	0.00677	0.0396	-	0.0188 (run-off)	0.00144 (run-off)	0.0013
	stream - sed	0.0299	0.00336	0.0299	0.0541 (0.0109)	0.0274	0.00153	-

NB. Peak concentrations arise due to drift inputs unless otherwise stated.
†13,14-beta-dihydro-C17-pseudoaglycone-175-L metabolite PECs were calculated assuming the maximum occurrence (23 %) and correcting for molecular mass, from maximum XDE-175-L concentrations (621/760).

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PEARL vers.4.4.4 Scenarios (list of names): Chateaudun, Hamburg, Kremsmunster, Piacenza, Porto, Sevilla, Thiva Crop: Vines XDE-175-J Geometric mean parent $DT_{50lab:}$ 16.1 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). arithmetic mean parent K_{OC}: 2544.1, $^1/_n$= 0.95. XDE-175-L Geometric mean parent $DT_{50lab:}$ 11.8 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). arithmetic mean parent K_{OC}: 2813.7, $^1/_n$= 0.87. N-demethyl-175-J Geometric mean $DT_{50lab:}$ 123 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). arithmetic mean parent K_{OC}: 2397.1, $^1/_n$= 0.91. Formation: 100 % from XDE-175-J N-demethyl-175-L Geometric mean $DT_{50lab:}$ 71.2 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). arithmetic mean parent K_{OC}: 2410.7, $^1/_n$= 0.85. Formation: 100 % from XDE-175-L
Application Rate	Application rate: 32.4 g/ha XDE-175-J; 10.8 g/ ha XDE-175-L. No. of applications: 3; Application interval: 7 days Time of application (month or season): Final application 1 week before harvest.

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1m)

	Scenario	XDE-175-J (µg/L)	XDE-175-L (µg/L)	Metabolite (µg/L)	
				N-demethyl-175-J	N-demethyl-175-L
FOCUS PEARL	Chateaudun	< 0.000001	< 0.000001	< 0.000001	< 0.000001
	Hamburg	< 0.000001	< 0.000001	< 0.000001	< 0.000001
	Kremsmunster	< 0.000001	< 0.000001	< 0.000001	< 0.000001
	Piacenza	< 0.000001	< 0.000001	< 0.000001	< 0.000001
	Porto	< 0.000001	< 0.000001	< 0.000001	< 0.000001
	Sevilla	< 0.000001	< 0.000001	< 0.000001	< 0.000001
	Thiva	< 0.000001	< 0.000001	< 0.000001	< 0.000001

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	No information provided
Photochemical oxidative degradation in air ‡	DT_{50} of 0.336 hours for XDE-175-J and 0.276 hours for XDE-175-L derived by the Atkinson model (version 1.91). OH (12 h) concentration assumed = 1.5 x 10^6 cm^{-3}.
Volatilisation ‡	No information provided
	No information provided
Metabolites	No information provided

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and Atkinson half life.

$PEC_{(a)}$

Maximum concentration	Negligible

Residues requiring further assessment

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: total parent XDE-175 (comprising both parent factors XDE-175-J and XDE-175-L) and the major metabolites N-demethyl-175-J and N-demethyl-175-L Surface Water: total parent XDE-175 (comprising both parent factors XDE-175-J and XDE-175-L) and the major soil and aqueous photolytic metabolites metabolites N-demethyl-175-J and N-demethyl-175-L, and the major aqueous photolysis only metabolite 13,14-beta-dihydro-C17-pseudoaglycone-175-L Sediment: total parent XDE-175 (comprising both parent factors XDE-175-J and XDE-175-L) and the major soil

	and aqueous photolytic metabolites metabolites N-demethyl-175-J and N-demethyl-175-L, and the major aqueous photolysis only metabolite 13,14-beta-dihydro-C17-pseudoaglycone-175-L Ground water: total parent XDE-175 (comprising both parent factors XDE-175-J and XDE-175-L), the major soil metabolites from field dissipation studies N-demethyl-175-J, N-demethyl-175-L. Air: total parent XDE-175 (comprising both parent factors XDE-175-J and XDE-175-L)

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

Soil (indicate location and type of study)	None available.
Surface water (indicate location and type of study)	None available.
Ground water (indicate location and type of study)	None available.
Air (indicate location and type of study)	None available.

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

Candidate for R53.

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds				
Bobwhite quail (*Colinus virginianus*)	Technical XDE-175 (85.8% purity)	Acute (oral)	LD_{50} >2250	-
Mallard duck (*Anas platyrhynchos*)	Technical XDE-175 (85.8% purity)	Acute (oral)	LD_{50} >2250	-
Bobwhite quail (*Colinus virginianus*)	'GF 1587' (11.2% a.s.)	Acute (oral)	LD_{50} >2250	-
Bobwhite quail (*Colinus virginianus*)	Technical XDE-175 (85.8% purity)	Short-term	LDD_{50} >2044	LC_{50} >5620
Mallard duck (*Anas platyrhynchos*)	Technical XDE-175 (85.8% purity)	Short-term	LDD_{50} >1981	LC_{50} >5620
Bobwhite quail (*Colinus virginianus*)	Technical XDE-175 (85.8% purity)	Long-term	NOEL 95	NOEC 1000
Mallard duck (*Anas platyrhynchos*)	Technical XDE-175 (85.8% purity)	Long-term	NOEL 149	NOEC 1000
Mammals				
Rat	Technical XDE-175 75J:25L (85.8% pure)	Acute (oral)	LD_{50} >5000	-
Rat	XDE-175 85J:15L (86.3% pure)	Acute (oral)	LD_{50} >5000	-
Rat	GF-1587 (11.2% a.s.)	Acute (oral)	LD_{50} >5000	-
Rat	N-demethyl-175-J (98% pure)	Acute (oral)	LD_{50} = 3129	-
Rat	N-formyl-175-J (100% pure)	Acute (oral)	LD_{50} >5000	-
Rat	Technical XDE-175 (85.8% purity)	Long-term (2-generation repro. study)	NOAEL 10 (for both parental toxicity and reproductive effects)	-
Additional higher tier studies				
No higher tier studies reported				

LDD = lethal dietary dose

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

Crop and application rate: Grapevines – up to three spray applications made at a minimal interval of 10 days and at a maximum individual dose of 0.3 litres product /ha (≡ 36g technical XDE-175 /ha)

Indicator species/Category	Time scale	ETE mg kg /bw	TER	Annex VI Trigger
Tier 1 (Birds)				
Small insectivorous bird	Acute	1.95	> 1154	10
	Short-term	1.09	> 1817	10
	Long-term	1.09	87	5
Earthworm-eating bird	Long-term	0.544	175	5
Fish-eating bird	Long-term	0.06315	1504	5
Small bird (drinking water exposure – via contaminated surface water)	Acute	0.00303	>742721	10
	Short-term	0.00303	>653925	10
	Long-term	0.00303	31359	5
Higher tier refinement (Birds): Not required				
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	7.23	> 692	10
	Long-term	2.4	**4.2**	5
Earthworm-eating mammal	Long-term	0.693	14.4	5
Fish-eating mammal	Long-term	0.03909	256	5
Small mammal (drinking water exposure – via contaminated surface water)	Acute	0.00180	>2777778	10
	Long-term	0.00180	5556	5
Higher tier refinement (Mammals)				
Small herbivorous mammal	Long-term	1.2#	8.3	5

includes a refinement to ground level interception levels for 'short-grass' –spray deposition of 30% being assumed based on FOCUS 2000 spray interception estimates for flowering vine crops (as opposed to 60% at 'Tier 1').

Toxicity data for aquatic species: most sensitive relevant endpoints for each aquatic group are indicated in bold and were used in risk assessment (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance # (purity)	Time-scale (Test type)	End point	Toxicity[1] (µg/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss (Rainbow trout)	Technical XDE-175 (83%)	96-h Static	LC_{50}	>3460 mm
Oncorhynchus mykiss (Rainbow trout)	Technical XDE-175 (85.8%)	96-h Flow through	LC_{50}	>3480 mm
Lepomis macrochirus (Bluegill sunfish)	Technical XDE-175 (85.8%)	96-h Flow through	LC_{50}	**2690** mm
Cyprinodon variegatus (Sheepshead minnow)	Technical XDE-175 (85.8%)	96-h Static	LC_{50}	>2050 mm
Lepomis macrochirus (Bluegill sunfish)	GF-1587 (11.2%)	96-h Static renewal (at 24, 48 & 72 hours)	LC_{50}	>5400 mm
Pimephales promelas (Fathead minnow)	Technical XDE-175 (85.8%)	32-d ELS Flow-through	NOEC	**182** mm
Cyprinodon variegatus (Sheepshead minnow)	Technical XDE-175 (85.8%)	37-d ELS Flow-through	NOEC	1530 mm
Lepomis macrochirus (Bluegill sunfish)	GF-1587 (11.2% a.s.)	96-h Static renewal (at 24, 48 & 72 hours)	LC_{50}	>5400 mm
Lepomis macrochirus (Bluegill sunfish)	N-demethyl-175-J (99%)	96-h Static renewal (at 24 & 48 hours)	LC_{50}	**2980** mm
Lepomis macrochirus (Bluegill sunfish)	N-demethyl-175-L (98%)	96-h Static renewal (at 24 & 48 hours)	LC_{50}	**1550** mm
Aquatic invertebrate				
Daphnia magna	Technical XDE-175 (83%)	48-h Static	EC_{50}	>3170 mm
Daphnia magna	Technical XDE-175 (85.8%)	48-h Static	EC_{50}	**228** mm
Daphnia magna	Technical XDE-175 (85.8%)	48-h Static renewal (at 24 hours)	EC_{50}	3400 mm
Daphnia magna	GF-1587 (11.2%)	48-h Static renewal (at 24 hours)	EC_{50}	>4790
Daphnia magna	Technical XDE-175 (83%)	21-d Flow-through	NOEC	**0.0624** mm
Daphnia magna	Technical XDE-175 (85.8%)	21-d study, single pulsed dose over first 48 hours (static renewal at 2, 4, 8, 24 hours & daily thereafter)	NOEC (mortality & growth effects only, adult reproductive life stages not exposed)	0.951 (mean measured of single peak concentration)

Group	Test substance # (purity)	Time-scale (Test type)	End point	Toxicity[1] (µg/L)
Daphnia magna	Technical XDE-175 (85.8%)	21-d flow through with repeat (x3) pulsed doses on days 1, 10 and 20)	NOEC (mortality & growth) NOEC (reproduction) LOEC (reproduction)	1.56 Not determined (effects at lowest test dose) 1.56 (mean measured of peak concentrations on days 1, 10 & 20)
Daphnia magna	Technical XDE-175 (85.8%)	21-d static renewal study - 4 peaking exposure events on days 0, 5, 10 and 15 (3 day DT_{50})	NOEC (including mortality, growth and reproduction)	**0.33** (mean measured of peak concentrations on days 0, 5, 10 & 15)
Daphnia magna	GF-1587 (11.2% a.s.)	48-h Static renewal (at 24 hours)	EC_{50}	> 4790
Daphnia magna	N-demethyl-175-J (99%)	48-h Static	EC_{50}	**19.8** mm
Daphnia magna	N-demethyl-175-J (93%)	48-h Static renewal (at 24 hours)	EC_{50}	11000 mm
Daphnia magna	N-demethyl-175-J (99%)	21-d Flow-through	NOEC	**0.03** mm
Daphnia magna	N-demethyl-175-J (99%)	21-d static renewal study - 4 peaking exposure events on days 0, 5, 10 and 15 (3 day DT50)	NOEC (including mortality, growth and reproduction)	**0.29** (mean measured of peak concentrations on days 0, 5, 10 and 15)
Daphnia magna	N-demethyl-175-L (98%)	48-h Static	EC_{50}	**101** mm
Daphnia magna	N-demethyl-175-L (93%)	48-h Static renewal (at 24 hours)	EC_{50}	2100 mm
Daphnia magna	N-demethyl-175-L (98%)	21-d Flow-through	NOEC	**0.027** mm
Americamysis bahia (saltwater mysid)	Technical XDE-175 (83%)	96-h Flow-through	LC_{50}	355 mm
Americamysis bahia	XDE-175 85:15 (86.3%)	96-h Flow-through	LC_{50}	535 mm
Americamysis bahia	Technical XDE-175 (83%)	28-d Flow-through	NOEC	35.2 mm
Americamysis bahia	XDE-175 85:15 (86.3%)	28-d Flow-through	NOEC	8.74 mm
Crassostrea virginica (saltwater 'Eastern oyster')	Technical XDE-175 (83%)	96-h Flow-through	LC_{50} EC_{50} (shell growth)	>1200 mm 393 mm
Sediment dwelling organisms				
Chironomus riparius (chironomid midge)	Technical XDE-175 (83%)	28-d spiked water, chronic toxicity	NOEC	**0.75 µg a.s./l** (initial nominal concentration in overlying water)

Group	Test substance # (purity)	Time-scale (Test type)	End point	Toxicity[1] (µg/L)
Chironomus riparius	Technical XDE-175 (83%)	28-d spiked sediment, chronic toxicity	NOEC	**97.2 µg a.s./kg dw sediment** (initial measured concentration)
Leptocheirus plumulosus (saltwater amphipod)	Technical XDE-175 (85.8%)	10 day spiked sediment, acute toxicity	LC_{50}	83300 µg a.s. /kg dw sediment (nominal)
Chironomus riparius	N-demethyl-175-J (99%)	28-d spiked water (static), chronic toxicity	NOEC	**0.617** (initial measured concentration in overlying water)
Algae				
Pseudokirch-neriella subcapitata	Technical XDE-175 (83%)	96-h Static	72h EC_{50} (cell density) 72h E_bC_{50} 72h E_rC_{50} 96h E_rC_{50}	160 mm 278 mm 1060 mm 1040 mm
Navicula pelliculosa	Technical XDE-175 (83%)	96- h (static)	72h EC_{50} (cell density) 72h E_bC_{50} 72h E_rC_{50} 96h E_rC_{50}	**77.9 mm** 79.5 mm 127 mm 117 mm #
Anabaena flos- aquae	Technical XDE-175 (83%)	96- h Static	72h EC_{50} (cell density) 72h E_bC_{50} 72h E_rC_{50} 96h E_rC_{50}	>13400 mm >13400 mm >13400 mm >12300 mm
Skelotonema costatum	Technical XDE-175 (83%)	96- h Static	72h EC_{50} (cell density) 72h E_bC_{50} 72h E_rC_{50} 96h E_rC_{50}	94.3 mm 158 mm >209 mm >205 mm
Navicula pelliculosa	XDE-175 85:15 (86.3%)	96- h Static	72h EC_{50} (cell density) 72h E_bC_{50} 72h E_rC_{50} 96h E_rC_{50}	233 mm 224 mm 311 mm 218 mm
Navicula pelliculosa	GF-1587 (11.2% a.s.)	96- h Static	72h EC_{50} (cell density) 72h E_bC_{50} 72h E_rC_{50} 96h E_rC_{50}	89.9 mm (0.8 mg GF-1587/L) 109 mm 156 mm 127 mm (1.134 mg GF-1587/L)
Navicula pelliculosa	N-demethyl-175-J (99%)	96- h Static	72 E_yC_{50}	**125** mm
Navicula pelliculosa	N-demethyl-175-L (98%)	96- h Static	72 E_bC_{50}	**51.6** mm
Higher plant				
Lemna gibba	Technical XDE-175 (83%)	7-d (static renewal)	EC_{50} (biomass & growth rate)	**>14200** mm
Microcosm or mesocosm tests: None conducted.				

[1] where endpoints based on measured concentrations they relate to pure active substance or metabolite.
# Technical XDE-175 consisted of a mixture of XDE-175-J and XDE-175J present in ratio of 75J:25L
mm = mean measured concentration

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2): FOCUS Step1

Crop and application rate: Grapevines – up to three spray applications made at a minimal interval of 10 days and at a maximum individual dose of 0.3 litres product /ha (≡ 36g technical XDE-175 /ha) from 'fruit set' growth stage (BBCH 71) until 'softening of berries'(BBCH 85). Northern and Southern Europe Member States.

Test substance	Organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or met. /L or kg dw sediment)	Maximum PEC# (µg a.s. or met. /L or kg dw sediment)	TER *	Annex VI Trigger
XDE-175 (technical)	*Lepomis macrochirus* (Bluegill sunfish)	Acute: 96h LC50	2690	11.0	245	100
	Pimiphales promelas (fathead minnow)	Chronic: 32d NOEC	182	11.0	17	10
	Daphnia magna (water flea)	Acute: 48h EC50	228	11.0	**21**	100
	Daphnia magna	Chronic: 21d NOEC	0.0624	11.0	**0.01**	10
	Navicula pelliculosa (green alga)	72h EbC50	77.9	11.0	**7.08**	10
	Lemna minor	14d EbC50	14200	11.0	>1291	10
	Chironomus riparius (sediment dwelling midge)	Chronic 28 day NOEC (spiked water)	0.75	11.0	**0.07**	10
	Chironomus riparius (sediment dwelling midge)	Chronic 28 day NOEC (spiked sediment)	97.2 µg a.s. /kg sediment	225.5 µg a.s. /kg sediment	**0.43**	10
N-demethyl-175-J (metabolite)	*Lepomis macrochirus*	Acute: 96h LC50	2980	10.13	294	100
	Daphnia magna	Acute: 48h EC50	19.8	10.13	**1.95**	100
	Daphnia magna	Chronic 21d NOEC (flow through)	0.03	10.13	**0.003**	10
	Navicula pelliculosa	72h EyC50	125	10.13	12	10
	Chironomus riparius (sediment dwelling midge)	Chronic 28 day NOEC (spiked water)	0.617	10.13	**0.06**	10
N-demethyl-175-L (metabolite)	*Lepomis macrochirus*	Acute: 96h LC50	1550	3.37	460	100
	Daphnia magna	Acute: 48h EC50	101	3.37	**30**	100
	Daphnia magna	Chronic 21d NOEC (flow through)	0.027	3.37	**0.008**	10
	Navicula pelliculosa	72h EbC50	51.6	3.37	15	10
	Chironomus riparius (sediment dwelling midge)	Chronic 28 day NOEC (spiked water)	0.75 #	3.37	**0.22**	10

*TERs in breach of the Annex VI trigger indicated in bold

Sediment dweller N-demethyl-175-L metabolite toxicity endpoint derived from XDE-175 spiked water *Chironomid* chronic toxicity study assuming equivalent toxicity

FOCUS Step 2

Crop and application rate: Grapevines – details as for FOCUS Step 1.

Test substance	Organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or met. /l or kg dw sediment)	Maximum PEC# (µg a.s. or met. /l or kg dw sediment)	TER*	Annex VI Trigger
XDE-175 (technical)	*Daphnia magna* (water flea)	Acute: 48h EC50	228	1.32 (N & S)	173	100
	Daphnia magna	Chronic: 21d NOEC	0.0624	1.32 (N & S)	**0.047**	10
	Navicula pelli-culosa (green alga)	72h EbC50	77.9	1.32 (N & S)	59	10
	Chironomus riparius (sediment dwelling midge)	Chronic 28 day NOEC (spiked water)	0.75	1.32 (N & S)	**0.568**	10
	Chironomus riparius(sediment dwelling midge)	Chronic 28 day NOEC (spiked sediment)	97.2 µg a.s. /kg sediment	22.01 µg /kg(N) 25.94 µg /kg (S)	**4.42 (N)** **3.75 (S)**	10
N-demethyl-175-J (metabolite)	*Daphnia magna*	Acute: 48h EC50	19.8	1.19 N 1.34 S	**17 (N)** **15 (S)**	100
	Daphnia magna	Chronic 21d NOEC	0.03	1.19 N 1.34 S	**0.03 (N)** **0.02 (S)**	10
	Chironomus riparius (sediment dwelling midge)	Chronic 28 day NOEC (spiked water)	0.617	1.19 N 1.34 S	**0.52** **0.46**	10
N-demethyl-175-L (meta-bolite)	*Daphnia magna*	Acute: 48h EC50	101	0.40 N 0.44 S	252 (N) 230(S)	100
	Daphnia magna	Chronic 21d NOEC	0.027	0.40 N 0.44 S	**0.07 (N)** **0.06 (S)**	10
	Chironomus riparius (sediment dwelling midge)	Chronic 28 day NOEC (spiked water)	0.75 #	0.40 N 0.44 S	**1.87 (N)** **1.70 (S)**	10

*TERs in breach of the Annex VI trigger indicated in bold.

Sediment dweller N-demethyl-175-L metabolite toxicity endpoint derived from XDE-175 spiked water *Chironomid* chronic toxicity study – assuming equivalent toxicity to XDE-175

FOCUS Step 3

Crop and application rate: Grapevines – details as for FOCUS Step 1.

Test substance	Scenario	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or met. /l or kg dw sediment)	Maximum PEC# (µg a.s. or met. /l or kg dw sediment)	TER*	Annex VI trigger
XDE-175 (technical)	D6	Ditch	*Daphnia magna* (water flea)	Chronic: 21 day NOEC	0.0624	0.864	**0.07**	10
	R1	Pond				0.0537	**1.16**	10
	R1	Stream				0.452	**0.14**	10
	R2	Stream				0.605	**0.10**	10
	R3	Stream				0.637	**0.10**	10
	R4	Stream				0.451	**0.14**	10
XDE-175 (technical)	D6	Ditch	*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (spiked water)	0.75	0.864	**0.87**	10
	R1	Pond				0.0537	14	10
	R1	Stream				0.452	**1.66**	10
	R2	Stream				0.605	**1.24**	10
	R3	Stream				0.637	**1.18**	10
	R4	Stream				0.451	**1.66**	10
XDE-175 (technical)	D6	Ditch	*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (spiked sediment)	97.2 µg a.s. /kg d.w. sediment	3.414	28	10
	R1	Pond				0.490	198	10
	R1	Stream				0.123	790	10
	R2	Stream				0.121	803	10
	R3	Stream				1.308	74	10
	R4	Stream				0.300	324	10
N-demethyl-175-J	D6	Ditch	*Daphnia magna* (water flea)	Acute: 48 hour EC_{50}	19.8	0.209	**94**	100
	R1	Pond				0.0139	1424	100
	R1	Stream				0.111	178	100
	R2	Stream				0.148	134	100
	R3	Stream				0.156	127	100
	R4	Stream				0.201	**99**	100
N-demethyl-175-J	D6	Ditch	*Daphnia magna* (water flea)	Chronic: 21day NOEC	0.03	0.209	**0.14**	10
	R1	Pond				0.0139	**2.16**	10
	R1	Stream				0.111	**0.27**	10
	R2	Stream				0.148	**0.20**	10
	R3	Stream				0.156	**0.19**	10
	R4	Stream				0.201	**0.15**	10
N-demethyl-175-J	D6	Ditch	*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (spiked water)	0.617	0.209	**0.13**	10
	R1	Pond				0.0139	**1.94**	10
	R1	Stream				0.111	**0.24**	10
	R2	Stream				0.148	**0.18**	10
	R3	Stream				0.156	**0.17**	10
	R4	Stream				0.201	**0.13**	10
N-demethyl-175-L	D6	Ditch	*Daphnia magna* (water flea)	Chronic: 21day NOEC	0.027	0.0235	26	10
	R1	Pond				0.00153	403	10
	R1	Stream				0.0148	42	10
	R2	Stream				0.0175	35	10
	R3	Stream				0.0187	33	10
	R4	Stream				0.0438	14	10
N-demethyl-175-L	D6	Ditch	*Chironomus riparius* (sediment dwelling	Chronic 28 day NOEC (spiked	0.75 ##	0.0235	32	10
	R1	Pond				0.00153	490	10
	R1	Stream				0.0148	51	10
	R2	Stream				0.0175	43	10

Test substance	Scenario	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or met. /l or kg dw sediment)	Maximum PEC# (µg a.s. or met. /l or kg dw sediment)	TER*	Annex VI trigger
	R3	Stream	midge)	water)		0.0187	40	10
	R4	Stream				0.0438	17	10

*TERs in breach of the Annex VI trigger indicated in bold.
Maximum PECsw – highest value from a single or multiple applications
Sediment dweller N-demethyl-175-L metabolite toxicity endpoint derived from XDE-175 spiked water *Chironomid* chronic toxicity study – assuming equivalent toxicity to XDE-175

Refined aquatic risk assessment using higher tier FOCUS modelling:

FOCUS Step 4.1: no buffer zones (3 metre distance between grapevine crop and waterbody)
Crop and application rate: Grapevines – details as for FOCUS Step 1.

Test substance	Scenario	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or metabolite /l)	Maximum PEC# (µg a.s. or metabolite /l)	TER*	Annex VI trigger
XDE-175 (technical)	D6	Ditch	*Daphnia magna* (water flea)	Chronic 21 day NOEC (static renewal, mean measured of max. 'peaked' exposures on days 0, 5, 10 & 15)	0.33	0.639	**0.52**	10
	R1	Pond				0.0273	12.09	10
	R1	Stream				0.452	**0.73**	10
	R2	Stream				0.605	**0.55**	10
	R3	Stream				0.637	**0.52**	10
	R4	Stream				0.452	**0.73**	10
XDE-175 (technical)	D6	Ditch	*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (static spiked water, mean measure of initial water concentration)	0.75	0.639	**1.17**	10
	R1	Pond				0.0273	27.47	10
	R1	Stream				0.452	**1.66**	10
	R2	Stream				0.605	**1.24**	10
	R3	Stream				0.637	**1.18**	10
	R4	Stream				0.452	**1.66**	10
N-demethyl-175-J	D6	Ditch	*Daphnia magna* (water flea)	Chronic 21 day NOEC (static renewal, mean measured of max. pulsed exposures on days 0, 5, 10 & 15)	0.29	0.164	**1.77**	10
	R1	Pond				0.00756	38.36	10
	R1	Stream				0.111	**2.61**	10
	R2	Stream				0.148	**1.96**	10
	R3	Stream				0.156	**1.86**	10
	R4	Stream				0.111	**2.61**	10
N-demethyl-175-J	D6	Ditch	*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (static spiked water, mean measure of initial water concentration)	0.617	0.164	**3.76**	10
	R1	Pond				0.00756	81.61	10
	R1	Stream				0.111	**5.56**	10
	R2	Stream				0.148	**4.17**	10
	R3	Stream				0.156	**3.96**	10
	R4	Stream				0.111	**5.56**	10
N-demethyl-175-L	D6	Ditch	*Daphnia magna* (water flea)	Chronic 21 day NOEC (extrapolated from XDE-175 'peaked exposures' study - details above)	0.33	0.0189	17.46	10
	R1	Pond				0.00082	402.44	10
	R1	Stream				0.0131	25.19	10
	R2	Stream				0.0175	18.86	10
	R3	Stream				0.0184	17.93	10
	R4	Stream				0.0131	25.19	10

*TERs in breach of the Annex VI trigger indicated in bold.
Maximum PECsw – highest value from single or multiple applications

FOCUS Step 4.2: including a 30 metre no spray aquatic buffer zone (spray drift mitigation) – Runoff scenarios

Crop and application rate: Grapevines – details as for FOCUS Step 1.

Test substance	Scenario	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or meta-bolite /l)	Maximum PEC# (µg a.s. or meta-bolite /l)	TER*	Annex VI trigger
XDE-175 (technical)	R1	Pond	*Daphnia magna* (water flea)	Chronic 21 day NOEC (static renewal, mean measured of max. peak exposures at 0, 5, 10 & 15 days)	0.33	0.0057	57.89	10
	R1	Stream				0.0225	14.67	10
	R2	Stream				0.0301	10.96	10
	R3	Stream				0.103	**3.20**	10
	R4	Stream				0.159	**2.08**	10
XDE-175 (technical)			*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (static spiked water, mean measure of initial water concentration)	0.75			
	R1	Pond				0.0057	131.58	10
	R1	Stream				0.0225	33.33	10
	R2	Stream				0.0301	24.92	10
	R3	Stream				0.103	**7.28**	10
	R4	Stream				0.159	**4.72**	10
N-demethyl-175-J			*Daphnia magna* (water flea)	Chronic 21 day NOEC (static renewal, mean measured of max. peak exposures at 0, 5, 10 & 15 days)	0.29			
	R1	Pond				0.00172	168.60	10
	R1	Stream				0.0404	**7.18**	10
	R2	Stream				0.0156	18.59	10
	R3	Stream				0.0384	**7.55**	10
	R4	Stream				0.0786	**3.69**	10
N-demethyl-175-J			*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (static spiked water, mean measure of initial water concentration)	0.617			
	R1	Pond				0.00172	358.72	10
	R1	Stream				0.0404	15.27	10
	R2	Stream				0.0156	39.55	10
	R3	Stream				0.0384	16.07	10
	R4	Stream				0.0786	**7.85**	10

*TERs in breach of the Annex VI trigger indicated in bold.

Maximum PECsw – highest value from single or multiple applications

FOCUS Step 4.3: including a 30 meter no spray aquatic buffer zone (spray drift mitigation) plus 20 meter vegetative strip (run-off mitigation) – Runoff scenarios

Crop and application rate: Grapevines – details as for FOCUS Step 1.

Test substance	Scenario	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or metabolite /l)	Maximum PEC# (µg a.s. or metabolite /l)	TER*	Annex VI trigger
XDE-175 (technical)			*Daphnia magna* (water flea)	Chronic 21 day NOEC (static renewal, mean measured of max. peak exposures at 0, 5, 10 & 15 days)	0.33			
	R1	Pond				0.0057	57.89	10
	R1	Stream				0.0225	14.67	10
	R2	Stream				0.0301	10.96	10
	R3	Stream				0.0317	10.41	10
	R4	Stream				0.0396	**8.33**	10
XDE-175 (technical)			*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (static spiked water, mean measure of initial water concentration)	0.75			
	R1	Pond				0.0057	131.58	10
	R1	Stream				0.0225	33.33	10
	R2	Stream				0.0301	24.92	10
	R3	Stream				0.0317	23.66	10
	R4	Stream				0.0396	18.94	10
N-demethyl-175-J			*Daphnia magna* (water flea)	Chronic 21 day NOEC (static renewal, mean measured of max. peak exposures at 0, 5, 10 & 15 days)	0.29			
	R1	Pond				0.00154	188.31	10
	R1	Stream				0.00936	30.98	10
	R2	Stream				0.00749	38.72	10
	R3	Stream				0.00911	31.83	10
	R4	Stream				0.0188	15.43	10
N-demethyl-175-J			*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (static spiked water, mean measure of initial water concentration)	0.617			
	R1	Pond				0.00154	400.65	10
	R1	Stream				0.00936	65.92	10
	R2	Stream				0.00749	82.38	10
	R3	Stream				0.00911	67.73	10
	R4	Stream				0.0188	32.82	10

*TERs in breach of the Annex VI trigger indicated in bold.
Maximum PECsw – highest value from single or multiple applications

Maximum PECsw (µg/ L) and PECsed (µg/ kg) for XDE-175, a 25 m no spray aquatic buffer zone (spray drift mitigation) – Drainage scenario (D6)

Crop and application rate: Grapevines - details as for FOCUS Step 1.

Test substance	Scenario[1]	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or metabolite /l)	Maximum PEC (µg a.s. or metabolite /l)	TER*	Annex VI trigger
XDE-175 (technical)	D6	Ditch	*Daphnia magna* (water flea)	Chronic 21 day NOEC (static renewal, mean measured of max. peak exposures at 0, 5, 10 & 15 days)	0.33	0.0334	**9.88**	10
XDE-175 (technical)	D6	Ditch	*Chironomus riparius* (sediment	Chronic 28 day NOEC (static spiked water, mean	0.75	0.0334	22.45	10

Test substance	Scenario[1]	Water body type	Test organism	Time scale & endpoint measured	Toxicity end point (µg a.s. or metabolite /l)	Maximum PEC (µg a.s. or metabolite /l)	TER*	Annex VI trigger
			dwelling midge)	measure of initial water concentration)				
N-demethyl-175-J	D6	Ditch	*Daphnia magna* (water flea)	Chronic 21 day NOEC (static renewal, mean measured of max. peak exposures at 0, 5, 10 & 15 days)	0.29	0.0195	14.87	10
N-demethyl-175-J	D6	Ditch	*Chironomus riparius* (sediment dwelling midge)	Chronic 28 day NOEC (static spiked water, mean measure of initial water concentration)	0.617	0.0195	31.64	10

*TERs in breach of the Annex VI trigger indicated in bold.

Bioconcentration				
Parameter measured	XDE-175-J	XDE-175-L	N-demethyl-175-J	N-demethyl-175-L
Log P_{OW}	4.09	4.49	4.3	4.6
Fish bioconcentration factor (BCF)[1] ‡	BCF (max) = 114 # BCF_K = 46 #	BCF (max) = 305* BCF_K = 348*	-	-
Annex VI Trigger for bioconcentration factor	3.0	3.0	3.0	3.0
Whole fish clearance time CT_{50} (days, maximum values for high or low level exposure)	4.6	5.2	-	-
Whole fish clearance time CT_{90} (days, maximum values for high or low level exposure)	15.4	17.3	-	-
Level and nature of residues (%) in fish after the 14 day depuration phase (maximum values for high or low level exposure)	15% of peak C_{14} residues on day 14 of clearance phase. No HPLC residue analysis in clearance phase (day 27 exposure analysis indicates 30% a.s. & 70% metabolites)	13% of peak C_{14} residues on day 14 of clearance phase. HPLC residue analysis day 5 indicates 10% a.s. & 90% metabolites.	-	-

[1] Based on measured total C_{14} radio-activity in whole fish from water exposure to C_{14} labelled XDE-175.
BCF (max) of 114 derived from results of 'high' concentration level and (kinetic) BCF_K of 46 from 'low' concentration level treatment (ref. Woodburn KB et al 2005, Section B.9.2.1.3 ii) of Vol. 3 DAR)
* BCF (max) of 305 and (kinetic) BCF_K of 348 both derived from results of 'high' concentration level treatment (ref. Woodburn KB et al 2005, Section B.9.2.1.3 i) of Vol. 3 DAR)

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

Standard laboratory oral and dermal toxicity studies:		
Test substance	**Acute oral toxicity (LD_{50} µg/bee)**	**Acute contact toxicity (LD_{50} µg/bee)**
Technical XDE-175 ǂ	48h LD_{50}: 0.14 µg a.s./bee 72h LD_{50}: 0.11 µg a.s./bee	24h LD_{50}: 0.039 µg a.s./bee 48h LD_{50}: 0.024 µg a.s./bee
XDE-175 (85:15)[1]	-	48h LD_{50}: 0.011 µg a.s./bee 72h LD_{50}: 0.010 µg a.s./bee 96h LD_{50}: 0.009 µg a.s./bee
'GF-1587' (120g XDE-175 /litre)	48h LD_{50}: 0.043 µg a.s./bee 72h LD_{50}: 0.037 µg a.s./bee 96h LD_{50}: 0.036 µg a.s./bee	48h LD_{50}: 0.03 µg a.s./bee 72h LD_{50}: 0.023 µg a.s./bee 96h LD_{50}: 0.019 µg a.s./bee
N-demethyl-XDE-175-J	-	48h LD_{50}: 0.063 µg met./bee 72h LD_{50}: 0.057 µg met./bee 96h LD_{50}: 0.056 µg met./bee
N-demethyl-XDE-175-L	-	48h LD_{50}: 0.038 µg met./bee 72h LD_{50}: 0.030 µg met./bee 96h LD_{50}: 0.027 µg met./bee
Laboratory Foliar Residue Toxicity Test with technical XDE-175:		
No mortality or significant adverse effects to bees when exposed to foliar residues of XDE-175 treated 3, 6 or 24 hours previously at 110 g a.s./ha.		
Semi-field (tunnel) foraging bee toxicity study:		
Test scenario	**Test item**	**Effects/observations**
100 g a.s./ha Spray treatment 7 days prior to *Phacelia* flowering & bee foraging	GF-1640 (25% XDE-175)	Mortality: No effect Foraging: No effect Brood: Visual inspection 16 days after initial exposure indicated no adverse effects.
36 g a.s./ha Spray treatment 7 days prior to *Phacelia* flowering & bee foraging	GF-1587 (11.2% XDE-175)	Mortality: No effect Foraging: No effect Brood: Visual inspection 16 days after initial exposure indicated no adverse effects.
36 g a.s./ha Spray treatment at full flowering of *Phacelia* & in the evening after bee flight	GF-1587 (11.2% XDE-175)	Mortality: No differences in mean 0-7DAA dead bee numbers recorded between this (T2) treatment and the water control. First assessment conducted during active bee foraging in the morning following previous evening treatment. Foraging: No effect. Brood: Assessments 8 days after initial exposure indicated no adverse effects.
36 g a.s./ha Spray treatment at full flowering of Phacelia & during bee flight	GF-1587 (11.2% XDE-175)	Mortality: Daily mortality increased over that in water control by 4 times at 0DAA and by 16 times at 1DAA, with mean mortality for 0-7 DAA assessment period statistical significant higher ($p \leq 0.05$) – 0-7day mean treated and control dead bees /replicate /day = 53.9 and 22.7 respectively. Foraging: No statistically significant effect. Brood: Visual inspection 8 days after initial exposure indicated no adverse effects.

[1] This study was performed to determine the effect of a slightly different ratio of XDE-175-J and XDE-175-L (85:15) on toxicity. Other studies with XDE-175 were conducted with the typical (technical) 75:25 (i.e. 3:1) ratio.

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

Crop and application rate: Grapevines – up to three spray applications made at a minimal interval of 10 days and at a maximum individual dose of 0.3 litres product /ha (≡ 36g technical XDE-175 /ha).

Test substance	Route	Endpoint µg a.s./bee	Hazard quotient	Annex VI Trigger
XDE-175 (75J:25L)	Oral	72h LD_{50}: 0.11	**327**	50
XDE-175 (75J:25L)	Contact	48h LD_{50}: 0.024	**1500**	50
XDE-175 (85J:15L)	Contact	96h LD_{50}: 0.009	**4000**	50
GF 1587	Oral	96h LD_{50} 0.036	**1000**	50
GF 1587	Contact	96h LD_{50} 0.019	**1895**	50

Note: The results of the semi-field foraging bee study, together with the results of the laboratory foliar residue toxicity study (no residual effects on bees), support the conclusion that in order to avoid significant bee mortality and other possible adverse effects, XDE-175 should only be applied when bees are not present in the crop.

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

Laboratory glassplate residual toxicity studies with standard sensitive arthropod species:

Species	Test Substance	End point measured	LR_{50} (inert substrate) g a.s./ha #
Typhlodromus pyri (protonymphs)	GF-1587 (11.2% w/w XDE-175)	Mortality	**0.132**
Typhlodromus pyri (protonymphs)	GF-1640 (25% w/w XDE-175)	Mortality	0.1375
Aphidius rhopalosiphi (adults)	GF-1587 (11.2% w/w XDE-175)	Mortality	0.128
Aphidius rhopalosiphi (adults)	GF-1640 (25% w/w XDE-175)	Mortality	**0.0885**

The most sensitive endpoints (included in bold) have been used in first tier risk assessment

First tier terrestrial arthropod risk assessment:

Crop and application rate: Grapevines – up to three spray applications made at a minimal interval of 10 days and at a maximum individual dose of 0.3 litres 'GF1587' /ha (≡ 36g technical XDE-175 /ha)

Species	Predicted in-field (accumulated) exposure rate g a.s./ha	LR_{50} g a.s. /ha	In-field HQ	Off-field HQ (at 3 metre #)
A. rhopalosiphi	82.8	0.0885	**936**	**65**
T. pyri	82.8	0.132	**627**	**43**

Based on maximum predicted off-field predicted (accumulated) exposure rate of 5.71 g a.s. /ha
HQs in bold are in breach of the ESCORT 2 trigger values of 2

Further laboratory and 'extended laboratory' studies:

'Extended laboratory' foliar residual toxicity studies conducted with *Typhlodromus pyri* and *Aphidius rhopalosiphi*

Species	Test Substance	End point measured	LR_{50} (foliar substrate) g a.s./ha
Typhlodromus pyri (protonymphs)	GF-1587 (11.2% w/w XDE-175)	Mortality	0.426
Typhlodromus pyri (protonymphs)	GF-1640 (25% w/w XDE-175)	Mortality	0.476
Aphidius rhopalosiphi (adults)	GF-1587 (11.2% w/w XDE-175)	Mortality	0.300
Aphidius rhopalosiphi (adults)	GF-1640 (25% w/w XDE-175)	Mortality	0.671

Other extended laboratory non-target arthropods toxicity studies conducted using 'GF-1640' (WDG formulation containing 250g a.s./kg)

Species	**Treatment details g a.s./ha**	**Exposure timing & Endpoint**	**Effects (Abbott corrected % mortality & % reduction in fecundity from control)***
Coccinella septempunctata larvae (foliar dwelling ladybird)	4 x 150 g.a.s./ha to foliage, at spray interviews of 7, 28 & 7 days respectively	**From 0DAA4 (upto adult emergence):** Mortality &fecundity (% difference from control in number of viable eggs /female)	13.5% & -27.4%
		ER_{50} > 150 g a.s./ha	
Aleochara bilineata adults (ground dwelling rove beetle)	Four different treatment regimes: 4 x 150g a.s./ha; 4 x 75g a.s./ha; 2 x 43.8 + 2 x 23.6g a.s./ha. Each treatment including four surface sprays made in the lab to a moist sand substrate (4 cm deep) at application intervals of 7, 28 & 7 days respectively.	**From 0DAA4 (28days exposure):** Mortality & Parasitism# (4 x 150g a.s./ha) Mortality & Parasitism# (4 x 75g a.s./ha) Mortality & Parasitism# (2 x 43.8 + 2 x 23.6g a.s./ha) **From 1WAA4 (28days exposure):** Mortality & Parasitism# (4 x 150g a.s./ha) Mortality & Parasitism# (4 x 75g a.s./ha) Mortality & Parasitism# (2 x 43.8 + 2 x 23.6g a.s./ha) **From 2WAA4 (28days exposure):** Mortality & Parasitism# (4 x 150g a.s./ha) Mortality & Parasitism# (4 x 75g a.s./ha) Mortality & Parasitism# (2 x 43.8 + 2 x 23.6g a.s./ha)	25.7% & 77.8% -4.3% & 41.4% 0% & 23.7% 8.1% & 17.8% 1.4% & 13.6% -5.4% & 11.2% 0% & 12.1% -1.4% & 11.4% 0% & 10.3%
		ER_{50} > 75 g a.s./ha	
Aphidius rhopalosiphi (aged residue test, using field treated leaves)	Three foliar sprays in apple orchards at 9-10 day intervals at 24g or 100g a.s. /ha /application.	**0DAA3** Water control mortality Mortality & Parasitism (3 x 24g a.s./ha) Mortality & Parasitism (3 x 100g a.s./ha) **1WAA3** Water control mortality Mortality & Parasitism (3 x 24g a.s./ha) Mortality & Parasitism (3 x 100g a.s./ha) **2WAA3** Water control mortality Mortality & Parasitism (3 x 24g a.s./ha) Mortality & Parasitism (3 x 100g a.s./ha)	Actual mortality: 18% 100% & N/A 100% & N/A Actual mortality: 18% 31% & 5.9% 23% & 11.8% Actual mortality: 18% -9% & 8.7% 32% & 21.7%
		Data indicates much reduced effects from exposure one week or more after treatment.	

N/A = Not applicable

* Negative figures indicate increased survival / fecundity over that of control population

Measured by comparing numbers of adult beetles emerging from onion fly pupae in treatment and water control

Summary of effects of 'GF-1587' in grapevine non-target arthropod grapevine field study

Treatment	**Population effects (from leaf and beat sampling assessments made up to four months after treatment)***
'Drift rate' treatments of 'GF-1587': 2 or 3 applications at 1.3 g XDE-175 /ha (both including two post-flowering applications with a 10 day spray interval).	No consistent or statistical significant treatment related adverse effects on non-target arthropod populations.
One post-flowering application (13/6/07) of 'GF-1587' at 48g a.s./ha	Consistent treatment related population reductions in 5 taxonomic groups (statistical significant in two: *Phytoseiidae* mites 78% & *Psocoptera* 68%), with recovery within 3 months of treatment.
Two post-flowering applications (13/6/07 and 23/6/07), each at 36g a.s./ha.	Consistent treatment related population reductions in 6 taxonomic groups (statistical significant in two: *Phytoseiidae* mites 87% & *Psocoptera* 95%), with recovery within 3 months of treatment.
One pre-flowering and two post-flowering applications (18/5/07, 13/6/07 and 23/6/07) each at 36g a.s./ha	Consistent treatment related population reductions in 8 taxonomic groups (statistical significant in five: *Phytoseiidae* mites 95%, *Psocoptera* 92%, *Collembola* 100%, *Cicadellidae* 82%, *Lathridiidae* 57%), with population recovery occurring mostly (except for *Lathridiidae*) within 3 or 4 months of treatment. Numbers of *Lathridiidae* beetles were 57% less than control populations -in the final October assessment.

*Percentages quoted are the maximum levels of statistically significant ($P \leq 0.05$) population reductions recorded during the 4 month post-treatment assessment period

Higher tier terrestrial arthropod risk assessment conclusions:

The proposed use of XDE-175 (formulated as 'GF1587') in grapevines may have an initial adverse effect on some non-target arthropod populations present within the 'in-field' treated area. Although the results of the *Aphidius* aged foliar residue study suggest the possibility for in-field recovery (effects at 1 and 2WAA3 being much reduced compared with that at 0DAA3) and results of the grapevine field trial indicate recovery within 4 months of treatment for the majority of assessed taxonomic groups, this was not specifically demonstrated in the field study for *Lathridiidae* beetles and also no evidence has been provided in relation to effects on Lepidoptera – which may be particularly sensitive given that the target pest species in vines is a member of this group.

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

Test organism	Test substance	Time scale	End point #
Earthworms:			
Eisenia fetida	Technical XDE-175 (85.8% w/w purity)	Acute 14 days	LC_{50} > 500 mg a.s./kg d.w. soil #
		Chronic 56 days	NOEC 9.325 mg a.s./kg d.w. soil #
Eisenia fetida	GF-1587 (11.2% w/w a.s.)	Acute 14 days	LC_{50} > 479.5 mg a.s./kg d.w. soil #
		Chronic 56 days	NOAEC 5.45 mg a.s./kg d.w. soil
Eisenia fetida	N-demethyl-175-J (99% purity)	Acute 14 days	LC_{50} > 500 mg a.s./kg d.w. soil #
		Chronic 56 days	NOEC 10 mg a.s./kg d.w. soil #
Eisenia fetida	N-demethyl-175-L (99% purity)	Acute 14 days	LC_{50} > 500 mg a.s./kg d.w. soil #
		Chronic 56 days	NOEC 10 mg a.s./kg d.w. soil #
Other soil macro-organisms:			
Folsomia candida (collembola)	N-demethyl-175-J (99% purity)	Chronic 28 days	NOEC 10 mg a.s./kg d.w. soil (highest test dose, 5% OM in test soil)
Soil micro-organisms:			
Nitrogen mineralisation	Technical XDE-175 (85.8% w/w purity)	Effects at day 28	< 25% effects at 4 mg a.s. /kg dw soil *
	GF-1587 (11.2% w/w a.s.)	Effects at day 28	< 25% effects at 11.45 mg product /kg dw soil (= 1.282 mg a.s./kg dw soil) *
	N-demethyl-175-J (99% purity)	Effects at day 28	< 25% effects at 4 mg metabolite /kg dw soil *
	N-demethyl-175-L (99% purity)	Effects at day 28	< 25% effects at 4 mg metabolite /kg dw soil *
Carbon mineralisation	Technical XDE-175 (85.8% w/w purity)	Effects at day 28	< 25% effects at 4 mg a.s. /kg dw soil *
	GF-1587 (11.2% w/w a.s.)	Effects at day 28	< 25% effects at 11.45 mg product /kg dw soil (=1.282 mg a.s./kg dw soil) *
	N-demethyl-175-J (99% purity)	Effects at day 28	< 25% effects at 4 mg metabolite /kg dw soil *
	N-demethyl-175-L (99% purity)	Effects at day 28	< 25% effects at 4 mg metabolite /kg dw soil *
Field studies: None reported			

Endpoint includes EPPO correction factor of 2 where indicated due to high (10%) organic matter content of test soil and log Pow of test substance > 2.0.

* Compares with maximum soil PECs of 0.127 mg XDE-175 /kg dw soil, 0.0746 mg N-demethyl-175-J /kg dw soil and 0.0079 mg N-demethyl-175-L /kg dw soil.

Toxicity/exposure ratios for soil organisms (earthworms and other macro-organisms)

Crop and application rate: Grapevines – up to three spray applications made at a minimal interval of 10 days and at a maximum individual dose of 0.3 litres 'GF1587' /ha (≡ 36g technical XDE-175 /ha)

Test organism	Test substance	Time scale	Maximum PEC_{soil} (mg a.s. or metabolite /kg soil)	TER	Trigger
Earthworms					
Eisenia fetida	Technical XDE-175 (85.8% w/w purity)	Acute 14 days	0.127	> 3937	10
		Chronic 56 days	0.127	73	5
Eisenia fetida	GF-1587 (11.2% w/w a.s.)	Acute 14 days	0.127	> 3776	10
		Chronic 56 days	0.127	43	5
Eisenia fetida	N-demethyl-175-J (99% purity)	Acute 14 days	0.0746	6702	10
		Chronic 56 days	0.0746	134	5
Eisenia fetida	N-demethyl-175-L (99% purity)	Acute 14 days	0.0079	63291	10
		Chronic 56 days	0.0079	1266	5
Other soil macro-organisms					
Folsomia candida (collembola)	N-demethyl-175-J (99% purity)	Chronic 28 days	0.0746	134	5

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

Preliminary screening data:

A standard GLP compliant seedling emergence and vegetative vigour study was conducted according to EPA guidelines using a spray application of 'GF-1640' (a water dispersible granule containing 25% w/w XDE-175) at 150g a.s./ha on six dicot and four monocot species. Phytotoxic effects were either absent or present at a low level. There were no phytotoxic effects of greater than 25% compared to the control.

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

Test type/organism	End point
Activated sludge	Respiratory inhibition: 3hour EC_{50} >10mg a.s./L; NOEC = 10 mg a.s./L.

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

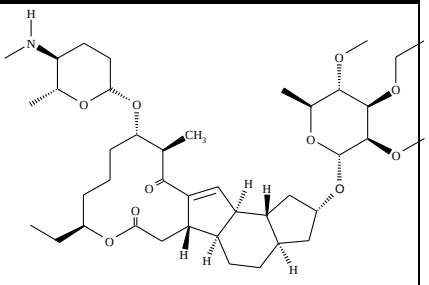
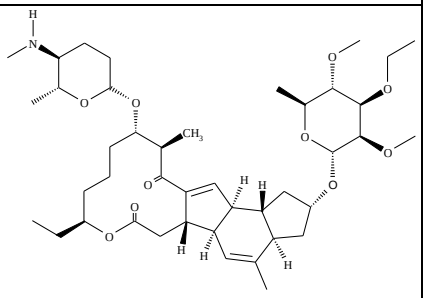
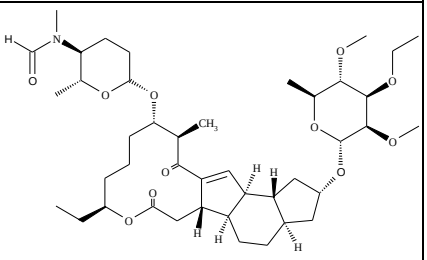
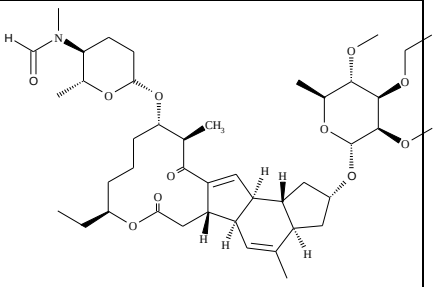
Compartment	Substance
soil	XDE-175 (factors J and L), N-demethyl-175-J and N-demethyl-175-L
water	XDE-175 (factors J and L), N-demethyl-175-J and N-demethyl-175-L
sediment	XDE-175 (factors J and L), N-demethyl-175-J and N-demethyl-175-L
groundwater	None
air	total parent XDE-175 (comprising both parent factors XDE-175-J and XDE-175-L)

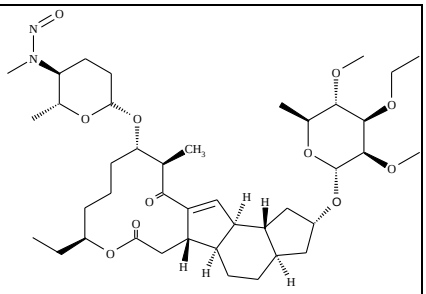
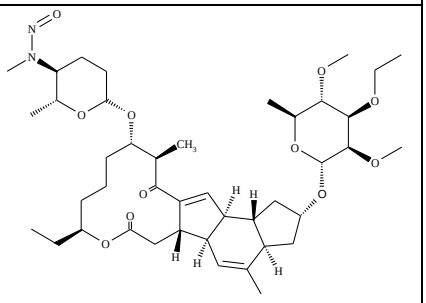
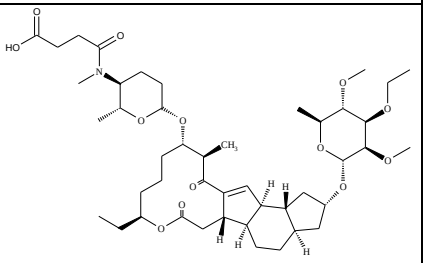
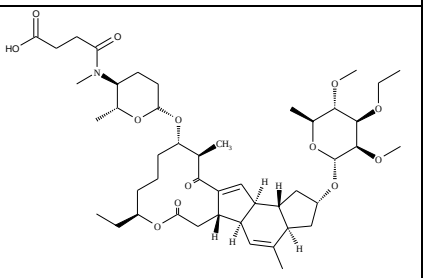
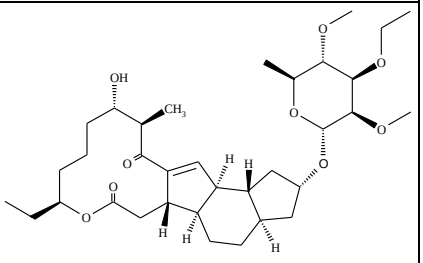
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

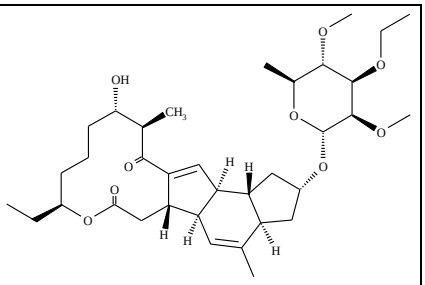
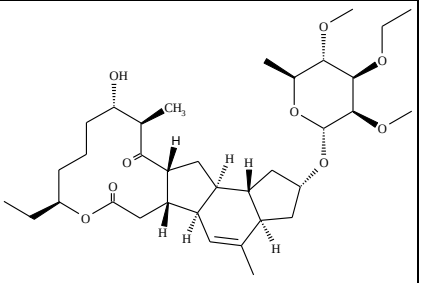
	RMS/peer review proposal*
Active substance	Under Dir. 67/548/EEC: R50 & R53. Under Reg. (EC) 1272/2008: H400 & H410, M-factor = 1000.

* It should be noted that classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 or Regulation (EU) No 188/2011 are not formal proposals.

APPENDIX B – USED COMPOUND CODES

Code/Trivial name*	Chemical name	Structural formula
N-demethyl-175-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-9-ethyl-14-methyl-13-{[(2S,5S,6R)-6-methyl-5-(methylamino)tetrahydro-2H-pyran-2-yl]oxy}-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranoside	
N-demethyl-175-L	(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-9-ethyl-4,14-dimethyl-13-{[(2S,5S,6R)-6-methyl-5-(methylamino)tetrahydro-2H-pyran-2-yl]oxy}-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranoside	
N-formyl-175-J	(2R,3S,6S)-6-({(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranosyl)oxy]-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-13-yl}oxy)-2-methyltetrahydro-2H-pyran-3-yl(methyl)formamide	
N-formyl-175-L	(2R,3S,6S)-6-({(2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranosyl)oxy]-9-ethyl-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-13-yl}oxy)-2-methyltetrahydro-2H-pyran-3-yl(methyl)formamide	

N-demethyl-N-nitroso-175-J	(2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-9-ethyl-14-methyl-13-{[(2*S*,5*S*,6*R*)-6-methyl-5-(1-methyl-2-oxohydrazino)tetrahydro-2*H*-pyran-2-yl]oxy}-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranoside	
N-demethyl-N-nitroso-175-L	(2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-9-ethyl-4,14-dimethyl-13-{[(2*S*,5*S*,6*R*)-6-methyl-5-(1-methyl-2-oxohydrazino)tetrahydro-2*H*-pyran-2-yl]oxy}-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranoside	
N-succinyl-175-J	4-[[(2*R*,3*S*,6*S*)-6-({(2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-2-[(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranosyl)oxy]-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-13-yl}oxy)-2-methyltetrahydro-2*H*-pyran-3-yl](methyl)amino]-4-oxobutanoic acid	
N-succinyl-175-L	4-[[(2*R*,3*S*,6*S*)-6-({(2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-2-[(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranosyl)oxy]-9-ethyl-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-13-yl}oxy)-2-methyltetrahydro-2*H*-pyran-3-yl](methyl)amino]-4-oxobutanoic acid	
C17-pseudyaglycone-175-J	(2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-9-ethyl-13-hydroxy-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranoside	

C17-pseudyaglycone-175-L	2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-9-ethyl-13-hydroxy-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1H-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-O-ethyl-2,4-di-O-methyl-alpha-L-mannopyranoside	
13,14-beta-dihydro-C17-pseudoaglycone-175-L	(2*S*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,15a*R*,16a*S*,16b*S*)-9-ethyl-13-hydroxy-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,15a,16,16a,16b-octadecahydro-1*H*-*as*-indaceno[3,2-*d*]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranoside	

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

ABBREVIATIONS

1/n	slope of Freundlich isotherm
λ	wavelength
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
ADME	adsorption, distribution, metabolism and excretion
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AUC	area under curve
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstracts Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DFR	dislodgeable foliar residue
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
FID	flame ionisation detector
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
GI	gastrointestinal
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
IV	intravenous
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
LLNA	local lymph node assay
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
mN	milli-newton
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
NPD	nitrogen phosphorous detector
OECD	Organisation for Economic Co-operation and Development
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
pF	preferred flow
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
REACH	Registration, Evaluation, Authorisation of CHemicals
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
STOT-RE	specific target organ toxicity — repeated exposure
$t_{1/2}$	half-life (define method of estimation)
TC	transfer coefficient
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
WAA	weeks after application
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year