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CONCLUSION ON PESTICIDE PEER REVIEW

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

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SUMMARY

Difenoconazole is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002,[3] as amended by Commission Regulation (EC) No 1095/2007.[4]

Difenoconazole was included in Annex I to Directive 91/414/EEC on 1 January 2009 pursuant to Article 11b of the Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007 (hereinafter referred to as 'the Regulation'). In accordance with Article 12a of the Regulation the European Food Safety Authority (EFSA) is required to deliver by 31 December 2010 its view on the draft review report submitted by the Commission of the European Communities (hereinafter referred to as 'the Commission') in accordance with Article 12(1) of the Regulation. This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

Sweden being the designated rapporteur Member State submitted the DAR on difenoconazole in accordance with the provisions of Article 10(1) of the Regulation, which was received by the EFSA on 22 December 2006. The peer review was initiated on 6 March 2007 by dispatching the DAR for consultation of the Member States and the notifier Syngenta Ltd. Following consideration of the comments received on the DAR, it was concluded that EFSA should conduct a focused peer review in the areas of mammalian toxicology, environmental fate and behaviour and ecotoxicology and deliver its conclusions on difenoconazole.

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

No critical areas of concern were identified in the physical-chemical properties section. However, data gaps were identified for data to support the ranges of the *cis/trans* isomers in the technical specification, the biological activity of the isomers, the validation of the isomer method, the

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[1] On request from the European Commission, Question No EFSA-Q-2009-00244, issued on 17 December 2010.

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[3] OJ L224, 21.08.2002, p.25

[4] OJ L 246, 21.9.2007, p.19

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consequence for the physical-chemical properties of the active substance of the wide range of isomer content and the formulation's adhesion to seeds.

No critical areas of concern were identified in the mammalian toxicology section. Two data gaps were identified: for an assessment of the toxicological relevance of some impurities; and to clarify the uncertainties related to the isomer ratio of the tested compound (for which reference values have been derived), the isomer ratio to which the workers will be exposed and the relative toxicity of the different isomers.

Based on the metabolism studies conducted on four plant groups, the residue in plants was defined as difenoconazole for monitoring and provisionally as difenoconazole and TDM for risk assessment. Residue definitions were also proposed for animal products. No critical areas of concern were identified in the residue section. Data gaps were identified to provide information on the possible residues of TDM metabolites in primary crops, rotational crops, processed commodities and animal products. Additional residue trials and processing studies on carrots are also required. No acute or chronic intake concerns were identified for consumers, but this evaluation has to be considered provisional, since the contribution of the TDM metabolites and the isomeric composition of the residues were not taken into account.

The data available on environmental fate and behaviour were generally sufficient to carry out the required environmental exposure assessments at the EU level for the representative uses assessed. The potential for groundwater contamination consequent to these uses by difenoconazole and the metabolites 1,2,4-triazole and CGA 205375 above the parametric drinking water limit of 0.1 µg/L was assessed as low. However, data gaps were identified for identification of the metabolites V3 and M4 formed in soil incubation, and for the rate of dissipation of difenoconazole in the field under Southern European conditions. The assessment of the environmental behaviour and consequent exposure levels of individual enantiomers of difenoconazole was not finalised.

Data gaps were identified in the ecotoxicology section. Further refinement of the risk to aquatic sediment-dwelling organisms for the use in cereals is necessary. Furthermore, the potential endocrine disruption effects in fish should be addressed. A data gap was also identified to demonstrate that the increase in body weight would not lead to adverse effects on earthworm populations in order to be able to use the reproduction NOEC from the reproduction study. Data gaps were identified to address the chronic risk to earthworms and *Collembola*. The possible impact on the ecotoxicity and the environment of potential enantio-selective biologically mediated metabolism/degradation or transformation needs to be addressed in order to the risk assessment for non-target organisms.

KEY WORDS

Difenoconazole, peer review, risk assessment, pesticide, fungicide.

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BACKGROUND

Difenoconazole is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002[5], as amended by Commission Regulation (EC) No 1095/2007.[6]

Difenoconazole was included in Annex I to Directive 91/414/EEC on 1 January 2009 pursuant to Article 11b of the Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007 (hereinafter referred to as 'the Regulation'). In accordance with Article 12a of the Regulation the European Food Safety Authority (EFSA) is required to deliver by 31 December 2010 its view on the draft review report submitted by the Commission of the European Communities (hereinafter referred to as 'the Commission') in accordance with Article 12(1) of the Regulation (European Commission, 2008). This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

Sweden being the designated rapporteur Member State submitted the DAR on difenoconazole in accordance with the provisions of Article 10(1) of the Regulation, which was received by the EFSA on 22 December 2006 (Sweden, 2006). The peer review was initiated on 6 March 2007 by dispatching the DAR to Member States and the notifier Syngenta Ltd. 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 rapporteur Member State for compilation and evaluation in the format of a Reporting Table. The comments were evaluated by the rapporteur Member State in column 3 of the Reporting Table.

The scope of the peer review was considered in a telephone conference between the EFSA, the rapporteur Member State, and the Commission on 13 July 2010. On the basis of the comments received and the rapporteur Member State's evaluation thereof it was concluded that the EFSA should organise a consultation with Member State experts in the areas of mammalian toxicology, environmental fate and behaviour and ecotoxicology.

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

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

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as a fungicide on pome fruit, carrot, wheat, barley, triticale, rye and oats, as proposed by the notifier. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a

[5] OJ L224, 21.08.2002, p.25
[6] OJ L 246, 21.9.2007, p.19

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, 2011) comprises the following documents:

- the comments received on the DAR,
- the Reporting Table (revision 1-1; 13 July 2010),
- the Evaluation Table (13 December 2010),
- the reports of the scientific consultation with Member State experts (where relevant).

Given the importance of the DAR including its addendum (compiled version of November 2010 containing all individually submitted addenda; Sweden, 2010) and the peer review report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Difenoconazole is the ISO common name for 3-chloro-4-[(2*RS*,4*RS*;2*RS*,4*SR*)-4-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-2-yl]phenyl 4-chlorophenyl ether (IUPAC).

The representative formulated products for the evaluation were 'Score' an emulsifiable concentrate (EC) containing 250 g/l difenoconazole and 'Dividend 030 FS' a flowable concentrate for seed treatment (FS) containing 30 g/l difenoconazole.

The representative uses evaluated for the formulation 'Score' are outdoor foliar spraying in pome fruit and carrots. The representative uses evaluated for the formulation 'Dividend 030 FS' are as a seed treatment for cereals. Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

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

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

The minimum purity of the active substance as manufactured is 940 g/kg. The ranges for the *cis* and *trans* isomers are the subject of a data gap. Information on the biological activity of the isomers is also the subject of a data gap. Toluene was considered as a relevant impurity, its maximum content in the technical material is 5 g/kg.

The main data regarding the identity of difenoconazole and its physical and chemical properties are given in Appendix A. As the isomer range is so wide, a data gap was identified to address the effect of this on the physical and chemical properties of the active substance. A data gap was identified for adherence to seed for the formulation 'Dividend 030 FS'. It should be noted that the rinsed residue result was high for the formulation 'Dividend 030 FS' so appropriate labelling should be considered.

A data gap was identified for validation of the HPLC method for the isomer ratio in the technical material.

LC-MS/MS methods are available to analyse difenoconazole in plants and difenoconazole and CGA 205375 in products of animal origin and soil. Water can be analysed for difenoconazole by GC-ECD and air by LC-MS/MS. A method of analysis for body fluids and tissues is not required because the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

The following guidance documents were used 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, May 2009 (European Commission, 2009).

Difenoconazole was discussed during the PRAPeR meeting 83 (October 2010). With regard to the technical specification, a data gap was identified to assess the toxicological relevance of some impurities but the batches used in the toxicological studies can be considered as representative of the technical specification (Sweden, 2010).

Extensively absorbed after oral administration, difenoconazole did not show any potential for accumulation in body tissues. Based on the acute oral toxicity results, the classification **Xn**, **R22 “Harmful if swallowed”** is proposed for difenoconazole, whereas no classification is triggered for the acute toxicity after dermal or inhalation exposure, for skin or eye irritation or for skin sensitisation.

In repeated dose studies, the liver was the main target organ, showing adverse effects but also adaptive changes in short-term studies in mice and rats. The effects triggering the NOAELs include reduced body weight (gain) and/or decreased organ weights. Cataract formation was observed in dogs (in the 28-week study only) and hens, and the relationship with treatment could not be excluded. However, this effect only appeared after high dose exposure with a sufficient margin between the NOAEL and the reference values (~200). The relevant short-term NOAEL in the rat is 20 mg/kg bw/day based on the first 90-day study with Wistar rats; the short-term NOAEL in the mouse is 34 mg/kg bw/day (90-day study) and the short-term NOAEL in the dog is 31 mg/kg bw/day (28-week study). The relevant long-term NOAELs are 1.0 mg/kg bw/day for the rat and 4.7 mg/kg bw/day for the mouse. Difenoconazole is unlikely to be genotoxic *in vivo* and unlikely to pose a carcinogenic risk to humans.

In the rat multigeneration study, no adverse effect was observed on the reproductive parameters up to the highest dose tested (189 mg/kg bw/day) and the relevant NOAEL for the offspring and for the parental animals is 16.8 mg/kg bw/day. In the developmental toxicity studies, an increased number of resorptions was observed in rats and rabbits, whereas an increased incidence of skeletal variations was only noted in rat foetuses. The relevant maternal and developmental NOAELs are the same, i.e. 25 mg/kg bw/day for the rabbit, and 15.6 mg/kg bw/day for the rat (after correction for actual concentration of 78 % in the test material for the rat study).

No neurotoxicity studies were performed. No effects indicative of neurotoxicity were observed in any of the available studies.

In a mechanistic study, difenoconazole showed an enzyme induction profile (in the mouse liver) resembling phenobarbitone. Several plant metabolites were tested with an Ames test (CGA 189138, CGA 205374, CGA 205375: all negative) and with a mouse oral acute toxicity test (CGA 205374, CGA 205375: LD_{50}>2000 mg/kg bw). Based on the available data for the triazole derivative metabolites, and including an additional rat multigeneration study for 1,2,4-triazole showing a more critical NOAEL (Young et al., 2005), specific reference values were agreed for 1,2,4-triazole (ADI 0.02 mg/kg bw/d, ARfD 0.06 mg/kg bw), for triazole alanine (ADI and ARfD 0.1 mg/kg bw(/day)) and for triazole acetic acid and triazole lactic acid (ADI and ARfD of 1,2,4-triazole because of the limited database available).

For difenoconazole, the agreed Acceptable Daily Intake (ADI) is 0.01 mg/kg bw/day based on the 2-yr rat study; the agreed Acceptable Operator Exposure Level (AOEL) is 0.16 mg/kg bw/day and the Acute Reference Dose (ARfD) is 0.16 mg/kg bw, both based on the developmental rat study. All reference values were derived with a safety factor of 100. The agreed dermal absorption values were 2 % for the concentrate and 4 % for the dilution of the formulation ‘Score’, and 4 % for the concentrate of ‘Dividend 030 FS’ (not diluted for seed treatment in the representative uses). The operator exposure estimate during the use of ‘Score’ in pome fruit and carrots is below the AOEL without the use of personal protective equipment (PPE) (ranging from 2 to 75 % of the AOEL according to the German Model and UK POEM). During the use of ‘Dividend 030 FS’ on seed, the operator exposure estimate is 37 % of the AOEL without the use of PPE based on the Seed Tropex model. For both products, worker (without use of PPE) and bystander exposure estimates are well below the AOEL.

It is noted that the ratio of isomers to which the workers will be exposed when re-entering treated crops is unknown, as well as the relative toxicity of the four different isomers. Additionally, there is also some uncertainty related to the isomer ratio that has been tested in the toxicological studies (see data gap in section 1). Therefore data gaps have been identified.

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 in plant was investigated in four plant groups: fruit crops (tomato, grape), cereals (wheat), tuber/root crops (potato) and on oilseeds/pulses crops (oilseed rape), using ^{14}C-difenoconazole labelled in the phenyl or the triazole ring and foliar applications with a total of 2 to 6 treatments. Samples were collected for analysis at interim intervals and 6 to 40 days after the final application. In addition, metabolism was also considered in cereals following seed application.

The metabolism was seen to be similar in all four crop types. The parent difenoconazole remained the major component of the residues in the majority of the plant parts (mostly >40 % TRR), with the exception of the cereal grains, potato tubers and rape seeds, where it accounted for less than 10 – 15 % of the TRR. In these crops, and for the triazole labelling, TRRs are mainly composed of the triazole derivative metabolites (TDM): triazole alanine (56 % and 79 % TRR in rape seeds and potato tubers) and triazole acetic acid (20 % TRR in cereal grain). In addition, triazole alanine was detected up to 42 % TRR in tomato fruits and 1,2,4-triazole up to 12 % in grape. TDM were also the major components of the residues in cereal grains following seed treatment and the major metabolites in the succeeding crop studies. Metabolites CGA 205374 (ketone), CGA 205375 (alcohol) and CGA 189138 (benzoic acid) were also identified in low proportions (below 5 % TRR). Based on the different structures identified, the following metabolic pathway in plants was proposed. As a first step, the metabolism involves hydrolysis of the dioxolane ring to form the ketone metabolite which is then reduced to the corresponding alcohol. Further oxidation of the difenoconazole-alcohol metabolite results in the cleavage of the alkyl bridge to form the difenoconazole-benzoic acid metabolite and the 1,2,4-triazole which is further metabolised to triazole alanine and triazole acetic acid. Based on these data, the residue for monitoring was defined as the parent compound difenoconazole. For risk assessment, considering that TDM are toxicologically relevant metabolites present in significant proportions in primary and rotational crops, two separate plant residue definitions were proposed: 1) difenoconazole and 2) provisionally, Triazole Derivative Metabolites. No final definition can be proposed for TDM at this stage, since a global and harmonized approach is needed for all compounds of the triazole chemical class.

A sufficient number of supervised residue trials conducted according to the critical GAPs was provided to propose MRLs on cereals (seed treatment), pome fruits and carrot. On pome fruits, the MRL calculation was derived from the Southern data only, since the GAP defined for this zone was seen to be more critical than the Northern one. Additional trials on carrot are however required in order to complete the residue dataset. No information was provided on the residue levels of TDM in primary crops. Cold rotational crop studies were provided where difenoconazole was applied to the bare soil at a rate of 750 g/ha (2N) one month prior to planting and samples were analysed for difenoconazole and triazole alanine. Residues were below the LOQs but further information on TDM residues in rotational crops are still required since this study was limited to a single plant back interval and to two crops only (spinach and carrots). These residue data are supported by the storage stability study showing difenoconazole residues to be stable up to 2 years in various plant matrices when stored at -20°C. Difenoconazole was found to be stable under standard hydrolysis conditions simulating pasteurisation, baking and sterilisation. Processing studies were provided for apple only and it was concluded that additional processing studies on carrot are required.

Several metabolism studies on goats and laying hens were submitted where animals were fed with ^{14}C-difenoconazole labelled on the phenyl and triazole ring. Difenoconazole was more extensively metabolised in animals than in plants, occurring at less than 10 % TRR in nearly all matrices. Difenoconazole-alcohol (CGA 205375) was by far the most abundant metabolite detected, up to 60 – 90 % TRR in goat and poultry fat. Beside CGA 205375, the metabolite 1,2,4-triazole resulting from cleavage of the parent structure was also observed in significant proportions in milk (46 % TRR) and eggs (32 – 75 % TRR). Based on these studies, the residue definition for monitoring was limited to the metabolite difenoconazole-alcohol only. For risk assessment, as for plants, two separate residue definitions are proposed: 1) difenoconazole-alcohol expressed as difenoconazole and 2) provisionally, Triazole Derivative Metabolites. Only 1,2,4-triazole was detected in the animal metabolism studies, but the presence of the other TDM (CGA 131013, CGA 142586 and CGA 205369) in animal feed was not considered. Their transfer to the animal products cannot be excluded and the definition for TDM can not be limited to the 1,2,4-triazole only. As for plants, no final residue definition can be proposed for TDM, since the fate of CGA 131013, CGA 142586 and CGA 205369 were not investigated and a global and harmonized approach is needed for all compounds of the triazole chemical class. A feeding study on cow was provided where samples were analysed for difenoconazole and difenoconazole-alcohol. Difenoconazole was not detected in any animal matrices, even at the highest dose level (15N for beef cattle), except in liver (highest residue 0.02 mg/kg). MRLs were derived for ruminant products from the difenoconazole-alcohol residue levels.

No chronic or acute consumer concerns were identified, the highest TMDI being 44 % of the ADI (DE child) and the highest IESTI 17 % of the ARfD (apples). However, this consumer risk assessment has to be considered as provisional since the contribution of the TDM metabolites present in primary crops, rotational crops, processed commodities and in animal matrices was not taken into account and the impact of isomeric composition of the residues could not be considered.

4. Environmental fate and behaviour

The application dossier provides no information on the behaviour of each individual difenoconazole enantiomer or each diastereoisomer pair in the environment. The notifier confirmed that the chromatographic conditions that they had used in the analyses in their studies had not enabled the diastereoisomers to be resolved, though this could have been technically possible with non-chiral chromatographic methods. It is not known if either isomer is degraded more quickly than the other or if any other conversion may occur in the environmental matrices studied. Consequently this issue is identified as a data gap.

In soil laboratory incubations under aerobic conditions in the dark, difenoconazole exhibits moderate to high persistence forming the major metabolite 1,2,4-triazole (exhibiting low to moderate persistence).[7] Moreover, two minor transient metabolites (ascribed the codes V3 and M4) were formed but not identified or further addressed in the risk assessment.[8] The notifier has provided some indication that V3 is very likely to be 1,2,4-triazole, which is already included in the assessment available. However, since this could not be unequivocally confirmed with the data available, a data gap remains for identification of the metabolites V3 and M4. In a radiolabelled field dissipation study, GCA 205375 was identified as a major breakdown product.

[7] Major metabolites are defined as metabolites, which account for more than 10 % of the amount of active substance added in soil at any time during soil incubation or field dissipation studies.

[8] Minor transient metabolites are defined as metabolites, which a) account for more than 5 % of the amount of the active substance added in soil in at least two sequential measurements during the studies; or b) for which at the end of the soil degradation studies the maximum of formation is not yet reached.

Available laboratory soil incubations and field dissipation studies suggested that there could be a dose dependence of the degradation rate. This issue was however discussed at the teleconference of Member State experts (PRAPeR TC 41), where it was concluded that the evidence provided was not strong enough to affirm dose dependent degradation. In the available aerobic laboratory incubations mineralisation of the triazole and chlorophenyl ring radiolabels to carbon dioxide accounted for 2 % (after 90 – 100 days) and 4 – 19 % (after 90 – 120 days) respectively. The formation of unextractable residues (not extracted using acetonitrile:water) for the triazole and chlorophenyl ring radiolabels accounted for 12 – 37 % (after 90 – 100 days) and 14 – 34 % (after 90 – 120 days) respectively. Under anaerobic soil conditions difenoconazole was stable, while 1,2,4-triazole and GCA 205375 exhibited medium and high persistency respectively. In field dissipation studies the persistency of difenoconazole was moderate to high. These studies were conducted in Germany and Switzerland and satisfactory field dissipation information covering Southern European conditions was not available. This is identified as a data gap. Since the DT_{90} of difenoconazole exceeded one year, soil accumulation was investigated in four soil accumulation studies. Under the conditions present at these trial sites in the UK, Switzerland and Italy, soil accumulation did not occur.

Difenoconazole exhibited immobility to medium mobility in soil. 1,2,4-triazole exhibited high to very high mobility, whereas CGA 205375 exhibited low mobility or was immobile. There was no evidence that the adsorption of these compounds was affected by soil pH.

In laboratory incubations in dark aerobic natural sediment water systems, difenoconazole exhibited high persistence, forming the major metabolite CGA 205375 (max. ca. 11 % AR in sediment, exhibiting high persistence). Non-extractable sediment fraction was the major sink for the applied chlorophenyl ring radiolabel accounting for 9 – 14 % AR (after 183 days) while mineralisation accounted for 3.0 – 3.9 % AR (after 183 days).

Difenoconazole and CGA 205375 were both considered to be stable in laboratory studies on photochemical transformation in water under sterile conditions

The necessary surface water and sediment exposure assessments (predicted environmental concentrations (PEC)) were carried out for difenoconazole as well as the metabolites 1,2,4-triazole and GCA 205375 using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 1.1 of the Steps 1 – 2 in FOCUS calculator). For difenoconazole FOCUS (2001) step 3 and step 4 calculations were also provided.[9.] The step 4 calculation appropriately followed the FOCUS (FOCUS, 2007) guidance, with no-spray drift buffer zones implemented for the use assessed on apples (‘late’ spray drift values reducing spray drift by 90.4 to 90.7 % with a buffer width of up to 20 m). Combined no-spray buffer zones with vegetative buffer strips were implemented for carrots (a 5 m no spray buffer reducing drift by 72.9 to 73.5 % and reducing runoff flux with a vegetative strip by 50 %).

The necessary groundwater exposure assessments were carried out using FOCUS (FOCUS, 2000) scenarios and the model PEARL 2.2.2,[10.]for difenoconazole, GCA 205375 and 1,2,4-triazole. The potential for groundwater exposure from the representative uses for these compounds above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios.

5. Ecotoxicology

The risk assessment was based on the followings documents: European Commission (2002a, 2002b, 2002c), SETAC (2001), EFSA (2009).

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[9] Simulations utilised a Q10 of 2.2 and Walker equation coefficient of 0.7.
[10] Simulations utilised a Q10 of 2.2 and Walker equation coefficient of 0.7.

Isomerisation of difenoconazole cannot be excluded. No reliable information on the ecotoxicity, conversion or preferential degradation of isomers was submitted. This adds additional uncertainty to the environmental risk assessment.

The metabolism of difenoconazole in a range of plant species has demonstrated 56 – 79% of measurable residues in rape seeds and potato tubers may exist as the metabolite triazole alanine (CGA 131013). As a worst case assumption, it was proposed that 100 % of the parent compound is transformed to the metabolite (correction for molecular weight, 156 g/mole, compared to 406 g/mole for the parent, or a factor of 0.38 was taken into account).

The acute and short-term risk to birds via dietary exposure from difenoconazole and its metabolite triazole alanine was assessed as low at first tier for all the representative uses. Triazole alanine was not found in the residue study with pome fruit and therefore the risk assessment for this metabolite in pome fruit use was not performed.

The long-term risk to granivorous, medium herbivorous and small herbivorous birds from difenoconazole and the metabolite triazole alanine was assessed as low based on measured residues decline of difenoconazole in shoots emerging from treated seeds, and on measured data on dissipation of difenoconazole from treated seeds for the use in cereals.

The long-term risk of difenoconazole to insectivorous birds was assessed as low, based on a focal species (blue tit) and PT refinement for the use on pome fruit. The long-term risk of the metabolite triazole alanine to birds was assessed as low at the first tier for the use on carrots. The long-term risk of difenoconazole to medium herbivorous and insectivorous birds was assessed as high at the first tier based on the old guidance document (European Commission, 2002c) for the use on carrots. The Member State experts in PRAPeR TC 42 agreed to perform the risk assessment on the basis of the new guidance document (EFSA, 2009). The worst case scenario for late growth stages of carrot root and stem vegetables with a BBCH >40 where the focal species was woodlark (omnivore; 25 % crop leaves, 25 % weed seeds, 50 % ground arthropods) was used in the risk assessment. A calculation of the reproductive TER for this focal species was provided by the rapporteur Member State after the teleconference and presented in the addendum (Sweden, 2010). The long-term risk to woodlark was assessed as low for the use on carrots.

The acute risk to mammals via dietary exposure from difenoconazole was assessed as low at tier 1 for all representative uses. The long-term risk to granivorous and small herbivorous mammals was assessed as low based on a focal species (woodmouse), and measured residues decline of difenoconazole in emerging shoots, for the use in cereals. The long-term risk to herbivorous mammals was assessed as low based on the use of crop interception values for the use in pome fruit. The long-term risk of difenoconazole to mammals via dietary exposure was assessed as low for the use in carrots. The risk to mammals via dietary exposure from the metabolite triazole alanine was assessed as low at the first tier, for the use in cereals and carrots.

The risk assessment for fish-eating birds and mammals and earthworm-eating birds and mammals was required since log P_{ow} was 4.4. The risk assessment from secondary poisoning to birds and mammals was assessed as low for all representative uses. Additionally, the risk to birds and mammals from consumption of contaminated water was assessed as low for all representative uses.

During the peer-review process concerns were raised regarding the potential endocrine disrupting properties of difenoconazole (DMI-fungicide family). There were indications in open literature that difenoconazole is an aromatase inhibitor, but information from the toxicology section gave no indications of endocrine disruption. Therefore, the Member State experts at PRAPeR TC 42 agreed that concern for endocrine disruptive effects in birds and mammals was low. It was noted that the information on birds and mammals would not be appropriate to cover the potential endocrine disruption on fish.

Difenoconazole is very toxic to aquatic organisms. The formulations 'Dividend 030 FS' and 'Score' were less toxic than the technical active substance. In the *Chironomus riparius* study on difenoconazole, no measurements of sediment concentrations were conducted. Therefore the sediment concentrations in the test system were recalculated from the measured water concentrations (PRAPeR TC 42). The Member State experts confirmed that the PEC_{sed} plateau should be used in the risk assessment for *C. riparius.* The RMS updated the list of endpoints with the agreed TER.

EFSA notes that the aquatic risk assessment should be done with the highest PEC_{sw} available. These usually correspond with the PEC_{sw} estimated for single application instead of the PEC_{sw} for multiple applications used by the rapporteur Member State in the risk assessment. However, in this case there were a few scenarios where the PEC_{sw} for the multiple applications were higher than PEC_{sw} for a single application. Therefore EFSA calculated the TER values for the aquatic organisms using the highest PEC_{sw} available for the Step 3 and Step 4 assessment for the use on pome fruit and carrots.

The risk of difenoconazole to fish and algae and the acute risk to aquatic invertebrates was assessed as low at FOCUS step 1 for ***use on cereals***. The chronic risk to aquatic invertebrates was assessed as low at FOCUS step 2. The risk to *C. riparius* was assessed as high at FOCUS step 2 for the use in cereals and there were no accepted PEC_{sw} FOCUS step 3 available. Therefore the risk to *C. riparius* needs to be further addressed and a data gap was identified for the representative use on cereals.

The risk of difenoconazole to aquatic organisms was assessed as high at FOCUS step 2 for ***use on pome fruit***, with the exception of the acute risk to fish. The risk to algae was assessed as low for the use on pome fruit at $FOCUS_{sw}$ step 3 for all relevant scenarios. However, the chronic risk to fish and the acute and chronic risk to aquatic invertebrates were assessed as high for seven out of ten scenarios. Furthermore, the chronic risk to *C. riparius* was assessed as high for four out of ten scenarios (D3 ditch, D4 pond, D5 pond and R1 pond) where the TERs values were below the Annex VI trigger values at $FOCUS_{sw}$ step 3. At $FOCUS_{sw}$ step 4, the chronic risk to fish, the acute and chronic risk to *D. magna* and the risk to *C. riparius* were assessed as low for the majority of scenarios, based on risk mitigation measures (e.g. non-spray buffer zones of 14 m for the use on pome fruit).

The risk to algae and the acute risk of difenoconazole to fish and aquatic invertebrates were assessed as low at FOCUS step 2 for ***use on carrots***. At FOCUS step 3 a low chronic risk to fish was identified for the majority of the relevant scenarios (four out of seven scenarios). However, at $FOCUS_{sw}$ Step 3 the chronic risk to aquatic invertebrates and *C. riparius* was assessed as high for the majority of the relevant scenarios. At $FOCUS_{sw}$ step 4 the chronic risk to aquatic invertebrates was assessed as low. The risk to *C. riparius* was assessed as low including risk mitigation measures (e.g. non-spray buffer zones of 5 m for the use on carrots) in the full FOCUS scenarios D3, D6 and the part scenario R1 pond.

The risk from the metabolites 1,2,4-triazole and CGA 205375 was assessed as low for aquatic organisms for all representative uses.

A bioconcentration factor of 330 obtained for whole fish may indicate some potential for bioaccumulation however the risk from secondary poisoning was assessed as low (see above assessment for fish-eating birds and mammals).

The Member State experts at PRAPeR TC 42 agreed that the available information on fish would not be sufficient to assess the potential for endocrine disrupting effect of difenoconazole to fish. Therefore a data gap was identified to address the potential for endocrine disruption in fish.

Satisfactory field soil dissipation information for difenoconazole was not available to cover Southern European conditions. This information would be required to finalise the risk assessment to soil-dwelling organisms under Southern European conditions. A low acute risk to earthworms was identified from difenoconazole and its metabolites 1,2,4-triazole and CGA 205375. The selection of the chronic endpoint for difenoconazole was discussed at PRAPeR TC 42. It was concluded that the notifier would have to demonstrate that the increase in body weight would not lead to adverse effects on earthworm populations in order to use the reproduction NOEC from the available reproduction study. However, it was noted that with the reproduction NOEC a high risk would be identified for the use in pome fruits and carrots, and that further refinement of the risk would be needed for these uses if the reproduction NOEC would be accepted. A data gap was identified for the notifier to demonstrate that the increase in body weight would not lead to adverse effects on earthworm populations in order to be able to use the reproduction NOEC from the reproduction study. The chronic risk of 1,2,4-triazole metabolite to earthworms was assessed as low. For the metabolite CGA 205375, no chronic data on earthworms were available. Based on the persistence in soil of the metabolite CGA 205375, two data gaps were identified for the submission of data in order to address the chronic risk to earthworms and *Collembola*.

The risk to soil non-target macro-organisms was assessed as low for difenoconazole and the metabolite 1,2,4-triazole.

The risk to bees, non-target arthropods, non-target soil micro-organisms, non-target plants and waste water treatment plants was assessed as low for all representative uses.

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
Difenoconazole	Moderate to high persistence Single first order DT_{50} 53 – 235 (20°C, 40 – 48 % MWHC soil moisture) Field studies: Single first order DT_{50} 20 – 242 days (non normalised)	The acute risk of difenoconazole to earthworms was assessed as low. No NOEC could be derived from the reproductive earthworms study. Therefore the chronic risk to earthworms could not be finalised. The risk to non-target soil macro-organisms was assessed as low.
1,2,4-triazole (CGA 71019)	Low to moderate persistence Single first order DT_{50} 6 – 12 (20°C, 40 % MWHC soil moisture)	The acute and chronic risk of 1,2,4-triazole to earthworms was assessed as low.
CGA 205375	Medium to high persistence Single first order DT_{50} 83 – 152 (20°C, 40 %MWHC soil moisture)	The acute risk of CGA 205375 to earthworms was assessed as low. No long-term data on soil organisms were available, therefore the chronic risk to soil organisms could not be finalised.

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
Difenoconazole	Immobile to medium mobility K_{foc} 400 – 7730 mL/g	No	Yes	Yes	Very toxic to aquatic organisms, endpoint driving the aquatic risk assessment: *Daphnia magna* chronic NOEC = 0.0056 mg a.s./L (regulatory concentration including a safety factor of 10 = 0.00056 mg a.s./L). A high risk to the aquatic environment was indicated in the surface water risk assessment.
1,2,4-triazole (CGA 71019)	High to very high mobility K_{foc} 43 – 120 mL/g	No	No	Yes	Toxic to aquatic organisms, endpoint driving the aquatic risk assessment: fish chronic NOEC = 3.2 mg a.s./L (regulatory concentration including a safety factor of 10 = 0.32 mg a.s./L). A low risk to the aquatic environment was indicated in the surface water risk assessment.
CGA 205375	Immobile to low mobility K_{foc} 1680 – 5440 mL/g	No	No	Assessment not required. Mouse oral LD_{50} >2000 mg/kg bw. Ames test negative.	Very toxic to aquatic organisms, endpoint driving the aquatic risk assessment: fish acute EC_{50} = 0.74 mg a.s./L (regulatory concentration including a safety factor of 100 = 0.0074 mg a.s./L). A low risk to the aquatic environment was indicated in the surface water risk assessment.

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Difenoconazole	Very toxic to aquatic organisms, endpoint driving the aquatic risk assessment: *Daphnia magna* chronic NOEC = 0.0056 mg a.s./L (regulatory concentration including a safety factor of 10 = 0.00056 mg a.s./L). A high risk to the aquatic environment was indicated in the surface water risk assessment.
1,2,4-triazole (CGA 71019)	Toxic to aquatic organisms, endpoint driving the aquatic risk assessment: fish chronic NOEC = 3.2 mg a.s./L (regulatory concentration including a safety factor of 10 = 0.32 mg a.s./L). A low risk to the aquatic environment was indicated in the surface water risk assessment.
CGA 205375	Very toxic to aquatic organisms, endpoint driving the aquatic risk assessment: fish acute EC_{50} = 0.74 mg a.s./L (regulatory concentration including a safety factor of 100 = 0.0074 mg a.s./L). A low risk to the aquatic environment was indicated in the surface water risk assessment.

6.4. Air

Compound (name and/or code)	Toxicology
Difenoconazole	Rat LC_{50} > 3.3 mg/L (4h exposure, nose-only, highest technically achievable concentration).

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

- Specification range supported by the available data for the *cis* and *trans* isomers (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1).
- Biological activity of the isomers (relevant for all representative uses evaluated; data available but could not be taken into account due to the provisions in Regulation 1490/2002 and 1095/2007; see section 1).
- Validation of the HPLC method for the isomer ratio in the technical specification (relevant for all representative uses evaluated; data available but could not be taken into account due to the provisions in Regulation 1490/2002 and 1095/2007; see section 1).
- Adherence to seeds (relevant for the representative use evaluated as a seed treatment; submission date proposed by the notifier: unknown; see section 1).
- Given that the isomer range is so wide the effect of this on the physical, chemical and toxicological properties of the active substance is identified as a data gap (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1 and 2).
- A data gap was identified to assess the toxicological relevance of some impurities (relevant for all representative uses evaluated; data on one of the impurities but could not be taken into account due to the provisions in Regulation 1490/2002 and 1095/2007, submission date proposed by the notifier for data on the other impurities: unknown; see section 2).
- Additional supervised residue trials on carrots are required in order to complete the residue dataset, unless the stability of the residues in plant matrices is confirmed up to 33 months (relevant for the representative use evaluated in carrots; submission date proposed by the notifier: unknown; see section 3).
- Processing study on carrots (data already submitted but that could not be taken into account due to the provisions in Regulation 1490/2002 and 1095/2007; see section 3)
- Information on the possible residues of TDM metabolites in primary crops, rotational crops, processed commodities and in animal matrices are required in order to perform a sound consumer risk assessment (relevant for all representative use evaluated; no submission date proposed by the notifier, see section 3).
- Identification and further assessment of the minor transient metabolites V3 and M4 formed in soil incubation studies is outstanding (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 4).
- Satisfactory field soil dissipation information for difenoconazole was not available to cover Southern European conditions. This information would be required to finalise the risk assessment to soil-dwelling organisms under Southern European conditions (relevant for all representative uses evaluated in Southern Europe; submission date proposed by the notifier: unknown; see section 4).
- Difenoconazole consists of diastereo isomers. The preferential metabolism/degradation of each enantiomer in plants, animals, and the environment, as well as the possible impact on the toxicity, the consumer risk assessment, worker exposure and the environment needs to be addressed (relevant for all representative uses evaluated; data gap identified by EFSA during drafting of the

conclusion; submission date proposed by the notifier: unknown; applicable to sections 2, 3, 4 and 5).

- A high risk was identified from the use of difenoconazole for *C. riparius*. Further refinement of the risk to aquatic sediment-dwelling organisms was necessary (relevant for the representative use in cereals; submission date proposed by the notifier: unknown; see section 5).

- A data gap was identified for data to address the potential for endocrine disruption in fish (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5).

- A data gap was identified to demonstrate that the increase in body weight would not lead to adverse effects on earthworm populations in order to be able to use the reproduction NOEC from the reproduction study. As a consequence of the use of this NOEC, further refinement would be needed for the use on pome fruit and carrots (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5).

- A data gap was identified for an earthworm reproduction study on the soil metabolite CGA 205375 (relevant for all representative uses evaluated; data available but could not be taken into account due to the provisions in Regulation 1490/2002 and 1095/2007; see section 5).

- A data gap was identified for a *Collembola* reproduction study on the soil metabolite CGA 205375 (relevant for all representative uses evaluated; data available but could not be taken into account due to the provisions in Regulation 1490/2002 and 1095/2007; see section 5).

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

- The rinsed residue result was high for the formulation 'Dividend 030 FS' so appropriate labelling should be considered (see section 1).

- Risk mitigation measures corresponding to 14 m non-spray buffer zones and 5 m non-spray buffer zones were required to address the risk to aquatic organisms for the representative uses on pome fruit and carrots, respectively (see section 5).

ISSUES THAT COULD NOT BE FINALISED

- Possible impact on the toxicity, the consumer risk assessment, worker exposure and the environment of the variable isomer ratio in the technical and of the potential enantio-selective biologically mediated metabolism/degradation/transformation in plants, animals, and the environment needs to be addressed.

- The consumer risk assessment has to be considered provisional since the possible contribution of the TDM metabolites present in primary crops, rotational crops, processed commodities and products of animal origin to the overall consumer exposure was not considered. Moreover, the impact of the enantiomeric composition of the residues was not considered.

- Consequent to the data gap for further information to address the identity of soil metabolites V3 and M4, the groundwater exposure assessment for metabolites is not finalised.

- The risk to soil non-target organisms under Southern European conditions could not be finalised whilst the soil exposure assessment under Southern European conditions is not finalised.

- The chronic risk assessment to sediment-dwellers could not be finalised for the uses on cereals.

- The chronic risk assessment of difenoconazole to earthworms could not be finalised for all the representative uses. For the metabolite CGA 205375, the chronic risk could not be assessed for any of the representative uses.

CRITICAL AREAS OF CONCERN

- None.

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APPENDICES

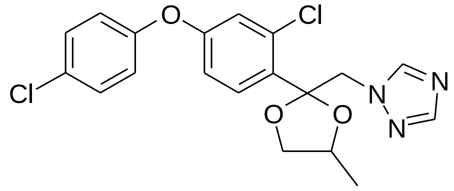
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

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

Rapporteur Member State	Sweden
Co-rapporteur Member State	Not assigned

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3-chloro-4-[(2*RS*,4*RS*;2*RS*,4*SR*)-4-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-2-yl]phenyl 4-chlorophenyl ether
Chemical name (CA) ‡	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole
CIPAC No ‡	687
CAS No ‡	119446-68-3
EC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification (including year of publication) ‡	No FAO specification available.
Minimum purity of the active substance as manufactured ‡	940 g/kg. Open for cis/trans ranges
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Toluene: 5 g/kg Open for others.
Molecular formula ‡	$C_{19}H_{17}Cl_2N_3O_3$
Molecular mass ‡	406.3 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	82.0-83.0°C (99.3%)
Boiling point (state purity) ‡	Not relevant at atmospheric pressure as decomposition occurs. 100.8°C at 3.7 mPa (99.3%)
Temperature of decomposition (state purity)	Decomposition starts at about 337°C (99.3%)
Appearance (state purity) ‡	Technical material: Off-white powder with a slightly sweetish odour, purity not stated. Purified material: White fine odourless crystalline powder, purity 99.3 %
Vapour pressure (state temperature, state purity) ‡	3.32×10^{-8} Pa at 25°C (99.0%)
Henry's law constant ‡	9.0×10^{-7} Pa m^3 mol^{-1} at 25°C
Solubility in water (state temperature, state purity and pH) ‡	15 mg/l ± 1.3 mg/l at pH 7.2 and 25 °C No pH effect is anticipated at environmentally relevant pH
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 25°C in g/L (94.6%): acetone: >500 g/l dichloromethane: >500 g/l ethyl acetate: >500 g/l hexane: 3.0 g/l methanol: >500 g/l octanol: 110 g/l toluene >500 g/l
Surface tension ‡ (state concentration and temperature, state purity)	62.8 mN/m at 20°C (90 % saturated solution)(94.6%)
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ = 4.36 ± 0.02 at 25 °C and a pH of approx. 8 (99.3%) No pH effect is anticipated at environmentally relevant pH.
Dissociation constant (state purity) ‡	pKa_1 = 1.07 ± 0.18 for the corresponding acid (i.e the neutral species is predominantly present at pH > 1.1) (99.3%)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Neutral media: λ_{max} [nm] ε (l x mol^{-1} x cm^{-1}) 215 28658 235 17392 275 1680
	Acidic media: λ_{max} [nm] ε (l x mol^{-1} x cm^{-1}) 215 29306 235 17556 275 1743
	Alkaline media: λ_{max} [nm] ε (l x mol^{-1} x cm^{-1}) 220 21210 235 17176 275 1542 No absorption maxima between 300 nm and 700 nm at any pH.
Flammability ‡ (state purity)	Flammability: Not highly flammable Auto-flammability: No self-ignition below the melting point Flash-point: Not applicable since the melting point is > 40 °C
Explosive properties ‡ (state purity)	Not explosive (91.8%)
Oxidising properties ‡ (state purity)	Not oxidising (91.8%)

Summary of representative uses evaluated (Difenoconazole)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc of as (i)	method kind (f-h)	growth stage & season (j)	number min-max (k)	interval between applications (min)	kg as/hL min-max	Water L/h min-max	kg as/ha min-max		
Pome fruit	EU (N/S)	Score A7402T	F	*Podosphaera leucotricha* *Venturia inaequalis*	EC	250 g/l	High vol spray or mist blower	Spray programme beginning at flowering (BBCH 61)	1-4	10-14	0.00375 0.0075	500 1500 500 1000	0.01875 0.05625 0.0375 0.0750	28 14	EU(N) [I] [IV] [V] [VI] EU (S) [I] [II] [IV] [V] [VI]
Carrot	EU (N/S)	Score A7402T	F	*Alternaria dauci* *Erysiphe heraclei*	EC	250 g/l	High vol spray	First application at BBCH 42/43	1-3	14	-	100 500	0.125	14	[I] [II] [IV] [V] [VI]
Wheat	EU (N/S)	Dividend 030 FS A9142G	F	*Fusarium spp. Tilletia spp.*	FS	30 g/l	Seed treatment	BBCH 00	1	-	0.03-0.06 kg as/tonne	-	0.005 0.012	-	kg as/ha rate depends on seeding rate [I] [II] [III] [IV] [V] [VI]
Barley	EU (N/S)	Dividend 030 FS A9142G	F	*Pyrenophorma granimea*	FS	30 g/l	Seed treatment	BBCH 00	1	-	0.03-0.06 kg as/tonne	-	0.005 0.012	-	kg as/ha rate depends on seeding rate [I] [II] [III] [IV] [V] [VI]
Triticale	EU (N/S)	Dividend 030 FS A9142G	F	*Fusarium spp. Tilletia spp.*	FS	30 g/l	Seed treatment	BBCH 00	1	-	0.03-0.06 kg as/tonne	-	0.005 0.012	-	kg as/ha rate depends on seeding rate [I] [II] [III] [IV] [V] [VI]
Rye	EU (N/S)	Dividend 030 FS A9142G	F	– *Fusarium spp. Urocystis occulata*	FS	30 g/l	Seed treatment	BBCH 00	1	-	0.03-0.06 kg as/tonne	-	0.005 0.012	-	kg as/ha rate depends on seeding rate [I] [II] [III] [IV] [V] [VI]

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc of as (i)	method kind (f-h)	growth stage & season (j)	number min-max (k)	interval between applications (min)	kg as/hL min-max	Water L/h min-max	kg as/ha min-max		
Oats	EU (N/S)	Dividend 030 FS A9142G	F	*Ustilago avenae* *Pyrenphora avenae* *Cochliobolus sativum* *Fusarium culmorum* *Gibberella avenacea* *Pythium ultimum*	FS	30 g/l	Seed treatment	BBCH 00	1	-	0.03-0.06 kg as/tonne	-	0.005 0.012	-	kg as/ha rate depends on seeding rate [I] [II] [III] [IV] [V] [VI]

[I] The groundwater exposure assessment for metabolites that may be formed in soil was not finalised.
[II] The risk assessment to soil dwelling organisms from exposure to difenoconazole under southern European conditions was not finalised.
[III] The chronic risk assessment to sediment dwelling organisms from the exposure to difenoconazole could not be finalised for the representative uses on cereals.
[IV] The chronic risk of difenoconazole to earthworms could not be finalised.
[V] The consumer risk assessment has to be considered provisional since the possible contribution of the TDM metabolites to the overall consumer exposure was not considered.
[VI] Possible impact on the toxicity, the consumer risk assessment, worker exposure and the environment of the variable isomer ratio in the technical and of the potential enantio-selective biologically mediated metabolism/degradation/transformation in plants, animals, and the environment needs to be addressed.

∗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)	GC-FID Open for validation of the isomer ratio method
Impurities in technical as (analytical technique)	GC-FID
Plant protection product (analytical technique)	HPLC-UV (Dividend 030 FS) and GC-FID (Score)

Analytical methods for residues (Annex IIA, point 4.2)
Residue definitions for monitoring purposes

Food of plant origin	Difenoconazole
Food of animal origin	Difenoconazole alcohol (CGA 205375) expressed as difenoconazole
Soil	Difenoconazole, data gap needs to be filled before Difenoconazole alcohol (CGA 205375) can be excluded.
Water surface	Difenoconazole
drinking/ground	Difenoconazole
Air	Difenoconazole

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	LC-MS/MS; 0.02 mg/kg (apple, lettuce), 0.05 mg/kg (wheat grain, oilseed rape) ILV available down to 0.01 mg/kg for all matrices
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Difenoconazole and CGA 205375: LC-MS/MS; LOQ 0.01 mg/kg (tissues, fat, eggs), 0.005 mg/kg (milk) ILV available down to LOQ
Soil (analytical technique and LOQ)	Difenoconazole and CGA 205375: LC-MS/MS; LOQ 0.01 mg/kg
Water (analytical technique and LOQ)	GC-ECD; LOQ 0.05 µg/l (drinking), 0.1 µg/l (surface)
Air (analytical technique and LOQ)	LC-MS/MS; 0.99 ng/L
Body fluids and tissues (analytical technique and LOQ)	Not required as the active substance is not classified as toxic or very toxic.

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

	RMS/peer review proposal
Active substance Difenoconazole	None

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	About 80 - 90% based on the biliary (73- 76%) and urinary (14 -9%) excretion within 48 hours.
Distribution ‡	Initially highest residues in fat, liver, brown fat, Harderian gland, adrenal gland and stomach. At 168 hours, residues above the plasma concentration only detected in fat.
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	Rapid and extensive within 48 hours mainly via faeces (>77%) and in urine (>12%). Entero hepatic recirculation demonstrated.
Metabolism in animals ‡	Extensively metabolised, mainly by hydrolysis of the ketal and hydroxylation; also by cleavage of the triazole (1, 2, 4- triazole determined to represent <10% in male rats).
Toxicologically relevant compounds ‡ (animals and plants)	Triazole derivative metabolites (1,2,4-triazole, triazole acetic acid, triazole alanine, triazole lactic acid).
Toxicologically relevant compounds ‡ (environment)	Difenoconazole

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	1453 mg /kg bw	R22
Mouse LD_{50} oral	> 2000 mg/kg bw	
Rabbit LD_{50} dermal ‡	>2010 mg/kg bw	
Rat LC_{50} inhalation ‡	> 3.3 mg/L (4h exposure, nose-only, highest technically achievable concentration)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non- irritant	
Skin sensitisation ‡	Non-sensitiser (modified Buehler test)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Rat: reduced body weight, heart and carcass weight, reduced food and water consumption; liver (at high doses after oral exposure); liver and thyroid (follicular hypertrophy) after dermal exposure Mouse: reduced bodyweight gain, reduced ovary weight, liver (increased weight with enlargement, vacuolization and coagulative necrosis) Dog: decreased body weight gain, liver (increased weight and changes in clinical chemistry), cataract formation (at high doses)	
Relevant oral NOAEL ‡	Rat: 20 mg/kg bw/d (90-day) Mouse: 34 mg/kg bw/d (90-day) Dog: 31 mg/kg bw/d (28-week)	
Relevant dermal NOAEL ‡	Rat: 100 mg/kg bw/d (28-day)	
Relevant inhalation NOAEL ‡	No data – not required.	

Genotoxicity ‡ (Annex IIA, point 5.4)

	Equivocal increases in chromosomal aberrations in CHO cells *in vitro*. Difenoconazole is unlikely to be genotoxic *in vivo*.	

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

Target/critical effect ‡	Rat: reduced body weight gain; liver (increased relative weight, hepatocyte hypertrophy) Mouse: reduced body weight (gain); liver (increased weight, histopathological changes including necrosis, hypertrophy, fatty change and bile stasis.

Relevant NOAEL ‡	Rat: 1.0 mg/kg bw/d (2-yr) Mouse: 4.7 mg/kg bw/d (18-mo)	
Carcinogenicity ‡	Liver adenomas/carcinomas in mice, only at high doses where toxicity was observed. Difenoconazole is considered unlikely to pose a carcinogenic risk to humans.	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: reduced body weight (gain) Offspring: reduced body weight through lactation Reproductive: no adverse effect	
Relevant parental NOAEL ‡	16.8 mg/kg bw/d	
Relevant reproductive NOAEL ‡	189 mg/kg bw/d	
Relevant offspring NOAEL ‡	16.8 mg/kg bw/d	

Developmental toxicity

Developmental target / critical effect ‡	Developmental: skeletal variations (rat), increased number of resorptions (rat, rabbit) Maternal: reduced body weight gain/reduced food consumption (rat, rabbit); abortions (2) and death (1) (rabbit)	
Relevant maternal NOAEL ‡	Rat: 15.6* mg/kg bw/d Rabbit: 25 mg/kg bw/d	
Relevant developmental NOAEL ‡	Rat: 15.6* mg/kg bw/d Rabbit: 25 mg/kg bw/d	

*corrected for actual concentration of 78% in the test material

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data available, no indication of neurotoxic properties in the available acute toxicity studies, no data required.	
Repeated neurotoxicity ‡	No data available, no indication of neurotoxic properties in the available acute toxicity studies, no data required.	
Delayed neurotoxicity ‡	No data available – not required	

Other toxicological studies (Annex IIA, point 5.8)

	Dietary treatment of chickens with 5000 ppm difenoconazole during 8 weeks led to cataract development in some animals after one month of treatment.
Mechanism studies ‡	Supplementary study on enzyme induction performed: difenoconazole is considered to be a reversible inducer of metabolising enzymes in the mouse liver with an enzyme induction profile resembling phenobarbitone.
Studies performed on metabolites or impurities ‡	Studies submitted for the plant metabolites: **CGA 189138:** bacterial reverse mutation test negative **CGA 205374:** mouse acute oral LD_{50} >5000 mg/kg bw, bacterial reverse mutation test negative **CGA 205375:** mouse acute oral LD_{50} 2309 mg/kg bw, bacterial reverse mutation test negative
	Several studies were submitted for the triazole derivative metabolites (as plant metabolites), and were already considered during the meeting PRAPeR 14 (January 2007). Based on these data and including an additional multigeneration study performed with 1,2,4-triazole and showing a more critical NOAEL (Young, 2005), specific reference values were agreed for the triazole metabolites (see also PRAPeR 14): - **1,2,4-triazole**: ADI 0.02 mg/kg bw/d based on the 2-generation rat study by Young (2005) (SF 1000); ARfD 0.06

	mg/kg bw based on the rat developmental study (SF 500). - **triazole acetic acid** and **triazole lactic acid**: ADI and ARfD of 1,2,4-triazole (because of limited database available) - **triazole alanine**: ADI and ARfD 0.1 mg/kg bw(/d) based on the rat developmental study (SF 1000).

Medical data ‡ (Annex IIA, point 5.9)	No detrimental effects on health in manufacturing personnel.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/d	2-yr rat	100
AOEL ‡	0.16 mg /kg bw/d	developmental, rat	100
ARfD ‡	0.16 mg /kg bw	developmental, rat	100

Dermal absorption ‡ (Annex IIIA, point 7.3) Formulation ((SCORE® 250 EC (A 7402 G, EC) (23.2% w/w, 250 g/L); DIVIDEND®030FS (A9142G) (2.86%w/w, 30 g/L))	SCORE® 250 EC (A 7402 T): no data available. Data obtained for SCORE® 250 EC (A 7402 G) used to represent type A 7402 T: 2% undiluted formulation, 4% diluted spray solution, based on rat *in vivo* and comparative *in vitro* human/rat skin. DIVIDEND®030FS (A9142G): no data available. Data obtained for diluted SCORE® 250 EC (A 7402 G) (i.e. 4%) used for **undiluted** DIVIDEND®030FS (A9142G).

Exposure scenarios (Annex IIIA, point 7.2)

	Exposure estimates in % of AOEL (without use of PPE*)		
Operators using **SCORE® 250 EC** (A-7402 T)	Crop – application – Zone	German model	UK POEM (5L bottle)
	Pome fruit – tractor – North	2	16
	Pome fruit – tractor – South	3	19
	Pome fruit – hand held - North	3	14
	Pome fruit – hand held – South	4	15
	Carrot – tractor	3	75
	Carrot – hand held	-	63
Operators using **DIVIDEND® 030 FS** (A-9142 G)	Estimated exposure according to SEEDTROPEX model (all tasks combined) is 37% of the AOEL without use of PPE.		
Workers re-entering crop treated with **SCORE® 250 EC** (A-7402 T)	Crop	EUROPOEM estimates in % AOEL(without use of PPE)	
	Pome fruit	3.4 (after one application)	
	Carrot	3.1 (after one application)	
Workers loading and sowing seed treated with **DIVIDEND® 030 FS** (A-9142 G)	Estimated exposure according to SEEDTROPEX model is 6.9% of the AOEL.		
Bystanders	**SCORE® 250 EC :** <1% of AOEL for bystanders situated at 10 m distance from the orchards and exposed during 5 minutes. **DIVIDEND®030 FS :** Incidental exposure in seed treatment facilities is not expected to exceed the operator exposure during seed treatment.		

*PPE: personal protective equipment

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

	RMS/peer review proposal
Difenoconazole	Xn; R22

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

Plant groups covered	Foliar treatment: Cereals (spring wheat) Root vegetables (potato) Fruits (tomato, grapes) Pulses/oilseeds (oilseed rape) Seed treatment: Cereals (spring wheat)
Rotational crops	Leafy vegetables (lettuce, spinach), root vegetables (carrot, sugarbeet, turnip), cereals (spring and winter wheat, maize), oilseeds (mustard)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes, in part. No residues of parent difenoconazole were found. Residues mainly composed of TDM metabolites: triazole alanine (TA), triazole acetic acid (TAA) and triazole lactic acid (TLA).
Processed commodities	Difenoconazole stable under standard hydrolysis conditions representative of pasteurisation/baking/sterilisation (more than 96% TRR consisted of parent difenoconazole).
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Difenoconazole
Plant residue definition for risk assessment	Two separate residue definitions: 1) Difenoconazole 2) Triazole derivative metabolites (TDM) (provisional, pending the definition of a common and harmonised approach for all the active substances of the triazole chemical class)
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	Ruminant (goat), poultry (hen)
Time needed to reach plateau concentration in milk and eggs	48 hours in milk [^{14}C-phenyl]-difenoconazole 144 hours in milk [^{14}C-triazole]-difenoconazole 168 hours in egg yolk [^{14}C-phenyl] and [^{14}C-triazole] 120 hours in eggs white [^{14}C-triazole]-difenoconazole
Animal residue definition for monitoring	Difenoconazole alcohol (CGA-205375) expressed as difenoconazole
Animal residue definition for risk assessment	Two separate residue definitions: 1) Difenoconazole alcohol (CGA-205375) expressed as difenoconazole 2) Triazole derivative metabolites (provisional, pending information on metabolism of TDM in animals and pending the definition of a common and harmonised approach for all the active substances of the triazole chemical class)
Conversion factor (monitoring to risk assessment)	Not concluded
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes

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

	Residues of difenoconazole in human food commodities of succeeding crops (lettuce, carrot, spinach) not expected to exceed 0.01 mg/kg. In one study conducted with the [^{14}C-triazole-] label, TRRs in mature maize and wheat grain were 0.211 and 0.341 mg/kg, consisting mainly of TDM [triazole alanine (44-66.2%), triazole acetic acid (25.9%) and triazole lactic acid (9.7%)]

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

	Difenoconazole stable when stored frozen at -20°C, up to: - 24 months in potato, tomato, cotton (cottonseed oil) and wheat (straw, forage and grain) - 12 months in lettuce (head), soybean (beans) and banana. Difenoconazole stable at least 12 months in animal matrices (Eggs, milk, poultry breast and beef liver) when stored frozen at -20°C. Difenoconazole and Difenoconazole alcohol (CGA-205375) stable at least 10 months in animal matrices (milk, liver, kidney, fat and muscle) when stored frozen at -18°C.

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)	Yes 0.23/0.65 mg/kg DM Dairy/Beef cattle	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 study[a] (residues of **difenoconazole-alcohol** (CGA 205375) for the feeding rate 10 mg/kg DM corresponding to a 43N and 15N dose rate for dairy and beef cattle) Residue levels in matrices : **mean (Max) mg/kg CGA 205375**		
Muscle	0.022 (0.024)	--	--
Liver	0.303 (0.350)	--	--
Kidney	0.044 (0.052)	--	--
Fat	0.077 (0.095)	--	--
Milk	0.008 (0.009)		
Eggs		--	

[a]: Parent also analysed for in the feeding study. At the highest feeding rate (10 mg/kg DM), all values below LOQs (0.005 mg/kg milk, 0.01 mg/kg other matrices), except in liver (HR 0.02 mg/kg).

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 Southern Region, field or glasshouse	**Trials results relevant to the representative uses** (a)	**Recommendation/comments**	**MRL** estimated from trials according to representative use	**HR** (c)	**STMR** (b)
Wheat	Northern and Southern	**Grain:** 2x <0.01, 6x <0.02 (North) 2x <0.01, 4x <0.02 (South)		0.02	0.02	0.02
		Straw: 2x <0.01, 2x <0.02, 2x <0.04, 0.04, 0.05 (North) 2x <0.01, 3x <0.04, 0.05 (South)			0.05	0.04
Apple and Pear	Northern	**cGAP: 0.056 g/ha, PHI 28 days** 0.01, 0.02, 0.03, 0.04, 2x 0.05, 0.06, 2x 0.07	MRL derived from trials conducted in the Southern region, since Southern GAP leads to higher residue levels. R_{max}= 0.31; R_{ber}= 0.30	0.3	0.07	0.05
	Southern	**cGAP: 0.075 g/ha, PHI 14 days** 0.04, 0.05, 0.07, 0.08, 0.10, 0.11, 0.13, 0.14, 0.15, 0.16, 0.28			0.28	0.11
Carrot	Northern	2x 0.02, 0.03, 0.04, 0.05, 0.07, 0.11, 0.12	MRL derived from merged northern and southern datasets, as similar residue levels in both zones. R_{max}= 0.17; R_{ber}= 0.22 3 additional trials required in Southern EU	0.2	0.13	0.05
	Southern	0.02, 0.03, 0.07, 0.11, 0.13				

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

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

ADI	**0.01 mg/kg bw/day**
TMDI (% ADI) according to EFSA PRIMo rev2	Highest TMDI: 44% ADI (DE child) (Provisional, TDM contribution and isomeric composition of the residues not considered)
TMDI (% ADI) according to WHO European diet	-
TMDI (% ADI) according to national (to be specified) diets	-
IEDI (WHO European Diet) (% ADI)	-
NEDI (specify diet) (% ADI)	Not calculated (TMDI < 100%)
Factors included in IEDI and NEDI	Not applicable
ARfD	**0.16 mg/kg bw**
IESTI (% ARfD) according to EFSA PRIMo rev2	17% ARfD (Apples) 16% ARfD (Pears) 5% ARfD (Carrots)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	-
Factors included in IESTI and NESTI	Highest residue (HR)

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

Crop/process/processed product	Number of studies	**Processing factors**		Amount transferred (%) (Optional)
		Transfer factor **Mean** (values)	Yield factor	
Apple/Washed fruit	2	**0.78** (0.71, 0.84)		
Apple/Wet pomace	4	**4.3** (3.5, 6.5, 4.0, 3.0)		
Apple/Dry pomace	1	**16**		
Apple/Juice (before/after pasteurisation)	1[a]	0.02/0.02		
Apple/Puree	1	0.14		

[a]: 4 studies available for apple juice, but 3 studies disregarded as residues in RAC and juice at/close to the LOQ

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

Plant products (difenoconazole)

Pome fruit	0.3 mg/kg
Carrot	0.2 mg/kg
Cereal grain	0.05* mg/kg

Ruminant products (difenoconazole alcohol expressed as difenoconazole)

Liver	0.05 mg/kg
Other ruminant products	0.01* 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°, standard moisture conditions: [^{14}C-triazole]-label: 0.2% (91 d), 1.6% (100 d) and 2.1% (90 d) (n=3) [^{14}C-chlorophenyl]-label: 18.1% (100 d), 3.7% (106 d), 5.5% (90 d), 19.3% (90 d), 11.3% (120 d), 14.4% (120 d), 15.2% (120 d) (n=7) study on 1,2,4-triazole at 20°: 15.4% and 33.0%, both after 120 d (n=2) study on [^{14}C-triazole]-labelled CGA 205375 at 20°: 10.0%, 2.8%, 0.2% (all after 84 days) (n=3)
Non-extractable residues after 100 days ‡	20°, standard moisture conditions: [^{14}C-triazole]-label: 11.9% (91 d), 21.8% (100 d) and 36.6% (90 d) (n=3) [^{14}C-chlorophenyl]-label: 22.8% (100 d), 20.6% (106 d), 13.8% (90 d), 33.7% (90 d), 17.4% (120 d), 18.1% (120 d), 19.2% (120 d) (n=7) study on 1,2,4-triazole at 20°: 64.7% and 40.1%, both after 120 d (n=2) study on [^{14}C-triazole]-labelled CGA 205375 at 20°: 15.6%, 17.2%, 15.6% (all after 84 days) (n=3)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	CGA 205375: max. 4.4-9.7% after 56-120 d [^{14}C-triazole] and [^{14}C-chlorophenyl] labels (n=7) in laboratory incubations: Max 11.9% found in radiolabelled field dissipation study. CGA 71019: max. 20.6-23.4% after 190/271 d [^{14}C-triazole]-label (n=2)

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

Anaerobic degradation ‡

Mineralization after 100 days	0.1% after 110 d [^{14}C-triazole]-label (n=1)
Non-extractable residues after 100 days	11.6% after 110 d [^{14}C-triazole]-label (n=1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None

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 ‡

Difenoconazole	Aerobic conditions						
Soil type	g/ha[1]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d)[3] 20 °C pF2/10kPa	St. (r^2)	Method of calculation
loam	141	7.2	20 / 40	104 / 345	64	0.999	SFO
loam	143	7.2	20 / 40	118 / 392	72	0.998	SFO
Geomean loam (n=2)				**111** / 368	**111**		
sandy loam	75	5.0	20 / 40	**123**[4] / 409	**123**	0.913	SFO
silt loam	750	7.2	20 / 48	456[4] / >>273	456	0.892	SFO
silt loam	750	7.2	30 / 48	175[2] / >>178[2]	-	0.977	SFO
silt loam	750	7.2	20 / 24	709[2,4] / >>281[2]	-	0.855	SFO
silt loam	750	7.2	20 / 48	345[4] / >>281	345	0.973	SFO
silt loam	750	7.2	10 / 48	602[2,4] / >>281[2]	-	0.952	SFO
silt loam	75	7.2	20 / 48	83 / 277	83	0.950	SFO
Geoman silt loam (n=3)				**235** / >277	**235**		

loam	128	7.2	20 / 22	136[2] / 452[2]	-	0.986	SFO
loam	128	7.2	10 / 43	338[2,4] / >1000[2]	-	0.993	SFO
loam	12.8	7.2	20 / 43	**53** / 175	**53**	0.995	SFO
loam sterile	128	7.2	20 / 43	>1000[2,4] / >1000[2]	-	-	-
sandy loam	193	7.4	20 / 40	**149** / 496	**136**	0.977	SFO
sandy loam/loamy sand	193	7.5	20 / 40	**186** / 617	**177**	0.939	SFO
silty clay loam	193	6.7	20 / 40	**187** / 620	**151**	0.972	SFO
Geometric mean (n=7)				136 / > 390	130		
Median (n=7)				149 / ≥ 409	136		

[1] *Test concentration re-calculated into corresponding g a.s./ha dose for comparison with the representative uses.*
[2] *Values not included in the mean/median because they were obtained from test at 10/30ºC, dry moisture or sterile conditions.*
[3] *In case the same soil was tested under standard conditions, the variations in temperature and moisture were not considered for mean/median values of normalised data.*
[4] *DT_{50} value extrapolated beyond the durations of the study.*

CGA 71019	Aerobic conditions						
Soil type	pH	t. ºC / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
sandy loam	6.4	20 / 40	6.3 / 21	-	5.0	0.75	SFO
loamy sand	5.8	20 / 40	9.9 / 33	-	9.9	0.81	SFO
silt loam	6.7	20 / 40	12 / 41	-	8.2	0.95	SFO
Geometric mean			9.1 / 30.5		7.4		
Median			9.9 / 33		7.7		

CGA 205375	Aerobic conditions						
Soil type	pH	t. ºC / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
sandy loam	7.4	20 / 40	93 / 309	-	85	0.980	SFO
sandy loam/loamy sand	7.5	20 / 40	83 / 275	-	79	0.995	SFO
silt loam	5.8	20 / 40	152 / 504	-	123	0.996	SFO
Geometric mean			106 / 350		94		
Median			93 / 309		85		

Field studies ‡

Difenoconazole									
Soil type (indicate if bare or cropped soil was used).	Location	g/ha[1]	pH	Depth (cm)[2]	DT_{50} (d) actual	DT_{90}(d) actual	Chi2 (%)	DT_{50} (d) Norm. 20ºC	Method of calculation
silt loam bare	Germany	>>250	7.4	0-20	160	532	18.6	-	SFO
silt loam bare	Germany	500	6.6	0-10	20	68	13.0	-	SFO
loamy sand bare	Germany	500	6.2	0-10	59	195	18.3	-	SFO
silt loam bare	Germany	500	6.8	0-20	64	211	14.1	-	SFO
loamy sand bare	Germany	500	5.6	0-10	61	202	14.8	-	SFO
sandy loam bare	Germany	750	6.0	0-20	265	879	18.6	-	SFO
silt loam bare	Germany	750	6.0	0-20	242	802	20.9	-	SFO
silt loam bare	Germany	750	5.7	0-20	118	394	21.8	-	SFO
clay loam bare	Switzerland	125	7.3	0-10	83	277	-	-	SFO
Geometric mean					92	305			
Median					83	277			

[1] *Treatment rate (g a.s./ha) used in studies.*
[2] *Indicates depth considered.*

pH dependence ‡ (yes / no) (if yes type of dependence)	No

Soil accumulation and plateau concentration ‡	No accumulation observed after up to 10 years use under the following conditions: <u>10-yr study in Switzerland (sandy loam):</u> 7 years appl. of 125 g/ha to wheat, 2 years appl. of 125 g/ha to rape and 1 year 3x125 g/ha to sugar beet. Taking crop interception (90% by wheat and sugar beet and 80% by rape, FOCUS GW) into account the “effective doses” would have been 12.5 g/ha for 7 years, 25 g/ha for 2 years and 37.5 g/ha for 1 year. <u>4-yr study in N Italy (sandy loam):</u> Annual application to pome fruit at 250 g/ha. Assuming standard crop interception (50-65%, FOCUS GW) the annual “effective dose” would have been 87.5-125 g/ha. <u>4-yr study in N Italy (silt clay):</u> Annual application to sugar beets at 202-241 g/ha. Assuming crop interception of 90% the “effective dose” would have been within 20-24 g/ha each year. <u>3-yr study in UK (sandy loam and clay):</u> 3-yr appl. to winter wheat or bare ground, at 75 g/ha and 150 g/ha. Assuming 90% crop interception by wheat the net application rates would have been 7.5 and 15 g/ha. (this study considered as supplementary)

Laboratory studies ‡

Difenoconazole	Anaerobic conditions						
Soil type	g/ha[1]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
loam	128	7.2	20 / flooded	stable	-	-	-
Geometric mean/median				-	-		

[1] Test concentration re-calculated into corresponding g a.s./ha dose for comparison with the representative uses.

CGA 71019	Anaerobic conditions						
Soil type	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
silt loam	7.3	20 / flooded	81 / 268	-	-	0.972	SFO
Geometric mean/median			-	-	-		

CGA 205375	Anaerobic conditions						
Soil type	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
sandy loam/loamy sand	7.5	20 / flooded	213 / 706	-	-	0.986	SFO
Geometric mean/median			-	-	-		

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Difenoconazole ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
sand	0.36	7.9	-	-	12.8	3870	0.74
sandy loam	1.98	7.8	-	-	63.0	3520	0.76
silt loam	1.74	6.5	-	-	54.8	3470	0.85
silty clay loam	0.67	6.9	-	-	47.2	7730	0.91
clay	2.79	5.9	-	-	97.8	3470	0.89
sand	0.52	6.5	-	-	2.1	400	0.80
silt loam	0.58	7.5	-	-	35.0	5660	0.88
sandy loam	0.58	8.5	-	-	11.5	1960	0.94
Arithmetic mean					40	3760	0.85
Median					41	3495	0.87
pH dependence, Yes or No			No				

CGA 71019 ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
silty clay	0.70	8.8	-	-	0.83	120	0.90
clay loam	1.74	6.9	-	-	0.75	43	0.83
silty clay loam	0.70	7.0	-	-	0.72	104	0.92
sandy loam	0.81	6.9	-	-	0.72	89	1.02
Arithmetic mean					0.75	89	0.91
Median					0.74	82	0.91
pH dependence (yes or no)			No				

CGA 205375 ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
loamy sand	2.17	5.7	-	-	118	5440	0.81
silty clay loam	1.16	6.6	-	-	45.5	3920	0.76
clay	2.63	6.7	-	-	44.1	1680	0.76

sandy loam	1.17	6.8	-	-	22.6	1930	0.72
loam	1.22	7.6	-	-	23.6	1930	0.77
Arithmetic mean					51	2980	0.76
Median					44	1930	0.76
pH dependence (yes or no)			No				

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

Column leaching ‡	Eluation: 200 mm Time period: 2 d
	Difenoconazole did not move out of the zone of application in any of four soils tested. Study used only to support results from adsorption/desorption tests.
Aged residues leaching ‡	Not submitted, not required
Lysimeter/ field leaching studies ‡	Not submitted, not required

PEC (soil) (Annex IIIA, point 9.1.3)

Difenoconazole Method of calculation	DT_{50} (d): 265 days Kinetics: SFO Field or Lab: longest DT_{50}s from field studies (n=9).
Application data	Crop: Seed treatment; Spray on apples; Spray on carrots Depth of soil layer: 5 cm (for plateau PECsoil mixing in 20 cm considered for carrots and seed treatment scenarios, except for the last year) Soil bulk density: 1.5 g/cm^3 % plant interception: Seed treatment: no interception; Apples: 65% Carrots: 80% Number of applications: 1 (seed treatment); 4 (apples); 3 (carrots) Interval (d): 10 d (apples); 14 d (carrots) Application rates: 12.3 g a.s./ha (seed treatment); 4 x 75 g a.s./ha (apples); 3 x 125 g a.s./ha (carrots)

PEC$_{(s)}$ (mg/kg) Difenoconazole Seed treatment		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.016		-	
Short term	24h	0.016	0.016	-	-
	2d	0.016	0.016	-	-
	4d	0.016	0.016	-	-
Long term	7d	0.016	0.016	-	-
	28d	0.015	0.016	-	-
	50d	0.014	0.015	-	-
	100d	0.013	0.014	-	-
Plateau concentration		0.00257 mg/kg (lower part of the "saw-tooth" curve; before annual applications, 20 cm depth) 0.0190 mg/kg (upper part of the "saw-tooth" curve; after annual applications, 5 cm depth)			

PEC$_{(s)}$ (mg/kg) Difenoconazole Apples	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.035		0.135	

PEC$_{(s)}$ (mg/kg) Difenoconazole Apples		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Short term	24h	-	-	0.135	0.135
	2d	-	-	0.134	0.135
	4d	-	-	0.134	0.134
Long term	7d	-	-	0.133	0.134
	28d	-	-	0.125	0.130
	50d	-	-	0.118	0.127
	100d	-	-	0.104	0.119
Plateau concentration		0.0912 mg/kg (lower part of the "saw-tooth" curve; before annual applications, 5 cm depth) 0.219 mg/kg (upper part of the "saw-tooth" curve; after annual applications, 5 cm depth)			

PEC$_{(s)}$ (mg/kg) Difenoconazole Carrots		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.033		0.0955	
Short term	24h	-	-	0.0953	0.0954
	2d	-	-	0.0950	0.0953
	4d	-	-	0.0945	0.0950
Long term	7d	-	-	0.0938	0.0946
	28d	-	-	0.0888	0.0921
	50d	-	-	0.0838	0.0895
	100d	-	-	0.0735	0.0840
Plateau concentration		0.0161 mg/kg (lower part of the "saw-tooth" curve; before annual applications, 20 cm depth) 0.112 mg/kg (upper part of the "saw-tooth" curve; after annual applications, 5 cm depth)			

CGA 71019 Method of calculation	Initial PECs= Max parent PECs x Max. metabolite in soil x Mol. Wt fraction. where: Max. parent PECs: 0.016 mg/kg (seed treatment); 0.135 mg/kg (apples); 0.0955 mg/kg (carrots) Max. CGA 71019 in soil: 23% Molecular weight fraction: 0.170.
Application data	Use of difenoconazole as Seed treatment; Spray in apples; Spray in carrots.

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Seed treatment				
Initial	0.0006		-	
Apples				
Initial	-		0.00528	
Carrots				
Initial	-		0.00373	

CGA 205375 Method of calculation	Initial PECs= Max parent PECs x Max. metabolite in soil x Mol. Wt fraction. where: Max. parent PECs: 0.016 mg/kg (seed treatment); 0.135 mg/kg (apples); 0.0955 mg/kg (carrots) Max. CGA 205375 in soil: 10% (a value of 11.9% should have been used) Molecular weight fraction: 0.862.
Application data	Use of difenoconazole as Seed treatment; Spray in apples; Spray in carrots.

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Seed treatment				
Initial	0.0014		-	
Apples				
Initial	-		0.0116	
Carrots				
Initial	-		0.00823	

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	Difenoconazole: No degradation observed at pH 5, 7 and 9 (25ºC, 30 days)
	CGA 71019: No degradation observed at pH 5, 7 and 9 (25ºC, 30 days)
	CGA 205375: No degradation observed at pH 4, 7 and 9 (50ºC, 5 days)
Photolytic degradation of active substance and metabolites above 10 % ‡	Difenoconazole: Stable (<10% transformation over 15 days, continuous irradiation)
	CGA 205375: Stable (<10% transformation over 15 days, continuous irradiation)
Quantum yield of direct phototransformation in water at λ> 290 nm	0.0155. Predicted half-lives were between 12 and >10000 years at 52ºN latitude depending on season.
	CGA 205375: 0.0266. Predicted half-lives were between 14 and >10000 years at 52ºN latitude depending on season.
Readily biodegradable ‡ (yes/no)	No

Degradation in water / sediment

Difenoconazole	Distribution of total radioactivity in Pond/River systems (20ºC): Max. in water 88/80% day 0. Decreased to 20/32% by day 3 and to <10% by day 7/14. Given the short $DisT_{50}$ from water <1% of applied difenoconazole was estimated to remain in the water column after 7 and 14 days. Distribution of Difenoconazole in Pond/River systems (8ºC): Max. in water 83/87% day 0. Decreased to 15/36% by day 3 and to 2.3/12% by day 14. Max. in sediment 99.8/96.5% day 42. Metabolites identified (20ºC, ^{14}C-chlorophenyl label): CGA 205375 max. 4.9% in pond system (days 32 and 127), max. 11.6-11.4% in river system (days 90-183).									
Water / sediment system	pH water phase	pH sed	t. ºC	DT_{50}/DT_{90} whole sys. Degradation	St. (r^2)	DT_{50}/DT_{90} water Dissipation	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Pond	-	6.9	20	ca 324/>1000	0.998	1.0 / 3.3	0.987	-		SFO
River	-	7.2	20	ca 307/>1000	0.999	2.0 / 6.6	0.968	-		SFO
Geometric mean				315 / >1000		1.1 / 4.6		-		

CGA 205375	Distribution of CGA 205375 in Pond/River systems: Max. in water 97/96% day 0. Decreased to <10% by day 7/14. Max. in sediment 91/87% day 62/28. Metabolites identified (^{14}C-triazole label): CGA 71019 max. 3.2% in pond system (day 148), max. 14.1% in river system (day 148).

Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys. Degradation	St. (r^2)	DT_{50}-DT_{90} water Dissipation	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Pond	7.97	7.09	20	ca 630/>1000	0.765	1.4 / 4.7	0.958	-	-	SFO
River	8.1	7.46	20	ca 301/>1000	0.932	3.1 / 10.2	0.985	-	-	SFO
Geometric mean				ca 435/>1000		2.1 / 6.9				

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)
Parent; Pond, 20°	-	6.9	3.0 % (183 d)[1]	-	13.9 % (183 d)[1]
Parent; River, 20°	-	7.2	3.9 % (183 d)[1]	-	8.7 % (183 d)[1]
Parent; Pond, 8°	-	7.2	1.9 % (183 d)[1]	-	11.4 % (183 d)[1]
Parent; River, 8°	-	7.2	2.9 % (181 d)[1]	-	9.8 % (181 d)[1]
CGA 205375; Pond	7.97	7.09	0.5 % (148 d)[2]	-	8.2 % (148 d)[2]
CGA 205375; River	8.1	7.46	0.4 % (148 d)[2]	-	13.0 % (148 d)[2]

[1] ^{14}C-Chlorophenyl radiolabel
[2] ^{14}C-triazole radiolabel

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

Difenoconazole Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 406 Water solubility (mg/L): 15 K_{OC} (mL/g): 3759.4 (mean value) DT_{50} soil (d): 86 (previous arithmetic mean of normalised lab values) (note that geomean normalised DT_{50} soil 130 d would be the correct value to use) DT_{50} water/sediment system (d): 315.5 (mean value) DT_{50} water (d): 315.5 (mean value, degradation whole system) DT_{50} sediment (d): 315.5 (mean value, degradation whole system) Crop interception (%): 0 (seed treatment); 70 (apples and carrots) "No drift" option used for seed treatment scenario (Steps 1-2). Plateau PECsed calculated as: (max PECsed after 1 year of treatment) ÷ $(1 – e^{-k \times t})$, where: k= ln 2/315.5 days
Parameters used in FOCUSsw step 3	Version control no.'s of FOCUS software: SWASH 1.1; Drift calculator 1.1; PRZM_SW 1.1.1; MACRO 4.4.2; TOXSWA 1.1.1 Vapour pressure: 0 (worst case) 1/n: 0.8 (mean value) (note that 0.85 would be the correct value to use) Q10 2.2 Other parameters set to the same value as in Steps 1 and 2. Plateau PECsed calculated using same eq. as in Steps 1-2.
Parameters used in FOCUSsw step 4	Version control no.'s of FOCUS software: As in Step 3 except TOXSWA ver. 2.2.1 Other parameters set to the same value as in Steps 3. Plateau PECsed calculated using same eq. as in Steps 1-2.
Risk mitigation applied in FOCUSsw step 4	Buffers of 14 m and 20 m used for apples to reduce spray drift. Vegetative buffer strip of 5 m used for carrots to reduce spray drift and run-off (run-off reduction 50%).
Application rate	Seed treatment (Steps 1 and 2): 12.3 g a.s./ha Apples (Steps 1-4): 4 x 75 g a.s./ha (7 d interval) (late application drift values) Carrots (Steps 1-4): 3 x 125 g a.s./ha (at Steps 3 and 4 scenario R2 also 6 x 125 g a.s./ha was simulated to account for 2 annual crops grown) (14 d interval) Application window for 1st treatment, Step 3: 1 March-18

April (apples); 2 March-15 June (carrots) Application window for 1st treatment, Step 4: 1 March-6 April (apples); 2 March-3 June (carrots)

Difenoconazole FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Seed treatment	0	0.693		26.0	
Apples	0	32.4		722	
Carrots	0	24.2		801	
				Max* Plateau PEC_{SED}: 1453	

* The plateau PECsed was based on the maximum PECsed, calculated for the use in carrots.

Difenoconazole FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Seed treatment N EU autumn planting	0	0.336		12.6	
Apples S EU, spring	0	4.23		128	
Carrots S EU, spring	0	2.73		96.5	
				Max* Plateau PEC_{SED}: 232	

* The plateau PECsed was based on the maximum PECsed, calculated for the use in apples.

Difenoconazole FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
Apples multiple applications						
D3	Ditch	0	1.789		3.875	
		7		0.326		3.686
		21		0.206		3.259
		28		0.191		3.111
					Plateau PEC_{SED} 7.026	
D4	Pond	0	0.241		3.937	
		7		0.219		3.937
		21		0.193		3.934
		28		0.185		3.932
					Plateau PEC_{SED} 7.138	
D4	Stream	0	1.677		0.255	
		7		0.018		0.242
		21		0.015		0.219
		28		0.015		0.209
					Plateau PEC_{SED} 0.462	
D5	Pond	0	0.240		**4.033**	
		7		0.219		4.033
		21		0.192		4.031
		28		0.185		4.029
					Plateau PEC_{SED} 7.312	
D5	Stream	0	1.806		0.287	
		7		0.020		0.271
		21		0.019		0.244
		28		0.014		0.232
					Plateau PEC_{SED} 0.520	
R1	Pond	0	0.227		3.723	
		7		0.205		3.723
		21		0.179		3.718
		28		0.172		3.714
					Plateau PEC_{SED} 6.750	
R1	Stream	0	1.372		0.718	

Difenoconazole FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
		7		0.034		0.695
		21		0.029		0.652
		28		0.023		0.634
					Plateau PEC_{SED} 1.302	
R2	Stream	0	1.819		1.568	
		7		0.026		1.548
		21		0.022		1.510
		28		0.019		1.492
					Plateau PEC_{SED} 2.843	
R3	Stream	0	**1.943**		1.849	
		7		0.130		1.740
		21		0.103		1.557
		28		0.096		1.489
					Plateau PEC_{SED} 3.353	
R4	Stream	0	1.380		1.761	
		7		0.093		1.690
		21		0.040		1.571
		28		0.036		1.522
					Plateau PEC_{SED} 3.193	

Difenoconazole FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
Carrots multiple applications						
D3	Ditch	0	0.573		0.979	
		7		0.093		0.937
		21		0.059		0.840
		28		0.044		0.800
					Plateau PEC_{SED} 1.775	
D6	Ditch	0	0.570		0.428	
		7		0.076		0.410
		21		0.026		0.374
		28		0.026		0.362
					Plateau PEC_{SED} 0.776	
R1	Pond	0	0.082		3.908	
		7		0.076		3.892
		21		0.068		3.854
		28		0.066		3.818
					Plateau PEC_{SED} 7.086	
R1	Stream	0	0.376		23.00	
		7		0.057		22.86
		21		0.030		22.59
		28		0.025		22.49
					Plateau PEC_{SED} 41.70	
R2, 1st crop	Stream	0	0.504		62.88	
		7		0.015		62.54
		21		0.007		61.09
		28		0.006		60.84
					Plateau PEC_{SED} 114.0	
R2, 2nd crop	Stream	0	0.504		**146.6**	
		7		0.022		145.3
		21		0.014		143.1
		28		0.012		142.8
					Plateau PEC_{SED} 265.8	
R3	Stream	0	0.530		7.356	
		7		0.050		7.314
		21		0.030		7.249

Difenoconazole FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
		28		0.025		7.234
					Plateau PEC_{SED} 13.34	
R4	Stream	0	**0.713**		18.15	
		7		0.190		17.85
		21		0.088		17.45
		28		0.085		17.19
					Plateau PEC_{SED} 32.91	

Difenoconazole FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	Plateau PEC_{SED}
Apples, 14 m buffer multiple applications						
D3	Ditch	0	0.326		0.777	1.409
D4	Pond	0	0.101		1.74	3.155
D4	Stream	0	0.351		0.056	0.102
D5	Pond	0	0.101		**1.78**	3.227
D5	Stream	0	0.378		0.062	0.112
R1	Pond	0	0.095		1.68	3.046
R1	Stream	0	0.287		0.508	0.921
R2	Stream	0	0.381		1.51	2.738
R3	Stream	0	0.407		0.769	1.394
R4	Stream	0	**0.444**		1.52	2.756

Difenoconazole FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	Plateau PEC_{SED}
Apples, 20 m buffer multiple applications						
D3	Ditch	0	0.325		0.515	0.934
D4	Pond	0	0.064		1.14	2.067
D4	Stream	0	0.183		0.030	0.054
D5	Pond	0	0.064		1.16	2.103
D5	Stream	0	0.197		0.033	0.060
R1	Pond	0	0.067		1.26	2.285
R1	Stream	0	0.230		0.478	0.867
R2	Stream	0	0.198		**1.50**	2.720
R3	Stream	0	0.292		0.623	1.130
R4	Stream	0	**0.444**		1.49	2.702

Difenoconazole FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	Plateau PEC_{SED}
Carrots, 5 m buffer multiple applications						
D3	Ditch	0	0.151		0.273	0.495
D6	Ditch	0	0.150		0.123	0.223
R1	Pond	0	0.044		2.20	3.989
R1	Stream	0	0.162		11.7	21.2
R2, 1st crop	Stream	0	0.180		32.0	58.0
R2, 2nd crop	Stream	0	0.180		**74.1**	134.4
R3	Stream	0	0.206		3.73	6.76
R4	Stream	0	**0.392**		9.24	16.8

Difenoconazole FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)
			Actual
Apples single application			
D3	Ditch	0	2.72

Difenoconazole FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)
			Actual
D4	Stream	0	2.46
D5	Stream	0	2.49
R1	Stream	0	2.08
R2	Stream	0	2.76
R4	Stream	0	2.08

Difenoconazole FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)
			Actual
Carrots single application			
D3	Ditch	0	0.783
D6	Ditch	0	0.781
R1	Stream	0	0.517
R2, 1st crop	Stream	0	0.682
R2, 2nd crop	Stream	0	0.694
R3	Stream	0	0.725

Difenoconazole FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)
			Actual
Apples, 14 m buffer single application			
D3	Ditch	0	0.464
D4	Stream	0	0.486
D5	Stream	0	0.492
R1	Stream	0	0.410
R2	Stream	0	0.544
R3	Stream	0	**0.578**

Difenoconazole FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)
			Actual
Carrots, 5 m buffer single applications			
D3	Ditch	0	0.211
D6	Ditch	0	0.211
R1	Stream	0	0.188
R2, 1st crop	Stream	0	0.248
R2, 2nd crop	Stream	0	0.253
R3	Stream	0	**0.264**

CGA 71019 Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 69 Water solubility (mg/L): 730 Soil or water metabolite: Both K_{OC} (mL/g): 89 (mean value) DT_{50} soil (d): 6.45 (arithmetic mean of normalised lab values) (note that geomean normalised DT_{50} soil 7.4 d would be the correct value to use) DT_{50} water/sediment system (d): 1000 (worst case assumption) DT_{50} water (d): 1000 (worst case assumption) DT_{50} sediment (d): 1000 (worst case assumption) Simulated together with parent compound: Crop interception (%): 0 (seed treatment); 70 (apples and carrots) "No drift" option used for seed treatment scenario. Max. occurrence observed (%), used to calculate dose and

	formation in aquatic systems: Water/Sediment: 9.6 (worst case assumption calc. by RMS) Soil: 23.4
Application rate	Seed treatment: 12.3 g a.s./ha Apples: 4 x 75 g a.s./ha (7 d interval) Carrots: 3 x 125 g a.s./ha (14 d interval)

CGA 71019 FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L) Actual	PEC_{SED} (µg/kg) Actual
Seed treatment	0	0.148	0.132
Apples	0	3.76	3.11
Carrots	0	4.43	3.89

CGA71019 FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L) Actual	PEC_{SED} (µg/kg) Actual
Seed treatment N EU autumn planting	0	0.0482	0.0429
Apples S EU, spring	0	0.272	0.237
Carrots S EU, spring	0	0.176	0.155

<u>CGA 205375</u> Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 350 Water solubility (mg/L): 100 (assumed value) Soil or water metabolite: Both K_{OC} (mL/g): 2979.4 (mean value) DT_{50} soil (d): 71.5 (previous arithmetic mean of normalised lab values) (note that geomean normalised DT_{50} soil 94 d would be the correct value to use) DT_{50} water/sediment system (d): 465.5 (arithmetic mean) DT_{50} water (d): 465.5 (mean value, degradation whole system) DT_{50} sediment (d): 465.5 (mean value, degradation whole system) Simulated together with parent compound: Crop interception (%): 0 (seed treatment); 70 (apples and carrots) "No drift" option used for seed treatment scenario. Max. occurrence observed (%),used to calculate dose and formation in aquatic systems: Water/Sediment: 11.6 Soil: 9.7 Plateau PECsed calculated as: (max PECsed after 1 year of treatment) ÷ $(1 – e^{-k\ x\ t})$, where: k= ln 2/435 days
Application rate	Seed treatment: 12.3 g a.s./ha Apples: 4 x 75 g a.s./ha (7 d interval) Carrots: 3 x 125 g a.s./ha (14 d interval)

CGA 205375 FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L) Actual	PEC_{SED} (µg/kg) Actual
Seed treatment	0	0.0679	2.02
Apples	0	3.20	57.8
Carrots	0	2.38	62.6
			Max* Plateau PEC_{SED}: 142

* The plateau PECsed was based on the maximum PECsed, calculated for the use in carrots.

CGA205375 FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
		Actual	Actual
Seed treatment N EU autumn planting	0	0.0327	0.973
Apples S EU, spring	0	0.457	11.0
Carrots S EU, spring	0	0.274	7.61

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	Model used: FOCUS PEARL 2.2.2 Scenarios: Difenoconazole and the metabolites CGA71019 and CGA 205375 were simulated in separate model runs. For use in apples all 9 FOCUS scenarios were run. For use in carrots Châteaudun, Hamburg, Kremsmünster, Porto and Thiva were run with two annual crops assumed, and Jokioinen was run with one annual crop assumed. The results from the simulations in apples and carrots are considered to cover also the use of difenoconazole in seed treatment. Crops: Apples and carrots. Difenoconazole: DT_{50} soil (d): 86.0 (previous arithmetic mean of normalised lab values) (note that geomean normalised DT_{50} soil 130 d would be the correct value to use) Koc (mL/g): 3759.4 (mean value) 1/n: 0.8 (mean value) (note that 0.85 would be the correct value to use) CGA 71019: DT_{50} soil (d): 6.45 (arithmetic mean of normalised lab values) (note that geomean normalised DT_{50} soil 7.4 d would be the correct value to use) Koc (mL/g): 89 (mean value) 1/n: 0.9 (mean value) CGA 205375: DT_{50} soil (d): 71.5 (previous arithmetic mean of normalised lab values) (note that geomean normalised DT_{50} soil 94 d would be the correct value to use) Koc (mL/g): 2979.4 (mean value) 1/n: 0.8 (mean value) Q10 for all compounds 2.2
Application rate	Difenoconazole: Application rate: 4 x 75 g a.s./ha, 7 d interval (apples); 3 x 125 g a.s./ha or 6 x 125 g a.s./ha, 14 d interval (carrots) No. of applications: 4 (apples); 3 (carrots, Jokioninen) 6 (carrots, remaining scenarios) Time of application: BBCH 61 (apples); BBCH 42-43 (carrots) Application window for 1st treatment: 22 March - 17 May (apples); 10-19 April (carrots) Crop interception (%): 65 (apples); 70 (carrots) CGA 71019: Application rate: 4 x 2.98 g a.s./ha, 7 d interval (apples); 3 x 4.97 g a.s./ha or 6 x 4.97 g a.s./ha, 14 d interval (carrots) (calc. as appl. rate parent x max. metabolite in soil (23.4%) x mol. wt fraction (69/406)). Other parameters as for parent.

CGA 205375: Application rate: 4 x 6.07 g a.s./ha, 7 d interval (apples); 3 x 10.12 g a.s./ha or 6 x 10.12 g a.s./ha, 14 d interval (carrots) (calc. as appl. rate parent x max. metabolite in soil (9.4%) x mol. wt fraction (350/406)). Other parameters as for parent.

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

	Scenario	Difenoconazole (µg/L)	Metabolites (µg/L)	
			CGA 71019	CGA 205375
PELMOI /Apples	Chateaudun	<0.001	<0.001	<0.001
	Hamburg	<0.001	<0.001	<0.001
	Jokioinen	<0.001	<0.001	<0.001
	Kremsmunster	<0.001	<0.001	<0.001
	Okehampton	<0.001	<0.001	<0.001
	Piacenza	<0.001	<0.001	<0.001
	Porto	<0.001	<0.001	<0.001
	Sevilla	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001

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

	Scenario	Difenoconazole (µg/L)	Metabolites (µg/L)	
			CGA 71019	CGA 205375
PELMOI /Carrots	Chateaudun	<0.001	<0.001	<0.001
	Hamburg	<0.001	<0.001	<0.001
	Jokioinen[1]	<0.001	<0.001	<0.001
	Kremsmunster	<0.001	<0.001	<0.001
	Porto	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001

1 One carrot crop per season assumed; in the other scenarios two annual carrot crops assumed.

PEC(gw) From lysimeter / field studies

Parent/metabolites	1st year	2nd year	3rd year
Annual average (µg/L)	not available, not requested	not available, not requested	not available, not requested

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

Direct photolysis in air ‡	Not submitted, not required
Quantum yield of direct phototransformation	Difenoconazole: 0.0155 (in water) CGA 205375: 0.0266 (in water)
Photochemical oxidative degradation in air ‡	DT_{50} 5 hours derived by the Atkinson method (AOP 1.85). OH (12 h) concentration assumed: 1.5 x 10^6 radicals/cm^3.
Volatilisation ‡	Volatilisation from soil: <0.05% after 24 hours (measured as % ^{14}C in absorption trap).
	Volatilisation from plants and soil: <9% after 24 hours (measured as % loss).
Metabolites	None identified.

PEC (air)

Method of calculation	Expert judgement based on vapour pressure, Henry's Law constant and experimental data on volatilisation.

PEC$_{(a)}$

Maximum concentration	Expected to be negligible.

Residues requiring further assessment

Environmental occurring metabolite requiring further	Soil: Difenoconazole, CGA 71019 and CGA 205375

assessment by other disciplines (toxicology and ecotoxicology) or for which a groundwater exposure assessment is triggered.	Surface water: Difenoconazole, CGA 71019 and CGA 205375 Sediment: Difenoconazole, CGA 205375 Groundwater: Difenoconazole, CGA 71019 and CGA 205375 Air: Difenoconazole

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

Soil (indicate location and type of study)	Not submitted, not required
Surface water (indicate location and type of study)	Not submitted, not required
Ground water (indicate location and type of study)	Not submitted, not required
Air (indicate location and type of study)	Not submitted, not required

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

Not readily biodegradable. 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 ‡				
Japanese quail.	difenoconazole	Acute	LD50 >2000	-
	metabolite CGA131013	Acute	no data	-
Mallard duck	difenoconazole	Short-term	5 d LC_{50} >349	5 d LC50 >5000
Mallard duck	metabolite CGA131013	Short term	5 d LC_{50} >1342	5 d LC_{50} >5000
Bobwhite quail	difenoconazole	Long-term	NOEL 9.71	NOEL 100
	metabolite CGA131013	Long-term	no data	-
Mammals ‡				
Rat.	difenoconazole	Acute	LD_{50} >1453	-
	DIVIDEND 030FS	Acute	LD_{50} >3000	-
	SCORE 250EC	Acute	LD_{50} >3000	-
	metabolite CGA 131013	Acute	LD_{50} >5000	-
Rat	difenoconazole	Long-term	NOAEL 17.3	-
	metabolite CGA 131013	Long-term	NOAEL 100	-
Additional higher tier studies ‡				
no further data				

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)
Seed treatment to cereals, 60 mg/kg seed

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
granivorous bird, a.s.	Acute	22.8	>88	10
granivorous bird, metabolite		8.66	>230	10
medium herbivorous bird, a.s.		22.8	>44	10
medium herbiv. bird, metabolite		17.5	110	10
small herbivorous bird, a.s.		63.6	31.4	10
small herbivorous bird, metabolite		24.4	82	10
granivorous bird, a.s.	Short-term	22.8	15	10
granivorous bird, metabolite		8.66	155	10
medium herbivorous bird, a.s.		22.8	15	10
medium herbiv. bird, metabolite		8.74	154	10
small herbivorous bird, a.s.		31.8	11	10
small herbivorous bird, metabolite		12.2	110	10
granivorous bird, a.s.	Long-term	7.60	**1.3**	5
granivorous bird, metabolite		2.89	**3.4**	5
medium herbivorous bird, a.s.		3.88	**1.3**	5
medium herbiv. bird, metabolite		2.97	**3.3**	5
small herbivorous bird, a.s.		10.8	**0.91**	5
small herbivorous bird, metabolite		4.14	**2.4**	5
fish-eating bird, a.s.		0.046	210	5
earthworm-eating bird, a.s.		0.061	160	5
exposure via contaminated water		<<0.001	>20000	5
Higher tier refinement (Birds)				
granivorous bird, a.s.*	Long-term	1.89	5.1	5
granivorous bird, metabolite*		0.72	13	5
medium herbivorous bird, a.s.**		0.093	105	5
medium herbiv. bird, metabolite**		0.034	287	5
small herbivorous bird, a.s.**		0.13	75	5
small herbiv. bird, metabolite**		0.049	200	5

*refinement based on measured residues of difenoconazole in shoots emerging from treated seeds
**refinement based on measured data on dissipation of difenoconazole from treated seeds and diet composition of skylark in April (Green, 1978).

Tier 1 (Mammals)				
granivorous mammal, a.s.	Acute	13.8	105	10
granivorous mammal, metabolite		5.24	954	10
small herbivorous mammal*, a.s.		83.4	17.4	10
small herbiv. mammal*, metab.		31.7	158	10
granivorous mammal, a.s.	Long-term	4.54	**3.8**	5
granivorous mammal, metabolite		1.73	58	5
small herbivorous mammal*, a.s.		14.2	**1.2**	5
small herbiv. mammal*, metab.		5.39	19	5
medium herbivorous mammal*, a.s		2.86	6.1	5
medium herbiv. mammal*, metab.		1.09	92	5
fish-eating mammal, a.s.		0.029	604	5
earthworm-eating mammal, a.s.		0.076	229	5
exposure via contaminated water		<<0.001	>200000	5
Higher tier refinement (Mammals)				
granivorous mammal, a.s.	Long-term	2.57	6.7	5
small herbivorous mammal*, a.s.		0.17	102	5
medium herbivorous mammal*, a.s		0.034	509	5

* in higher tier refinement a medium sized herbivore was used, since small herbivorous mammals (default used in the first tier assessment) would avoid open areas with no or little vegetation cover.

Pome fruit, 4 applications of 75 g as/ha, 7 days interval (Southern EU), covers also pome fruit, 4 applications of 56.25 g as/ha, 7 days interval (Northern EU).

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
insectivorous bird	Acute	4.06	493	10
insectivorous bird	Short-term	2.26	154	10
insectivorous bird	Long-term	2.26	**4.3**	5
fish-eating bird, a.s.		0.29	25	5
earthworm-eating bird, a.s.		0.45	20	5
exposure via contaminated water		0.022	442	5
Higher tier refinement (Birds)				
insectivorous bird*	Long-term	1.38	7.1	5
Tier 1 (Mammals)				
herbivorous mammal, a.s.	Acute	9.57	152	10
herbivorous mammal, metabolite		3.64	1374	10
herbivorous mammal, a.s.	Long-term	8.33	**2.1**	5
herbivorous mammal, metabolite		3.17	32	5
fish-eating mammal, a.s.		0.18	98	5
earthworm-eating mammal, a.s.		0.63	28	5
exposure via contaminated water		<0.01	>5000	5
Tier 2 refinement (Mammals)				
herbivorous mammal, a.s. (Southern EU, 4x75 g as/ha)**	Long-term	4.89	**3.5**	5
Tier 3 refinement (Mammals)				
herbivorous mammal, a.s. (Southern EU, 4x75 g as/ha)***	Long-term	2.89	6.0	5

*refinement for insectivorous birds based on PT 0.61. Focal species blue tit.
**refinement for mammals based on interception values from FOCUSgw.
***refinement for mammals based on interception values from FOCUSgw and diet composition data for field vole.

Carrots, 3 applications of 125 g as/ha, 14 days interval

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
medium sized herbiv. bird, a.s.	Acute	10.7	>186	10
medium sized herbiv. bird, metab.		4.08	>490	10
insectivorous bird		6.76	>296	10
medium sized herbiv. bird, a.s.	Short-term	5.70	61	10
medium sized herbiv. bird, metab.		2.17	>618	10
insectivorous bird		3.77	93	10

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
medium sized herbiv. bird, a.s.	Long-term	3.65	**2.7**	5
medium sized herbiv. bird, metab.		1.15	8.5	5
insectivorous bird (SANCO GD)		3.77	**2.6**	5
Woodlark (EFSA GD 2009)*	Long-term	3.3	15	5
fish-eating bird, a.s.		0.18	53	5
earthworm-eating bird, a.s.		0.36	28	5
exposure via contaminated water		<0.02	>400	5
Higher tier refinement (Birds)				
medium sized herbiv. bird, a.s.**	Long-term	1.47	6.6	5
insectivorous bird**		1.88	5.2	5
Tier 1 (Mammals)				
herbivorous mammal, a.s.	Acute	3.96	367	10
herbivorous mammal, metabolite		1.50	3333	10
herbivorous mammal, a.s.	Long-term	1.2	14	5
herbivorous mammal, metabolite		0.46	217	5
fish-eating mammal, a.s.		0.11	152	5
earthworm-eating mammal, a.s.		0.45	39	5
exposure via contaminated water		<0.01	>5000	5

*based on the relevant scenario for carrot BBCH>40 in the new EFSA GD.
**refinement for birds based on PT 0.5. This was not fully accepted at PRAPeR TC 42, and therefore additional calculations according to the new EFSA GD were included in Tier I to replace the insectivore scenario.

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg as/L)
Laboratory tests ‡				
Fish				
Rainbow trout	difenoconazole	96 hr (flow-through)	Mortality, EC_{50}	1.1 (0.98-1.1)
Fathead minnow	difenoconazole	34 d (flow-through)	Larval weight NOEC	**0.0076**
Rainbow trout	DIVIDEND 030FS	96 hr (static)	Mortality, EC_{50}	0.70 (0.43 – 1.2)
Rainbow trout	SCORE 250EC	96 hr (static)	Mortality, EC_{50}	**0.65** (0.56 – 1.1)
Rainbow trout	SCORE 250EC	21 d (semi-static)	Growth NOEC	0.15 (mm)
Rainbow trout	Metab. CGA 71019	96 hr (static)	Mortality, EC_{50}	498 (378 – 657)
Rainbow trout	CGA 205375	96 hr (static)	Mortality, EC_{50}	0.74 (0.58 – 0.95)
Rainbow trout	CGA 71019	28 d (static-renewal)	Behaviour effects, NOEC	3.2
Aquatic invertebrate				
Daphnia magna.	difenoconazole	48 h (static)	Mortality, EC_{50}	0.77 (0.59 – 0.95)
Mysidopsis bahia	difenoconazole	96 h (flow-through)	Mortality, EC_{50}	**0.15** (0.11 – 0.22)
Crassostrea virginica	difenoconazole	96 h (flow-through)	Shell deposition, EC_{50}	>0.30
Daphnia magna.	difenoconazole	21 d (flow-through)	Reproduction, NOEC	**0.0056** (mm)
Daphnia magna.	DIVIDEND 030FS	48 h (static)	Mortality, EC_{50}	0.43 (0.3 – 0.6)
	SCORE 250EC	48 h (static)	Mortality, EC_{50}	0.62 – 1.38
Daphnia magna	Metab. CGA 71019	48 h (static)	Mortality, EC_{50}	>100
Daphnia magna.	CGA 205375	48 h (static)	Mortality, EC_{50}	1.4 (1.2 – 1.7)
Sediment dwelling organisms				
Chironomus riparius	difenoconazole	28 d (static)	NOEC via water	0.015 (0.0525 mg/kg).
Chironomus riparius	SCORE 250EC	28 d (static)	NOEC via water	0.075
Chironomus riparius	CGA 205375	28 d (static)	NOEC via water	0.4
Chironomus riparius	CGA 205375	28 d (static)	NOEC via sediment	10 mg/kg dw
Algae				
Scenedesmus subspicatus	difenoconazole	72 h (static)	Biomass: E_bC_{50}	0.032 (0.026 – 0.039)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg as/L)
Pseudokrchneriella subspicata	DIVIDEND 030FS	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	1.8 (1.3 – 2.6) >3.0 (2-8 - >3.0)
Scenedesmus subspicatus	SCORE 250EC	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	0.29 (0.22 – 0.60) 0.96 (0.62 – 1.75)
Selenastrum capricornutum	Metab. CGA 71019	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	8 >31
Selenastrum capricornutum	CGA 205375	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	1.2 (1.2 – 1.3) 3.1 (3.0 – 3.2)
Higher plant				
No reliable data, not required.				
Microcosm or mesocosm tests				
Not required.				

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

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

Maximum PECsw values and TER values for Difenoconazole – seed treatment to cereals, 60 mg as/kg seed

Scenario	PECini (mg/L)	PEC global max (mg/L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged
			Rainbow trout	**Fathead minnow (ELS)**	***Mysidopsis bahia***	***Daphnia magna***	***Scenedesmus subspicatus***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	ErC_{50}	NOEC
			0.65 mg/L	0.0076 mg/L	0.15 mg/L	0.0056 mg/L	0.032 mg/L	0.0525 mg/kg
FOCUS Step 1		0.00069	942	11	217	**8.1**	46	**1.1***
FOCUS Step 2								
North Europe South Europe		0.00034 -				16 -		**2.3***
Annex VI Trigger			100	10	100	10	10	10

*The TER values were based on PECplateau in the sediment compartment.

Maximum PECsw values and TER values for CGA 71019 – seed treatment to cereals, 60 mg difenoconazole/kg seed

Scenario	PECini (mg/L)	PEC global max (mg/L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged
			Rainbow trout	**Rainbow trout**	***Daphnia magna***	***Daphnia magna***	***Selenastrum capricornutum***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	EbC_{50}	NOEC
			498 mg/L	3.2 mg/L	>100 mg/L	No data	8 mg/L	No data
FOCUS Step 1		0.00015	3320000	21333	666667	-	546667	-

Maximum PECsw values and TER values for CGA 205375 – seed treatment to cereals, 60 mg difenoconazole/kg seed

Scenario	PECini (mg/L)	PEC global max (mg/L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged
			Rainbow trout	**Fathead minnow (ELS)**	***Daphnia magna***	***Daphnia magna***	***Selenastrum capricornutum***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	EbC_{50}	NOEC
			0.74 mg/L	No data	1.4 mg/L	No data	1.2 mg/L	10 mg/kg dw
FOCUS Step 1		0.000068	10882	-	20588	-	17647	2180*

*The TER value was based on PECplateau in the sediment compartment.

Maximum PECsw values and TER values for Difenoconazole – application to pome fruit in Southern EU, 4 x 75 g as/ha, 7 days interval between treatments (covers also pome fruit scenarios in Northern EU, 1 x 56.25 g as/ha, 7 days interval between treatments)

Scenario	**PECini (mg/L)**	**PEC global max (mg/L)**	**fish acute**	**fish prolonged**	**Daphnia acute**	**Daphnia prolonged**	**Algae**	**Sed. dweller prolonged***
			Rainbow trout	**Fathead minnow (ELS)**	***Mysidopsis bahia***	***Daphnia magna***	***Scenedesmus subspicatus***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	ErC_{50}	NOEC
			0.65 mg/L	0.0076 mg/L	0.15 mg/L	0.0056 mg/L	0.032 mg/L	0.0525 mg/kg**
FOCUS Step 1		0.032	**20**	**0.2**	**4.7**	**0.2**	**1.0**	**0.04**
FOCUS Step 2								
North Europe		-						
South Europe		0.0042	155	**1.8**	**36**	**1.3**	**7.6**	**0.23**
FOCUS Step 3								
D3 / ditch		0.00272	238.9	2.79	55.146	2.0	11.771	7.5
D4 / pond		0.000241***	2697	31.5	622	23	133	7.4
D4 / stream		0.00246	264.2	3.1	60.91	2.27	13.0	114
D5 / pond		0.000240***	2708	31.7	625	23	133	7.2
D5 / stream		0.00249	261.04	3.0	60.2	2.2	12.85	101
R1 / pond		0.000227	2863.4	33.4	660.7	24.6	140.9692	7.8
R1 / stream		0.00208	312.5	3.656	72.11	2.69	15.38	40.3
R2 / stream		0.00276	235.5	2.75	54.34	2.02	11.59	18.5
R3 / stream		0.00293	221.8	2.59	51.19	1.91	10.92	15.7
R4 / stream		0.00208	312.5	3.65	72.11	2.69	15.38	16.4
Annex VI Trigger**			100	10	100	10	10	10

*The TER values were based on PECplateau in the sediment compartment.

.*** The PECsw value for multiple applications is higher for these scenarios. Therefore, the worst case PECsw from 4x **56.25 g as/ha,** were used in the risk assessment.

Maximum PECsw values and TER values for CGA 71019 – application to pome fruit in Southern EU, 4 x 75 g as/ha, 7 days interval between treatments (covers also pome fruit scenarios in Northern EU, 4 x 56.25 g as/ha, 7 days interval between treatments)

Scenario	PECini (mg/L)	PEC global max (mg/L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged
			Rainbow trout	**Rainbow trout**	***Daphnia magna***	***Daphnia magna***	***Selenastrum capricornutum***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	EbC_{50}	NOEC
			498 mg/L	3.2 mg/L	>100 mg/L	No data	8 mg/L	No data
FOCUS Step 1		0.0038	131053	842	26316	-	2158	-

Maximum PECsw values and TER values for CGA 205375 – application to pome fruit in Southern EU, 4 x 75 g as/ha, 7 days interval between treatments (covers also pome fruit scenarios in Northern EU, 4 x 56.25 g as/ha, 7 days interval between treatments)

Scenario	PECini (mg/L)	PEC global max (mg/L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged
			Rainbow trout	**Fathead minnow (ELS)**	***Mysidopsis bahia***	***Daphnia magna***	***Selenastrum capricornutum***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	EbC_{50}	NOEC
			0.74 mg/L	No data	1.4 mg/L	No data	1.2 mg/L	10 mg/kg dw
FOCUS Step 1		0.0032	231	-	438	-	375	76*

*The TER value was based on PECplateau in the sediment compartment.

Maximum PECsw values and TER values for Difenoconazole – application to carrots, 1 x 125 g as/ha, 14 days interval between treatments

Scenario	PECini (mg/L)	PEC global max (mg/L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged*
			Rainbow trout	**Fathead minnow (ELS)**	***Mysidopsis bahia***	***Daphnia magna***	***Scenedesmus subspicatus***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	ErC_{50}	NOEC
			0.65 mg/L	0.0076 mg/L	0.15 mg/L	0.0056 mg/L	0.032 mg/L	0.0525 mg/kg**
FOCUS Step 1		0.024	**27**	**0.32**	**6.3**	**0.23**	**1.3**	**0.04**
FOCUS Step 2								
North Europe		-						
South Europe		0.0027	241	**2.8**	56	**2.1**	12	**0.30**
FOCUS Step 3								
D3 / ditch		0.000783	830.14	9.7	191.5 9	7.15	40.85	9.6
D6 / ditch		0.000781	832.26	9.7	192.06	7.17	40.9	67.7
R1 / pond		0.000082***	7927	93	1829	68	390	7.4
R1 / stream		0.00069	936.5	10.9	216.1	8	46.1	1.3
R2 / stream, 2nd crop		0.000504***	1290	15	298	11	63	0.2
R3 / stream		0.000725***	896.5	10.5	206.7	7.7	44.1	3.9
R4 / stream		0.000713***	912	11	210	8	45	1.6
Annex VI Trigger**			100	10	100	10	10	10

*The TER values were based on PECplateau in the sediment compartment.

*** The PECsw value for multiple applications is higher for these scenarios. Therefore, the worst case PECsw from 3 x **125 g as/ha,** were used in the risk assessment.

Maximum PECsw values and TER values for CGA 71019 – application to carrots, 3 x 125 g as/ha, 14 days interval between treatments

Scenario	PECini (mg/L)	PEC global max (mg/L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged
			Rainbow trout	**Rainbow trout**	***Daphnia magna***	***Daphnia magna***	***Scenedesmus subspicatus***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	ErC_{50}	NOEC
			498 mg/L	3.2 mg/L	>100 mg/L	No data	8.2 mg/L	No data
FOCUS Step 1		0.0044	113182	727	22727	-	1864	-

Maximum PECsw values and TER values for CGA 205375 – application to carrots, 3 x 125 g as/ha, 14 days interval between treatments

Scenario	PECini (mg/L)	PEC global max (mg/L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged*
			Rainbow trout	**Fathead minnow (ELS)**	***Mysidopsis bahia***	***Daphnia magna***	***Scenedesmus subspicatus***	***Chironomus riparius***
			LC_{50}	NOEC	EC_{50}	NOEC	ErC_{50}	NOEC
			0.74 mg/L	No data	1.4 mg/L	No data	1.2 mg/L	10 mg/kg dw
FOCUS Step 1		0.0024	308	-	583	167	500	70

*The TER value was based on PECplateau in the sediment compartment.

FOCUSsw step 4

TER calculations for the most critical endpoints (Daphnia chronic NOEC 0.0056 mg/L and Chironomus chronic NOEC 0.0525 mg/kg) including different mitigation options for FOCUS Step 4 Scenario – application to pome fruit at 1 x 75 g a.s./ha, 7 days between treatments

Mitigation options	**14 m non-spray buffer zone**				**20 m non-spray buffer zone**			
	PECsw	**PECsed, plateau**	**TERsw**	**TERsed**	**PECsw**	**PECsed, plateau**	**TERsw**	**TERsed**
FOCUS Step 4*								
D3 / ditch	0.000464	1.409	12.06	37.3	0.325	0.934	17	56.2
D4 / pond	0.101**	3.155	55	16.6	0.064	2.067	88	25.4
D4 / stream	0.000486	0.102	11.59	517.1	0.183	0.054	31	965.2
D5 / pond	0.101**	3.227	55	16.3	0.064	2.103	88	25.0
D5 / stream	0.000492	0.112	11.38	467.0	0.197	0.060	28	877.4
R1 / pond	0.095**	3.046	59	17.2	0.067	2.285	84	23.0
R1 / stream	0.00041	0.921	13.65	57.0	0.230	0.867	24	60.6
R2 / stream	0.000544	2.738	10.29	19.2	0.198	2.720	28	19.3
R3 / stream	0.000578	1.394	9.68	37.7	0.292	1.130	19	46.5
R4 / stream	0.444**	2.756	13	19.0	0.444	2.702	13	19.4

*it should be noted that the NOEC value was based on very conservative estimate of the concentration in the sediment (see Addendum B.9, 0ctober 2010), and no effects were seen at the highest test concentration.

** The PECsw value for multiple applications is higher for these scenarios. Therefore, the worst case PECsw from 4 x **75 g as/ha,** were used in the risk assessment.

TER calculations for the most critical endpoints (Daphnia chronic NOEC 0.0056 mg/L and Chironomus chronic NOEC 0.0525 mg/kg) including different mitigation options for FOCUS Step 4 Scenario – application to carrots at 1 x 125 g a.s./ha, 14 days between treatments

Mitigation options	**5 m non-spray buffer zone**			
	PECsw	**PECsed**	**TERsw**	**TERsed**
FOCUS Step 4*				
D3 / ditch	0.000211	0.495	26.54	106
D6 / ditch	0.000211	0.223	26.54	235
R1 / pond	0.044**	3.989	127	13.2
R1 / stream	0.000188	21.21	29.78	**2.5**
R2 / stream, 2nd crop	0.000253	134.4	22.13	**0.4**
R3 / stream	0.000264	6.763	21.21	**7.8**
R4 / stream	0.000392**	16.75	14	**3.1**

*it should be noted that the NOEC value was based on very conservative estimate of the concentration in the sediment (see Addendum B.9, 0ctober 2010), and no effects were seen at the highest test concentration.

** The PECsw value for multiple applications is higher for these scenarios. Therefore, the worst case PECsw from 3 x **125 g as/ha,** were used in the risk assessment.

Bioconcentration			
	Active substance	**Metabolite CGA 205375**	**Metabolite CGA 71019**
$\log P_{O/W}$	4.36	3.8	-1
Bioconcentration factor (BCF) ‡	330*	no data, not needed	-
Annex VI Trigger for the bioconcentration factor			
Clearance time (days) (CT_{50})	1 day	-	-
(CT_{90})	ca 3 days	-	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	not relevant	-	-

* based on total ^{14}C

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

Test substance	Acute oral toxicity (LD_{50} µg as/bee)	Acute contact toxicity (LD_{50} µg as/bee)
difenoconazole ‡	>177	>100
Field or semi-field tests		
No significant effects on bee mortality, foraging behaviour, flight activity or brood health in semi-field study with the formulation SCORE 250EC.		

Hazard quotients for honey bees (Annex IIIA, point 10.4)
Seed treatment of 60 mg as/kg seed, corresponding to 12.3 g as/ha.

Test substance	Route	Hazard quotient	Annex VI Trigger
difenoconazole	Contact	not relevant	50
difenoconazole	oral	0.069	50
Preparation	Contact	not relevant	50
Preparation	oral	not relevant	50

Spray application to pome fruit, 75 g as/ha.

Test substance	Route	Hazard quotient	Annex VI Trigger
difenoconazole	Contact	0.75	50
difenoconazole	oral	0.42	50
Preparation	Contact	not relevant	50
Preparation	oral	not relevant	50

Spray application to carrots, 125 g as/ha.

Test substance	Route	Hazard quotient	Annex VI Trigger
difenoconazole	Contact	1.25	50
difenoconazole	oral	0.71	50
Preparation	Contact	not relevant	50
Preparation	oral	not relevant	50

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)
Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g as/ha)
Typhlodromus pyri ‡	difenoconazole	Mortality	112
Aphidius rhopalosiphi ‡	difenoconazole	Mortality	178

Seed treatment of 60 mg as/kg seed, corresponding to 12.3 g as/ha.

Test substance	Species	Effect (LR_{50} g as/ha)	HQ in-field	HQ off-field	Trigger
SCORE 250EC	*Typhlodromus pyri*	178	0.069	not relevant	2
SCORE 250EC	*Aphidius rhopalosiphi*	112	0.11	not relevant	2

Spray application to pome fruit, 4 x 75 g as/ha, 7 days interval.

Test substance	Species	Effect (LR_{50} g as/ha)	HQ in-field (foliar/soil)	HQ off-field[1] (foliar)	Trigger
SCORE 250EC	*Typhlodromus pyri*	178	1.49/0.91	0.15	2
SCORE 250EC	*Aphidius rhopalosiphi*	112	0.94/0.57	0.094	2

[1] distance assumed to be 3 m in calculation of the drift rate

Spray application to carrots, 3 x 125 g as/ha, 14 days interval.

Test substance	Species	Effect (LR_{50} g as/ha)	HQ in-field (foliar/soil)	HQ off-field[1] (foliar)	Trigger
SCORE 250EC	*Typhlodromus pyri*	178	1.7/0.64	0.028	2
SCORE 250EC	*Aphidius rhopalosiphi*	112	1.1/0.40	0.020	2

[1] distance assumed to be 1 m in calculation of the drift rate

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)[1,2]	End point	Effect[3]	Trigger value
Aleochara bilineata	adults	DIVIDEND 030FS, treated seeds in moistened sand	23.2 g ai/ha (60 mg as/kg seed and seed density of 379 kg/ha	LR_{50}	>23.2 g as/ha (22.2% effect)	50% effect
Poecilus cupreus	adults	DIVIDEND 030FS, treated seeds in moistened sand	18.8 g ai/ha (60 mg as/kg seed and seed density of 307 kg/ha	LR_{50}	>18.8 g as/ha (no effect)	50% effect
Poecilus cupreus	larvae	DIVIDEND 030FS, treated seeds in moistened sand	56.4 g ai/ha (60 mg/kg seed and seed density of 937 kg/ha	LR_{50}	>56.4 g as/ha (no effect)	50% effect
Aphidius rhopalosiphi	juveniles	SCORE 250EC, fresh residues on glass plates.	5, 127, 253	LR_{50} NOER	≥253 g as/ha 5.06 g as/ha	50% effect
Typhlodromus pyri	proto-nymphs	SCORE 250EC, fresh residues on glass plates.	5, 127, 253	ER_{50} NOER	>127 g as/ha 5.06 g as/ha	50% effect
Chrysoperla carnea	larvae	SCORE 250EC, fresh residues on glass plates	4, 100, 200	ER_{50} NOER	>200 g as/ha 101 g as/ha	50% effect
Pardosa spp.	adults	SCORE 250EC, direct spray over adults, food and substrate (sand).	4, 100, 200	ER_{50}	>200 g as/ha (no effect)	50% effect
Poecilus cupreus	adults	SCORE 250EC, direct spray over adults, food and substrate (sand).	6, 30, 150, 300	ER_{50}	>300 g as/ha (no effect)	50% effect
Typhlodromus pyri	proto-nymphs	SCORE 250EC, fresh residues on bean leaves	6, 30, 150, 300	LR_{50} NOER	210 (165-267) g as/ha 30 g as/ha	50% effect

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)[1,2]	End point	Effect[3]	Trigger value
Chrysoperla carnea	larvae	SCORE 250EC, fresh residues on bean leaves	14, 28, 75, 125, 202, 288	ER_{50} NOER	>288 g as/ha No reliable NOER	50% effect
Orius laevigatus	nymphs	SCORE 250EC, fresh residues on maize plants	6 30 150 300	% effect	0% 7% 10% 18%*	50% effect
Trichogramma cacoeciae	adults	SCORE 250EC, fresh and 14-day old residues on broad beans.	15, 75, 125, 288	ER_{50} NOER	>288 g as/ha 125 g as/ha	50% effect
Coccinella septempunctata	larvae	SCORE 250EC, fresh and 14-day aged residues on broad beans.	4 appl. of 125 g ai/ha at 14-day intervals	ER_{50} NOER	>4 x 125 g as/ha No reliable NOER	50% effect
Episyrphus balteatus	larvae	SCORE 250EC, 14-day aged residues on broad beans.	15, 75, 125, 288	LR_{50} NOER	>288 g as/ha for aged residues based on mortality. Results from fresh residues not reliable due to high control mortality. No reliable NOER.	50% effect
Episyrphus balteatus	larvae	SCORE 250EC, fresh residues on broad beans.	288	Number of viable eggs per female. Aged residues not tested for reproduction. Potential for recovery considered likely.	62% effect when an outlier was excluded.	50% effect

[1] indicate whether initial or aged residues
[3] indicate if positive percentages relate to adverse effects or not

Field or semi-field tests
SCORE 250EC, field study on predatory mites in apple orchards in Italy. 4 applications of 79.5 g as/ha at intervals of 10 or 11 days. No significant effect on population density of predatory mites up to 28 days after the last application, except for an increased population on day 28 after the last application. SCORE 250EC, field study on predatory mites in apple orchards in Germany. 4 applications of 59.6 g as/ha at intervals of 9 or 12 days. No significant effect on population density of predatory mites up to 28 days after the last application.

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

Test organism	Test substance	Time scale	End point[1]
Earthworms			
Eisenia foetida	difenoconazole ‡	Acute 14 days	LC_{50} >610 mg a.s./kg dw soil
Eisenia foetida	difenoconazole ‡	Chronic	no reliable data, assessment based on representative formulation studies
Eisenia foetida	DIVIDEND 030FS	Chronic 56 days, reproduction	NOEC **0.2** mg a.s./kg dw soil

Test organism	Test substance	Time scale	End point[1]
Eisenia foetida	SCORE 250EC	Acute	LC_{50} **40** (36 – 44) mg a.s./kg dw soil (mg a.s/ha)
Eisenia foetida	SCORE 250EC	Chronic 56 days, reproduction	no reliable data
Eisenia foetida	Metabolite CGA 71019	Acute	LC_{50} **>1000** mg a.s./kg dw soil
Eisenia foetida	Metabolite CGA 71019	Chronic 28 days, reproduction	NOEC **1.0** mg a.s./kg dw soil
Eisenia foetida	Metabolite CGA 205375	Acute	LC_{50} **312** (284 – 343) mg a.s./kg dw soil
Other soil macro-organisms			
Collembola			
Folsomia candida	difenoconazole ‡	Chronic 28 days	NOEC **500** mg a.s./kg dw soil
	Metabolite CGA 71019	Chronic 28 days	NOEC **1.8** mg a.s./kg dw soil
Soil micro-organisms			
Nitrogen mineralisation	difenoconazole ‡	28 days	<25% effect at day 28 at 1.67 and 16.7 mg a.s./kg dw soil in silty loam, 60% increase in loamy sand
	Metabolite CGA 71019	28 days	<25% effect at day 28 at 0.035 and 0.353 mg a.s./kg dw soil
	Metabolite CGA 205375	28 days	<25% effect at day 28 at 0.09 and 0.22 mg a.s./kg dw soil
	SCORE 250EC	28 days	<25% effect at day 28 at 0.33 and 1.67 mg a.s./kg dw soil
Carbon mineralisation	difenoconazole ‡	28 days	<25% effect at day 28 at 1.67 and 16.7 mg a.s./kg dw soil
	Metabolite CGA 71019	28 days	<25% effect at day 28 at 0.035 and 0.353 mg a.s./kg dw soil
	Metabolite CGA 205375	28 days	<25% effect at day 28 at 0.09 and 0.22 mg a.s./kg dw soil
	SCORE 250EC	28 days	<25% effect at day 28 at 0.33 and 1.67 mg a.s./kg dw soil
Single species tests			
Marasmius oraede	difenoconazole	6 days	NOEC 1.64 mg as/kg
Mucor circinelloides	difenoconazole	3 days	NOEC 4.9 mg as/kg
Paecilomyces marquandii	difenoconazole	17 days	NOEC 16.4 mg as/kg
Phytophtora nicotianae	difenoconazole	17 days	NOEC 16.4 mg as/kg
Field studies[2]			
In a litter bag study with SCORE 250EC, a 17% reduction in decomposition rate was observed at direct overspray of 506 g as/ha compared to the control after 168 days. Exposure conditions considered as worst case compared to the representative use of difenoconazole in carrots, pome fruit and as seed treatment.			

[1] The values are not corrected due to log Pow >2.0 (e.g. LC_{50corr}). The correction is included in the TER calculation.
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies
*not fully reliable

Toxicity/exposure ratios for soil organisms
Seed treatment of 60 mg as/kg seed, corresponding to 12.3 g as/ha.

Test organism	Test substance	Time scale	Soil PEC (mg as/kg dw, initial)	TER	Trigger
Earthworms					
	difenoconazole ‡	Acute	0.016 (0.019)**	>19000 >16000	10
	difenoconazole ‡	Chronic	0.016 (0.019)**	no data	5
	DIVIDEND 030FS	Chronic	0.016 (0.019)**	6.3 (5.3)	5
	Metab. CGA 71019	Acute	0.0006	>770000	10
	Metab. CGA 71019	Chronic	0.0006	1667	5
	Metab. CGA 205375	Acute	0.0014	111000	10
	Metab. CGA 205375	Chronic	0.0014	no data	5
Other soil macro-organisms					
Collembola	difenoconazole ‡	Chronic	0.016	31200	5

Test organism	Test substance	Time scale	Soil PEC (mg as/kg dw, initial)	TER	Trigger
			(0.019)**	26000	
	CGA 71019	Chronic	0.0006	3000	5
	CGA 205375	Chronic	0.0014	no data	5

**values within parentheses represents plateau concentrations in soil

Pome fruit Southern EU, 4 x 75 g as/ha, 7 days interval between treatments (covers also pome fruit in Northern EU, 4 x 56.25 g as/ha, 7 days interval between treatments).

Test organism	Test substance	Time scale	Soil PEC (mg as/kg dw, initial)	TER	Trigger
Earthworms					
	difenoconazole ‡	Acute	0.135 (0.219)**	148 91	10
	difenoconazole ‡	Chronic	0.135 (0.219)**	no data	5
	SCORE 250EC	Acute	0.135 (0.219)**	148 (91)	10
	SCORE 250EC	Chronic	0.135 (0.219)**	no data	5
	Metab. CGA 71019	Acute	0.005	190000	10
	Metab. CGA 71019	Chronic	0.005	200	5
	Metab. CGA 205375	Acute	0.012	13000	10
	Metab. CGA 205375	Chronic	0.012	no data	5
Other soil macro-organisms					
Collembola	difenoconazole ‡	Chronic	0.135 (0.219)**	3700 (2300)	5
	CGA 71019	Chronic	0.005	360	5
	CGA 205375	Chronic	0.012	no data	5

**values within parentheses represents plateau concentrations in soil

Carrots, 3 x 125 g as/ha, 14 days interval between treatments.

Test organism	Test substance	Time scale	Soil PEC (mg as/kg dw, initial)	TER	Trigger
Earthworms					
	difenoconazole ‡	Acute	0.096 (0.112)**	208 178	10
	difenoconazole ‡	Chronic	0.096 (0.112)**	no data	5
	SCORE 250EC	Acute	0.096 (0.112)**	208 178	10
	SCORE 250EC	Chronic	0.096 (0.112)**	no data	5
	Metab. CGA 71019	Acute	0.004	260000	10
	Metab. CGA 71019	Chronic	0.004	268	5
	Metab. CGA 205375	Acute	0.008	19000	10
	Metab. CGA 205375	Chronic	0.008	no data	5
Other soil macro-organisms					
Collembola	difenoconazole ‡	Chronic	0.096 (0.112)**	5200	5
	CGA 71019	Chronic	0.004	450	5
	CGA 205375	Chronic	0.012	no data	5

**values within parentheses represents plateau concentrations in soil

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

Not available.

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha) emergence	Exposure[1] (g as/ha)	TER	Trigger
Avena sativa, Brassica napus, Glycine maxima	difenoconazole	>10 mg as/kg dw soil (incorporation)	>10 mg as/kg dw soil (incorporation)	not relevant	not relevant	5
Glycine maxima	SCORE 250EC	>100 g as/ha, (spray application)	100 g as/ha, (spray application)	12 (pome fruit) 3.5 (carrots)	8.1 (pome fruit) 28 (carrots)	5

[1] exposure has been estimated for spray applications based on Ganzelmeier drift data at 1 m distance for carrots, 3 m distance for pome fruit. Multiple applications were taken into account. For seed treatment, off-field exposure not relevant.

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

Not required.

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

Test type/organism	end point
Activated sludge, 3 hours exposure	NOEC 32 mg/L, EC_{50} >100 mg/L

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

Compartment	
soil	Parent (difenoconazole), data gap needs to be filled before Difenoconazole alcohol (CGA 205375) can be excluded.
water	Parent (difenoconazole)
sediment	Parent (difenoconazole)
groundwater	None

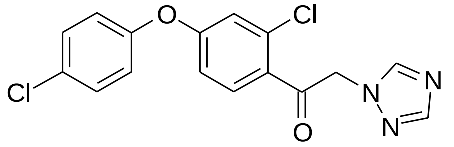
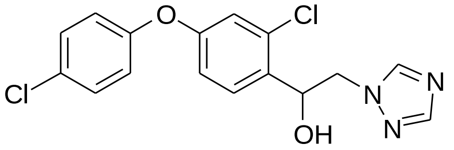
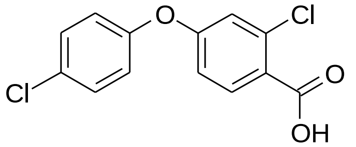
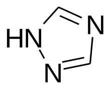
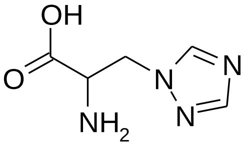
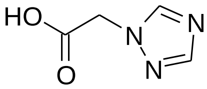
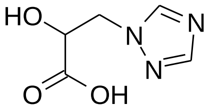
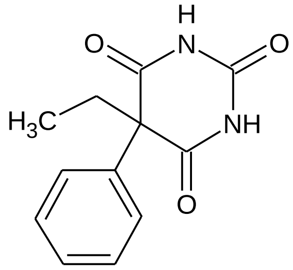
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R50/53

	RMS/peer review proposal
DIVIDEND 030FS	R52/53

	RMS/peer review proposal
SCORE 250EC	R51/53

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name	Structural formula
Difenoconazole-ketone **CGA-205374**	1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-[1,2,4]triazol-1-yl-ethanone	
Difenoconazole-alcohol **CGA-205375**	1-[2-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-1H-[1,2,4]triazol-yl]-ethanol	
Difenoconazole-benzoic acid **CGA-189138**	2-chloro-4-(4-chloro-phenoxy)-benzoic acid	
1,2,4-triazole CGA 71019	1H-1,2,4-triazole	
Triazole alanine (TA) **CGA 131013**	2-amino-3- [1,2,4] triazol-1-yl-propionic acid	
Triazole acetic acid (TAA) **CGA 142586**	[1,2,4]triazol-1-yl-acetic acid	
Triazole lactic acid (TLA) **CGA 205369**	[1,2,4]triazol-1-yl-lactic acid	
Phenobarbitone		

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

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
Ct	clearance time
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
ECD	electron capture detector
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 ionization 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
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
ILV	inter laboratory validation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
LR	lethal residue
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose

MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect residue
OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RAC	raw agricultural commodity
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TDM	triazole derivative metabolite
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment

w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year