CONCLUSION ON PESTICIDE PEER REVIEW

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

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ABSTRACT

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

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KEY WORDS

ipconazole, peer review, risk assessment, pesticide, fungicide, seed treatment

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SUMMARY

Ipconazole is a new active substance for which in accordance with Article 6(2) of Council Directive 91/414/EEC the United Kingdom (hereinafter referred to as the 'RMS') received an application from Kureha GmbH, Germany, for approval. Complying with Article 6(3) of Directive 91/414/EEC the completeness of the dossier was checked by the RMS. The European Commission recognised in principle the completeness of the dossier by Commission Decision 2008/20/EC of 20 December 2007.

The RMS provided its initial evaluation of the dossier on ipconazole in the Draft Assessment Report (DAR). In accordance with Commission Regulation (EU) No 188/2011 Article 11(6) additional information was requested. The RMS's evaluation of the additional information was submitted to the EFSA in the format of a revised DAR, which was received by the EFSA on 22 November 2011. The peer review was initiated on 1 February 2012 by dispatching the DAR for consultation of the Member States and the applicant (Kureha GmbH, Germany).

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

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of ipconazole as a fungicide for seed treatment of wheat and barley as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

In the area of identity, physical/chemical/technical properties and methods of analysis a data gap for further methods of analysis was identified, no areas of concern were identified.

No gaps or areas of concern were identified in the mammalian toxicology section.

No data gaps or areas of concern were identified in the section of residues.

No major gaps or critical areas of concern were identified in the environmental fate and behaviour section, but the lack of data with regard to the metabolism/degradation of each isomers lead to an issue 'not finalised'.

Several data gaps were identified in the section on ecotoxicology. The long-term risk for small granivorous birds was identified as a concern.

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BACKGROUND

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

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

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

In accordance with Article 6(2) of Council Directive 91/414/EEC (hereinafter referred to as the 'RMS') received an application from Kureha GmbH, Germany, for approval of the active substance ipconazole. Complying with Article 6(3) of Directive 91/414/EEC, the completeness of the dossier was checked by the RMS. The European Commission recognised in principle the completeness of the dossier by Commission Decision 2008/20/EC of 20 December 2007.[6]

The RMS provided its initial evaluation of the dossier on ipconazole in the Draft Assessment Report (DAR). In accordance with Commission Regulation (EU) No 188/2011 Article 11(6) additional information was requested. The RMS's evaluation of the additional information was submitted to the EFSA in the format of a revised DAR, which was received by the EFSA on 22 November 2011 (united Kingdom, 2011). The peer review was initiated on 1 February 2012 by dispatching the DAR for consultation of the Member States and the applicant (Kureha GmbH, Germany). In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 8(3) of the Regulation were considered in a telephone conference between the EFSA, the RMS, and the European Commission on 24 May 2012. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof it was concluded that additional information should be requested from applicant and that the EFSA should

[3] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ No L 309, 24.11.2009, p. 1-50.
[4] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1-32, as last amended.
[5] Commission Regulation (EU) No 188/2011 of 25 February 2011 laying down detailed rules for the implementation of Council Directive 91/414/EEC as regards the procedure for the assessment of active substances which were not on the market 2 years after the date of notification of that Directive. OJ No L 53, 26.2.2011, p. 51-55.
[6] Commission Decision 2008/20//EC of 20 December 2007, recognising in principle the completeness of the dossiers submitted for detailed examination in view of the possible inclusion of ipconazole and maltodextrin in Annex I to Council Directive 91/414/EEC. OJ No L 1, 4.1.2008, p. 5-6

organise an expert consultation in the areas of mammalian toxicology, residues, fate and behaviour, and ecotoxicology.

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

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

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in March 2013.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as a fungicide for seed treatment of wheat and barley, as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2013) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the DAR,
- the Reporting Table (24 May 2012),
- the Evaluation Table (25 March 2013)
- the report of the scientific consultation with Member State experts (where relevant),
- the comments received on the assessment of the additional information (where relevant),
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its addendum (compiled version of March 2013 containing all individually submitted addenda (United Kingdom, 2013)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Ipconazole is the ISO common name for (1*RS*,2*SR*,5*RS*;1*RS*,2*SR*,5*SR*)-2-(4-chlorobenzyl)-5-isopropyl-1-(1*H*-1,2,4-triazol-1-ylmethyl) cyclopentanol (IUPAC).

The representative formulated product for the evaluation was 'Rancona 15ME' a micro-emulsion (ME) containing 15 g/l ipconazole.

The representative uses evaluated are as a fungicide for seed treatment of wheat and barley. 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 ipconazole is a mixture of two diasteroisomer pairs, 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 "ipconazole" have to be considered as "sum of isomers". The possible impact of each individual enantiomer on the environment was not evaluated. A general data gap, applicable for sections 4 and 5, was therefore identified to address the impact of the isomeric composition of the substance. For the other sections this was not an issue for the representative uses.

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

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

The minimum purity of the active substance as manufactured is 955 g/kg it consists of two diasteroiomers 875-930 g/kg cis-isomer and 65-95 g/kg trans-isomer.

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

Residues of ipconazole can be determined in plants using the multi-residue method DFG S19 however a data gap has been identified for further ILV data in line with the current guidance document. An LC-MS/MS method is available for products of animal origin but no ILV is available, a data gap is not identified for this as no MRLs are proposed. LC-MS/MS methods are available for soil, water and air. However, as 1,2,4-triazole is included in the residue definition for surface water and soil a data gap is identified for validated methods. A method of analysis for body fluids and tissues is not required as the active substance is not proposed for classification as toxic or very toxic.

2. Mammalian toxicity

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

Ipconazole was discussed in the Pesticides Peer Review expert meeting 95 (September-October 2012).

Ipconazole is almost extensively absorbed after oral administration in rodents, is widely distributed and extensively metabolised and excreted. It is harmful if swallowed (R22 proposed*, or H302); it is not acutely toxic after skin and inhalation administration; it is not a skin and eye irritant, or a skin sensitiser. After repeated oral administration the relevant short-term toxicity No Observed Adverse Effect Levels (NOAELs) are 4.4 and 7 mg/kg bw per day in mouse and rat, respectively, based on hepatocyte vacuolation (mouse) and renal mineralisation (rat). In the 90-day study in dogs the lowest dose tested of 2 mg/kg bw per day was a Lowest Observed Adverse Effect Level (LOAEL) based on

reduced thymus weight. Based on the finding of cataracts in dogs, R48/22 has been proposed* ("Danger of serious damage to health by prolonged oral exposure", or H373 "May cause damage to organs through prolonged or repeated oral exposure). Two repeated dose studies are also available through skin and inhalation administration, with respective NOAELs of 30 mg/m3 and 150 mg/kg bw per day. Ipconazole did not show any evidence of genotoxicity and carcinogenicity: in long-term toxicity and carcinogenicity studies ipconazole caused liver histopathological effects in the mouse and forestomach lesions in rats (not relevant to humans) with relevant NOAELs of 1.9 and 12.6 mg/ kg bw per day, respectively. In multigeneration toxicity studies ipconazole did not show reproductive toxicity potential: the relevant NOAELs are 9 mg/kg bw per day (parental, based on reduced body weight gain), 22 mg/kg bw per day (reproductive, highest dose tested) and 8 mg/kg bw per day (offspring, based on reduced bw gain, delayed vaginal opening). In developmental toxicity assays ipconazole caused malformations (microphthalmia and kinky/short tail in the rat, short tail in the rabbit, cleft palate in rat and rabbit, and malformations of the aortic arch in the rat). For these reasons the experts proposed the classification as R63* ("Possible risk of harm to the unborn child" or H361d "Suspected of damaging the unborn child"). The relevant maternal toxicity NOAELs are 10 mg/kg bw per day in both rats and rabbits, whereas the developmental toxicity NOAELs are 3 and 10 mg/kg bw per day in rats and rabbits, respectively. Ipconazole did not show effects indicative of a neurotoxicity potential (no acute neurotoxicity studies were available, nor needed; the NOAEL of a repeated dose study was 33 mg/kg bw per day). No adverse reactions in any operator handling either ipconazole technical or the formulated product have been recorded to date (agricultural and industry workers). The proposed Acceptable Daily Intake (ADI) is 0.015 mg/kg bw per day, based on the subchronic (1-year) NOAEL of 1.5 mg/kg bw per day in dogs, with an uncertainty factor (UF) of 100; the Acute Reference Dose (ARfD) and the Acceptable Operator Exposure Level (AOEL) are 0.015 mg/kg bw (per day) as well, but they are derived from the rat developmental toxicity NOAEL with an UF of 200 (the majority of the experts decided to have the same margin as with the ADI between the reference values and the teratogenic effects occurring at 10 mg/kg bw per day, therefore an increased UF was applied). The estimated exposure for the operator and for the bystander during seed treatment and seed sowing is below the AOEL. For the concerned scenario, no re-entry exposure is anticipated (based on this also the potential exposure to isomers formed in the environment after application has no relevance).
* It should be noted that classification is formally proposed and decided in accordance with Regulation (EC) No 1272/2008. Proposals for classification made in the context of the evaluation procedure under Regulation (EC) No 1107/2009 are not formal proposals.

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.

The metabolism of ipconazole was investigated in wheat following seed treatment and foliar application of benzyl methylene or triazole labelled ipconazole, and in addition in soy bean with seed treatment application of triazole labelled ipconazole.

Wheat grain and soybean seeds following seed treatment showed similar residue profiles with triazole alanine (TA) (56 - 68%TRR), triazole acetic acid (TAA) 10 - 32% TRR) and triazole pyruvic acid (TPA) (3 - 4% TRR) present as major metabolites, and with parent ipconazole not detected. Absolute residue levels were low, and none of the identified compounds is expected to largely exceed 0.01 mg/kg at the cGAP application rate. In foliar treated wheat plants, ipconazole was present at low levels and proportions in the grain (3 - 9% TRR, <0.01 mg/kg) while the major metabolites were triazole alanine (29%TRR), triazole acetic acid (14% TRR) and the O-glycoside of ipconazole (18% TRR). No metabolites specific to the benzyl methylene portion of the molecule were detected.

The metabolic picture in wheat straw, forage and soy bean forage and hay was very similar, with few exceptions. Parent ipconazole was present in slightly higher proportions when compared to grains/seeds, and ipconazole was also found to be hydroxylated and conjugated to hydroxy ipconazole

conjugates. The cis-cis (cc) and cis-trans (ct) isomers ratio investigated in wheat straw did not change significantly between application and harvest, and it can be concluded that there is no diastereoisomer specific metabolism of ipconazole in wheat. It is unknown whether or not there was a change in the ratio of enantiomers.

The metabolism of ipconazole was also investigated in succeeding leafy, root and cereal crops with radio-labelled ipconazole. The findings indicated preferential uptake by all of the crops of the triazole ring-containing metabolites, and uptake of these metabolites was generally increased at each successive plant back interval. Triazole acetic acid and triazole alanine were the predominant residues, ipconazole was not detected.

The residue definition for risk assessment for cereal and oilseed crops was set as 1) Ipconazole and 2) Triazole derivative metabolites (TDMs). The residue definition for TDMs is pending the detailing of the definition upon the finalisation of a harmonised assessment approach for TDMs and triazole active substances. For monitoring, it was proposed to include ipconazole by default in the residue definition.

Investigation of residues in livestock was not triggered by the representative uses due to insignificant livestock dietary exposure, and hence no MRLs for food of animal origin are proposed. However, the metabolism of ipconazole was studied in goats. In view of the very low total residue levels recovered in the study, the residue definition could be set as ipconazole by default. Data on poultry were not available. If in the future additional uses as feed items are supported, a global residue data package addressing the TDMs in animal matrices might be necessary.

The representative uses are sufficiently supported by residue data in wheat and barley. Analytical methods were sufficiently validated to determine the residues of ipconazole, and metabolites triazole alanine, triazole acetic acid, and triazole pyruvic acid in cereal grain and straw. Valid storage stability data are available to confirm ipconazole and metabolites as being stable under freezer storage conditions. Cereal processing data were not required due to insignificant residues in grain.

The consumer risk assessment performed with the EFSA Pesticides Residues Intake Model (PRIMo) indicated that the maximum chronic dietary exposure (TMDI) for wheat and barley is less than 1 % of the ADI of 0.015 mg/kg bw per day for ipconazole. In an acute consumer risk assessment the calculated maximum exposure was less than 1 % of the ARfD of 0.015 mg/kg bw for all cereal commodities.

Due to high contamination levels with TDMs in untreated samples in the residue trials, actual residue levels of triazole alanine and triazole acetic acid in cereal grain resulting from the representative uses could not be determined with certainty. The differences were in many cases marginal, which is supported by the findings in the radiolabel metabolism study where residues of triazole alanine and triazole acetic acid were individually present around 0.01 mg/kg, so that this value could be used in lieu of the STMR to assess chronic consumer exposure to triazole alanine and triazole acetic acid. The highest residue level (i.e. the difference between determined level in treated and untreated sample) in the residue trials was 0.05 mg/kg for each, triazole alanine and triazole acetic acid, respectively. Residues of triazole pyruvic acid were consistently below the LOQ of 0.01 mg/kg in all samples.

The consumer risk assessment individually performed for triazole alanine and triazole acetic acid with the EFSA Pesticides Residues Intake Model (PRIMo), assuming a residue level of 0.01 mg/kg in lieu of the STMR, indicated that the chronic dietary exposure for wheat and barley is less than 1 % of the ADI of 0.1 mg/kg bw per day for triazole alanine, and also less than 1% of the ADI of 0.02 mg/kg bw per day for triazole acetic acid. In an acute consumer risk assessment the calculated maximum intakes on the basis of the highest residues were less than 1 % of the ARfD of 0.1 mg/kg bw for triazole alanine in all cereal commodities, and 1% of the ARfD of 0.06 mg/kg bw for triazole acetic acid for wheat.

A consumer risk assessment has not been performed for triazole pyruvic acid since no toxicological reference values were available.

Moreover, a combined risk assessment considering simultaneous dietary exposure of consumers to residues of parent ipconazole and TDMs is pending a general methodology on the risk assessment of triazole compounds and their triazole derivative metabolites.

4. Environmental fate and behaviour

The following evaluation of section 4 has been completed having consideration of the following guidance: EFSA PPR (2004), EFSA PPR (2007), European Commission (2002b), FOCUS (2000, 2001, 2006, 2007, 2008, 2009). Ipconazole was discussed at the Pesticides Peer Review Expert teleconference 80 in November 2012.

It should be noted that ipconazole used in the environmental fate and behaviour studies is present as two isomers, cis-cis (cc) and cis-trans (ct). The methods of analyses used in the radio labelled soil and water studies were able to distinguish between the isomers and there was no evidence of significant change in isomer ratio over the duration of the studies. However, information on the different environmental behaviour of the individual enantiomers was not available and therefore a data gap was identified.

The original submission for approval of ipconazole included aerobic route and rate of degradation studies on four soils conducted with the active substance radio-labelled in the triazole and in the benzyl methylene positions. In these studies mineralisation was limited with up to 9.8% at 122 days, indicative of the slow degradation under standard laboratory conditions. Unextracted residues at 120-122 days formed up to 33.2% AR. Aerobic degradation led to the formation of a number of minor metabolites, none of which exceeded 5% AR at any sampling time. However, during the EU peer review an additional soil metabolism study on ipconazole conducted to US EPA guidelines and to GLP, was submitted and evaluated (Addendum 3, United Kingdom, 2013). In this study the maximum observed occurrence of the metabolite 1,2,4-triazole was 23.7% AR at 31 days after treatment in the sandy loam soil tested. The fate experts considered the study acceptable and relevant to the EU regulatory procedure. As a consequence a new environmental exposure assessment of ipconazole and metabolite 1,2,4-triazole was required and presented in Addendum 7 (United Kingdom, 2013). The following evaluation reflects the inclusion of this new information as agreed by the peer review. In particular, persistence endpoints for metabolite 1,2,4 triazole are derived from the latest data package provided by the Triazole Derivative Metabolite Group (TDMG) and revised by the UK[7] (Addendum 7, United Kingdom, 2013).
Ipconazole exhibited high to very high persistence in soil and metabolite 1,2,4 triazole exhibited high persistence in the US soil. The extent of degradation of ipconazole under anaerobic conditions was slightly less than seen under aerobic conditions, but no novel metabolites were observed. A study investigating photolytic route of degradation of ipconazole on a single soil was also conducted using both radio labelled positions. Apparently greater degradation of ipconazole was seen during the course of this study than under dark conditions, with one major photolysis product (1,2,4-triazole) formed at a maximum of 10.4% AR on day 8. The representative use of ipconazole is as a cereal seed treatment, so residues of ipconazole are unlikely to be present on the soil surface. Thus the photolytic route of degradation for ipconazole is not relevant to the exposure assessment for this use. Ipconazole exhibited low to slight mobility in soil and no pH influence on soil adsorption was detected.

Field dissipation studies were conducted in Germany (two sites), Italy and Spain (one site each). Applications were made in December/January period and the bare soil applications were immediately incorporated, presumably to mimic application as a seed treatment and to minimise any soil surface

[7] A group of notifiers of triazole fungicides have formed a task force called the Triazole Derivative Metabolite Group (TDMG) to produce a common data package to cover the risk assessment to common triazole metabolites. At the time of writing this conclusion for ipconazole, the new 1,2,4-triazole evaluation had been through the EFSA peer review procedure and was awaiting noting at the Standing Committee on the Food Chain and Animal Health.

losses by photolysis and volatilisation. Only ipconazole was analysed for. With the exception of the Spanish field dissipation result, the field dissipation values are all considerably shorter than those seen in the laboratory studies, indicating that ipconazole exhibits medium to high persistence under field conditions. Based on the endpoints provided by the TDMG evaluation, metabolite 1,2,4 triazole exhibits moderate to high persistence (derived from best fit kinetics of DissT50 values from 4 dissipation field trials in Germany, UK, Italy and Spain).

The PEC (Predicted Environmental Concentration) in soil that calculate accumulation estimates from use over successive years, covering the representative uses assessed, can be found in Appendix A.

In a dark water-sediment study conducted on 2 natural aerobic aquatic systems, ipconazole dissipated rapidly from the water phase and was found predominantly in the sediment phase of both systems. No major metabolites (> 10% AR) were detected in water or sediment. Both unextracted radioactivity and mineralization to CO_2 were low. Unextractable residues peaked at ≤ 9.3% AR, with a maximum of ≤1.1% AR CO_2 detected in both systems after 100 days. In the natural sediment water systems, ipconazole exhibited high persistence. No data are required on aqueous photolysis, as there is no significant absorption of ipconazole at wavelengths greater than 220 nm. The necessary surface water and sediment exposure assessments (PEC calculations) were carried out for parent ipconazole and the metabolite 1,2,4-triazole using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 1.1 of the Steps 1-2 in FOCUS calculator). For the active substance ipconazole, satisfactory step 3 calculations were also available (Addendum 7, United Kingdom, 2013). As the study performed to investigate toxicity of ipconazole to sediment dwelling organisms was dosed by spiking in the water phase and the NOEC expressed as a water concentration (mg/L), pseudo PECsw values were also calculated. As degradation of ipconazole in sediment occurs slowly, the potential for accumulation of residues in this compartment was also considered and evaluated using these pseudo PECsw values.

Appropriate groundwater exposure assessments for ipconazole and its soil metabolite 1,2,4-triazole were available. Input parameters for degradation and soil adsorption of 1,2,4-triazole were obtained from the TDMG database. The 80th percentile annual average PECgw concentrations for ipconazole and 1,2,4-triazole at 1 m soil depth were ≤ 0.001 µg/L for all the scenarios simulated using FOCUS-PEARL v.4.4.4.

5. Ecotoxicology

The following documents were considered in the risk assessments: European Commission 2002a and 2002b, SETAC 2000, and EFSA 2009.

It is noted that although there was no evidence of significant change in the cis/trans isomeric ratio of ipconazole in the environment (see chapter 4), the possible impact of each individual enantiomer on the environment was not evaluated. Therefore a general data gap, applicable for sections 4 and 5, was identified.

The first tier risk assessments for granivorous and herbivorous birds and for granivorous mammals resulted in a high risk via long-term dietary exposure. Therefore higher tier risk assessments were performed for these scenarios. The higher tier risk assessments with the refinement steps and the underlying data were discussed at the Pesticides Peer Review Experts' Meeting 99 (November, 2012). In line with the discussions (e.g. on use of TWA factor), the higher tier risk assessments were updated after the meeting (see Appendix A for the relevant TER values). As a result, a high risk was only identified for small granivorous birds at long-term scale and a data gap was concluded for all of the representative uses for this scenario. Furthermore, additional data gaps were identified at the meeting of experts to address further uncertainties associated with the available risk assessments for birds and mammals, including a data gap for potential endocrine mediated effects in birds. For the relevant plant metabolite a low risk to birds and mammals was concluded.

With regard to the aquatic organisms, the necessary data for a risk assessment were available. However the experts of the Pesticides Peer Review Meeting 99 agreed that further information is needed to address the risk to fish from potential endocrine mediated effects, therefore a data gap was identified for this issue. The risk assessment using the available data resulted in a low risk for aquatic organisms. The only exception was the chronic risk to fish in the case of one of the surface water scenarios (R4) for the winter cereal uses (at FOCUS step 3). Therefore a data gap was concluded to further address the risk for the European situations represented by the R4 FOCUS surface water scenario for the winter cereal uses. A low risk to aquatic organisms was concluded for the metabolite 1,2,4-triazole.

A low risk to bees was concluded on the basis of the available data on foliar residues and degradation, the representative uses and the low toxicity of ipconazole to bees. The available assessments using the standard tier 1 test species as well as additional species, indicated a low risk to non-target arthropods for the representative uses of ipconazole.

A low risk to earthworms and soil micro organisms was concluded for ipconazole. However, considering the persistence of ipconazole (see section 4), further consideration for soil organisms was triggered. The experts at the Pesticides Peer Review Meeting 99 discussed the need for further information and identified a data gap for further assessments for soil macro organisms. They agreed that a study on collembolan or field studies investigating biologically relevant effects on soil macro organisms could be useful to address this data gap. On the basis of the available information, a low risk for soil organisms was concluded for the metabolite 1,2,4-triazole.

A low risk was concluded for non-target plants and organisms involved in biological methods for sewage treatment on the bases of the available data and the low exposure.

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
Ipconazole	Single first order lab DT_{50} 170-391 days (20° C and pF2/10kPa) Exhibits high to very high persistence Field DT_{50} 66-228 days	Data gap was concluded for further assessments for soil macro-organisms.
1,2,4-triazole	Single first order lab DT_{50} 119 days (20° C and pF2/10kPa; US EPA study) Exhibits moderate to high persistence Field DT_{50} normalised to 20° C and pF2: 25.1-126 days (slow phase DFOP kinetics)	A low risk was concluded for soil organisms.

6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
Ipconazole	K_{Foc} 1724 to 3214 mL/g low to slight mobility	No	Yes	Yes	Yes

1,2,4-triazole	K_{Foc} 43 to 202 mL/g very high to medium mobility	No	No data, data not needed	Yes	No (a low risk was concluded for aquatic organisms)

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Ipconazole	Data gaps were concluded to further address the risk to fish
1,2,4-triazole	A low risk was concluded for aquatic organisms

6.4. Air

Compound (name and/or code)	**Toxicology**
Ipconazole	Not acutely toxic via inhalation

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

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

- ILV data for the method of analysis for plants (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)
- Method of analysis for 1,2,4-triazole in soil and surface water (relevant for all representative uses evaluated; data gap identified by EFSA; no submission date proposed; see section 1).
- Ipconazole consists of two diasteroisomer pairs. The preferential metabolism/degradation of each enantiomer in the environment and its impact on the risk assessment, needs to be addressed (relevant for all representative uses evaluated; data gap identified by EFSA; no submission date proposed; applicable to sections 4 and 5).
- The long-term risk to small granivorous birds needs to be further addressed (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5).
- The long-term risk to granivorous birds and mammals from seeds remaining on the soil surface in EU regions where the available residue decline study is not relevant (e.g. Southern EU-MS) needs to be further addressed (relevant for all representative uses evaluated for EU regions where the available residue decline study is not relevant; submission date proposed by the applicant: unknown; see section 5)
- The long-term risk to granivorous birds from seeds, below the soil surface needs to be further addressed (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5).
- The risk to birds from potential endocrine mediated effects needs to be further addressed (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5)
- The risk to fish for the European situations represented by the R4 FOCUS surface water scenario for the winter cereals uses needs to be further addressed (relevant for the representative use in winter cereals for situations represented by the R4 FOCUS surface water scenario; submission date proposed by the applicant: unknown; see section 5).
- The risk to fish from potential endocrine mediated effects needs to be further addressed (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5).
- The risk to soil macro organisms needs to be further addressed (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5).

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

- Gloves have to be worn during seed treatment and coverall during seed sowing to reduce exposure below the AOEL.

9. Concerns

9.1. Issues that could not be finalised

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

1. Possible impact on the environmental risk assessment of the potential enantio-selective biologically mediated metabolism/degradation needs to be addressed.

Representative use		**winter barley and wheat**	**spring cereals barley and wheat**
Operator risk	Risk identified		
	Assessment not finalised		
Worker risk	Risk identified		
	Assessment not finalised		
Bystander risk	Risk identified		
	Assessment not finalised		
Consumer risk	Risk identified		
	Assessment not finalised		
Risk to wild non target terrestrial vertebrates	Risk identified	X[5]	X[5]
	Assessment not finalised	X[1,2,3]	X[1,2,3]
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified		
	Assessment not finalised	X[1,4]	X[1,4]
Risk to aquatic organisms	Risk identified	1 out of 9 FOCUS scenarios	
	Assessment not finalised	X[1,3]	X[1,3]
Groundwater exposure active substance	Legal parametric value breached		
	Assessment not finalised		
Groundwater exposure metabolites	Legal parametric value breached		

2. The long-term risk to birds feeding on seeds, below the soil surface.

	Parametric value of 10µg/L[(a)] breached		
	Assessment not finalised		
Comments/Remarks			

3. The risk to birds and fish from potential endocrine mediated effects.

4. The risk to soil macro-organisms considering the persistence of ipconazole.

9.2. Critical areas of concern

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

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

5. The long-term risk to small granivorous birds

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

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

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

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APPENDICES

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

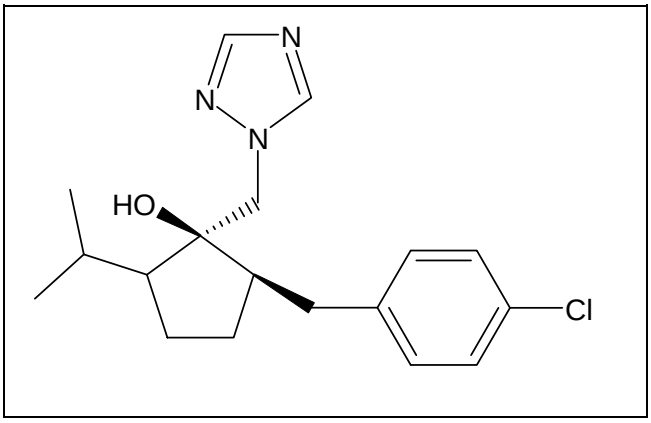
Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	ipconazole
Function (*e.g.* fungicide)	fungicide
Rapporteur Member State	UK
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(1*RS*,2*SR*,5*RS;*1*RS*,2*SR*,5*SR*)-2-(4-chlorobenzyl)-5-isopropyl-1-(1*H*-1,2,4-triazol-1-ylmethyl) cyclopentanol
Chemical name (CA) ‡	2-[(4-chlorophenyl)methyl]-5-(1-methylethyl)-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CIPAC No ‡	798
CAS No ‡	125225-28-7 (mixture of diastereoisomers) 115850-69-6 (ipconazole cc, cis isomer) 115937-89-8 (ipconazole ct, trans isomer)
EC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification (including year of publication) ‡	Not applicable
Minimum purity of the active substance as manufactured ‡	955 g/kg Ipconazole cc: 875 – 930 g/kg Ipconazole ct: 65-95 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_{18}H_{24}ClN_3O$
Molecular mass ‡	333.9 g/mol

Structural formula ‡



Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	81-89 °C (99.7 % pure)
Boiling point (state purity) ‡	> 400 ± 0.5 °C (99.7 % pure cc) > 400 ± 0.5 °C (99.7 % pure ct)
Temperature of decomposition (state purity)	Not applicable
Appearance (state purity) ‡	White crystalline powder (99.3 % pure cc) White fine powder (98.3 % pure ct) White powder (98.1 % tech)
Vapour pressure (state temperature, state purity) ‡	3 x 10^{-6} Pa at 25 °C (99.7 % pure)
Henry's law constant ‡	3 x 10^{-5} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	(99.2 % pure cc): 9.34 mg/L in pure water (Milli-Q) 9.86 mg/L in pH 5 buffer 8.68 mg/L in pH 7 buffer 9.13 mg/L in pH 9 buffer (99.0 % pure ct): 4.97 mg/L in pure water (Milli-Q) 5.79 mg/L in pH 5 buffer 4.60 mg/L in pH 7 buffer 4.71 mg/L in pH 9 buffer
Solubility in organic solvents ‡ (state temperature, state purity)	98.1 % (tech) at 20 ± 0.5 °C

Solvent:	Solubility (g/L):
Acetone	570.4
1,2-Dichloroethane	424.8
Dichloromethane	583.1
Ethyl acetate	428.1
Heptane	1.90
Methanol	678.7
n-Octanol	229.6
Toluene	156.0
Xylenes	151.0

Surface tension ‡ (state concentration and temperature, state purity)	56.5 mN/m at 20 °C (90 % saturated solution) (98.1 % tech)
Partition co-efficient ‡ (state temperature, pH and purity)	Log Pow = 4.49 at 20 °C (99.6 % pure cc) Log Pow = 4.28 at 20 °C (100 % pure ct) pH not investigated

Dissociation constant (state purity) ‡	Potential dissociated species: pKa = -5.43, -2.42, 2.32 and 17.34 (calculated values)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	(99.3 % pure cc): Neutral solution (water/acetonitrile; 3:2): λmax 276 nm; ε = 315 Acidic solution (HCl/acetonitrile; 3:2): λmax 276 nm, ε = 304 Basic solution (NaOH/acetonitrile; 3:2): λmax 276 nm, ε = 312 (98.3 % pure ct): Neutral solution (water/acetonitrile; 3:2): λmax 276 nm; ε = 312 Acidic solution (HCl/acetonitrile; 3:2): λmax 276 nm, ε = 293 Basic solution (NaOH/acetonitrile; 3:2): λmax 276 nm, ε = 305
Flammability ‡ (state purity)	Not flammable (98.1 % tech)
Explosive properties ‡ (state purity)	Not explosive (98.1 % tech)
Oxidising properties ‡ (state purity)	Not oxidising (98.1 % tech)

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

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

Summary of representative uses evaluated (*name of active substance or the respective variant*)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Wheat	France UK	'Rancona 15ME'	F	Soil and seed borne diseases	ME	15 g/L	Seed treatment	Seed before planting	1	Not applicable	**1.5 g ipconazole / 100 kg seed** 1.0 L product/tonne seed At a maximum seed rate of 220 kg/ha, the application rate is equivalent to 3.3 g ipconazole/ha.			Not applicable	ME Micro emulsion
	Czech Republic Hungary Poland Slovakia Romania Bulgaria	'Rancona 15ME'	F	Seed borne diseases	ME	15 g/L	Seed treatment	(BBCH growth stage 00)	1	Not applicable	**1.5 g ipconazole / 100 kg seed** 1.0 L product/tonne seed At a maximum seed rate of 350 kg/ha, the application rate is equivalent to 5.25 g ipconazole/ha.			Not applicable	
Barley	France UK	'Rancona 15ME'	F	Seed borne diseases	ME	15 g/L	Seed treatment	Seed before planting	1	Not applicable	**2.0 g ipconazole / 100 kg seed** 1.33 L product/tonne seed At a maximum seed rate of 220 kg/ha, the application rate is equivalent to 4.4 g			Not applicable	ME Micro emulsion

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

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

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
											ipconazole/ha				
	Czech Republic Hungary Poland Slovakia	'Rancona 15ME'	F	Seed borne diseases	ME	15 g/L	Seed treatment	(BBCH growth stage 00)	1	Not applicable	**2.0 g ipconazole / 100 kg seed** 1.33 L product/tonne seed At a maximum seed rate of 350 kg/ha, the application rate is equivalent to 7.0 g ipconazole/ha			Not applicable	
	Romania Bulgaria	'Rancona 15ME'	F	Seed borne diseases	ME	15 g/L	Seed treatment		1	Not applicable	**1.95 g ipconazole / 100 kg seed** 1.33 L product/tonne seed At a maximum seed rate of 350 kg/ha, the application rate is equivalent to 6.8 g ipconazole/ha			Not applicable	

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the applicant 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
(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

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

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

used must be indicated	

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Methods of Analysis

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV (detection at 220 nm)
Impurities in technical as (analytical technique)	HPLC-UV (detection at 220 nm)
Plant protection product (analytical technique)	HPLC-UV (detection at 220 nm)

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Ipconazole
Food of animal origin		Not applicable
Soil		Ipconazole and 1,2,4 triazole
Water	surface	Ipconazole and 1,2,4 triazole
	drinking/ground	Ipconazole
Air		Ipconazole

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	LC-MS/MS (dry, high water, high acid and high oil crops). ILV (dry crops) LOQ = 0.01 mg/kg DFG-S19 (dry, high water, high acid and high oil crops). ILV (dry crops) LOQ = 0.01 mg/kg
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	LC-MS/MS (meat, milk, eggs, fact, kidney, liver) LOQ = 0.01 mg/kg tissues and eggs; LOQ = 0.01 mg/L milk.
Soil (analytical technique and LOQ)	LC-MS/MS (sandy loam and clay soils) LOQ = 0.001 mg/kg Open for 1,2,4 triazole
Water (analytical technique and LOQ)	LC-MS/MS (drinking, ground and surface water) LOQ = 0.05 µg/kg Open for 1,2,4 triazole in surface water

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Methods of Analysis

Air (analytical technique and LOQ)	LC-MS/MS LOQ = 0.0004 mg/m^3
Body fluids and tissues (analytical technique and LOQ)	Not applicable

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

	RMS/peer review proposal
Active substance	None

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Mammalian toxicology

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	>90% based mostly on biliary excretion within 48h (oral dose of 2 mg/kg bw)
Distribution ‡	At 120h , widely distributed with highest residues in liver
Potential for accumulation ‡	Limited accumulation on repeat dosing
Rate and extent of excretion ‡	>70% excreted within 24h (mostly in faeces)
Metabolism in animals ‡	Extensively metabolised (max of 2% of dose excreted unchanged) with large number of metabolite fractions (each mostly <10 % of dose)
Toxicologically relevant compounds ‡ (animals and plants)	Parent and the following metabolites: Triazole alanine (plants) Triazole acetic acid (plants)
Toxicologically relevant compounds ‡ (environment)	None

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	888 mg/kg bw (females)	R22 H302
Rat LD_{50} dermal ‡	>2000 mg/kg bw	
Rat LC_{50} inhalation ‡	>3.53 mg/l	
Skin irritation ‡	Non irritant	
Eye irritation ‡	Non irritant	
Skin sensitisation ‡	Non sensitiser (Magnusson and Kligman)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Skin reddening, lens opacity, reduced thymus weight (dog) Hepatocyte vacuolation (mouse) Renal mineralisation (rat)	
Relevant oral NOAEL ‡	1.5 mg/kg bw per day (1-year dog) < 2 mg/kg bw per day (90-day dog) 4.4 mg/kg bw per day (90-day mouse)	R48/22 H373

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Mammalian toxicology

	7.0 mg/kg bw per day (90-day rat)	
Relevant dermal NOAEL ‡	150 mg/kg bw per day for systemic effects Irritant effects at all dose levels attributed to self grooming	
Relevant inhalation NOAEL ‡	30 mg/m^3 for systemic effects Irritant effects at 30 mg/m^3 and above	

Genotoxicity ‡ (Annex IIA, point 5.4)

Ipconazole is not genotoxic	

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

Target/critical effect ‡	Liver histopathology (mouse) No relevant effects (rat); forestomach lesions in rat not relevant to humans	
Relevant NOAEL ‡	1.9 mg/kg bw per day (18-month, mouse) 12.6 mg/kg bw per day (2-year, rat)	
Carcinogenicity ‡	Ipconazole is not oncogenic	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: reduced bw gain Reproductive: no adverse effects Offspring: reduced bw gain, delayed vaginal opening	
Relevant parental NOAEL ‡	9 mg/kg bw per day	
Relevant reproductive NOAEL ‡	22 mg/kg bw per day	
Relevant offspring NOAEL ‡	8 mg/kg bw per day	

Developmental toxicity

Developmental target / critical effect ‡	Rat: Parental: reduced bw gain and food consumption	R63 H361d

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Mammalian toxicology

	Developmental: malformations of eyes and major blood vessels in presence of moderate maternal toxicity (main study); malformations of eyes and tail in presence of marked maternal toxicity (prelim study) Rabbit: Parental: reduced bw gain Developmental: skeletal abnormalities indicative of fetal toxicity in presence of moderate maternal toxicity (main study); malformations of tail in presence of marked maternal toxicity (prelim study)	
Relevant maternal NOAEL ‡	10 mg/kg bw per day, rat 10 mg/kg bw per day, rabbit	
Relevant developmental NOAEL ‡	3 mg/kg bw per day, rat 10 mg/kg bw per day, rabbit	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data available – not required	
Repeated neurotoxicity ‡	No effect, 90-day rat (NOAEL 33 mg/kg bw per day)	
Delayed neurotoxicity ‡	No data available – not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data available- not required
Studies performed on metabolites or impurities ‡	No

Medical data ‡ (Annex IIA, point 5.9)

No evidence of adverse effects in manufacturing personnel or in workers involved with experimental agricultural use of ipconazole

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Mammalian toxicology

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.015 mg/kg bw per day	One-year dog	100
AOEL ‡	0.015 mg/kg bw per day	Rat developmental	200*
ARfD ‡	0.015 mg/kg bw	Rat developmental	200*

*the UF was increased to have the same margin as with the ADI between the reference values and the teratogenic effects occurring at 10 mg/kg bw per day

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Rancona 15 ME = UBI 6931.02 based on a study with UBI 6919, another 15g/l ME)	5% for concentrate and dilute product

Exposure scenarios (Annex IIIA, point 7.2)

Operator	**Treating seed** French SeedTropex model (70th percentile values): of exposure for operators treating seeds with Crusoe are within acceptable levels for operators wearing gloves for all tasks except bagging: 90% of AOEL, Scenario 2. -UK SeedTropex: gloves worn during the calibration, mixing/loading and cleaning tasks and coveralls are worn during bagging: 18% and 27% of the AOEL. **Sowing treated seed** worker wearing coverall: 23% of the AOEL.
Workers	No re-entry scenario expected
Bystanders	**During Seed Treatment** <1% to <4% of the AOEL **During seed sowing** 39% of systemic AOEL

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

Peer review proposal

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Mammalian toxicology

Substance classified (ipconazole)	R22, R48/22, Toxic to reproduction Category 3 R63 Acute tox 4 H302, STOT-RE 2, H373, Repro cat 2 H361d

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Residues

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

Plant groups covered	Wheat (cereal), Soybean (pulse/oilseed) seed treatment
Rotational crops	Wheat, lettuce and carrot
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Not applicable, study not triggered.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Ipconazole
Plant residue definition for risk assessment	1) Ipconazole 2) Triazole derivative metabolites (TDMs) pending further detailing when a harmonised assessment approach for triazole compounds and TDMs has been agreed
Conversion factor (monitoring to risk assessment)	Not applicable

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

Animals covered	Not applicable (animal intakes < 0.1 mg/kg)
Time needed to reach a plateau concentration in milk and eggs	n/a
Animal residue definition for monitoring	n/a
Animal residue definition for risk assessment	n/a
Conversion factor (monitoring to risk assessment)	n/a
Metabolism in rat and ruminant similar (yes/no)	n/a
Fat soluble residue: (yes/no)	n/a

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

Based on the total radioactive residues in the rotational crop metabolism study it is unlikely that significant residues (> 0.01 mg/kg) would result from the intended use.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Residues

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

Ipconazole was stable for up to 13 months in wheat (grain, forage, hay and straw) and maize (cobs, forage and straw).

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

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

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Residues

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

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Wheat	N Europe	Grain: 14 x < 0.01 mg/kg Straw: 14 x < 0.01 mg/kg	Residues in wheat grain were below the LOQ of the analytical method (i.e. <0.01 mg/kg) in all trials conducted in the Northern and Southern EU A MRL of 0.01 mg/kg is proposed for wheat grain. By extrapolation an MRL of 0.01 mg/kg is also proposed for barley grain.	0.01 mg/kg (wheat and barley)	< 0.01 mg/kg	< 0.01 mg/kg
Wheat	S Europe	Grain: 14 x < 0.01 mg/kg Straw: 14 x < 0.01 mg/kg			< 0.01 mg/kg	< 0.01 mg/kg

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

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Residues

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

ADI	0.015 mg/kg bw per day
TMDI (% ADI) according to European diet	< 1 % (WHO Cluster B diet) [EFSA PRIMo]
TMDI (% ADI) according to national (to be specified) diets	n/a
IEDI (WHO European Diet) (% ADI)	n/a
NEDI (specify diet) (% ADI)	< 1 % (UK diet, all sub-populations)
Factors included in IEDI and NEDI	n/a
ARfD	0.05 mg/kg bw/day
IESTI (% ARfD)	Wheat: 0.3 % (UK 4-6 year old child) [EFSA PRIMo]
NESTI (% ARfD) according to national (to be specified) large portion consumption data	< 1 % (UK diet, all sub-populations)
Factors included in IESTI and NESTI	n/a

TDMs

ADI **Triazole alanine (TA)**	0.1 mg/kg bw per day
IEDI (WHO European Diet) (% ADI)	< 1 % (WHO Cluster B diet) [EFSA PRIMo]
NEDI (specify diet) (% ADI)	<1 % (IT, child/toddler) [EFSA PRIMo]
ARfD	0.1 mg/kg bw/day
IESTI (% ARfD)	Wheat: 0.7 % (UK 4-6 year old child) [EFSA PRIMo]
ADI **Triazole acetic acid (TAA)**	0.02 mg/kg bw per day
IEDI (WHO European Diet) (% ADI)	< 1 % (WHO Cluster B diet) [EFSA PRIMo]
NEDI (specify diet) (% ADI)	<1 % (IT, child/toddler) [EFSA PRIMo]
ARfD	0.06 mg/kg bw/day
IESTI (% ARfD)	Wheat: 1.2 % (UK 4-6 year old child) [EFSA PRIMo]
Triazole pyruvic acid (TPA)	Assessment not conducted as no ADI/ ARfD available

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

	Processing studies have not been conducted as for the low residues in grain, and were not triggered by current data requirements.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Residues

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

Wheat grain	*0.01 mg/kg
Barley grain	*0.01 mg/kg

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

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

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

Mineralization after 100 days ‡	0.2 – 4.3% AR after 120 - 122 d, [^{14}C-triazole]-label (n= 4), EU studies 9.8% AR after 122 d, [^{14}C-benzyl methylene]-label (n= 1), EU study 12.4% AR after 119 days, eqimolar mixture of [^{14}C-triazole] and [^{14}C-benzyl methylene]-labels, US study
Non-extractable residues after 100 days ‡	14.2 – 33.2% AR after 120-122 d, [^{14}C-triazole]-label (n= 4), EU studies 13.8% AR after 122 d, [^{14}C-benzyl methylene]-label (n= 1), EU study 22.7% AR after 119 days, eqimolar mixture of [^{14}C-triazole] and [^{14}C-benzyl methylene]-labels, US study
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	None trigger assessment from EU studies. KNF-317-M-1 and KNF-317-M-11 <5% AR. 1,2,4-triazole 23.7% AR at 31 d in US study

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

Anaerobic degradation ‡

Mineralization after 100 days	0.6% AR after 120 d, [^{14}C-triazole]-label (n= 1) 3.6% AR after 120 d, [^{14}C-benzyl methylene]-label (n= 1)
Non-extractable residues after 100 days	12.3% AR after 120 d, [^{14}C-triazole]-label (n= 1) 11.7% AR after 120 d, [^{14}C-benzyl methylene]-label (n= 1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None trigger assessment

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	1,2,4-triazole – 10.4 % AR at 8 d (equiv. to 32.6 days 40˚N summer sunlight) (n= 1) 4-chlorobenzaldehyde – 6.3 % AR at 8 d (equiv. to 32.5 days 40˚N summer sunlight) (n= 1)

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

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

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X[8]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20°C pF2/10kPa	St. (χ^2)	Method of calculation
Sandy loam[1]		5.3	20°C / pF2	294 / 977	294	2.8	SFO
Sandy clay loam[1]		7.2	20°C / pF2	170 / 564	170	3.5	SFO
Silt loam[1]		5.4	20°C / pF2	225 / 748	225	4.1	SFO
Clay loam[1]		6.5	20°C / pF2	184 / 612	184	5.6	SFO
Sandy loam[2]		7.7[3]	25°C / 75% 1/3 bar	194 / 998	391	2.5	DFOP (SFO for 20°C)
Geometric mean/median					240		SFO
Sandy clay loam		7.2	10°C / pF2	593 / 1969		1.7	SFO

[1] = EU soil, [2] = US soil, [3] = pH measured in water

1,2,4-triazole	Aerobic conditions						
Soil type	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f.	DT_{50} /DT_{90}(d) 20°C pF2/10kPa	St. (χ^2)	Method of calculation
Sandy loam (US soil)	7.7[3]	25°C / 75% 1/3 bar	136 / 453 76 / 251	0.62 1.0	213 / 711 119 / 394	20.4 42.9	DFOP-SFO SFO-SFO

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

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (χ^2)	DT_{50} (d) Norm.	Method of calculation
Silt loam, bare soil, incorporated	Hesse, Germany		7.2	0-20	96.3	320	16.42	-	SFO
Loam	Bavaria, Germany[1]		6.5	0-20	66	219	27.54	-	SFO
Clay	Italy[1]		7.4	0-20	135	264.3	10.15	-	HS[2]
Sandy loam	Spain[1]		7.5	0-20	228*	757*	19.46*	-	SFO
Geometric mean/median**					-	-	-	-	-

[1] application made to bare soil followed by incorporation

[2] HS kinetics calculated including initial lag phase where no degradation occurs (k1 = 0.000, k2 = 0.012, Tb = 79.361)

* dry soil conditions

** not calculated for non-normalised DT50/DT90 values as not all calculated using the same kinetics

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	No studies submitted. See PECsoil calculation

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

Field studies ‡

metabolite 1,2,4-triazole (applied as test compound)

(Endpoints derived from the Triazole Derivative Metabolite Group database, revised by UK, January 2013)

Location	Kinetic Model	un-normalised DT50 [days]	DT90 [days]	Visual Assess*	Chi^2
Germany	SFO	22.9	75.9	-	24.9
	FOMC	**7.8** **α 0.4454**	**366.7** **β 2.0966**	+	**15.2**
	DFOP	11.3 k1 0.1149	241.6 k2 0.0051 g 0.6602	O	18.5
Italy	SFO	48.8	162.2	O	17.9
	FOMC	16.3 α 0.3883	>1000 β 3.2894	+	11.3
	DFOP	**21.2** **k1 0.3500**	**207.4** **k2 0.0086** **g 0.4000**	+	**10.7**
UK	SFO	21.8	72.3	O	25.4
	FOMC	8.1 α 0.5728	188.4 β 3.4434	+	20.2
	DFOP	**6.8** **k1 0.4863**	**109.3** **k2 0.0154** **g 0.4633**	+	**17.8**
Spain	SFO	85.6	284.4	O	21.8
	FOMC	28.6 α 0.3618	>1000 β 4.9336	+	12.6
	DFOP	**28.1** **k1 0.0632**	**717.6** **k2 0.0020** **g 0.5732**	+	**13.3**

*Visual assessment: + = good O = medium -- = bad

1,2,4-triazole (applied as parent)	Aerobic conditions, kinetics calculated timestep **normalised to 20ºC and pF2 moisture** for modelling purpose. Bare soil with grass sown immediately after application (with exception of Spain site where no grass sown).								
Soil type	Location		pH	Depth (cm)	DT_{50} (d) Fast phase	DT_{50} (d) Slow phase	'g'	St. ($\chi 2$)	Method of calculation
Silt loam	Germany		6.4	0-30	2.5	70.7	0.655	18.8	DFOP
Silty clay loam	Italy		7.6	0-40	1.4	59.8	0.364	10.6	DFOP
Sandy loam	UK		7.4	0-40	0.5	25.1	0.458	18.1	DFOP
Loam	Spain		5.8	0-30	4.6	126.0	0.489	12.7	DFOP
Geometric mean ('g' value is arithmetic mean)					1.68	60.5	0.489		DFOP

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

Laboratory studies ‡

Parent	**Anaerobic conditions**						
Soil type	X[9]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Sandy loam (anaerobic part of study only)		5.6	20˚C	779 / 2587		0.5	SFO
Geometric mean/median			n.a.				
Parent	**Soil photolysis**						
Sandy loam		5.3	20˚C, dry	147 / 490[a]		3.7	SFO

[a] = DT50 and DT90 are equivalent days under 40˚N summer sunlight, assuming 12 hour day/night cycles

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	2.8	5.2			90	3214	0.7842
Sandy loam	5.6	7.1			107	1911	0.8073
Clay loam	4.3	7.1			108	2512	0.8077
Sandy loam	1.6	5.9			45	2813	0.8121
Silt loam	1.95	5.9			47	2410	0.8582
Loamy sand	0.3	6.2			5.2	1724	0.792
Arithmetic mean/median					67/68.5	2431/2461	0.81/0.81
pH dependence, Yes or No			No				

Metabolite 1,2-4 triazole ‡ **(Endpoints derived from the Triazole Derivative Metabolite Group database, January 2013)**							
Soil Type(USDA)	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	K_F (mL/g)	K_{Foc} (mL/g)	1/n
Silty clay	0.70	8.8			0.833	120	0.897
Clay loam	1.74	6.9			0.748	43	0.827

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

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

Sand	0.12	4.8			0.234	202	0.885[1]
Silty clay loam	0.70	7.0			0.722	104	0.922
Sandy loam	0.81	6.9			0.720	89	1.016
Arithmetic mean (of 4 values excluding the very low OC sand that was considered not representative of agricultural soils)					0.756	89	0.9155
pH dependence (yes or no)			No				

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

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

Column leaching ‡	Not submitted, not required
Aged residues leaching ‡	Aged for (d): 30 d Time period of elution (d): 2 d Elution (mm): 200 mm
	Analysis of soil residues post ageing (soil residues pre-leaching): not performed
	Leachate: undetectable (<0.1% AR) residues/radioactivity in leachate 96.9 – 99.7% AR retained in top 5 cm. 80.4 – 86.0% AR extractable, >99.9% of extractable comprised ipconazole. Radioactivity not detectable in any other column segment.

Lysimeter/ field leaching studies ‡	Not submitted, not required.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

PEC (soil) (Annex IIIA, point 9.1.3)

Parent ipconazole	DT_{50} (d): 391 days
Method of calculation	Kinetics: SFO Field or Lab: worst case from aerobic lab studies.
Application data	Crop: barley Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: seed treatment, therefore no crop interception Number of applications: 1 Interval (d): not applicable Application rate(s): 7 g as/ha

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.009			
Short term 24h	0.009	0.009		
2d	0.009	0.009		
4d	0.009	0.009		
Long term 7d	0.009	0.009		
28d	0.009	0.009		
50d	0.008	0.009		
100d	0.008	0.009		
Plateau concentration	Maximum 0.020 mg/kg after 10 yr Steady state 0.010 mg/kg after 10 years			

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

Metabolite 1,2,4-triazole Method of calculation	Calculated with Escape v 2.0 Parent DT50 391 days (SFO, worst case lab) or 228 days (SFO worst case field)* Metabolite DT_{50} (d): 28.1 days, DT90 717.6 days (k1 = 0.0632, k2 = 0.0020, g= 0.5732) Kinetics: DFOP Field or Lab: worst case from field studies. Formation fraction 1.0 Parent MW 333.9 g/mol Metabolite MW 69.1 g/mol
Application data	Crop: barley Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: seed treatment, therefore no crop interception Number of applications: 1 Interval (d): not applicable Application rate(s): 7 g as/ha

*Peak accumulated PECsoil for metabolite 1,2,4-triazole is 1 x 10^{-5} mg/kg (0.01 µg/kg) irrespective of parent DT50.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 4 or 5: *stable at 25°C and 50°C* Parent: 90.9 %AR (30 d, 25°C, pH 5), 95.3 %AR (7 d, 50°C, pH 4) No relevant metabolites >10%.
	pH 7: *stable at 25°C and 50°C* Parent: 96.4 %AR (30 d, 25°C), 101.5 %AR (7 d, 50°C) No relevant metabolites >10%.
	pH 9: *stable at 25°C and 50°C* Parent: 92.1 %AR (30 d, 25°C), 97.5 %AR (7 d, 50°C) No relevant metabolites >10%.
Photolytic degradation of active substance and metabolites above 10 % ‡	No data required, as there is no significant absorption of ipconazole at wavelengths above 290 nm.
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not applicable. Molar absorption co-efficient (ε) 11600 at 222 nm
Readily biodegradable ‡ (yes/no)	No

Degradation in water / sediment

Parent	Distribution (eg max in water 92.3 %AR after 0 d. Max. sed 87.7 %AR after 30 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90}* water	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Clay loam (Bury Pond)	7.44	7.7	20	241 799	0.93	2.0 17.6	>0.99	244 810	0.99	SFO
Sandy loam (Emperor Lake)	7.72	6.4	20	490 1628	0.85	2.8 19.3	>0.99	441 1466	>0.99	
Geometric mean/median			-	344 1141		2.4 18.4		328 1098		

* represents dissipation from water phase, calculated using FOMC kinetics. χ^2 values not available. Pseudo SFO DT50 (FOMC DT90/3.322) for water phase dissipation are 5.3 days (clay loam) and 5.8 days (sandy loam).

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

Maximum metabolite level, 5.8% AR at 59 DAT (metabolite M-1) in sediment. Maximum individual metabolite level in water, 1.4% AR at 0 DAT (metabolite ASd3).

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)
Clay loam (Bury Pond)	7.44	7.7	1.1	9.3 (100 DAT)	9.3
Sandy loam (Emperor Lake)	7.72	6.4	0.7	6.1 (100 DAT)	6.1

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

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

Parent ipconazole Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: v1.1 Molecular weight (g/mol): 333.9 Water solubility (mg/L): 11 mg/l (20°C)[1] K_{OC}/K_{OM} (L/kg): 2431 DT_{50} soil (d): 240 days (Lab geometric mean. In accordance with FOCUS SFO) DT_{50} water/sediment system (d): 344 days (representative worst case from sediment water studies) DT_{50} water (d): 1000 (default to represent no degradation as a.s. rapidly dissipated in water. In accordance with FOCUS Degradation Kinetics guidance.) DT_{50} sediment (d): 344 (geometric mean of total system DT50. In accordance with FOCUS Degradation Kinetics guidance) Crop interception (%): 0 [1] Note solubility in purified water of cc isomer = 9.34 mg/l; ct isomer = 4.97. Value used in calculations likely to result in lower simulated volatilisation losses.
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: SWASH 3.1, MACRO 4.4.2, PRZM 1.5.6 and TOXSWA 3.3.1 Vapour pressure: 3×10^{-6} Pa (25°C) Kom/Koc: 1410.09/ 2431 l/kg 1/n: (Freundlich exponent general or for soil, susp. solids or sediment respectively) 0.81 Q10: 2.58
Application rate	Crop: winter cereals and spring cereals Crop interception: 0 Number of applications: (i) 1 (single) (ii) 8 (split dose) Interval (d): (i) n/a (ii) 1 d Application rate(s): (i) 7 g as/ha (ii) 0.9 g as/ha Application window: <u>Step 1-2:</u> Crop type – no drift October-February, March – May and June-July. (Results shown for Oct-Feb, as these were higher

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

than for Mar-May and Jun-Jul). Step 3: Spring cereals (within 8 Mar-4 Jun, depending on scenario). Winter cereals (within 15 Sept – 31 Dec, depending on scenario). MACRO – 'soil incorporation' option. PRZM – CAM 8 option, DEPI 1 cm and 2cm Crop uptake factor - 0

Step 1, PECsw max 0.5501 µg/l, PECsed max 13.3739 µg/kg

Step 2, N Europe, October-February, PECsw max 0.2719 µg/l, PECsed max 6.6102 µg/kg

Step 2, N Europe, March - May, PECsw max 0.1088 µg/l, PECsed max 2.6441 µg/kg

Step 2, N Europe, June - September, PECsw max 0.1088 µg/l, PECsed max 2.6441 µg/kg

Step 2, S Europe, October-February, PECsw max 0.2175 µg/l, PECsed max 5.2881 µg/kg

Step 2, S Europe, March - May, PECsw max 0.2175 µg/l, PECsed max 5.2881 µg/kg

Step 2, S Europe, June - September, PECsw max 0.1631 µg/l, PECsed max 3.9661 µg/kg

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

FOCUSsw Step 3 Winter Cereals

Scenario	Water body	Max PECsw (µg/l)	Max PECsed (µg/kg)	TWA PECsw 21days (µg/l)	TWA PECsw 28days (µg/l)
D1	Ditch	<0.000001	<0.000001	Not calculable	Not calculable
	Stream	<0.000001	<0.000001	Not calculable	Not calculable
D2	Ditch	0.000009	0.000045	0.000001	0.000001
	Stream	0.000005	0.000016	<0.000001	<0.000001
D3	Ditch	<0.000001	<0.000001	Not calculable	Not calculable
D4	Pond	<0.000001	0.000003	<0.000001	<0.000001
	Stream	0.000003	0.000001	<0.000001	<0.000001
D5	Pond	<0.000001	0.000002	<0.000001	<0.000001
	Stream*	failed	failed	failed	failed
D6	Ditch*	failed	failed	failed	failed
R1[#]	Pond	0.00469	0.0909	0.00343	0.00317
	Stream	0.0318	0.0330	0.00166	0.00127
R3[#]	Stream	0.0372	0.0428	0.00178	0.00134
R4[#]	Stream	**0.0489**	0.0515	0.00213	0.00205

*Failed simulations: no PECs reported. Relevant TOXSWA reports showed substance concentration in drained water was 0.00 µg/l. Given the relative vulnerabilities of D5s and D6d and the relatively strong soil adsorption of ipconazole, the RMS considers is extremely unlikely that surface water concentrations as a result of drainage from these two sites would be greater than those predicted at D2.

[#] Results shown for Run-off (R) scenarios simulated assuming 1 cm seed depth.

Highest global maximum PECsw/sed and TWA 21 and 28 day PECsw values highlighted in **bold**.

Not calculable = 'simulated period too short'.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

FOCUSsw Step 3 Spring Cereals

Scenario	Water body	Max PECsw (µg/l)	Max PECsed (µg/kg)	TWA PECsw 21days (µg/l)	TWA PECsw 28days (µg/l)
D1	Ditch	<0.000001	<0.000001	Not calculable	Not calculable
	Stream	<0.000001	<0.000001	<0.000001	<0.000001
D3	Ditch	<0.000001	<0.000001	Not calculable	Not calculable
D4	Pond	<0.000001	0.000007	<0.000001	<0.000001
	Stream	0.000003	0.000002	<0.000001	<0.000001
D5	Pond	<0.000001	0.000002	<0.000001	<0.000001
	Stream*	failed	failed	failed	failed
R4 #	Stream	**0.0430**	**0.0837**	**0.00595**	**0.00447**

*Failed simulations: no PECs reported. Relevant TOXSWA reports showed substance concentration in drained water was 0.00 µg/l.

Results shown for Run-off (R) scenarios simulated assuming 1 cm seed depth.

Highest global maximum PECsw/sed and TWA 21 and 28 day PECsw values highlighted in **bold**.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

Pseudo PECsw for use in ipconazole risk assessment for sediment dwelling organisms

Using the outputs from the FOCUS SW Step 1 and 2 results, the total loading (mg/m^2) into the water body from drift and from run-off/ drainage was multiplied by 3.32 (a conversion factor of mg/m^2 to µg/l for a static 30 cm deep water body) as shown below.

FOCUSsw Step 1-2 Outputs:

At Step 1: loading to water body via drift = 0.00 mg/m^2
Loading to water body via run-off/drainage = 0.700 mg/m^2
(0.00 + 0.7) x 3.32 = 2.324 µg/l

At Step 2: loading to water body via drift = 0.00 mg/m^2
Loading to water body via run-off/drainage = 0.3460 mg/m^2
(0.00 + 0.3460) x 3.32 = 1.149 µg/l

Potential for ipconazole accumulation in sediment

As degradation of ipconazole in sediment occurs slowly, (geometric mean DT50 of 328 days), the potential for accumulation of residues in this compartment needs to be considered.

Pseudo PECsw values of 2.324 µg/l and 1.149 µg/l have been calculated above, using the FOCUSsw Step 1 and 2 outputs, respectively. DT50 values for ipconazole in the two sediment systems tested i.e. 244 d and 441 d, can be assumed to give rise to accumulation factors of *ca* 1.6x and 2.3x respectively.

The highest PEC from a single application (i.e. pseudo PECsw values above) can be multiplied by these accumulation factors:

Step 1 pseudo PECsw: 2.324 µg/l x 1.6 (acc. factor for DT50 244d) = 3.72 µg/l
2.324 µg/l x 2.3 (acc. factor for DT50 441d) = 5.35 µg/l

Step 2 pseudo PECsw: 1.149 µg/l x 1.6 (acc. factor for DT50 244d) = 1.84 µg/l
1.149 µg/l x 2.3 (acc. factor for DT50 441d) = 2.65 µg/l

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

1,2,4-triazole Steps 1-2

Parameters used in PECsw model for 1,2,4-triazole (FOCUS Steps 1-2)

Parameter	Value
Molecular mass of a.s.	333.9
Molecular mass of 1,2,4-triazole	69.1
Water solubility	700,000 mg/l
K_{OC}	89 l/kg
DT_{50} in soil	60.5 days
DT_{50} in water	300 days [c]
DT_{50} in sediment	300 days
DT_{50} in the total water/sediment system	300 days
Maximum occurrence in water/sediment	0.001%
Maximum occurrence in soil	23.7%
Application rate	7 g/ha
Number of applications	1
Crop interception	'no interception'
Crop type	'no drift (incorporated or seed treatment)'

1,2,4-triazole was not detected in water/sediment studies. As FOCUSsw Steps 1-2 cannot accept a value of 0 for occurrence in studies, a nominal value of 0.001% was input. DT50 in water and sediment was set at a default value of 300 days.

FOCUS Step 1 PECsw/sed values for 1,2,4-triazole from ipconazole

DAT	Water (µg/l)		Sediment (µg/kg dry weight)	
	Actual PEC	TWA PEC	Actual PEC	TWA PEC
0	**0.1023**	-	**0.0910**	-
1	0.1021	0.1022	0.0908	0.0909
2	0.1018	0.1021	0.0906	0.0908
4	0.1014	0.1018	0.0902	0.0906
7	0.1007	0.1015	0.0896	0.0903
14	0.0990	0.1007	0.0882	0.0896
21	0.0975	0.0999	0.0867	0.0889
28	0.0959	0.0991	0.0853	0.0882
42	0.0928	0.0975	0.0826	0.0868
50	0.0911	0.0966	0.0811	0.0860
100	0.0812	0.0913	0.0723	0.0813

TWA Time-weighted average.
Highest global maximum PECsw/sed highlighted in bold.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

FOCUS Step 2 PECsw/sed values for 1,2,4-triazole from ipconazole (N. EU)

Northern Europe

Time after max. (days)	October - February				March - May			
	Water (µg/L)		Sediment (µg/kg dry weight)		Water (µg/L)		Sediment (µg/kg dry weight)	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max.	**0.0489**	-	**0.0435**	-	0.0195	-	0.0174	-
1	0.0487	0.0488	0.0434	0.0434	0.0195	0.0195	0.0174	0.0174
2	0.0486	0.0487	0.0433	0.0434	0.0195	0.0195	0.0173	0.0174
4	0.0484	0.0486	0.0431	0.0433	0.0194	0.0195	0.0172	0.0173
7	0.0481	0.0485	0.0428	0.0431	0.0192	0.0194	0.0171	0.0173
14	0.0473	0.0481	0.0421	0.0428	0.0189	0.0192	0.0168	0.0171
21	0.0465	0.0477	0.0414	0.0424	0.0186	0.0191	0.0166	0.0170
28	0.0458	0.0473	0.0408	0.0421	0.0183	0.0189	0.0163	0.0168
42	0.0443	0.0466	0.0395	0.0414	0.0177	0.0186	0.0158	0.0166
50	0.0435	0.0461	0.0387	0.0411	0.0174	0.0185	0.0155	0.0164
100	0.0388	0.0436	0.0345	0.0388	0.0155	0.0175	0.0138	0.0155

TWA Time-weighted average
Highest global maximum PECsw/sed values highlighted in **bold**.

Table B.8.43 Applicant's FOCUS Step 2 PECsw/sed values for ipconazole (S. EU)

Southern Europe

Time after max. (days)	October - February				March - May			
	Water (µg/L)		Sediment (µg/kg dry weight)		Water (µg/L)		Sediment (µg/kg dry weight)	
	Actual	TWA	Actual	TWA	Actual	TWA	Actual	TWA
Max.	**0.0391**	-	**0.0348**	-	**0.0391**	-	**0.0348**	-
1	0.0390	0.0390	0.0347	0.0347	0.0390	0.0390	0.0347	0.0347
2	0.0389	0.0390	0.0346	0.0347	0.0389	0.0390	0.0346	0.0347
4	0.0387	0.0389	0.0345	0.0346	0.0387	0.0389	0.0345	0.0346
7	0.0385	0.0388	0.0342	0.0345	0.0385	0.0388	0.0342	0.0345
14	0.0378	0.0385	0.0337	0.0342	0.0378	0.0385	0.0337	0.0342
21	0.0372	0.0382	0.0331	0.0340	0.0372	0.0382	0.0331	0.0340
28	0.0366	0.0379	0.0326	0.0337	0.0366	0.0379	0.0326	0.0337
42	0.0355	0.0373	0.0316	0.0332	0.0355	0.0373	0.0316	0.0332
50	0.0348	0.0369	0.0310	0.0329	0.0348	0.0369	0.0310	0.0329
100	0.0310	0.0349	0.0276	0.0311	0.0310	0.0349	0.0276	0.0311

TWA Time-weighted average
Highest global maximum PECsw/sed values highlighted in **bold**.

At FOCUS Step 2 the highest PEC values for 1,2,4-triazole were for N. Europe, October – February, with a maximum PECsw and PECsed of 0.0489 µg/l and 0.0435 µg/kg, respectively occurring on day 0.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PEARL v.4.4.4 Crop: (i) spring cereals (ii) winter cereals Scenarios: spring cereals: (i) Châteaudun, Hamburg, Kremsmünster, Okehampton, Jokioinen, Porto winter cereals: (ii) Châteaudun, Hamburg, Kremsmünster, Okehampton, Jokioinen, Piacenza, Porto, Sevilla, Thiva Parent Molecular weight = 333.9 Geometric mean parent DT_{50lab} = 240 d (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.58). K_{OM}: parent, arithmetic mean 1410 ml/g, $^1/_n$= 0.81. Vapour pressure = $3x10^{-6}$ Pa at 25°C Solubility = 11 mg/l at 20°C Metabolite 1,2,4-triazole Molecular weight = 69.1 Geometric mean DT_{50lab} = 60.5 d at 20°C at pF2 Formation fraction = 0.2 K_{OM}: 51.6 ml/g, $^1/_n$= 0.9155. Vapour pressure = $1x10^{-10}$ Pa at 20°C Solubility = 700,000 mg/l at 20°C Plant uptake factor for simulated substances – 0 Soil incorporation taken into account, PEARL incorporation depth 0.05m.
Application rate	Application rate: 7 g/ha. No. of applications: 1 Time of application (month or season): Relative applications, 7 days before emergence for all scenarios and both crops.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

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

	Scenario	Ipconazole (µg/L)	Metabolite (µg/l)
			1,2,4-triazole
PEARL /spring cereals	Châteaudun	<0.001	<0.001
	Hamburg	<0.001	0.001
	Jokioinen	<0.001	<0.001
	Kremsmünster	<0.001	0.001
	Okehampton	<0.001	0.001
	Porto	<0.001	<0.001

	Scenario	Ipconazole (µg/L)	Metabolite (µg/L)
			1,2,4-triazole
PEARL /winter cereals	Châteaudun	<0.001	<0.001
	Hamburg	<0.001	0.001
	Jokioinen	<0.001	<0.001
	Kremsmünster	<0.001	<0.001
	Okehampton	<0.001	0.001
	Piacenza	<0.001	<0.001
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	<0.001

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

Direct photolysis in air ‡	No data submitted. None are required, based on intended use of ipconazole as a seed treatment, limiting exposure to air.
Quantum yield of direct phototransformation	No data submitted. None are required.
Photochemical oxidative degradation in air ‡	DT_{50} of 5.1 hours derived by the Atkinson model (version 1.88). OH (12h) concentration assumed = 1.5×10^6 per cm^3.
Volatilisation ‡	No data submitted. None are required, based on vapour pressure of 3×10^{-6} Pa at 25°C, Henry's Law constant of 3×10^{-5} $Pa.m^3.mol^{-1}$ and intended use of ipconazole as a seed treatment
Metabolites	Not relevant.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Fate and behaviour in the environment

PEC (air)

Method of calculation	PECair not calculated, nor required. Expert judgement, based on low vapour pressure, dimensionless Henry's Law Constant and intended use of ipconazole as a seed treatment.

$PEC_{(a)}$

Maximum concentration	Considered likely to be negligible.

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil : parent, 1,2,4-triazole Surface Water: parent, 1,2,4-triazole Sediment: parent, 1,2,4-triazole Ground water: parent, 1,2,4-triazole Air: parent

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

Soil (indicate location and type of study)	New active substance, none available
Surface water (indicate location and type of study)	New active substance, none available
Ground water (indicate location and type of study)	New active substance, none available
Air (indicate location and type of study)	New active substance, none available

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

Candidate for R53

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ǂ				
Colinus virginianus	ipconazole	Acute	LD_{50} 962 mg a.s./kg bw	-
Colinus virginianus	ipconazole	Short-term	LDD_{50} >300.0 mg a.s./kg bw/day	LC_{50} >5620 mg a.s./kg feed
Colinus virginianus	ipconazole	Long-term	NOEL: 4.3 mg a.s./kg bw/day	NOEC: 50 mg a.s./kg feed
Anas platyrhynchos	ipconazole	Long-term	NOEL: 27.1 mg a.s./kg bw/day	NOEC: 200 mg a.s./kg feed
Mammals ǂ				
Mouse (female)	ipconazole	Acute	468 mg a.s./kg bw	-
Rat (female)	Crusoe'[1]	Acute	>2000 mg formulation/kg bw	-
Rat	ipconazole	Long-term	8 mg a.s./kg bw/day	100 mg/kg feed
Additional higher tier studies ǂ				
no data available				

[1]'Crusoe' micro-emulsion seed treatment containing 15 g ipconazole/L

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

Seed treatment to spring and winter sown cereals, seed loading of 20 mg a.s./kg seed.

Indicator species/Category	Time scale	Toxicity endpoint mg a.s./kg bw/day	DDD mg a.s./kg bw/day	TER[1]	Annex VI Trigger
Tier 1 (Birds)					
Granivorous bird	Acute	LD_{50} 962 mg a.s./kg bw	6 mg a.s./kg bw/day	160	10

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

Indicator species/Category	Time scale	Toxicity endpoint mg a.s./kg bw/day	DDD mg a.s./kg bw/day	TER[1]	Annex VI Trigger
Herbivorous bird	Acute	LD_{50} 962 mg a.s./kg bw	2 mg a.s./kg bw/day[4]	481	10
Granivorous bird	Long-term	NOEL: 4.3 mg a.s./kg bw/day	6 mg a.s./kg bw/day	**0.717**	5
Herbivorous bird[2]	Long-term	NOEL: 4.3 mg a.s./kg bw/day	2 mg a.s./kg bw/day[4]	**2.15**	5
Earthworm-eating bird[2]	Long-term	NOEL: 4.3 mg a.s./kg bw/day	0.232 mg a.s./kg bw/day	18.5	5
Fish-eating bird[2]	Long-term	NOEL: 4.3 mg a.s./kg bw/day	0.0248 mg a.s./kg bw/day	174	5
Higher tier refinement: risk to granivorous and herbivorous birds					
Granivorous bird (refined TWA and geometric mean endpoint)	Long-term	NOEL: 10.8 mg a.s./kg bw/day	1.30 mg a.s./kg bw/day	8.29	5
Granivorous bird (refined TWA and lowest endpoint)	Long-term	NOEL: 4.3 mg a.s./kg bw/day	1.30 mg a.s./kg bw/day	**3.30**	5
Skylark (refined TWA, FIR/bw and PD) [3]	Long-term	NOEL: 4.3 mg a.s./kg bw/day	0.358 mg a.s./kg bw/day	12.0	5
Woodpigeon (refined TWA, FIR/bw)	Long-term	NOEL: 4.3 mg a.s./kg bw/day	0.577 mg a.s./kg bw/day	7.45	5
Yellowhammer (refined TWA, FIR/bw and PD) [3]	Long-term	NOEL: 4.3 mg a.s./kg bw/day	1.25 mg a.s./kg bw/day	**3.44**	5
Herbivorous bird (refined residue value)[2]	Long-term	NOEL: 4.3 mg a.s./kg bw/day	0.01 mg a.s./kg bw/day[4]	430	5
Tier 1 (Mammals)					

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

Indicator species/Category	Time scale	Toxicity endpoint mg a.s./kg bw/day	DDD mg a.s./kg bw/day	TER[1]	Annex VI Trigger
Granivorous mammal	Acute	468 mg a.s./kg bw/day	4.8 mg a.s./kg bw/day	97.5	10
Granivorous mammal	Long-term	8 mg a.s./kg bw/day	4.8 mg a.s./kg bw/day	**1.67**	5
Herbivorous mammal	Acute	468 mg a.s./kg bw/day	0.96 mg a.s./kg bw/day	488	10
Herbivorous mammal[2]	Long-term	8 mg a.s./kg bw/day	0.96 mg a.s./kg bw/day	8.33	5
Earthworm-eating mammal[2]	Long-term	8 mg a.s./kg bw/day	0.283 mg a.s./kg bw/day	28.3	5
Fish-eating mammal[2]	Long-term	8 mg a.s./kg bw/day	0.0221 mg a.s./kg bw/day	362	5
Higher tier refinement (Mammals)					
Granivorous mammal (refined TWA)	Long-term	8 mg a.s./kg bw/day	1.04 mg a.s./kg bw/day	7.68	5

TERs highlighted in **bold** are less than the respective Annex VI trigger value

[2] No TWA was considered in the risk assessment for earthworm-eating, fish-eating and herbivorous birds and mammals.

[3] Residues in other feed items such as seedlings were not taken into account

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]
Laboratory tests ǂ				
Fish				
Oncorhynchus mykiss	ipconazole	96 hr (flow-through)	Mortality, $_{mm}LC_{50}$	1.5 mg a.s./L
Lepomis macrochirus	ipconazole	96 hr (flow-through)	Mortality, $_{mm}LC_{50}$	1.3 mg a.s./L

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1]
Pimephales promelas	ipconazole	Early-life stage (flow-through)	$_{mm}$NOEC: based on fry weight and length	0.44 µg a.s./L
Oncorhynchus mykiss	'Crusoe'	96 hr (flow-through)	Mortality, $_{mm}LC_{50}$	0.977 mg a.s./L
Aquatic invertebrate				
Daphnia magna	ipconazole	48 h (flow-through)	Mortality, $_{mm}EC_{50}$	1.7 mg a.s./L
Daphnia magna	ipconazole	21 d (static)	Reproduction, $_{mm}$NOEC	10.9 µg a.s./L[2]
Daphnia magna	'Crusoe'	48 h (static)	Mortality, $_{mm}EC_{50}$	95.7 mg formulation/L (1.33 mg a.s./L)
Sediment dwelling organisms				
Chironomus riparius	ipconazole	28 d (spiked water, static)	NOEC, emergence and development rate	3.52 mg a.s./L (highest dose tested)
Algae				
Pseudokirchneriella subcapitata	ipconazole	72 h (static)	Biomass: $_{mm}E_bC_{50}$	0.62 mg a.s./L
			Growth rate: $_{mm}E_rC_{50}$	>2.2 mg a.s./L
Pseudokirchneriella subcapitata	'Crusoe'	72 h (static)	Biomass: $_{mm}E_bC_{50}$	45.6 mg formulation/L (0.634 mg a.s./L)
			Growth rate: $_{mm}E_rC_{50}$	E_rC_{50} = 185 mg formulation/L (2.57 mg a.s./L)
Microcosm or mesocosm tests				
No data available - Not required.				

[1] Nominal ($_{nom}$) or mean measured concentrations ($_{mm}$).
[2] Based on the arithmetic mean concentration

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

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

FOCUS Step1

7 g a.s./ha application rate as a seed treatment to winter and spring sown cereals

Test substance	Time scale	Organism	Toxicity endpoint µg a.s./L (mg/L 1,24-triazole)		FOCUS Step 1 initial PEC µg a.s./L	TER	Annex VI trigger value
ipconazole	Acute	Fish	LC_{50}	1300	0.5501	2363.2	100
ipconazole	chronic	Fish	NOEC	0.44	0.5501	**0.8**	10
ipconazole	Acute	Aquatic invertebrate	EC_{50}	1700	0.5501	3090.3	100
ipconazole	Chronic	Aquatic invertebrates	NOEC	10.9	0.5501	19.8	10
ipconazole	-	Algae	E_bC_{50}	620	0.5501	1127.1	10
			E_rC_{50}	>2200	0.5501	3999.3	10
1,2,4-triazole	Acute	Fish	LC_{50}	498[1]	0.1023	4868035	100
1,2,4-triazole	chronic	Fish	NOEC	3.2[1]	0.1023	31281	10
1,2,4-triazole	Acute	Aquatic invertebrates	EC_{50}	> 100[1]	0.1023	977517	100
1,2,4-triazole	-	Algae	E_bC_{50}	8.2[1]	0.1023	80156	10
			E_rC_{50}	22.5[1]	0.1023	219941	10

TERs highlighted in **bold** are less than the respective Annex VI trigger value

[1:] endpoints derived from PRAPeR expert meeting 13 (2007)

FOCUS Step 2

7 g a.s./ha application rate as a seed treatment to winter and spring sown cereals

Test substance	Time scale	Organism	Toxicity endpoint µg a.s./L	FOCUS Step 2 initial PEC µg a.s./L	TER	Annex VI trigger value

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

ipconazole	chronic	Fish	NOEC	0.44	0.2716	**1.62**	10
ipconazole	chronic	Sediment dwelling invertebrate	NOEC	3520	5.35[1]	658	10

TERs highlighted in **bold** are less than the respective Annex VI trigger value
[1] Accumulated pseudo PECsw value

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Scenario water body combination	FOCUS Step 3 max PEC µg a.s./L	Chronic fish NOEC µg a.s./L	FOCUS step 3 TER	Annex VI trigger value
8 x 0.875 g a.s./ha seed treatment application to winter cereals*				
D1 Ditch	<0.000001	0.44	440000	10
D1 Stream	<0.000001	0.44	440000	10
D2 Ditch	0.000009	0.44	48889	10
D2 Stream	0.000005	0.44	88000	10
D3 Ditch	<0.000001	0.44	440000	10
D4 Pond	<0.000001	0.44	440000	10
D4 Stream	0.000003	0.44	146667	10
D5 Pond	<0.000001	0.44	440000	10
R1[#] Pond	0.00469	0.44	93.8	10
R1 Stream	0.0318	0.44	13.8	10
R3[#] Stream	0.0372	0.44	11.8	10
R4[#] Stream	**0.0489**	0.44	**9.00**	10
8 x 0.875 g a.s./ha seed treatment application spring cereals*				
D1 Ditch	<0.000001	0.44	440000	10
D1 Stream	<0.000001	0.44	440000	10
D3 Ditch	<0.000001	0.44	440000	10
D4 Pond	<0.000001	0.44	440000	10
D4 Stream	0.000003	0.44	146667	10
D5 Stream	<0.000001	0.44	440000	10
D5 Pond	<0.000001	0.44	440000	10
R4 [#] Stream	0.0430	0.44	10.2	10

TERs highlighted in **bold** are less than the respective Annex VI trigger value.
* FOCUS surface water modelling assumed a split application of 8 applications of 0.875 g a.s./ha to reflect the slow release of ipconazole from the treated seed.

Bioconcentration

Parameter	Value
Log P_{ow}	4.65 for the cis-isomer and 4.44 for the trans-isomer

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

Bioconcentration factor (BCF) (whole-fish)	283
Annex VI Trigger for the bioconcentration factor	100*
Clearance time (days) (CT_{50})	0.37 days
(CT_{90})	1.61 days

* ipconazole is not readily bio-degradable (Section B.8.4.3) and therefore the Annex VI trigger value is 100.

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

Test substance	Acute oral toxicity	Acute contact toxicity
ipconazole ǂ	LD_{50} >100 µg a.s./bee	LD_{50} >100 µg a.s./bee
Field or semi-field tests		
~~Indicate if not required~~ No data available		

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

Test substance	Route	Hazard quotient	Annex VI Trigger
ipconazole	Contact	n/a[1]	50
ipconazole	oral	n/a[1]	50

[1] Calculation of hazard quotients not suitable for a.s. which are proposed only for seed treatment use.

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ǂ	'CA11F317L'	Mortality	7-day LR_{50} = 17.4 g a.s./ha
Aphidius rhopalosiphi ǂ	'CA11F317L'	Mortality	48-hour LR_{50} = 35.1 g a.s./ha

'CA11F317L': soluble concentrate (SL) formulation containing 9.21% w/w ipconazole

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

Further laboratory and extended laboratory studies ǂ

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)[1]	End point	% effect	Trigger value
Pardosa spp.[2]	Adult	'Crusoe' treated wheat seed	Sowing rate of 30 seeds/64 cm^2 (equivalent to 3500 kg seed/ha); 1.81 g a.s./100 kg seed	Mortality Prey consumption	Compared to unseeded control: **Mortality: 11.5%** **Mean prey consumption: 1% reduction** at	30 %[1]
Aleochara bilineata	Adult	'Crusoe' treated wheat seed	Sowing rate of 90 seeds/176 cm^2 (equivalent to 3500 kg seed/ha) 1.81 g a.s./100 kg seed	Reproductive capacity	Compared to the seeded control **Reduction in reproduction: 11%**	30 %[1]

[1] ESCORT 1 trigger value of 30%
[2] Validity criterion for control mortality was not met

Risk assessment
Calculation of ESCORT 2 Hazard Quotients are not appropriate for active substances which are to be used as seed treatments. Off-field: Risk acceptable on the basis there is very limited exposure to off-crop environments from the proposed use as a seed treatment. In-field: Risk acceptable on the basis that there were less than 30% (i.e. ESCORT 1 trigger value) effects on *Aleochara bilineata* and *Paradosa spp.* at 10 times the maximum sowing density of 350 kg seed/ha. Also, ipconazole is of low toxicity to *Aphidius rhopalosiphi* and *Typhlodromus pyri*.

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

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			
	ipconazole ǂ	Acute 14 days	LC_{50} 597 mg a.s./kg d.w. soil
			LC_{50CORR}: 298.5 mg a.s./kg d.w. soil[1]
	ipconazoleǂ	Chronic 8 weeks	NOEC: 0.78 mg a.s./kg d.w. soil
			$NOEC_{CORR}$: 0.39 mg a.s./kg d.w. soil[1]
Soil micro-organisms			
Nitrogen mineralisation	Ipconazole ǂ	28-day	-17.08% effect at day 28 at 2.88 mg a.s./kg soil (10 x 108 g a.s./ha)
Carbon mineralisation	Ipconazole ǂ	28-day	16.3% effect at day 28 at 2.88 mg a.s./kg soil (10 x 108 g a.s./ha)
Field studies			
~~None required~~ No data available			

[1] Log P_{ow} of ipconazole is 4.65 for the cis-isomer and 4.44 for the trans-isomer, therefore endpoints corrected to take in to account the different amount of organic carbon in laboratory and field soils

Toxicity/exposure ratios for soil organisms

Seed treatment to spring and winter sown cereals at equivalent to 7 g a.s./ha

Test organism	Test substance	Time scale	Initial soil PEC mg a.s./kg dw soil	TER	Trigger
Earthworms	ipconazole ǂ	Acute	0.02	14925	10
	ipconazole. ǂ	Chronic	0.02	19.5	5
	1,2,4-triazole[1]	Acute	0.00001	1000000000	10
	1,2,4-triazole[1]	Chronic	0.00001	100000	5
Collembola	1,2,4-triazole[1]	Chronic	0.00001	180000	5

[1]: toxicological endpoints derived from PRAPeR expert meeting 13 (2007)

List of end points (based on EPCO Manual E4 - rev. 4 (September 2005))

Rapporteur Member State	Month and year	Active Substance (Name)
United Kingdom	January 2013	Ipconazole

Ecotoxicology

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

Ipconazole cc and ct isomers showed a high fungicidal activity against a wide range of plant disease pathogens, both in laboratory (culture) and green house tests, and as both a seed treatment and a spray application. Both isomers showed similar fungicidal activities against the pathogens.

The plant growth regulatory activity of ipconazole ct was slightly higher than that of ipconazole cc when seeds of plant were treated in the chemical solution.

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

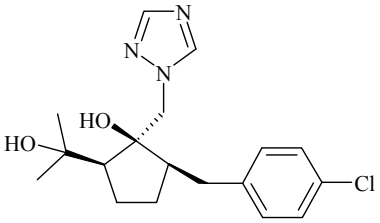
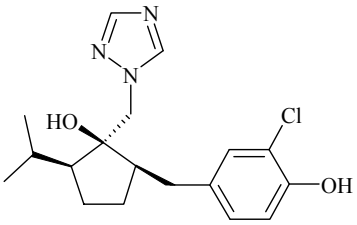
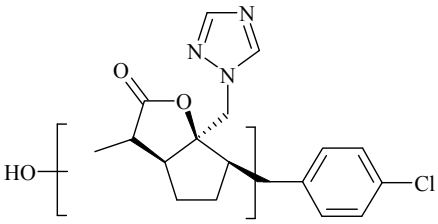
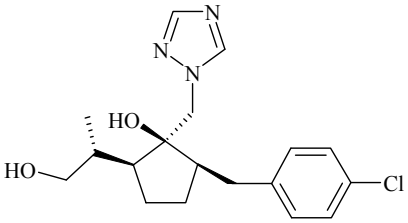
Test type/organism	end point
Activated sludge	EC_{50} >100 mg a.s./L

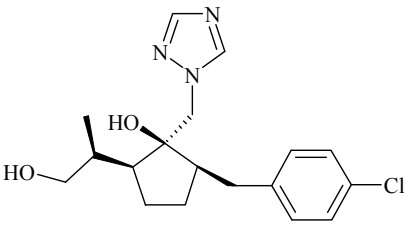
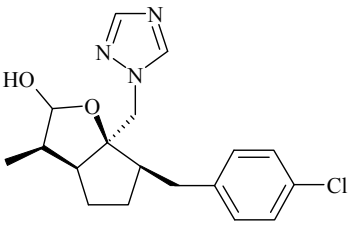
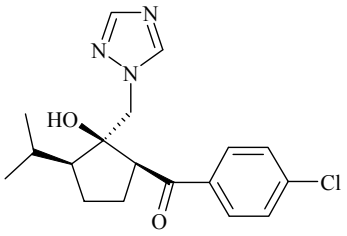
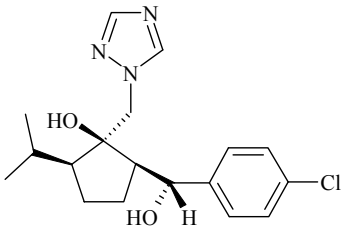
Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

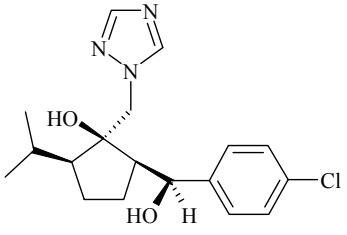
Compartment	
soil	ipconazole
water	ipconazole
sediment	ipconazole

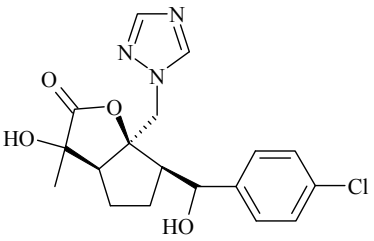
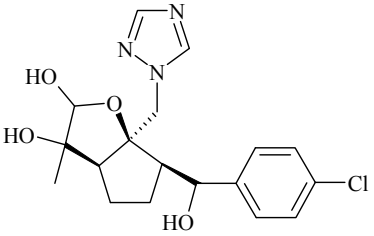
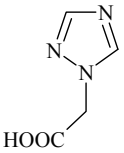
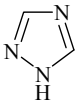
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	N R50 R53, H410

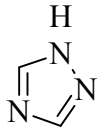
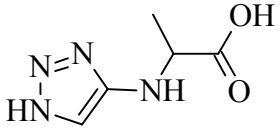
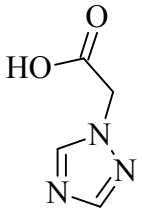
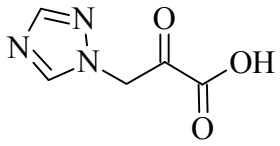
Code/Trivial name	Chemical name	Structural formula
KNF-317-M-1	(1*RS*,2*SR*,5*RS*)-2-(4-chlorobenzyl)-5-(1-hydroxy-1-methylethyl)-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclo pentanol	
KNF-317-M-2	(1*RS*,2*SR*,5*RS*)-2-(3-chloro-4-hydroxybenzyl)-5-isopropyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclo pentanol	
KNF-317-M-4		
KNF-317-M-5	(1*RS*,2*SR*,5*RS*)-2-(4-chlorobenzyl)-5-[(1*SR*)-2-hydroxy-1-methylethyl]-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

Code/Trivial name	Chemical name	Structural formula
KNF-317-M-6	(1*RS*,2*SR*,5*RS*)-2-(4-chlorobenzyl)-5-[(1*RS*)-2-hydroxy-1-methylethyl]-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
KNF-317-M-7,8	(3*RS*,3a*SR*,6*RS*,6a*SR*)-6-(4-chlorobenzyl)-3,3a,4,5,6,6a-hexahydro-2-hydroxy-3-methyl-6a-(1*H*-1,2,4-triazol-1-ylmethyl)-2H-cyclopenta [b]furan.	
KNF-317-M-11	(1*RS*,2*SR*,5*SR*)-2-(4-chlorobenzoyl)-5-isopropyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
KNF-317-M-12	(1*RS*,2*RS*,5*SR*)-2-[(1*RS*)-(4-chlorophenyl)hydroxymethyl]-5-isopropyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

Code/Trivial name	Chemical name	Structural formula
KNF-317-M-13	(1*RS*,2*RS*,5*SR*)-2-[(1*SR*)-(4-chlorophenyl)hydroxymethyl]-5-isopropyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

KNF-317-M-14	(3a*RS*,6*RS*,6a*SR*)-6-[(4-chlorophenyl)hydroxymethyl]-3,3a,4,5,6,6a-hexahydro-3-hydroxy-3-methyl-6a-(1*H*-1,2,4-triazol-1-ylmethyl)-2H-cyclopenta[b]furan-2-one.	
KNF-317-M-18,19	(3a*SR*,6*RS*,6a*SR*)-6-[(4-chlorophenyl)hydroxymethyl]-2,3-dihydroxy-3,3a,4,5,6,6a-hexahydro-3-methyl-6a-(1*H*-1,2,4-triazol-1-ylmethyl)-2H-cyclopenta[b]furan-2-one	
KNF-317-M-21	1*H*-1,2,4-triazole-1-acetic acid	
KNF-317-M-22	1*H*-1,2,4-triazole	

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name**	Structural formula**
1,2,4-triazole	1H-1,2,4-triazole	
Triazole alanine	N-1H-1,2,3-triazol-4-ylalanine	
Triazole acetic acid	1H-1,2,4-triazol-1-ylacetic acid	
Triazole pyruvic acid	2-oxo-3-(1H-1,2,4-triazol-1-yl)propanoic acid	

* The metabolite name in bold is the name used in the conclusion.
** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

(Please highlight additional entries in Turquoise)

1/n	slope of Freundlich isotherm
λ	wavelength
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
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 Abstracts Service
CFU	colony forming units
cGAP	Critical good agricultural practice
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FID	flame ionisation detector
FIR	Food intake rate

FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
ME	Micro-emulsion
mg	milligram
mL	millilitre
mm	millimetre
mN	milli-newton
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity

NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NPD	nitrogen phosphorous detector
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
Pa	pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
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
PRIMo	Pesticides Residue Intake Model
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
REACH	Registration, Evaluation, Authorisation of CHemicals
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TDM	Triazole Derivate Metabolite
TDMG	Triazole Derivate Metabolite Group
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