Conclusion regarding the peer review of the pesticide risk assessment of the active substance

epoxiconazole

Finalised: 26 March 2008

SUMMARY

Epoxiconazole is one of the 79 substances of the third stage Part A of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Germany being the designated rapporteur Member State submitted the DAR on epoxiconazole in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 28 April 2005. The peer review was initiated on 7 October 2005 by dispatching the DAR for consultation of the Member States and the sole applicant BASF as identified by the rapporteur Member State. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed on during a written procedure in July – September 2006. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in March 2007 (in all sections) and in May 2007 (only ecotox).

A final discussion of the outcome of the consultation of experts took place in a written procedure with the Member States in February-March 2008 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as a fungicide on cereals and sugar beet. Full details of the GAP can be found in the attached end points. The representative formulated product for the evaluation was "Opus", a suspension concentrate (SC).
Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (The German S19 method has been validated). For the other matrices only single methods are available to determine residues of epoxiconazole.

[1] OJ No L 224, 21.08.2002, p. 25, as last amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. It has been identified that more information is necessary to enable the impact of potential different isomer ratios on the risk assessments to be better characterised

Mammalian toxicology of epoxiconazole was assessed in a row of tests. Epoxiconazole is absorbed rapidly but only to a limited extent (about 50%) after oral administration in rats. It is widely distributed in the body and although epoxiconazole has no potential for accumulation its elimination is slow. The substance is mainly excreted via faeces (about 78%) and urine (about 17%). Metabolism is rapid and extensive. At least 47 different metabolites have been identified in the rat. The active substance is of low acute toxicity by the oral, dermal and inhalation route. It is neither irritant to the skin nor to the eyes and has no skin sensitising potential.

The liver has been identified as the main target of toxicity in repeated dose tests with rats, mice and dogs. Epoxiconazole does not have genotoxic potential *in vitro* and *in vivo*. In a 24-months study in rats liver toxicity was observed and additionally ovary- and adrenal gland tumours were seen. In a 18-month carcinogenicity study in mice a treatment related increase in liver tumours has been observed based on which a classification of epoxiconazole as Xn; Carc. Cat. 3 R40 "Harmful; Limited evidence of a carcinogenic effect" was proposed. Based on the effects on reproduction seen in a two-generation study in rats (dystocia, impaired fertility, prolonged gestation and vaginal haemorrhages) it was concluded to propose a classification with Xn; Repr. Cat. 3 R62 "Harmful; Possible risk of impaired fertility". Based on developmental effects such as increases in number of resorptions, skeletal variations and malformations observed in relevant studies in rats and rabbits also a classification with Xn; Repr. Cat. 3 R 63 "Harmful; Possible risk of harm to the unborn child" was proposed. Results from new *in vitro* studies and a new developmental study in rats confirm that epoxiconazole has endocrine disrupting properties but do not merit changing relevant NOAELs or revising the proposed classification according to an evaluation by the rapporteur Member State. However, these new data have not been peer reviewed.

The acceptable daily intake (ADI) is 0.008 mg/kg bw/d derived from an 18-month carcinogenicity study in mice applying a safety factor of 100. An acute reference dose (ARfD) of 0.023 mg/kg bw has been derived based on the effects observed in two generation reproduction study in rats applying a safety factor of 100. The acceptable operator exposure level (AOEL) of 0.008 mg/kg bw/d was derived from a subchronic dog study applying a safety factor of 100. In consideration of a dermal absorption of 50% both for the concentrate and the diluted preparation (the default value agreed upon by the majority of experts at PRAPeR 19, March 2007) the exposure estimates for operators were 39% and 700% of the AOEL when wearing personal protective equipment (PPE) with the German model and the UK POEM respectively. When no PPE is worn the values rise to 991% and 4918% respectively. Exposures for re-entry workers were amounted to 55.8% (without PPE) and 2.8% (with PPE) of the systemic AOEL respectively. Exposure of bystanders was estimated to amount to 3.75% of the systemic AOEL.

The metabolism of epoxiconazole in plants after foliar application is limited. Accordingly the proposed residue definition for monitoring is restricted to the parent compound. Indications are present that the accumulation of triazole metabolites in cereal grains is limited but due to some inadequacies in the design of the wheat metabolism study a firm conclusion on this is not possible.
A sufficient amount of supervised residue trials are available and MRL can be proposed covering the representative uses in cereals and sugar beets in both Northern and Southern European regions.
The nature of the residue is not altered by processing. Processing data show that residues are preferably transferred to the bran fraction during the milling process and that no residue above the limit of quantification (LOQ) is expected to be present in beer from the brewing process.
Uptake of soil residues by rotational crops is not expected to lead to epoxiconazole residues above the LOQ. In contrast, a significant uptake of triazole metabolites (triazole alanine and triazole acetic acid) has been demonstrated at least for cereals.
Feed commodities from cereals and sugar beets may represent a significant source of exposure to epoxiconazole residues for animals. Livestock metabolism studies in lactating goats and laying hens are available and based on the metabolic pattern in animal tissues the residue definition for monitoring can be restricted to the parent compound. Feeding studies in dairy cows are available and appropriate MRLs for animal products can be proposed.
For the time being the residue definition in plant and animal products for risk assessment is restricted to the parent compound. Inclusion of triazole derivative metabolites in this definition will need to be considered at a later stage.
These compounds (mainly triazole, triazole alanine and triazole acetic acid) which are common metabolites of all triazole fungicides have been recognized as hazards given their impact on reproduction. Toxicological reference values have been agreed by the PRAPeR expert meeting 14 on toxicology in January 2007.
Chronic and acute consumer exposures assessments have been carried out for parent compound only and were found to be well below the respective toxicological trigger values of epoxiconazole.
Therefore provisionally no risk for the consumer has been identified under restriction of an uncertainty related to the isomer ratio consumer is actually exposed to. A robust conclusion on the risk will be possible when information on the actual level of triazole derivative metabolites in primary crops, rotational crops, and products of animal origin will be available. It must be noted that this lack of data is a generic issue and concerns all active substances of the triazole chemical class when their degradation pathway in primary crops, soil and livestock involves a cleavage of the triazole ring.

Sufficient data were available to demonstrate that in soil epoxiconazole exhibits medium to very high persistence. The available laboratory studies did not identify any major (> 10% AR) soil metabolites. One metabolite appearing in minor (max. 6.6% AR after 175 days) amounts is 1,2,4-triazole. Other possible degradation products after separation of the aromatic rings are simple monohalogenated acids. Metabolite 1,2,4-triazole is rapidly degraded by soil micro-organisms and it has low persistence, with a reported laboratory mean half-life of 8 days. In anaerobic soils, the first step in degradation is cleavage of the oxirane ring resulting in the formation of the alcohol, which is readily

dehydrated to the alkene BF 480 entriazole (max. 8.6% AR after 120 days). Epoxiconazole is quite stable at soil surfaces under the influence of light.

Epoxiconazole is slightly to moderately adsorbed to soil and the leaching potential is low. Lysimeter studies were not triggered and FOCUS PEC groundwater calculations revealed no risk for groundwater contamination for the active substance or 1,2,4-triazole. A plateau concentration in soil of 0.167 mg/kg for epoxiconazole was calculated based on field accumulation studies.

Epoxiconazole and 1,2,4-triazole are hydrolytically stable at pH 5, 7 and 9. They are also stable under the influence of light in aqueous buffer solutions. However, in a sensitized photolysis study with natural water, epoxiconazole degraded with a half life of 52 days.

After a rapid sorption of the parent compound to the sediment, the predominant metabolite in both investigated water/sediment systems was BF 480-entriazole, being almost exclusively detected in the sediment phase (max. 32.3% AR after 59 days). Once in the sediment, BF 480-entriazole degrades with first order DT_{50} of 32-65 days. Besides CO_2, no further degradation products of epoxiconazole were detected in significant amounts in both test systems during the incubation period. The calculated first order half lives of epoxiconazole for the total systems were 68 and 172 days. Some uncertainties were found in the assessment of the accumulation potential of BF 480-entriazole in sediment.

The volatilization experiments showed that epoxiconazole exhibits a very low average volatilization rate from plant and soil surfaces. It is not a relevant pathway for dissipation. If it however reached the troposphere it would be degraded with a half life of 4 days indicating a potential for long range atmospheric transport. After the experts' meeting the rapporteur Member State re-estimated a half-life of 1.83 days, but the calculation is not peer reviewed.

The first tier TER values indicated a potential high long-term risk to birds and mammals. Measured residues were accepted in the expert meeting to refine the RUD values for herbivorous birds and mammals and to set the multiple application factor (MAF) to 1 provided that the residue studies were conducted with an application interval equal or lower than the interval of 21 days as suggested GAP. Whether it is sufficiently justified to use a MAF of 1 although intervals between applications were above 21 days for about half of the residues studies needs to be evaluated further at Member State level. The DT_{50} refinement for residue decline in plants was also discussed and it is suggested to use the geometric mean value of 14.5 days based on the available residue data. The suggested refinements of PT and PD used in the long-term risk assessment for birds were not sufficiently supported by data and therefore rejected in the meeting of experts. A data gap was identified for further refinement of the long-term risk assessment for birds.

The hare (*Lepus europaeus*), common vole (*Microtus arvalis*) and wood mouse (*Apodemus sylvaticus*) were chosen as focal species to refine the long-term risk assessment for herbivorous mammals. The experts agreed to use the hare and the wood mouse as focal species in the refined risk assessment as suggested in addendum 2. The proposed PT value of 0.3 for hare was not accepted by the meeting since it was not based on radio-tracking data. It was considered not appropriate to derive an exact PT value from the submitted information. However the TER is >5 even without PT refinement and hence the risk to medium herbivorous mammals is considered as low. The suggested PT refinement for wood mouse was not agreed. The experts concluded that the submitted information

is not sufficient to derive a robust quantitative PT refinement. The use of interception factors for residues on arthropods was also rejected. The suggested PD refinement was accepted. The resulting long-term TER of 3.9 is below the trigger of 5 indicating the need for further refinement of the risk assessment. A new long-term risk assessment for wood mouse was submitted by the applicant and assessed by the rapporteur Member State in addendum 4(not peer-reviewed).The risk from secondary poisoning of earthworm- and fish-eating birds and mammals was assessed as low as well as the risk from uptake of contaminated drinking water.

Algae and *Lemna gibba* were the most sensitive tested organisms. In order to detect long-term effects on fish a 28 d prolonged toxicity test, an early life stage test and three full life cycle tests were performed in order to investigate potential endocrine effects. A new test with *Lemna gibba* was perfumed and evaluated in addendum 2. The experts agreed to the assessment of the rapporteur Member State. The endpoint (7d EbC_{50} = 0.0043 mg a.s./L) derived from standard test conditions should be used in the risk assessment. The endpoint derived from the test system with sediment present was considered as not being of direct use in the risk assessment since epoxiconazole partitions rapidly to the sediment and thus reducing the exposure of free floating Lemna fronds. The TERs were above the trigger of 10 in only 2 FOCUS step3 part scenarios (D4 pond, D5 pond) out of 9. No full FOCUS step 3 scenario resulted in TERs above the trigger. The available full life cycle studies with fish were discussed in the expert meeting. It was agreed that the latest study where fish were exposed to a single peak of epoxiconazole could be used in the risk assessment. The experts agreed that a NOEC of 0.03 mg a.s./L can be used in the risk assessment. The effect observed on male vitellogenin levels (NOEC = 0.012 mg a.s./L) was considered as not relevant since it did not affect the reproductive performance of the tested animals. The long-term TERs for fish were above the trigger of 10 for all 9 FOCUS part scenarios as well as the TERs calculated with time weighted PECsw and the lower long-term endpoint for fish (NOEC of 0.01 mg a.s./L) which was based on effects on growth in one of the fish full life cycle tests conducted under flow-through conditions. Epoxiconazole was of similar toxicity to algae when formulated but was significantly more toxic to fish. The acute TERs for fish were above the trigger of 100 in the FOCUS step3 part scenarios D4 (pond) and D5 (pond). In the part scenario D4 (stream) a TER of 99 was calculated which is close to the trigger of 100. Taking into consideration that part of the active substance reach the surface water via drainage and run-off and thus not as the intact formulation the rapporteur Member State concludes that the acute risk to fish from the formulation BAS 480 13 F to fish is addressed for the full FOCUS scenario D4 (pond and stream). EFSA agrees to the opinion of the rapporteur Member State. The risk of bioaccumulation (BCF = 70) was assessed as low. The metabolites 1,2,4-triazole and BF480-entriazole were less toxic to aquatic organisms and the risk posed to aquatic organisms was assessed as low for the representative uses in cereals. The TERs for sediment dwellers was calculated as 5.3 and 40.3 (depending on the test system from which the endpoint was derived). Overall it is concluded that the aquatic risk assessment needs further refinement and/or risk mitigation such as no-spray buffer zones.

The acute risk of epoxiconazole to earthworms is low but the first tier long term TER values were below the Annex VI trigger of 5. Field studies were conducted to assess the effects of continued use of epoxiconazole on earthworm populations in treated fields and also a terrestrial model ecosystem

study. The presented studies had some limitations but the long-term risk to earthworms and soil dwelling arthropods was sufficiently addressed for the representative uses evaluated if all the available information is considered together

The risk to bees, other non-target arthropods, soil non-target micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low for the representative uses evaluated.

Key words: epoxiconazole, peer review, risk assessment, pesticide, fungicide.

TABLE OF CONTENTS

BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Epoxiconazole is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 designating Germany as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Germany submitted the report of its initial evaluation of the dossier on epoxiconazole, hereafter referred to as the draft assessment report, to the EFSA on 28 April 2005. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the revised version of the draft assessment report was distributed for consultation on 7 October 2005 to the Member States and the sole applicant BASF as identified by the rapporteur Member State. Makhteshim Agan ICC originally also notified for this substance but withdrew the notification on 23 July 2003.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed during a written procedure in July – September 2006 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings in March 2007 (all sections) and in May 2007 (only ecotoxicology). The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States in February-March 2008 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

In accordance with Article 11(4) of the Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received;
- the resulting reporting table (rev. 1-1 of 2 October 2006)

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation;
- the evaluation table (rev. 2-1 of 4 March 2008).

Given the importance of the draft assessment report including its addendum (compiled version of February 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report (Volume 3 B.5) which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can be found in the original draft assessment report together with the peer review report, both of which are publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Epoxiconazole is the ISO common name for (2*RS*, 3*SR*)-1-[3-(2-chlorophenyl)-2,3-epoxy-2-(4-fluorophenyl)propyl]-1*H*-1,2,4-triazole (IUPAC). The structure would suggest that there is a possibility of diastero isomers however; epoxiconazole as defined by the ISO common name consists of only one of the possible pairs. Therefore epoxiconazole consists of one pair of enantiomers and it is racemic.

Epoxiconazole is a conazole fungicide; other examples of members of this class are fenbuconazole and myclobutanil. It causes inhibition of C-14-demethylase in sterol biosynthesis. It is a preventative and curative fungicide. It is used as a broad-spectrum fungicide, with preventative and curative action, for control of diseases caused by ascomycetes, basidiomycetes, and deuteromycetes
The representative formulated product for the evaluation was "Opus", a suspension concentrate (SC).

The evaluated representative uses are as a fungicide on cereals and sugar beet. Full details of the GAP can be found in the attached end points.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of epoxiconazole as manufactured should not be less than 920 g/kg. At the moment no FAO specification exists. The technical material contains no relevant impurities.
The content of epoxiconazole in the representative formulation is 125 g/L (pure).
The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of epoxiconazole or the respective formulation.

The main data regarding the identity of epoxiconazole and its physical and chemical properties are given in appendix 1.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of epoxiconazole in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. epoxiconazole in plants and animals as well as in soil and water and air. It should be noted that the residue definition for plants and animals is provisional refer to chapter 3. However, ILV data are not available for the plant method. ILV data were submitted in addendum 3 however, some of the %RSD values were high. In addition to this the data have not been peer reviewed and this must remain as a data gap.

Residues in food of plant origin can be determined with a multi-method (the German S19 method has been validated) and it has an LOQ of 0.05 mg/kg. In addition to this there was also a confirmatory LC-MS/MS method. Products of animal origin are analysed by GC-ECD with an LOQ of 0.001 mg/kg for milk and 0.01 mg/kg for muscle, liver, kidney, fat and egg. A GC-MS/MS method is available for confirmation.

The monitoring method for soil is by GC-ECD with an LOQ of 0.01 mg/kg. GC-MS and GC-PND are available as confirmatory methods. Water (ground/drinking and surface water) are analysed by GC-MS with an LOQ of 0.05 µg/l a GC-ECD method is available for confirmation. Air is analysed by GC-ECD with an LOQ of 0.09 µg/m^3.

Methods of analysis for body fluids and tissues are not required as epoxiconazole is not classified as toxic or very toxic. It should be noted however that there is a GC-ECD and GC-MS method available for blood.

2. Mammalian toxicology

The active substance was discussed at the PRAPeR meeting of experts for mammalian toxicology (PRAPeR 19, round 4) in March 2007.

EFSA note: During the meeting of experts (PRAPeR 19) the need for further information with regard to the composition of the batches used in the toxicological tests was identified. The rapporteur Member State has provided a table with the composition of the batches used in the different tests together with the proposed specification for the active substance in an addendum to the DAR (October, 2007). These data have not been peer reviewed.

EFSA note: After the meeting of experts, a Member State commented that the issue of the toxicological profile of epoxiconazole isomers was not addressed. No relevant information on the toxicology of epoxiconazole isomers is available.

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Epoxiconazole is absorbed to an extent of about 50% when given orally to rats based on urinary and biliary excretion and amount in carcass. Absorption is rapid as peak plasma concentrations are observed within 2 h after oral administration. It is widely distributed, mainly to blood, liver, kidneys, spleen, lung and adrenals. Epoxiconazole has no potential for accumulation in tissues, however, elimination from blood is slow. More than 95% of the active substance is excreted (~17% via urine) (~78% via faeces), within 168 hours after administration. The active substance is rapidly and extensively metabolised and at least 47 metabolites have been identified in the rat.

2.2. Acute toxicity

Epoxiconazole is of low acute toxicity in rats by the oral, dermal and inhalation route. It is neither irritant to the skin nor to the eye of rabbits and did not show a potential for skin sensitisation in a Guinea Pig Maximisation Test. No classification for acute toxicity is warranted.

2.3. Short term toxicity

Short term toxicity of epoxiconazole was investigated in repeated dose studies with rats, mice and dogs and is characterised by effects on the liver in all three species.

In rats, in a 28-day oral (range finding) study no NOAEL was set since increased clinical parameters indicating liver damage were seen even at the lowest dose. In a 21-day dermal study a NOAEL of 400 mg/kg bw/d was derived based on liver effects (increased weight, hypertrophy). A NOAEL of 7

mg/kg bw/d was set based on increased clinical liver parameters, hepatocyte hypertrophy, increased liver- and adrenal weight in a 90-day oral study.
In mice, in a 28-day oral study liver hypertrophy occurred even at the lowest dose and a LOAEL of 73 mg/kg bw/d was set. In two oral 90-day studies an overall NOAEL of 4 mg/kg bw/d based on effects on the liver (hypertrophy, cell degeneration, changes in clinical parameters) was derived.
In dogs, a NOAEL of 1.9 mg/kg bw/d has been derived in a 90-day oral study based on liver effects (clinical changes hypertrophy). A NOAEL of 1.6 mg/kg bw/d was derived from findings obtained in two 12-month feeding studies (altered clinical parameters, hepatitis, anaemia).

2.4. GENOTOXICITY

No evidence of genotoxic activity was found in a battery of *in vitro* and *in vivo* studies.

2.5. LONG TERM TOXICITY

In a 24-month rat study reduced food consumption and bodyweight gain, increased liver weight, hepatocellular hypertrophy, changes in clinical parameters and occurrence of ovarian cysts (females) were observed.
A second 24-month study was carried out and increases in liver weight, hepatocellular hypertrophy, reduced food consumption and body weight gain, liver foci and additionally in females also higher incidences of adrenal gland cortex neoplasms and a dose-related increase of ovarian cysts and ovarian theca granulosa cell tumours were found. Based on mechanistic data the tumours in rats were considered as non-relevant for human risk assessment. An overall non-oncogenic NOAEL has been set at 1 mg/kg bw/d.
Similarly, also in an 18-month carcinogenicity study in mice the liver was the target of toxicity since increased organ weight, hyperthrophy, hyperplasia, focal necrosis and increase in eosinophilic cell foci have been recorded. A substance related increase in liver adenoma and carcinoma in males was observed. It was concluded, based on the results obtained in the genotoxicty section and mechanistic studies that epigenetic mechanisms should be considered as being responsible for tumour formation. The NOAEL in mice was set at 0.8 mg/kg bw/d. Since a non-relevance of the tumours (liver neoplasia) seen in mice for human risk-assessment could not be excluded, classification of epoxiconazole as **Xn; Carc. Cat. 3 R40 "Harmful; Limited evidence of a carcinogenic effect"** was proposed (this is also the current ECB classification).

2.6. REPRODUCTIVE TOXICITY

A two-generation study and three developmental studies (one with dermal application) have been carried out with rats. One developmental study has been carried out in rabbits.
In the two-generation study the findings in the F0 females (reduced food consumption, dystocia, vaginal haemorrhages), the F1 parental animals (dystocia, impaired fertility, prolonged gestation, vaginal haemorrhages, liver effects) and their respective offspring (reduction of viable pups, increase of perinatal deaths) lead to a parental, reproductive and offspring NOAEL of 2.3 mg/kg bw/d. Based on the effects observed in this study also a classification of epoxiconazole as **Xn; Repr. Cat. 3 R62**

"Harmful; Possible risk of impaired fertility" (this is also the current ECB classification) was proposed.

In a first developmental study with rats the maternal and developmental NOAEL were set at 15 mg/kg bw/d based on reduced food consumption and reduced body weight gain in the dams and on a slightly increased number of resorptions, postimplantation losses and marked increases in skeletal variations. In a second developmental study where only one dose was tested (180 mg/kg bw/d), marked maternal (e.g. effects on food consumption, anaemia, liver effects and increased placental weights) and foetal toxicity (e.g. increased postimplantation losses, increased incidence of various malformations) were observed. Dermal application of the active substance in rats caused increased placental weights in the dams and increased number of skeletal variations in the offspring resulting in a maternal NOAEL of 1000 mg/kg bw/d and a foetal NOAEL of 400 mg/kg bw/day.

In a third developmental study with rabbits reduced food consumption and reduced body weight gain in dams and increased postimplantation loss and resorptions were observed leading to NOAELs of 5- and 20 mg/kg bw/d for maternal and developmental effects respectively. It was concluded to propose a classification of epoxiconazole as **Xn; Repr. Cat. 3 R 63 "Harmful; Possible risk of harm to the unborn child"** (also the current ECB classification) based on the effects observed in rat- and rabbit studies.

EFSA note: New data on the endocrine disrupting properties[2,3] of epoxiconazole have been made available after PRAPeR 19, March 2007. In a written statement (of 17th January 2007) the rapporteur Member State concluded that, overall, the results from the new *in vitro* studies and the new developmental study in rats confirm that epoxiconazole has endocrine disrupting properties and added that already in previous studies on epoxiconazole the occurrence of impaired reproductive/developmental parameters had been attributed to the interference of the substance with hormonal substances (DAR Vol.3, B.6.6 Reproductive toxicity and B.6.8 Further toxicological studies). The rapporteur Member State is of the opinion that the new data justify neither changing relevant NOAELs nor the proposed classification. Neither the new data nor the written statement have been peer reviewed.

2.7. NEUROTOXICITY

The results from an acute neurotoxicity study in rats suggest that the active substance has no neurotoxic potential. Based on the systemic effects observed (decreased body weight gain) a NOAEL of 500 mg/kg bw was established in this study. Likewise did the substance not exert neurotoxic effects in a 90-day repeated dose study in the same species and a NOAEL of 16 mg/kg bw/d could

[2]Birkhoj Kjaerstad M, Andersen HR, Taxvig C, Hass U, Axelstad M, Metzdorff and Vinggaard AM (2007) Effects of azole fungicides on the function of sex and thyroid hormones. Pesticides Research No 111.

[3]Taxvig C, Hass U, Axelstad M, Dalgaard M, Bober J, Andersen HR and Vinggaard AM (2007) Endocrine disrupting activities *in vivo* of the fungicides tebuconazole and epoxiconazole. Toxicological Sciences 2007 100(2):464-473.

only be set based on observations of general systemic toxicity (i.e. reduced food intake and body weight gain) at 50 mg/kg bw/d.

2.8. FURTHER STUDIES

No studies on the toxicity of epoxiconazole metabolites were submitted. In order to elucidate the mode of action leading to tumour formation in rats and mice two mechanistic studies (one in rats and one in mice) were carried out. In these studies it could be demonstrated that the active substance induces liver enzyme activities with equal or even higher strength as phenobarbitone, a substance known to cause liver tumours by hepatic enzyme induction and liver growth. The results suggest a comparable mode of action for the induction of liver tumours by epoxiconazole. To investigate the mechanism leading to the reproductive effects observed, hormone levels were measured in rats of both genders and it could be demonstrated that epoxiconazole leads to an irregular and prolonged oestrus cycle in females, decreased corticosterone levels and increased androgen and follicle stimulating hormone (FSH) levels in both sexes. The findings suggest an inhibitory effect of epoxiconazole on aromatase, an enzyme that converts androgens into oestradiol. Oestradiol deficiency results in increased luteinising hormone and FSH leading to a continuous stimulation of ovarian cells that could be cause for the ovarian tumours observed in the chronic rat study. Two further *in vitro* studies corroborate the *in vivo* findings by showing inhibition of aromatase by epoxiconazole in different mammalian cell types. The higher incidences of adrenal gland cortex neoplasms were, based on the findings in the study in rats, attributed to the continuous stimulation of adrenal cortical cells by increased ACTH levels that are a consequence of the inhibition of 11- or 21-hydroxylase by epoxiconazole.

2.9. MEDICAL DATA

Neither have adverse health effects been reported from exposed laboratory and manufacturing personnel nor could reports about such effects be found in the public literature.

2.10. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

ADI

The ADI was set at 0.008 mg/kg bw/d derived from the NOAEL of the 18-month carcinogenicity study in mice (0.8 mg/kg bw/d) and using as safety factor of 100.

AOEL

The AOEL of 0.008 mg/kg bw/d was derived from the NOAEL of the 12-month dog study (1.6 mg/kg bw/d) applying a safety factor of 100 and a correction factor of 50% for oral absorption.

ARfD

The ARfD was set at 0.023 mg/kg bw based on the NOAEL obtained in the two generation reproduction study in rats (2.3 mg/kg bw/d) applying a safety factor of 100.

2.11. DERMAL ABSORPTION

An overall dermal absorption rate of 3% (for the concentrate and the dilution of the preparation) was derived from the results of an *in vivo* and an *in vitro* rat dermal absorption study in the original DAR. During the meeting of experts (PRAPeR 19) substantial shortcomings of the *in vivo* study have been identified and the value for dermal absorption to be used for the calculation of exposures was set at 50% (applying the 100% default value and taking into consideration the results obtained in the *in vitro* study).

EFSA Note : In an addendum to the DAR (October, 2007) a new *in vivo* dermal penetration study with rats[4] has been reported by the rapporteur Member State. The rapporteur Member State is of the opinion that the lower dermal absorption values derived from this study are more realistic and thus the rapporteur Member State does not support using the default values (agreed at PRAPeR 19, March 2007) instead of these. However, this new study has not been peer reviewed.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product 'BAS 480 27 F' is formulated as suspension concentrate containing 125g/L epoxiconazole. It is used as a fungicide to protect cereals and sugar beets against leaf spot diseases.

EFSA note: In an addendum to the DAR (January, 2007) the rapporteur Member State submitted new exposure assessements that are based on the agreed (at PRAPeR 19, March 2007) dermal absorption value of 50% both for the concentrate and the diluted preparation (that is not supported by the rapporteur Member State). The new information has not been peer reviewed.

Operator exposure

According to the intended uses submitted by the applicant the maximum applied dose of epoxiconazole is 125 g/ha and the minimum volume is 150 L water/ha. The maximum numbers of applications per year is two. The supported use is vehicle mounted or drawn boom spraying with hydraulic nozzles. The estimated exposures (assuming a dermal absorption of 50 %) are presented below.

The estimated exposure presented in % of AOEL (0.008 mg/kg bw/day), according to calculations with the German and UK POEM model.

Model	Without PPE	With PPE:
German BBA	991	39
UK POEM	4918	700

[4] Fabian E and Landsiedel R (2007) Study on the dermal penetration of ^{14}C-BAS 480 F in BAS 480 31 F in rats. Unpublished. BASF Report, Project 01B0277/36011.

*PPE (personal protective equipment): gloves during mixing/loading and during application in the UK POEM and gloves during mixing/loading and gloves and garment during application in the German BBA.

Worker exposure

The predicted exposures (assuming a dermal absorption of 50%) based on the German re-entry model[5] for re-entry workers using a refined re-entry scenario (i.e. a work rate of 2h) are 55.8% and 2.8% of the AOEL without and with PPE respectively.

Bystander exposure

Predicted exposure (assuming a dermal absorption of 50%) for a bystander[6] from application of Opus (BAS 480 27 F) is 3.75% of the systemic AOEL of 0.008 mg/kg bw/d.

3. Residues

The active substance was discussed at the PRAPeR experts meeting for residues (PRAPER 20, round 4) in March 2007.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of epoxiconazole has been investigated in wheat, bananas, coffee beans and sugar beets after foliar application. The metabolic pathway was elucidated in wheat only and proceeds through hydroxylation of the chlorophenyl and oxirane rings, cleavage of the oxirane ring and further conjugation processes. In other tested plants, only epoxiconazole was identified as predominant component of the residue.

All these studies suggest that after foliar application parent epoxiconazole accounts for the major part of the toxicological burden the consumer is exposed to. Two to three months after application, unchanged epoxiconazole represents at least 75 % of the organic extract in straw. There is no indication that structurally related metabolites, individually or globally, may add a significant contribution to the toxicological burden.

The information related to the potential accumulation by cereals grains of the triazole derivative metabolites is limited. A metabolism study in spring wheat with radiolabelling in the triazole ring is available but the compound was applied at a too early growth stage (BBCH 49). In this study conducted at normal application, TRR in grains were low (0.05 mg/kg). A great part of the radioactivity was associated to the starch fraction and no parent epoxiconazole was detected. Triazole

[5]Hoernicke E, Nolting H-G, Westphal D (1998) Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflanzenschutzmitteln behandelten Kulturen (worker re-entry) Nachrichtenblatt des Deutschen Pflanzenschutzdienstes. Vol 50 (10) 1998.

[6]Ganzelmeier H, Rautmann D, Spangenberg R, Streloke M, Herrmann M, Wenzelburger H-J, Walter HF (1995) Studies on the spray drift of plant protection products. Mitteilungen aus der Biologischen Bundensanstalt für Land- und Forstwirtschaft Berlin-Dahlem. Heft 305, 1995.

alanine and triazole acetic acid levels were not reported but it seems from the original report that they were not used as reference compounds.

The expert meeting considered that no further metabolism study in cereals was needed as available study shows that the extent of epoxiconazole metabolism is very limited and proposed to define the residue for monitoring and risk assessment as epoxiconazole.

Nevertheless it is the opinion of EFSA, considering the here above mentioned deficiencies of the wheat metabolism study, considering that supervised residue trials show measurable residues of parent compound in cereal grains when the product is applied at growth stage BBCH 69 and considering the presence of triazole alanine and triazole acetic acid in rotational crops, that more information about the presence of these compounds in primary crops are needed before a final residue definition for risk assessment can be concluded.

The PRAPeR expert meeting 14 on mammalian toxicology agreed in January 2007 to set acute and chronic reference values for these metabolites, related to their reproductive toxicity.

In case of significant presence of triazole derivatives in cereal grains, the question on whether epoxiconazole and the free triazole metabolites are or not acting cumulatively on a same toxicological effect, in particular in the area of reproductive and developmental toxicity, and on how an eventual cumulative action needs to be calculated was not discussed during the peer-review. This part of the risk assessment related to epoxiconazole uses will have to be re-examined later, at the light of an opinion of the PPR panel of the EFSA on cumulative risk assessment.

A sufficient number of supervised field residue trials in cereals and sugar beets have been submitted covering all the supported representative uses. In all these trials epoxiconazole only was analysed in food and feed commodities, in accordance with the residue definition for monitoring. On basis of these trials, human and animal exposures to epoxiconazole residues can be assessed, and MRL proposals in relevant commodities established. The validity assessment of the residue data in cereals was conducted on the basis of the proposed PHI irrespective of the latest growth stage of application. Considering growth stage as the most appropriate parameter for selecting relevant data would result in lower MRL proposals for grains of the barley and wheat groups.

These results are supported by storage stability studies demonstrating that epoxiconazole residues are stable under deep-freeze conditions for periods up to 24 months.

In buffer solution and in standard conditions simulating processing (pasteurisation, baking, boiling, brewing and sterilisation), the nature of epoxiconazole is not altered. Processing studies show that during the milling process residues are preferably transferred to the bran fraction, and that no residue in beer is to be expected above 0.01 mg/kg resulting from the brewing process.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Confined rotational crops studies indicate a low potential for transfer of intact epoxiconazole residues from soil to rotational crops. Only one metabolite structurally related to the parent compound was identified at extremely low level. Metabolism in primary and rotational crops can be considered as similar.

Under labelling of the triazole ring, TRR in rotational crops are markedly higher than under chlorophenyl or fluorophenyl labelling. In cereal grains this has been shown to be related to a clear

uptake of triazole alanine and triazole acetic acid forming 80 % of the TRR. In beans, carrots and lettuce, identification of the nature of the radioactivity under triazole labelling was however not performed.

Field studies are available and show that under practical conditions parent compound residues are below the limit of quantification (0.05 mg/kg) in edible parts of rice, cucumber, spinach, potato, radish, soybean, oilseed rape, turnips and sugar beet cultivated as rotational crop after cereals.

The actual transfer of triazole metabolites to rotational crops was not investigated under realistic conditions.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The metabolism of epoxiconazole has been investigated in lactating goats and laying hens. The metabolic pathway in livestock involves opening of the oxirane ring, hydroxylation of the chlorophenyl ring, and (observed in hens only) cleavage of the carbon bridge between the two aromatic nuclei. Compounds resulting from these metabolic reactions are further transformed into glucuronide and/or sulphate conjugates. Livestock and rat metabolisms are similar. A tendency to accumulation of residues was observed in eggs but not in milk.

Possible release of free 1,2,4-triazole, as observed in animal metabolism of other triazole compounds was not investigated as no metabolism study is available with triazole labelling. Nevertheless indirect evidence from the available studies, which failed to detect metabolites without the triazole moiety, suggests that formation of free triazole during metabolic transformation to an appreciable extent is rather unlikely.

In all animal tissues the most abundant compound identified is the parent compound and represents the major part of the toxicological burden. Therefore as in plants the proposed residue definition for monitoring and risk assessment is parent epoxiconazole.

As for plant commodities the EFSA suggests that a final residue definition for risk assessment should need to consider triazole derivative metabolites present in animal commodities as a result of either the animal metabolism of the parent compound or of direct transfer of these metabolites from feed items.

A feeding study in lactating cows was conducted, at feeding levels representative of the critical exposure rate of beef and diary cattle. This study allows establishing MRL proposals for ruminant products. The results of this study can also be used for pig products, considering the related potential exposure.

For poultry, no feeding study was conducted. It is however predictable from the metabolism study that no determinable residues of epoxiconazole is to be expected in any edible poultry product, considering the potential exposure of this species.

3.3. CONSUMER RISK ASSESSMENT

Provisionally, no risk for the consumer resulting from the use of epoxiconazole according to the representative uses in cereals and sugar beets has been identified.

This conclusion is provisional as reliable exposure assessments are at this stage only possible for the parent compound.

The contribution of the triazole derivative metabolites (free triazole, triazole alanine and triazole acetic acid) to the risk is not possible to assess on the basis of the available information. Data are lacking on their actual occurrence in cereal grains, as well as in animal commodities and rotational crop. In addition the assessment of their potential to act toxicologically in a cumulative way with the parent compound needs to be assessed on the basis of related opinion and guidance of the EFSA PPR panel.
In addition, the risk assessment was performed disregarding the possible impact of a change of the enantiomer ratio due to plant or livestock metabolism as this was not investigated by the notifier.

Chronic and acute exposure assessments were carried out in accordance with the WHO calculation models.

Chronic exposure

International and national theoretical maximum daily intake (TMDI) assessments have been conducted by the rapporteur Member State using national German and UK diets as well as the WHO European diet. These diets cover all categories of consumers including infants and toddlers, and also address especially high consumptions patterns. Residues in cereals, sugar beet roots and animal products were considered to be at the level of respective proposed MRLs. A concentration factor of 4.2 was used for bran. Chronic exposures were shown to be significantly below (less than 20 %) the ADI of epoxiconazole in all cases.

Acute exposure

Considering the toxicological end point used for setting the ARfD, all categories of consumer need to be considered in the acute dietary risk assessment. National Estimates of Short Term Intakes (NESTI) were carried out by the rapporteur Member State on the basis of German and UK national large portion consumption data for adults and toddlers with Case 3 calculation method. This means that residues in cereals and their processed commodities were considered to be at the level of the respective STMR-P levels. Based on this, calculated NESTIs for adults and toddlers were equal or below 11 % the ARfD of epoxiconazole for all commodities.

3.4. PROPOSED MRLS

Considering the results of supervised residue trials as well as feeding studies in lactating cow, the following MRLs are proposed to be set in accordance with the representative uses of epoxiconazole in cereals and sugar beets.

Epoxiconazole:

Commodity	***Proposed MRL (mg/kg)***
Sugar beet roots	0.05
Wheat, rye, triticale	0.2
Barley, oats	1
Ruminant liver	0.2

Commodity	*Proposed MRL (mg/kg)*
Swine liver	0.05
Milk	0.002
Other products of animal origin	0.01*

* Indicates that the MRL is proposed to be set at the level of the LOQ.

4. Environmental fate and behaviour

Epoxiconazole was discussed at the PRAPeR experts' meeting for environmental fate and behaviour PRAPeR 17 in March 2007. The fate and behaviour characteristics of its potential very minor soil metabolite 1,2,4-triazole[7] (a metabolite with the potential to be formed by several triazole moiety containing active substances) was also discussed at the PRAPeR experts' meeting for environmental fate and behaviour PRAPeR 12 in January 2007. It should also be noted that the methods of analysis used in all the fate and behaviour studies were not stereoselective. Therefore the regulatory dossier provides no information on the behaviour of each individual epoxiconazole enantiomer in the environment. Therefore all residues reported as epoxiconazole in this conclusion are for the sum of the 2 enantiomers. It is not known if either isomer is degraded more quickly than the other in the environmental matrices studied.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation was investigated under laboratory conditions with epoxiconazole labelled at the oxirane- and triazine-moiety. In the reliable study with oxirane labelled epoxiconazole, metabolism in soil was investigated under dark conditions at 20 ºC in two soils (pH: 6.9-7.1; clay content: 2.6-41.6%; organic carbon content: 1.4-2.8%). The study was run for up to 336 days. Mineralization was only 5.5-7.2% of the applied radioactivity (AR) after 84 days of incubation and 10-38% AR at the end of the study. In the organo-soluble radioactive residues, the main portion was identified as parent compound (34% AR and 67% AR at 336 d). No metabolites appeared in major (> 10% AR) amounts. Non extractable residues accounted for a maximum of about 20 % AR, with most portion of radioactivity bounded to the humin fraction of soil. Investigations with epoxiconazole labelled in the triazine moiety provided further information on soil metabolism. Results showed that the parent compound is the major compound after application to soil, and 1,2,4-triazole was identified as the metabolite with the highest formation rate with up to 6.6% AR after 175 d and 5% AR after 343 d. The degradation behaviour of 1,2,4-triazole was investigated in a separated study, were 3,5-^{14}C triazole was aerobically incubated in three soils at 20ºC in the dark at a moisture content of 40% MWHC. The dissipation from soil was accompanied by fast and high (max. 74% AR at 61 d, and 70% AR and 61% AR at 30d) formation of bound residues in all soils, whereas the formation of CO_2 was relatively high in one soil, and low in the other two. Besides triazole, some further degradation products were found (triazol-acetic acid with max 7% AR and 1,2,4-hydroxytriazole with max 2.6%

[7] 1*H*-1,2,4-triazole

AR). In addition the results of a study with o-chloro benzoic acid as starting material provided evidences that – if ever o-chloro benzoic acid is formed during metabolism of epoxiconazole - this possible intermediate would be readily mineralised to CO_2 much faster than it would be built upon the relatively slow degradation of the active substance itself.

The anaerobic degradation was investigated at 20 ºC with the fluorophenyl labelled test compound in a loamy sand soil. Mineralisation was negligible with CO_2 formation of 1.6% AR after 120 days. The major peak was confirmed to consist of parent epoxiconazole which decreased to 55% AR at 120 days. Two minor metabolites were detected: BF 480-entriazole[8] (max. 8.6% AR at 120 d) and BF 480-alcohol[9], which remained constant at 1.2% AR from 63 d to 120 d.

Epoxiconazole was quite stable at the soil surface of the soil photolysis study and no metabolites appeared in amounts greater than 1% of the applied radioactivity.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The soil degradation of epoxiconazole was determined in 28 experiments with different incubation conditions with eight different soils. Reliable rates of degradation of epoxiconazole were calculated for 15 different experimental conditions. Incubation temperatures ranged from 10 ºC up to 20.7 ºC and moisture conditions were 20, 40, 60 and 80% of MWHC. The calculated first-order DT_{50} values (with $r^2 > 0.7$) ranged from 170 to 1064 days. The DT_{50} values were standardised to FOCUS reference conditions (20 ºC and soil moisture at pF 2) to account for the different soil moisture and temperature conditions during incubation. Individual normalised half lives for each soil investigated under different conditions were provided in addendum 4 (October 2007). The normalised first order DT_{50} values ranged from 98 to 694 days (geometric mean = 226 days), indicating that epoxiconazole is medium to very high persistent.

The metabolite 1,2,4-triazole degraded in laboratory soil experiments with single first order DT_{50} of 6-12 days (20ºC and 40% MWHC, 3 different soils). The geometric mean of the values normalised to 20ºC and pF2 soil moisture content resulted in a first order DT_{50} of 8 days. Because of this relatively rapid transformation rate compared to the breakdown rate of epoxiconazole, soil residues of this metabolite would be expected to present at only very low levels.

Under anaerobic conditions epoxiconazole is degraded with a half-life of 154 days.

Field soil dissipation studies were provided from 8 sites in northern Germany and 2 sites from southern Spain. Three different formulations were sprayed onto bare soil in April or May with a single application rate of 125 or 500 g a.s./ha.. A re-evaluation of the DT_{50} values from field dissipation studies was submitted and evaluated in addendum 2. The trials were evaluated with different models (SFO single first order, FOMC first order multi compartment, DFOP model and SFORB single first order reversible binding) according to the recommendations of the FOCUS kinetics group. For six out of ten trials the degradation of epoxiconazole could adequately be described with SFO kinetics, when a $r^2 > 0.7$ is used as acceptance criterion. The overall $DT_{50field}$

[8] BF 480-entriazole = 1-[(2Z)-3-(2-chlorophenyl)-2-(4-fluorophenyl)-2 propenyl]-1H-1,2,4-triazole
[9] BF 480-alcohol = 1-(2-chlorophenyl)-2-(4-fluorophenyl)-1-hydroxy-3-(1H-1,2,4-triazol-1-yl)propane

values ranged from 52 to 226 days, with the exception of DT_{50} = 1 day, calculated from the Utrera (Spain) field trial. The experts discussed the reliability of the Spanish field trials, as they were originally excluded by the applicant from the standardisation procedure. It was agreed that these field trials can be considered valid and the resulting decline patterns for epoxiconazole can be appropriately described by the FOMC kinetic model. The experts also considered the new PECsoil calculations evaluated in addendum 2. It was agreed that the use of the non-normalized SFO $DT_{50field}$ value of 226 days from the "Birkenheide" (Germany) trial site is appropriate for PECsoil calculations as this value represents the worst case from field dissipation experiments.

Due to the persistency of epoxiconazole, two soil accumulation studies were performed in Germany (Boehl and Niederhofen). In one study an annual application rate of 437 g a.s./ha (split into 3 applications every year) was made onto cereals over a 6 year period. Soil plateau concentration can be regarded as reached after 3 years, with maximum residue levels in the top soil layer (0-25 cm) after last application of 0.11 mg a.s./kg soil. In the second study, the accumulation behaviour of epoxiconazole under field conditions was investigated in Germany over a 9 year period an application rate of 312 g a.s./ha (split into 2 annual applications). Six years of repeated application were needed to reach the maximum residues levels (0.12-0.19 mg a.s./kg) after last application.

An evaluation of the long-term degradation behaviour of epoxiconazole in soil was performed based on the two field soil accumulation studies. The respective SFO DT_{50} values ranged between 251 and 420 days. The degradation rates after multiple applications were reported from the measured data using the software package for parameter estimation TOPFIT. The approach used to calculate the accumulation plateau was challenged during the evaluation procedure. Revised maximum PECsoil calculations after long-tem application of epoxiconazole were provided in addendum 2 but considered unacceptable by the experts. Following the recommendation from the experts' meeting the calculation of a new plateau concentration in soil after applications over several years were recalculated based on the worst case SFO DT_{50} of 403 days (geometric mean from the field accumulation study in Niederhofen). Revised $PEC_{soil,\ accu}$ values, together with further information on the calculation of the dissipation rates derived from the field accumulation studies, were reported in addendum 4 and therefore are not peer reviewed. However, the EFSA is content with the calculations and the information submitted. It should be noted that the DT_{50} value of 403 days was provided by the applicant in the original study[10] but a graphical assessment of the fit to the measured data was not available.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Two adsorption/desorption studies for epoxiconazole were available. Data from a total of five soils indicated that there is no dependency on the organic carbon content, on the clay content or the pH of the soils. K_{foc} values ranged from 280-2647 mL/g (1/n from 0.766 to 0.910), indicating that epoxiconazole is slight to medium mobile in soil. Due to the high variation of the values, the arithmetic mean of 1073 mL/g was used for PEC calculations. In a separate study, metabolite 1,2,4-

[10] Tilting N., 2007. Predicted environmental concentrations in soil for BAS 480 F (epoxiconazole) according to FOCUS recommendations. BASF DocID 2007/1005103.

triazole was basically classified as being high to very high mobile (K_{oc} = 43 – 120 mL/g, n = 4), with an increasing sorption with increasing pH of soil. However, it was agreed in PRAPeR 12 that the adsorption of this metabolite is not pH dependent.

The leaching behaviour of epoxiconazole was investigated in three soils. No epoxiconazole residues could be detected in the leachates above the limit of determination of 0.05 µg/L.

Four aged residues column leaching studies were available with 30, 175 and 343 aging period. Amounts between 0.7 to 1.3% of the applied radioactivity were found in the leachates. Extractable residues from the soil segments showed only unchanged epoxiconazole. In an additional laboratory column leaching study of 1,2,4-triazole aged residues, no triazole was identified in the leachates.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Epoxiconazole and the metabolite 1,2,4-triazole are hydrolytically stable in the investigated pH-range between pH 5 and pH 9. The active substance and the metabolite are also photolytically stable in sterile water as could be demonstrated in a photolysis study. In natural water 20% of the active substance was degraded after 15 days.

A ready biodegradability test (OECD 301F) indicated that epoxiconazole is “not readily biodegradable” using the criteria defined by the test.

The degradation and partitioning behaviour of epoxiconazole was investigated in two natural water/sediment systems using two different labelling positions (chlorophenyl-U and fluorophely-U-[^{14}C]epoxiconazole). One system was a clayey sediment with a higher organic carbon content (8.5%) and the other system a sandy sediment with 0.5% organic carbon. In both systems and for both labels, the radioactivity was increasingly partitioned to the sediment phase (maximum 71% AR and 50% AR after 30 and 13 days respectively). At the study end (100 d) less than 8% AR remained in the water phase and less than 5% AR was mineralised to carbon dioxide in both systems. Within the sediment epoxiconazole is metabolised to BF 480 entriazole to a maximum of 6.6% AR and 34% AR after 59 days in the two systems. Formation of other metabolites was low (< 2.5 % AR). Bound residues were found in moderate amounts (19.2% - 21.9% AR after 100 d). The calculated first order half lives of epoxiconazole for the total systems were 172 and 68 days. The corresponding DT_{50} values for the water phase were 38 and 93 days for the systems A and B. The first order degradation half-life of the metabolite BF 480-entriazole in sediment was calculated to be 32 and 65 days, respectively. A more in-depth description of the compartment model used for the estimation of the degradation and dissipation half-lives was provided in addendum 2 and accepted by the experts.

New FOCUSsw Step 3 calculations with the temperature for DT_{50} in water set to 20ºC were provided. The meeting of experts agreed these PEC surface water values presented in addendum 2 were appropriate for use in risk assessment, although not in accordance with most recent FOCUS kinetics guidance for the estimation of the water/sediment degradation parameters. They also agreed that estimation of concentrations in sediment under consideration of potential accumulation for epoxiconazole and the metabolite B 480-entriazole is necessary to ensure an appropriate risk assessment to sediment dwelling organisms. The applicant submitted higher tier estimations of

$PEC_{sed,accu,max}$ for epoxiconazole and metabolite B 480-entriazole and were considered acceptable by rapporteur Member State (addendum 4). Even though the new calculations have not been peer reviewed, the EFSA considers the results for epoxiconazole appropriate to be used for risk assessment to sediment dwellers, as the approach follows the FOCUS recommendations for $PEC_{sed,accu,max}$ estimations. Regarding the metabolite B 480-entriazole, the EFSA noted that a different $DT_{50\ sed}$ value (= 45 d) from the value agreed by the experts (= 61.4 d) was used, and therefore estimations for accumulation PEC value in sediment for B 480-entriazole can not be considered valid.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The simulation models FOCUS-PELMO 2.2.2 and FOCUS MACRO 3.3.1 were used for the calculation of the predicted environmental concentrations in groundwater (PECgw) for the parent compound epoxiconazole and 1,2,4-triazole. The geometric mean of the field DT_{50} values normalised to 20ºC (= 74 days) for epoxiconazole was considered in the calculations. For the metabolite the use of the standardised laboratory DT_{50} of 8 days (geometric mean) was in line with the agreed (PRAPeR 12) list of end points, whereas a worst case K_{foc} of 43 L/kg was used in place of the mean value (= 89 L/kg). The PECgw values for both substances are far below the 0.1 µg/L level in all 9 FOCUS scenarios. Therefore, the potential for groundwater exposure by epoxiconazole and the metabolite 1,2,4-triazole is concluded to be low.

4.3. FATE AND BEHAVIOUR IN AIR

Less than 5% of epoxiconazole volatilise within 24 hours after application both from soil and plant surface. Considering these experimental results and the low vapour pressure ($< 1 \times 10^{-5}$ Pa at 20ºC) it can be concluded that the active substance ha no tendency to enter the air. Volatilisation is not a relevant pathway for dissipation of epoxiconazole. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals (5×10^5 cm^{-3}) resulted in an half life estimated of 4 days, indicating a potential for long range atmospheric transport. Therefore, after the experts' meeting the EFSA identified a data gap for monitoring data for residues in air and evaluation of the long-range atmospheric transport potential. In February 2008, the rapporteur Member State recalculated the photochemical oxidative degradation of epoxiconazole with a newer version (v. 1.91) of AOPWIN and considering a hydroxyl radical concentration of 5×10^5 cm^{-3}. The estimated DT_{50} in air resulted to be 1.83 days, but this value is not peer reviewed.

5. Ecotoxicology

Epoxiconazole was discussed at the PRAPeR experts' meeting for ecotoxicology PRAPeR 18 in March 2007 and PRAPeR 23 in May 2007. A risk assessment was conducted by the rapporteur Member State for the representative use in cereals but no environmental risk assessment was presented in the DAR for the representative use in sugar beet. The rapporteur Member State informed that the use in sugar beet was withdrawn by the applicant.

Epoxiconazole belongs to the triazole fungicides which are suspected to have potential endocrine disrupting properties. The experts agreed that the risk of endocrine disrupting effects which have an impact on the reproductive performance is covered by the endpoints from available reproduction studies (rats, birds and fish full life cycle study). Uncertainty remains with regard to delayed reproductive effects. New information on endocrine disrupting effects was submitted by one Member State to the rapporteur Member State after the expert meeting. The rapporteur Member State assessed the new information on the endocrine disrupting potential in a statement from January 2008. From the not-peer reviewed statement it appears that endocrine disrupting effects were observed at doses higher (15 mg a.s./kg bw/d) than the endpoints used in the mammal risk assessment (2.3 mg a.s./kg bw/d).

In the environmental risk assessment it was not considered that epoxiconazole consists of a racemic mixture of two enantiomers. No information was made available on the toxicity of the different isomers or on potential different degradation rates of the isomers in the environment. This adds additional uncertainty to the ecotoxicological risk assessment and needs to be addressed further.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The representative use of epoxiconazole comprises 1-2 applications during early and late growth stages of cereals. The first tier TER values for the acute and short-term risk to birds and the acute risk to mammals were above the Annex VI trigger of 10. However the long-term TERs were below the trigger for herbivorous mammals and large herbivorous birds (scenario cereals early) and insectivorous birds (scenario cereals early and late applications).

Measured residues were accepted to refine the RUD values for herbivorous birds and mammals and to set the multiple application factor (MAF) to 1 provided that the residue studies were conducted with an application interval equal or lower than the interval of 21 days as suggested GAP. This information was not available in the meeting and an open point was set for the rapporteur Member State to check the interval used in the residue trials. An extensive re-evaluation of the residue studies was submitted by the applicant. It is obvious from the data presented in addendum 4 (not peer-reviewed) that about half of the studies were done with an application interval of >21 days. The data suggest a slight reduction of RUD values with increasing application interval. Whether it is sufficiently justified to use a MAF of 1 although intervals between applications were above 21 days for about half of the residues studies needs to be evaluated further at Member State level.

The DT_{50} value derived from the residue trials to refine the f(twa) value was discussed in the meeting. The experts noted that the median DT_{50} value of 10.7 days is close to the default value of 10 days. A high variability was observed in the residue decline data and the experts proposed to use the geometric mean value of 14.5 days in the risk assessment. A new DT_{50} calculation (resulting DT_{50} = 9.7d) based on single first order kinetics was submitted by the applicant and evaluated by the rapporteur Member State in the not-peer reviewed addendum 4. The rapporteur Member State suggested using the default DT_{50} value of 10 in the risk assessment. If Member States wish to use the

information provided in addendum 4 then it should be considered that the expert meeting proposed using the geometric mean DT_{50} of 14.5 days that is longer than the default value of 10.
In addition to refinements based on measured residues also PD and PT refinements were proposed in the risk assessment for large herbivorous birds (geese). The suggested PT and PD refinement for large herbivorous birds were not supported by data and therefore rejected in the meeting of experts. Based on measured residues but without refinement of PT and PD the resulting TER was 1.3 and hence a data gap for further refinement was identified. In the addendum 4 (not peer-reviewed) further information on feeding and habitat use of geese were included. The information suggests that the PT may be set to a value of <1. However, the PT would need to be lowered to 0.3 to achieve a TER of 5. Also a risk assessment for a medium herbivorous bird (grey partridge, *Perdix perdix*) was conducted. The use of an interception factor to refine residues in weeds was rejected in the meeting since extrapolation from deposition on soil surface to deposition on weeds was considered not correct. A PT value of 0.25 was applied in the risk assessment for grey partridge. The robustness of this value was questioned during the commenting period since the underlying radio-tracking data reflect only the occurrence of grey partridge in different habitats but information demonstrating active time spent feeding in cereal fields is missing. The suggested PT refinement for grey partridge was erroneously not discussed in the expert meeting. If Member States wish to consider grey partridge in addition to geese in their risk assessment then a degree of caution should be applied when the presented data are used to quantify the PT value. However the overall conclusion for a medium herbivorous bird does not change since also the TER including the rejected refinements was below 5.

The refined risk assessment for insectivorous birds was based on yellowhammer (*Emberiza citrinella*) for early growth stages and on marsh-warbler (*Acrocephalus palustris*) as focal species and refinement of PT and PD values. The meeting agreed to use yellowhammer as a focal species and suggested also skylark (*Alauda arvensis*). The suggested PT of 0.02 value was not agreed in the meeting. PT values of 1 (90%tile) were observed in studies in UK. Without PT refinement the TER for yellowhammer is 1.2. Therefore a data gap was identified to refine the risk to insectivorous birds. A new refined risk assessment for yellowhammer and skylark were submitted by the applicant and presented in addendum 4(not peer-reviewed).

The hare (*Lepus europaeus*), common vole (*Microtus arvalis*) and wood mouse (*Apodemus sylvaticus*) were chosen as focal species to refine the long-term risk assessment for herbivorous mammals. In addendum 2 a revised risk assessment was presented by the rapporteur Member State. The meeting agreed to use the hare and wood mouse as focal species in the refined risk assessment as suggested in addendum 2. The proposed PT value of 0.3 for hare was not accepted by the meeting since it was not based on radio-tracking data. It was considered not appropriate to derive an exact PT value from the submitted information. However the TER is >5 even without PT refinement and hence the risk to medium herbivorous mammals is considered as low.

The suggested PT refinement for wood mouse was not agreed in the expert-meeting. The experts concluded that the submitted information is not sufficient to derive a robust quantitative PT

refinement. The use of interception factors for residues on arthropods was also rejected. The suggested PD refinement was accepted. The rapporteur Member State presented a recalculation of the TER based on the recommendations from the expert meeting in addendum 4. The resulting long-term TER of 3.9 is below the trigger of 5 indicating the need for further refinement of the risk assessment. A new long-term risk assessment for wood mouse was submitted by the applicant and assessed by the rapporteur Member State in addendum 4(not peer-reviewed).

The risk from secondary poisoning of earthworm- and fish-eating birds and mammals was assessed as low as well as the risk from uptake of contaminated drinking water.

Triazolyl alanine (TA) and Triazolyl acetic acid (TAA) were identified as major residues in wheat grain for wheat which was grown on soil containing residues aged for 30 days. Residues for TA and TAA in wheat grain was 54 % total radioactivity residues (TRR) and 26 % TRR respectively. In contrast, straw contained a high percentage of unchanged parent (36 % TRR). Other major metabolites were TAA (10 % TRR) and triazoly hydroxyl propionic acid (THPA) with 16 % TRR.
The most sensitive endpoints for investigated metabolites TA and TAA indicate low acute toxicity to mammals (LD_{50} > 5000 mg/kg bw in rats) and to birds (LD_{50} > 1354 mg/kg bw for TA and an LD_{50}/NOEL of ≥ 2000 mg/kg bw for TAA). For the structural analogues TPHA no toxicity data is given but on the basis of the strong structural similarity with the metabolites TA and TAA no indication exists for an increased toxicity to mammals and birds. Given the low acute and short-term toxicity of the tested metabolites it is concluded that the risk from the major plant metabolites is covered by the risk assessment for epoxiconazole.

In the expert meeting it was discussed whether potential endocrine effects on birds are covered by the risk assessment. It was agreed by the experts that the reproductive endpoints cover endocrine modulated effects on reproduction but that some uncertainty remains with regard to delayed reproductive effects. The majority of the experts were of the opinion that it is not necessary to increase the safety factor to cover potential delayed adverse effects on reproduction of birds.

5.2. RISK TO AQUATIC ORGANISMS

Algae and *Lemna gibba* were the most sensitive tested organisms. The 72 h EbC_{50} for algae was 1.19 mg a.s./L and the 14 d EbC_{50} for *L. gibba* was 0.0081 mg a.s./L. The acute toxicity to the tested fish was in the range of 3.14 – 8.27 mg a.s./L with rainbow trout being the most sensitive species. In order to detect long-term effects on fish a 28 d prolonged toxicity test, an early life stage test and three full life cycle tests were performed in order to investigate potential endocrine effects. A new test with *Lemna gibba* was performed and evaluated in addendum 2. The experts agreed to the assessment of the rapporteur Member State. The endpoint (7d EbC_{50} = 0.0043 mg a.s./L) derived from standard test conditions should be used in the risk assessment. The endpoint derived from the test system with sediment present was considered as not being of direct use in the risk assessment since epoxiconazole partitions rapidly to the sediment and thus reducing the exposure of free floating Lemna fronds. The

TERs were above the trigger of 10 in only 2 FOCUS step3 part scenarios (D4 pond, D5 pond) out of 9. No full FOCUS step 3 scenario resulted in TERs above the trigger.

The available full life cycle studies with fish were discussed in the expert meeting. It was agreed that the latest study where fish were exposed to a single peak of epoxiconazole could be used in the risk assessment. It was noted that it is likely that all sensitive life stages were exposed since three groups were tested which were exposed to the peak concentration either as egg, juvenile or mature fish. The meeting agreed that a NOEC of 0.03 mg a.s./L could be derived from the study which can be used in the risk assessment. The effect observed on male vitellogenin levels (NOEC = 0.012 mg a.s./L) was considered as not relevant since it did not affect the reproductive performance of the tested animals. It was agreed that the NOEC of 0.03 mg a.s./L should be compared to initial maximum PECsw concentrations. The TERs were above the trigger of 10 for all 9 FOCUS part scenarios. The lower long-term endpoint for fish (NOEC of 0.01 mg a.s./L) was based on effects on growth in one of the fish full life cycle tests under flow-through conditions. A NOEC of 0.01 mg a.s./L based on effects on growth was also observed in a 28-d chronic study with *Oncorhynchus mykiss*. The meeting agreed that the observed effects on growth are due to prolonged exposure rather than due to a single exposure peak. The experts proposed to compare the NOEC of 0.01 mg a.s./L with appropriate time weighted average PECsw values taking into consideration the potential exposure profiles from different FOCUS scenarios. Comparing the NOEC of 0.01 mg a.s./L to a 28-d time weighted average PEC then the resulting TERs are above the trigger of 10 for all 9 FOCUS part scenarios.

Epoxiconazole was of similar toxicity to algae when formulated but was significantly more toxic to fish. The acute TERs for fish were above the trigger of 100 in the FOCUS step3 part scenarios D4 (pond) and D5 (pond). In the part scenario D4 (stream) a TER of 99 was calculated which is close to the trigger of 100. Taking into consideration that part of the active substance reach the surface water via drainage and run-off and thus not as the intact formulation the rapporteur Member State concludes that the acute risk to fish from the formulation BAS 480 13 F to fish is addressed for the full FOCUS scenario D4 (pond and stream). EFSA agrees to the opinion of the rapporteur Member State.

The risk of bioaccumulation (BCF = 70) was assessed as low. The metabolites 1,2,4-triazole and BF480-entriazole were less toxic to aquatic organisms and the risk posed to aquatic organisms was assessed as low for the representative uses in cereals.

The TER values for the sediment dwelling *Chironomus riparius* was calculated to be above the trigger of 10 in all 9 FOCUS part scenarios for epoxiconazole and the metabolite BF 480-entriazole. This calculation was based on nominal water concentrations in the test system compared to the water concentration of the FOCUS scenarios. However the concentration of the active and the metabolite in the sediment of the test system should be calculated and compared to the accumulated PEC in sediment from the FOCUS scenarios or alternatively the accumulated PEC in sediment should be expressed as a concentration in water and than compared to the surface water PECs. The argumentation of the rapporteur Member State provided in addendum 4 (not peer reviewed) that the

comparison of nominal water concentrations in the test system and the PEC surface water would lead to a conservative TER estimate is not agreed by EFSA and needs to be supported by an appropriate TER calculation as suggested above.

The rapporteur Member State provided a worst case TER calculation based on sediment concentrations in the test system. Since sediment concentration continuously increases during the course of the experiment time-weighted average concentration of the active substance in the sediment for the whole course of the experiment was used. From the course of % of initial total radioactivity (ITR) and the calculated concentrations in the sediment in the test with the lower nominal water concentration (6.25 µg/L) a time-weighted average of 14.15 % ITR (=5.78 µg/kg dry sediment) can be calculated for the 21 days period in the natural sediment system. For the artificial sediment system at the lower test concentration (6.25 µg/L) the time-weighted average is 53.78 % ITR (=43.96 µg/kg dry sediment). Assuming a similar kinetic for the higher test concentration would result in a value of 57.8 µg/kg for the natural sediment system and 439.6 µg/kg dry sediment for the artificial test system. The resulting TER considering the calculated worst case $PEC_{plateau,\ sediment}$ of 10.91 µg/L would be 5.3 and 40.3 for the natural and artificial test system respectively. The TER trigger value of 10 is breached if the endpoint for Chironomus is based on the behaviour observed in the test system with natural sediment. No TER calculation as suggested above was provided for the metabolite BF 480-entriazole. The observed NOEC for BF 480-entriazole is lower than for epoxiconazole. Therefore it cannot be concluded that the risk is covered by the risk assessment for the parent epoxiconazole and a TER calculation based on sediment concentrations is considered necessary. Further risk refinement or risk mitigation measures are required.

No full FOCUS step 3 scenario resulted in TERs above the trigger for aquatic plants. No reliable FOCUS step4 calculations were made available. No risk assessment for sediment dwelling organisms was conducted for the metabolite BF 480-entriazole. Overall it is concluded that a high risk to aquatic organisms cannot be excluded for the majority of the geoclimatic conditions represented by the FOCUS scenarios. Further risk refinement and/or risk mitigation measures are required.

5.3. RISK TO BEES

The acute oral and contact toxicity to bees was tested with the technical and formulated epoxiconazole. The HQ values were <50 for acute oral and dermal exposure indicating a low risk to bees from the representative uses.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory tests on glass plates/quartz sand were conducted with *Aphidius rhopalosiphi*, *Typhlodromus pyri*, *Coccinella septempunctata* and *Poecilus cupreus*. From the study with *T. pyri* the LR_{50} value was calculated to be 2.1 L/ha. Only one dose was tested in the other tests. The LR_{50} was assumed to be > 2 L/ha since the observed mortality was less than 50 %. The in-field and off-field HQ values were calculated as 0.95 and 0.045 for *T. pyri* and <1 and <0.048 for *A. rhopalosiphi* . A vegetation distribution factor (VDF) of 5 was used in the off-field risk assessment. If the standard

VDF is used for the calculations the resulting off field HQ values would be even lower. It is concluded that the risk from the representative uses posed to non-target arthropods is low.

5.5. RISK TO EARTHWOMS

The acute risk of epoxiconazole to earthworms is low but the first tier long term TER values were below the Annex VI trigger of 5. Field studies were conducted to assess the effects of continued use of epoxiconazole on earthworm populations in treated fields and also a terrestrial model ecosystem study. The long-term risk assessment for earthworms was discussed in the expert meeting. The presented studies had some limitations (e.g. start of monitoring 6 years after the first application, lack of a positive control, extrapolation from Enchytraeidae to Lumbricidae). However, the experts agreed that the long-term risk to earthworms from the representative use in cereals is sufficiently addressed if all the available information is considered together provided that the accumulated peak PEC soil was reached in the studies. The soil concentrations in the field study of Krieg (2000) were measured and reported in the study of Keller 2000. The results indicate that soil concentrations similar to the maximum plateau PEC were reached one year after application of 2 x 0.125 kg a.s./ha and 3 x 0.125 kg a.s./ha. Therefore it is likely that soil concentrations comparable to the accumulated peak PECsoil were reached in the field studies where the same application pattern as in the study of Krieg (2000) was applied in two consecutive years.

The acute and long-term risk of the metabolite 1,2,4-triazole was assessed as low.
Overall it is concluded that the risk to earthworms is low for the representative uses.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

Field biomonitoring and litterbag studies were conducted to address the potential risk to soil dwelling non-target organisms. A new statistical evaluation of effects on collembola species was submitted by the applicant and evaluated by the rapporteur Member State in addendum 2. The experts agreed to the conclusion of the rapporteur Member State that the risk to other soil dwelling non-target organisms can be considered as low for the representative uses evaluated provided that the accumulated peak PECsoil is covered by the tests. The same application pattern is applied as in the earthworms field studies and hence it is likely that concentrations comparable to the accumulated peak PECsoil were reached (see point 5.5.)

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects on soil respiration and nitrification was tested with formulated epoxiconazole and the soil metabolite 1,2,4-triazole. No effects of > 25% were observed at treatment levels of up to 10 times the application rate of the GAP indicating a low risk. A field study was conducted with concentrations at PECplateau level after a multi year use. No clear treatment related effect was observed in the field study. The risk posed to soil non-target micro-organisms is considered to be low for the representative uses.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

The effects of the formulation BAS 480 27 F on growth was tested with oat (*Avena sativa*), onion *Allium cepa*), cabbage (*Brassica oleacea*), pea (*Pisum sativum*), carrot (*Daucus carota*), sunflower (*Helianthus annuus*), cucumber (*Cucumis sativus*), sugar beet (*Beta vulgaris*). Some visual damages were observed for sugar beet at the dose of 2 L/ha. But no statistical significant effects on growth were observed at the dose rate of 2 L/ha. Since 2 L/ha is the two fold of a single use rate the risk to non-target flora is considered to be low for the representative uses evaluated.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The risk to biological methods of sewage treatment is considered to be low. No significant inhibition of respiration was observed in a test with activated sewage sludge up to the highest tested concentration of 1014 mg a.s./L and no inhibition of oxygen consumption was measured in a test with *Pseudomonas putida* up to a concentration of 1000 mg a.s./L.

6. Residue definitions

Soil

Definitions for risk assessment: epoxiconazole

Definitions for monitoring: epoxiconazole

Water

Ground water

Definitions for exposure assessment: epoxiconazole

Definitions for monitoring: epoxiconazole

Surface water

Definitions for risk assessment: epoxiconazole, BF 480 entriazole[11] (only sediment)

Definitions for monitoring: epoxiconazole

Air

Definitions for risk assessment: epoxiconazole

Definitions for monitoring: epoxiconazole

Food of plant origin

Definitions for risk assessment: epoxiconazole (provisional)

Definitions for monitoring: epoxiconazole

[11] BF 480 entriazole = 1-[(2Z)-3-(2-chlorophenyl)-2-(4-fluorophenyl)-2 propenyl]-1H-1,2,4-triazole

Food of animal origin

Definitions for risk assessment: epoxiconazole (provisional)

Definitions for monitoring: epoxiconazole

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
epoxiconazole	Medium to very high persistence Single first order labDT_{50} 98-694 days (20°C, pF2) Single first order or biphasic, field DT_{50} 1-226 days, DT_{90}>1year (German and Spanish field studies)	The acute toxicity and risk to earthworms is low. The long-term TERs indicated a potential long-term risk. On the basis of the available field studies it was concluded that the long-term risk to soil dwelling organisms is low. The risk to soil micro-organsims was assessed as low.

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 activity**	**Ecotoxicological activity**
epoxiconazole	Slight to medium mobility 280-2647 mL/g	no	Yes	Yes	Yes

Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Epoxiconazole (water and sediment)	Toxic to fish (LC_{50} = 3.14 mg/L), invertebrates (EC_{50} = 8.69 mg/L), algae (EbC_{50} = 1.19 mg/L), very toxic to aquatic plants (EbC_{50} = 0.0043). The TER trigger was met in only 2 out of 9 FOCUS step3 part scenarios.
BF 480 entriazole (sediment only)	The 28-d NOEC for *Chironomus riparius* is 0.03 mg/L. The risk assessment is not finalised no conclusion can be drawn if the Annex VI TER trigger of 10 is exceeded based on PECsed concentrations.

Air

Compound (name and/or code)	**Toxicology**
epoxiconazole	Low acute toxicity by inhalation in rats (LC_{50} > 5.3 mg/L)

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

- ILV data are required for the method of analysis for plants (relevant for all uses evaluated, data requirement identified by PRAPeR 16 March 2007, data available in addendum 3 but it has not been peer reviewed, refer to chapter 1).
- The composition of the batches used for the toxicological investigations (relevant for all uses evaluated, has been provided after the meeting of experts (PRAPeR 19, March 2007) in an addendum to the DAR (October, 2007) but has not been peer reviewed; refer to point 2).
- A comparison of the mode of action of epoxiconazole and the triazole metabolite derivatives is required in order to assess possible cumulative toxicity resulting of the combined exposure to these compounds (relevant for all uses evaluated, data gap identified by EFSA after the expert meetings; refer to chapter 3).
- Information allowing the assessment consumer exposure to triazole metabolite derivatives in primary crops, rotational crops, and products of animal origin (relevant for all uses evaluated; no submission date proposed by the applicant; data gap identified by EFSA after the expert meeting; refer to chapter 3)
- Impact of different isomer ratios on the consumer risk assessment of epoxiconazole is to be addressed (relevant for all applied for intended uses; data gap identified by EFSA after the experts' meeting; no submission date proposed; refer to point 3.3).
- Estimation of concentrations in sediment under consideration of potential accumulation ($PEC_{sed,accu}$) for metabolite B 480-entriazole to ensure an appropriate risk assessment for sediment dwelling organisms (relevant for all representative uses evaluated; study submitted by the applicant in August 2007 and evaluated in addendum 4 of October 2007 but not peer reviewed; refer to point 4.2.1).
- Monitoring data for residues in environmental matrices to address the potential of long-range atmospheric transport (relevant for all representative uses evaluated; data gap identified by EFSA, no submission date proposed by the applicant; new calculation provided by RMS is available but not peer reviewed; refer to point 4.3).
- The long-term risk assessment for birds and mammals need further refinement (relevant for all representative uses evaluated, data gap identified in the expert meeting for ecotoxicology, PRAPeR 23 in May 2007; no submission date proposed; refer to point 5.1.)
- The aquatic risk assessment needs further refinement (relevant for all uses evaluated, data gap identified by EFSA after the expert meeting; no submission date proposed; refer to point 5.2.)
- Epoxiconazole consists of 2 isomeres. This needs to be taken into account in the environmental risk assessment. Information on the toxicity and/or on the degradation of the 2 isomeres in the environment is needed. (relevant for all representative uses evaluated; open point identified after the expert meeting; no submission date proposed by the applicant; refer to section 5).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as a fungicide on cereals and sugar beet. Full details of the GAP can be found in the attached end points. The representative formulated product for the evaluation was "Opus", a suspension concentrate (SC).

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in food of plant origin can be determined with a multi-method (The German S19 method has been validated). For the other matrices only single methods are available to determine residues of epoxiconazole.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. It has been identified that more information is necessary to enable the impact of potential different isomer ratios on the risk assessments to be better characterised

Epoxiconazole is absorbed rapidly but only to a limit extent (about 50%) after oral administration in rats. It is widely distributed and although it has no potential for accumulation, the elimination is slow. The substance is mainly excreted with the faeces (about 78%) and urine (about 17%).Metabolism is rapid and extensive. The active substance is of low acute toxicity, not irritant to skin or to eyes and has no sensitisation potential. The liver was the main target of epoxiconazole mediated toxicity in repeated dose tests with rats, mice and dogs. The lowest short term NOAEL of 1.1 mg/kg bw/day was obtained in a 12-month dogs study based on increases seen in clinical parameters indicating liver damage. Epoxiconazole is not genotoxic. In a 24-month study in rats again the liver was the main target of epoxiconazole toxicity, and a second 24-month carcinogenicity study in addition to liver toxicity also ovary and adrenal gland tumours were observed. In an 18-months carcinogenicity study in mice an increase in liver tumours has been observed and classification of epoxiconazole as **Xn; Carc. Cat. 3 R40 "Harmful; Limited evidence of a carcinogenic effect"** was proposed. Based on the effects seen in a two-generation study in rats (dystocia, impaired fertility, prolonged gestation and vaginal haemorrhages) it was concluded to propose a classification with **Xn; Repr. Cat. 3 R62 "Harmful; Possible risk of impaired fertility**". Based on developmental effects such as increases in number of resorptions, skeletal variations and malformations observed in relevant studies in rats and rabbits also a classification **Xn; Repr. Cat. 3 R 63 "Harmful; Possible risk of harm to the unborn child"** is proposed. Results from new *in vitro* studies and a new developmental study in rats confirm that epoxiconazole has endocrine disrupting properties but do not merit changing relevant NOAELs or revising the proposed classification according to an evaluation by the rapporteur Member State. However, these new data have not been peer reviewed.

The acceptable daily intake (ADI) is 0.008 mg/kg bw/day derived from an 18-month carcinogenicity study in mice applying a safety factor of 100. An acute reference dose (ARfD) of 0.023 mg/kg bw has been derived based on the effects observed in the two generation reproduction study in rats applying a safety factor of 100. The acceptable operator exposure level (AOEL) of 0.008 mg/kg bw/day was derived from a subchronic dog study applying a safety factor of 100. In consideration of a dermal

absorption of 50% both for the concentrate and the diluted preparation, a default value agreed upon by the experts at PRAPeR 19, March 2007, but are not supported by the rapporteur Member State, the exposure estimates for operators were 39% and 700% of the AOEL when wearing personal protective equipment (PPE) with the German model and the UK POEM respectively. When no PPE is worn the values rise to 991% and 4918% respectively. Exposures for re-entry workers were estimated to amount to 55.8% (without PPE) and 2.8% (with PPE) of the systemic AOEL respectively. Exposure of bystanders was estimated to amount to 3.75% of the systemic AOEL.

The metabolism of epoxiconazole in plants after foliar application is limited. Accordingly the proposed residue definition for monitoring is restricted to the parent compound. Indications are present that the accumulation of triazole metabolites in cereal grains is limited but due to some inadequacies in the design of the wheat metabolism study a firm conclusion on this is not possible.
A sufficient amount of supervised residue trials are available and MRL can be proposed covering the representative uses in cereals and sugar beets in both Northern and Southern European regions.
The nature of the residue is not altered by processing. Processing data show that residues are preferably transferred to the bran fraction during the milling process and that no residue above the limit of quantification (LOQ) is expected to be present in beer from the brewing process.
Uptake of soil residues by rotational crops is not expected to lead to epoxiconazole residues above the LOQ. In contrast, a significant uptake of triazole metabolites (triazole alanine and triazole acetic acid) has been demonstrated at least for cereals.
Feed commodities from cereals and sugar beets may represent a significant source of exposure to epoxiconazole residues for animals. Livestock metabolism studies in lactating goats and laying hens are available and based on the metabolic pattern in animal tissues the residue definition for monitoring can be restricted to the parent compound. Feeding studies in dairy cows are available and appropriate MRLs for animal products can be proposed.
For the time being the residue definition in plant and animal products for risk assessment is restricted to the parent compound. Inclusion of triazole derivative metabolites in this definition will need to be considered at a later stage.
These compounds (mainly triazole, triazole alanine and triazole acetic acid) which are common metabolites of all triazole fungicides have been recognized as hazards given their impact on reproduction. Toxicological reference values have been agreed by the PRAPeR expert meeting 14 on toxicology in January 2007.
Chronic and acute consumer exposures assessments have been carried out for parent compound only and were found to be well below the respective toxicological trigger values of epoxiconazole.
Therefore provisionally no risk for the consumer has been identified under restriction of an uncertainty related to the isomer ratio consumer is actually exposed to. A robust conclusion on the risk will be possible when information on the actual level of triazole derivative metabolites in primary crops, rotational crops, and products of animal origin will be available. It must be noted that this lack of data is a generic issue and concerns all active substances of the triazole chemical class whose degradation pathway in primary crops, soil and livestock involves a cleavage of the triazole ring.

The environmental exposure assessments available for epoxiconazole were sufficient to complete the necessary EU level estimates of Predicted Environmental Concentrations (PEC) for the representative uses applied for, for annex 1 listing. Because of the persistence of epoxiconazole in soil and aquatic sediment it was necessary for exposure assessment to take into account the potential accumulation of epoxiconazole in these environmental matrices from potential use in consecutive years. However, the EFSA found the assessment (not peer reviewed) of the accumulation potential of metabolite BF 480-entriazole in sediment uncertain and consequently not valid for the risk assessment to sediment dwellers. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals (5×10^5 cm^{-3}) resulted in an half life estimated of 4 days, indicating a potential for long range atmospheric transport. Therefore monitoring data for residues in environmental matrices might be needed to address the potential of long range atmospheric transport. A new calculation of the half life in air was provided by the rapporteur Member State but has not been peer reviewed.

The first tier TER values indicated a potential hig long-term risk to birds and mammals. Measured residues were accepted in the expert meeting to refine the RUD values for herbivorous birds and mammals. The suggested refinements of PT and PD were not accepted resulting in data gaps for further refinements of the long-term risk to insectivorous and herbivorous birds. Whether it is sufficiently justified to use a MAF of 1 although intervals between applications were above 21 days for about half of the residues studies needs to be evaluated further at Member State level. The experts agreed to use the hare and the wood mouse as focal species in the refined risk assessment for mammals as suggested in addendum 2. The proposed PT refinements were not agreed by the experts. The TER for hare was >5. However for wood mouse the TER is <5 and hence further risk refinement is required.

Algae and *Lemna gibba* were the most sensitive tested organisms. In order to detect long-term effects on fish a 28 d prolonged toxicity test, an early life stage test and three full life cycle tests were performed in order to investigate potential endocrine effects. A new test with *Lemna gibba* was performed and evaluated in addendum 2. The experts agreed to the assessment of the rapporteur Member State. The endpoint (7d EbC_{50} = 0.0043 mg a.s./L) derived from standard test conditions should be used in the risk assessment. The endpoint derived from the test system with sediment present was considered as not being of direct use in the risk assessment since epoxiconazole partitions rapidly to the sediment and thus reducing the exposure of free floating Lemna fronds. The TERs were above the trigger of 10 in only 2 FOCUS step3 part scenarios (D4 pond, D5 pond) out of 9. No full FOCUS step 3 scenario resulted in TERs above the trigger. The available full life cycle studies with fish were discussed in the expert meeting. It was agreed that the latest study where fish were exposed to a single peak of epoxiconazole could be used in the risk assessment. The experts agreed that a NOEC of 0.03 mg a.s./L can be used in the risk assessment. The effect observed on male vitellogenin levels (NOEC = 0.012 mg a.s./L) was considered as not relevant since it did not affect the reproductive performance of the tested animals. The long-term TERs for fish were above the trigger of 10 for all 9 FOCUS part scenarios as well as the TERs calculated with time weighted PECsw and the lower long-term endpoint for fish (NOEC of 0.01 mg a.s./L) which was based on effects on

growth in one of the fish full life cycle tests conducted under flow-through conditions. Epoxiconazole was of similar toxicity to algae when formulated but was significantly more toxic to fish. The acute TERs for fish were above the trigger of 100 in the FOCUS step3 part scenarios D4 (pond) and D5 (pond). In the part scenario D4 (stream) a TER of 99 was calculated which is close to the trigger of 100. Taking into consideration that part of the active substance reach the surface water via drainage and run-off and thus not as the intact formulation the rapporteur Member State concludes that the acute risk to fish from the formulation BAS 480 13 F to fish is addressed for the full FOCUS scenario D4 (pond and stream). EFSA agrees to the opinion of the rapporteur Member State. The risk of bioaccumulation (BCF = 70) was assessed as low. The metabolites 1,2,4-triazole and BF480-entriazole were less toxic to aquatic organisms and the risk posed to aquatic organisms was assessed as low for the representative uses in cereals. The TERs for sediment dwellers was calculated as 5.3 and 40.3 (depending on the test system from which the endpoint was derived). Overall it is concluded that the aquatic risk assessment needs further refinement and/or risk mitigation such as no-spray buffer zones. The acute risk of epoxiconazole to earthworms is low but the first tier long term TER values were below the Annex VI trigger of 5. Field studies were conducted to assess the effects of continued use of epoxiconazole on earthworm populations in treated fields and also a terrestrial model ecosystem study. The presented studies had some limitations but the long-term risk to earthworms and soil dwelling arthropods was sufficiently addressed for the representative uses evaluated if all the available information is considered together

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

- Risk mitigation measures such as no-spray buffer zones are required to protect aquatic organisms. Only 2 out of 9 FOCUS step3 part scenarios but no full FOCUSstep3 scenario resulted in TERs above the trigger. No calculations of the required no-spray buffer zones were provided to give an indication of the required risk mitigation measured.

Critical areas of concern

- A final consumer risk assessment covering the toxicological burden of the triazole derivative metabolites is at this stage not possible to conduct due to lacking data on their occurrence in primary crops, rotational crops and products of animal origin.
- The long-term risk assessment for birds and mammals needs further refinement.
- The risk assessment for aquatic organisms (aquatic plants and sediment dwelling organisms) needs further refinement.

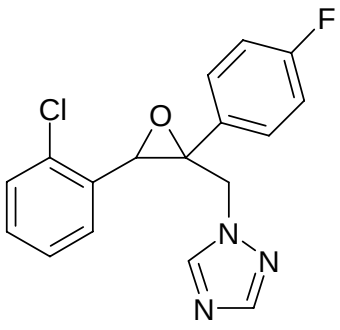
APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

(Abbreviations used in this list are explained in appendix 2)

Appendix 1.1 Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	epoxiconazole
Function (*e.g.* fungicide)	fungicide
Rapporteur Member State	Federal Republic of Germany
Co-rapporteur Member State	none

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(2*RS*, 3*SR*)-1-[3-(2-chlorophenyl)-2,3-epoxy-2-(4-fluorophenyl)propyl]-1*H*-1,2,4-triazole
Chemical name (CA) ‡	*cis*-1-[[3-(2-chlorophenyl)-2-(4-fluorophenyl)oxiranyl]methyl]- 1*H*-1,2,4-triazole
CIPAC No ‡	609
CAS No ‡	135319-73-2 (formerly 106325-08-0)
EC No (EINECS or ELINCS) ‡	406-850-2
FAO Specification (including year of publication) ‡	none
Minimum purity of the active substance as manufactured ‡	920 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	none
Molecular formula ‡	$C_{17}H_{13}ClFN_3O$
Molecular mass ‡	329.76 g/mol
Structural formula ‡	

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

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	136.2 – 137 °C (99.9%)
Boiling point (state purity) ‡	not applicable
Temperature of decomposition (state purity)	> 310 °C (99.9%)
Appearance (state purity) ‡	colourless solid (99.9%)
Vapour pressure (state temperature, state purity) ‡	$< 1 \cdot 10^{-5}$ Pa (20 °C) (99.1%) extrapolated from measurements at 70 °C
Henry's law constant ‡	$< 4.7 \cdot 10^{-4}$ Pa m^3 mol^{-1} (20°C)
Solubility in water (state temperature, state purity and pH) ‡	7.1 mg/L (deionized water) (99.9%) pH 3: 8.4 mg/L all at 20 °C
Solubility in organic solvents ‡ (state temperature, state purity)	at 20 °C [g/L] (99.8%) Acetone 140 Acetonitrile 70 Dichlormethane 290 Ethyl acetate 100 *n*-Heptane 0.5 Methanol 30 1-Octanol 10 Toluene 40
Surface tension ‡ (state concentration and temperature, state purity)	68.7 mN/m (0.5% w/w) (99.1%) 72.9 mN/m (6.4 mg/L) (99.6%)
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ = 3.3 (25 °C, deionised water) (99.8%) no dependence on the pH value
Dissociation constant (state purity) ‡	Epoxiconazole does not dissociate in water, no pK_a value could be determined (99.9%)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	λ_{max} [nm] ε 204 32000 263 390 No absorption above 290 nm (baseline).
Flammability ‡ (state purity)	The test substance is not considered highly flammable. The test substance shows no self-ignition up to 400 °C (93.7%)
Explosive properties ‡ (state purity)	No thermal or mechanical sensitivity with respect to shock or friction was observed. (93.7%)
Oxidising properties ‡ (state purity)	No oxidising properties (theoretical assessment)

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

Summary of representative uses evaluated (*Epoxiconazole*)*

Crop and/ or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (days)	kg as/hL min max	water L/ha min max	kg as/ha min max	(l)	(m)
Cereals (Wheat, Rye, Barley, Oat, Triticale, Spelt)	Northern and Southern Europe	BAS 480 27 F Opus	F	*Erysiphe graminis, Puccinia spp., Rhynchosporium secalis, Pseudocercosporella herpotrïchoides, Septoria spp.*	SC	125	spraying	25 – 69	1 - 2	21 - 42	0.0313 – 0.0833	150 - 400	0.125	35	[1]
Sugar beets	Northern and Southern Europe	BAS 480 27 F Opus	F	*Erysiphe betae, Uromyces betae, Cercospora beticola*	SC	125	spraying	39 - 49	1- 2	21 - 42	0.023 – 0.0833	150 - 400	0.092 – 0.125	28	Use withdrawn by notifier

[1] The risk assessment for birds and mammals and the aquatic risk assessment needs further refinement.

Remarks:
* Uses for which risk assessment could not been concluded due to lack of essential data are marked grey
(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
(g) All abbreviations used must be explained
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

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

Appendix 1.2 Methods of Analysis

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

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

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Epoxiconazole (provisional)
Food of animal origin		Epoxiconazole (provisional)
Soil		Epoxiconazole
Water	surface	Epoxiconazole
	drinking/ground	Epoxiconazole
Air		Epoxiconazole

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	GC-ECD	LOQ = 0.05 mg/kg (wheat, barley rye, oat, sugar beet, banana, coffee)
	GC-MS	LOQ = 0.01 mg/kg (tomato, lemon, wheat grain) LOQ = 0.02 mg/kg (rape seed)
	Open for ILV data for the GC method.	
	HPLC-MS/MS	LOQ = 0.01 mg/kg (gry crops) LOQ = 0.05 mg/kg (all kinds of crops)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	GC-ECD	LOQ = 0.001 mg/kg (milk) LOQ = 0.01 mg/kg (muscle, liver, kidney, fat, egg)
	GC-MS/MS	LOQ = 0,001 mg/kg (milk) LOQ = 0.01 mg/kg (egg, meat, fat, kidney and liver)
Soil (analytical technique and LOQ)	GC-ECD	LOQ = 0.01 mg/kg
	GC-MS	LOQ = 0.01 mg/kg
	GC-PND	LOQ = 0.01 mg/kg
Water (analytical technique and LOQ)	GC-MS	LOQ = 0.05 µg/L (tap water, surface water)
	GC-ECD	LOQ = 0.05 µg/L (tap water) LOQ = 0.5 µg/L (surface water)
Air (analytical technique and LOQ)	GC-ECD	LOQ = 0.09 µg/m3

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

Body fluids and tissues (analytical technique and LOQ)	An analytical method is not required (the substance is neither classified as T nor as T+). GC-ECD LOQ = 0.01 mg/kg (blood) GC-MS LOQ = 0.01 mg/kg (blood)

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

	RMS/peer review proposal
Active substance	none

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

Appendix 1.3 Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Rapid, about 50 % within 48 h, based on urinary and biliary excretion and amount in carcass
Distribution ‡	Wide, highest residues in blood, liver, kidneys, spleen, lung and adrenals after 168 h; plasma: AUC = 15-22 µg h/g, $t_{1/2}$ = 5-6 h
Potential for accumulation ‡	No potential for accumulation in tissue, but slow elimination from blood
Rate and extent of excretion ‡	> 95 % within 168 h (ca 17 % via urine and ca 78 % via faeces)
Metabolism in animals ‡	Extensively metabolised with at least 47 metabolites occuring; main pathways: opening of the oxirane ring, hydroxylation and conjugation
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolites (1,2,4-triazole, triazole alanin, triazole acetic acid)
Toxicologically relevant compounds ‡ (environment)	Parent compound and metabolites (1,2,4-triazole, triazole alanin, triazole acetic acid)

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	5000 mg/kg bw (m)	-
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	-
Rat LC_{50} inhalation ‡	> 5.3 mg/L air (4 h, nose only, highest obtainable concentration)	-
Skin irritation ‡	Not irritant	-
Eye irritation ‡	Not irritant	-
Skin sensitisation ‡	Not sensitising (M&K test)	-

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver (increased organ wt, clinical chemistry, chronic hepatitis); slight anaemia	
Relevant oral NOAEL ‡	1-yr, dog: 1.6 mg/kg bw/d	
Relevant dermal NOAEL ‡	21-d, rat: 400 mg/kg bw/d	
Relevant inhalation NOAEL ‡	No data, not necessary	

Genotoxicity ‡ (Annex IIA, point 5.4)

Not genotoxic	-

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

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

Target/critical effect ‡	Liver (increased organ wt, clinical chemistry, histology); adrenals; ovar	**R40**
Relevant NOAEL ‡	18-mo, mouse: 0.8 mg/kg bw/d	
Carcinogenicity ‡	Benign tumours of adrenals and ovaries in rats liver cell adenomas and carcinomas in mice	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: decreased body weight, vaginal haemorrhages	**R62**
	Offspring: perinatal mortality increased, oedema	
	Reproductive: impaired fertility, prolonged gestation, dystocia	
Relevant parental NOAEL ‡	2-gen., rat: 2.3 mg/kg bw/d	
Relevant reproductive NOAEL ‡	2-gen., rat: 2.3 mg/kg bw/d	
Relevant offspring NOAEL ‡	2-gen., rat: 2.3 mg/kg bw/d	

Developmental toxicity

Developmental target / critical effect ‡	Maternal: Decreased body weight, clinical signs, reduced food consumption, clinical chemistry	**R63**
	Developmental: malformations (cleft palates in the rat) and a higher abortion and resorption rate	
Relevant maternal NOAEL ‡	Rat, oral: 15 mg/kg bw/d Rat, dermal: 1000 mg/kg bw/d Rabbit, oral: 5 mg/kg bw/d	
Relevant developmental NOAEL ‡	Rat, oral: 15 mg/kg bw/d Rat, dermal: 400 mg/kg bw/d Rabbit, oral: 20 mg/kg bw/d	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No neurotoxic potential Systemic toxicity: NOAEL, rat:.500 mg/kg bw	-
Repeated neurotoxicity ‡	No neurotoxic potential Systemic toxicity: NOAEL 90-d, rat:16 mg/kg bw	
Delayed neurotoxicity ‡	No data, not necessary	

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

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Mechanistic studies suggesting hormonal imbalances to cause carcinogenic (adrenals, ovaries) and reproductive/developmental effects. Liver toxicity including tumours is related to microsomal enzyme induction. Evidence for aromatase inhibition in vitro and in vivo.
Studies performed on metabolites or impurities ‡	No further data required.

Medical data ‡ (Annex IIA, point 5.9)

	No evidence of adverse effects. No poisoning incidents reported so far.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.008 mg/kg bw	18 mo, mouse	100
AOEL ‡	0.008 mg/kg bw/d	1-yr, dog (50% oral absorption)	100
ARfD ‡	0.023 mg/kg bw	2-gen., rat	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50 % EC)	<u>In consideration to a formal not submitted but valid study reported in Addendum 3:</u> <u>'Opus' (SC formulation BAS 480 31 F):</u> 3 % for the concentrate (applied dose appr. 1.25 mg/cm^2) and 18 % for the dilution (applied dose appr. 0.006 mg/cm^2) based on rat in vivo
Formulation (e.g. name 50 % EC)	In consideration of the discussion at PRAPeR: 50 % default value for the concentrate and the dilution

Exposure scenarios (Annex IIIA, point 7.2)

Operator	<u>In consideration to a formal not submitted but valid study to the dermal absorption:</u> Acceptable for proposed uses (fungicide in cereal crops and sugar beets: 0.125 kg as/ha) according to the German model; not acceptable according to the UK POEM. – 12.6 % of the systemic AOEL (German model; gloves during mixing/loading, and gloves and garment during application) – 220 % of the systemic AOEL (UK-POEM, 5 L cont.;

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

	gloves during mixing/loading and application)
Operator	In consideration of the dermal absorption discussed at PRAPeR: Acceptable for proposed uses (fungicide in cereal crops and sugar beets: 0.125 kg as/ha) according to the German model; not acceptable according to the UK POEM. – 39 % of the systemic AOEL (German model; gloves during mixing/loading, and gloves and garment during application) – 700 % of the systemic AOEL (UK-POEM, 5 L cont.; gloves during mixing/loading and application)
Workers	Acceptable for proposed uses
Bystanders	Acceptable for proposed uses

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

	RMS/peer review proposal
Active substance	R40, R62, R63

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

Appendix 1.4 Residues

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

Plant groups covered	Cereals (wheat), fruits (bananas), and coffee beans, all as foliar application
Rotational crops	Wheat, green beans, carrots and lettuce
Metabolism in rotational crops similar to metabolism in primary crops?	yes
Processed commodities	Wheat (milling fractions); barley (milling fractions, brewing fractions)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	yes
Plant residue definition for monitoring	Parent compound epoxiconazole
Plant residue definition for risk assessment	Parent compound epoxiconazole (provisional)
Conversion factor (monitoring to risk assessment)	not concluded

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

Animals covered	Lactating goats, laying hens
Time needed to reach a plateau concentration in milk and eggs	5-7 days
Animal residue definition for monitoring	Parent compound epoxiconazole
Animal residue definition for risk assessment	Parent compound epoxiconazole (provisional)
Conversion factor (monitoring to risk assessment)	not concluded
Metabolism in rat and ruminant similar (yes/no)	yes
Fat soluble residue: (yes/no)	yes (log Pow = 3.3)

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

Epoxiconazole residues in succeeding crops under field conditions (wheat, potatoes, barley, oilseed rape, turnips) were all below the limit of determination of 0.05 mg/kg Triazolyl alanine and triazolyl acetic acid were found in wheat grain

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

residues are stable during storage periods up to 2 years at – 18 °C

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

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 4.0 (cow)-9.5 (beef) mg/kg feed dry matter (or 0.15-0.41 mg/kg bw)	yes 0.8 mg/kg feed dry matter (or 0.05 mg/kg bw)	yes 0.9mg/kg feed dry matter (or 0.04 mg/kg bw)
Potential for accumulation:	no	yes	no
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues	yes	no	yes
	Feeding studies (low (for cows) and middle (for beef) dosing levels relevant, corresponding to 0.12 and 0.39 mg/kg bw respectively) Residue levels in matrices : Mean (max) mg/kg		
Muscle	< 0.01	no poultry feeding study conducted since it is concluded from results of metabolism study that residues will be below 0.01 mg/kg (LOQ)	no pig feeding study conducted since it is concluded from lowest dose level of cow feeding study that residues will be below 0.01 mg/kg (LOQ) except for liver (anticipated residue: 0.05 mg/kg)
Liver	0.1		
Kidney	< 0.01		
Fat	< 0.01		
Milk	< 0.001 – 0.001		
Eggs			

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

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 and rye grain	North, field	N = 14: < 0.01; 4 x 0.02; 3 x 0.03; 4 x < 0.05; 0.06; 0.07 mg/kg		0.20	0.07	0.03
wheat and rye grain	Mediterranean, field	N = 8 : 4 x < 0.01; 0.03; 0.04; < 0.05; 0.10 mg/kg		0.20	0.10	0.02
barley and oats grain	North, field	N = 12 : 2 x < 0.05; 2 x 0.06; 2 x 0.07; 1 x 0.08; 1x 0.09; 1 x 0.1; 1 x 0.11; 1 x 0.14; 1 x 0.24 mg/kg		1.00	0.24	0.075
barley and oats grain	Mediterranean, field	N = 8 : 2 x < 0.03; 2 x < 0.09; 0.19; 0.29; 0.31; 0.39 mg/kg		1.00	0.39	0.14
cereal straw	North and Mediterranean, field	N = 35 : 0.56; 0.74; 0.78; 1.00; 1.03; 1.14; 1.33; 1.42; 1.44; 1.59; 1.68; 1.68; 1,71; 2.00; 2.14; 2.22; 2.40; 2.42; 2,49; 2,65; 2.91; 3.54; 3.90; 4.27; 4.43; 4.55; 4.83; 4.85; 5.61; 6.29; 6.63; 6.69; 9.29; 10.2; 15.4 mg/kg		-	15.4	2.42
sugar beet roots	North and Mediterranean, field	N = 18 : 17 x < 0.05; 0.05		0.05	0.05	0.05
sugar beet tops	North and Mediterranean, field	N = 18 : 0.06; 0.07; 0.09; 0.16; 0.19; 0.23;2 x 0.25; 0.40; 0.41; 0.62; 0.74; 0.95; 1.19; 1.24; 1.26; 1.30; 1.44		0.41	1.44	0.68

(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

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

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

ADI	0.008 mg/kg bw/d
TMDI (% ADI) according to WHO regional European diet	13%
TMDI (% ADI) according to national (to be specified) diets	16 % (German VELS model, 2- <5 year old children) based on intended uses
IEDI (WHO European Diet) (% ADI)	not relevant
NEDI (specify diet) (% ADI)	not relevant
Factors included in IEDI and NEDI	none
ARfD	0.023 mg/kg bw
IESTI (% ARfD)	max 11 % (7-10 years old children, PSD model), max 8 % (children up to 5 years, VELS model)
NESTI (% ARfD) according to national (to be specified) large portion consumption data	10 % (consumption of 64 g/d of oat bran, 97.5 percentile, German children, aged 2 –< 5 years)
Factors included in IESTI and NESTI	-processing factors of 4.2 for bran, STMR values

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Wheat (flour type 550)	1 (4 trials)	<< 0.6		
Wheat (whole meal flour)	1 (4 trials)	1.3		
Wheat germs	1(4 trials)	2.5		
Wheat (coarse/total bran)	1(4 trials)	4.2		
Barley (brewing malt)	1(4 trials)	0.59		
Barley (malt germ)	1(4 trials)	0.9		
Beer	1(4 trials)	< 0.08		

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

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

Plant matrices.	Sugar beet roots : 0.05 mg/kg Wheat, rye and triticale grains : 0.20 mg/kg Barley and oats grains : 1.0 mg/kg
Animal matrices	*Cattle products:* 0.01* mg/kg for ruminant meat 0.2 mg/kg for ruminant liver 0.01* mg/kg for ruminant kidney 0.01* mg/kg for ruminant fat 0.002 mg/kg for milk *Chicken products:* 0.01* mg/kg for meat 0.01* mg/kg for liver 0.01* mg/kg for fat 0.01* mg/kg for eggs *Pig products:* 0.01* mg/kg for pork meat 0.05 mg/kg for pork liver 0.01* mg/kg for pork kidney 0.01* mg/kg for pork fat

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

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

Appendix 1.5 Fate and behaviour in the environment

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

Mineralisation after 100 days ‡	- Oxirane ^{14}C-labelled epoxiconazole: Clay/clay loam: 5.5 % CO_2 after 84 days 10.3 % CO_2 after 336 days (study end) Sand: 7.2 % CO_2 after 84 days 38.3 % CO_2 after 336 days (study end) - Metabolite [3,5-^{14}C] 1,2,4-triazole (rate study): Sandy loam 20/11 % CO_2 after 120 days (study end) Loamy sand: 1.4/1.6 % CO_2 after 120 days (study end) Silt loam: 34/32 % CO_2 after 120 days (study end) (higher mineralisation rates can be expected in soils pre-adapted to azole fungicides)
Non-extractable residues after 100 days ‡	- Oxirane ^{14}C-labelled epoxiconazole: Clay/clay loam: 8.9 % after 84 days 23.2 % after 336 days (study end) Sand: 12.1 % after 84 days 15.1 % after 336 days (study end) - Metabolite [3,5-^{14}C] 1,2,4-triazole (rate study): Sandy loam 63/66 % after 120 d (study end) Loamy sand: 54/65 % after 120 d (study end) Silt loam: 38/42 % after 120 d (study end)
Relevant metabolites - name and/or code, % of applied (range and maximum) ‡	Oxirane ^{14}C-labelled epoxiconazole: - Unknown fraction M2/M3 (only partly resolved, fraction M2 consisting of at least 4 further fractions) Clay/clay loam: max. 4.0 % after 84 d 2.3 % after 336 days (study end) Sand: max. 3.6 % after 28 d 1.1 % after 336 days (study end) Triazole ^{14}C-labelled epoxiconazole: Loamy sand: 5% 1,2,4-triazole after 343 days (only analysed after 343d) Triazole ^{14}C-labelled epoxiconazole: Sandy loam: 6,6% 1,2,4-triazole after 175 days (only analysed after 175d)

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

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

Anaerobic degradation ‡	Investigated: fluorophenyl ^{14}C-labelled epoxiconazole - loamy sand = silty sand Recoveries in % of total applied radioactivity (TAR): active substance 55.3 % after 120 days (study end) metab. BF 480-entriazol: max. 8.6 % after 120 days 5.7 % after 91 d metab. BF 480-alcohol: max. 1.2 % after 63/91/120 days each mineralisation: 1.6 % CO_2 after 120 d bound residues: 18.4/24.2 % after 120 d DT_{50} 154 days (1st order, nonlinear fit)
Soil photolysis ‡	Investigated: fluorophenyl ^{14}C-epoxiconazole in sandy loam, 40 % WHC, 22 °C. Continuous irradiation (Xe-lamp, SUNTEST apparatus 3 mW/cm²) for 15 d. Recoveries in % of total applied radioactivity: active substance 84.1 % after 15 days (study end) CO_2 1.9 % after 15 days bound residues 10.1 % after 15 days metabolites max 1 % after 15 days DT_{50} 67 days, continuous irridation

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	X12 mg/kg	pH	t. 'C / % MWHC	DT50 /DT90 (d)	DT50 (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Itingen, clay	-	6.9	20.5/ 40	673	384	0.73	SFO
Collombey, sand	-	7.1	20.5/ 40	254	264	0.94	SFO
Speyer 2.2, loamy sand	-	6.0	20.7/ 20	1064	431	0.88	SFO
Speyer 2.2, loamy sand	-	6.0	20.7/ 60	408	978 (649*)	0.84	SFO
Les Ecouvette, sandy loam	-	4.8	20.7/ 60	502	531	0.92	SFO
Bruch West, sandy loam	0.05	7.4	20/ 40	127	86	0.91	SFO
Bruch West, sandy loam	0.5	7.4	20/ 40	354	238 (143*)	0.75	SFO

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

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

Broom`s Barn, sandy loam	-	6.99	10/ 40	453	139	0.74	SFO
Broom`s Barn, sandy loam	-	6.99	15/ 60	206	124	0.76	SFO
Broom`s Barn, sandy loam	-	6.99	10/ 60	180	73 (108*)	0.91	SFO
Shuttleworth, clay loam	-	6.37	15/ 60	281	145	0.94	SFO
Shuttleworth, clay loam (application rate: 1 mg/kg)	-	6.37	10/ 60	221	77	0.76	SFO
Shuttleworth, clay loam	-	6.37	10/ 80	327	140	0.80	SFO
Shuttleworth, clay loam (application rate: 0.05 mg/kg)	-	6.37	10/ 60	170	59 (98*)	0.71	SFO
Woburn, loamy sand	-	5.7	15/ 60	192	129	0.83	SFO
Geometric mean/median					226 / 204		

* geometric mean of different soil treatments in one soil

Met.: 1,2,4-triazole	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Laacher Hof AXXa, sandy loam		6.4	20/ 40	6	-	5	-	SFO
BBA 2.2, loamy sand		5.8	20/ 40	10	-	10	-	SFO
Laacher Hof A III, silt loam		6.7	20/ 40	12	-	9	-	SFO
Geometric mean/median						8		

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

Field studies ‡ soils with $r^2 > 0,7$ (considered models: SFO, DFOP, FOMC)

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country) : :	X1	pH	Depth (cm)	DT50 (d) actual	DT90(d) actual	St. (r^2)	DT50 (d) Norm.	Method of calculation
Silty clay	Achtum (Germany)		7.5		52	174	0.89	-	SFO
Loamy silt	Boehl (Germany)		7.5		120	>5000	0.72	-	DFOP**
Loamy sand	Bothkamp (Germany)		4.6		216 111 137	719 - 1180	0.72 0.91 0.90	-	SFO FOMC* DFOP**
Sandy loam	Havixbeck (Germany)		6.3		112 82 79	372 1077 >5000	0.88 0.97 0.98	-	SFO FOMC* DFOP**
Loam	Stetten (Germany)		6.9		74 56 58	247 1016 >5000	0.82 0.94 0.97	-	SFO FOMC* DFOP**
Sandy loam	Oberding (Germany)		6.6		150 128 103	499 1026 >5000	0.84 0.89 0.86	-	SFO FOMC* DFOP**
Loamy sand	Birkenheide (Germany)		4.9		226 184 190	752 >5000 >5000	0.86 0.91 0.93	-	SFO FOMC* DFOP**
Sandy silt	Manzanilla (Spain)		7.7		141	$2x10^6$ 170	0.93 0.97	-	FOMC* DFOP**
Sand	Utrera (Spain)		7.2		1	313	0.99	-	FOMC*
Geometric mean/median					-	-		-	

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

*) FOMC Parameters (soils with r^2>0,7)			
Test site	Co	Alpha	beta
Bothkamp	0.2084	0.2584	8.1822
Havixbeck	0.3941	0.7619	55.1166
Stetten	0.3116	0.6410	28.7590
Oberding	0.2463	1.0199	131.4887
Birkenheide	0.2525	0.5347	69.4095
Manzanilla*	0.274	0.169	0.426
Utrera*	0.263	0.270	15.909

**) DFOP Parameters (soils with r^2>0,7)				
Test site	Co	K1	K2	dist
Böhl	0.02794	0.010186	1*10-11	0.725
Bothkamp	0.20581	0.001542	0.05340	0.617
Havixbeck	0.38759	1*10-10	0.01261	0.208
Stetten	0.30188	0.017393	1*10-11	0.784
Oberding	0.24636	1*10-10	0.00804	0.114
Birkenheide	0.25811	0.001887	0.02987	0.714
Manzanilla	0.27562	0.000516	0.06665	0.546

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	X[13]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Bruch West, silty sand*	-	7.5	20 /44.5	154			SFO
Geometric mean/median				-			

* epoxiconazole in soil was 55% of TAR after 120 d

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

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

Soil accumulation and plateau concentration ‡	Two field accumulation (Germany) studies with 6 to 9 years duration: Study 1: Niederhofen, Germany, 6 years duration, loamy sand/sandy loam, 437 g a.s./ha/year measured residues after last application (mg/kg soil) in 0 to 25 cm min. / max. trial 1 (cereals; no biomass withdrawal) 0.062 / 0.114 trial 2 (cereals; grain and straw harvested) 0.056 / 0.108 Calculated degradation rates (TOPFIT modelling, SFO): $DT_{50, trial\ 1}$: 420 d $DT_{50, trial\ 2}$: 387 d Geometric mean DT_{50}: 403 d Study 2: Boehl, Germany, 9 years duration, sandy loam, 312 g a.s./ha/year measured residues after last application (mg/kg) in 0 to 25 cm min. / max. trial 1 (bare soil) 0.09 / 0.19 trial 2 (cereals; grain harvested) 0.05 / 0.13 trial 3 (cereals; grain and straw harvested) 0.06 / 0.12 Calculated degradation rates (TOPFIT modelling, SFO): $DT_{50, trial\ 1}$: 343 d $DT_{50, trial\ 2}$: 251 d $DT_{50, trial\ 3}$: 389 d Geometric mean DT_{50}: 322 d Soil accumulation modelling with ModelMaker 3 2 x 125 g a.s./ha every year for 26 year, interval 21 days, 1.5 kg/L bulk density, with interception (FOCUS) for cereal scenario f = 0.5 (BBCH 25) and 0.7 (BBCH 61), DT_{50} 403 days (geometric mean from study 1 in Niederhofen) Max. residue in top 5 cm: $PEC_{soil, accu\ overall}$: 0.167 mg kg^{-1}

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ [L/kg]	Epoxiconazole: K_{foc} 280 – 2647 (2 studies), arithmetic mean 1073 (n=5): soil — pH — K_{foc} — K_f — 1/n 2.1, sand — 6.0 — 957 — 4.79 — 0.766 (90,9 % sand, 3.8 % silt, 5.3 % clay, 0.5 % org.C.) Les.EV, sandy loam — 4.75 — 2647 — 19.59 — 0.813 (53,7 % sand, 29.3 % silt, 17 % clay, 0.74 % org.C.) Itingen, clay/clay loam — 6.87 — 1100 — 21.78 — 0.808 (33.6 % sand, 24.8 % silt, 41.6 % clay, 1.98 % org.C.) Sandy silty loam — 7.1 — 280 — 7.25 — 0.882 (40.4 % sand, 43 % silt, 16.9 % clay, 2.6 % org.C.) Clayey loam — 6.8 — 380 — 7.50 — 0.910 (19.1 % sand, 40.2 % silt, 41 % clay, 2.0 % org.C.) no correlation of k_f with parameters oc, clay and pH was observed metabolite 1,2,4-triazole K_{foc}: 43-120, arithmetic mean 89 (n=4) soil — pH — K_{foc} — K_f — 1/n Sandy loam — 6.9 — 89 — 0.720 — 1.016 (62 % sand, 21 % silt, 17 % clay, 1.4 % org. matter, Corg 0.812 %.) Clay loam — 6.9 — 43 — 0.748 — 0.827 (26 % sand, 46 % silt, 28 % clay, 3.0 % org. matter, Corg 1.74 %.) Silty clay — 8.8 — 120 — 0.833 — 0.897 (11 % sand, 44 % silt, 45 % clay, 1.2 % org.C matter, Corg 0.696) Silty clay loam — 7.0 — 104 — 0.722 — 0.922 (9 % sand, 62 % silt, 29 % clay, 1.2 % org. matter, Corg 0.696)
pH dependence ‡	no (for 1,2,4-triazole agreed by PRAPeR 12).

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

Column leaching ‡	Guideline: BBA IV 4-2. Three studies with 3 LUFA soils each: German standard soils LUFA 2.1, 2.2 (loamy sand), 2.3 (sandy loam), saturated soil moisture, room temp. Applied: 1 L BAS 480 13 F or BAS480 03 F or BAS 483 00 F/ha = 125 g as/ha in 2 studies, 3rd study 187 g as/ha, 200 mm irrigation. Concentrations in leachate: Epoxiconazole conc. were < 0.05 µg/L in all leachates of the two studies (< 0.2 % of applied amount).
Aged residues leaching ‡	(1) Guideline: BBA IV 30 day ageing in the dark, 22 °C, 21.1 % WHC, 10.2 % field capacity. Application rate 1 mg as/kg (509 g as/ha), ^{14}C-labelled. Soil: LUFA 2.1 (90 % sand, 3.8 % silt, 5.3 % clay, 0.48 % org. C., pH 6.0) Very low radioactive residues in the 4 percolates (about 100 ml each): 0.1 - 0.4 % of applied radioactivity, sum 0.8 % (0.8 µg total). Epoxiconazole: in soil segments 1, 2 and 3: 16.6, 74.8 and 1.5 % of applied radioactivity. (2) Guideline EPA 163-1 Test conditions as described above. 10 percolate fraction of 100 mL but 205 g as/ha.

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

	Very low radioactive residues in percolates: 0.0 - 0.2 % of applied radioactivity, sum 0.7 % (0.352 µg total). Epoxiconazole: in soil segments 1, 2 and 3: 68.5, 21.0 and 0.4 % of applied radioactivity. (3) Guideline: BBA IV 4-2 and EPA 163-1 175 day ageing in the dark, 22 °C, application rate 0.5 mg as/kg, triazole-^{14}C labelled = 255 g as/ha. Soil: Sand, LUFA 2.1 (93.3 % sand, 4.7 % silt, 2.0 % clay, 0.74% org. C., pH 5.4) Sandy loam (74 % sand, 10 % silt, 16 % clay, 0.9 % org. C., pH 7.2) : Very low radioactive residues in the 4 percolates: BBA guideline evaluation 1.3 % of applied radioactivity, epoxiconazole: in segments 1, 2 and 3: 82.2, 17.9 and 0.5 % of applied radioactivity. EPA evaluation 1.1 % = 0.226 µg total). epoxiconazole: in segments 1, 2 and 3: 57.8, 35.6 and 3.9 % of applied radioactivity. (4) Guideline: BBA IV 4-2 343 day ageing in the dark, 22 °C, application rate 0.5 mg as/kg oxirane- and triazole-^{14}C labelled. Soil: Sandy loam (81 % sand, 12 % silt, 7 % clay, 1.0 % org. C., pH 6.3). Very low radioactive residues in the 5 percolates: oxirane-labelled: < 0.01-0.6 % of applied radioactivity, sum 0.72 % (0.311 µg total). Epoxiconazole: in segments 1, 2 and 3: 64.6, 28.6, 0.5 % of applied radioactivity. triazole-labelled: sum in percolate 1.3 % TAR, Epoxiconazole: in soil segments 1, 2 and 3: 61.4, 33.5, 0.6 % of applied radioactivity. Metabolite 1,2,4-triazole 31 day ageing in the dark, application rate 1 mg triazole = 215 g/ha. Soil: Sandy loam and silt loam, 31 d ageing. 520 mm irrigation throughout 91 d. 42 - 46 % of applied radioactivity in the leachates, 54 - 58 % remained in soil, one half of it in the upper 5 cm. No triazole was identified in the leachates.
Lysimeter/ field leaching studies ‡	not performed, not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	SFO kinetic Worst case of non-standardised $DT_{50field}$ out of 8 studies: 226 days ("Birkenheide") 5 cm soil layer, 1.5 kg/L bulk density with interception (FOCUS) for cereal scenario f = 0.5 (BBCH 25) and 0.7 (BBCH 61) Interval between applications 21 d.
Application rate	2 × 0.125 kg active substance /ha

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

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	-		0.128	
Long term 21d	--	--		0.124

Metabolite 1,2,4-triazole

Method of calculation

PEC: 1st order kinetic, DT_{50Lab} worst case standardised to 15 °C of 3 studies: 18 d, 5 cm soil layer, 1.5 kg/L bulk density, with interception (FOCUS) for cereal scenario f = 0.5 (BBCH 25) and 0.7 (BBCH 61). Interval between applications 21 d. ModelMaker, *k*1_deg = 1st order rate constant for BAS 480 F to metabolite 1,2,4-triazole 0.0038/d, *k*2_deg = 1st order rate constant for elimination of metabolite 1,2,4-triazole 0.039/d, molar mass correction BAS 480 F to metabolite 1,2,4-triazole 0.211 (69.1 g/mol/329.8g/mol).

Application rate

2 x 0.125 kg active substance /ha

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial			0.00211	

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature) ‡

pH 3:	parent: 65 % decrease at 70 °C after 20 d	
pH 5:	parent: stable at 25 °C, stable at 75 °C for 29 d, 20 % decrease at 90 °C after 29 d	
	1,2,4-triazole:	stable at 25 °
pH 7:	parent:	stable at 25 °C, 75 °C, 90°C
	1,2,4-triazole:	stable at 25 °
pH 9:	parent:	stable at 25 °C, 75 °C, 12 % decrease at 90 °C
	1,2,4-triazole:	stable at 25 °

Photolytic degradation of active substance and relevant metabolites ‡

Active substance
- absorption coefficient < 10 L/mol x cm.
- no photolysis in sterile buffer solution after 31 days, 3 mg as/L, pH 7, 25 °C, natural sunlight mimic, 1800 µEinstein (SUN-TEST apparatus), 12 h cycle light/dark. ^{14}C-labelled as.
- 20 % degradation in natural water after 15 days, 3.3 mg as/L, pH 8.2, DOC 11.7, TOC 11.2 mg/L; nitrate 0.84 mg/L. 22 °C, natural sunlight mimic, 3 mW/cm² (SUNTEST-apparatus), constant light. As not labelled.

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

	Epoxiconazole: slow photolysis, DT_{50} 52 d, 1st order. No metabolites investigated Metabolite: 1,2,4-triazole, ^{14}C-labelled - 80 mg/L triazole in distilled water containing humic acid (Fluka). No photochemical loss after 30 days (natural sun light). absorption coefficient < 10 L/mol x cm
Readily biodegradable ‡	no (OECD 301F)
Dissipation in water/sediment	Water/sediment, 2 systems, ^{14}C-U-chlorophenyl and ^{14}C-U-fluorophenyl labelled epoxiconazole, application rate 125 g as/ha. 2 systems (A = Millstream Pond, sediment: clayey loam; B = Swiss lake, sediment: sand)

Active substance

Epoxiconazole as: (ModelMaker 3.0.4, 1st order)

	system A	system B
Degradation in water/sediment - DT_{50} water ‡		
$DT_{50,water}$	38.4 d	93.1 d
- DT_{90} water ‡		
$DT_{90,water}$	127.6 d	309.4 d
r^2	0.987	0.975
- DT_{50} whole system ‡		
$DT_{50,system}$	172 d	67.5 d
- DT_{90} whole system ‡		
$DT_{90,system}$	573 d	224 d
r^2	0.997	0.989
- DT_{50} sediment ‡		
$DT_{50,sediment}$	-	61.4 d
- DT_{90} sediment ‡		
$DT_{90,sediment}$	-	204 d
r^2	-	0.975

Dissipation - DT_{50} water ‡

ModelMaker 4.0	system A	system B	
$DT_{50,water\ degradation}$	2.8 d	6.4 d	best fit

Metabolite

Metabolite: BAS 480-entriazole

Degradation in water/sediment - DT_{50} sediment ‡ - DT_{90} sediment ‡

	system A	system B
$DT_{50,sediment}$	-/-*	65.2 d
$DT_{90,sediment}$	-/-*	216 d
r^2	0.987	0.975

* no reliable fit in ModelMaker calculations

Mineralisation	after 100 days (study end) in % TAR: ^{14}C-U-chlorophenyl / ^{14}C-U-fluorophenyl labelled epoxiconazole system A: 4.2 / 3.3 system B: 3.8 / 3.2
Non-extractable residues	after 100 days (study end) in % TAR: ^{14}C-U-chlorophenyl / ^{14}C-U-fluorophenyl labelled epoxiconazole system A: 21.9 / 21.6 system B: 19.7 / 19.2
Distribution in water / sediment systems (active substance) ‡	Maximum values: (as in % TAR) epoxiconazole, 14C-U-chlorophenyl / 14C-U-fluorophenyl label System A: 71.0/67.7 % in sediment after 30 days System B: 48.3/50.0 % in sediment after 13 days

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

BAS 480 F in % total applied radioactivity (TAR) (as: chloro-/fluorophenyl-^{14}C label)

days after applicat.	(A) **water** (B)		(A) **sediment** (B)	
0	93.6/91.1	93.4/91.1	< LOD/3.2	2.0/2.7
1	66.7/67.5	76.8/78.1	26.9/26.0	18.1/15.8
3	49.4/43.0	64.4/62.5	45.4/48.6	31.2/30.3
7	24.9/25.7	47.8/49.9	65.7/62.2	42.8/41.0
13	12.9/22.7	37.7/32.3	69.9/60.3	48.3/50.0
30	8.0/9.6	21.6/15.2	71.0//67.7	36.4/40.7
59	4.5/4.7	12.8/12.8	66.4/63.8	38.5/35.0
100	3.6/4.5	6.3/6.6	64.0/58.5	33.6/37.2

Distribution in water / sediment systems (metabolites) ‡

Maximum values: (BAS 480 entriazole in % TAR)
System A: 6.1/6.6 % in sediment after 30/59 days
System B: 32.7/34.0 % in sediment after 100/59 days

BAS 480 entriazole in % TAR (as: chloro-/fluorophenyl-^{14}C label)

days after applicat.	(A) **water** (B)		(A) **sediment** (B)	
0	< LOD/1.4	< LOD/1.7	< LOD	< LOD
1	< LOD/0.7	< LOD/0.9	< LOD/0.4	< LOD
3	< LOD	< LOD/0.8	< LOD/0.8	< LOD/0.9
7	< LOD	< LOD	1.3/2.6	2.5/2.4
13	< LOD	< LOD	3.9/5.7	6.4/7.0
30	< LOD	< LOD	6.1/5.6	27.0/27.4
59	< LOD	< LOD	3.1/6.6	30.6/34.0
100	< LOD	< LOD	3.7/5.7	32.7/28.1

other unknown metabolites:
water A: max. 0.8/1.7 %TAR at day 0
water B: max. 1.4/1.3 %TAR at day 0
sediment A: max. 2.3/2.5 %TAR after 30 resp. 100 d
sediment B: max. 2.1/1.8 % TAR after 100 d

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

Parent

Method of calculation	FOCUS surface water Step 3, 9 different FOCUS locations with 9 scenarios. Input parameters: $DT_{50,\ water}$ from water/sediment study 59.8 d, $DT_{50,sediment}$ 149.7 d (geometric means). Median of standardised $DT_{50,soil}$ 73 d.; Koc 1073 L/kg *; 1/n 0.836. Vapour pressure < $1 \cdot 10^{-5}$ Pa 20°C, molar enthalpy of vaporisation 95000 J/mol, water solubility 7.05 mg/L at pH 7, molar enthalpy of dissolution 27000 J/mol, diffusion coefficient in water 4.3×10^{-5} m²/d, diffusion coefficient in air 0.43 m²/d. Scenario: spring [2)]cereals, BBCH code 25 and 69
Application rate	2 x 125 g as/ha with an interval of 21 days.
Main routes of entry	Run off and Spray drift

* arithm. mean of 5 Koc and 1/n values (broad range of individual values)
[2)] crop scenario with worst case max. concentrations

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

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D1	ditch	0 h	0.896		5.020	
		24 h	0.825	0.858	5.020	5.020
		2 d	0.774	0.828	5.019	5.020
		4 d	0.704	0.782	[1)]	5.020
		7 d	0.634	0.733	[1)]	5.019
		14 d	0.515	0.652	[1)]	5.009
		21d	0.418	0.590	[1)]	5.005
		28 d	0.338	0.537	[1)]	5.002
		42 d	0.229	0.451	[1)]	4.989
D1	stream	0 h	0.608		2.539	
		24 h	0.192	0.469	[1)]	2.536
		2 d	0.013	0.269	[1)]	2.534
		4 d	0.004	0.206	[1)]	2.533
		7 d	0.002	0.205	[1)]	2.529
		14 d	0.001	0.199	[1)]	2.513
		21 d	0.001	0.197	[1)]	2.500
		28 d	0.001	0.196	[1)]	2.489
		42 d	0.190	0.195	[1)]	2.458
D3	ditch	0 h	0.691		0.589	
		24 h	0.469	0.585	0.543	0.583
		2 d	0.161	0.447	0.478	0.567
		4 d	0.015	0.253	0.385	0.523
		7 d	0.004	0.148	0.310	0.462
		14 d	0.001	0.075	0.231	0.373
		21 d	0.001	0.050	0.192	0.322
		28 d	0.000	0.038	0.167	0.288
		42 d	0.000	0.042	0.134	0.243

[1)] simulated period too short for calculation of PECsed

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

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D4	pond	0 h	0.068		0.675	
		24 h	0.068	0.068	0.675	0.675
		2 d	0.067	0.068	0.675	0.675
		4 d	0.067	0.068	0.675	0.675
		7 d	0.065	0.067	0.674	0.675
		14 d	0.060	0.066	0.672	0.675
		21d	0.056	0.064	0.669	0.674
		28 d	0.053	0.063	0.665	0.674
		42 d	0.054	0.061	0.653	0.672
D4	stream	0 h	0.593		0.238	
		24 h	0.0001	0.173	0.237	0.238
		2 d	0.000	0.104	0.232	0.237
		4 d	0.000	0.090	0.226	0.234
		7 d	0.000	0.071	0.223	0.231
		14 d	0.000	0.045	0.196	0.224
		21 d	0.000	0.042	0.174	0.215
		28 d	0.000	0.036	0.168	0.211
		42 d	0.000	0.026	0.215	0.203
D5	Pond	0 h	0.038		0.269	
		24 h	0.037	0.037	0.269	0.269
		2 d	0.036	0.037	0.269	0.269
		4 d	0.034	0.036	0.268	0.269
		7 d	0.033	0.035	0.268	0.269
		14 d	0.029	0.033	0.265	0.268
		21 d	0.027	0.031	0.261	0.268
		28 d	0.024	0.030	0.256	0.267
		42 d	0.020	0.027	0.246	0.265

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

FOCUS STEP 3 Scenario	Water Body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D5	stream	0 h	0.640		0.183	
		24 h	0.004	0.245	0.154	0.175
		2 d	0.001	0.123	0.130	0.162
		4 d	0.000	0.062	0.102	0.141
		7 d	0.000	0.036	0.080	0.121
		14 d	0.000	0.018	0.059	0.095
		21d	0.000	0.012	0.049	0.081
		28 d	0.000	0.009	0.043	0.072
		42 d	0.000	0.007	0.034	0.061
R4	stream	0 h	1.455		1.931	
		24 h	0.002	0.939	1.693	1.855
		2 d	0.002	0.885	1.508	1.762
		4 d	0.966	0.458	1.285	1.611
		7 d	0.002	0.397	1.448	1.554
		14 d	0.001	0.260	1.093	1.426
		21 d	0.000	0.173	0.931	1.298
		28 d	0.000	0.134	0.828	1.199
		42 d	0.000	0.089	0.691	1.056

Sediment accumulation for epoxiconazole	Estimated on the basis of the worst-case FOCUS surface water Step 3 scenario showing the highest initial and long-term concentrations in sediment and using ModelMaker v3.0.4 modelling (for details see Addendum 4).
PECsed,accu,max	10.91 µg/kg (to be compared to global max. PEC_{sed} of 5.020 µg/kg from D1 as worst-case FOCUSsw Step 3 scenario)

Metabolite

Method of calculation	not required, maximum 1.7 % in water phase of water/sediment study
Application rate	
Main routes of entry	

Sediment accumulation for BF 480-entriazole	Data available, not peer reviewed.

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

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUS-PELMO 2.2.2 and FOCUS-Macro 3.3.1 Epoxiconazole: Interception (FOCUS) for cereal scenario f=0.5 (BBCH 25) and 0.7 (BBCH 61). $DT_{50\ field}$, 74 (20°C standardised geom. mean). K_{oc} 280 L/kg, 1/n 0.882, water sol. 7.1 mg/L, pH independent, TSCF (crop uptake default 0.5. Metabolite 1,2,4-triazole: $DT_{50\ lab}$ 8 d (20°C, pF2 standardised). K_{oc} 43 L/kg, 1/n 0.827, water sol. 700 mg/L,pH independent, TSCF (crop uptake default 0.5
Application rate	2 x 0.125 g as/ha with an interval of 21 d days, BBCH growth stage 25-61

$PEC_{(gw)}$

Maximum concentration	0.001 µg/L
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	< 0.001 µg/L for 8 scenarios, 1 scenario 0.001 µg/L

PEC(gw) - FOCUS modelling results

	Scenario annual application	Parent (µg/l)	Metabolite (µg/l)		
			1,2,4-triazole	-	-
FOCUS-PELMO 3.3.2 / 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		
FOCUS-MACRO	Châteaudun	0.001	< 0.001		

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

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

Direct photolysis in air ‡	no calculation performed, not studied, not required
Quantum yield of direct photo transformation	criteria for the determination not reached (A > 10 L/mol x cm), determination is not necessary.
Photochemical oxidative degradation in air ‡	DT_{50} = **4** days, indicating a potential for long range aerial transport (calculation according to Atkinson 1987, considering a hydroxyl radical concentration of 5×10^5 cm^{-3}) A re-calculation with a newer version (v. 1.91) of AOPWIN is available in section 4.3, but not peer reviewed.
Volatilisation ‡	(circulation chamber, air flow 1 m/s, 21 ± 1 °C, rel. humidity 45 %.). from plant surfaces: < 5 % within 24 h after application
	from soil: ‡ < 5 % within 24 h after application

PEC (air)

Method of calculation	not performed

$PEC_{(a)}$

Maximum concentration	not required

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment for quantitation	Soil : epoxiconazole Water : epoxiconazole Sediment : epoxiconazole metabolite BF 480 entriazole [1)] Groundwater : epoxiconazole (by default) Air : epoxiconazole (by default) [1)] 1-[(2Z)-3-(2-chlorophenyl)-2-(4-fluorophenyl)-2 propenyl]-1H-1,2,4-triazole

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

Soil	USA, California. Soil survey of naturally occurring 1,2,4-triazole. 68 non-agricultural and agricultural samples. 45 % contained 1,2,4-triazole between 1.5 - 4.68 µg/kg. Intensity and frequency independent from agricultural practice.
Surface water	not available
Ground water	Germany, groundwater monitoring programme Data from 4 Federal States

	number				
	total	< LOQ	≤ 0.1	> 0.1-1.0	> 1.0 µg/L
2000	102	102	0	0	0
2001	114	114	0	0	0
2002	411	409	2	0	0
total	627	625	2	0	

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

Air (indicate location and type of study)	not available, data required to assess the long range atmospheric transport

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R 53

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

Appendix 1.6 Effects on non target species

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

Acute toxicity to mammals ‡	rat LD_{50} = 3160 mg as/kg bw
Long-term toxicity to mammals ‡	rat NOAEL = 25 mg as/kg diet (2 gen. reproduction) 2.3 mg as/kg bw
Acute toxicity to birds ‡	*Colinus virginianus* LD_{50} = > 2000 mg as/kg bw
Short term dietary toxicity to birds ‡	*Colinus virginianus* LD_{50} = > 907 mg as/kg bw > 5000 mg as/kg diet
Reproductive toxicity to birds ‡	*Colinus virginianus* NOEL = 10 mg as/kg diet 1.0 mg as/kg bw

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

Application rate (kg as/ha)	Crop	Category	Time-scale	TER	Annex VI Trigger
Tier 1 (Mammals)					
2 x 0.125	cereals, early	herbivorous mammal, small	acute	169	10
2 x 0.125	cereals, early	herbivorous mammal, small	long-term	0.27	5
2 x 0.125	cereals, late	insectivorous mammal	acute	4546	10
2 x 0.125	cereals, late	insectivorous mammal	long-term	5.75	5
Tier 2, long-term (Mammals)					
Refinement steps: - Focal species: Hare (early cereals), Wood mouse (early/late cereals) - RUD: 22. 86 mg/kg for cereal shoots and weeds, - DT_{50}: 14.5 d (f_{twa}: 0.63, MAF: 1.23) - PD factor and FIR/bw: Wood mouse: 31% grasses and cereal shoots, 31% non-grass herbs, 34% weed seeds, 4% arthropods					
2 x 0.125	cereals, early	Herbivorous mammal (hare)	long-term	23	5
2 x 0.125	cereals, early/late	Omnivorous mammal (Wood mouse)	long-term	3.9	5
Tier 1 (Birds)					
2 x 0.125	cereals, early	herbivorous bird, large	acute	213	10
2 x 0.125	cereals, early	herbivorous bird, large	short-term	176	10
2 x 0.125	cereals, early	herbivorous bird, large	long-term	0.37	5
2 x 0.125	cereals, early	insectivorous bird	acute	296	10
2 x 0.125	cereals, early	insectivorous bird	short-term	241	10
2 x 0.125	cereals, early	insectivorous bird	long-term	0.27	5
Tier 2, long-term (Birds)					
Refinement steps: - Focal species: Goose, Grey Partridge, Skylark, Yellowhammer - RUD: 22. 86 mg/kg for cereal shoots and weeds, - DT_{50}: 14.5 d (f_{twa}: 0.63, MAF: 1.23) - PD factor and FIR/bw: Grey Partridge: 31% grasses and cereal shoots, 31% non-grass herbs, 34% weed seeds, 4% arthropods Yellowhammer: 82 % large arthropods and 10 % small arthropods, 8% seeds Skylark: 50 % grasses and cereal shoots, 20 % weed seeds and 30 % large arthropods					

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

2 x 0.125	cereals, early	herbivorous bird (goose)	long-term	1.3	5
2 x 0.125	cereals, early/late	insectivorous bird (skylark)	long-term	0.9	5
2 x 0.125	cereals, early/late	insectivorous bird (yellowhammer)	long-term	1.2	5

Toxicity data for aquatic species (most sensitive species of each group or relevant for risk assessment, respectively) (Annex IIA, point 8.2, Annex IIIA, point 10.2)‡

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l) *
Pseudokirchneriella subcapitata	epoxiconazole	72 h acute	E_bC_{50} biomass E_rC_{50} growth rate NOEC biomass NOEC growth rate	1.19 > 10 0.0078 -
Daphnia magna	epoxiconazole	48 h acute	EC_{50} immobilisation	8.69
Oncorhynchus mykiss	epoxiconazole	96 h acute	LC_{50}	3.14
Lemna gibba	epoxiconazole	7 d	E_bC_{50} biomass E_rC_{50} growth rate E_bC_{10} biomass E_rC_{10} growth rate	0.0043** 0.0138** 0.00098** 0.0019**
Daphnia magna	epoxiconazole	21 d	NOEC reproduction	0.63
Oncorhynchus mykiss	epoxiconazole	28 d	NOEC juvenile growth	0.01
P. promelas	epoxiconazole	FLC	NOEAEC growth F2	0.01
Danio rerio, 3 different life stages, with sediment, static	epoxiconazole	FLC	NOEAEC (EC_{10}) sex ratio	0.030
Danio rerio	epoxiconazole	FLC	NOEAEC reproduction F1	0.012
Chironomus riparius	epoxiconazole	28 d	NOEC emergence LC_{50} emergence	0.0625 > 0.0625
Pseudokirchneriella subcapitata	formulated product	72 h	E_bC_{50} biomass E_rC_{50} growth rate NOEC biomass NOEC growth rate	0.81 (0.1 as) - 0.02 (0.0024 as) -
Daphnia magna	formulated product	48 h	EC_{50} immobilisation	1.8 (0.22 as)
Daphnia magna	formulated product	21 d	NOEC reproduction	0.625 (0.08 as)
Oncorhynchus mykiss	formulated product	96 h	LC_{50}	0.50 (0.059 as)
Oncorhynchus mykiss	formulated product	28 d	NOEC feed consumption	0.1 (0.012 as)
Pseudokirchneriella subcapitata	metabolite 1,2,4-triazole	72 h	E_bC_{50} biomass E_rC_{50} growth rate NOEC biomass NOEC growth rate	14 31 3.1 6.8
Daphnia magna	metabolite 1,2,4-triazole	48 h	EC_{50} immobilisation	> 100
Oncorhynchus mykiss	metabolite 1,2,4-triazole	96 h	LC_{50}	760
Oncorhynchus mykiss	metabolite 1,2,4-triazole	28 d	NOEC juvenile growth	3.2
Chironomus riparius	metabolite BF480-entriazole	28 d	NOEC emergence LC_{50} emergence	0.03 1.55

* nominal concentrations, confirmed by chemical analyses ** initial measured concentrations

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

Microcosm or mesocosm tests
not required

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER > trigger number of (sub)scenarios out of 9	Annex VI Trigger
Epoxiconazole as (BAS 480 F)						
2 x 0.125	cereals	*Lemna gibba*	acute	ditch 1m stream 1.5 m pond 3.5 m	2	10
2 x 0.125	cereals	*Danio rerio*	long-term FLC, with sediment		9	10
2 x 0.125	cereals	*Danio rerio*	long-term FLC		8	10
Formulation BAS 480 13 F						
2 x 0.125	cereals	*Oncorhynchus mykiss*	acute	see above	2	100
2 x 0.125	cereals	*Oncorhynchus mykiss*	long-term		9	10
Metabolite 1,2,4-triazole						
2 x 0.125	cereals	*Pseudokirchneriella subcapitata*	acute	ditch 1m stream 1.5 m pond 3.5 m	9	10
2 x 0.125	cereals	*Oncorhynchus mykiss*	long-term		9	10
Metabolite BF 480-entriazole						
2 x 0.125	cereals	*Chironomus riparius*	long-term	see above	9	10

Bioconcentration

Bioconcentration factor (BCF) ‡	whole fish (trout): highest mean value 70 (steady state)
Annex VI Trigger for the bioconcentration factor	100
Clearance time (CT_{50})	whole fish: 0.72 days
(CT_{90})	whole fish: 1.6 days
Level of residues (%) in organisms after the 14 day depuration phase	after 7 days depuration phase: 5 µg/L 5.7 % TAR in whole fish, 4.8 % in inedible tissue, 11.3 % in edible tissue 1 µg/L: 6.8 % TAR in whole fish, 5.4 % in inedible tissue, 11.5 % in edible tissue

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

Acute oral toxicity ‡	LD_{50} > 83 µg as/bee (active substance) LD_{50} > 69.9 µg as/bee (formulation)
Acute contact toxicity ‡	LD_{50} > 100 µg as/bee (active substance) LD_{50} > 59.7 µg as/bee (formulation)

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

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.125		contact (48 h)	2.1	50
0.125		oral (48 h)	1.79	50

Field or semi-field tests
not required

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

Species	Stage	Test substance	Dose (kg as/ha)	Endpoint	Effect	Trigger
Laboratory tests with inert substrate						
Typhlodromus pyri	proto-nymphs	formulation BAS 480 27 F		mortality	LR_{50} 2.1 L product/ha 258 g as/ha	30 % *
			0.086 0.123 0.185 0.283 0.431	mortality and reproduction	mortality / repro. 10 % / 44.4 % 10 % / 41.3 % 17.6 % / 31.7 % 57.9 % / - 82.8 % / -	
Aphidius rhopalosiphi	adults			mortality	LR_{50} > 2 L product/ha > 246 g as/ha	30 % *
			0.246	mortality	40.8 %	
			0.246	reproduction	18.2 %	
C. septempuncta	adult	BAS 480 13 F	0.188	mortality	2.0 %	30 % *
				reproduction	- 4.3 %	30 % *
P. cupreus	adult	BAS 480 13 F	0.188	mortality	0 %	30 % *
				food cons.	- 2.4 %	30 % *
Extended laboratory tests with natural substrate						
Aphidius rhopalosiphi	adults	BAS 480 27 F	0.246	mortality	0 %	50 % **
		BAS 480 27 F	0.246	reproduction	not valid	

* Trigger according to Annex VI 91/414/EEC ** Trigger at field rate according to Sanco/10329/2002

Hazard quotients for other arthropod species: in-crop scenario

Application rate (kg as/ha)	Test species	Test substance	LR_{50} (g product/ha)	in-crop HQ	off-crop HQ	Trigger *
2 × 0.125	*Aphidius rhopalosiphi*	BAS 480 27 F	> 2.0	< 1	< 0.048	2
	Typhlodromus pyri	BAS 480 27 F	2.1	0.95	0.045	2

* according to SANCO/10329/2002

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

Toxicity/exposure ratios for arthropod species: off-crop scenario (most sensitive species)

Application rate (kg as/ha)	Test species	Test substance	PEC off-crop, distance 1 m (g product/ha)	LR_{50} (g product /ha)	TER	Trigger *
Laboratory tests with inert substance						
2 x 0.125	*Typhlodromus pyri*	BAS 480 27 F	9.52	2100	221	10
Extended laboratory tests with natural substrate						
2 x 0.125	*Aphidius rhopalosiphi*	BAS 480 27 F	47.6	> 2000	> 42	5

* used by the German Federal Environmental Agency (Schulte et al., 1999: UWSF 11(5) 261-266).

PEC off-crop = Single application rate × 2 × drift (2.38 %)/VDF(5). Without VDF if product is sprayed on plants

Field or semi-field tests
No field tests were triggered on basis of the intended field uses and data available

Effects on earthworms (Annex IIA, point 8.4, Annex IIIA, point 10.6)

Acute toxicity ‡	techn. as: LC_{50} > 1000 mg as/kg soil dw LC_{50} corrected > 500 mg as/kg soil dw Formulation (related to as): LC_{50} > 125 mg as/kg soil dw LC_{50} corrected > 62,5 mg as/kg soil dw Metabolite 1,2,4-triazole: LC_{50} > 1000 mg /kg soil dw
Reproductive toxicity ‡	NOEC 1 L product/ha = 0.167 mg as/kg soil dw (depth 5 cm) NOEC corrected 0.084 mg as/kg soil dw Terrestrial Model Ecosystem (TME): NOEC 2 x 1.0 L product/ha (125 g as/ha; Enchytraeidae) Metabolite 1,2,4-triazole: NOEC 0.0708 mg/kg soil dw
Field study	Monitoring study: NOEC 3 x 1.0 L product/ha (125 g as/ha; adapted earthworm populations of an arable field site)

Toxicity/exposure ratios for earthworms (Annex IIIA, point 10.6)

Application rate (kg as/ha)	Crop	Time-scale	$PEC_{soil, ini}$	TER	Annex VI Trigger
Epoxiconazole					
2 x 0.125	cereals	acute	0.128 mg as/kg soil	> 3906	10
Formulation (related to as)					
2 x 0.125	cereals	acute	0.128 mg as/kg soil	>488	5
2 x 0.125 (labor)	cereals	sublethal	0.128 mg as/kg soil	0.7	5
2 x 0.125 (TME)	cereals	sublethal	2 x 0.125 kg as/ha	1 (in-field) > 1 (off-field)*	n.a.

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

Application rate (kg as/ha)	Crop	Time-scale	$PEC_{soil, ini}$	TER	Annex VI Trigger
2 x 0.125 (field study / monitoring)	cereals	sublethal	2 x 0.125 kg as/ha	> 1 (in-field)	n.a.
Metabolite 1,2,4-triazole					
2 x 0.125	cereals	acute	0.0021 mg/kg soil	> 473934	10
2 x 0.125	cereals	sublethal	0.0021 mg/kg soil	34	5

* under consideration of spray drift, lower PEC values are calculated for off-crop area

Effects on other soil macro-organisms (Annex IIIA, point 10.6.2)

Reproductive toxicity with collembolan species *Folsomia candida*				Metabolite 1,2,4-triazole: 28 day reproduction test mortality: LC_{50} 214 mg/kg soil dw reproduction: NOEC 1.8 mg/kg soil dw
Terrestrial Model Ecosystem (TME)				Effects on total, species or group abundance, dominances and species composition of Collembola, Enchytraeida, Acari, Nematoda. NOER: 2 x 1.0 L BAS 480 28 F/ha (2 x 125 g as/ha) for Collembola NOER: 2 x 1.0 L BAS 480 F/ha for Enchytraeidae
Field study: Decomposition of organic matter (litter bag test) and monitoring of soil dwelling macro-organisms (Collembola species)				Arable land site, Dannstadt/Rheinland-Pfalz, Germany; Plant protection products (i.e. herbicides) according to conventional standards for the region were applied on both the control and all treatment plots. Historic test site with $PEC_{plateau}$ level after multi-year use since 1992. Plots were spray-treated with 1, 2 or 3 applications of the formulation BAS 480 21 F.
Application rate (kg as/ha)	Crop	Test level (kg as/ha)	Time-scale	Effects
2 x 0.125	cereals	1, 2, or 3 x 0.125	around 11 months	Decomposition of organic matter (litter bag test): no significant impairment on organic matter degradation by repeated treatments neither in winter wheat nor in oilseed rape plots up to highest application rate of 3 L product/ha.
				Collembola: monitoring study on arable land was performed, might be used for the on-crop risk assessment NOEC 3 x 1.0 L product/ha (3 x 125 g as/ha; adapted Collembola populations of an arable field site)

Toxicity/exposure ratios for soil macro-organisms

Application rate (kg as/ha)	Crop	Time-scale	Organism	$PEC_{soil, ini}$	TER	Trigger
Formulation (related to as)						
2 x 0.125	cereals	sublethal	Collembola (field study / monitoring)	2 x 0.125 kg as/ha	> 1	n.a.
2 x 0.125	cereals	sublethal	Collembola, (TME)	2 x 0.125 kg as/ha	< 1 (in-field) > 1 (off-field)*	n.a.
Metabolite 1,2,4-triazole						
2 x 0.125	cereals	reproduction 28 d	Collembola	0.0021 mg/kg soil	857	5

* under consideration of spray drift, lower PEC values are calculated for off-crop area

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

Effects on soil micro-organisms (Annex IIA, point 8.5, Annex IIIA, point 10.7)

Nitrogen mineralisation ‡	in loamy sand and sandy loam: no effects at 1.5 L or 15 L product/ha (0.188 kg or 1.88 kg as/ha = (2 µL or 20 µL formulation/kg soil dw)
Carbon mineralisation ‡	in loamy sand and sandy loam: no effects at 1.5 L or 15 L product/ha (0.188 kg or 1.88 kg as/ha = (2 µL or 20 µL formulation/kg soil dw)
Terrestrial Model Ecosystem (TME)	Effects of 1 x and 2 x 1.0 L/ha BAS 480 28 F on microbial biomass, nitrogen transformation, enzyme activity. NOER: 2.0 L BAS 480 28 F/ha (0.334 g as/kg soil dw)
Field study	Additional information: Arable land site, Dannstadt/Rheinland-Pfalz, Germany; Plant protection products (i.e. herbicides) according to conventional standards for the region were applied on both the control and all treatment plots. Historic test site with $PEC_{plateau}$ level after multi-year use since 1992. Plots were spray-treated with 1, 2 or 3 applications of the formulation BAS 480 21 F. No reference substance. No indication of a clear trend of epoxiconazole related influences on microbial turnover rates (N-transformation, microbial biomass) up to 3 x 1.0 L/ha application of BAS 480 27 F (= 3 x 0.167 mg as/kg soil dw)

Impact on water treatment procedures (Annex IIA, point 8.7)

Oxygen consumption by activated sludge ‡	EC_{20} respiration: > 1014 mg as/L (highest test conc.)
Oxygen consumption by *Pseudomonas putida*	NOEC respiration: > 1000 mg as/L (highest test conc.)

Effects on other non-target organisms (flora and fauna) (Annex IIA, point 8.6)

Species	Parameter	Test Substance	Dose (kg as/ha)	Effect plant weight	Effect visible damage	Trigger *
Limit test, 14 days, application: spraying, post-emergence BBCH code 13-14						
Avena sativa	mean plant weight and visible damage	formulation BAS 480 27 F	0.250	4 % reduction n.s.	0 %	50 %
Allium cepa				3 % increase n.s.	0 %	
Beta vulgaris				16 % reduction n.s	20 %	
Brassica oleracea				5 % reduction n.s	0 %	
Cucumis sativus				1 % reduction n.s.	0 %	
Daucus carota				2 % increase n.s	0 %	
Helianthus annuus				7 % reduction n.s	0 %	
Pisum sativum				36 % increase n.s	0 %	

* Trigger at field rate according to Sanco/10329/2002
n.s. not significant different from control

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	R 50/53, N, dangerous for the environment

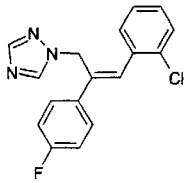
‡ Endpoints identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median

LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
1,2,4-triazole BF 480-16	1,2,4-triazole	
BF 480-entriazole	1-[(2Z)-3-(2-chlorophenyl)-2-(4-fluorophenyl)-2 propenyl]-1H-1,2,4-triazole	
BF 480-alcohol	1-(2-chlorophenyl)-2-(4-fluorophenyl)-1-hydroxy-3-(1H-1,2,4-triazol-1-yl)propane