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

triticonazole

finalized: 22 June 2005

(revision of 7 July 2005 with a minor clarification in the ecotoxicological risk assessment)

SUMMARY

Triticonazole is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. 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 (RMS) and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Austria being the designated rapporteur Member State submitted the DAR on triticonazole in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 29 September 2003. Following a quality check on the DAR, the peer review was initiated on 4 December 2003 by dispatching the DAR for consultation of the Member States and the sole notifier BASF. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting in 25 May 2004. 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 September and October 2004.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 18 May 2005 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 fungicide as proposed by the notifier which comprises seed treatment to control a broad range of fungi belonging to several groups of plant pathogens in wheat seeds at application rate up 50 g triticonazole per tonne seed (equals up to 12.5 g/ha). Triticonazole can be used only as fungicide. The representative formulated product for the evaluation was "Premis 25 FS", a flowable concentrate for seed treatment (FS), registered in several countries in Europe.

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25

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 triticonazole. An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed.
Sufficient analytical method 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.

Triticonazole is rapidly and almost completely absorbed. Triticonazole is of low acute toxicity by the oral, dermal and inhalative route, it is not irritating to skin and eyes and shows no sensitizing properties. The main target organs identified were the liver and the adrenals. The **ADI and AOEL is 0.025 mg/kg bw/d**, based on the NOAEL of 2.5 mg/kg bw/d from the 1-yr dog study, safety factor 100. The **ARfD is 0.05 mg/kg bw**, based on the maternal NOAEL of 5 mg/kg bw/d from the rabbit developmental study, with a safety factor of 100. The dermal absorption rate used for the calculation of operator exposure is proposed to be 11 % for the Premis 25 FS formulation. Calculations according to the Seed TROPEX model indicate that the estimated exposure for the intended use (seed treatment of cereals) is below the AOEL for the operator, when PPE is considered, and bystanders and workers.

The metabolism of triticonazole in cereals after seed dressing is well understood and does not yield metabolites of toxicological concern. No residues of triticonazole were quantified in any of the cereal grain or straw samples from field trials conducted according critical good agricultural practice (GAP). Triticonazole turned out to be persistent in soil. However, significant residues (>0.01 mg/kg) in crops growing in rotation with seed treated cereals are not anticipated. Furthermore, there is no significant exposure of livestock to triticonazole residues in feed items.
Using a residue level equal to the limit of quantification (LOQ) of 0.01 mg/kg for grain in the chronic dietary risk assessment and the short term exposure risk assessment leads to estimated intakes for consumers that are significantly below (less than 1 %) of the proposed allowed daily intake (ADI) and acute reference dose (ARfD).
The degradation of triticonazole in soil is initiated with the hydroxylation to a number of dihydroxy metabolites. Three metabolites amounted for more that 10 % AR in at least one soil: **RPA 404766, RPA 407922** and **RPA 406341**. Mineralization was generally low. Unextractable radioactivity amounted to a maximum of 17.9 % AR after 1 year. Light induces the trans-cis isomerization of triticonazole to yield metabolite **RPA 406203**.
Triticonazole is highly persistent under laboratory conditions (DT_{50} = 151 – 429 d). First order half life of metabolites RPA 406341 (DT_{50} = 165 – 330 d), RPA 407922 (DT_{50} = 3.7 – 5.1 d) and RPA 404766 (DT_{50} = 21 - 46 d) was obtained in soil under aerobic conditions. Under anaerobic conditions there is no significant degradation of triticonazole in soil. Results from field studies confirm the high persistence of triticonazole with mean half life in soil above 100 d.
Triticonazole has potential for accumulation in soil with a theoretical plateau attained after 11 years of continuous application. Field accumulation study confirms theoretical estimates.

Adsorption / desorption studies indicate that triticonazole may be classified as having medium mobility in soil, RPA 406341 high mobility, RPA 407922 medium to low mobility and RPA 4074766 high mobility. For metabolite RPA 407922 Koc values showed a pH related trend.
Two lysimeters were investigated in Germany using triticonazole formulated as seed treatment. The equivalent concentration in the leachate exceeded 0.1 µg/ L for several samples. Analyses of selected samples during the second and third monitoring year show that no triticonazole was detectable in the leachate.
Triticonazole is hydrolytically stable at environmental relevant pH (pH = 5 to 9). When irradiated triticonazole undergoes cis-trans isomerization. Triticonazole is not ready biodegradable.
In water / sediment systems degradation of triticonazole was very slow with half lives for the whole system of 392 and 224 d. Triticonazole is adsorbed to the sediment with a DT_{50} = 8 -9 d (disappearance time from the water phase). Recalculation with Model maker v. 4 (presented in the FOCUS sw calculation) result in a half life in the water phase of 85.1 d for one of the systems**.** Less than 2 % AR evolved as CO_2 after 105 d.
FOCUS sw Step 3 calculations show that PEC sw for parent triticonazole are equal or below 0.001 µg / L for the use as seed treatment in all the scenarios.
On the basis of FOCUS-PELMO model simulations neither triticonazole nor the degradation products RPA 407922, RPA 404766 are expected to exceed the 0.1 µg / L trigger in ground water when used as seed treatment in cereals. Degradation product RPA 406341 may exceed the 0.1 µg / L trigger under vulnerable situations (winter cereals, Piacenza scenario).
Concentrations of triticonazole in the air compartment are expected to be negligible, due to low volatility and short persistence in the atmosphere.

The risk to aquatic organisms, bees, earthworms, soil organic matter breakdown, non-target terrestrial plants and biological methods for sewage treatment is low with respect to triticonazole and the metabolites as far as investigated.
The risk to non-target arthropods can be regarded as low based on the available studies but to allow a full assessment of the risk of the representative use an additional laboratory study that addresses the effects of the intended seed treatment on sensitive life stages should be submitted. The EPCO 13 expert meeting on ecotoxicology agreed that based on the low toxicity to other species, this data requirement is confirmatory rather than a requirement for Annex I listing. A study to address this was submitted by the notifier and evaluated by the RMS who considers the study not valid for risk assessment purpose because the tested application rate is lower than the representative use rate of 12.5 g a.s./ha. EFSA agrees with the conclusion of the RMS.
The risk to soil non-target micro-organisms from triticonazole is considered to be low. It is noted by EFSA that no studies with the major soil metabolites RPA 404766 and RPA 406341 are available. Therefore, EFSA proposes that a study or at least a solid argumentation regarding the effects of these metabolites on soil non-target micro-organisms should be made available. The need for these data was not discussed at an EPCO expert meeting. The RMS made an argumentation regarding this issue available after the evaluation meeting of 18 May 2005. This argumentation was added by EFSA to the final addendum. This argumentation was not peer reviewed.

The acute, short and long term risk to herbivorous birds, the acute and short-term risk to granivorous birds and the acute and long term risk to granivorous and herbivorous mammals can be considered as low from the representative use of triticonazole as a seed treatment in wheat.
The long-term (reproductive) risk to granivorous birds is considered high based on the data available at the EPCO expert meeting on ecotoxicology (EPCO 13). Further data to address this risk have been submitted by the notifier after the expert meeting and were evaluated by the RMS but not peer reviewed due to the late submission date. A full risk assessment for granivorous birds can only be concluded after further consideration of this evaluated data. The meeting agreed that the focus should be on spring sowing, being the normal breeding season for birds, and if this risk is addressed, the risk from autumn sowings should be covered as well.

Key words: triticonazole, peer review, risk assessment, pesticide, fungicide

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Triticonazole is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Austria as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Austria submitted the report of its initial evaluation of the dossier on triticonazole, hereafter referred to as the draft assessment report, to the EFSA on 29 September 2003. 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 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 4 December 2003 to the Member States and BASF, the main applicant as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives of the Member States identified and agreed in an evaluation meeting on 25 May 2004 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier was attending this meeting.

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 organised on behalf of the EFSA by the EPCO-Team at the Pesticide Safety Directorate (PSD) in York, UK, in September and October 2004. 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 on 18 May 2005 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 8(7) of the amended Regulation (EC) No 451/2000, 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. 1-2 of 1 July 2004)
- the consultation report

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. 1-1 of 27 May 2005)

Given the importance of the draft assessment report including its addendum (compiled version of May 2005 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.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Triticonazole is the ISO common name for (*RS*)-(*E*)-5-(4-chlorobenzylidene)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol (IUPAC).

Triticonazole belongs to the class of conazole fungicides. Triticonazole can be used only as fungicide and it is used for the control a broad range of fungi belonging to several groups of plant pathogens (*Ascomycetes, Adelomycetes, Basidiomycetes*) in wheat seeds. Triticonazole is taken up slowly by the seedlings via the seed, teguments and roots and act as a C-14 demethylation inhibitor in the sterol biosynthesis pathway. The soil around the roots acts as a reservoir to feed the plant with triticonazole for several months after sowing.

The representative formulated product for the evaluation was "Premis 25 FS", a flowable concentrate for seed treatment (FS), registered in several countries in Europe.

The representative uses evaluated comprise seed treatment to control a broad range of fungi belonging to several groups of plant pathogens in wheat seeds at application rate up 50 g triticonazole per tonne seed (equals up to 12.5 g/ha). Triticonazole can be used only as fungicide.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of triticonazole as manufactured should not be less than 950 g/kg (dry material).
At the moment no FAO specification exists. The technical material contains no relevant impurities.
The assessment of the data package revealed no particular area of concern.
The main data regarding the identity of triticonazole 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 triticonazole 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. triticonazole in food of plant origin, soil, water and air.

An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2).

2. Mammalian toxicology

2.1. ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Triticonazole is almost completely and rapidly absorbed following a single low dose. Based on the recoveries of radioactivity obtained in urine, bile and tissue, the absorption rate from the gastrointestinal tract for both sexes can be estimated at > 98 %. Absorption of a single high dose was not so extensive, implying that saturation of absorption from the gastro-intestinal tract was occurring.

Pharmacokinetic parameters were investigated following single oral doses of 5 or 500 mg/kg bw. There were no sex differences in either dose groups. In both dose groups, a rapid peak in blood radioactivity concentration (0.5 to 2 hour post-dose) was followed by a rapid decline over 24 – 48 hours and then a slow elimination thereafter with terminal elimination half-lives of 116 - 120 hours at the low dose level and 96 - 106 hours at the high dose level, respectively.
Following oral administration to rats, radioactivity was widely distributed into the tissues. However, the levels of radioactivity remaining in the tissues after 168 hours were low in all dose groups with highest tissue concentrations observed in skin and fur, liver, plasma and adrenals for both sexes. In all experiments, the levels of radioactivity in male tissues tended to be slightly higher than in female. There was no evidence of a potential for bioaccumulation.

In rats triticonazole was almost completely excreted with more than 98 % of the administered dose following single high dose and > 95 % within 72 hours after single low dose administration. Animals in the multiple low dose experiment excreted > 89 % in urine and faeces within 72 hours. Rates and routes of excretion in the single and repeated low dose experiments were similar indicating no effects on pharmacokinetics resulting from repeated administration. The major route of elimination in the rat was via faeces and the remainder of the doses were found in the urine. In a biliary excretion study in rats, significant excretion of radioactivity via bile was demonstrated.

Metabolism of triticonazole was found to be rapid and extensive at the low dose level (single and repeated application), with no parent material excreted via urine and only very low amounts found in the faeces 24 hours after dosing only. At the high dose level, triticonazole was identified the major compound in the faecal extracts after 24 hours indicating limited absorption. Analysis by HPLC revealed a total of 10 and 12 components in faecal and urinary extracts, respectively. The metabolite profiles obtained for males and females were qualitatively very similar and differed rather in quantitative terms. Based on the identified metabolites in urine and faeces by LC/MS, a metabolic pathway was proposed which involved hydroxylation at different positions of the molecule.

2.2. ACUTE TOXICITY

Acute toxicity tests with triticonazole demonstrated that this compound is of low acute toxicity to rats by the oral (LD_{50} > 2000 mg/kg bw), dermal (LD_{50} > 2000 mg/kg bw) and also respiratory routes (LC_{50} > 5.61 mg/L air). Triticonazole is non-irritating to the skin and to the eyes of the New Zealand White rabbit, and is a non-sensitizer in the Buehler test and in the Magnusson and Kligman dermal maximization study conducted in guinea pig as well.

2.3. SHORT TERM TOXICITY

The short term toxicity of triticonazole has been investigated in rats and mice following a 90 day exposure period and in dogs following a 1-year treatment period. The dosages of these studies were selected based on the results of 4 to 6-week preliminary studies. In addition, a 21-day dermal study was conducted in rats:

In a 90 day dietary study in the rat, there was clear evidence of systemic toxicity at high dose level (12500 and 25000 ppm). Treatment-related findings included reductions in body weight gain and food consumption, haematological and clinical chemistry changes, organ weight effects and histopathological findings. The liver and the adrenals were identified as the major target organs. Vacuolation of the adrenal cortex was noted in all groups but, based on severity grade and microscopic appearance, the findings at the dose levels of 25 and 250 ppm were considered to be typical of spontaneous changes commonly found in untreated animals. The short term NOAEL for triticonazole in the rat can be set at 250 ppm (equivalent to 19.8 (males) and 22.3 (females) mg/kg bw/d).

Also in mice, continuous dietary treatment during 90 days produced severe systemic toxicity at all dose levels with the liver being identified as the major target organ showing organ weight changes associated with histopathological alterations (hypertrophy, fatty vacuolation, necrosis, and increased

mitotic activity). However, being a preliminary range-finding study, no short-term NOAEL could be determined in mice.

In the 1-yr dog-study, clear systemic toxicity was evident at the high dose (150 mg/kg) including cataractogenic effects, decreased body weight gains, haematological and clinical chemistry findings and increased liver and adrenal weights. Increased adrenal weights were associated with histopathological changes. Clinical chemistry findings together with organ weight effects suggest toxicological effects on the liver, but there were no histopathological alterations seen in the liver. Based on a moderate reduction in body weight gain and also clinical chemistry findings in females at 25 mg/kg bw/d, the NOAEL for this study is considered to be 2.5 mg/kg bw/d. This conclusion was also agreed at the Expert Meeting in October 2004 (EPCO 14).

Dermal application of triticonazole at dose levels up to 1000 mg/kg bw/d to rats for 21 days did neither produce local effects nor systemic toxicity. The NOAEL for this study was 1000 mg/kg bw/d (the highest dose tested).

2.4. GENOTOXICITY

Triticonazole was tested in *in vitro* and *in vivo* mutagenicity assays measuring different end points of potential mutagenicity such as gene mutation in bacteria and in mammalian cells, and chromosomal aberration and UDS in somatic cells. Results from these studies showed that triticonazole did not induce gene mutation in any of the bacterial tester strains of *S.typhimurium*, or gene mutation in mammalian cells in culture (CH-V79 assay). No potential for clastogenicity was observed in the *in vitro* chromosome aberration assay in human lymphocytes or in the *in vitro* UDS assay in rat hepatocytes as well.

In the *in vivo* mouse micronucleus assay, a clear negative result was obtained. Therefore, it can be concluded that triticonazole has no genotoxic potential of relevance to human risk assessment.

2.5. LONG TERM TOXICITY

In a 2-year combined chronic toxicity/carcinogenicity study in rats, continuous dietary administration of triticonazole produced clear evidence of toxicity at 5000 ppm. In addition to reduced body weight gain and reduced efficiency of food conversion, there were some changes in haematology and clinical chemistry in both sexes, and also histopathological non-neoplastic findings in the liver and the adrenal cortex. Changes in the eye lens (evident in males at 5000 ppm after 98 weeks of treatment only) were considered to be normal age-related changes and not an effect of treatment. Although the poor survival rate limits the value of the rat carcinogenicity study, there was no convincing evidence of any treatment-related hyperplastic or oncogenic response. Increased incidences of benign pituitary adenoma and keratoacanthoma of the skin were noted but were considered to be coincidental and not indicative of an oncogenic potential. Further evidence suggesting that triticonazole is not oncogenic is demonstrated by the lack of any oncogenic effect in the valid mouse carcinogenicity study and the negative genotoxicity studies. The NOAEL for this chronic toxicity/carcinogenicity study in the rat was considered to be 750 ppm (equivalent to 29.4 in males and 38.3 mg/kg bw/d in females, repsectively).

In the mouse carcinogenicity study, continuous dietary administration of triticonazole for 78 weeks produced clear evidence of toxicity at 1500 ppm. Body weight gain was reduced during throughout the dosing period and increased liver weight was associated with histopathological non-neoplastic changes (hepatocytic fatty vacuolation).There was no indication of oncogenic potential at any dose level. On the basis of these results, the dose level of 150 ppm (equivalent to 17.4 in males and 20.1 mg/kg bw/d in females, repsectively) was the NOAEL of this study.
Overall there was no evidence of a carcinogenic potential

2.6. REPRODUCTIVE TOXICITY

In the 2-generation reproductive study in rats, distinct parental toxicity was produced at the dietary concentration of 5000 ppm (premature deaths, significant reductions in body weight gain and food consumption as well, and necropsy findings in adrenals, liver and ovary). Adverse effects on reproductive parameters in both generations at 5000 ppm included decreased fertility (F_1), increased pup mortality, decreased pup viability and decreased pup bodyweights and weight gain (F_0 and F_1). These adverse effects on reproductive parameters are considered as consequence of distinct maternal toxicity at this very high dose level, exceeding the maximum tolerated dose. There were no significant parental or reproductive findings at 48.4 mg/kg bw/day which was considered the NOAEL for both parental and reproductive effects as well.

In the teratology study in the rat, there was evidence of slight maternal toxicity at 1000 mg/kg bw/d. There were also incidences of pale areas in the liver at 200 and 1000 mg/kg bw/d indicative of maternal toxicity. Foetal survival and growth was not affected in any dose group. However, there was an increase in the incidence of foetuses with an additional 14th rib or pair of ribs at all dose levels, but this was only outside the historical background range at 1000 mg/kg bw/d. These findings were not regarded as a major malformation and it is considered that no teratogenic effect was observed at any dose level. The NOAEL for maternal toxicity was 40 mg/kg bw/d and for developmental toxicity 200 mg/kg bw/d.
In the oral teratology study in rabbits, marked maternal toxicity (30 % mortality) was noted at 75 mg/kg bw/d with the MTD being exceeded. There was also one treatment-related death at the next lower dose level of 50 mg/kg bw/d. Treatment-related body weight loss during the first two days of treatment and reduced food consumption were observed at the dose level of $\geq$ 25 mg/kg bw/d. A slight, but not statistically significant increase in both pre- and post-implantation losses were noted at 75 mg/kg bw/d. Skeletal anomalies considered treatment-related were noted at $\geq$ 25 mg/kg bw/d. However, there was no teratogenic effect observed at any dose level. On the basis of these results, the dose level of 5 mg/kg bw/d can be considered the maternal and the foetal NOAEL.

2.7. NEUROTOXICITY

Triticonazole does not belong to a chemical family for which testing for delayed neurotoxicity is required. However, there was indication of neurotoxicity seen at the top dose in the 1-yr dog study (tremors, ataxia, convulsions), but no microscopic findings in brain, spinal cord or ischiatic nerves were observed. For further clarification, studies on neurotoxicity after acute and repeated oral

exposure to rats have been performed: In the acute oral neurotoxicity study in rats, no evidence for neurotoxicity was seen up to dose levels of 2000 mg/kg bw. Also after repeated dose administration via the diet, no neurobehavioral or neuro morphological effects occurred following 13 weeks of continuous exposure. Based on the study results a NOAEL of 10000 ppm (554 – 931 mg/kg bw/d for males and 704 – 937 mg/kg bw/d for females) was derived.

2.8. FURTHER STUDIES

Studies on metabolites

RPA 406341 (a hydroxylated metabolite of triticonazole found in cereals following seed treatment) and RPA 406203 (cis-isomer of triticonazole; soil photo-metabolite) were of low acute oral toxicity in rats and showed no indication of mutagenic properties when tested in the bacterial reverse mutation assay. It can be concluded that these metabolites are of similar toxicity to triticonazole in terms of acute oral and mutagenic potential (investigated by Ames-test only).

For the impurity RPA 402570, low acute toxicity in the rat by the oral and dermal routes was demonstrated. In a 14-day comparative oral toxicity study in the rat using gavage-dosing, RPA 402570 was of similar toxicity to triticonazole with similar effects observed at the top dose of 1000 mg/kg bw/d. The possible adverse effects limited to RPA 402570 were increased kidney weight in females receiving 100 and 1000 mg/kg bw/d, and acanthosis and hyperkeratosis in the stomach of males treated with 1000 mg/kg bw/d RPA 402570. Finally, mutagenicity of RPA 402570 was investigated in the Ames-test with no indication of a mutagenic effect.

Effects on hormone system

Some findings in subchronic and chronic toxicity studies such as a marked decrease in prostata weight in dogs, histological lesions in the adrenals and a slight increase in pituitary adenomas in the long term rat study as well as the impaired reproduction performance and ovary lesions in the multigeneration study in rats suggest a potential of triticonazole to have an impairment effect on the hormone system. However, these findings were confined to very high dose levels only where general toxicity was evident in all studies. The potential for endocrine disrupting effects of triticonazole was discussed at the Expert Meeting in October 2004. It was concluded that although specific interactions with the hormone system at the high dose levels cannot be excluded totally, it can be assumed that these signs of disturbance on hormonal balance are most likely the consequence of general toxicity.

2.9. MEDICAL DATA

No documentation was submitted other than a statement by the notifier concerning the possible occupational exposure of manufacturing plant personnel. It was stated that no clinical cases or poisoning incidents have been reported from possible exposure to triticonazole amongst the general population in the countries where triticonazole containing formulations has been approved.

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

ADI

Given the results from all relevant studies, the lowest NOAEL of 2.5 mg/kg bw/d was found in the 1-yr dog study. This NOAEL was based on reduced body weight gain and treatment-related effects on clinical chemistry findings at the next higher dose level of 25 mg/kg bw/d. It can be concluded that triticonazole exhibits no mutagenic, teratogenic; neurotoxic or oncogenic potential. Therefore, it is considered appropriate to apply an uncertainty factor of 100 to the NOAEL of 2.5 mg/kg bw/d from the dog study mentioned, resulting in an **ADI of 0.025 mg/kg bw/d**.

ARfD

Triticonazole is of low acute oral toxicity. There was also no evidence of genotoxicity, neurotoxicity or teratogenicity seen in relevant studies. However, in the rabbit teratology study, dose-related maternal body weight losses were observed at dose levels of 25, 50 and 75 mg/kg bw/d triticonazole during the first two days of treatment. This effect can be considered as a result from a single oral exposure. Bodyweights of animals receiving 5 mg/kg bw/d were unaffected by treatment. This dose level was also the maternal (and foetal) NOAEL for the study. Applying a 100-fold assessment factor the **ARfD of 0.05 mg/kg bw is derived** based on the NOAEL of 5 mg/kg bw/day from the teratology study in rabbits.

AOEL

The lowest NOAEL of all relevant studies was found in the 52-week dog study, which is considered a mid-term study. This NOAEL of 2.5 mg/kg bw/d was based on reduced body weight gain and clinical chemistry findings at the next higher dose level of 25 mg/kg bw/d.

Since the oral absorption of triticonazole is considered to be extensive (>98 % after single low dose application), no correction for oral absorption is required. It is also considered appropriate to use a 100 fold assessment factor. The **AOEL is 0.025 mg/kg bw/d**.

2.11. DERMAL ABSORPTION

Two studies (one *in vivo* study in rats and one comparative *in vitro* study on rats and human skin are evaluated in the DAR. For the purposes of exposure estimates, the low dose formulation (15 g/l) has been considered, since the proposed representative formulation “PREMIS 25 FS” contains a similar concentration of 25 g triticonazole/l.

In the *in vivo* rat study following an 8 hour exposure; only small amounts of the total dose applied could be clearly defined as absorbed as they were detected in urine, faeces and carcass. However, a large portion of radioactivity was associated in the treated skin. Considering the highest value of 3.14% for the systemically absorbed dose (total amounts detected in urine, faeces and carcass at 72 hours) plus the respective value of 32.7% for the skin content detected in the *in vivo* rat study, a total dermal absorption rate of approx. 36% in the rat can be assumed. This approach can be considered conservative since further data from the study indicate that only a minor amount of material located in the skin is actually systematically absorbed. Also in the comparative *in vitro* study, low dermal

penetration of radio labelled triticonazole was demonstrated for both human (0.77%) and rat skin (2.61%) with a significantly lower skin penetration rate through human skin than through rat skin with a ratio of 1:3.4.

Consideration of this correction factor results in an **overall dermal absorption rate of 11 % for triticonazole in a 25 g/l FS-formulation** to be used for the purposes of exposure calculations.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Operator exposure:

The representative formulation is Premis 25 FS which is a flowable concentrate containing 25 g triticonazole/L and is applied as seed dressing in wheat. The application rate is maximum 12.5 g/ha. The proposed GAP is 5 g triticonazole/100 kg seed, equivalent to 200 ml Premis 25 FS/100 kg seed. Calculations for operator exposure were made using the Seed TROPEX model and assuming a worst case scenario with the same operator doing all tasks: calibration, mixing/loading, 8 hours of bagging and cleaning. Calculations were performed covering the cases without dilution of the concentrate and with dilution with water (ratio 1:5). It is further assumed in this model that operators wear cotton coverall and gloves.

According to this Seed TROPEX model, the estimated exposure was below the AOEL for the 50 kg bag scenario considering all tasks for both the concentrate and the dilution as well.

For the 25 kg bag scenario, total systemic exposure was exceeding the proposed systemic AOEL for both application forms. However, these calculated exposures for the 25 kg bag scenario are based on "Seed TROPEX French data" from a plant with insufficient ventilation during manual bagging. If additional use of respiratory protective equipment (RPE) during the tasks "bagging" and "cleaning" are considered (equivalent to filtering respirator FFP2 to reduce potential exposure by 90%), total systemic exposures for the 25 kg bag scenario were below the AOEL.

When PSD Seed TROPEX modification (the revision is based on recent inhalation data determined in UK seed treatment plants) is used for the calculations, the estimated exposure was below the AOEL for the conditions with adequate local exhaust ventilation as well as poor local exhaust ventilation, see table blow. These calculations with the assumption that one operator conducts all the tasks demonstrate that the intended use for seed treatment is below the AOEL if the operator is wearing appropriate protective clothing.

Estimated operator exposure, % of AOEL (0.025 mg/kg bw/d), according to calculation with Seed Tropex.

Seed Tropex scenario	**Seed treatment with concentrate**		**Seed treatment with aqueous dilution**	
	PPE[§]	RPE*	PPE[§]	RPE*
50 kg	84%		48%	
25 kg (French data)	168%	80%	132%	64%
25/50 kg (PSD modification, poor ventilation)	92%		76%	
25/50 kg (PSD modification, adequate ventilation)	68%		52%	

[§] Coverall and gloves, *filtering respirator FFP2

It has to be emphasised that the Seed TROPEX model is only considering operator exposure covering “large scale users” in seed treatment facilities. A study on operator exposure covering "small scale users" was evaluated and exposure below the AOEL was demonstrated. However, considering the limitations of this study (e.g. only 1 - 2 operators were monitored during their work at 6 farm-based seed treatment stations using 6 different technical equipments with different procedures of working conditions and working methods), a general applicability of the results obtained to "small scale users" seems not appropriate. Moreover it can be assumed that, different methods and technical conditions (e.g. technical equipment) of seed treatment on farm level which usually are applied in other Member States are not covered by this surrogate study.

Therefore, operator exposure assessment of "small scale users" has to be evaluated on Member State level considering the different methods and conditions, which are usually applied in the different regions.

Furthermore, given the packaging description originally submitted (1 L, 5L, 200 L and 1000 L) containers, the small sizes (1 L and 5 L) cannot be supported since the notifier pointed out that only professional use is intended.

Bystander

The estimated exposure for bystanders (fork lift drivers in a seed treatment plant) was below the AOEL.

Worker exposure

Calculations on worker exposure (farmers loading and sowing/drilling seed) according to Seed TROPEX demonstrated an estimated exposure below the AOEL when coveralls are considered

3. Residues

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of triticonazole was studied in barley and wheat after seed treatment using two radiolabelled forms. Triticonazole was metabolised in growing cereal plants via hydroxylation following separation and destruction of the triazole moiety with incorporation of triazole derived material into natural products to form polar residues.

After application of *phenyl-labelled* triticonazole the major residue in grain was triticonazole, present at harvest up to 33 % of the present radioactivity (equal to 0.02 mg/kg). . In the other plant parts analysed, again triticonazole was found to be the largest amount of compounds detected. (whole plants up to 63 %, straw up to 35 % TRR). A few hydroxylated metabolites of triticonazole (RPA 406 780, RPA 404 766, RPA 404 886, RPA 406 341) exceeded 10 % TRR in the analysed cereal matrices.

The investigation of the metabolism of *triazole-labelled* triticonazole shows a different metabolic pattern: The majority of the recovered radioactivity in nearly all plant parts investigated was shown to be a number of polar and natural compounds (up to 88% in whole plants; 91 % in ears; 93 % in grains and up to 52% in straw) with a water soluble nature.

The parent triticonazole and hydroxylated triticonazole (RPA 406 780, RPA 404 766, RPA 404 886) could be detected in amounts greater 10% of the recovered radioacitivity in whole plants and straw.

Although the residues found in the study with *phenyl-labelled* triticonazole are significantly lower than *triazole-labelled* study, it is proposed by RMS to base the residue definition on the phenyl study only. As the toxicity of the identified hydroxylated compounds is not considered to be relevant compared to that of triticonazole and due to the application regime (seed dressing), the residues in of concern is defined as triticonazole for risk assessment and monitoring purposes. Due to the fact, that the investigation of the metabolic behaviour of triticonazole is limited to seed dressing on cereals only, a residue definition for plants in general can not be proposed.

The magnitude of triticonazole residues in grain and straw was determined in a total of 40 cereal field residue trials (17 in barley, 21 in wheat and to in rye) conducted over three growing seasons in locations representative of major crop production areas in Northern and Southern European regions. Field-testing parameters, such as application rate, number of applications, application time, sampling time and intervals were consistent with critical GAP. All residues were analyzed using validated methods. Triticonazole was the only residue determined. Grain residues were determined at a limit of quantification (LOQ) of 0.01 mg/kg. and straw residues at a limit of quantification (LOQ) of 0.05 mg/kg in all trials. At harvest (PHI ranged from 105 to 311 days) no residues were found in any of the cereal grain or straw samples.

Because no quantifiable triticonazole residues (<0.01 mg/kg) were found in cereal grains at the time of harvest an investigation of effects of industrial or household processing was not necessary.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Crop rotation studies were undertaken to address the potential incorporation of soil residues into succeeding and rotational crops, as triticonazole is highly persistence in soil. (see 4.1.2) In a study applying radiolabelled triticonazole to soil at 20-times the intended application rate, the edible parts of the plants of the first rotation contained total radioactive residues of 0.23 mg/kg (roots of radish), 0.048 mg/kg (leaves of lettuce) and 0.003 mg/kg (grain of wheat). Total radioactive residues declined with the planting interval. The main part of the radioactivity recovered was found to be triticonazole.

5 field studies showed after sowing of seed treated wheat no triticonazole residues greater 0.01 mg/kg in crops planted after harvest of wheat (protein peas, sugar beet root, sunflower seed, oilseed rape and grains of wheat).

Based on the findings, it is concluded that the application of triticonazole to seeds of cereals will not lead to quantifiable residues in succeeding crops.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

No quantifiable triticonazole residues were found in cereal grains and straw at the time of harvest and triticonazole and/or its metabolites are not deemed to accumulate in animal tissue. Therefore metabolism studies in livestock are not necessary as long as cereal green forage is not used in animal diet and a definition of residues in food of animal origin has not to be proposed.

3.3. CONSUMER RISK ASSESSMENT

The chronic dietary risk assessment for consumers is based on the information obtained from Northern European residue trials in cereals and on consumption data from the WHO/GEMS Food European diet and on the German diet of a 4-6 year old girl. The dietary estimates include contributions from the raw agricultural commodities (cereal) and processed fractions (e.g. flour, pasta, baked goods etc.) In the calculations the proposed MRL of 0.01* mg/kg is used. The contribution of dietary exposure to the ADI of 0.025 mg/kg bw is less than 1 % for adults and children, respectively.

The short term exposure risk assessment showed that the National estimated Short Term Intake (NESTI), using the UK model for adults and toddlers, is significantly below (less than 1 %) the ARfD of 0.05 mg/kg bw/day.

3.4. PROPOSED MRLS

It is proposed to set the maximum residue level (MRL) in cereal grain to the limit of quantification (LOQ) of the analytical method of 0.01 mg/kg, resulting in an MRL of 0.01* mg/kg for for grains of cereals (wheat, barley, triticale, oats, rye).

Triticonazole is approved in non-EU countries; however no Codex MRLs have been established or proposed yet and need to be considered.

4. Environmental fate and behaviour

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of triticonazole in soil was investigated under dark aerobic conditions at 22 ºC and 75 % of 0.33 bar field capacity in one study with three soils. Formation of the main metabolites was also investigated in two additional soils in two studies performed to measure the rate of degradation of triticonazole at 25 ºC and in one additional soil in a study performed to measure the rate of degradation at 22 ºC and 75 % of 0.33 bar field capacity. Two additional studies were performed to reach a better identification of some of the degradation products. The soils covered a range of pH values (5.7-6.4), clay contents (7.7 % - 64.3 %) and organic matters content (1.2 % - 32.2 %). The range of pH in the soils tested is very narrow, however the product is hydrolytically stable at the environmental relevant pH (5-9) and it is not expected that pH may have a significant impact on the route or rate of degradation of triticonazole in soil.

The degradation of triticonazole in soil is initiated with the hydroxylation to a number of closely related dihydroxy metabolites. However, due to the slow degradation of the parent compound the build up of these metabolites was limited. Maximum amount of parent triticonazole remaining one year after the initiation of the study amounted to 25 - 74.5 % AR. Eleven metabolites were identified, three of them amounted for more that 10 % AR in at least one soil. Those metabolites are **RPA 404766** ((E)-2-(4-chlorobenzylidene)-5,5-dimethyl-1-((1*H*)-1,2,4-triazol-1-ylmethyl)-cyclopentan-1,3-diol, maximum 12.3 % AR at study termination after 363 d at 22 ºC), **RPA 407922**((1RS, E)-5-(4-chloro-3-hydroxybenzylidene)-2,2-dimethyl-1-((1*H*)-1,2,4-triazol-1-ylmethyl)-cyclopentan-1-ol, maximum 12.8 % AR after 266 d at 22 ºC), **RPA 406341**((1R*, 3R*, E)-2-(4-chlorobenzylidene)-5,5-dimethyl-1-((1*H*)-1,2,4-triazol-1-ylmethyl)-cyclopentan-1,3-diol, maximum 20.2 % AR after 240 d). Mineralization after 90 – 112 d was generally low (0 – 8.1 % AR) increasing slightly at the end of the studies (2.1 – 23.8 % AR after 1 year). Unextractable radioactivity amounted to a maximum of 17.9 % AR after 1 year.

A soil photolysis study shows that photolysis may contribute to the dissipation of triticonazole in soil. Light induces the trans-cis isomerization of triticonazole given rise to major metabolite **RPA 406203** (cis isomer of triticonazole, (1RS, Z)-5-(4-chlorobenzylidene)- 2, 2- dimethyl- 1- ((1*H*)- 1,2,4-triazol-1-ylmethyl)-cyclopentan-1-ol, maximum 11 % AR at the end of the study after 30 d of continuous irradiation).

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

Degradation rate of triticonazole was investigated in the same degradation studies used to establish soil metabolism at 22 ºC and in two additional studies with two soils at 25 ºC with a 50 % field

capacity moisture. Three additional experiments were performed with one of the soils at 10 ºC, under reduced moisture to 20 % field capacity and with reduced application rate (one tenth of normal rate). Another study investigates the degradation rate at 10 ºC in four soils and at 22 ºC in one of them with a moisture of 75 % of 0.33 bar field capacity. Data of the eight degradation experiments performed at 22 ºC and 25 ºC in these studies were evaluated using TopFit 2.0 software assuming a multi-compartmental model that includes the parent, the three major soil metabolites and a sink compartment (minor metabolites, unextractable and CO_2). First-order kinetics was assumed for all degradation steps. Degradation and formation constants were obtained as applicable for each of the compounds. These first order degradation constants were employed to calculate the corresponding DT_{50} and DT_{90}. The results of this analysis show that triticonazole is highly persistent in soil under laboratory conditions (DT_{50} = 151 – 429 d). This kinetic analysis did not allow obtaining reliable parameters for the metabolites.

Degradation of metabolites was investigated at 20 ºC at 45 % of water holding capacity in three additional studies where the corresponding metabolites were applied as parent in three soils. First order half life of metabolites RPA 406341 (DT_{50} = 165 – 330 d), RPA 407922 (DT_{50} = 3.7 – 5.1 d) and RPA 404766 (DT_{50} = 21 - 46 d) was calculated. Due to the fact that appearance of metabolite RPA 407922 above 10 % AR was only very occasional and the low persistence in the laboratory studies RMS proposed not to consider further this metabolite with respect to the soil compartment. RMS provided the arguments in an addendum that was discussed in Experts Meeting on Fate and Behaviour in the Environment (EPCO 12, September 2004). The arguments of the RMS were accepted by the experts at the meeting.

Under anaerobic conditions at 25 ºC there is no significant degradation of triticonazole in soil.

One outdoor study with radiolabelled material, two field studies and two field soil accumulation studies are available. Final report of one of these accumulation studies was presented in an addendum to be discussed in the Fate and behaviour experts meeting (EPCO 12, September 2004). Degradation of triticonazole has been investigated in a total of 13 sites in Europe. Only in the outdoor study and one of the field studies the product is applied as seed dressing. In the other studies the product is sprayed and subsequently incorporated into soil. Results from these studies confirm the high persistence of triticonazole with mean half life in soil above 100 d.

PECs soil for the representative use proposed were recalculated by the RMS in an addendum. The PEC soil are calculated with worst case $DT_{50field}$ = 267 d with an application rate of 12.5 g/ha. The calculation addressed the potential accumulation of triticonazole in soil after yearly repeated applications. The theoretical plateau was attained after 11 years of continuous application. Results of the calculation were comparable to the data obtained in the field accumulation study when corrected for the lower application.

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

Batch adsorption / desorption studies are available for triticonazole and metabolites RPA 406341, RPA 407922 and RPA 4074766. The values obtained in these studies indicate that triticonazole (Koc = 184 – 563 mL/g) may be classified as having medium mobility in soil, RPA 406341 (Koc = 61 –

163 mL/g) high mobility, RPA 407922 (Koc = 407 - 1305 mL/g) medium to low mobility and RPA 4074766 (Koc = 35 – 133 mL/g) high mobility. For metabolite RPA 407922 Koc values showed a pH related trend with higher values obtained in the lower pH soils.

A column leaching study with non aged and aged residues is available. The results of this study show the dependency of triticonazole mobility on the type of soil. For all the soils the amount of leached residue was low (< 2 %) with the exception of the sand (35 % AR in the leachate after 30 d ageing). The vast majority of the material present in these experiments was unchanged triticonazole with small amounts of RPA 406341 and RPA 4074766.

One lysimeter study with two square lysimeters was performed in Germany during three consecutive years using triticonazole formulated as seed treatment. The equivalent concentration in the leachate exceeded 0.1 µg/ L for several samples resulting in annual averages of 0.089 µg/ L and 0.042 µg/ L during the second year and of 0.18 µg/ L and 0.084 µg/ L for the third year. Analysis of selected samples during the second and third monitoring year show that no triticonazole or the two metabolites (RPA 404766 and RPA 406341) were detectable in the leachate and that the vast majority of the radioactivity correspond to a number of polar components.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

In sterile aqueous buffer solutions at 25 ºC, triticonazole is hydrolytically stable at environmental relevant pH (pH = 5 to 9). When irradiated in aqueous solution triticonazole undergoes cis-trans isomerization to yield **RPA406203** (cis-isomer of triticonazole, (Z)-2-(4-chlorobenzylidene)-5,5-dimethyl-1-(1,2,4-triazol-1-ylmethyl)-cyclopentan-1-ol).

Triticonazole is not ready biodegradable.

A study with two water / sediment systems is available. The study was performed in natural water / sediments with neutral, slightly alkaline water (pH = 7.7, 8.0) and slightly acidic sediments (pH = 6.9, 6.8). Degradation of triticonazole was very slow in both systems not being possible to determine the half life in the whole system. The fact that more than 70 % of applied radioactivity remained as triticonazole after 105 d indicates that the half life is greater than 6 months. Recalculation presented within the FOCUS sw modelling results in a half life for the whole system of 392 and 224 d. Triticonazole is adsorbed to the sediment with a DT_{50} = 8 -9 d and a DT_{90} = 87 – 98 d (disappearance time from the water phase). Recalculation with Model maker v. 4 (presented in the FOCUS sw calculation) result in a half life in the water phase of 85.1 d (reliable value may be obtained only for one of the systems)**.** Less than 2 % AR evolved as CO_2 after 105 d.

Initial assessment in the DAR did not provide PEC sw calculation. Assessment based on spray drift was not possible for the only representative use proposed by the notifier (seed treatment). Therefore, acknowledging that assessment based on FOCUS sw modelling is not routinely required for the second list of substances under revision within the frame of directive 91/414/EEC, EFSA considered that in this case the use of FOCUS sw scheme was justified and necessary to facilitate the assessment of the representative use proposed.

The notifier presented a surface water assessment based on FOCUS sw that has been summarised and assessed by the RMS in the addendum to the DAR (rev. 2). A conservative worst case DT_{50} = 392 d

for the water phase was selected as input parameter for the calculation from the water sediment (whole system). Since no degradation is observed in the sediment a DT_{50} = 1000 d was used as half life of triticonazole into the sediment. Step 1 calculations were performed for soil metabolites RPA 406341, RPA 407922 and RPA 404766. Step 1, Step 2 and Step 3 calculations were performed only for the parent triticonazole based on seed treatment applications in spring and winter cereals. Calculations were repeated by the RMS adjusting some parameters such as soil DT_{50} and depth incorporation. While the calculations were not peer reviewed by the fate and behaviour in the environment expert meeting, EFSA supports the assessment made by the RMS. The study was performed before the release of the EFSA opinion on application of FOCUS sw for non sprayed products[3] but the approach followed is in line with the principles given in this opinion. FOCUS sw Step 3 calculations show that PEC sw for parent triticonazole are equal or below 0.001 µg / L for the use as seed treatment in all the scenarios.

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

Updated modelling was presented in an addendum and reviewed by the expert meeting. On the basis of FOCUS-PELMO model simulations neither triticonazole nor the degradation products RPA 407922, RPA 404766 are expected to exceed the 0.1 µg / L trigger in ground water when used as seed treatment in cereals. Degradation product RPA 406341 may exceed the 0.1 µg / L trigger under vulnerable situations (winter cereals, Piacenza scenario; for relevance of this metabolite see table in the residue definition section).

4.3. FATE AND BEHAVIOUR IN AIR

Concentrations of triticonazole in the air compartment are expected to be negligible, due to low volatility and short persistence in the atmosphere.

5. Ecotoxicology

5.1. RISK TO TERRESTRIAL VERTEBRATES

The risk to birds and mammals is calculated according to the Guidance Document on Birds and Mammals (SANCO/4145/2000). The risk was calculated for granivorous and herbivorous birds and mammals.

All calculated first tier TER values for herbivorous birds and mammals and the acute TER values for granivorous birds and mammals and the short-term TER for granivorous birds do not breach the appropriate Annex VI trigger value and hence the acute, short and long term risk to herbivorous birds and the acute and long term risk to herbivorous mammals and the acute risk to granivorous birds and

[3] Opinion of the Scientific Panel on Plant health, Plant protection products and their Residues on a request from EFSA on the appropriateness of using the current FOCUS surface water scenarios for estimating exposure for risk assessment in aquatic ecotoxicology in the context of Council Directive 91/414/EEC (Question N° EFSA-Q-2004-55). *The EFSA Journal* (2004) 145, 1-31. (http://www.efsa.eu.int/science/ppr/ppr_opinions/772_en.html)

mammals and the short-term risk to granivorous birds can be considered as low from the representative use of triticonazole as a seed treatment in wheat.

The long term TER values for granivorous birds and mammals breach the appropriate Annex VI trigger value. These risk assessments were revised by the RMS in addendum rev. 1 of September 2004.

The long-term risk to granivorous birds was discussed in the EPCO 13 expert meeting on ecotoxicology in September 2004 and the used approach was not accepted by this meeting as it was felt by the meeting that the seeds could be available on the field for more than 4 days prior to germination. The use of the house sparrow as a relevant model was agreed by the meeting and that the grey partridge was not a suitable model when used in isolation for this refinement. The meeting ruled out de-husking as a possible route of refinement. The meeting noted furthermore that no uncertainty factor was taken into account in the calculation of the number of wheat grains per day to be consumed by a house sparrow to induce reproductive effects. Therefore, the meeting agreed to set a data requirement for the notifier to submit further information to enable refinement of the long term risk to granivorous birds. The meeting agreed that the focus should be on spring sowing, being the normal breeding season for birds, and if this risk is addressed, the risk from autumn sowings should be covered as well.

A further refinement of the risk to granivorous birds was made available by the notifier after the EPCO 13 expert meeting on ecotoxicology and was evaluated by the RMS in the addendum rev. 2 to the DAR (January 2005). The evaluation of this refinement of the risk assessment was not peer reviewed by EFSA or by an EPCO expert meeting.

The long term risk to granivorous mammals was discussed in the EPCO 13 expert meeting on ecotoxicology. To refine this long term risk a case for refinement of the proportion in the diet (PD value) from 1 to 0.6 for wood mouse was presented as it is assumed that 60% of the diet of woodmouse consists of cereals/seeds. This figure was the maximum intake through the period March to December (covering the period when both autumn and spring wheat is sown). The expert meeting accepted this refinement of the PD value. Therefore the long term risk to granivorous mammals can be regarded as low based on the refined risk assessment.

Also the risk from secondary poisoning was assessed as the log Pow exceeds 3.

The scenario for fish eating birds and mammals was not considered relevant by the RMS as the representative use evaluated for triticonazole is a seed treatment and no contamination of surface water via spray drift occurs. As contamination of surface water is possible via drainage and run-off a risk assessment for fish eating birds and mammals is presented in the addendum by EFSA. The resulting long term TER values are above the respective trigger value indicating a low risk to fish eating birds and mammals from the representative use of triticonazole as a seed treatment in wheat.

The risk for earthworm eating birds and mammals can be considered low for the representative use evaluated.

5.2. RISK TO AQUATIC ORGANISMS

On an acute time scale *Scenedesmus subspicatus* is the most sensitive species from all aquatic species tested with triticonazole and a formulation. *Onchorhynchus mykiss* is the most sensitive species on a

chronic time scale from all aquatic species tested with triticonazole. EFSA noted that no studies on the chronic toxicity of the lead formulation to aquatic organisms are available but does not consider such studies necessary as no long term exposure from the lead formulation to surface water is expected due to the use as a seed treatment. The risk assessment was revised in addendum rev. 1 of September 2004. This addendum was discussed in the EPCO 13 expert meeting on ecotoxicology.
The EPCO expert meeting agreed that the acute risk to aquatic organisms can be regarded as low based on the TER-values calculated with FOCUS step 1 PEC_{sw} values (see point 4.2.1 above). The EPCO 13 expert meeting had some concerns about the use of time weighted average PEC_{sw} values to calculate the chronic risk to aquatic organisms. However the meeting noted that the chronic risk to aquatic organisms can be regarded as low based on TER values calculated with initial FOCUS step 3 PEC_{sw} values.

Triticonazole can be found in concentrations above 10% of the AR in the sediment. Therefore the risk to sediment dwelling organisms needs to be addressed. This risk assessment is available in the addendum rev. 1 of September 2004. The effects of the a.s. were tested on *Chironomus riparius*. The resulting TER value does not breach the Annex VI trigger value and hence the risk from the a.s. can be regarded as low.

Furthermore studies on the toxicity to *Daphnia magna* of the metabolites RPA 404766, RPA 407922 and RPA 406341 are available. The acute risk to *Daphnia magna* from these metabolites can be regarded as low based on the TER-values calculated with FOCUS step 1 PEC_{sw} values. No major surface water metabolites were identified in the section on fate and behaviour and hence no further studies are considered necessary.

Studies on bio-accumulation in fish are available as the logPow exceeds 3 and the DT_{50} in water exceeds 10. The resulting BCF is below the Annex VI trigger value of 100 for not readily biodegradable compounds indicating a low risk for bioconcentration in fish.

5.3. RISK TO BEES

An acute contact and oral toxicity study with triticonazole is available. No HQ values were calculated as the calculation of these values is considered not appropriate for seed dressing use. Triticonazole shows systemic activity, being translocated within the plant and so there is the possibility of exposure of foraging bees via the nectar of treated crops. However aphid populations would not be high enough to produce significant quantities of honeydew until quite late growth stages, by which time residue levels of triticonazole would be low. Furthermore the oral toxicity of triticonazole to bees is low (LD_{50} > 155.5 µg a.s./bee) Therefore the risk to bees from the representative use of triticonazole as a seed treatment in wheat is considered low.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Toxicity to non-target arthropods was low in laboratory studies on the two indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri* with the lead formulation. Further testing with formulations

differing from the lead formulation, applied as treated barley seed, indicated no adverse effects on adults of *Poecilus cupreus* and *Aleochara bilineata*. However, these studies are not considered to allow a full assessment of the risk of wheat seeds dressed with the lead formulation Premis 25 FS to sensitive stages of soil dwelling arthropods. Therefore the RMS set a level 4 data requirement for the notifier to submit an additional laboratory study that addresses the effects of the intended seed treatment with Premis 25 FS on sensitive life stages, e.g. larvae of *Poecilus cupreus*. Alternatively, studies conducted with *Hypoaspis aculeifer* or *Folsomia candida*, as recommended in the "Guidance document on Terrestrial Ecotoxicology" (Oct. 2002), are an option. This Level 4 data requirement was discussed in the EPCO 13 expert meeting on ecotoxicology. The meeting agreed that based on the low toxicity to other species, the data requirement is confirmatory rather than a requirement for Annex I listing. After the EPCO 13 expert meeting on ecotoxicology the notifier submitted a study to address this issue. This study was evaluated by the RMS and considered not valid for risk assessment purpose because the tested application rate is lower than the representative use rate of 12.5 g a.s./ha. EFSA agrees with the conclusion of the RMS.

5.5. RISK TO EARTHWORMS

Studies on the acute toxicity to earthworms from triticonazole, the lead formulation and the metabolites RPA 406341, RPA 404766 and RPA 407922 are available. The risk assessment for triticonazole was revised in addendum rev. 1 of September 2004. The endpoints for triticonazole were corrected for the high logPow. The TER-values resulting from the endpoints derived from these studies do not breach the Annex VI trigger value indicating a low acute risk to earthworms for the representative use.

A study on the long term toxicity to earthworms from the active substance is available. As for the acute risk a revised risk assessment is available in the addendum rev. 1 of September 2004 and a correction factor was taken into account. Also this TER-value, based on the NOEC corrected for the LogPow, does not breach the Annex VI trigger value, indicating a low long term risk to earthworms from triticonazole for the representative use evaluated. Due to the high DT_{90} (DT_{90lab} > 365 days) for metabolite RPA 406341 a long term study for this metabolite is triggered. No study is available and the need for such a study was discussed in the EPCO 13 expert meeting on ecotoxicology. The meeting agreed with the argumentation of the RMS that no long term toxicity study with the metabolite RPA 406341 is necessary due to the very low acute risk observed for RPA 406341 and the structural similarity of this metabolite to the parent for which low long term toxicity was observed.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

Given the persistency in soil ($DT_{90field}$ > 365 days) a litterbag study was conducted for this substance. The tested concentrations cover the peak PEC_{soil} taking into account accumulation. No significant effects on litter decomposition were observed. Hence the risk to soil organic matter breakdown from the representative use of triticonazole as a seed treatment in wheat is low.

It is noted by EFSA that also for the metabolite RPA 406341 a litterbag study is triggered due to its persistency (DT_{90lab} > 365 days). EFSA considers the risk to soil organic matter breakdown from this metabolite covered by the available study with the parent.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of triticonazole were tested on soil microbial respiration and nitrogen transformation. No deviations of more than 25% after 28 days were observed (i.e. no breaching of the Annex VI trigger value) at concentrations above the max. PECs and hence the risk to soil non-target micro-organisms is considered to be low.

It is noted by EFSA that no studies with the major soil metabolites RPA 404766 and RPA 406341 are available. Therefore, EFSA proposes that a study or at least a solid argumentation regarding the effects of these metabolites on soil non-target micro-organisms should be made available. The need for these data was not discussed at an EPCO expert meeting. The RMS made an argumentation regarding this issue available after the evaluation meeting of 18 May 2005. This argumentation was added by EFSA to the final addendum. This argumentation was not peer reviewed.

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

The exposure of non-target plants is considered negligible when triticonazole is applied as a seed treatment and hence the RMS considered that no data are required.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

A study was made available with triticonazole. The risk for biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: triticonazole, RPA 406203 (cis isomer of triticonazole, produced by photolysis), RPA 406341, RPA 404766 (Note: Metabolite RPA 40792 was assessed as not relevant by experts meeting on fate and behaviour due to the fact that its appearance > 10 % AR was only very occasional and the low persistence in soil)

Definitions for monitoring: triticonazole

Water

Ground water

Definitions for risk assessment: triticonazole, RPA 406341, RPA 404766, RPA 407922.

Definitions for monitoring: triticonazole

Surface water

Definitions for risk assessment: triticonazole, RPA 406203 (cis isomer of triticonazole, produced by photolysis).

Definitions for monitoring: triticonazole

Air

Definitions for risk assessment: triticonazole

Definitions for monitoring: triticonazole

Food of plant origin

Definitions for risk assessment: triticonazole

Definitions for monitoring: triticonazole

Food of animal origin

Definitions for risk assessment: not required/ not proposed

Definitions for monitoring: not required/ not proposed

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
triticonazole	High persistent ($DT_{50lab\ 22°C\text{-}25°C}$ = 151 – 429 d; $DT_{50field}$ > 100 d)	See points 5.5, 5.6 and 5.7.
RPA 404766	Moderately persistent ($DT_{50\ lab\ 20°C}$ = 21 - 46 d)	Acute risk to earthworms is considered to be low (trigger not breached) and is lower than the risk from the parent. No study with soil micro-organisms is available.
RPA 407922	Low persistent ($DT_{50\ lab\ 20°C}$ = 3.7 – 5.1 d) Due to the fact that its appearance > 10 % AR was only very occasional and the low persistence in the laboratory studies it was considered to be not relevant with respect to the residue definition in soil.	Acute risk to earthworms is considered to be low (trigger not breached) and is lower than the risk from the parent. No study with soil micro-organisms is available.
RPA 406341	High persistent ($DT_{50\ lab\ 20°C}$ = 165 – 330 d)	Acute risk to earthworms is considered to be low (trigger not breached) and is lower than the risk from the parent. Long term risk to earthworms and the risk to other soil non-target macro-organisms is expected to be low (see point 5.6 and 5.7). No study with soil micro-organisms is available.
RPA 406203 (cis isomer of triticonazole) Not relevant for the representative use (seed treatment)	Photolysis metabolite. Not investigated, not relevant for the representative use proposed (seed treatment)	No assessment required. No data available.

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
triticonazole	Medium mobility (Koc = 184 – 563 mL/g)	FOCUS-PELMO: No	Yes	Yes	Yes
RPA 404766	High mobility (Koc = 35 – 133 mL/g).	FOCUS-PELMO: No	No assessment required. No data on the pesticidal activity available.	No assessment required. No data available.	No assessment required. Data available (*D. magna*). The risk is lower than the risk from the parent.
RPA 407922	Medium to low mobility (Koc = 407 - 1305 mL/g) pH dependence with higher values in the lower pH soils.	FOCUS-PELMO: No	No assessment required. No data on the pesticidal activity available.	No assessment required. No data available.	No assessment required. Data available (*D. magna*). The risk is lower than the risk from the parent.
RPA 406341	High mobility (Koc = 61 – 163 mL/g)	FOCUS-PELMO: Yes, one scenario > 0.1 µg / L for winter cereals	No data on the pesticidal activity available.	Not toxicologically relevant. LD_{50} > 2000mg/kg bw	Assessed not to be ecotoxicological relevant.

Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Triticonazole (water and sediment phases)	See point 5.2.
RPA 406203 (cis isomer of triticonazole) Not relevant for the representative use (seed treatment)	No assessment required. No data available.

Air

Compound (name and/or code)	**Toxicology**
Triticonazole	See point 2.2 and 2.3

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

- further information to enable refinement of the long term risk to granivorous birds (relevant for all representative uses evaluated; data made available to the RMS after the EPCO 13 expert meeting on ecotoxicology and evaluated but not peer reviewed; refer to point 5.1)
- an additional laboratory study that addresses the effects of the intended seed treatment with Premis 25 FS on sensitive life stages, e.g. larvae of *Poecilus cupreus*. Alternatively, studies conducted with *Hypoaspis aculeifer* or *Folsomia candida*, as recommended in the "Guidance document on Terrestrial Ecotoxicology" (Oct. 2002), are an option. This data requirement was proposed to be confirmatory by the EPCO 13 expert meeting on ecotoxicology. (relevant for all representative uses evaluated; data made available after the expert meeting and evaluated by the RMS but not peer reviewed (EFSA agrees with the RMS conclusion); refer to point 5.4)
- a study or at least a solid argumentation on the effects of the metabolites RPA 404766 and RPA 406341 on soil non-target micro-organisms This data requirement is proposed by EFSA and has not been discussed in an EPCO expert meeting. The RMS made an argumentation regarding this issue available after the evaluation meeting of 18 May 2005. This argumentation was added by EFSA to the final addendum. This argumentation was not peer reviewed. (relevant for all representative uses evaluated; no submission date yet proposed by the notifier; refer to point 5.7)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide as proposed by the notifier which comprises seed treatment to control a broad range of fungi belonging to several groups of plant pathogens in wheat seeds at application rate up 50 g triticonazole per tonne seed (equals up to 12.5 g/ha). Triticonazole can be used only as fungicide. The representative formulated product for the evaluation was "Premis 25 FS", a flowable concentrate for seed treatment (FS), registered in several countries in Europe.

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 triticonazole. An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed.

Sufficient analytical method 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.

Triticonazole is rapidly and almost completely absorbed from the rat gastrointestinal tract and also rapidly excreted. The main part of the active substance is excreted via urine and bile mainly as hydroxylated parent compound.
Triticonazole is of low acute toxicity by the oral and dermal LD50 > 2000 mg/kg bw and inhalative LC50 > 5.61 mg/L, it is not irritating to skin and eyes and shows no sensitizing properties.
In subchronic and chronic toxicity studies conducted in rats, mice and dogs, the main target organs identified were the liver and the adrenals. At very high dose levels, some findings in subchronic to chronic studies suggest a potential of triticonazole to interact with the hormone system. However, in all these studies clear NOAELs at lower dose levels have been established and no risk to humans is anticipated. Further data for triticonazole did not support evidence of genotoxic, carcinogenic or development disturbing properties.
The **ADI and AOEL is 0.025 mg/kg bw/d**, based on the NOAEL of 2.5 mg/kg bw/d from the 1-yr dog study, with a 100-fold safety factor. The **ARfD is 0.05 mg/kg bw**, based on the maternal NOAEL of 5 mg/kg bw/d from the rabbit developmental study, with a safety factor of 100.
Based on an *in vivo* study in rats and an *in vitro* study in human and rat skin performed with the Premis 25 FS formulation the dermal absorption rate used for the calculation of operator exposure is proposed to be 11 %. Calculations according to the Seed TROPEX model indicate that the estimated exposure for the intended use (seed treatment of cereals) is below the AOEL for the operator, when PPE is considered, as well as for bystanders and workers.

The metabolism of triticonazole in cereals after seed dressing is well understood and does not yield metabolites of toxicological concern. No residues of triticonazole were quantified in any of the cereal grain or straw samples from field trials conducted according critical good agricultural practice (GAP). Triticonazole turned out to be persistent in soil. However, significant residues (>0.01 mg/kg) in crops growing in rotation with seed treated cereals are not anticipated. Furthermore, there is no significant exposure of livestock to triticonazole residues in feed items.
Using a residue level equal to the limit of quantification (LOQ) of 0.01 mg/kg for grain in the chronic dietary risk assessment and the short term exposure risk assessment leads to estimated intakes for consumers that are significantly below (less than 1 %) of the proposed allowed daily intake (ADI) and acute reference dose (ARfD).

The degradation of triticonazole in soil is initiated with the hydroxylation to a number of closely related dihydroxy metabolites. Eleven metabolites were identified and three of them amounted for more that 10 % AR in at least one soil: RPA 404766, RPA 407922 and RPA 406341. Mineralization was generally low. Unextractable radioactivity amounted to a maximum of 17.9 % AR after 1 year.
Photolysis may contribute to the dissipation of triticonazole in soil. Light induces the trans-cis isomerization of triticonazole given rise to metabolite RPA 406203.
The results of the kinetic analysis of soil degradation studies show that triticonazole is highly persistent under laboratory conditions (DT_{50} = 151 – 429 d). Degradation of metabolites was investigated in three additional studies. First order half life of metabolites RPA 406341 (DT_{50} = 165 – 330 d), RPA 407922 (DT_{50} = 3.7 – 5.1 d) and RPA 404766 (DT_{50} = 21 - 46 d) was obtained.

Under anaerobic conditions at 25 ºC there is no significant degradation of triticonazole in soil.

Results from field studies confirm the high persistence of triticonazole with mean half life in soil above 100 d.

The PEC soil calculation addressed the potential accumulation of triticonazole in soil after yearly repeated applications. The theoretical plateau was attained after 11 years of continuous application. Results of the calculation were comparable to the data obtained in the field accumulation study when corrected for the lower application.

Adsorption / desorption studies indicate that triticonazole (Koc = 184 – 563 mL/g) may be classified as having medium mobility in soil, RPA 406341 (Koc = 61 – 163 mL/g) high mobility, RPA 407922 (Koc = 407 - 1305 mL/g) medium to low mobility and RPA 4074766 (Koc = 35 – 133 mL/g) high mobility. For metabolite RPA 407922 Koc values showed a pH related trend with higher values obtained in the lower pH soils.

A column leaching study shows that the vast majority of the material present in these experiments was unchanged triticonazole. One lysimeter study with two lysimeters was performed in Germany during three consecutive years using triticonazole formulated as seed treatment. The equivalent concentration in the leachate exceeded 0.1 µg/ L for several samples. Analysis of selected samples during the second and third monitoring year show that no triticonazole was detectable in the leachate and that the vast majority of the radioactivity corresponds to a number of polar components.

Triticonazole is hydrolytically stable at environmental relevant pH (pH = 5 to 9). When irradiated in aqueous solution triticonazole undergoes cis-trans isomerization to yield RPA406203. Triticonazole is not ready biodegradable.

A study with two water / sediment systems is available. Degradation of triticonazole was very slow in both systems not being possible to determine the half life in the whole system (DT_{50} > 6 months). Recalculation presented within the FOCUS sw modelling results in a half life for the whole system of 392 and 224 d. Triticonazole is adsorbed to the sediment with a DT_{50} = 8 -9 d and a DT_{90} = 87 – 98 d (disappearance time from the water phase). Recalculation with Model maker v. 4 (presented in the FOCUS sw calculation) result in a half life in the water phase of 85.1 d (reliable value may be obtained only for one of the systems)**.** Less than 2 % AR evolved as CO_2 after 105 d.

Initial assessment in the DAR did not provide PECsw calculation. Subsequently, the notifier presented a surface water assessment based on FOCUS sw that has been summarised and assessed by the RMS in the addendum to the DAR (rev. 2). FOCUS sw Step 3 calculations show that PEC sw for parent triticonazole are equal or below 0.001 µg / L for the use as seed treatment in all the scenarios.

On the basis of FOCUS-PELMO model simulations neither triticonazole nor the degradation products RPA 407922, RPA 404766 are expected to exceed the 0.1 µg / L trigger in ground water when used as seed treatment in cereals. Degradation product RPA 406341 may exceed the 0.1 µg / L trigger under vulnerable situations (winter cereals, Piacenza scenario).

Concentrations of triticonazole in the air compartment are expected to be negligible, due to low volatility and short persistence in the atmosphere.

The risk to aquatic organisms, bees, earthworms, soil organic matter breakdown, non-target terrestrial plants and biological methods for sewage treatment is low with respect to triticonazole and the metabolites as far as investigated.

The risk to non-target arthropods can be regarded as low based on the available studies but to allow a full assessment of the risk of the representative use an additional laboratory study that addresses the effects of the intended seed treatment with Premis 25 FS on sensitive life stages, e.g. larvae of *Poecilus cupreus* should be submitted. Alternatively, studies conducted with *Hypoaspis aculeifer* or *Folsomia candida*, as recommended in the "Guidance document on Terrestrial Ecotoxicology" (Oct. 2002), are an option. The EPCO 13 expert meeting on ecotoxicology agreed that based on the low toxicity to other species, the data requirement is confirmatory rather than a requirement for Annex I listing. A study to address this was submitted by the notifier and evaluated by the RMS who considers the study not valid for risk assessment purpose because the tested application rate is lower than the representative use rate of 12.5 g a.s./ha. EFSA agrees with the conclusion of the RMS.

The risk to soil non-target micro-organisms from triticonazole is considered to be low. It is noted by EFSA that no studies with the major soil metabolites RPA 404766 and RPA 406341 are available. Therefore, EFSA proposes that a study or at least a solid argumentation regarding the effects of these metabolites on soil non-target micro-organisms should be made available. The need for these data was not discussed at an EPCO expert meeting. The RMS made an argumentation regarding this issue available after the evaluation meeting of 18 May 2005. This argumentation was added by EFSA to the final addendum. This argumentation was not peer reviewed.

The acute, short and long term risk to herbivorous birds and the acute and long term risk to herbivorous mammals and the acute risk to granivorous birds and mammals and the short-term risk to granivorous birds can be considered as low from the representative use of triticonazole as a seed treatment in wheat. Also the long term risk to granivorous mammals can be regarded as low after refinement of the risk assessment.

The long-term (reproductive) risk to granivorous birds is considered high based on the data available at the EPCO 13 expert meeting on ecotoxicology. Further data to address this risk has been submitted by the notifier after the EPCO 13 expert meeting on ecotoxicology and was evaluated by the RMS but not peer reviewed due to the late submission date. A full long-term risk assessment for granivorous birds can only be concluded after further consideration of this evaluated data. The EPCO 13 expert meeting on ecotoxicology agreed that the focus should be on spring sowing, being the normal breeding season for birds, and if this risk is addressed, the risk from autumn sowings should be covered as well.

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

- Appropriate PPE (i.e. coverall and gloves) is considered in the estimations of operator exposure in order to be below the AOEL.

- Environmental risk assessment is based on the specificities of seed treatment use. For other kind of uses extensive reassessment may need to be performed taking into consideration the high persistence of triticonazole.
- MS to pay particular attention to metabolite RPA 406341 for potential ground water contamination under vulnerable conditions. This metabolite has been assessed to be neither toxicological or ecotoxicological relevant but no information is available on its pesticidal activity.

Critical areas of concern

- Operator exposure assessments were performed based on Seed TROPEX model covering ”large scale users” in seed treatment facilities. With respect to seed treatment systems operating on farm level (small scale users) risk assessment has to be evaluated on Member State level taking into account the different methods and conditions, which are usually applied in the different regions.
- For operators adequate PPP (i.e. coverall and gloves) has to be considered.
- Given the packaging description originally submitted (1 L, 5L, 200 L and 1000 L containers) the small sizes (1 L and 5 L) cannot be supported since only professional use is intended.
- High persistence in soil and water compartments.
- The long-term risk to granivorous birds is considered high based on the data available at the EPCO 13 expert meeting on ecotoxicology. Further data to address this risk has been submitted by the notifier after the expert meeting and was evaluated by the RMS but not peer reviewed due to the late submission date. A full long-term risk assessment for granivorous birds can only be concluded after further consideration of this evaluated data (refer to point 5.1).

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

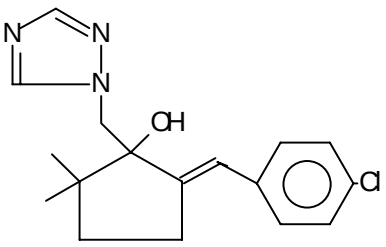
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Triticonazole (draft approved ISO), no synonyms
Function (e.g. fungicide)	Fungicide for seed treatment

Rapporteur Member State	Austria
Co-rapporteur Member State	---

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(±) - (E) -5-(4-chlorobenzylidene) -2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
Chemical name (CA) ‡	(5*E*)-5-[(4-chlorophenyl)methylene]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CIPAC No ‡	652
CAS No ‡	131983-72-7
EEC No (EINECS or ELINCS) ‡	not yet allocated
FAO Specification ‡ (including year of publication)	---
Minimum purity of the active substance as manufactured ‡ (g/kg)	950 g/kg (dry compound)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	No relevant impurities
Molecular formula ‡	$C_{17}H_{20}ClN_3O$
Molecular mass ‡	317.82
Structural formula ‡	

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

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	First crystalline form: 137 °C, second crystalline form: 141 °C (Purity: 998.5 g/kg)
Boiling point (state purity) ‡	Not measurable
Temperature of decomposition	Starts slightly decomposing after melting. Significant decomposition above 180 °C.
Appearance (state purity) ‡	White powder with or without agglutinated mass (technical grade: purity: 959 and 957 g/kg)
Relative density (state purity) ‡	D^R_4 = 1.21 (at 22.5 °C) (purity: 99.9 %)
Surface tension	σ = 51.7 mN/m at 23.5 ± 0.5 °C and c = 13.7 mg/l
Vapour pressure (in Pa, state temperature) ‡	< 0.1 x 10^{-5} Pa at 50 °C
Henry's law constant (Pa m^3 mol^{-1}) ‡	KH 3.0 x 10^{-5} Pa m^3 mol^{-1}
Solubility in water ‡ (g/l or mg/l, state temperature)	Dist. Water (pH 7.3 – 8.7; 20 °C): 9.3 mg/l buffer solution pH 5 (20 °C): 7.7 mg/l buffer solution pH 9 (20 °C): 8.3 mg/l
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	Solvent — solubility at 20 °C [g/l] Hexane 0.12 Toluene 12.6 Methanol 18.2 2-Propanol 7.6 1-Octanol 6.2 Dichloromethane 191.0 Acetone 74.5 Ethyl acetate 48.6
Partition co-efficient (log POW) ‡ (state pH and temperature)	log P_{ow} = 3.29 ± 0.04 at 20 °C
Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	Stable after a 30-day hydrolysis at pH 5, 7 and 9 at 25 ± 1 °C
Dissociation constant ‡	No dissociation expected based on the structure and the water solubility
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	Neutral medium (MeOH/water 100 : 10) wavelength [nm] — molar absorption coefficient [l x mol-1 x cm-1] 212 — 23879 263 — 25731 No significant modification was observed between the spectrum obtained in neutral, acid and basic media.

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

Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	The degradation kinetics of triticonazole was not pseudo-first order neither 0 order. Therefore, the half-lives were determined graphically. "Suntest" apparatus: Half-life: 75.9 h (1st phase: 12.1 h, 2nd phase: 154 h) Summer sunlight in Florida: Half-life: 3.0 d (1st phase: 0.47 d, 2nd phase: 6 d) (pH 5; 25 ± 1 °C)
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	Φ = 0.05 molecules of triticonazole degraded per photon absorbed
Flammability ‡	Not highly flammable.
Explosive properties ‡	Not explosive

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

List of representative uses evaluated*

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Wheat	Northern and Southern Region of Europe	Premis 25 FS	F	Seed and soil-borne desease (Fusarium Tilletia caries, Septoria Ustilago Puccinia)	FS	25	seed treat-ment	-	1	-	Max. 50 g a.i./t seed	-	0.009 – 0.0125	-	

Remarks:				
	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
	(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)	(i)	g/kg or g/L
	(b)	Outdoor or field use (F), glasshouse application (G) or indoor application (I)	(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
	(c)	*e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds		
	(d)	*e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

‡ Endpoint identified by 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 (principle of method)	Reversed phase HPLC with acetonitrile/water/trifluoroacetic acid as mobile phase and UV detection at 250 nm, external standard calibration.
Impurities in technical as (principle of method)	1) HPLC on reversed phase and detected by UV-absorption 2) Karl Fischer method (water) 3) GC-FID (solvents)
Plant protection product (principle of method)	Reversed phase HPLC with acetonitrile/water as mobile phase and UV detection at 280 nm, external standard calibration.

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Extraction with water/acetone, purification of the extract using an octadecyl cartridge followed by an aminopropyl cartridge, quantification by gaschromatography with thermoionic specific detector or liquid chromatography using tandem spectrometric detection. LOQ (grain) = 0.01 mg/kg LOQ (straw) = 0.05 mg/kg
	Multi-residue enforcement method (DFG S19): Extraction with water/acetone, partition into acetone/ethyl acetate/cyclohexane, purification by gel permeation chromatography and silica gel column fraction, quantification by GC-NPD, GC/MS/MS or GC-MS. LOQ (grain) = 0.005 mg/kg LOQ (straw) = 0.01 mg/kg
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	No analytical method is required as no MRLs and no residue definition for food of animal origin is proposed
Soil (principle of method and LOQ)	Extraction with acetone/ammonium hydroxide, purification of the extract using an octadecyl cartridge, quantification by reversed phase LC/MS/MS. LOQ = 0.002 mg/kg for triticonazole, LOQ = 0.002 mg/kg for RPA406341 and LOQ = 0.002 mg/kg for RPA404766
Water (principle of method and LOQ)	Extraction with dichloromethane, by silica gel column, quantification by GC-MS. LOQ = 0.05 µg/l
Air (principle of method and LOQ)	Adsorbed on a cartridge filled with porous styrene/divenylbenzene copolymer, desorbed by extraction with toluene, quantified by GC/ECD, confirmation by GC-MS. LOQ = 0.75 µg/m^3.

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

Body fluids and tissues (principle of method and LOQ)	No analytical method is required as triticonazole is not classified as toxic or very toxic

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	no classification required
with regard to toxicological data	no classification required
with regard to fate and behaviour data	R 53
with regard to ecotoxicological data	N, R 51/53

‡ Endpoint identified by 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 in mammals (Annex IIA, point 5.1)

Rate and extent of absorption ‡	Rapid; > 98 %. Excretion mainly in faeces following excretion in bile.
Distribution ‡	widely distributed (highest levels found in skin & fur, liver, plasma and adrenals)
Potential for accumulation ‡	no potential for accumulation
Rate and extent of excretion ‡	Rapid; > 98%, urinary (>10 %) and biliary (>80 %) after single low dose and > 89 % (multiple low dose), within 72 hours; mainly via faeces (bile). Nearly 100 % after 168 hours after repeat dose.
Metabolism in animals ‡	extensively metabolized in rats after single and repeated low dose (only < 1.5 % of dose as parent compound in faeces) via hydroxylation at different positions of the molecule
Toxicologically significant compounds ‡ (animals, plants and environment)	Parent compound and hydroxylated metabolites. The metabolites RPA 406341 (plant, low levels in rats) and RPA 406203 (soil) were determined to be of non-toxicological relevance.

Acute toxicity (Annex IIA, point 5.2)

Rat LD50 oral ‡	> 2000 mg/kg bw
Rat LD50 dermal ‡	> 2000 mg/kg bw
Rat LC50 inhalation ‡	> 5.61 mg/L (4 hours, nose only)
Skin irritation ‡	not irritant
Eye irritation ‡	not irritant
Skin sensitization ‡ (test method used and result)	not sensitizing (M & K test, Buehler test)

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Biochemical changes indicative of liver effects in females. Other target organs affected at doses >LOAEL were the adrenals (rat; dog: cortical fatty vacuolation and degeneration of *zona reticularis*) and eye (dog: cataracts at high dose level).
Lowest relevant oral NOAEL / NOEL ‡	1-yr dog: 2.5 mg/kg bw/d
Lowest relevant dermal NOAEL / NOEL ‡	21-d rat: > 1000 mg/kg bw/d
Lowest relevant inhalation NOAEL / NOEL ‡	no data –not required

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

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	no evidence of genotoxic potential

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

Target/critical effect ‡	liver (increased organ weight, fatty vacuolation and hypertrophy)
Lowest relevant NOAEL / NOEL ‡	18 months mouse: 17.4 mg/kg bw/d
Carcinogenicity ‡	overall no evidence of a carcinogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	decreased fertility indices; reduced viability and growth of pups at 330 mg/kg bw/day, a dose level causing severe parental toxicity
Lowest relevant reproductive NOAEL / NOEL ‡	48.4 mg/kg bw/d for parental and reproduction toxicity
Developmental target / critical effect ‡	foetal effects (increased incidence of additional 14th ribs in rats, increased incidence of skeletal anomalies in rabbits) at maternal toxic dose levels; no evidence of teratogenic potential
Lowest relevant developmental NOAEL / NOEL ‡	rabbit: 5 mg/kg bw/d, developmental and maternal effects

Neurotoxicity / Delayed neurotoxicity ‡ (Annex IIA, point 5.7)

.....	no evidence of neurotoxicity after acute (NOAEL > 2000 mg/kg bw) and subchronic (13 week) oral administration (NOAEL > 500 mg/kg bw/d) in rat

Other toxicological studies ‡ (Annex IIA, point 5.8)

.....	**RPA 406341** (plant metabolite and found in rats at low levels) and **RPA 406203** (soil metabolite only): Oral LD50 value > 2000 mg/kg bw no evidence of genotoxic activity (Ames test) **RPA 402570** (major impurity): Oral and dermal toxicity LD50 values > 2000 mg/kg bw No evidence of genotoxic activity (Ames test).

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

	Short term toxicity NOAEL 10 mg/kg bw/day, 14 day rat The impurity was present in the batches used in the toxicity studies.

Medical data ‡ (Annex IIA, point 5.9)

.....	Available data indicate no detrimental effects on health of plant personnel in manufacturing of triticonazole. No clinical cases or poisoning incidents have been reported

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.025 mg/kg bw/d	1-yr, dog, dog	100
AOEL ‡	0.025 mg/kg bw/d	1-yr, dog, dog	100
ARfD ‡ (acute reference dose)	0.05 mg/kg bw	developmental study, rabbit	100

Dermal absorption (Annex IIIA, point 7.3)

.....	11 % (FS formulation) based on in vivo rat study (36%, residues in skin included) and comparative in vitro human skin/rat skin study (ratio 1 : 3.4)

Acceptable exposure scenarios (including method of calculation)

Operator

Estimated exposure (% of AOEL) of Premis 25 FS a flowable concentrate used for seed dressing based on the Seed TROPEX model. Application rate 5 g triticonazole/100 kg seed, equivalent to 200 ml Premis 25 FS/100 kg seed or 12.5 g/ ha with PPE (coverall and gloves)

Bag size	Concentrate	Aq. dilution
50 kg	84%	48%
PSD modification:		
25/50 kg bag size (poor ventilation)	92%	76%
25/50 kg bag size (adequate ventilation)	68%	52%

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

Workers	The estimated exposure for bystanders (fork lift drivers in a seed treatment plant) was below the AOEL.
Bystanders	Calculations on worker exposure (farmers loading and sowing/drilling seed) according to Seed TROPEX demonstrated an estimated exposure below the AOEL when coveralls are considered

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	no classification required

‡ Endpoint identified by 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 (barley, wheat) (seed treatment)
Rotational crops	Radish, lettuce, wheat
Plant residue definition for monitoring	Parent compound (triticonazole), based on seed treatment
Plant residue definition for risk assessment	Parent compound (triticonazole), based on seed treatment
Conversion factor (monitoring to risk assessment)	---

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

Animals covered	No studies submitted; not regarded as necessary
Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor (monitoring to risk assessment)	---
Metabolism in rat and ruminant similar (yes/no)	---
Fat soluble residue: (yes/no)	Yes (parent compound)

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

.....	No detectable residues in succeeding crops to be expected

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

.....	stable for 12 months (maize – grain; wheat – grain and straw)

‡ Endpoint identified by 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)

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: yes/no	Poultry: yes/no	Pig: yes/no
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-	-	-
Eggs	-	-	-

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

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)
Wheat, barley, rye	Northern Region	PHI = 105 - 311 days: 20 x <0.01		0.01 *)	-
	Southern Region	PHI = 124 - 246 days: 20 x <0.01		0.01 *)	-

*) indicates lower limit of analytical determination

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

‡ Endpoint identified by 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	0.025 mg/kg bw
TMDI (European Diet) (% ADI)	TMDI (European Diet): 0.14 % ADI TMDI (German diet; girl of 13.5 kg bw): 0.30 %
NEDI (% ADI)	---
Factors included in NEDI	---
ARfD	0.05 mg/kg bw
Acute exposure (% ARfD)	IESTI (adults): 0.1 % IESTI (children): 0.3 %

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
-	-	-	-

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

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

wheat	0.01 mg/kg *)

*) indicates lower limit of analytical determination

‡ Endpoint identified by 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)

Mineralization after 100 days ‡	Phenyl ring labelled 14C-Triticonazole: Day 84-112: 1-8.1% Mean: 3.4% Triazole ring labelled 14C-Triticonazole: Day 90: 0.2%
Non-extractable residues after 100 days ‡	Phenyl ring labelled 14C-Triticonazole: Day 84-112: 3.4-9.6% Mean: 6.8% Triazole ring labelled 14C-Triticonazole: Day 90: 8.3%
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	RPA 406341: Max. 20.2% AR day 240 (25°C) RPA 404766: Max. 12.3% AR day 365 (22°C) RPA 407922: Max. 12.8% AR day 266 (22°C) (found only in one study >10% AR)

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

Anaerobic degradation ‡	No significant degradation
Soil photolysis ‡	Not relevant due to the use as seed treatment

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

Method of calculation	TopFit 2.0 (5 compartment model) Triticonazole: 8 soils; 22°C-25°C; 75% 0.33 bar WHC or 50% FC or 20% FC
Laboratory studies ‡ (range or median, with n value, with r^2 value)	DT_{50lab} (22-25°C, aerobic): 151-429 days; Mean: 237 days B value: 0.79-0.98
	DT_{90lab} (22-25°C, aerobic): 501-1425 days; Mean: 788 days B value: 0.79-0.98
	Linear regression analysis: r^2: 0.68-0.99; 3 soils (6 samples) DT_{50lab} (10°C, aerobic): 224-707 days; Mean: 430 days One extrapolated value: 614 days
	DT_{50lab} (20°C, anaerobic): No significant degradation
	degradation in the saturated zone: no data; no significant leaching of Triticonazole

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

Relevant metabolites	1st order analysis
Laboratory studies	20°C; 45% MWHC; 3 soils each, RPA 406341: DT_{50}: 165-330 days, mean: 230 days; r^2: 0.78-0.97 DT_{90}: 549-1095 days, mean: 764 days RPA 407922: DT_{50}: 3.7-5.1 days, mean: 4.5 days; r^2: 0.74-0.81 DT_{90}: 12.3-17 days, mean: 15 days Stat. Model SAS 6.12 20°C; FC; 3 soils RPA 404766: DT_{50}: 21-46 days, mean: 32.7 days; r^2: 0.83-0.97 DT_{90}: 69-152 days, mean: 108 days

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

Field studies (state location, range or median with n value)	2-year field dissipation study, Triticonazole formulated (EXP80441A); Spray application and incorporation to ca. 5 cm preplanting; 240 g a.i./ha 1st order kinetics: DT_{50f}: Germany: 178 d Italy: 105 d mean = 138 days UK : 104 d (1.5th order kinetics) mean = 171 days 187 d (if 1st order applied) (1st order values) UK : 139 d (seed treatment) France: 164 d (1.5th order kinetics) 247 d (if 1st order applied) DT_{90f}: Germany: 592 d Italy: 347 d mean = 560 days UK : 545 d mean = 569 days 622 d (if 1st order applied) (1st order values) UK: 461 d (seed treatment) France: 857 d 822 d (if 1st order applied) RPA 406341 found only sporadically at low levels, with a peak concentration of 22.5 g Triticonazole equivalents/ha (after 6 months). 2-year field dissipation study, Triticonazole 240 g ai/ha with incorporation, seeding of wheat (1st year) and grass (2nd year) 1st order kinetics (r^2 0.84-0.94): DT_{50f}: MS Excel "Solver" Simple 1st order UK: 159 d 267 d Germany: 104 d 193 d Spain: 97 d 122 d N. France: 57 d 96 d mean: 104 days 169 days DT_{90f}: MS Excel "Solver" Simple 1st order UK: 530 d 886 d Germany: 345 d 640 d Spain: 323 d 404 d N. France: 190 d 320 d Mean: 347 days 562 days RPA 404766: peak concentration 0.014 mg/kg dw, RPA 406341: peak concentration 0.032 mg/kg dw (after 6-8 months). No significant leaching into deeper soil layers (>30 cm) of Triticonazole and the two metabolites.

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

Soil accumulation and plateau concentration	Soil accumulation testing: Annual application of Triticonazole formulated at a rate of 112.5 g ai/ha for 4 years in Germany and UK. Results for 30 cm soil layer: Peak concentrations 0.02-0.04 ppm Plateau concentration in the range of 0.01 ppm Corrected for application rate (if 12.5 g ai/ha are applied): Peak concentrations: 0.0022-0.0044 mg/kg Plateau concentration in the range of 0.001 mg/kg RPA 406341: Below LOQ (0.002 mg/kg), except six times at German site: 0.002-0.005 ppm

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	Triticonazole: 9 soils: K_{OC}: 394 (184*)-812, mean: 504 K_f: 1.7-14.4 (31.7*), mean: 6.9 1/n: 0.813-0.964 mean: 0.879 1 sediment: K_{OC}: 344 K_f: 11.7 1/n: 0.890 *high organic soil RPA 406341: 4 soils: K_{OC}: 61-163, mean: 123 K_f: 0.82-2.65 mean: 1.90 1/n: 0.840-0.868 mean: 0.855 1 sediment: K_{OC}: 127 K_f: 3.31 1/n: 0.877 RPA 407922: 4 soils: K_{OC}: 467-1305, mean: 761 K_f: 3.88-19.13 mean: 12.35 1/n: 0.708-0.825 mean: 0.778 1 sediment: K_{OC}: 407 K_f: 10.57 1/n: 0.865 RPA 404766: 4 soils: K_{OC}: 35-133, mean: 82.8 K_f: 0.67-1.51 mean: 3.63 1/n: 0.825-0.884 mean: 0.853 1 sediment: K_{OC}: 62 K_f: 1.62 1/n: 0.877

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

	Triticonazole: 9 soils: K_d: 2.36-20.74 (36.13*) mean: 10.03 1 sediment: K_d: 18.57 *high organic soil RPA 406341: 4 soils: K_d: 1.71-4.78 mean: 3.09 1 sediment: K_d: 4.27 RPA 407922: 4 soils: K_d: 11.25-53.4 mean: 28.73 1 sediment: K_d: 14.91 RPA 404766: 4 soils: K_d: 1.30-2.49 mean: 2.00 1 sediment: K_d: 2.15
pH dependence (yes/no) (if yes type of dependence)	No

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

Column leaching ‡	<1% AR in the leachates except with the sand soil: 75% leached through the soil column, predominantely Triticonazole.
Aged residues leaching ‡	Ageing period 30 days, 95% AR remained as parent. ≤2% AR in the leachates except with the sand soil: 32% leached through the soil column. Small amounts of dihydroxylated metabolites.
Lysimeter/ field leaching studie ‡	Lysimeter study with benze-ring-U-^{14}C labelled Triticonazole formulated (EXP 80472B) as a seed dressing to winter wheat (seeding 16. Nov.) In the 2nd year untreated winter barley. Actual application rates: 13.13 and 13.12 g a.i./ha Silty sand soil (Gleyic Cambisol): pH 5.6 ($CaCl_2$), 1.32% OC, 76.4% sand Findings: No radioactivity was detected in any of the leachate samples during the entire 1st monitoring year at or above the LOD (i.e. ca. 0.012 µg/l Triticonazole equivalents). The total amount of radioactivity in the crop was 0.89% and 0.85% AR for the two lysimeters respectively. Total amounts of radioactivity in the leachates of the 2nd year were 0.93% and 0.99% AR. Maximum conc. of equivalents in leachate: 0.073 µg/l and 0.051 µg/l. Lysimeter study with triazole-ring-^{14}C labelled Triticonazole formulated (EXP 80472B) as a seed dressing to winter wheat (in the 1st year; seeding 17.Nov.). In the 2nd year untreated winter barley was seeded in one lysimeter and treated winter barley seeds in the other (seeding 26. Oct.). Actual application rates: 12.4 g a.i./ha, 13.1 g a.i./ha in

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

	the 2nd year (one of the two lysimeters). Silty sand soil (Gleyic Cambisol): pH 5.6 ($CaCl_2$), 1.32% OC, 76.4% sand Findings: Radioactivity in the leachate of the 1st year was only detected at two individual occasions with 0.03 µg/l and 0.02 µg/l in one of the two lysimeters. The total amount of radioactivity in the 1st crop was 2.55% and 2.21% AR for the two lysimeters respectively. Total amounts of radioactivity in the leachates of the 2nd year were 0.89% and 1.99% AR. Maximum conc. of equivalents in leachate: 0.16 µg/l and 0.08 µg/l. Mean conc. of equivalents in leachate of 2nd year: 0.089 and 0.042 µg/l. 2nd crop: 1.32% and 0.85% AR. Total amounts of radioactivity in the leachates of the 3rd year were 2.15% (lys. with 2 treatments) and 1.99% AR (lys. with 1 treatment). Max. conc. of equivalents in leachates: 0.23 µg/l and 0.098 µg/l. Mean conc. of equivalents in leachates of 3rd year: 0.18 µg/l and 0.084 µg/l. In crops of the 3rd year: 1.06% and 0.77 % AR. Amount of radioactivity in the soil at the end of the 3rd year: 52.7% and 51.3% AR. Only found in the upper three 10 cm-soil layers, with the majority found in the upper 10 cm layer. About half of radioactivity remained non-extractable. Extractable: Traces of triticonazole, RPA 406341, RPA 404766 and polar material. Triticonazole and its soil metabolites were not identified in the leachates. Radioactivity mainly consisted of very polar components, none single component expected to exceed 0.1 µg/l.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	$PEC_s(t) = \sum_{i=1}^{n} PEC_{s,\ init,\ i} \bullet e^{-k(t-t_i)}$ $TWAC_{1\ day}(T_j) = \frac{PEC(T_{j-1}) + PEC(T_j)}{2} \bullet (T_j - T_{j-1})$ $TWAC_{m\ days}(T_j) = \frac{1}{m} \bullet \sum_{k=1}^{m} TWA_{1\ day}(T_{j+1-k})$

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

Application rate	Triticonazole: 12.5 g/ha RPA 406341: 1.32 g/ha RPA 407922: 1.32 g/ha RPA 404766: 1.32 g/ha Plant interception: 0% Mixing depth: 20 cm Soil bulk density: 1.5 g/cm^3 Dissipation half-life in soil: Triticonazole: 267 d, worst case field DT_{50} RPA 406341: 346 d, worst case laboratory value RPA 407922: 5.1 d, worst case laboratory value RPA 404766: 46 d, worst case laboratory value

PEC $_{(s)}$ mg/kg		Single application Actual	Single application TWA	Single application Actual	Single application TWA
		Triticonazole		RPA 406341	
initial		0.0042	0.0042	4.4E-04	4.4E-04
short term	24 h	0.0042	0.0042	4.4E-04	4.4E-04
	2d	0.0041	0.0042	4.4E-04	4.4E-04
	4d	0.0041	0.0041	4.4E-04	4.4E-04
long term	7 d	0.0041	0.0041	4.3E-04	4.4E-04
	14 d	0.0040	0.0041	4.3E-04	4.3E-04
	28 d	0.0039	0.0040	4.1E-04	4.3E-04
	50 d	0.0037	0.0039	4.0E-04	4.2E-04
	100 d	0.0032	0.0037	3.6E-04	4.0E-04
Plateau concentrations					
PEC $_{(s)}$ mg/kg		Single application Actual	Single application TWA	Single application Actual	Single application TWA
		RPA 407922		RPA 404766	
initial		4.4E-04	4.4E-04	4.4E-04	4.4E-04
short term	24 h	3.8E-04	4.1E-04	4.3E-04	4.4E-04
	2d	3.3E-04	3.8E-04	4.3E-04	4.3E-04
	4d	2.5E-04	3.4E-04	4.1E-04	4.3E-04
long term	7 d	1.7E-04	2.8E-04	4.0E-04	4.2E-04
	14 d	< 0.0001	2.0E-04	3.6E-04	4.0E-04
	28 d	< 0.0001	1.1E-04	2.9E-04	3.6E-04
	50 d	< 0.0001	< 0.0001	2.1E-04	3.1E-04
	100 d	< 0.0001	< 0.0001	0.0001	2.3E-04

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

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)	Not relevant
Photolytic degradation of active substance and relevant metabolites ‡	Not relevant
Readily biodegradable (yes/no)	No
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡	158 d (8.9 d from study of Wyss Benz, 1995)* (97.9 d)*
- DT_{50} whole system ‡ - DT_{90} whole system ‡	392 d Not calculated because of very slow degradation of the air
Mineralization	1.3 – 1.7 % after 105 d
Non-extractable residues	14.5 – 25.5 % after 105 d
Distribution in water / sediment systems (active substance) ‡	Distribution of the ai at the end of test after 105 d: Water: 8.9 % (S1), 10.2 % (S2) Sediment: 70.9 % (S1), 61.2 % (S2)
Distribution in water / sediment systems (metabolites) ‡	Metabolites after 105 d: Water: 0.6 % (S1), 1.4 % (S2) Sediment: 2.1 % (S1), 2.2 % (S2)

*Values calculated in the study of Wyss Benz, 1995, recalculation of DT_{50} values for the water phase resulted in higher DT_{50} values (see Beigel C., 2004)

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

Parent

Method of calculation	FOCUS version 1.1, step 1, 2 and 3 calculations were conducted for triticonazole, step 1 calculations were conducted for the soil metabolites RPA 406341, RPA 407922 and RPA 404766
Application rate	seed treatment, 1 x 12.5 g/ha
Main routes of entry	drainage, runoff

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

Triticonazole PEC (sw) µg/L		FOCUS step 1		FOCUS step 2 North Europe (Oct.-Feb.)	
		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
initial		2.492	-	1.228	-
short term	24 h	2.488	2.490	1.225	1.226
	2 d	2.483	2.488	1.224	1.225
	4 d	2.475	2.483	1.220	1.224
long term	7 d	2.461	2.477	1.216	1.221
	28 d	2.372	2.431	1.182	1.204
	50 d	2.281	2.385	1.148	1.187
	100 d	2.088	2.284	1.074	1.149

FOCUS step 3 calculations for the drainage and runoff scenarios for winter (D1 - D6, R1 - R4) and spring cereals (D1 – D5, R4) resulted in maximum $PEC_{(sw)}$ values of 0.001 µg ai/L or below. 0.001 µg/L is the limit of accuracy of the FOCUS surface water program.

PEC (sw) µg/L		RPA 406341		RPA 407922	
		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
initial		0.762	-	0.320	-
short term	24 h	0.761	0.762	0.320	0.320
	2 d	0.761	0.761	0.320	0.320
	4 d	0.760	0.761	0.319	0.320
long term	7 d	0.758	0.760	0.319	0.320
	28 d	0.747	0.754	0.314	0.317
	50 d	0.736	0.749	0.309	0.315
	100 d	0.711	0.736	0.299	0.309

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

PEC (sw) µg/L		RPA 404766	
		Single application Actual	Single application Time weighted average
initial		0.486	-
short term	24 h	0.486	0.486
	2 d	0.486	0.486
	4 d	0.485	0.486
long term	7 d	0.484	0.485
	28 d	0.477	0.482
	50 d	0.470	0.478
	100 d	0.454	0.470

PEC (sediment)

Parent

Method of calculation	FOCUS version 1.1, step 1, 2 and 3 calculations were conducted for triticonazole, step 1 calculations were conducted for the soil metabolites RPA 406341, RPA 407922 and RPA 404766
Application rate	seed treatment, 12.5 g/ha

Triticonazole PEC (sed) µg/kg		FOCUS step 1		FOCUS step 2 North Europe (Oct.-Feb.)	
		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
initial		12.56	-	6.187	-
short term	24 h	12.54	12.55	6.182	6.184
	2 d	12.52	12.54	6.174	6.181
	4 d	12.47	12.52	6.158	6.174
long term	7 d	12.41	12.48	6.133	6.161
	28 d	11.95	12.25	5.963	6.076
	50 d	11.50	12.02	5.791	5.988
	100 d	10.52	11.51	5.416	5.795

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

FOCUS step 3 calculations for the drainage and runoff scenarios for winter (D1 - D6, R1 - R4) and spring cereals (D1 – D5, R4) resulted in maximum $PEC_{(sed)}$ values of 0.001 µg ai/L or below (0.001 µg/L is the limit of accuracy of the FOCUS surface water program)

PEC (sw) µg/L		RPA 406341		RPA 407922	
		Single application Actual	Single application Time weighted average	Single application Actual	Single application Time weighted average
initial		0.937	-	2.437	-
short term	24 h	0.936	0.937	2.436	2.437
	2 d	0.936	0.936	2.434	2.436
	4 d	0.934	0.936	2.431	2.434
long term	7 d	0.932	0.935	2.426	2.432
	28 d	0.919	0.928	2.391	2.414
	50 d	0.905	0.921	2.354	2.396
	100 d	0.874	0.905	2.274	2.355

PEC (sw) µg/L		RPA 404766	
		Single application Actual	Single application Time weighted average
initial		0.403	-
short term	24 h	0.402	0.403
	2 d	0.402	0.402
	4 d	0.402	0.402
long term	7 d	0.402	0.402
	28 d	0.395	0.399
	50 d	0.389	0.396
	100 d	0.376	0.389

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUS PELMO 3.3.2
Application rate	12.5 g a.i./ha Input parameters: Triticonazole: K_{OC}: 504; 1/n: 0.879; DT_{50}: 185 d Formation metabolites: k_{12} (RPA 406341): 0.001616 k_{13} (RPA 407922): 0.000313

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

	k_{14} (RPA 404766): 0.001423 k_{15} (NER, CO_2, minor m.): 0.000398 RPA 406341: K_{OC}: 123; 1/n: 0.855; k: 0.00312 (DT_{50}: 222 d) RPA 407922: K_{OC}: 761; 1/n: 0.778; k: 0.1529 (DT_{50}: 4.5 d) RPA 404766: K_{OC}: 83; 1/n: 0.843; k: 0.0229 (DT_{50}: 30.3 d) Average formation fractions: RPA 406341: 0.431 RPA 407922: 0.084 RPA 404766: 0.379 Degradation scheme (5-compartment model) : Figure B.8.1.2.1-1 in the DAR

$PEC_{(gw)}$

Maximum concentration	Triticonazole <0.001 µg/l RPA 406341 = 0.112 µg/l
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	80th percentiles of the predicted annual concentrations: Triticonazole: <0.001 µg/l for all scenarios RPA 406341: Winter cereals / Spring cereals Châteaudun: 0.014 µg/l / 0.005 µg/l Hamburg: 0.062 µg/l / 0.047 µg/l Jokioinen: 0.002 µg/l / <0.001 µg/l Kremsmünster: 0.041 µg/l / 0.022 µg/l Okehampton: 0.066 µg/l / 0.039 µg/l Piacenza: **0.112** µg/l / -- Porto: <0.001 µg/l / <0.001 µg/l Sevilla: <0.001 µg/l / -- Thiva: 0.007 µg/l / -- RPA 407922: <0.001 µg/l for all scenarios RPA 404766: <0.001 µg/l for all scenarios

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

Direct photolysis in air ‡	No data, not required
Quantum yield of direct phototransformation	No data, not required
Photochemical oxidative degradation in air ‡	AOPWIN calculation: Half-life: 0.113 days when a 12-hour day is considered and 0.057 days when a 24 hour day is considered.
Volatilization ‡	from plant surfaces: no data, not required from soil: no data, not required

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

PEC (air)

Method of calculation	Estimated to be negligible

$PEC_{(a)}$

Maximum concentration	Due to the short half-life of Triticonazole in the air and due to its low tendency for volatilisation (vapour presssure: 0.1×10^{-5} Pa at 50°C, H = $<3.8 \times 10^{-10}$ atm.M^3.Mol^{-1} at 20°C) no significant residues are expected in the atmosphere.

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil: Triticonazole, RPA 406341, RPA 404766 Water and sediment: Triticonazole Groundwater: Triticonazole Air: Triticonazole

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

Soil (indicate location and type of study)	No data available
Surface water (indicate location and type of study)	No data available
Ground water (indicate location and type of study)	No data available
Air (indicate location and type of study)	No data available

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	R 53

‡ Endpoint identified by 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 ‡	LD50 > 2000 mg/kg bw (rats)
Acute toxicity to birds ‡	LD50 > 2000 mg/kg bw (6 species)
Dietary toxicity to birds ‡	LC50 > 5200 ppm / LD50 > 693 mg/kg bw (bobwhite quail)
Reproductive toxicity to birds ‡	NOAEC = 250 ppm / NOAEL = 19.5 mg/kg bw/d (bobwhite quail)
	NOAEC = 750 ppm / NOAEL = 49 (♂) / 48 (♀) mg/kg bw/d (2-generations rat)

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

Application rate (g as/ha)	Crop	Category (e.g. insectivorous bird)	Time-scale	TER	Annex VI Trigger
12.5 g as/ha 50 mg/kg seed	wheat (seed treatment)	granivorous bird	acute	> 105	10
		bird feeding young shoots	acute	> 1176	10
		granivorous bird	short-term	> 36	10
		bird feeding young shoots	short-term	> 408	10
		granivorous bird	long-term	1	5
		bird feeding young shoots	long-term	65	5
		earthworm-eating bird	long-term	2167	5
		granivorous mammal	acute	> 174	10
		mammal feeding young shoots	acute	> 625	10
		granivorous mammal	long-term	4.2[1] 7[2]	5
		mammal feeding young shoots	long-term	80	5
		Earthworm-eating mammal	long-term	4800	5

[1] tier 1
[2] refinement 1: PD refined according to wood mouse diet

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

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests				
Oncorhynchus mykiss	Triticonazole	96 h	LC50 / NOEC	> 3.6 / 1.4
Daphnia magna	Triticonazole	48 h	EC50 / NOEC	9 / 1.8
Selenastrum capricornutum	Triticonazole	96 h	EbC50 ErC50	> 1 > 1
Anabaena flos-aquae	Triticonazole	5 d	EC50 / NOEC	>2.6 / < 2.6
Lemna gibba	Triticonazole	14 d	Biomass EC50 / NOEC	1.1 / 0.33
Oncorhynchus mykiss	Triticonazole	28 d	NOEC	0.01
Daphnia magna	Triticonazole	21 d	NOEC	0.092
Chironomus riparius	Triticonazole	26 d	NOEC	0.0777
Daphnia magna	RPA 404766	48 h	EC50	> 100
Daphnia magna	RPA 407922	48 h	EC50	> 100
Daphnia magna	RPA 406341	48 h	EC50	50
Oncorhynchus mykiss	CRLD 001002 (Formulation)	96 h	LC50	79 / equivalent to 0.89 mg ai/l
Daphnia magna	EXP 10642A (Formulation)	48 h	EC50	69 / equivalent to 0.78 mg ai/l
Scenedesmus subspicatus	EXP 10642A (Formulation)	72 h	EbC50 ErC50	57 / equivalent to 0.64 mg ai/l 86 / equivalent to 0.97 mg ai/l
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	FOCUS PEC cal-culation	TER	Annex VI Trigger
Triticonazole						
1 x 0.0125	Cereals	Oncorhynchus mykiss	96 h	step 1	1444	100
1 x 0.0125	Cereals	Daphnia magna	48 h	step 1	3611	100

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	FOCUS PEC cal-culation	TER	Annex VI Trigger
1 x 0.0125	Cereals	Selenastrum capricornutum	96 h	step 1	401	10
1 x 0.0125	Cereals	Oncorhynchus mykiss	28 d	step 3	10000	10
1 x 0.0125	Cereals	Daphnia magna	21 d	step 3	92000	10
1 x 0.0125	Cereals	Chironomus riparius	26 d	step 1	31.1	10
1 x 0.0125	Cereals	Lemna gibba	14 d	step 3	$330 * 10^3$	10
Metabolite RPA 404766						
1 x 0.0125	Cereals	Daphnia magna	48 h	step 1	$205 * 10^3$	100
Metabolite RPA 407922						
1 x 0.0125	Cereals	Daphnia magna	48 h	step 1	$312 * 10^3$	100
Metabolite RPA 406341						
1 x 0.0125	Cereals	Daphnia magna	48 h	step 1	$65 * 10^3$	100
Formulation CRLD 001002						
1 x 0.0125	Cereals	Oncorhynchus mykiss	96 h	step 1	357	100
Formulation EXP 10642A						
1 x 0.0125	Cereals	Daphnia magna	96 h	step 1	313	100
1 x 0.0125	Cereals	Scenedesmus subspicatus	96 h	step 1	257	100

Bioconcentration

Bioconcentration factor (BCF) ‡	BCFss = 94, BCFk = 72.6
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	after 3 d more than 99 % eliminated
Level of residues (%) in organisms after the 14 day depuration phase	after 3 d more than 99 % eliminated

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

Acute oral toxicity ‡	> 155.5 µg triticonazole/bee
Acute contact toxicity ‡	> 100 µg triticonazole/bee

‡ Endpoint identified by 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				
12.5	wheat (seed treatment)	exposure negligible	not appropriate	not appropriate

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/ formulation	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Laboratory tests						
Aphidius rhopalosiphi	adults	EXP80523A (25 g ai/kg DS)	11.5 100	mortality fecundity mortality fecundity	0 < 30 % 86 % n.a.	30 %
Aphidius rhopalosiphi	adults	Premis 25FS	up to 12.5 25 50	mortality fecundity mortality fecundity mortality fecundity	0 not red. 2.5 % 33.9 % red. 0 22.9 % red.	30 %
Typhlodromus pyri	proto-nymphs	EXP80523A (25 g ai/kg DS)	11.5 + 100	mortality fecundity	no effect	30 %
Typhlodromus pyri	nymphs	Premis 25FS	up to 50 (4 dosages)	mortality fecundity	no effect	30 %
Lab tests with treated barley seed						
Poecilus cupreus	adults	EXP80560B triticonazole+ iprodione	120	mortality food consumption	0 11 % reduced	30 %
Poecilus cupreus	adults	EXP80527B triticonazole+ guazatine	60	mortality food consumption	0 14 % reduced	30 %

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

Species	Stage	Test Substance/ formulation	Dose (g as/ha)	Endpoint	Effect	Annex VI Trigger
Aleochara bilineata	adults	EXP80527B triticonazole+ guazatine	48	parasitation capacity	12 % increased	30 %
Aleochara bilineata	adults	EXP80560B triticonazole+ iprodione	120	parasitation capacity	4 % increased	30 %

Field or semi-field tests
-

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

Acute toxicity ‡	Triticonazole: 14-day LC50: >1000 mg/kg (LC50corr.: >500 mg/kg) NOEC: 1000 mg/kg (NOECcorr.: 500 mg/kg) RPA 406341: 14-day LC50: >1000 mg/kg NOEC: 667 mg/kg LOEC: 1000 mg/kg RPA 404766: 14-day LC50: >1000 mg/kg NOEC: 250 mg/kg LOEC: 500 mg/kg RPA 407922: 14-day LC50: >1000 mg/kg NOEC: 556 mg/kg LOEC: 1000 mg/kg EXP 80472B: 14-day LC50: >1000 mg/kg (Formulation) LOEC: >1000 mg/kg NOAEC: 1000 mg/kg
Reproductive toxicity ‡	Triticonazole: 56-day NOEC: 500 mg/kg (NOECcorr.: 250 mg/kg)

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

Application rate (g as/ha)	Crop	Time-scale	Compound	TER	Annex VI Trigger
12.5	Seed dressing	14 days	Triticonazole	> 36 764 $TER_{corr.}$: >18 382	10
12.5	Seed dressing	14 days	RPA 406341	> 312 500	10

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

Application rate (g as/ha)	Crop	Time-scale	Compound	TER	Annex VI Trigger
12.5	Seed dressing	14 days	RPA 404766	> 625 000	10
12.5	Seed dressing	14 days	RPA 407922	> 625 000	10
12.5	Seed dressing	8 weeks	Triticonazole	18 382 TER_{corr}.: 9 191	5

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

Nitrogen mineralization ‡	No significant effects (<15%) at rates of 320 g a.i./ha and 1600 g a.i./ha
Carbon mineralization ‡	No significant effects (<15%) at rates of 320 g a.i./ha and 1600 g a.i./ha

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N, R 51/53

‡ Endpoint identified by 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
NOEC	no observed effect concentration
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