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

Tetraconazole

Finalised: 31 July 2008

SUMMARY

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

Italy being the designated rapporteur Member State submitted the DAR on tetraconazole in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 15 July 2005. The peer review was initiated on 5 February 2007 by dispatching the DAR for consultation of the Member States and the sole applicant ISAGRO S.p.A. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in March - April 2008.

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

The conclusion was reached on the basis of the evaluation of the representative uses as fungicide as proposed by the applicant. Full details of the GAP can be found in the attached list of end points.

The representative formulated product for the evaluation was “Eminent 40 ME”, a micro-emulsion (ME) containing 40 g/L tetraconazole.

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

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. Adequate methods are available to monitor tetraconazole residues in food/feed of plant and animal origin, soil and water; however additional ILV and confirmatory methods are required. There is no acceptable monitoring method for air.

Mammalian toxicology of tetraconazole has been assessed in a series of tests. It is absorbed rapidly orally to an extent of about 80%. It is widely distributed in the body. It does not accumulate and is excreted rapidly and completely. It is extensively metabolised. Tetraconazole is of moderate acute toxicity by the oral and of low toxicity by the dermal and inhalation route. It is neither a skin nor an eye irritant and has no skin sensitising properties. A classification as **Xn; R22 "Harmful; Harmful if swallowed"** is proposed. In several short-term dietary studies liver and kidneys were the target organs of toxicity (the lowest NOAEL of 2.95 mg/kg bw/d was found in dogs). Tetraconazole is not genotoxic. In a chronic rat study liver effects and at higher doses also effects on bones and incisors (fluorosis) and thyroid tumours were seen. In a carcinogenicity study with mice liver tumours were observed. Neither the thyroid tumours in rats nor the liver tumours in mice were considered relevant for human risk assessment. In a two-generation study dystocia and prolonged gestation periods were observed in dams and classification as **Xn; Repr. Cat. 3 R62 "Harmful; Possible risk of impaired fertility"** was proposed. In a developmental study with rats extra ribs, hydrourether and hydronephrosis occurred in the pups and classification as **Xn; Repr. Cat. 3 R63 "Harmful; Possible risk of harm to the unborn child"** was proposed. The acceptable daily intake (ADI) was set at 0.004 mg/kg bw/d , the acceptable operator exposure level (AOEL) was fixed at 0.03 mg/kg bw/d and the ARfD was set at of 0.05 mg/kg bw. Using the worst case scenario of all suggested uses for preparation EMINENT 40 ME (tractor mounted/trailed boom sprayer; hydraulic nozzles on sugar beet and wheat) the calculated exposures were 305.13% and 48.17% and 51.26% and 39.56% with and without PPE (personal protective equipment) respectively of the AOEL in the UK POEM and in the German model. Estimated maximum exposure using worst case scenarios amount to 5.5% of the AOEL for bystanders and to 28% of the AOEL for re-entry workers.

The metabolism of tetraconazole in plants was investigated upon foliar application to wheat, sugar beet and grapes and in carrots, lettuce and wheat planted as succeeding crops.
Based on the studies a residue definition including tetraconazole and the triazole derivative metabolites (triazole alanine, triazole acetic acid) has been provisionally established. A final plant residue definition for risk assessment is pending the clarification on the toxicological properties of metabolite triazole hydroxypropionic acid. This metabolite had not been identified in metabolism studies with other triazole pesticide compounds assessed in the peer review.
The nature of the residue is not altered by processing. From processing studies transfer factors to juice, wine and dry apple pomace could be derived.
A sufficient number of supervised residue trials are only available to cover the representative uses in wheat and sugar beets in all Europe and hence MRLs can be proposed for these crops. The representative uses in grapes and apples were initially not supported by residue trials matching the

notified GAP criteria. Trials submitted during the peer review process could not be considered in view of the restrictions concerning the acceptance of new studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007.

Uptake of soil residues by rotational crops is not expected to lead to residues of tetraconazole per se above the LOQ. In contrast, a significant uptake of triazole derivative metabolites is expected, but the available field studies were not considered sufficient to address residues in following crops. Hence a data gap for a new field rotational crop study has been set.

Feed commodities may represent a significant source of exposure to tetraconazole residues for animals. Metabolism studies in lactating goats and laying hens are available, and based on the metabolic pattern in animal tissues a residue definition was proposed. However, due to data gaps the livestock dietary intake estimates cannot be finalised and thus appropriate MRLs for animal products can currently not be proposed.

The consumer risk assessment for the notified representative uses can currently not be finalised. Excluding the uses on apples and grapes and only considering residues of tetraconazole alone, the RMS has submitted a provisional and none-peer reviewed chronic and acute consumer risk assessment indicating consumer exposure being below the toxicological reference values for tetraconazole. A robust conclusion on the consumer risk will only be possible when the identified data gaps are addressed and sufficient data and information regarding the assessment of triazole derivative metabolites in primary crops, rotational crops, and products of animal origin is available.

Degradation of tetraconazole in soil under dark aerobic laboratory conditions was negligible. Photolysis of tetraconazole in soil was negligible.

Degradation of tetraconazole was also investigated in three soils under aerobic outdoor conditions, exposed to sunlight. The applicant attributed degradation to a combined effect of photochemical and microbial degradation. RMS considered the reliability of the study doubtful since no clear mechanism may explain degradation. The experts considered that further experiments investigating effect of higher temperatures in dark under controlled moisture conditions and indirect aqueous photochemical studies could help to understand the mechanism of degradation prevailing in the environment. Therefore, a data gap was identified for these additional studies.

Dissipation of tetraconazole under field conditions was investigated in five sites (4 in Germany and 1 Northern Italy). In the five soils dissipation followed biphasic behaviour. Tetraconazole was high to very high persistent during the second phase. The meeting of experts agreed that the field half lives cannot be used in FOCUS modelling with the current lack of understanding of the mechanism causing loss. For PEC soil the meeting of experts agreed that the longest second phase field DT_{50} of 1688 d should be used. Potential accumulation of tetraconazole may not be excluded since about 20 – 40 % AR remains as tetraconazole one year after application. Assuming yearly application and tillage, EFSA calculated a plateau background concentration over the 20 cm horizon after 36 years and peak concentration after last application. Tetraconazole is low mobile in acidic soils. Adsorption / desorption of potential metabolites M 14360-acid and TAA were investigated in different studies. Metabolite M 14360-acid may be considered high to very high mobile in soil and TAA very high mobile in soil. Potential metabolite M 14360-alcohol may be considered very high mobile in soil.

A two years lysimeter study with two soil monoliths was performed in Switzerland. Product containing labelled tetraconazole was applied the first year. No product was applied the second year. Residue leachate concentrations observed were 0.53 – 0.54 µg / L and 0.27 µg / L parent equivalents for the first and second year respectively. The two major fractions were M11 (47 % - 66 % of radioactivity in the leachate; corresponding to 0.11 – 0.18 µg/L) and M10 (15 – 21 % of the radioactivity in the leachate; corresponding to 0.03 – 0.08 µg/L). A data gap was identified for the characterization of tetraconazole lysimeter metabolites M10 and M11 and to address its potential for ground water contamination.

Tetraconazole is stable to hydrolysis and is not expected to be degraded by photolysis in water. Tetraconazole is not readily biodegradable.

A dissipation study of tetraconzole in two water/sediment systems under dark aerobic conditions at 20 ºC is available. Degradation only occurs in the sediment by formation of non extractable residue. Virtually no degradation product was observed. Mineralization was negligible over the duration of the study (100 d). Tetraconazole was very high persistent in both systems ($DT_{50\ whole\ system}$ = 310 – 372 d).

New PEC SW values calculated according FOCUS SW and FOCUS kinetics were presented in the Addendum 1 to the DAR. These PEC_{SW} are based on FOCUS SW Step 2 and were agreed by the meeting of experts. However, some MSs may require Step 3 calculations. With respect to PEC_{SED} a data gap to address the potential accumulation of tetraconazole in the sediment was identified.

FOCUS GW calculations presented for the parent compound in Addendum 2 were agreed by the meeting of experts. None of the uses and scenarios simulated resulted in 80th percentile annual average leachate concentration above the trigger of 0.1 µg / L. For the metabolites the meeting of experts did not agree on the calculations presented. Lysimeter metabolite M11 exceed 0.1 µg parent eq / L the year of application and the subsequent year. Lysimeter metabolite M10 reach concentrations slightly below the trigger (0.08 µg parent eq / L) the year of application; since the substance has been applied only one season, it may not be excluded that this metabolite also exceeds the trigger of 0.1 µg parent eq / L when tetraconazole is applied in successive seasons.

On basis of the vapour pressure (1.8 10^{-4} Pa) and the water solubility (196 mg /L) a Henry's Law constant of 3.6 · 10^{-4} Pa m^3 mol^{-1} was calculated. Half life in the troposphere due to photochemical reaction with OH· radicals was calculated to be of 1.16 d.

The acute risk assessment to insectivorous birds in orchards and sugar beets indicated a low risk, where as the acute risk to insectivorous birds in cereals and herbivorous birds in sugar beets was assessed to be high and calls for further refinements. The short-term risk to birds from all intended uses was considered to be low, whereas the long-term risk to birds from all intended uses was found to be high. A refined long-term risk assessment for birds for all intended uses was required, taking into account the recommendations from the expert meeting. Only the long-term risk assessment to mammals was provided in the DAR, as the acute toxicity endpoint for mammals was found not to be valid by RMS. However, the mammalian toxicity experts agreed that the acute study was valid, and EFSA subsequently calculated acute TER values for mammals. The risk was found to be low for all uses. The long-term risk assessment to mammals indicated a low risk to insectivorous mammals from use in cereals and a high risk to herbivorous mammals from uses in sugar beets, grapes and apples.

Refinements were required to address the long-term risk to herbivorous mammals for uses in sugar beets, grapes and apples. The risk assessment for secondary poisoning indicated a low risk to fish-eating birds and mammals and earthworm-eating mammals. The risk to earthworm-eating birds was found to be high and further refinements were required. The risk from uptake of contaminated drinking water was considered to be low for birds and mammals. A data gap to address the risk for potential endocrine effects on birds was identified.

Tetraconazole is very toxic to aquatic organisms. However, acute and chronic TER values were far above the Annex VI trigger for all organisms included in the aquatic risk assessment, based on FOCUSsw Step 2 South European calculation for the worst case sugar beet application. A data gap was identified for the applicant to address the potential risk of endocrine disrupting effects in fish.

Standard glass plate tests were provided for *Aphidius rhopalosiphi, Typhlodromus pyri, Crysoperla carnea and Poecilus cupreus.* No effects were found in the two latter species. The study with *T. pyri* was considered insufficient to address the risk due to high escape rates during the study. Even though in-field and off-field HQ indicated at low risk to *A. rhopalosiphi*, reproductive effects above 50% were derived in extended laboratory study with *A. rhopalosiphi* at exposure rates comparable to in-field uses. Aged residue studies, however, indicated that the effects on mortality and reproduction never exceeded 50% even at day 0 of ageing. Field studies covering all intended uses indicated a low risk to *T. pyri.* The expert meeting agreed to require an extended lab study (with fresh residues) with *T. pyri* to conduct an off-field risk assessment in order to see if the off-field risk to mites/spiders will be addressed also for species with longer reproductive cycles than *T. pyri* (i.e. species with lower capacity to re-colonise the in-field area).

The formulation Eminent 125 EW had no significant effect on organic matter decomposition over a six months period in a litter bag test with worst a case application rate

The risk from tetraconazole to bees, earthworms, soil non-target micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

As uncertainties remains for potential soil metabolites, no final conclusion can be drawn for the risk from metabolites to aquatic organisms, earthworms, soil non-target micro- and macro organisms.

Key words tetraconazole, peer review, risk assessment, pesticide, fungicide

TABLE OF CONTENTS

BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stage of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000 as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Tetraconazole is one of the 79 substances of the third stage Part A covered by the amended Regulation (EC) No 1490/2002 designating Italy as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Italy submitted the report of its initial evaluation of the dossier on tetraconazole, hereafter referred to as the draft assessment report, received by EFSA on 15 July 2005. The draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1490/2002 on 5 February 2007 to the Member States and the main applicant ISAGRO S.p.A 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, EFSA identified and agreed on lacking information to be addressed by the applicant as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the applicant, a scientific discussion took place in expert meetings in March - April 2008. 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 during a written procedure with the Member States in June - July 2008 leading to the conclusions as laid down in this report.

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

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

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial

evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received
- the resulting reporting table (rev.1-1 of 22 January 2008)
- 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.2-1 of 31 July 2008)

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

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Tetraconazole is the ISO common name for (*RS*)-2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propyl-1,1,2,2-tetrafluoroethyl ether (IUPAC). It is a racemic mixture.

Tetraconazole belongs to the class of conazole fungicides alternatively classified as N-substituted triazole fungicides. It is a systemic fungicide with protectant, curative and eradicant properties. Tetraconazole belongs to the Sterol Biosynthesis Inhibitors (SBI) group, it acts by inhibiting the metabolic pathway leading to fungal sterol production by blocking the lanosterol demethylation reaction. Tetraconazole is used in agriculture, viticulture, horticulture, home gardening to control a range of fungal diseases.

The representative formulated product for the evaluation was "Eminent 40 ME", a micro-emulsion (ME) containing 40 g/L tetraconazole, registered under different trade names in Europe.

The representative uses evaluated comprise foliar spraying against *Erysiphe graminis*, *Puccinia* spp., *Septoria tritici* in wheat, from growth stage of BBCH 51 up to flowering, in all EU countries, at single application rate of 125 g a.s./ha, and foliar spraying against *Podosphaera leucotricha* in apple, *Uncinula necator* in grapes up to growth stage of BBCH 75-83 and BBCH 75 respectively, in all EU countries, up to a maximum 3 applications at a maximum application rate per treatment of 30 g a.s./ha, with an interval of 14 days between applications; and foliar spraying against *Erysiphe betae*, *Cercospora beticola* in sugar beet, up to growth stage of BBCH 49, in all EU countries, up to a maximum 2 applications at a maximum application rate per treatment of 100 g a.s./ha, with an interval of 20 days between applications.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of tetraconazole is 950 g/kg. No FAO specifications exist.

PRAPeR 41 meeting (April 2008) proposed a data gap for the applicant to submit a new technical specification justifying the presence/absence and the limits for the impurities based on the 5 batch data, however the experts agreed that if the non relevant impurities below 1 g/kg are removed from the specification, no further justification is required. The meeting also proposed a data gap for the confirmation of the identity of one impurity in the technical material.
Toluene was considered a relevant impurity by the experts at PRAPeR Meeting 44 (April 2008) but the levels proposed in the current specification are of no toxicological concern.

Since clarification is required with respect to certain impurities, the specification for the technical material as a whole should be regarded as provisional for the moment.
The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of tetraconazole or the respective formulation.
The main data regarding the identity of tetraconazole and its physical and chemical properties are given in appendix 1.

Adequate analytical methods (GC-FID) are available for the determination of tetraconazole in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material (GC-FID).
Sufficient test 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.

Adequate methods are available to monitor tetraconazole residues in food/feed of plant and animal origin; however data gaps were set for ILV of the primary methods and for confirmatory methods for both matrices.
The extended version of the German modular multi-method DFG S19 with modified extraction is the enforcement method for the determination of residues of tetraconazole in plant materials with LOQ of 0.01 mg/kg in wheat (grain), sugar beet and with LOQ of 0.02 mg/kg in wheat (straw), grape (bunches), apples and tomatoes.
Residues of tetraconazole in food of animal origin can be monitored with the extended version of the German modular multi-method DFG S19 with modified extraction with LOQ of 0.01 mg/kg in milk, and with LOQ of 0.02 mg/kg in meat, fat and eggs.
Adequate methods are available (DFG S19, extended revision, GC-MS) to monitor tetraconazole in soil with LOQ of 0.05 mg/kg and in water (GC-NPD) with LOQ of 0.1µg/kg, however for water a data gap was set for confirmatory method.

There are no acceptable analytical methods to determine residues of tetraconazole in air.
Since tetraconazole is not classified as acute toxic or very toxic, analytical methods for the determination of residues of tetraconazole in body fluids and/or tissues are not needed.

2. Mammalian toxicology

Tetraconazole was discussed at the meeting of experts for mammalian toxicology in April 2008 (PRAPeR 44, round 9).

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

Based on urinary excretion in repeated dose experiments with rats, it has been shown that tetraconazole is absorbed orally to an extent of more than 80%. Absorption is rapid, as concentrations in the blood reach a maximum already between 8 and 36 hours after oral application. It is widely distributed in the body and the highest amounts of tissue residues are found in liver, adrenals, kidneys, gastrointestinal tract, muscle and fat. It has no potential for accumulation. Excretion is rapid and complete (> 99% within 72 hours), mainly via the urine (~76%). It is extensively metabolised (to an extent of about 84%); less than 9% of a given dose were detected as parent compound in urine and faeces. The major metabolic pathways include oxidation and reduction, involving ether formation and displacement of triazole by glutathione. The end metabolites and displaced triazole are excreted eventually with the urine.

2.2. Acute toxicity

EFSA note: A new acute oral toxicity study was provided with the addendum to the DAR but could not be considered in view of the restrictions concerning the acceptance of new studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007. However, the experts agreed that the study provided in the original DAR was valid and could be used for risk assessment.

In rats tetraconazole is of moderate acute toxicity by the oral (LD_{50} = 1031 mg/kg bw) and of low toxicity by the dermal (LD_{50} > 2000 mg/kg bw) and inhalation route (LC_{50} > 3.66 mg/L). It is neither a skin nor an eye irritant and has no skin sensitising properties. Based on the data available on acute toxicity a classification as **Xn; R22 "Harmful; Harmful if swallowed"** is proposed.

2.3. Short term toxicity

A 28-day and a 90-day dietary study have been carried out with rats. With dogs a 1-year dietary study is reported. The experts agreed to set the NOAEL in the 28-day dietary study at 3.9 mg/kg bw/d based on increased liver weights and sizes. They also agreed to establish a NOAEL of 4.10 mg/kg bw/d based on changes in liver parameters in the 90-day rat study and to set a set a NOAEL of 2.95 mg/kg bw/d in the 1-year dog study based on changes in blood chemistry parameters paralleled by increased organ weights and pathology in liver and kidneys at the highest dose. A 21-day dermal study with

rabbits with a formulation containing 125 g/L tetraconazole was reported in the DAR and since no adverse effects were observed the NOAEL was fixed at the highest dose of 240 mg/kg bw/d (value corrected for content of active substance).

2.4. GENOTOXICITY

Tetraconazole did not show a genotoxic potential in an adequate battery of tests.

2.5. LONG TERM TOXICITY

A 2-year combined chronic toxicity/carcinogenicity study with rats and an 80-week carcinogenicity study with mice are presented in the DAR. The experts agreed to set a systemic NOAEL of 0.4 mg/kg bw/d (10 ppm) in the rat, based on observations of increased liver weights and toxicity at the next higher dose (80 ppm). At doses of 640 ppm and 1280 ppm also effects on bones and incisors (fluorosis) were observed that were attributed to the high fluorine content of tetraconazole. The experts confirmed also that the increased number of thyroid lesions seen at high doses were secondary to liver toxicity and not relevant for human risk assessment. With regard to the increased incidences of absent corpora lutea and squamous metaplasia (that were not seen in the two generation reproduction study) the experts noted that it could not be excluded that they were caused by hormonal effects of tetraconazole in particular since other triazoles have been shown already to possess endocrine disrupting properties. In the mouse study the systemic NOAEL was set at 1.5 mg/kg bw/d based on general toxicity at the higher dose levels (reduced body weight gain, increased liver and kidney weights and liver, kidney and brain pathology). Taken into account a series of mechanistic investigations (see chapter 2.8) the experts agreed that the increased incidences in benign and malignant liver tumours in mice were attributable to microsomal liver enzyme induction and considered not relevant for man.

2.6. REPRODUCTIVE TOXICITY

A two-generation study, a developmental study in rats and one in rabbits are presented in the DAR. The results obtained in these studies were extensively discussed at the meeting of experts. It was agreed to set an overall NOAEL for reproduction, parental and developmental effects in the two-generation study at 3.6 mg/kg bw/d based on increased liver weights (parental), occurrence of prolonged gestation periods and dystocia (reproduction) an adverse effect common to triazoles) in dams and reduced body weight gain and survival in the offspring (development) and to also propose a classification as **Xn; Repr. Cat. 3 R62 "Harmful; Possible risk of impaired fertility"** based on the occurrence of dystocia and prolonged gestation periods. In the rat developmental study the maternal NOAEL was set at 5 mg/kg bw/d based on clinical signs and decreased body weight gain at a dose of 22.5 mg/kg bw/d which was the NOAEL for developmental effects since at the highest dose of 100 mg/kg bw/d hydronephrosis, hydroureter and extra ribs were observed in the pups. In the rabbit, a maternal NOAEL of 15 mg/kg bw/d was established based on reduced bodyweight gain while no adverse effects on offspring could be detected up to the highest dose of 30 mg/kg bw/d. Based on the

effects observed in rat foetuses a classification as **Xn; Repr. Cat. 3 R63 "Harmful; Possible risk of harm to the unborn child"** was proposed.

2.7. NEUROTOXICITY

Tetraconazole does not have a structure related to organophosphates and no effects indicative of neurotoxicity have been observed in any of the investigations presented in the DAR. Therefore, specific neurotoxicity studies were considered not necessary.

2.8. FURTHER STUDIES

Mechanistic studies on effects on liver and thyroid

A series of mechanistic studies has been carried out in order to elucidate the mechanisms leading to liver tumours in mice and thyroid tumours in rats after chronic application of tetraconazole. It could be demonstrated in three 4-week oral studies that tetraconazole induces hepatic phase I and phase II enzymes in rats and mice. In a one-week study in rats, tetraconazole induced cell growth activity in hepatocytes and caused increased liver weights. In a further 4-week study in rats it could be shown that tetraconazole induces also thyroxin glucuronyltransferase, leading to increased thyroxin clearance, consequently to increased levels of TSH and eventually to thyroid hypertrophy. This mechanism is considered not relevant for man. In another 4-week study in rats it was confirmed that the elevated TSH levels and the reduced T4 levels are a consequence of the inductive (indirect) action of tetraconazole and that the active substance exerts no direct toxicity on the thyroid. Overall, the mechanistic studies indicate that the liver tumours in mice and the thyroid tumours in rats are secondary to hepatic enzyme induction and are not relevant for human risk assessment.

Mechanistic studies on effects of the fluoride moiety

In two mechanistic studies with rats it could be demonstrated that fluoride was systemically available after application of tetraconzole and that both tetraconazole and fluoride had similar effects in terms of inducing fluorosis. The experts agreed that this can be considered as indirect evidence that the fluorine moiety is causative of the effects on cranium and incisors (fluorosis) observed in subchronic and chronic studies with tetraconazole.

Studies on metabolites

The tetraconazole metabolite M14360-acid[2] yielded negative results in a bacterial mutagenicity test and in an *in vitro* mutation assay with mouse lymphoma cells but was positive in an *in vitro* clastogenicity assay with human lymphocytes. *In vivo* M14360-acid did not induce micronuclei in murine bone marrow cells. With the tetraconazole metabolite M14360-alcohol[3] an acute oral toxicity study with rats (LD_{50} > 2000 mg/kg bw) and a bacterial mutagenicity assay and an *in vivo* micronucleus test (both negative) are presented in the DAR.

[2] 2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid
[3] 2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propan-1-ol

The metabolite M14360-difluoroacetic acid[4] was negative in a bacterial mutagenicity test and its LD_{50} in rats was higher than 5000 mg/kg bw. Acute oral toxicity of a mixture of metabolites M14360-DCP-3OH[5] (48.13%) and M14360-DCP-5OH[6] (37.94%) yielded a LD_{50} > 2000 mg/kg bw. A series of investigations are presented on the tetraconazole metabolites triazole acetic acid (TAA)[7] and triazole aniline (TA)[8] in the DAR. These two metabolites are common to other triazole fungicides and have been discussed already at PRAPeR 14, January 2007 where based on the available data reference values have been established. They are 0.02 mg/kg bw/d for the ADI and 0.06 mg/kg bw/d for both ARfD and AOEL of TAA and 0.1 mg/kg bw/d for the ARfD and ADI (no AOEL set) for TA.

2.9. MEDICAL DATA

There are no reported cases of tetraconazole poisoning.

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

The experts agreed to set an **ADI** of 0.004 mg/kg bw/d based on the NOAEL obtained in the 2-year rat study, applying a safety factor of 100.

The experts agreed to set an **AOEL** of 0.03 mg/kg bw/d based on the NOAEL obtained in the 1-year dog study, applying a safety factor of 100.

The experts agreed to set an **ARfD** of 0.05 mg/kg bw derived from the maternal NOAEL established in the developmental study in rats, applying a safety factor of 100.

2.11. DERMAL ABSORPTION

In the original DAR only an *in vivo* skin penetration study with rats (with the dermal absorption values based on it) is provided. The applicant has submitted (as part of the post-submission dossier prior to the submission of the DAR to the EFSA) an *in vitro* dermal absorption test with rat and human skin membranes that had been integrated by the RMS together with revised exposure calculations in an addendum to the DAR.

The experts agreed to set the dermal absorption of the preparation "EMINENT 40 ME" at 1% for the concentrate and at 20% for the spray dilution based on an *in vivo* skin penetration test with rats in combination with an *in vitro* dermal absorption test with rat and human skin membranes as presented in the addendum to the DAR.

[4] 5-(2,4-dichlorophenyl)-2,2-difluoro-6-(1*H*-1,2,4-triazol-1-yl)-3-oxahexanoic acid
[5] 2-(2,4-dichloro-3-hydroxyphenyl)-3-(1*H*-1,2,4-triazol-1-yl)-propyl-1,1,2,2-tetrafluoroethyl ether
[6] 2-(2,4-dichloro-5-hydroxyphenyl)-3-(1*H*-1,2,4-triazol-1-yl)-propyl-1,1,2,2-tetrafluoroethyl ether
[7] 1*H*-1,2,4-triazol-1-ylacetic acid
[8] (*R*,*S*)-2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid; {3-(1*H*-1,2,4-triazol-1-yl)-D,L-alanine}

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant product "EMINENT 40 ME" is formulated as a microemulsion containing 40 g/L tetraconazole. It is used as a systemic fungicide with protectant, curative and eradicant properties on sugar beet and wheat (field crop application) and on grapes and apple (vineyard/orchard application). New exposure calculations (based on a revised AOEL and dermal absorption values) have been provided with an addendum to the DAR.

Operator exposure

According to the intended uses submitted by the applicant the maximum applied dose of tetraconazole is 125 g/ha and the minimum volume is 200 L water/ha with maximal number of 3 applications per year.

The values in the tables below represent the calculated exposures in percentages of the systemic AOEL of 0.03 mg/kg bw/d using the UK POEM and the German model.

UK POEM

Application mode	Without PPE	With PPE*
Tractor mounted/trailed boom sprayer; hydraulic nozzles (sugar beet & wheat)	305.13%	48.17%
Tractor mounted/air-assisted sprayer (grapes & apples)	43%	29.90%
Hand held sprayer with hydraulic nozzles (grapes & apples)	50.78%	17.43%

*PPE (personal protective equipment): gloves during spray application & mixing and loading.

German model

Application mode	Without PPE	With PPE**
Tractor mounted/trailed boom sprayer; hydraulic nozzles (sugar beet & wheat)	51.26%	39.56%
Tractor mounted/trailed broadcast air-assisted sprayer (grapes & apples)	27.7%	4.21%
Hand held sprayer; hydraulic nozzles (grapes & apples)	15.49%	2.37%

**PPE (personal protective equipment): gloves during spray application & mixing and loading and standard protective garment during application.

Bystander exposure

Two different exposure predictions for bystanders have been presented, both applying worst case scenarios of application of EMINENT 40 ME in orchards. Depending on the input parameters used in

the calculations the exposures amounted to either 0.16 % or to 5.5% of the systemic AOEL of 0.03 mg/kg bw/d.

Worker exposure

The predicted exposure for re-entry workers using the worst case scenario (application in orchards) was calculated according to Krebs et al. 2000[9] with the addition of the indications from the workshop SCORA[10] and amounted to 28% when no PPE is used and to 2.8 % when PPE is worn of the AOEL.

3. Residues

Tetraconazole was discussed in the meeting of experts PRAPeR 45 in March 2008.

Tetraconazole is a racemic mixture of isomers. The analytical methods used in the residue studies were not specific for the *R*- and *S*-isomer of tetraconzole. Therefore it is not possible to state whether a change of the isomer ratio occurred in plant and livestock studies e.g. by preferential metabolism or degradation of one isomer. The reported results always refer to the sum of isomers, any ratio.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The fate of tetraconazole in plants was investigated in wheat, sugar beet and grapes using the active substance labelled in the triazole and phenyl ring, respectively. Study designs were representative of the supported uses in these crops.

Based on the identified metabolites in the wheat and sugar beet studies, the main primary steps of metabolism of tetraconazole in these crops include hydroxylation of the phenyl ring, hydrolysis of the tetrafluoroethylether group as well cleavage of the phenyl-triazole ring system. Several metabolites were found in a conjugated form. The triazole derivative metabolites were identified as triazole alanine, triazole acetic acid and triazole hydroxypropionic acid[11] in wheat and sugar beet.

In wheat straw, sugar beet and grapes, tetraconazole represented the major compound of the terminal residue at harvest (around 50% TRR or even above) while metabolites were present in amounts one order of magnitude lower (1 to 10% TRR). Only in cereal grain the triazole derivative metabolites

[9] Krebs B, Maasfeld W, Schrader J, Wolf R, Hoernicke E, Nolting HG, Backhaus GF, Westphal D (2000) Einheitliche Grundsätze zur Sicherung des Gesundheitsschutzes für Beschäftigte beim Wiederbetreten behandelter Kulturen nach Applikation von Pflanzenschutzmitteln (Uniform principles for safeguarding the health of workers re-entering crop growing areas after application of plant protection products). Nachrichtenblatt des Deutschen Pflanzenschutzdienstes Germany, 2000, 52 (1) 5-9.

[10] SCORA (Successful consumer and operator risk assessment) held in York (U.K.) at the CSL (Central Science Laboratory) on 13th February 2003.

[11] (*R,S*)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid

triazole alanine (50.1% TRR) and triazole acetic acid (24.9% TRR) were present in clearly higher amounts than tetraconazole (6.3 % TRR). In addition, the metabolite triazolyl hydroxyl propionic acid was found in sugar beet leaves (7.1% TRR). This metabolite had not been identified in metabolism studies with other triazole compounds assessed in the peer review.
In grapes only small amounts of metabolites were produced in the metabolism study, and only two of them were tentatively identified. However it was agreed that the metabolic pathway of tetraconazole should be comparable in the three crops after foliar treatment.

The amount of produced metabolites which are structurally related to tetraconazole is low and their contribution to the overall toxicological burden is not considered significant. As far as the triazole derivative metabolites are concerned, the PRAPeR experts meeting 14 on toxicology in January 2007 concluded that toxicological end points and reference values should be adopted, as a result of their effect on reproduction and development. This conclusion applied to triazole, triazole alanine and triazole acetic acid. Triazole hydroxypropionic acid was not considered at that time. For triazole hydroxypropionic acid no information has been available on the toxicity and hence no conclusion can currently be drawn (PRAPeR 44).
Based on the toxicologists' conclusion it was agreed by the PRAPeR expert meeting 15 on residues in January 2007 that a robust consumer risk assessment related to the compounds of the triazole chemical class needs to take these derivatives into account.
Therefore, regarding tetraconzole the meeting of experts PRAPeR 45 agreed that for the risk assessment it is necessary to set separate residue definitions, taking into account 1) tetraconazole and 2) triazole alanine, triazole acetic acid and provisionally triazole hydroxypropionic acid (data gap). The meeting took also into consideration the results of the confined rotational crop study with regard to the triazole derivative metabolites (see point 3.1.2 of this document). The residue definition for monitoring was provisionally proposed as tetraconazole only. Pending finalisation of the risk assessment on triazole compounds and the triazole derivative metabolites these metabolites may also need to be monitored in future.

Supervised residue trials were submitted for the representative uses. Usually, only tetraconazole residues were analysed in these trials. No information is available on the occurrence of the triazole derivative metabolites under field conditions. A study on analysis of tetraconazole, triazolyalanine and triazolyl acetic acid in wheat was considered not acceptable by the RMS. All residue trial data considered acceptable were therefore assessed with regard to tetraconazole residues only and in view of possibilities of MRL setting.
For apples and grapes the initially submitted residue data were not considered in the DAR because the number of applications and the application rate were both higher than those notified as representative. It was therefore required to generate further data according to the notified cGAP (data gap). A new set of submitted residue trial data in apples and grapes has been evaluated in the addendum of November 2007. However, in view of the restrictions concerning the acceptance of new studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review. Presentation, evaluation and related

assessments in the addendum concerning these residue trials should therefore not be considered peer reviewed. Due to the data gap the risk assessment on the apple and grape uses cannot be finalised.

The information provided in support of the representative uses in sugar beets and cereals was sufficient. Residues were consistently below the Limit of Quantification (LOQ, ranging from < 0.005 to < 0.02 mg/kg, depending on the trial) in sugar beet root and in cereal grains in both Northern and Southern European region. Positive results where found in feed items (sugar beet leaves and cereal straw) with Supervised Trials Median Residues (STMR) values ranging from 0.5 to 1.1 mg/kg, depending on the item and region.

These results can be considered as reliable based on storage stability studies showing that tetraconazole residues are stable under deep freeze conditions in cereals (grain and straw), apple, grapes and sugar beet root for at least 3 years.

Tetraconazole was shown to be stable under standard hydrolytic condition in buffer solutions simulating pasteurization, boiling, baking, brewing, and sterilisation. Processing studies indicated that tetraconazole residues are preferably transferred to pomace during apple juice and wine making. Transfer factors to juice, wine and dry apple pomace could be derived.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

The potential uptake, translocation and metabolism of soil residues by rotational crops were investigated with tetraconazole labelled either in the phenyl or in the triazole ring. Together with unchanged tetraconazole the triazole derivative metabolites triazole alanine, triazole acetic acid and triazole hydroxypropionic acid were found as major components in succeeding crops carrots, lettuce and wheat. The triazole derivative metabolites were present in amounts one order of magnitude higher than tetraconazole. Other metabolites identified were present at much lower levels. Altogether, it was concluded that the metabolism in rotational crops is comparable to the metabolic pathway in primary crops.

Rotational field studies were conducted and demonstrated that under practical conditions of use, residues of tetraconazole compounds above LOQ are unlikely to occur in usual agricultural crop rotation. The available field studies were however not considered to fully address the issue of residues in following crops because they do not include leafy vegetables. Moreover the triazole compounds were not analysed while they have been shown to be the main residue in the radiolabel study with rotated crops. Therefore the experts proposed a new data gap for a new field rotational crop study.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Tetraconazole metabolism studies in goats were conducted using phenyl and triazole ring labelling respectively. The main metabolic pathway consists in oxidative degradation of the tetrafluoroethyl moiety and cleavage of the phenol- triazole ring system. Rat and goat metabolisms are considered as being similar.

Tetraconazole and free triazole together account for 90% of the residue present in the edible animal tissues. Milk and meat contain predominantly triazole residues while liver and fat contain essentially unchanged tetraconazole.

The meeting of experts agreed that for the risk assessment it is necessary to set separate residue definitions for 1) tetraconazole and 2) 1,2,4-triazole, because this metabolite was found at significant levels in animal commodities. The proposed residue definition for monitoring is tetraconazole, as it is a valid indicator in all edible ruminant commodities. It should be considered as fat soluble compound. However, as for plants the proposal is pending finalisation of the risk assessment on triazole compounds and triazole derivative metabolites. The outstanding assessment may demonstrate the need to monitor animal products for 1,2,4-triazole residues in future.
Considering the potential livestock exposure to tetraconazole residues through consumption of treated feed items (sugar beet roots and leaves, wheat, apple pomace), feeding studies indicate that measurable residues may be present in the range of the analytical LOQ in meat and milk and above the LOQ in fat, liver and kidneys. A processing study clearly showed that residues present in milk are essentially present in cream. Amounts of 1,2,4-triazole appear to be lower than expected from metabolism studies.

The tetraconazole metabolism in poultry was not investigated given the expected low exposure level resulting from the representative uses.
Also a pig metabolism study was not a requirement; however the meeting of experts noted that for pigs significant intake is expected. It was agreed that for pigs it is possible to extrapolate residue levels from cattle and hence a livestock feeding study with pigs is therefore not required.

The meeting of experts confirmed that MRLs for animal commodities are required. However the livestock intake calculation needs to be revised according to current agreed methodology and also considering the use of sugar beet leaves in animal diet. Subsequently MRL proposals for livestock commodities will have to be recalculated accordingly. For the moment, with the identified data gaps in the residue section it will not be possible to conclude on final MRL proposals for food of animal origin.

3.3. CONSUMER RISK ASSESSMENT

For different reasons the consumer risk assessment with regard to the representative uses of tetraconzole in sugar beet, wheat, apples and grapes cannot be finalised.

Data to address the level of relevant residues in apples and grapes when treated according to notified GAP criteria could not be considered in the peer review in view of the restrictions concerning the acceptance of new studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007.
Moreover, with the data submitted for the peer review a reliable consumer exposure assessment would only be possible for residues of unchanged parent compound tetraconazole. The contribution of the triazole derivative metabolites (free triazole, triazole alanine, triazole acetic acid and triazole hydroxypropionic acid) to consumer exposure and risk is not possible to assess on the basis of the available information. Data is lacking on their actual occurrence in primary crops, animal

commodities and rotational crops but also with respect to hazard assessment (triazole hydroxypropionic acid).

In addition, their potential to act toxicologically in a cumulative way with the parent compound needs to be assessed on the basis of a related opinion and guidance of the EFSA PPR panel. It must be noted that this lack of data is a generic issue and concerns all active substances of the triazole chemical class whose degradation pathway in primary crops, soil and livestock involves a molecule cleavage to form triazole ring structures.

It should be also noted that tetraconazole is a racemic mixture of isomers. The risk assessment in the DAR was performed disregarding the impact of a possible change of the enantiomer ratio due to plant or livestock metabolism as this was not investigated by the applicant. The experts concluded the applicant should address the consumer exposure to the two tetraconzole isomers, whether a change of the isomer ratio may occur when tetraconazole is metabolised or degraded and whether a possibly changed ratio of isomers can be considered covered by the available toxicological data and information.

The assessment of human and livestock exposure and consumer risk initially done in the DAR and amended in the addendum of November 2007 was not accepted by the meeting of experts since it needed substantial revision.

A revised assessment of human and livestock exposure to residues of tetraconzole alone, and only based on data eligible for consideration in the review process, and moreover limited to the uses in wheat and sugar beet was submitted to EFSA by the RMS after the meeting of experts, and as such can only be presented as a provisional assessment in this document. This assessment was neither peer neither reviewed nor made available in an addendum to the DAR.

Chronic exposure and risk assessment: International and national theoretical maximum daily intake (TMDI) estimates were conducted using national German and UK diets as well as the GEMS Food WHO European cluster diets. These diets cover all categories of consumer including infants and toddlers. Residues in cereals and sugar beet roots were considered to be at the level of the proposed MRLs, and residues in animal products were estimated from the cattle feeding study upon revision of the livestock dietary burden estimates. The maximum chronic intakes were estimated for the UK infants and toddler (0.0067 and 0.0065 mg/kg bw/day respectively), corresponding to above 160% of the ADI of tetraconazole of 0.004 mg/kg bw /day. Refined estimates of the daily intake (NEDI), using STMR values for the relevant plant and animal commodities demonstrated exposure of the critical consumer group of young children being below the ADI of 0.004 mg/kg bw /day (infant 88% and toddler 78% ADI).

Acute exposure: International Estimates of Short Term Intakes (IESTI) were carried out by the RMS on the basis of WHO large portion consumption data for the general population and for children. Highest acute exposure in both categories was due to consumption of cattle liver (23% and 37% ARfD respectively), exposure to other commodities was significantly below the ARfD of tetraconzole of 0.05 mg/kg bw/day.

It is again noted that none of the above presented results in the chapter 3.3 on consumer risk assessment is peer reviewed. Moreover, a final consumer risk assessment for the notified representative uses is pending

- the conclusion of a final plant residue definition for risk assessment with regard to whether or not metabolite triazole hydroxypropionic acid needs to be included
- the consideration of residue levels occurring in apples and grapes upon treatment with tetraconazole according to representative GAP criteria
- an human and animal intake assessments of triazole derivative metabolites resulting from the use of tetraconazole, when adequate data on their levels in food and feed are available
- an assessment of the potential of triazole derivative metabolites to act toxicologically in a cumulative way with tetraconazole
- submission of data or information on the fate of isomers of tetraconazole in plants and livestock.

3.4. PROPOSED MRLS

Sugar beet	0.02* mg/kg (tetraconzole)
Wheat	0.02* mg/kg (tetraconzole)
Apples, Grapes	No MRL proposed; residue trials supporting the notified uses were not available for the peer review (refer to point 3.1.1 of this document).

Food of animal origin

The meeting of experts confirmed that MRLs for food of animal origin are required. For the moment, it will however not be possible to conclude on final MRL proposals for these commodities (refer to point 3.4 of this document).

4. Environmental fate and behaviour

Fate and behaviour of tetraconazole in the environment was discussed in the meeting of experts PRAPeR 42 (March – April 2008) on basis of the DAR (2005) and addenda I (November 2007) and II (March – 2008). Tetraconazole technical is a racemic mixture. The racemic mixture of purified tetraconazole has been used in all the fate and behaviour studies. However, no enantioselective method has been used to analyze the samples in the studies and no conclusion may be derived on potential enantioselective degradation in the environment. Nevertheless, the risk assessment presented assumes practically no degradation and, therefore, the issue of potential enantioselective enrichment is not relevant for it. A number of data gaps have been identified to clarify weather and under which conditions significant degradation in the environment may actually occur. Applicant should consider the issue of potential enantioselective degradation when addressing the data gaps identified.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Route of degradation under dark aerobic conditions at 25 °C was investigated in one soil (pH 6.9, OM 2.0 %, clay 9%) with tetraconazole ^{14}C-labelled either in the triazole ring or the dichlorophenil ring. Degradation was negligible after 364 d (97.8 % AR as tetraconazole) and unextractable residues were found at levels between 5.6 % (14 DAT) and 15.8 % (364 DAT) AR. Similar results were obtained in one study with three additional soils (pH 5.6 – 6.4, OC 0.6 – 2.3 %, clay 1.9 – 9.5 %) at 20 °C were the rate of degradation was investigated (89.8 – 92.5 % AR as tetraconazole and 4.9 -6.9 % AR as bounded residue after 100 d).

In the rate outdoor study (see following section) M14360-alcohol[3] (max. 15.5 % AR after 30 d) and TAA[7] (max. 14.11 % AR after 150) were major metabolites. M14360-acid[2] (max. 7.94 % AR after 150 d) exceeded 5 % AR in two or more consecutive sampling dates and therefore it was considered to need further assessment for potential groundwater contamination. These metabolites may only be considered as potential soil metabolites due to the uncertainties associated with the study where they have been found.

Route of degradation in soil under dark anaerobic conditions was not investigated. Taking into consideration the representative uses and the persistence of tetraconazole, residues of this active ingredient may be exposed to anaerobic conditions in soil. The meeting of the experts agreed that information on the route and rate of degradation under anaerobic conditions is needed. The risk assessment presented assumes no degradation under anaerobic conditions. Photolysis of tetraconazole, ^{14}C labelled in the triazole ring, was investigated in soil surface. Samples were irradiated with a Xenon lamp at 20 °C for 16 d, corresponding to 36.6 d of summer sun light. Degradation of tetraconazole observed in this experiment was negligible.

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

Rate of degradation of tetraconazole was investigated in one dark aerobic study in three soils (pH 5.6 – 5.4; OC 0.62 – 2.32 %; clay 1.9 – 9.5 %). As for the route study, degradation of tetraconazole was less than 10 % AR after 100d (89.8 – 92.5 % AR remaining as tetraconazole at the end of the study). From the data in this study it was not possible to estimate a reliable degradation rate in soil.

In a second study the degradation of tetraconazole was investigated in the same three aerobic soils under outdoor conditions, exposed to sunlight. Tetraconazole ^{14}C-labelled at the triazole ring was applied over 4 mm depth soil layers in trays at a rate equivalent to 133 g a.s / ha. The trays were kept outdoors from April – October (soil moisture= WFC, night temperature = 0-24 °C, day temperature = 11 – 46 °C). No traps for volatiles were used in these experiments. Tetraconazole was moderate to high persistent (DT_{50} = 51.2 – 191.4 d) in these studies. The applicant attributed degradation to a combined effect of photochemical and microbial degradation. RMS considered the reliability of the study doubtful since no clear mechanism may explain degradation. The meeting of the experts considered that since no aqueous photolysis was observed and no information on indirect photolysis is available, there is no experimental support to the hypothesis of the applicant. Also the meeting

noted the wide range of temperatures and the possible effect of high temperatures on the degradation. The experts considered that further experiments investigating effect of higher temperatures in dark under controlled moisture conditions and indirect aqueous photochemical studies could help to understand the mechanism of degradation prevailing in the environment. Therefore, a data gap was identified for these additional studies. In the lack of this information, the risk assessment was performed assuming that degradation of tetraconazole in soil is negligible under all conditions.

Rate of degradation of potential soil metabolite M14360-acid ^{14}C-labelled at the triazole ring was investigated under dark aerobic conditions at 20 °C in three soils (pH 5.8 – 6.6; OC 0.56 – 2.19 %; clay 1.7 – 8.1 %). Soils were treated at a rate equivalent to 125 g a.i / ha. This metabolite is medium to high persistent under these conditions (DT_{50} = 92.5 – 221.4 d).

Rate of degradation of potential soil metabolite M14360-alcohol ^{14}C-labelled at the triazole ring was investigated under dark aerobic conditions at 20 °C in three soils (pH 5.7 – 6.5; OC 0.5 – 2.17 %; clay 3.8 – 9.6 %). Soils were treated at a rate equivalent to 125 g a.i / ha. This metabolite is very low persistent under these conditions (DT_{50} = 0.2 – 0.45 d).

Rate of degradation of potential soil metabolite TAA ^{14}C-labelled at the triazole ring was investigated under dark aerobic conditions at 20 °C in three soils (pH 5.2 – 6.3; OC 0.9 – 2.3 %; clay 2 – 7.5 %). Soils were treated at a rate equivalent to 125 g a.i / ha. This metabolite is low to moderately persistent under these conditions (DT_{50} = 8.4 – 18.7 d).

Dissipation of tetraconazole under field conditions was investigated in two field dissipation studies in a total of five sites (4 in Germany and 1 Northern Italy). Tetraconazole was applied on bare soil in May / June 1992 at rates of 128 g a.i / ha for the German sites and 120 g a.i/ha for the Italian one. In the five soils dissipation followed biphasic behaviour. Second phase started after 7- 27 d. Tetraconazole was high to very high persistent during the second phase. The meeting of experts agreed that the field half lives cannot be used in FOCUS modelling with the current lack of understanding of the mechanism causing loss. For PEC soil the meeting of experts agreed that the longest second phase field DT_{50} of 1688 d should be used. Potential accumulation of tetraconazole may not be excluded since about 20 – 40 % AR remains as tetraconazole one year after application. RMS presented after the meeting new PEC soil calculations (addendum 3) using the input parameters agreed by the meeting. However, EFSA identified an error on the use of program ESCAPE. Assuming yearly application and tillage EFSA calculated a plateau background concentration over the 20 cm horizon of 0.124 mg / Kg after 36 years of continuous use. This will result on a peak concentration of 0.204 mg / Kg over the 5 cm horizon. These figures may be considered to represent a realistic worst case for the uses proposed.

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

Adsorption / desorption of tetraconazole in soil was investigated in a study with four soils (pH 5.3-6.0; OC 0.7 – 28.5 %; clay 5.1 – 49.0). Tetraconazole is low mobile in acidic soils (Koc = 531 – 1922 mL / g). Adsorption / desorption of potential soil metabolites M 14360-acid and TAA were investigated in different studies with four or three soils respectively (M 14360-acid: pH 6.0 – 8.0; OC 0.6 – 2.3 %; clay 2.5 – 26.8 % / TAA: pH 3.4 – 7.55; OC 0.9 – 14.4 %; clay 2.7 – 15.25 %).

Metabolite M 14360-acid may be considered high to very high mobile in soil (K_{oc} = 33.9 – 125.0 mL / g) and TAA very high mobile in soil (K_{oc} = 1.04 - 21 mL / g). The adsorption coefficient of M 14360-alcohol was estimated by the HPLC method due to its instability in soil. The calculated value indicated that M 14360-alcohol may be considered very high mobile in soil (Koc = 51 mL / g).

Two column leaching studies were performed with tetraconazole in three soils (pH 5.3 – 7.25; OC 2.5 – 28.5 %; clay 29 – 63 %). Very low radioactivity was found in the leachate (0.02 – 0.13 %AR) but the soils do not represent worst case soils because the high clay and organic carbon content. An additional column leaching study was performed in a sandy loam soil (pH 6.1; OC 2.6 %; clay 6.4 %). In this study slightly higher levels of radioactivity were found in the leachate (0.17 – 0.37 % AR). In a third column leaching study mobility was investigated in the same three soils employed in the batch adsorption / desorption study. In this study the highest levels of radioactivity were found in the leachate (0.43 – 0.60 % AR). However, overall the column leaching experiments confirm the low mobility of tetraconazole. Two aged residue column leaching studies were performed after ageing in dark and under sunlight (53 d). In the dark ageing study no degradation of tetraconazole occurred. Levels of radioactivity in the leachate were in the same range observed in the non aged studies (0.15 % AR, 0.1 µg / L; soil: pH 6.0, OC 0.59 %, clay 2.5 %). In the aged residue under sunlight column leaching study formation and leaching of metabolites M14360-DFA (10 % AR), TAA (5.69 % AR), M14360-acid (4.12 % AR), 1,2,4 triazole (1.88 % AR), M14360-alcohol (0.44 % AR) and of six unknown compounds was observed.

The leaching behaviour of tetraconazole metabolites M14360-DFA, TAA, M14360-acid, 1,2,4 triazole and M14360-alcohol was investigated in a column leaching study in one soil (pH 5.9, OC 0.62 %, clay 1.9 %). The study confirmed the potential mobility of these metabolites in soil.

A two years lysimeter study with two soil monoliths (pH 4.95 – 5.6; OC 0.00 – 1.77 %; sand 80.9 – 99.1 %) was performed in Switzerland. Product containing ^{14}C triazol labelled tetraconazole was applied twice at a rate of 125 g a.i. / ha with 25 d interval in the first year. No product was applied the second year. Rainfall and temperatures higher than average were observed during the first experimental year. Residue leachate concentrations observed were 0.53 – 0.54 µg / L and 0.27 µg / L parent equivalents for the first and second year respectively. This residue consisted in at least twelve radioactive chromatographic fractions that did not match any of the reference standards for the already known soil metabolites. The two major fractions were M11 (47 % - 66 % of radioactivity in the leachate; corresponding to 0.11 – 0.18 µg/L) and M10 (15 – 21 % of the radioactivity in the leachate; corresponding to 0.03 – 0.08 µg/L). The rest of the fractions were below 10 % of the radioactivity in the leachate or below 0.1 µg/L parent equivalents. Whereas not fully identified, determination of molecular weight of compounds M10 and M11 was attempted by size exclusion chromatography. The meeting of experts considered this determination highly unreliable and not according the state of the art. Therefore, the experts considered that concentrations of M10 and M11 have to be reported on basis to parent molecular mass and concluded that both metabolites have the potential to exceed the annual average trigger of 0.1 µg / L. A data gap was identified for the characterization of tetraconazole lysimeter metabolites M10 and M11 and to address its potential for ground water contamination.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Tetraconazole is stable to hydrolysis and it is not expected to be degraded by photolysis in water.
Tetraconazole is not readily biodegradable.
A dissipation study of tetraconzole in two water/sediment systems under dark aerobic conditions at 20 ºC is available. Tetraconazole re-distributed from surface water to sediment. Equilibrium was reached after about 30 d , 7.5 – 9.5 % AR remained in the water phase at equilibrium. Degradation only occurs in the sediment by formation of non extractable residue. Virtually no degradation product was observed. Mineralization was negligible over the duration of the study (100 d). Tetraconazole was very high persistent in both systems ($DT_{50\ whole\ system}$ = 310 – 372 d).
New PEC SW values calculated according FOCUS SW and FOCUS kinetics were presented in the Addendum 1 to the DAR. These PEC_{SW} are based on FOCUS SW Step 2 and were agreed by the meeting of experts. However, it was noted that some MSs may require Step 3 calculations to ensure that higher values are not obtained in some of the Step 3 scenarios. With respect to PEC_{SED} a data gap to address the potential accumulation of tetraconazole in the sediment taking into consideration the high persistence of tetraconazole in water / sediment systems was identified.

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

Potential ground water contamination by tetraconazole and its soil metabolites was addressed by FOCUS GW calculations in Addendum 1 and updated in Addendum 2 with more appropriate input parameters. Calculations presented for the parent compound in Addendum 2 were agreed by the meeting of experts. However, it was noted that for future calculations the experimental arithmetic mean 1/n = 0.92 should be used. None of the uses and scenarios simulated resulted in 80th percentile annual average leachate concentration above the trigger of 0.1 µg / L. For the metabolites the meeting of experts did not agree on the calculations presented. Lysimeter metabolite M11 exceed 0.1 µg parent eq / L the year of application and the subsequent year. Lysimeter metabolite M10 reach concentrations slightly below the trigger (0.08 µg parent eq / L) the year of application; since the substance has only been applied for one season, it may not be excluded that this metabolite also exceeds the trigger of 0.1 µg parent eq / L when tetraconazole is applied in successive seasons. However, no new calculations are possible before fulfilling the data gaps identified for the route of 0.1 µg parent eq / L degradation in soil and the identification of metabolites found in the lysimeter experiments.

4.3. FATE AND BEHAVIOUR IN AIR

On basis of the vapour pressure (1.8 10^{-4} Pa) and the water solubility (196 mg /L) a Henry's Law constant of 3.6 · 10^{-4} Pa m^3 mol^{-1} was calculated. Half life in the troposphere due to photochemical reaction with OH· radicals was calculated to be of 1.16 d.

5. Ecotoxicology

Tetraconazole was discussed at the PRAPeR Expert's Meeting on ecotoxicology (PRAPeR 43) in March-April 2008, on basis of the DAR (May 2005), addendum 1 (November 2007), addendum 2 (March 2008) and addendum 3 (May 2008).

Tetraconazole belongs to the group of triazole fungicides which are suspected to have potential endocrine disrupting properties. The expert meeting on mammalian toxicology agreed that it could not be excluded that tetraconazole may exert endocrine disrupting effects on mammals, even if effects is low compared to other triazoles (see section 2). No information was submitted by the applicant to address this point with regard to potential effects on birds and fish (e.g. a fish full life cycle test or a specific two generation study with birds). The ecotoxicology expert meeting agreed that the applicant should address the concern with regard to endocrine disruption for fish (see section 5.2). The potential endocrine effects on birds were never addressed in the ecotoxicology section of the DAR or during the review process. EFSA, therefore, consider that a data gap remains for the applicant to address the ecotoxicological risk to birds from endocrine effects of tetraconazole.

It was not considered during the peer-review if the current technical specification would cover the batches used in the ecotox studies. EFSA recommends a data gap for the applicant to assess if the current technical specification covers the batches used in the ecotox studies. Nor was it assessed during the peer-review if toluene should be considered as a relevant impurity. EFSA consider that toluene is an ecotoxicological relevant impurity. This would be in agreement with the toxicological assessment (see section 2).

5.1. RISK TO TERRESTRIAL VERTEBRATES

The representative evaluated use of Tetraconazole is as fungicide in sugar beets, wheat, grapes and apples. Tetraconazole can be applied twice to sugar beets with a maximum rate of 100 g a.s./ha at 20 days interval, and once on wheat with an application rate of 125 g a.s./ha. For grapes and apples the application is up to three times at a rate of 30 g a.s./ha with an interval of 10 and 14 days respectively. The risk to birds and mammals was assessed in accordance with the Guidance Document on Risk Assessment for Birds and Mammals (SANCO/4145/2000).

At tier 1 in the DAR the acute TER_a values for birds were above the Annex VI triggers for all uses, indicating a low risk. It was pointed out in the peer-review that the acute toxicity endpoint of > 63 mg/kg bw obtained from the study with mallard duck (*Anas platyrhynchos*) should be preferred in the risk assessment, as no emetic effects were observed at this dose. The RMS provided a revised acute risk assessment in addendum 2 (March, 2008). TER_a values were 7.1 and 11.7 for herbivorous and insectivorous birds respectively for sugar beet uses and 9.3 and 38.8 for insectivorous birds in cereal crops and orchards respectively. It was noted during the expert meeting that the MAF applied in the acute risk assessment for herbivorous birds should be corrected from 1.4 to 1.2 resulting in a TER_a value of 7.9 for the herbivorous bird following use in sugar beets. For uses in sugar beets the expert meeting concluded that the acute risk to insectivorous birds was considered to be low whereas the acute risk to herbivorous birds was high and a data gap remains for the applicant to address the acute risk to herbivorous birds. For the use in orchards the acute risk to insectivorous birds was considered

low, whereas the risk to insectivorous birds in cereals was considered to be high and a data gap remains for the applicant to address this risk.

At tier 1 in the DAR the short-term TER values for birds were above the Annex VI triggers for all uses, indicating a low risk. In addendum 1 (November 2007) the daily dose LD_{50} for Mallard duck was corrected from 128 mg/kg bw/day to of 55.5 mg/kg bw/day due to peer-review comments. The revised daily dietary LD_{50} was based exclusively on the group of Mallard ducks exposed to 325 mg/kg bw, due to food avoidance at higher exposure levels. The recalculated TER_{st} values were still above the Annex VI trigger indicating a low risk for all uses.

The long-term risk assessment was based on the reproductive endpoint of 1.6 mg a.s./kg bw/day. The long-term TER_{lt} was below the Annex VI trigger for all uses (leafy crop TER_{lt}: 0.8 for medium herbivorous bird and 0.5 for insectivorous bird; cereals TER_{lt}: 0.4 for insectivorous birds; orchards TER_{lt}: 1.8 for insectivorous birds) indicating a need for further refinement to the risk assessment. The risk assessment to herbivorous birds in leafy crop was refined by the applicant by applying mean time-weighted-average residues over 21 days from 11 sugar beets residue trials located around Europe. As the measured residue levels were a result of multiple applications, no MAF was considered necessary for the adjustment. The Ftwa value of 0.53 was still applied. The refined TER_{lt} of 3.2 for a medium herbivorous bird was still indicating a high risk to herbivorous birds. PD and PT were hereafter refined for both herbivorous birds and insectivorous birds. PT was set to 0.1 in both cases and PD was stated to be 85% insects and 15% molluscs for insectivorous birds and 88% leaves and 6% seed and insects for herbivorous birds. The PT and PD refinements for insectivorous birds were applied for all uses. The resulting TER_{lt} was 35.5 and 15.8 respectively for herbivorous and insectivorous birds in leafy crop and 4.49 and 19.9 for insectivorous birds in cereals and orchards respectively. RMS concluded in the DAR that the refinements provided by the applicant (e.g. PT and PD) would require further supporting data. Also further information from the field residue trials in sugar beets were requested during the peer-review. A revised long-term risk assessment to birds was provided in addendum 1 (November, 2007), including further information on the residue trials in sugar beets. The first refinements provided by the applicant were based on refined residue levels and residue decline data in sugar beets and small insects. Arithmetic mean $RUD_{twa(20\ d)}$ of 9.9 ppm and 16.3 ppm in sugar beets was calculated from 10 South European field trials (Italy and Greece) and 4 Northern European field trials (France and UK) respectively. Residue decline in pea aphids representing small insects was investigated under standardised laboratory conditions. An insect DT_{50} of 0.61 days was derived and used to calculate a RUD_{twa} for each exposure scenario. TER_{lt} based on refined residue data indicated low risk to insectivorous bird from all used ($TER_{lt\ sugar\ beets}$=11.4; $TER_{lt\ cereals}$=10.0; $TER_{lt\ grapes}$=28.6; $TER_{lt\ apples}$=19.8) and a high risk to herbivorous birds ($TER_{lt\ sugar\ beets\ NE}$=1.1; $TER_{lt\ sugar\ beets\ SE}$=1.7). Further refinement was proposed by the applicant for PD and PT based on literature data. For sugar beet uses a Red-legged partridge (*Alectoris rufa*) was suggested in South Europe and a Wood pigeon (*Columba palumbus*) in North Europe as representative herbivorous birds, while a skylark (*Alauda arvensis*) was suggested as insectivorous bird covering whole Europe. For application to cereals a Corn bunting (*Miliaria calandra*) was suggested in South Europe and a Skylark in North Europe as representative insectivorous birds. For application to grapes a Stonechat (*Saxicola torquata*) was suggested in South Europe and a Blackbird (*Turdus merula*) in North Europe

as representative insectivorous birds. For application to apples a Stonechat was suggested in South Europe and a Blue tit (*Cyanistes caeruleus*) in North Europe as representative insectivorous birds. Specific PT and PD values were provided by the applicant and used for refined TER calculations. Refinements based on residue data for sugar beets and small insects and specific PT and PD values for representative species resulted in TER_{lt} values above the Annex VI trigger indicating a low risk to birds for all uses.

The refined long-term risk assessment to birds was discussed in the ecotox expert meeting. The $RUDs_{twa}$ based on the residue trails in sugar beets presented in addendum 1 (November, 2007) was confirmed in the expert meeting. The use of a MAF factor in the TER calculation for herbivorous birds was considered as not necessary since the refined RUD values was based on residues from multiple applications reflecting the GAP use in sugar beets. The residue study on insects was submitted to refine the risk to insectivorous birds after the DAR was finalised. However, in view of the restrictions concerning the acceptance of new studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new study could not be considered in the peer review. TER calculations needs to be based on refinements excluding residues in insects derived from the above mentioned study. The proposed focal species for sugar beets was accepted by the expert meeting. For use in cereals Skylark was agreed as focal species for North Europe. For South Europe investigations suggest that Corn bunting and Yellow wagtail (*Motacilla flava*) are the most abundant bird species in cereal fields. The growth stage of the cereals during application should be considered in the choice of the focal species. Yellow wagtail would be a focal species during early growth stages but not at the late growth stages when tetraconazole is applied. The Blue tit was agreed as focal species for orchards but further information was considered necessary to support the choice of the other focal species in apples and grapes (Blackbird and Stonechat). It was further more noted in the expert meeting that the derivation of RUD values for seeds, fruits, earthworms was not transparent, the suggested PT/PD refinements were not supported by data and the PD values presented in addendum 1 (November, 2007) did not sum up to 100%. The meeting agreed on a data gap for the applicant to provide a new long-term risk assessment for birds for all uses, taking into account the recommendations from the expert meeting.

The TER-values provided in the DAR indicated a low risk to earthworm- and fish-eating birds. The risk assessment to earthworm-eating birds was revised in addendum 2 (March, 2008) to be based on plateau PEC_{soil} values. The ecotox expert meeting did not agree with the calculation and a new calculation was provided after the expert meeting in addendum 3 (May, 2008). The new TER_{lt} of 2.12 indicated a high risk to earthworm-eating birds. EFSA recalculated a plateau PEC_{soil} of 0.204 mg as/kg soil when drafting the conclusion. Consequently, a TER value of 4.42 was recalculated for earthworm-eating birds by EFSA. A data gap remains for the applicant to address the risk to earthworm-eating birds.

A risk assessment for uptake of contaminated drinking water was provided in the DAR and addendum 1 (November, 2007). TER_a and TER_{lt} calculations were provided for insectivorous birds, medium herbivorous birds and large herbivorous birds based on both maximum FOCUSsw PEC

values and concentration in puddles of spray liquid or reservoirs held in the axils of leaves. All the scenarios exceed the Annex VI trigger and the risk from drinking water exposure was considered to be low. EFSA notes that it has been agreed in previous expert meeting that until further guidance was available for the assessment of risk from uptake of contaminated drinking water, only an acute risk assessment for small birds and mammals exposed to puddles of spray liquid or reservoirs held in the axils of leaves needs to be considered.

Only the long-term risk assessment to mammals was provided in the DAR, as the acute toxicity endpoint for mammals was not considered valid by RMS. An acute toxicity endpoint for mammals from a new study was provided by RMS in addendum 1 (November, 2007), including an acute risk assessment for mammals and a risk assessment for the consumption of contaminated water. The risk assessments were not discussed in the ecotox expert meeting as it was agreed that no new studies could be taken in to account at this stage of the peer-review according to Commission regulation 1095/2007. However, the mammalian toxicity experts did subsequently agree in their expert meeting that it was possible to derive a valid LD_{50} of 1031 mg/kg bw from the original dossier study on acute toxicity to rats. In response, EFSA calculated TER vales for the acute risk to mammals based on the agreed acute toxicity endpoint and following the guidance document for birds and mammals. TER values were above the Annex VI trigger indicating a low acute risk to mammals from all uses. Additionally EFSA calculated TER values for the risk from consumption of contaminated drinking water. TER values were above the Annex VI trigger, indicating a low risk to mammals from consumption of contaminated drinking water for all relevant uses[12].

The long-term risk to mammals was assessed for medium herbivorous mammals (hare) for sugar beet uses, for insectivorous mammals (shrew) for cereal uses and for small herbivorous mammals (vole) for uses in orchards (grapes and apples). The TER_{lt} for uses in sugar beets and cereals was above the Annex VI trigger, indicating a low risk. For uses in orchards the risk to small herbivorous mammals feeding on short grass was considered high (TER_{lt}=2.7). The risk assessment was refined based on residue level and decline data and from residue trials in young wheat plants, providing an experimental RUD of 36.5 and a DT_{50} in plants of 5.25 days. The refined risk assessment gave a TER_{lt} of 5.3.

The toxicological endpoint for the long-term mammal risk assessment was discussed in the ecotox expert meeting. The NOEL is 4.9 mg/kg bw/d (70 ppm) used in the DAR was an average value of effect concentrations for males and females. It was noted that at 4.9 mg/kg bw/d (70 ppm) effects on duration of pregnancy, organ weights and litter loss were observed. The experts agreed that the endpoint of 4.9 mg/kg bw/d should be used in the risk assessment provided that the effects on litter loss and prolongation of the gestation period are considered as not being of relevance by the experts on toxicology in derivation of the long-term endpoint for reproductive effects. It was noted in the

[12] MS had no remarks during the written commenting of this conclusion report, regarding the acute risk assessment to mammals, which was provided by EFSA after the peer-review. The acute risk to mammals including risk from consumption of contaminated drinking water has been addressed. Therefore, the data requirement originally identified by RMS in the DAR for an acute toxicity study and a risk assessment has been considered obsolete.

ecotox expert meeting that the first tier TER calculations in orchards was incorrect. A TER_{lt} of 2.6 was calculated in the meeting using of moving time window of 21 days. The refined risk assessment in the DAR for small herbivorous mammals in orchards was not accepted by the expert meeting. The refinement based on measured residues in wheat leading to a RUD of 36.5 (without interception) was rejected to replace the default values (including the DT50 values) since it is based on only one trial and a high variation in measured residues were observed in the sugar beet trials. The expert meeting calculated refined TER values using the default RUD, using 21d moving time window, twa factor of 0.99 for orchards and 1.16 for grapes and an interception factor for the respective growth stage as refinement steps. The refined risk assessment indicated a further need for refinement for grape uses. The meeting agreed on a data gap for a refined risk assessment to herbivorous mammals for uses in grapes. However, a final conclusion was pending on the outcome of the mammalian toxicology expert meeting regarding the endpoint to be used.
The toxicological endpoint for long-term mammals risk assessment was discussed at the mammalian toxicology expert meeting. A NOAEL of 70 ppm was agreed, resulting in a recalculated daily dose of 3.6 mg/kg bw/day based on male F0. The long-term risk assessment was updated accordingly by the RMS in addendum 3 (May, 2008), indicating a low risk to insectivorous mammals from the use in cereals (TER_{lt}=8.96) and a high risk to herbivorous mammals from uses in sugar beets (TER_{lt}=4.85), grapes (TER_{lt}=2.02) and apples (TER_{lt}=2.36). The risk assessment was confirmed by EFSA. A data gap remains for the applicant to address the long-term risk to mammals for uses in sugar beets, grapes and apples.

A long-term risk assessment from consumption of contaminated water was provided in the DAR for three different types of mammals (vole, hare and shrew). This assessment was not considered relevant as noted in the section above for risk assessment to birds from contaminated drinking water.

The risk to earthworm- and fish-eating mammals was assessed as low in the DAR. The risk to earthworm-eating mammals was revised in addendum 2 (March, 2008) to be based on plateau PEC_{soil} values. The ecotox expert meeting did not agree with the calculation and a new calculation was provided after the expert meeting in addendum 3 (May, 2008). The new TER_{lt} of 3.75 indicated a high risk to earthworm-eating mammals. However, EFSA recalculated a plateau PEC_{soil} of 0.204 mg as/kg soil when drafting the conclusion. Consequently, a TER value of 7.82 was recalculated for earthworm-eating mammals by EFSA. In conclusion the risk to earthworm- and fish-eating mammals was assessed to be low.

The risk to birds and mammals from metabolites was not assessed, as no major metabolites were found in the plant metabolism studies (see addendum 2, March 2002).

5.2. RISK TO AQUATIC ORGANISMS

Based on the available acute toxicity data, tetraconazole is proposed to be classified as very toxic to aquatic organisms. The lowest end point value for technical Tetraconazole was obtained for algae, with an EC_{50} of 0.27 mg a.s./L based on increase in biomass. Formulation studies were conducted

with the lead formulation Eminent 40 ME. The results did not indicate that the formulation would be more acutely toxic than expected from the content of tetraconazole. Acute and chronic TER values were fare above the Annex VI trigger for all organisms included in the aquatic risk assessment, based on FOCUSsw Step 2 south European calculation for the worst case sugar beet application. The risk to aquatic organisms from the intended uses of tetraconazole was considered to low by the RMS.
The risk to aquatic organisms was discussed in the ecotox expert meeting. Since the toxicity of tetraconazole was not increased of more than a factor of two in the formulation it was considered not necessary to conduct long-term studies with the formulation The need for an acute toxicity study with the formulation on *Americamysis bahia* was also discussed in the expert meeting, since *A. bahia* was about 8 times more sensitive than daphnia to the pure active substance. As there was no indication of increased toxicity of the formulation, the meeting did not see the need for such a study. Furthermore, was a long-term study with *A. bahia* not deemed necessary, as the experts was of the opinion that the uncertainty factor of 10 covers the uncertainty related to potential effects on aquatic invertebrates which are more sensitive than daphnids. The need for a fish full lifecycle test (FFLC) was discussed to investigate potential endocrine effects to fish. The experts in the meeting agreed on a data gap for the applicant to address the potential endocrine disrupting effects on fish, e.g. by a FFLC test.
Effects on sediment dwellers were examined in a water spiked study with *Chironimus riparus.* Based on water concentrations the TER value of 1578 was fare above the Annex VI trigger. After the peer-review EFSA recalculated a TER for *C. riparus* based on sediment concentrations given the multiple use, persistency and hydrophobic characteristics of tetraconazole. This sediment based TER value of 763 was lower, but still clearly above the trigger level. The risk to sediment dwellers was considered to be low.

The bioconcentration factor was determined to be 35.7 for whole fish with a clearance half-life of 0.189 days. The reliability of the study was discussed in the ecotox expert meeting. It was concluded that the study was robust enough to be included in the risk assessment. Hence the potential for bioaccumulation was considered as low.

Three metabolites M14360acid, M14360alcohol and triazolyl acetic acid (TAA) were included in the aquatic risk assessment of the DAR and revised in addendum 1 (November, 2007) with updated $FOCUS_{sw}$ Step 1 calculations. The assessment indicating a low risk to aquatic organisms. EFSA notes that the endpoints used for TAA in the DAR were in agreement with the endpoints agreed for this metabolite at PRAPeR 13[13]. No final conclusion can be derived for metabolites, as the fate of tetraconazole is not fully concluded (see section 4.12). A data gap remains to provide an aquatic risk assessment for potential metabolites (pending fate conclusion), in accordance with the ecotoxicological endpoints agreed at PRAPeR 13.

[13] PRAPeR 13 (16 – 18 January 2007) agreed on the endpoints to be used for the common metabolites of the triazoles.

5.3. RISK TO BEES

Oral and contact toxicity of technical tetraconazole and the formulation EMINENT 40 ME to bees is low. The hazard quotients are well below the Annex VI trigger indicating a low risk to bees.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Glass plate studies with the two indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri* were conducted with lead formulation Eminent 40 ME in a dose response related design. For *T. pyri* mortality was combined with high escape rates of 10% to 53% at different dose rates and the study was considered insufficient to address the risk. No effects of Eminent 40 ME were observed with *Crysoperla carnea and Poecilus cupreus* using the same dose. In-field and off-field HQ indicating at low risk to *A. rhopalosiphi* were provided in addendum 2 (March, 2008) covering all intended uses.

Corrected mortality of 30% was observed in an extended laboratory study with *A. rhopalosiphi* exposed up to 250 g a.s./ha. Reproduction was also affected at 125 and 250 g a.s./ha (51.6% and 70.8% respectively). Further testing in extended laboratory with aged residues was provided. Mortality was not affected even after exposure to freshly dried residues at any dose. The reduction of parasitation efficiency decreased from 0 days ageing (34.1% at 125 and 49.0% at 250 g a.i./ha) to 7 days (13.7% at 125 and 26.3% at 250 g a.i./ha) and 14 days ageing (14.7% at 125 and –4.6% at 250 g a.i./ha). Effects at the rate of 250 g a.s./ha (covering the intended use) did not exceed the 50% trigger for *A. rhopalosiphi* and no further testing was considered necessary.

Effects of tetraconazole 40 g/L ME and tetraconazole 100 g/L emulsifiable concentrate (Domark 10EC) indicated a low risk when applied up to 4 times at the application rate of 40 g a.s./ha in a field studies with *T. pyri.* In the field study carried out with tetraconazole 100 g/L EC formulation at 125 g a.s./ha x 2 applications and corrected according to Barrett *et al*. into 312.5 g a.s./ha x 2 applications (conversion from grape *vs* wheat), complete recovery of the mite population was observed 8 weeks after the second application while it resulted no different from the control to *T. pyri* at a 5% spray drift rate of 15.6 g a.s./ha.

RMS did not require further lab studies given the field studies available with *T. pyri.* However, it was noted in the ecotox expert meeting that an extended lab study with *T. pyri* was available. The meeting agreed to require an extended lab study (with fresh residues) with *T. pyri* to conduct an off-field risk assessment in order to see if the off-field risk to mites/spiders will be addressed also for species with longer reproductive cycles than *T. pyri* (i.e. species with lower capacity to re-colonise the in-field area).

5.5. RISK TO EARTHWORMS

Data on acute and reproductive toxicity of tetraconazole was provided both for the technical substance and the lead formulation. The TER-calculations presented in the DAR were above the Annex VI trigger for both acute and long-term effects. The risk assessment was revised in addendum 3 (May 2008) to include revised plateau PEC_{soil} values of 0.4263 mg a.s./kg soil calculated by RMS after the fate expert meeting. However, EFSA recalculated a plateau PEC_{soil} of 0.204 mg as/kg soil

when drafting the conclusion. Recalculated TER values of 93.7 and 16.5 still indicated a low risk for acute and long-term effects respectively based on updated PEC_{soil}.

Three metabolites M14360acid, M14360alcohol and triazolyl acetic acid (TAA) were included in the risk assessment for earthworms in the DAR and updated with new PEC_{soil} values in addendum 1 (November, 2007). The assessment indicated a low risk to earthworms from these metabolites. EFSA notes that the endpoints used for TAA in the DAR were in agreement with the conclusion for triazole metabolites decided at PRAPeR 13[14]. No final conclusion can be derived for metabolites, as the fate of tetraconazole is not fully concluded (see section 4.1.2). A data gap remains to provide a risk assessment to earthworms for potential metabolites (pending fate conclusion), in accordance with the ecotoxicological endpoints agreed at PRAPeR 13.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

The formulation Eminent 125 EW had no significant effect on organic matter decomposition over a six months period in a litter bag test at an application rate of 246 g a.s./ha (1st appl.) and 125 g a.s./ha (2nd appl.). The application rate was worst case compared to the intended uses. The risk to decomposition of organic matter was considered to be low.

Reproductive effects of the soil metabolites M14360-acid, M14360-alcohol and TAA were tested on collembola (*Folsomia candida*). A risk assessment was presented in the DAR. However, as the fate of tetraconazole was not fully concluded, no final conclusion can be derived for metabolites (see section 4.1.2). A data gap remains to provide a risk assessment to collembola for potential metabolites (pending on fate conclusion), in accordance with the ecotoxicological endpoints agreed at PRAPeR 13.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

Technical tetraconazole had no effects >25% after 28 days on soil respiration or nitrogen transformation at an application rate of 502 g a.s./ha when compared to the control. The exposure was equivalent to 0.67 mg as/kg soil (calculated by EFSA), which covers the expected plateau PECsoil (also calculated by EFSA). Nor did the metabolites M14360-acid or TAA have any effects >25% after 28 days on soil respiration or nitrogen transformation at application rates of up to 0.23 mg M14360-acid/kg soil and 0.08 mg TAA/kg soil respectively. However, as the fate of tetrazonazole was not fully concluded, no final conclusion can be derived for metabolites (see section 4.1.2). A data gap remains to provide a risk assessment to non-target soil micro-organisms from potential metabolites (pending on fate conclusion), in accordance with the ecotoxicological endpoints agreed at PRAPeR 13.The risk to soil non-target micro-organism from tetraconazole was considered to be low.

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

A study on the effects of Eminent 125 EW on seedling emergence and vegetative vigour of 10 crop species is available. There were no effects in these studies at 112 g a.s./ha. The risk assessment to

[14] PRAPeR 13 (16 – 18 January 2007) agreed on the endpoints to be used for the common metabolites of the triazoles.

non-target plants was revised in addendum 2 (March 2008) based on an NOEC of 112 g a.s./ha. TER-values were above the Annex VI trigger for all intended uses. The risk to non-target plants was considered to be low for all intended uses.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Data from an available test with technical tetraconazole gave an EC_{50} of >1000 mg a.s./L for inhibition of respiration rate of activated sludge micro-organisms. The risk to sewage treatment plants was considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: tetraconazole and potential metabolites (data gaps on aerobic and anaerobic degradation in soil need to be fulfilled before residue definition may be finalized).
Definitions for monitoring: not concluded

Water

Ground water

Definitions for exposure assessment: tetraconazole and potential metabolites (data gaps on aerobic and anaerobic degradation in soil and nature of lysimeter metabolites need to be fulfilled before residue definition may be finalized)
Definitions for monitoring: not concluded

Surface water

Definitions for risk assessment: tetraconazole and potential metabolites that move form soil to surface water (data gaps on aerobic and anaerobic degradation in soil need to be fulfilled before residue definition may be finalized).
Definitions for monitoring: not concluded

Air

Definitions for risk assessment: tetraconazole
Definitions for monitoring: tetraconazole

Food of plant origin

Definitions for risk assessment: 1) tetraconazole; 2) Triazole alanine and Triazole acetic acid (provisional awaiting information on triazolyl hydroxyl propionic acid)
Definitions for monitoring: tetraconazole (provisional pending the outcome of the risk assessment on the triazole derivative compounds)

Food of animal origin

Definitions for risk assessment: tetraconazole and 1,2,4-triazole

Definitions for monitoring: tetraconazole (provisional pending the outcome of the risk assessment on the triazole derivative compounds)

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
tetraconazole	Very high persistent (degradation observed under dark aerobic conditions was considered negligible)	The risk to earthworms, soil micro-organisms and organic matter breakdown was assessed as low for tetraconazole.
potential metabolites (data gaps on aerobic and anaerobic degradation in soil need to be fulfilled before residue definition may be finalized)	Potential metabolite M14360-acid is medium to high persistent (DT_{50} = 92.5 – 221.4 d). Potential metabolite M14360-alcohol is very low persistent (DT_{50} = 0.2 – 0.45 d). Potential metabolite TAA is low to moderately persistent (DT_{50} = 8.4 – 18.7 d). Further route degradation studies and information on the identity of lysimeter metabolites has been identified as data gap.	The risk from potential soil metabolites needs to be addressed.

Ground water

Compound (name and/or code)	**Mobility in soil**	**> 0.1 µg / L 1m depth for the representative uses** **(at least one FOCUS scenario or relevant lysimeter)**	**Pesticidal activity**	**Toxicological relevance**	**Ecotoxicological relevance**
tetraconazole	low mobile in acidic soils (Koc = 531 – 1922 mL / g)	Trigger not exceeded for any of the uses and scenarios modelled.	Yes	Yes	Yes
potential metabolites (data gaps on aerobic and anaerobic degradation in soil and nature of lysimeter metabolites need to be fulfilled before residue definition may be finalized)	No data available for lysimeter metabolites M10 and M11. Assessment not completed pending on data gaps identified.	Lysimeter metabolite M11 exceeds the trigger of 0.1 µg / L on the season of application and the next one. Lysimeter metabolite M10 has the potential to exceed the trigger of 0.1 µg / L if tetraconazole was applied in successive seasons. Assessment not completed pending on data gaps identified.	Needs to be addressed	Needs to be addressed	Needs to be addressed

Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
tetraconazole (water and sediment)	Tetraconazole is very toxic to aquatic organisms. The risk from tetraconazole is considered to be low for aquatic organisms.
potential metabolites that move from soil to surface water (data gaps on aerobic and anaerobic degradation in soil need to be fulfilled before residue definition may be finalized) (only water).	The risk from potential soil metabolites needs to be addressed.

Air

Compound (name and/or code)	**Toxicology**
Tetraconazole	Tetraconazole is of low acute inhalation toxicity (LC_{50} > 3.66 mg/L)

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

- A revised technical specification (relevant for all representative uses evaluated, data gap identified by PRAPeR 41 meeting (April 2008), date of submission unknown; refer to chapter 1)
- Confirmation of the identity of one impurity in the technical material (relevant for all representative uses evaluated, data gap identified in the PRAPeR 41 meeting (April 2008), date of submission unknown; refer to chapter 1)
- Independent laboratory validation for the primary monitoring methods of tetraconazole residues in food/feed of plant and animal origin (relevant for all representative uses evaluated, data gap identified in the PRAPeR 41 meeting (April 2008), study for plants provided to the RMS, not evaluated and not peer reviewed; date of submission unknown for the method for food of animal origin; refer to chapter 1)
- Confirmatory methods for the determination of tetraconazole residues in food/feed of plant and animal origin and water(relevant for all representative uses evaluated, data gap identified in the PRAPeR 41 meeting (April 2008), date of submission unknown; refer to chapter 1)
- Analytical method for the determination of residues in air (relevant for all representative uses evaluated, data gap identified in the PRAPeR 41 meeting (April 2008), date of submission unknown; refer to chapter 1)
- Data to address the toxicological potential of triazolyl hydroxyl propionic acid (relevant for the use in sugar beets and in addition for uses with succeeding crops (wheat); data gap identified in the PRAPeR 45 meeting (April 2008), no submission date proposed by the notifier; refer to chapter 3)
- A complete set of residue trials supporting the notified representative uses in grapes and in apples (relevant for the use in grapes and apples; data already submitted and evaluated in the addendum of November 2007 but not peer reviewed in view of the restrictions concerning the acceptance of new studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007; refer to chapter 3)
- A new rotational crop field study (relevant for the uses having following crops i.e. sugar beet and wheat; data gap identified in the PRAPeR 45 meeting (April 2008), no submission date proposed by the notifier; refer to chapter 3)
- The applicant should address the fate of tetraconazole isomers in plants and livestock with respect to the consumer risk assessment (relevant for all notified uses; data gap identified in the PRAPeR 45 meeting (April 2008), no submission date proposed by the notifier; refer to chapter 3)
- A general data gap is set with respect to the risk assessment for triazole derivative metabolites in primary crops, rotational crops, livestock commodities and possibly processed commodities (relevant for all notified uses; data gap identified in the PRAPeR 45 meeting (April 2008), no submission date proposed by the notifier; refer to chapter 3)

- A data gap for additional experiments to investigate the mechanism of tetraconazole degradation in soil, such that it is possible to identify under what conditions degradation will occur and when might not. The experiments need to address the potential formation of metabolites that may result from either of the rings. Potential enantioselective degradation should be considered when addressing this data gap. (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to point 4.1)
- A data gap has been identified for the characterization of tetraconazole lysimeter metabolites M10 and M11 to address its potential for ground water contamination (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to points 4.1.3 and 4.2.2).
- A data gap has been identified for tetraconazole route and rate of degradation in soil under anaerobic conditions. Potential enantioselective degradation should be considered when addressing this data gap. (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to points 4.1).
- A data gap has been identified to address potential water contamination by soil and lysimeter leachate metabolites (relevant for all representative uses evaluated; no submission date proposed by the notifier (the data gap may only be fulfilled once the data gaps on the route of degradation and the identity of the lysimeter metabolites are fulfilled); refer to points 4.2.2).
- A data gap to address the potential accumulation of tetraconazole in the sediment with appropriate PEC_{SED} accumulation calculations has been identified (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to points 4.2).
- It should be addressed whether the current active substance technical specification adequately covers those batches used in the ecotoxicological studies. (Relevant for all representative uses evaluated; data gap identified by EFSA after the peer-review; no submission date proposed by the applicant; refer to point 5)
- A data gap for a refined acute risk assessment for insectivorous birds has been identified. (Relevant for uses in cereals; data gap identified in the meeting expert (PRAPeR 43 in March-April 2008); no submission date proposed by the applicant; refer to point 5.1)
- A data gap for a refined acute risk assessment for herbivorous birds has been identified. (Relevant for uses in sugar beet; data gap identified in the meeting expert (PRAPeR 43 in March-April 2008); no submission date proposed by the applicant; refer to point 5.1)
- A data gap for a refined long-term risk assessment for birds has been identified. (Relevant for all representative uses evaluated; data gap identified in the meeting expert (PRAPeR 43 in March-April 2008); no submission date proposed by the applicant; refer to point 5.1)
- The risk to earthworm-eating birds needs to be addressed. (Relevant for all representative uses evaluated; data gap identified by RMS after the meeting expert (PRAPeR 43 in March-April 2008) and confirmed by EFSA; no submission date proposed by the applicant; refer to point 5.1)
- The long-term risk to herbivorous mammals needs to be addressed. (Relevant for uses in sugar beets, grapes and apples; data gap identified in the expert meeting (PRAPeR 43 in March-April 2008); no submission date proposed by the applicant; refer to point 5.1)

- The potential ecotoxicological risk of endocrine disrupting effects needs to be addressed for mammals and birds. (Relevant for all representative uses evaluated; data gap identified by EFSA after the peer-review; no submission date proposed by the applicant; refer to point 5.1)
- The risk to aquatic organisms from potential metabolites should be addressed (Relevant for all representative uses evaluated; data gap follows the fate expert meeting; no submission date proposed by the applicant; refer to point 5.2)
- The potential ecotoxicological risk of endocrine disrupting effects needs to be addressed for fish. (Relevant for all representative uses evaluated; data gap identified in the meeting expert (PRAPeR 43 in March-April 2008); no submission date proposed by the applicant; refer to point 5.2)
- The off-field risk assessment for species with longer reproductive cycles than *T. pyri* needs to be addressed by an extended lab study with *T. pyri.* (Relevant for all representative uses evaluated; data gap identified in the meeting expert (PRAPeR 43 in March-April 2008); no submission date proposed by the applicant; refer to point 5.4)
- The risk to earthworms from potential metabolites needs to be addressed (Relevant for all representative uses evaluated; data gap follows the fate expert meeting; no submission date proposed by the applicant; refer to point 5.5)
- The risk to non-target soil micro- and macro-organisms from potential metabolites needs to be addressed (Relevant for all representative uses evaluated; data gap follows the fate expert meeting; no submission date proposed by the applicant; refer to point 5.6 and 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 applicant on wheat, sugar beet, grapes and apple against several agriculturally important phytopathogens. For full details of the GAP please refer to the attached end points.

The representative formulated product for the evaluation was “Eminent 40 ME”, a micro-emulsion (ME) containing 40 g/L tetraconazole.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.

Tetraconazole residues in plants and food of animal origin can be determined with a multi-method (DFG S19, extended revision,) however no ILV is available and confirmatory methods are also missing.

Adequate analytical methods are available to monitor tetraconazole residues in soil and water, however confirmatory method for water is still needed. There is no acceptable monitoring method for air.

Tetraconazole is absorbed rapidly to an extent of about 80% when given orally to rats. It is widely distributed and has no potential for accumulation. Excretion is rapid and complete. It is extensively metabolised. Tetraconazole is of moderate acute toxicity by the oral and of low toxicity by the dermal and inhalation route. It is neither a skin nor an eye irritant and has no skin sensitising properties. Based on the data on acute toxicity a classification as **Xn; R22 "Harmful; Harmful if swallowed"** is proposed. In short-term dietary studies the liver and kidneys were the target organs of toxicity. The lowest short-term NOAEL of 2.95 mg/kg bw/d was derived from a 1-year dog study. Tetraconazole is not genotoxic. From a 24-month chronic study with rats a NOAEL of 0.4 mg/kg bw/d was derived based on liver effects, at higher doses fluorosis was observed. The thyroid tumours seen were considered not relevant for humans. Similarly the liver was the target of toxicity in an 18-month mouse study (NOAEL 1.5 mg/kg bw/d) and also the tumours occurring in the liver there were considered not relevant for humans. In a two-generation study in addition to the general toxicity seen in parental animals and offspring, in the dams dystocia and prolonged gestation periods were observed (overall NOAEL 3.6 mg/kg bw/d) leading to a proposal for classification as **Xn; Repr. Cat. 3 R62 "Harmful; Possible risk of impaired fertility".** While in a rabbit developmental study no foetal effects could be seen in the rat extra ribs, hydrourether and hydronephrosis were seen based on which a classification as **Xn; Repr. Cat. 3 R63 "Harmful; Possible risk of harm to the unborn child".** The acceptable daily intake (ADI) of 0.004 mg/kg bw/d was derived from the 24-month rat study applying a safety factor of 100. The acceptable operator exposure level (AOEL) of 0.03 mg/kg bw/d was derived from the 1-year dog study applying a safety factor of 100. The acute reference dose (ARfD) of 0.05 mg/kg bw was derived from the maternal NOAEL in the rat developmental study applying a safety factor of 100. Using the UK POEM the operator exposure estimates for the preparation EMINENT ME 40 in % of the systemic AOEL for tractor mounted/trailed boom sprayer (field crop application), for tractor mounted/air-assisted sprayer (vineyard application) and for hand held sprayer (orchard application) are 305.13%, 43% and 50.78% respectively when no personal protective equipment (PPE) is used. When PPE is used exposures amount to 48.17%, 29.90% and 17.43% respectively. Applying the German model the corresponding values are 51.26%, 27.7% and 15.49% (without PPE) and 39.56%, 4.21% and 2.37% (with PPE). Estimated maximum exposure using worst case scenario amount to 5.5% for bystanders and to 28 % for re-entry workers of the systemic AOEL.

The metabolism of tetraconazole in plants was investigated upon foliar application to wheat, sugar beet and grapes and in carrots, lettuce and wheat planted as succeeding crops.
Based on the studies a residue definition including tetraconazole and the triazole derivative metabolites (triazole alanine, triazole acetic acid) has been provisionally established. A final plant residue definition for risk assessment is pending the clarification on the toxicological properties of metabolite triazole hydroxypropionic acid. This metabolite had not been identified in metabolism studies with other triazole pesticide compounds assessed in the peer review.
The nature of the residue is not altered by processing. From processing studies transfer factors to juice, wine and dry apple pomace could be derived.

A sufficient number of supervised residue trials are only available to cover the representative uses in wheat and sugar beets in all Europe and hence MRLs can be proposed for these crops. The representative uses in grapes and apples were initially not supported by residue trials matching the notified GAP criteria. Trials submitted during the peer review process could not be considered in view of the restrictions concerning the acceptance of new studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007.

Uptake of soil residues by rotational crops is not expected to lead to residues of tetraconazole per se above the LOQ. In contrast, a significant uptake of triazole derivative metabolites is expected, but the available field studies were not considered sufficient to address residues in following crops. Hence a data gap for a new field rotational crop study has been set.

Feed commodities may represent a significant source of exposure to tetraconazole residues for animals. Metabolism studies in lactating goats and laying hens are available, and based on the metabolic pattern in animal tissues a residue definition was proposed. However, due to data gaps the livestock dietary intake estimates cannot be finalised and thus appropriate MRLs for animal products can currently not be proposed.

The consumer risk assessment for the notified representative uses can currently not be finalised. Excluding the uses on apples and grapes and only considering residues of tetraconazole alone, the RMS has submitted a provisional and none-peer reviewed chronic and acute consumer risk assessment indicating consumer exposure being below the toxicological reference values for tetraconazole. A robust conclusion on the consumer risk will only be possible when the identified data gaps are addressed and sufficient data and information regarding the assessment of triazole derivative metabolites in primary crops, rotational crops, and products of animal origin is available.

Degradation of tetraconazole in soil under dark aerobic laboratory conditions was negligible. Photolysis of tetraconazole in soil was negligible.

Degradation of tetraconazole was also investigated in three soils under aerobic outdoor conditions, exposed to sunlight. The applicant attributed degradation to a combined effect of photochemical and microbial degradation. RMS considered the reliability of the study doubtful since no clear mechanism may explain degradation. The experts considered that further experiments investigating effect of higher temperatures in dark under controlled moisture conditions and indirect aqueous photochemical studies could help to understand the mechanism of degradation prevailing in the environment. Therefore, a data gap was identified for these additional studies.

Dissipation of tetraconazole under field conditions was investigated in five sites (4 in Germany and 1 Northern Italy). In the five soils dissipation followed biphasic behaviour. Tetraconazole was high to very high persistent during the second phase. The meeting of experts agreed that the field half lives cannot be used in FOCUS modelling with the current lack of understanding of the mechanism causing loss. For PEC soil the meeting of experts agreed that the longest second phase field DT_{50} of 1688 d should be used. Potential accumulation of tetraconazole may not be excluded since about 20 – 40 % AR remains as tetraconazole one year after application. Assuming yearly application and tillage, EFSA calculated a plateau background concentration over the 20 cm horizon after 36 years and peak concentration after last application. Tetraconazole is low mobile in acidic soils. Adsorption /

desorption of potential metabolites M 14360-acid and TAA were investigated in different studies. Metabolite M 14360-acid may be considered high to very high mobile in soil and TAA very high mobile in soil. Potential metabolite M 14360-alcohol may be considered very high mobile in soil.

A two years lysimeter study with two soil monoliths was performed in Switzerland. Product containing labelled tetraconazole was applied the first year. No product was applied the second year. Residue leachate concentrations observed were 0.53 – 0.54 µg / L and 0.27 µg / L parent equivalents for the first and second year respectively. The two major fractions were M11 (47 % - 66 % of radioactivity in the leachate; corresponding to 0.11 – 0.18 µg/L) and M10 (15 – 21 % of the radioactivity in the leachate; corresponding to 0.03 – 0.08 µg/L). A data gap was identified for the characterization of tetraconazole lysimeter metabolites M10 and M11 and to address its potential for ground water contamination.

Tetraconazole is stable to hydrolysis and is not expected to be degraded by photolysis in water. Tetraconazole is not readily biodegradable.

A dissipation study of tetraconzole in two water/sediment systems under dark aerobic conditions at 20 ºC is available. Degradation only occurs in the sediment by formation of non extractable residue. Virtually no degradation product was observed. Mineralization was negligible over the duration of the study (100 d). Tetraconazole was very high persistent in both systems ($DT_{50\ whole\ system}$ = 310 – 372 d).

New PEC SW values calculated according FOCUS SW and FOCUS kinetics were presented in the Addendum 1 to the DAR. These PEC_{SW} are based on FOCUS SW Step 2 and were agreed by the meeting of experts. However, some MSs may require Step 3 calculations. With respect to PEC_{SED} a data gap to address the potential accumulation of tetraconazole in the sediment was identified.

FOCUS GW calculations presented for the parent compound in Addendum 2 were agreed by the meeting of experts. None of the uses and scenarios simulated resulted in 80th percentile annual average leachate concentration above the trigger of 0.1 µg / L. For the metabolites the meeting of experts did not agree on the calculations presented. Lysimeter metabolite M11 exceed 0.1 µg parent eq / L the year of application and the subsequent year. Lysimeter metabolite M10 reach concentrations slightly below the trigger (0.08 µg parent eq / L) the year of application; since the substance has been applied only one season, it may not be excluded that this metabolite also exceeds the trigger of 0.1 µg parent eq / L when tetraconazole is applied in successive seasons.

On basis of the vapour pressure (1.8 10^{-4} Pa) and the water solubility (196 mg /L) a Henry's Law constant of 3.6 · 10^{-4} Pa m^3 mol^{-1} was calculated. Half life in the troposphere due to photochemical reaction with OH· radicals was calculated to be of 1.16 d.

The acute risk assessment to insectivorous birds in orchards and sugar beets indicated a low risk, where as the acute risk to insectivorous birds in cereals and herbivorous birds in sugar beets was assessed to be high and calls for further refinements. The short-term risk to birds from all intended uses was considered to be low, whereas the long-term risk to birds from all intended uses was found to be high. A refined long-term risk assessment for birds for all intended uses was required, taking into account the recommendations from the expert meeting. Only the long-term risk assessment to mammals was provided in the DAR, as the acute toxicity endpoint for mammals provided in the dossier was found not to be valid by RMS. However, the mammalian toxicity experts agreed that the

acute study was valid, and EFSA subsequently calculated acute TER values for mammals. The risk was found to be low for all uses. The long-term risk assessment to mammals indicated a low risk to insectivorous mammals from use in cereals and a high risk to herbivorous mammals from uses in sugar beets, grapes and apples. Refinements were required to address the long-term risk to herbivorous mammals for uses in sugar beets, grapes and apples. The risk assessment for secondary poisoning indicated a low risk to fish-eating birds and mammals and earthworm-eating mammals. The risk to earthworm-eating birds was found to be high and further refinements were required. The risk from uptake of contaminated drinking water was considered to be low for birds and mammals. A data gap to address the risk for potential endocrine effects on birds was identified.

Tetraconazole is considered very toxic to aquatic organisms on basis of the available data. However, acute and chronic TER values were far above the Annex VI trigger for all organisms included in the aquatic risk assessment, based on FOCUSsw Step 2 South European calculation for the worst case sugar beet application. A data gap was identified for the applicant to address the potential risk of endocrine disrupting effects in fish.

Standard glass plate tests were provided for *Aphidius rhopalosiphi, Typhlodromus pyri, Crysoperla carnea and Poecilus cupreus.* No effects were found in the two latter species. The study with *T. pyri* was considered insufficient to address the risk due to high escape rates during the study. Even though in-field and off-field HQ indicated at low risk to *A. rhopalosiphi*, reproductive effects above 50% were derived in extended laboratory study with *A. rhopaloxiphi* at exposure rates comparable to in-field uses. Aged residue studies, however, indicated that the effects on mortality and reproduction never exceeded 50% even at day 0 of ageing. Field studies covering all intended uses indicated a low risk to *T. pyri*. The expert meeting agreed to require an extended lab study (with fresh residues) with *T. pyri* to conduct an off-field risk assessment in order to see if the off-field risk to mites/spiders will be addressed also for species with longer reproductive cycles than *T. pyri* (i.e. species with lower capacity to re-colonise the in-field area).

The formulation Eminent 125 EW had no significant effect on organic matter decomposition over a six months period in a litter bag test with worst a case application rate

The risk from tetraconazole to bees, earthworms, soil non-target micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

As uncertainties remains for potential soil metabolites, no final conclusion can be drawn for the risk from metabolites to aquatic organisms, earthworms, soil non-target micro- and macro organisms.

Critical areas of concern

- The consumer risk assessment for the notified representative uses is not finalised.
- There is no identified route for breakdown in soil

- Residue definition remains open for terrestrial and aquatic environmental compartments
- The assessment of leaching to groundwater of unidentified lysimeter metabolites cannot be finalised with the available data.
- Whether the current active substance technical specification adequately covers those batches used in the ecotoxicological studies needs to be addressed.
- The acute risk to insectivorous and herbivorous birds from use in cereals and sugar beet respectively need further refinements.
- The long-term risk assessment for birds needs further refinement.
- The long-term risk assessment for herbivorous mammals needs further refinement for uses in sugar beets, grapes and apples.
- The risk to earthworm-eating birds and mammals needs further refinement
- The potential of endocrine disrupting effects to birds is not addressed.
- The potential for endocrine disrupting effects to fish is not addressed
- The off-field risk assessment for non-target arthropod species with longer reproductive cycles needs to be addressed.
- The risk from potential soil metabolites to aquatic organisms, earthworms, soil non-target micro- and macro organisms needs to be addressed.

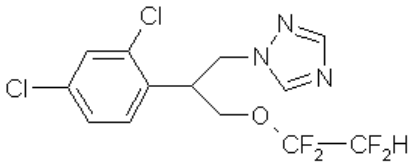
APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Chapter 2.1: Identity, Physical and Chemical Properties, Details of Uses, Further information, and Proposed Classification and Labelling

Active substance (ISO Common Name)	Tetraconazole
Function (e.g. fungicide)	Fungicide
Rapporteur Member State	Italy

Identity (Annex IIA, Point 1)

Chemical name (IUPAC)	(*RS*)-2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)-propyl-1,1,2,2-tetrafluoroethyl ether
Chemical name (CA)	(±)-1-[2-(2,4-dichlorophenyl)-3-(1,1,2,2-tetrafluoroethoxy)-propyl]-1*H*-1,2,4-triazole
CIPAC N°	726
CAS N°	112281-77-3
EEC N° (EINECS or ELINCS)	407-760-6
FAO Specification (including year of publication)	Not available
Minimum purity of the active substance as manufactured (g/kg)	950 g/kg (racemic mixture)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	Toluene, max. 13 g/kg
Molecular formula	$C_{13}H_{11}Cl_2F_4N_3O$
Molecular mass	372.14
Structural formula	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity)	-29.2 °C (glass transition; purity: 99.37%)
Boiling point (state purity)	Boiling point cannot be determined due to decomposition
Temperature of decomposition	235-240°C (purity: 99.94%)
Appearance (state purity)	Colourless viscous liquid (purity: 99.94%) Yellowish viscous liquid (purity: 94.16%)
Vapour pressure (state temperature, state purity)	1.8 x 10^{-4} Pa at 20°C (following extrapolation with Calpeyron-Clausius equation) (purity: 99.94%)
Henry's law constant	3.6 x 10^{-4} Pa m^3 $mole^{-1}$ at 20°C (by calculation)
Solubility in water (state temperature, state purity and pH)	at 20°C and purity: 99.94% pH=5 112.2 mg/L pH=7 156.6 mg/L un-buffered water 183.8 mg/L at 20°C and purity: 99.43% pH=9 153.7 mg/L
Solubility in organic solvents (state temperature, state purity)	xylene; acetone; ethyl acetate; 1,2-dichloromethane; methanol: > 300 g/L at 20°C, purity 95.40% n-hexane: 15 g/L at 20°C, purity 95.40%
Surface tension (state concentration and temperature, state purity)	49.94 ± 1.07 mN/m (111.8 mg/L in distilled water and 95.40% purity)
Partition co-efficient (log Pow) (state temperature, pH and purity)	3.56 at 20°C (the compound is not considered acidic or basic)
Dissociation constant (state purity)	pKa value is between 0.8 and 0.5; at pH>2 tetraconazole could be considered a non-protonated form (purity: 99.37 %)
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	No significant aborption at > 290 nm (ε < 10 M^{-1} cm^{-1}), although highest UV absorbtion maximum at 281 nm (ε < 310 M^{-1} cm^{-1}).
Flammability (state purity)	Tetraconazole is a liquid and does not evolve highly flammable gases. Flash point: 63°C (at 1 bar; purity: 95.60%)
Explosive properties (state purity)	Not explosive (95.60%) (EEC A 14)
Oxidizing properties (state purity)	Not oxidizing (consideration based on structure)

Summary of representative uses evaluated (*Tetraconazole*)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks:
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL (l) min – max	water L/ha min – max	kg as/ha (l) min – max		
Sugar beet	Northern and Southern Europe	EMINENT 40 ME	F	Cercospora Powdery mildew	ME	40 g/L	spray	1st)BBCH 38-39 Last) BBCH 49	1-2	20	0.0083-0.025	400-600	0.050-0.100	14 (south EU) 30 (north EU)	[1][2] [4]
Wheat	Northern and Southern Europe	EMINENT 40 ME	F	Powdery mildew Leaf spot Brown, yellow, black rust	ME	40 g/L	spray	from BBCH 51 (ear emergence) to flowering	1	-	0.021-0.062	200-600	0.125	application not later than flowering	[1] [4]
Grapes	Northern and Southern Europe	EMINENT 40 ME	F	Powdery mildew	ME	40 g/L	spray	1st) BBCH 55/57 (inflorescences developed / flowers separating) 3rd) BBCH 75 (berries pea sized)	2-3	10-14	0.0025-0.0030	1000	0.025-0.030	30	[1][2] [3] [4]
Apple	Northern and Southern Europe	EMINENT 40 ME	F	Powdery mildew	ME	40 g/L	spray	1st) BBCH 69 Last) BBCH 75-83	2-3	14	0.002-0.003	1000	0.02-0.03	14	[1][2] [3] [4]

* Uses for which the risk assessment can not be concluded are marked grey.
[1] Needs to be addressed: long-term risk to birds; risk to earthworm eating birds; acute risk to mammals; potential risk for endocrine disrupting effects on birds and fish; potential risk from metabolites on aquatic organisms and soil living organisms (earthworms and non-target micro- and macro-organisms); reproductive effects on non-target arthropods.
[2] The long-term risk to herbivorous mammals needs to be addressed
[3] No residue trial data available that support the notified cGAP [4] Consumer and livestock intake assessment not finalised

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (*e.g.* fumigation of a structure) (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I) (c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds (d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989 (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).** (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application (k) Indicate the minimum and maximum number of application possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha (m) PHI - minimum pre-harvest interval

Chapter 2.2 Methods of Analysis

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

Technical as (principle of method)	GC-FID
Impurities in technical as (principle of method)	GC-FID confidential (see Volume 4 Annex C)
Plant protection product (principle of method)	GC-FID

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Tetraconazole
Food of animal origin		Tetraconazole
Soil		Tetraconazole
Water	surface	Tetraconazole
	drinking/ground	Tetraconazole
Air		Tetraconazole

Monitoring/Enforcement methods (Annex IIA, point 4.2)

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	DFG method S19 with modified extraction (validated). Based on organic solvent extraction followed by GPC clean up and GC-MS analysis. LOQ: 0.01 mg/kg for wheat (grain), sugar beet; 0.02 mg/kg for wheat (straw), grape (bunches), apples and tomatoes. The submitted GC-MS method could not be accepted for confirmatory purposes, data required. No ILV data available, data required.
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	DFG method S19 with modified extraction (validated). Based on organic solvent extraction followed by GPC clean up and GC-MS analysis. LOQ: 0.01 mg/kg for milk (bovine); 0.02 mg/kg for fat (bovine), meat (bovine) and poultry eggs The submitted GC-MS method could not be accepted for confirmatory purposes, data required. No ILV data available, data required.
Soil (analytical technique and LOQ)	Accelerated Solvent Extraction (ASE) followed by GPC clean-up and GC-MS. German guideline DFG method S19 (extended revision); validated LOQ: 0.05 mg/kg tetraconazole in soil

Water (analytical technique and LOQ)	The analytical method is based on liquid-liquid partitioning followed by GC-NPD instrumental analysis. German guideline DFG method W5; validated LOQ: 0.1µg/kg tetraconazole in water The submitted GC-NPD method could not be accepted for confirmatory purposes, data required.
Air (analytical technique and LOQ)	The submitted validation data could not be considered acceptable, method required
Body fluids and tissues (analytical technique and LOQ)	Not required as active substance is not classified as Toxic or Very Toxic

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

	RMS/EPCO proposal	ECB decision
Active substance or variant	none	none

Chapter 2.3: Impact on Human and Animal Health

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

Rate and extent of absorption	More than 80 of absorption in the rat within 16-18 hours based on urinary excretion (repeated dose).
Distribution	Highest concentration in gastrointestinal tract, liver, muscle and fat (16-18 h)
Potential for accumulation	No evidence of accumulation
Rate and extent of excretion	Approx. 95% within 24 h mainly via urine (72.9%). More than 99% within 72 h mainly via urine (75.8%)
Metabolism in animals	Extensively metabolised (approx 84%), by oxidation / hydrolysis, cleavage of triazole-phenyl ring bridge, glutatione conjugation. Main metabolites: M14360-acid; M14360-alcohol; 1,2,4-triazole; P1 and P4 , fluorine.
Toxicologically significant compounds (animals, plants and environment)	Parent compound and metabolites

Acute toxicity (Annex IIA, point 5.2)

Rat LD50 oral	1031mg/kg bw **R22**
Rat LD50 dermal	> 2000 mg/kg
Rat LD50 inhalation	> 3.66 mg/L (maximum attainable concentration, 4 hrs whole body)
Skin irritation	Non irritant (rabbit)
Eye irritation	Non irritant (rabbit)
Skin sensitisation (test method used and results)	Non sensitising (guinea pig - Buehler test) Non sensitising (guinea pig - Maximisation test)

Short-term toxicity (Annex IIA, point 5.3)

Target / critical effect	Liver / adaptive modifications secondary to cytochrome P450 dependent enzymatic activities induction
Lowest relevant oral NOAEL	4.10 mg/kg bw/d (13 wk rat) 2.95 mg/kg bw/d (1-year dog)
Lowest relevant dermal NOAEL	240 mg/kg bw/d (21-day dermal rabbit) performed with the formulation and corrected for content of a.s..
Lowest relevant inhalation NOAEL	Not data, not required.

Genotoxicity (Annex IIA, point 5.4)

	No genotoxic potential

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

Target / critical effect	Liver / adaptive modifications secondary to cytochrome P450 dependent enzymatic activities induction, effects on bone and incisors (fluorosis).
Lowest relevant NOAEL	0.4 mg/kg/d (2-year rat). 1.5 mg/kg bw/d (18-month mouse)
Carcinogenicity	Liver tumours in mice and thyroid adenomas in rats not of relevance for humans

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect	Parental: Increased liver weight. Reproduction: Dystocia, prolonged gestation period. Offspring: Reduced body weight and decreased survival. **Repr. Cat. 3 R 62**
Lowest relevant reproductive NOAEL	Parental: 3.6 mg/kg bw/d. Reproduction: 3.6 mg/kg bw/d. Offspring: 3.6 mg/kg bw/d.
Developmental target / critical effect	Rat: Maternal: Decreased bodyweight gain. Foetal: Extra ribs, hydrourether and hydronephrosis. Rabbit: Maternal: Decreased bodyweight gain. Foetal: No effects. **Repr. Cat. 3 R63**
Lowest relevant developmental NOAEL / NOEL	Rat: Maternal: 5 mg/kg bw/d. Foetal: 22.5 mg/kg bw/d. Rabbit: Maternal: 15 mg/kg bw/d. Foetal: 30 mg/kg bw/d.

Neurotoxicity / Delayed neurotoxicity (Annex IIA, point 5.7)

	Not required, no concern from other studies.

Other toxicological studies (Annex IIA, point 5.8)

Metabolites	M14360-acid: -no genotoxic potential (4 in vitro studies) M14360-alcohol: -LD_{50} oral rat > 2000 mg/kg bw -no genotoxic potential (1 in vitro, 1 in vivo study) TAA (triazole acidic acid) : Reference values set at PRAPeR 14, January 2007: ADI: 0.02 mg/kg bw/d AOEL:0.06 mg/kg bw/d ARfD:0.06 mg/kg/bw/d TA (triazole alanine) : Reference values set at PRAPeR 14, January 2007: ADI: 0.1 mg/kg bw/d AOEL: not set (if needed should be the same as ADI) ARfD:0.1 mg/kg bw/d M14360-DFA: (Rat metabolite) -LD_{50} oral rat > 5000 mg/kg bw -Ames negative M14360-DCP-3OH/5OH: (Rat metabolite) -LD_{50} oral rat > 2000 mg/kg bw
Effect of the fluoride mojety of tetraconazole	The effects on teeth and bones observed in rodents are related to the fluorine content of tetraconazole (indirect demonstration in 2 mechanistic studies).

Medical data (Annex IIA, point 5.9)

	No effects in manufacturing plant personnel; no cases of poisoning or sensitisation ever registered

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI	0.004 mg/kg bw/d	2-year rat	100
AOEL systemic	0.03 mg/kg bw/d	1-year dog,	100
ARfD (acute reference dose)	0.05 mg/kg bw	developmental	100

	toxicity study in rats, maternal effects	

Dermal adsorption (Annex IIIA, point 7.3)

Dermal absorption of preparation EMINENT 40 ME: 1% for the concentrate and 20% for the spray dilution. (1:100) and (1:1000) dilutions were tested. Values are based on in vivo rat absorption study and comparative in vitro rat and human skin absorption study.

Acceptable exposure scenarios (including method of calculation)

Operator	UK POEM: Acceptable when gloves are used during mixing and loading and application for field crop scenario while the predicted exposure (% AOEL) is acceptable for orchard scenario and hand held application even if PPE are not worn. **Field crops** Tractor mounted//trailed boom sprayer; hydraulic nozzles application rate:3 L product/ha, exposure = 305,13% AOEL .(no PPE) 48,17 % AOEL (with PPE) **Orchards, Tractor mounted/air-assisted sprayer** application rate:0.75 L product/ha, exposure = 43% AOEL . (no PPE) 29,9 % AOEL (with PPE) **Orchards, Hand-held sprayer with hydraulic nozzles** application rate:0.75 L product/ha exposure = 50,78% AOEL .(no PPE) 17,5% AOEL (with PPE) German Model: All the intended uses show acceptable risk to the operator with the German Model even if PPE are not worn **FCTM scenario**: application rate:120g (a.s.)/ha, exposure = 51.26 % AOEL .(no PPE) 39.56% AOEL .(with PPE) **HCTM scenario:** application rate:30g (a.s.)/ha, exposure = 27.7% AOEL .(no PPE) 4.21% AOEL .(with PPE) **HCHH scenario**: application rate:30g (a.s.)/ha, exposure = 15.49% AOEL .(no PPE) 2.37% AOEL .(with PPE
Workers	**New calculation considering DA =20%, TF =4.500 cm^2/person h and DFR = 3 µg/cm^2/Kg a.s./ha (with and without PPE)** application rate:30 g (a.s.)/ha, exposure= 28% AOEL .(no PPE) **2,8% AOEL .(with PPE)**

Bystanders	**Worst case scenario (bystander exposure orchards)** The minimal amount of the ready-to-use diluted product which might reach a bystander has no toxicological relevance. application rate:30g (a.s.)/ha, exposure= 0.16 % AOEL indications of SCORA Workshop 2003. application rate:30g (a.s.)/ha, exposure= 5.5 % AOEL (acceptable)

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

	PRAPeR proposal	Current ECB classification
Active substance	Xn; R22, Xn; Repr.Cat.3 R62-63	Xn; R20/22; Xn; Carc. Cat.3 R40

Chapter 2.4: Residues

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

Plant groups covered	Cereals (wheat); root vegetables (sugar beet); fruiting vegetables (grapes)- foliar spraying
Rotational crops	Carrot, lettuce, sorghum, wheat
Metabolism in rotational crops similar to metabolism in primary crops?	The metabolism in rotational crops was similar to metabolism in primary crops. No unexpected new metabolite was observed.
Processed commodities	Tetraconazole is hydrolitically stable in the conditions of the test: pH 4, 20 minutes at 90°C pH 5, 60 minutes at 100°C pH 6, 20 minutes at 120°C
Residue pattern in processed commodities similar to residue pattern in raw commodities?	With respect to the residues found in raw commodities, tetraconazole concentrates in processed commodities such as wet and dry pomace and raisins. In juice, wine, must and sauce the residue is lower than in the raw commodity.
Plant residue definition for monitoring	Tetraconazole (provisional depending on outcome of the triazole compounds assessment)
Plant residue definition for risk assessment	Tetraconazole; Triazolyl alanine (TA) and Triazole acetic acid (TAA) (provisional awaiting information on THP)
Conversion factor (monitoring to risk assessment)	None

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

Animals covered	Lactating goats
Time needed to reach a plateau concentration in milk and eggs	Milk: plateau reached at day 3 (overall duration 5 days). 1,2,4-triazole did not reach the plateau
Animal residue definition for monitoring	Tetraconazole (provisional depending on outcome of the triazole compounds assessment)
Animal residue definition for risk assessment	Tetraconazole and 1,2,4-triazole
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	yes (Tetraconazole - Log Pow > 3) 1,2,4-triazole - ßßß

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

Field trials. Negligible tetraconazole residues are found in any rotational crops.

Despite a leafy vegetable was not included in this study, tetraconazole is expected to be negligible, considering the relevant metabolism in rotational crops in which tetraconazole residues in lettuce are the lowest among all the tested crops. However the levels of triazole derivative metabolites need to be addressed in rotational crop field trials for RA purposes. Data gap for the cold study

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

tetraconazole: plants: for three years at -20°C cereal grains and straw, vine grapes, apples, sugar beet roots No data on stability in animal tissues.

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes; no peer reviewed estimates available	No	No
Potential for accumulation (yes/no):	No	Not relevant	Not relevant
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Yes	Not relevant	Not relevant
Muscle		Not relevant	Not relevant
Liver		Not relevant	Not relevant
Kidney		Not relevant	Not relevant
Fat		Not relevant	Not relevant
Milk			
Eggs		Not relevant	

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

Note: Results only applicable to residues of tetraconazole, no data on residues of triazole derivative metabolites available

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Apple	N and S	No trials relevant to the representative uses available for peer review		pending assessment of new data	open	open
Grape	N and S	No trials relevant to the representative uses available for peer review		pending assessment of new data	open	open
Sugar beet root	S	5 × <0.01; 3 × <0.02	MRL can be set	0.02*	0.02	0.01
Sugar beet leaf	S	1 x 0.4; 1 x 0.5; 2 x 0.6; 1 x 0.7; 1 x 0.9; 1 x 1.0; 1 x 1.2		2	1.2	0.65
Sugar beet root	N	7 × <0.01; 1 × <0.02	MRL can be set	0.02*	0.02	0.01
Sugar beet leaf	N	1 x 0.21; 2 x 0.3; 1 x 0.5; 2 x 0.6; 1 x 0.7; 1 x 0.8		2	0.8	0.5
Wheat grain	S	8 × <0.005	MRL can be set	0.01*	0.005	0.005
Wheat straw	S	3 × 0.4; 1 × 0.5; 1 × 0.7; 1 × 0.9; 1 × 1.4; 1 × 1.9		3	1.9	0.6
Wheat grain	N	6 × < 0.02	MRL can be set	0.02*	0.02	0.02
Wheat straw	N	2 × 0.6; 1 × 1.0; 1 × 1.1; 1 × 1.9; 1 × 2.4		3	2.4	1.05

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

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

ADI	0.004 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	Consumer risk assessment is not finalised. Only provisional assessment by RMS after the meeting of experts available, no addendum, not peer reviewed (refer to EFSA conclusion chapter 3.3)
TMDI (% ADI) according to national (to be specified) diets	Consumer risk assessment is not finalised. Only provisional assessment by RMS after the meeting of experts available, no addendum, not peer reviewed (refer to EFSA conclusion chapter 3.3)
IEDI (WHO European Diet) (% ADI)	Consumer risk assessment is not finalised. Only provisional assessment by RMS after the meeting of experts available, no addendum, not peer reviewed (refer to EFSA conclusion chapter 3.3)
NEDI (specify diet) (% ADI)	Consumer risk assessment is not finalised. Only provisional assessment by RMS after the meeting of experts available, no addendum, not peer reviewed (refer to EFSA conclusion chapter 3.3).
Factors included in IEDI and NEDI	not applicable
ARfD	0.05 mg/kg bw/day
IESTI (% ARfD)	Consumer risk assessment is not finalised. Only provisional assessment by RMS after the meeting of experts available, no addendum, not peer reviewed (refer to EFSA conclusion chapter 3.3)

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

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

Note: Results only applicable to residues of tetraconazole

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
Apple/dry pomace	3*	4.2	-	-
Apple/juice	5*	0.35	-	-
Apple/sauce	1*	0.30	-	-
Apple/ washed apple	0*	Nd	-	-
Apple /wet pomace	1*	0.77	-	-
Grape/wine	8*	0.29	-	-
Grape/must	6*	0.49	-	-
Grape/juice	1*	0.45	-	-
Grape/marc	4*	2.7	-	-
Grape/wet pomace	2*	5.35	-	-
Grape/raisins	3*	2.28	-	-
Wheat/wholemeal flour	1*	1	-	-
Wheat flour	1*	1.3	-	-
Wheat/bran	1*	1.1	-	-
Milk/skimmed	2	0.18	-	-
Milk/cream	2	10.36	-	-
Liver/fried	1	1.15	-	-
Liver/braised	1	1.19	-	-
Liver/paté	1	0.83	-	-

*more studies were submitted for which residues in the RAC were < LOD

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

Apple	unable to be proposed
Grape	unable to be proposed
Wheat grain	0.02* mg/kg
Sugar beet root	0.02* mg/kg
Milk	assessment not finalised
Meat	assessment not finalised
Kidney	assessment not finalised
Liver	assessment not finalised
Fat	assessment not finalised

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

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

Chapter 2.5: Fate and Behaviour in the Environment

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

Mineralisation after 100 days	0.1% after 119 d, [^{14}C-Tr]Tetraconazole (triazole ring), (n=1) 0.1% after 119 d, [^{14}C-Ar]Tetraconazole (2,4-dichlorophenyl ring), (n=1)
Non-extractable residues after 100 days	10.8% after 119 d, [^{14}C-Tr]Tetraconazole (n=1) 10.6% after 119 d [^{14}C-Ar]Tetraconazole (n=1)
Metabolites requiring further consideration - name and/or code, % of applied (range and maximum)	Laboratory study (dark): no metabolite formation Data gap identified for additional experiments to investigate under what conditions degradation in soil might occur or not and the potential formation of metabolites arising from either ring.

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

Anaerobic degradation	
Mineralisation after 100 days	Data gap
Non-extractable residues after 100 days	Data gap
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	Data gap

Soil photolysis

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	500 W/m^2 intensity for 16 days (corresponding to 36.6 days of summer sunlight) [U-^{14}C-Triazole]Tetraconazole: no degradation Mineralisation: <0.12% Max non-extractable residues : 1.88% (day 16, wet sample), 1.64 (day 16, dry sample)

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

Laboratory studies							
Parent	Aerobic conditions						
Soil type	**X**	**pH**	**t. °C / % MWHC**	**DT_{50} /DT_{90} (d)**	**DT_{50} (d) 20°C pF2/10kPa**	**St. (r^2)**	**Method of calculation**
Slightly humous sand		5.9	20°C / 40%	No degradation	No degradation	-	-
Very humous loamy sand		5.6	20°C / 40%	No degradation	No degradation	-	-
Slightly humous sandy loam		6.4	20°C / 40%	No degradation	No degradation	-	-
Geometric mean/median				-	-	-	-

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

Field studies ‡									
Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (χ^2)	DT_{50} (d) Norm.	Method of calculation
Silty sand	Klein-Offenseth (Germany)		4.2	10	1026	3407	14.5		SFO
Loamy sand	Bad Oldesloe (Germany)		6.8	10	1688	5606	14.3		SFO
Strongly loamy sand	Moorfleet-Hamburg (Genmany)		6.7	10	310	1028	8.6		SFO
Loamy silt	Uslar-Verliehausen (Germany)		5.8	10	201	667	11.3		SFO
Sandy loam	Salerano sul Lambro (Italy)		4.47	10	136	453	11.3		SFO
Geometric mean/median					430/310	1428 / 1028			

pH dependence (yes / no) (if yes type of dependence)	no
Soil accumulation and plateau concentration	EFSA calculated a plateau background concentration over the 20 cm horizon of 0.124 mg / Kg after 36 years of continuous use. This will result on a peak concentration of 0.204 mg / Kg over the 5 cm horizon.

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)							
Parent							
Soil Type	OC %	Soil pH	K_d (mL/g)	K_{oc} (mL/g)	K_f (mL/g)	K_{foc} (mL/g)	1/n
Sandy	0.70	6.0			8.53	1219	0.89
Sandy loam	0.96	5.4			8.97	935	0.91
Clay	2.50	5.5			13.28	531	0.88
Clay loam	28.5	5.3			548.9	1922	0.99
Arithmetic mean					145	1152	0.92
pH dependence, Yes or No			no				

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

Column leaching

Phenyl-[^{14}C]Tetraconazole in 2 clay and 1 loamy peat soils:

elution: 560.5 mm

time period does not exceed infiltration capacity

elution time: 16 h ([A]-clay), 336 h ([B]-clay), 6 h ([C]-loamy-peat

[Triazole-^{14}C]Tetraconazole in 2 clay and 1 loamy peat soils:

elution: 560.5 mm

time period does not exceed infiltration capacity

elution time: 16 h ([A]-clay), 480 h ([B]-clay), 6 h ([C]-loamy-peat

[Phenyl-^{14}C]Tetraconazole and [Triazole-^{14}C] Tetraconazole in sandy loam soil:

elution: 560.5 mm

time period does not exceed infiltration capacity

elution time: 4 h and 45 min ([Phenyl-^{14}C]Tetraconazole), 5 h (and [Triazole-^{14}C] Tetraconazole)

^{14}C-M14360 EC 10 (formulate) in sand, loamy sand and sandy loam soils:

elution: 314.5 mm

time period: 2 days

Tetraconazole metabolites column leaching in slightly humous sand:

elution: 200 mm

time period : 2 days

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

	[Phenyl-^{14}C]Tetraconazole in 2 clay and 1 loamy peat soils: radioactivity in leachate: 0.117% ([A]-clay), <0.003% ([B]-clay), 0.03% ([C]-loamy-peat) radioactivity retained in the top 5 cm: 93.61% ([A]-clay), 66.30% ([B]-clay), 101.06% ([C]-loamy-peat) [Triazole-^{14}C]Tetraconazole in 2 clay and 1 loamy peat soils: radioactivity in leachate: : 0.1267% ([A]-clay), 0.0625% ([B]-clay), 0.0210% ([C]-loamy-peat) radioactivity retained in the top 5 cm: 94.74% ([A]-clay), 97.84% ([B]-clay), 97.12% ([C]-loamy-peat) [Phenyl-^{14}C]Tetraconazole and [Triazole-^{14}C] Tetraconazole in sandy loam soil: radioactivity in leachate: 0.17% ([Phenyl-^{14}C] Tetraconazole), 0.37% ([Triazole-^{14}C] Tetraconazole) radioactivity retained in the top 5 cm: 97.54% ([Phenyl-^{14}C]Tetraconazole), 99.58% ([Triazole-^{14}C] Tetraconazole) ^{14}C-M14360 EC 10 (formulate) in sand, loamy sand and sandy loam soils : radioactivity in leachate: 0.60% (SP-2.1), 0.43% (SP-2.2), 0.48% (SP-2.3) radioactivity retained in the top 5 cm: 99.41% (SP-2.1), 97.53% (SP-2.2), 85.10% (SP-2.3) Tetraconazole metabolites column leaching in slightly humous sand: M14360-alcohol: 67.84% (of applied M14360-alcohol) Triazole: 59.04% (of applied Triazole) M14360-acid: 89.39% (of applied M14360-acid) DFA: 71.54% (of applied DFA) TAA: 95.53% (of applied TAA)
Aged residues leaching	Aged for (d): 30 d Time period (d): 2 d Elution (mm): 200 mm
	Soil residues post ageing % of ^{14}C-Tetraconazole: 96.21%AR % of bound residues: 2.32%AR

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

	Analysis of leachate tetraconazole equivalents in the leachate: 0.15%AR bound residues: 2.13%AR
Lysimeter/ field leaching studies	Location: Switzerland, RCC Ltd Itingen Study type: lysimeter Soil properties: Horizon 0-30 cm: texture (loamy sand) = 6.47% clay, 12.7% silt, 80.9% sand; pH = 5.60; OC= 1.77%; MWHC = 30.9% Horizon 30-60 cm: texture (sand) = 3.67% clay, 6.17% silt, 90.2% sand; pH = 5.36; OC = 0.30%; MWHC = 25.2% Horizon 60-90 cm: texture (sand) = 0.93% clay, 0.40% silt, 98.7% sand; pH = 4.95; OC = 0.08%; MWHC = 23.9% Horizon 90-120 cm: texture (sand) = 0.71% clay, 0.22% silt, 99.1% sand; pH = 5.09; OC = 0.00%; MWHC = 25.2% Dates of application : May 31, 2002 (1st application); June 25, 2002 (2nd application) Crop : spring wheat and phacelia Number of applications: 1 year, 2 applications Duration: July 2002-July 2004 Application rate: 2 × 125 g/ha Average annual rainfall (mm): 1205.4 mm (1st year); 778.8 mm (2nd year) Average annual leachate volume (mm): 757.5 mm (1st year); 422.8 mm (2nd year) Maximum %radioactivity in leachate (without volatiles): lysimeter I: 0.21% (1st year); 0.07% (2nd year) lysimeter II: 0.18% (1st year); 0.06% (2nd year)

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

Individual annual maximum concentrations (without volatiles): no tetraconazole found in leachates; 12 metabolites detected, each of them at a concentration that does not exceed 0.1 µg/l

lysimeter I:

Maximum monthly average values

M10 = 0.14 µg of parent equivalent per litre (2002); 0.063 µg of parent equivalent per litre (2003); 0.039 µg of parent equivalent per litre (2004)

M11 = 0.31 µg of parent equivalent per litre (2002); 0.098 µg of parent equivalent per litre (2003); 0.083 µg of parent equivalent per litre (2004)

lysimeter II:

Maximum monthly average values

M10 = 0.06 µg of parent equivalent per litre (2002); 0.041 µg of parent equivalent per litre (2003); 0.029 µg of parent equivalent per litre (2004)

M11 = 0.26 µg of parent equivalent per litre (2002); 0.12 µg of parent equivalent per litre (2003); 0.089 µg of parent equivalent per litre (2004)

Individual annual average concentrations (including dissolved $^{14}CO_2$): no tetraconazole found in leachates; 12 metabolites detected, each of them at a concentration that does not exceed 0.1 µg/l

Leachate mean value (total amount found/total amount of leachates collected): 0.54µg/l parent equivalents (1st year); 0.27µg/l parent equivalents (2nd year)

Lysimeter I:

Yearly average values

M10 = 0.08 µg of parent equivalent per litre (2003); 0.03 µg of parent equivalent per litre (2004)

M11 = 0.18 µg of parent equivalent per litre (2003); 0.11 µg of parent equivalent per litre 2004)

Lysimeter II

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

	Yearly average values M10 = 0.04 µg of parent equivalent per litre (2003); 0.03 µg of parent equivalent per litre (2004) M11 = 0.18 µg of parent equivalent per litre (2003); 0.13 µg of parent equivalent per litre 2004)

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	DT_{50} (d): 1688 days Kinetics: SFO Representative worst case from field studies.
Application data	Number of applications: 2 Interval (d): 20 Application rate(s): 100 g as/ha Crop: sugar beet North/South EU Depth of soil layer: soil mixing depth of 20cm for the plateau and 5 cm for applications in the last year Soil bulk density: 1.5 kg/L % plant interception: Post-emergence therefore 70% interception

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.020		0.204	
Plateau concentration	0.124 mg/kg after 36 yr			

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

Hydrolytic degradation of the active substance and metabolites > 10%.	pH 4-7-9: no degradation over 120 hours
Photolytic degradation of active substance and metabolites above 10%	Photodegradation not expected being ε<10 M-1·cm-1 at λ>290 nm
Quantum yield of direct phototransformation in water at ☒ > 290 nm	Not necessary
Readily biodegradable (yes/no)	no

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

Parent Distribution (max in water 87.9/88.3% after 0 d. Max. sed 81.9/78.1 % after 14/30 d)

Water / sediment system	pH w	pH sed	t. (°C)	DT_{50}-DT_{90} whole sys.	χ^2	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Mill stream pond	7.86	7.6	20	372 / 1236	1.5	2 / 20	No data submitted	No data submitted	No data submitted	SFO (whole system); graphical interpretation (sw)
Iron hatch run-off	7.95	7.7	20	310 / 1029	2.0	2 / 30	No data submitted	No data submitted	No data submitted	SFO (whole system); graphical interpretation (sw)
Geometric mean/median				DT_{50}: 339.6/ 341.0 DT_{90}: 1127.8/ 1132.5		DT_{50}: 2/ 2 DT_{90}: 24.5/ 25.0				

Mineralization and non extractable residues

Water / sediment system	pH w	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Mill Stream Pond	7.86	7.6	n.d. (100 d)	13.0% (100 d)	13.0% (100 d)
Iron hatch run-off	7.95	7.7	n.d. (100 d)	16.6 (59 d)	16.0 (100 d)

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

Parent
Parameters used in FOCUSsw step 1 and 2

Version control no. of FOCUS calculator: 1.1
Molecular weight (g/mol): 372.16
Water solubility (mg/L): 189.8
K_{oc} (L/kg): 1152
DT_{50} soil (d): 1000 days (conventional worst case)
DT_{50} water/sediment system (d): 382 days (representative worst case from sediment water studies) DT_{50} water (d): 382 days

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

	DT_{50} sediment (d): 382 days Crop interception (%): 70% Tetraconazole does not degrade in water but it is rapidly re-distributed from the water to the sediment. Parent compound entry route: drift, runoff/drainage; metabolite entry route: runoff/drainage
Parameters used in FOCUSsw step 3 (if performed)	-
Application rate	Crop: sugar beat Crop interception: intermediate, 70% Number of applications: 2 Interval (d): 20 Application rate(s): 100 g as/ha Depth of water body: 30 cm Application window: June-September

FOCUS STEP 2 Scenario	**Day after overall maximum**	**PEC_{SW} (µg/L)**		**PEC_{SED} (µg/kg)**	
		Actual	**TWA**	**Actual**	**TWA**
Northern EU	0 h	2.346		25.15	
	24 h	2.183	2.264	25.10	25.13
	2 d	2.179	2.223	25.06	25.10
	4 d	2.171	2.199	24.97	25.06
	7 d	2.159	2.185	24.83	24.99
	14 d	2.132	2.165	24.52	24.83
	21 d	2.105	2.150	24.21	24.68
	28 d	2.079	2.135	23.90	24.52
	42 d	2.027	2.108	23.30	24.21
Southern EU	0 h	3.127		34.13	
	24 h	2.963	3.045	34.07	34.10
	2 d	2.957	3.002	34.01	34.07
	4 d	2.947	2.977	33.88	34.01
	7 d	2.931	2.961	33.70	33.91
	14 d	2.894	2.936	33.27	33.70
	21 d	2.857	2.916	32.85	33.49
	28 d	2.821	2.897	32.44	33.28
	42 d	2.750	2.860	31.63	32.86

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

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

Parent compound Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)	Two simulation models, FOCUS PEARL 3, and PRZM 2.4.1, were used Scenarios: all nine FOCUS scenarios where the crop is included. Crop: sugarbeet, wheat, grapes and apples Tetraconazole: DT_{50}: 1000 days, conventional worst case K_{oc}: 1152 (mean value); 1/n= 0.9 (default value).
Application rate	Application rate: sugar beets: 2 applications of 0.100 kg/ha wheat: 1 application of 0.125 kg/ha apples: 3 applications of 0.030 kg/ha vines: 3 applications of 0.030 kg/ha

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

PEC(gw) Tetraconazole- FOCUS modelling results (80th percentile annual average concentration at 1m). The highest values are in bold. All results are below 0.1µg/L

SCENARIO	PEARL	PRZM
SUGAR BEETS: 2 applications of 0.100 kg/ha		
Châteaudun	<0.001	<0.001
Hamburg	<0.001	<0.001
Jokioinen	<0.001	<0.001
Kremsmünster	<0.001	<0.001
Okehampton	<0.001	<0.001
Piacenza	<0.001	**0.023**
Porto	<0.001	<0.001
Sevilla	**0.001**	<0.001
Thiva	<0.001	<0.001
WHEAT: 1application of 0.125 kg/ha		
Châteaudun	<0.001	<0.001
Hamburg	**0.005**	<0.001
Jokioinen	<0.001	<0.001
Kremsmünster	**0.001**	<0.001
Okehampton	**0.016**	<0.001
Piacenza	**0.068**	**0.005**
Porto	<0.001	<0.001
Sevilla	<0.001	<0.001
Thiva	<0.001	<0.001
VINES: 3 applications of 0.030 kg/ha		
Châteaudun	<0.001	<0.001
Hamburg	<0.001	<0.001
Kremsmünster	<0.001	<0.001
Piacenza	<0.001	**0.031**
Porto	<0.001	<0.001
Sevilla	<0.001	<0.001
Thiva	<0.001	**0.001**
APPLES: 3 applications of 0.030 kg/ha		
Châteaudun	<0.001	<0.001
Hamburg	<0.001	<0.001
Jokioinen	<0.001	<0.001
Kremsmünster	<0.001	<0.001
Okehampton	**0.004**	<0.001
Piacenza	<0.001	**0.077**
Porto	<0.001	<0.001
Sevilla	<0.001	<0.001
Thiva	<0.001	<0.001

PEC$_{(gw)}$ From lysimeter / field studies

Parent	1st year	2nd year	3rd year
Annual average (µg/L)	Tetraconazole not found	Tetraconazole not found	Tetraconazole not found

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

Metabolite M10	1st year	2nd year	3rd year
Annual average (µg/L)	0.08 and 0.04 µg parent eq. per L	0.03 and 0.03 µg parent eq. per L	Not performed
Metabolite M11	1st year	2nd year	3rd year
Annual average (µg/L)	0.18 and 0.18 µg parent eq. per L	0.11 and 0.13 µg parent eq. per L	Not performed

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

Direct photolysis in air	Not required
Quantum yield of direct phototransformation	$\varepsilon < 10\ M^{-1}cm^{-1}$ at $\lambda > 290$ nm
Photochemical oxidative degradation in air	DT_{50} of 1.16 days (28 hours) - Atkinson model
Volatilisation	Not provided, not necessary
	Not provided, not necessary
Metabolites	Not relevant

PEC(a)	
Maximum concentration	Not relevant

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: tetraconazole, data gaps to be filled before it can be finalised (clarification of nature of aerobic and anaerobic soil residues). Surface water: tetraconazole, for metabolites that may move from soil to surface water data gap to be filled before it can be finalised Sediment: tetraconazole Groundwater: tetraconazole data gaps to be filled before it can be finalised (nature of soil residues and lysimeter study). Air: tetraconazole

Monitoring data, if available (Annex IIA 7.12)

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

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

Not readily biodegradable, candidate for R53.

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

Chapter 2.6: Effects on Non-target species

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

Species	Test substance	Time scale	Endpoint (mg/kg bw/d)	Endpoint (mg/kg feed)
Birds				
Bobwhite quail	a.s.	Acute	132	
Mallard duck	EMINENT 40 EW	Acute	> 63 a.s.	
Bobwhite quail, Mallard duck	TA Metabolite	Short-term		> 5000
Mallard duck	a.s.	Short-term	55.5[1]	422
Mallard duck	a.s.	Long-term	1.6[2]	10
Mammals				
Rat	a.s.	Acute	1031	
Rat	a.s.	Long-term	3.6[3]	70[4]
Additional higher tier studies				

[1]The daily intake was calculated for the groups receiving 325 ppm. From Hakin *et al*., 1989 (IIA, 8.1.2/01)
[2]calculated according to SANCO/4145/2000 and considering the mean body weight of 1090.5 g and the daily food consumption of 177.0 per bird per day, derived from Johnson *et al*., 1997 (IIA, 8.1.3/01)
[3]~~mean of F0 and F1 males and females values.~~ male F0
[4]Lowest dose with no effect of ecotoxicological relevance (survival rate, reproduction rate and development) among reproductive studies

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, point 10.1 and 10.3)
Sugar beet, 2 x 0.100 kg as/ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
medium herbivorous / leafy crops	Acute	7.93	**7.94**	10
insectivorous / leafy crops	Acute	5.4	11.65	10
medium herbivorous / leafy crops	Short-term	3.8	14.6	10
insectivorous / leafy crops	Short-term	3.02	18.4	10
medium herbivorous / leafy crops	Long-term	2.01	**0.8**	5
insectivorous / leafy crops	Long-term	3.02	**0.5**	5
Higher tier refinement (Birds)				

No refinements were agreed during the peer-review.

Tier 1 (Mammals)				
medium herbivorous / leafy crops	Acute	2.9	353*	10
medium herbivorous / leafy crops	Long-term	0.74	**4.85**	5

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

Higher tier refinement (Mammals)				

* Calculated by EFSA after the peer-review

Wheat, 1 x 0.125 kg as/ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
insectivorous / cereals (late)	Acute	6.8	**9.32**	10
insectivorous / cereals (late)	Short-term	3.8	14.7	10
insectivorous / cereals (late)	Long-term	3.77	**0.4**	5
Higher tier refinement (Birds)				
No refinements were agreed during the peer-review.				
Tier 1 (Mammals)				
insectivorous / cereals (late)	Acute	1.1	935*	10
insectivorous / cereals (late)	Long-term	0.4	8.96	5
Higher tier refinement (Mammals)				

* Calculated by EFSA after the peer-review

Orchards (apple/grape), 3 x 0.030 kg as/ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
insectivorous / orchards	Acute	1.62	38.83	10
insectivorous / orchards	Short-term	1.2	61.3	10
insectivorous / orchards	Long-term	0.9	1.8	5

Higher tier refinement (Birds)				
No refinements were agreed during the peer-review.				
Tier 1 (Mammals)				
small herbivorous / grapes/apples	Acute	3/4.6	194/224*	10
small herbivorous / grapes/apples	Long-term	1.78/1.52	**2.02/2.36**	5
Higher tier refinement (Mammals)				

* Calculated by EFSA after the peer-review

Drinking water from open bodies / Drinking water from axils of leaves*

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Insectivorous bird	Acute	13.50	10	10
Insectivorous mammal	Acute	7.8	131**	10

* Sugar beets application was used as a worst case scenario
** Calculated by EFSA after the peer-review

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

Secondary poisoning

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Earthworms eating	Long-term	0.755	**4.42**	5
Fish eating	Long-term	0.021	76.2	5
Tier 1 (Mammals)				
Earthworms eating	Long-term	0.961	**7.82**	5
Fish eating	Long-term	0.013	376.9	5

‡ Endpoints 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 (Test type)	Endpoint	Toxicity[1] (mg/L)
Laboratory tests				
Fish				
Lepomis macrochirus	a.s.	96 hr (flow-through)	Mortality, EC50	$4.3_{(nom)}$
Pimephales promelas	a.s.	28 d (flow-through)	Growth NOEC	$0.3_{(mm)}$
Brachydanio rerio	EMINENT 40 ME	96 hr (static)	Mortality, EC50	$>3.8_{(nom)}$
Oncorhynchus mykiss	M14360 acid Metabolite	96 hr (static)	Mortality, EC50	$61.4_{(nom)}$
Oncorhynchus mykiss	M14360 alcohol Metabolite	96 hr (semi static)	Mortality, EC50	$24_{(nom)}$
Oncorhynchus mykiss	TAA Metabolite	96 hr (static)	Mortality, EC50	$>100_{(nom)}$
Aquatic invertebrate				
Daphnia magna	a.s.	48 h (static)	Mortality, EC50	$3.0_{(mm)}$
Americamysis bahia	a.s.	96 h (flow-through)	Mortality, EC50	$0.42_{(mm)}$
Crassostrea virginica	a.s.	96 h (flow-through)	Mortality, EC50	$1.1_{(mm)}$
Daphnia magna	a.s.	21 d (semi static)	Reproduction, NOEC	$0.19_{(mm)}$
Daphnia magna	EMINENT 40 ME	48 h (static)	Mortality, EC50	$1.6_{(nom)}$
Daphnia magna	M14360 acid Metabolite	48 h (static)	Mortality, EC50	$>100_{(nom)}$
Daphnia magna	M14360 alcohol Metabolite	48 h (static)	Mortality, EC50	$68_{(mm)}$
Daphnia magna	TAA Metabolite	48 h (static)	Mortality, EC50	$>100_{(nom)}$
Sediment dwelling organisms				
Chironomus riparius	a.s.	28 d (static)	NOEC	$4.45_{(nom)}$
Algae				
Scenedesmus subspicatus	a.s.	72 h (static)	Biomass: E_bC50 Growth rate: E_rC50	$0.27_{(nom)}$ $0.41_{(nom)}$
Scenedesmus subspicatus	EMINENT 40 ME	72 h (static)	Biomass: E_bC50 Growth rate: E_rC50	$0.4^{2}_{(nom)}$ 1.5
Scenedesmus subspicatus	M14360 acid Metabolite	72 h (static)	Biomass: E_bC50 Growth rate: E_rC50	$>100_{(nom)}$ $>100_{(nom)}$

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

Group	Test substance	Time-scale (Test type)	Endpoint	Toxicity[1] (mg/L)
Scenedesmus subspicatus	TAA Metabolite	72 h (static)	Biomass: E_bC50 Growth rate: E_rC50	$12.2_{(nom)}$ $135.1_{(nom)}$
Higher plant				
Lemna gibba	a.s.	7 d (static)	Fronds, EC_{50}	$0.52_{(nom)}$
Microcosm or mesocosm tests: not required				

[1] (nom): nominal concentration; (mm): mean measured concentration
[2] this EC-value should be taken with caution, since the inhibition of r was lower than 50% up to the highest test concentration

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

FOCUS Step2
Sugar beet, 2 x 0.1 kg as/ha

Test substance	N/S[1]	Organism	Toxicity endpoint (mg/L)	Time scale	PEC (maximum value)	TER	Annex VI Trigger
a.s.	S	Fish	4.3	Acute	2.82	1524	100
a.s.	S	Fish	0.3	Chronic	2.82	106.4	10
a.s.	S	Aquatic invertebrates	0.42	Acute	2.82	148.9	100
a.s.	S	Aquatic invertebrates	0.19	Chronic	2.82	67.4	10
a.s.	S	Algae	0.27	Chronic	2.82	14.2	10
a.s.	S	Higher plants[2]	0.52	Chronic	2.82	11.3	10
a.s.	S	Sediment-dwelling organisms	4.45	Chronic	2.82 PEC_{sw}	1578	10
M14360 acid Metabolite	S	Fish	61.4	Acute	0.00717	8563.45	100
M14360 alcohol Metabolite	S	Fish	24	Acute	0.0132	1818.18	100
TAA Metabolite	S	Algae	12.2	Acute	0.0271	450	10

[1] Northern of Southern
[2] only required for herbicides

Bioconcentration				
	Active substance	M14360 acid	M14360 alcohol	TAA
logPow	3.56	<3	<3	<3
Bioconcentration factor (BCF)[1]	35.7[2]			
Annex VI Trigger for the bioconcentration factor	100			

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

Clearance time (days) (CT_{50})	0.189 (whole fish)			
(CT_{90})	not calculated			
Level and nature of residues (%) in organisms after the 14 day depuration phase	negligible			

[1]only required if log Pow >3.
[2]based on total ^{14}C

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

Test substance	Acute oral toxicity (LD 50 µg a.s./bee)	Acute contact toxicity (LD50 µg a.s./bee)
a.s.	> 130	63
EMINENT 40 ME	16.3	27.2

Field or semi-field tests: not required

Hazard quotients for honeybees (Annex IIIA, point 10.4)

Wheat 0.125 kg as/ha

Test substance	Route	Hazard quotient	Annex VI Trigger
EMINENT 40 ME	Contact	4.59	50
EMINENT 40 ME	oral	7.66	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	Endpoint	Effect (LR50 g/ha)
Typhlodromus pyri	ME formulation (40 g a.s./L)	Mortality	high mortality and high escaping rate
Aphidius rhopalosiphi	ME formulation	Mortality	125 g as/ha

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

Further laboratory and extended laboratory studies

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	Endpoint	% adverse effect	Trigger value
Chrysoperla carnea	Larvae, pupae, adults	ME formulation (40 g a.s./L) Glass plates 23 + 20 d	40, 80, 125, 250 a.s.	Mortality, reproduction	harmless up to 250 g as/ha 40 g a.i./ha 80 g a.i./ha 125 g a.i./ha 250 g a.i./ha	50%
Poecilus cupreus	adults	ME formulation (40 g a.s./L) 14 d	40, 80, 125, 250 a.s.	Mortality, food consumption	harmless up to 250 g as/ha 40 g a.i./ha 80 g a.i./ha 125 g a.i./ha 250 g a.i./ha	50%
Aphidius rhopalosiphi	adult	ME formulation (40 g a.s./L) Barley plants 48 + 24 h	80, 125, 250 a.s. initial residues	Mortality, reproduction	harmless at 80 g as/ha 80 g a.i./ha 125 g a.i./ha 250 g a.i./ha	50%
Aphidius rhopalosiphi	adult	ME formulation (40 g a.s./L) Barley plants 48 + 24 h	125, 250 a.s. 14 day aged residues	Mortality, reproduction	harmless 125 g a.i./ha 250 g a.i./ha	50%
*Typhlodromus pyri**						

* The need for an extended laboratory study with fresh residues and T. pyri to conduct an off-field risk assessment for mites/spiders with a lower recovery potential was identified during the peer-review.

Field or semi-field tests Both Tetraconazole 40 g/L microemulsion and Tetraconazole 100 g/L EC formulation have been tested in the field and resulted to be harmless when applied up to 4 times at the application rate of 40 g a.i./ha. In the field study carried out with Tetraconazole 100 g/L EC formulation at 125 g a.i./ha x 2 applications and corrected according to *Barrett et al.* into 312.5 g a.i./ha x 2 applications (conversion from grape vs wheat), complete recovery of the mite population was observed 8 weeks after the 2nd application while it resulted to be harmless to *Typhlodromus pyri* at a 5% spray drift rate of 15.6 g a.i./ha. In the field study carried out with Tetraconazole 40 g/L microemulsion at 125 g a.i./ha x 2 applications and 5% drift rate (6.25 g a.i./ha), it can be classified as harmless to the predatory mite *Typhlodromus pyri*.

Hazard quotients for no-target arthropods

Test substance	Route	Hazard quotient	Annex VI Trigger
ME formulation	In-field	1.36	2
ME formulation	Off-field	0.04	2

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

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

Test organism	Test substance	Time scale	Endpoint[1]
Earthworms			
Eisenia foetida	a.s.	Acute 14 days	LC50 71 mg a.s./kg d.w.soil
Eisenia foetida	a.s.	Chronic 4 weeks	NOEC 8.2 mg a.s./kg d.w.soil
Eisenia foetida	EMINENT 40 ME	Acute 14 days	$LC50_{corr}$ >19.12 mg a.s./kg d.w.soil
Eisenia foetida	EMINENT 40 ME	Chronic 4 weeks	$NOEC_{corr}$ >3.36 mg a.s./kg d.w.soil
Other soil macro-organisms			
Collembola			
Soil micro-organisms			
Nitrogen mineralisation	a.s.	Chronic 4 weeks	effect < 25% after 28d at 0.502 mg a.s./kg d.w soil
Carbon mineralisation	a.s.	Chronic 4 weeks	effect < 25% after 28d at 0.502 mg/kg d.w soil

Field studies[2]
In the study the 1st application rate (246 g a.s./ha) was in excess respect to the max concentrations expected in soil (even considering accumulation at plateau level after several years of application) and included the 1st seasonal application rate; the 2nd application (125 g a.s./ha) was done on bags exposed on the soil surface. Tetraconazole 125 g/L microemulsion is harmless regarding the degradability of organic matter also when applied under extreme worst conditions.
Indicate if not required

[1]toxicity endpoints, used in the risk assessment, are divided by 2 ($NOEC_{corr}$ and $LC50_{corr}$) in order to take into account the differences in organic carbon content between the natural and the artificial soil.
[2]litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

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

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
Eisenia foetida	EMINENT 40 ME	Acute	0.204 mg/kg soil (plateau)	93.7	10
Eisenia foetida	EMINENT 40 ME	Chronic	0.204 mg/kg soil (plateau)	16.5	5
Other soil macro-organisms					
Collembola					

Refined risk assessment[1]: not necessary
[1] to be completed where first Tier triggers are breached

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

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

Preliminary screening data

In both performed studies the NOEC of tetraconazole 125 g/L microemulsion for emergence, growth and vegetative vigor for all the 10 species tested was determined to be corresponding to 112 g a.i./ha and the EC_{25} was higher than 112 g a.i./ha.

Laboratory dose response tests

Most sensitive species	Test substance	ER50 (g/ha)[2] vegetative vigour	ER50 (g/ha)[2] emergence	Exposure[1] (g/ha)[2]	TER	Trigger
All tested species	tetraconazole	>112	>112	4.7191 (orchards)	23.73	5
All tested species	tetraconazole	>112	>112	2.77 (sugar beet and cereals)	40.43	5

[1] exposure has been estimated based on drift factor of 15.73% (orchards) and 2.77% (sugar beet and cereals) (Ganzelmeier drift data)
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation

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

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

Test type/organism	endpoint
Activated sludge	The effects of Tetraconazole on the respiration of activated sewage sludge gave a 30-minute and a 3-hour EC_{50} greater than 1000 mg/L (the highest tested dose).

Residues definition (consider all relevant metabolites requiring further assessment from the fate section)

Compartment	Ecotoxicologically relevant residue
soil	a.s.
water	a.s.
sediment	a.s.
groundwater	a.s.

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

	RMS/EPCO proposal	ECB decision
Active substance	R50/R53 N	Xn; N R: 20/22-51/53 S: (2-)36-61
Preparation	R51/R53 N	

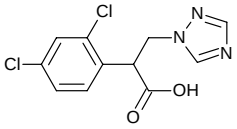
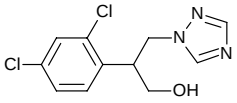
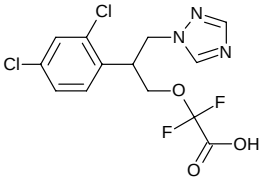
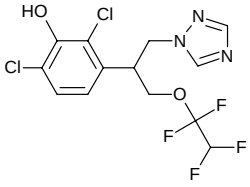
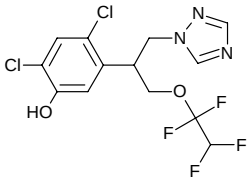
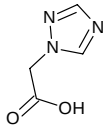
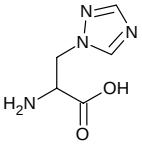
‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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
ER50	emergence rate, median
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

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
M14360-acid	2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid	
M14360-alcohol	2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propan-1-ol	
M14360-difluoroacetic acid	5-(2,4-dichlorophenyl)-2,2-difluoro-6-(1*H*-1,2,4-triazol-1-yl)-3-oxahexanoic acid [2-(2,4-dichlorophenyl)-3-(1*H*-1,2,4-triazol-1-yl)propoxy](difluoro)acetic acid	
M14360-DCP-3OH	2-(2,4-dichloro-3-hydroxyphenyl)-3-(1*H*-1,2,4-triazol-1-yl) propyl 1,1,2,2-tetrafluoroethyl ether	
M14360-DCP-5OH	2-(2,4-dichloro-5-hydroxyphenyl)-3-(1*H*-1,2,4-triazol-1-yl) propyl 1,1,2,2-tetrafluoroethyl ether	
TAA (triazole acetic acid)	1*H*-1,2,4-triazol-1-ylacetic acid	
TA (triazole aniline)	(*R*,*S*)-2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid 3-(1*H*-1,2,4-triazol-1-yl)-D,L-alanine	
THP (triazolyl hydroxy propionic acid)	(*R*,*S*)-2-hydroxy-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid