CONCLUSION ON PESTICIDE PEER REVIEW

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

etofenprox

Issued on 19 December 2008

SUMMARY

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

Italy being the designated rapporteur Member State submitted the DAR on etofenprox 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 and following a quality check on the DAR, on 14 February 2007. The peer review was initiated on 18 July 2007 by dispatching the DAR for consultation of the Member States and the sole applicant Landis Kane Consulting. 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 October 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in November-December 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 insecticide as proposed by the notifier, which comprise foliar spraying in oilseed rape, head cabbage, grapes, peach and apple for the control of biting and sucking insects. Full details of the GAP can be found in the endpoints.

[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)

The representative formulated product for the evaluation was 'TREBON 30EC', an emulsifiable concentrate (EC) containing 287.5 g/L etofenprox.

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 all compounds given in the respective residue definitions in food/feed of plant and animal origin and environmental matrices.

In the mammalian metabolism studies, etofenprox was rapidly but partially absorbed after oral administration. It was uniformly distributed through the body, and transferred via placenta and via milk. There was no evidence of bioaccumulation; etofenprox was rapidly eliminated, mainly via faeces, a major part as metabolites.
The acute toxicity was low, either by the oral, dermal or inhalation route; no eye or skin irritation was observed and no potential for skin sensitisation was found in a modified maximisation test. The main target organs of etofenprox were the liver and thyroid upon short-term or long-term exposure in the rat, which was the most sensitive species. The mouse presented also renal toxicity, but at much higher dose levels and the dog was less sensitive, showing effect only in the liver. The relevant NOAEL for short-term exposure was the dose level of 20 mg/kg bw/day from the 90-day rat feeding study; for long-term exposure, the NOAELs in rat and mouse were similar: 3.1 mg/kg bw/day in mouse and 3.7 mg/kg bw/day in rat. No potential for genotoxicity or neurotoxicity was observed. The aetiology of the formation of the thyroid adenomas observed in rats was elucidated in a mechanistic study and considered not relevant for human risk assessment. Marginally increased renal cortical tumours found only in male mice at high doses were also not considered relevant to humans. No effect on the reproduction, fertility or development was found, however, considering the increased mortality of offsprings during the lactation phase, classification with **R64, "May cause harm to breastfed babies"**, was proposed.
Further studies were provided on the plant metabolite α-CO[2], which showed that its toxicity is covered by the parent's toxicity studies.
The acceptable daily intake (ADI) of etofenprox was 0.03 mg/kg bw/day based on the long-term mouse study and applying a safety factor of 100, which is supported by the long-term rat study. The acceptable operator exposure level (AOEL) was 0.06 mg/kg bw/day based on the oral 90-day rat study, applying a safety factor of 100 and a correction factor of 30 % for low oral absorption. The acute reference dose (ARfD) was set at 1.0 mg/kg bw, based on the NOAEL of 100 mg/kg bw/day from the rabbit developmental toxicity study and a safety factor of 100. A default value of 30 % was agreed for dermal absorption.

[2] α-CO : 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate

The level of operator exposure calculated for the representative formulation "TREBON 30EC", at a maximum dose rate of 0.21 kg etofenprox/ha in high crops (grapes, peaches and apples) was below the AOEL when the use of gloves was considered; in field crops (oilseed rape and head cabbage), no personal protective equipment (PPE) was needed to achieve an operator exposure estimate below the AOEL, according to the German model. According to the UK POEM model, estimated operator exposure was above the AOEL, even when the use of PPE was considered. Estimated exposure of workers entering crops treated with etofenprox was below the AOEL, if PPE were worn (protective gloves, long-sleeved shirt and long trousers). Bystander exposure was estimated to be below the AOEL.

Concerning the plant and animal metabolism studies, the meeting of experts discussed the unusual way the experiments were conducted, using applications of a 1:1 mixture of both labelled forms in a single study, instead of two distinct radioactive labels from two separate studies. After discussion, the experts were of the opinion that such studies may only be accepted when no extensive cleavage of the parent molecule is observed. Thus, in the specific case of etofenprox, this practice could be accepted as no extensive metabolism was observed in plants and animals. Otherwise, in the case of an extensive metabolism and/or early cleavage of the parent molecule, the recovered levels of the different metabolites may be underestimated, when compared to the initial radioactive level of parent molecule. In such situation, the meeting re-enforced its opinion that metabolism studies must be conducted separately according to the different labelling forms, in order to depict the fate of each labelling portion of the molecule as completely as possible and to provide reliable quantitative information.

In plants, the metabolism of etofenprox has been investigated in rapeseed, grape and lettuce. The metabolism was limited and etofenprox was found to be the major compound of the residues, the other metabolites being detected in very low proportions, up to 7% of the TRR for the α-CO metabolite. However and considering that the α-CO metabolite was observed in proportions higher than 10 % of the etofenprox levels in the supervised residue trials, the meeting of experts decided to define the residue for risk assessment and monitoring as the "sum of etofenprox and α-CO expressed as etofenprox". Sufficient supervised residue trials were submitted to propose MRLs on rape seed (Northern GAP) and on head cabbage, grape, peach and apple (Southern GAP). The storage stability studies demonstrated that etofenprox and α-CO residues were stable under freeze storage conditions for at least two years in oil and water-containing matrices. A standard hydrolytic study was identified as a data gap and additionally, one balance study and three follow-up studies were requested for red wine and for raisin. Processing transfer factors could be calculated for some rape seed, apple and peach processed commodities.

For animals, the experts discussed the validity of the metabolism studies performed with the parent etofenprox only. Considering that the α-CO metabolite was shown to be a significant constituent of the residues in plants, the experts were of the opinion that information on the fate of this compound in the ruminant metabolism has to be requested. The parent etofenprox was found to be the major

residue in all goat and hen matrices, and the residue definition for monitoring and risk assessment was set provisionally as "etofenprox", awaiting the requested information on the α-CO metabolite. Based on the cow feeding study and the animal burden calculations, MRLs were proposed for milk and ruminant products.
The chronic and acute consumer risk assessments were performed using the EFSA and the UK PSD models. Using the MRLs proposed for plant and animal products, the calculated theoretical maximum daily intakes (TMDI) and international estimated short term intakes (IESTI) were shown to be below the ADI and ARfD values.

Degradation of etofenprox in soil under dark aerobic conditions at 20 °C occurred through oxidation at different parts of the molecule followed by breaking down in smaller moieties (DT_{50} = 7 – 57.7 days). In one study, one of the metabolites, α-CO, was observed to exceed 5 % AR in one of the soils (DT_{50} = 12 – 45 days). Unextracted radioactivity amounted to a maximum of 55.8 % AR after 55 days, and mineralization (CO_2) up to a maximum of 45.6 % AR after 120 days. Under dark anaerobic conditions at 20 °C, etofenprox is highly persistent in soil (DT_{50} = 174 days). Under these conditions metabolite 4'-OH[3] was identified as a major metabolite. Mineralization was negligible, and unextractable residue in soil amounted to 9.5 % AR after 121 days. Photolysis only slightly enhanced degradation of etofenprox in soil. PEC soil were calculated for etofenprox based on the soil half-life of 25 days for all representative uses. The meeting of experts agreed that these values could be used for the risk assessment.
According to the results of available soil batch adsorption/desorption experiments, etofenprox may be classified as immobile in soil (Koc = 8548 – 14923 mL / g). The meeting of experts identified a data gap for an additional batch soil adsorption/desorption study, but considered it not essential to finalize the EU risk assessment. The metabolites α-CO and 4'-OH were estimated to be immobile with PCKOCWIN (EPA).
Chemical hydrolysis is not expected to contribute to the environmental degradation of etofenprox. The photolysis of etofenprox is relatively rapid. The major aqueous photolysis metabolites were α-CO (max 63.6 %) and PENA[4] (max. 14.4 %). The metabolite α-CO was also found to reach up to 10% of the parent's applied amount in the outdoor mesocosm study.
On the basis of the available studies, etofenprox should be considered not ready biodegradable.
In water/sediment systems, partition of etofenprox to the sediment occurs during the first seven days. The meeting of experts agreed on the half-lives calculated for etofenprox in the whole system ($DT_{50\ \text{whole system}}$ = 6.5 days – 20.1 days). The metabolite **4'-OH** was identified as a major metabolite in the sediment phase of both systems.

[3] 4'-OH = 4'hydroxyetofenprox: 2-(4-ethoxyphenyl)-2-methylpropyl 3-(4-hydroxyphenoxy) benzyl ether
[4] PENA: 2-(4-ethoxyphenyl)-2-methylpropan-1-ol

The meeting of experts discussed the need to consider aqueous photolysis and photolysis metabolites for the EU risk assessment, and agreed that the risk assessment presented for the metabolite α-CO by the applicant could be regarded as conservative.
PEC_{SW} were calculated with FOCUS SW modelling for the relevant scenarios based on the soil half-life of 25 days. Degradation in the water phase was assumed to occur with a half-life of 1000 days, and the mean whole water/sediment system half-life was applied to the sediment phase. Step 3 and Step 4 (only oilseed rape; assuming 30m spray drift buffer zone) were calculated for the representative uses. PEC_{SW} of the aqueous photolysis metabolite α-CO was estimated to be 63.6 % of the PEC_{SW} of the parent compound. Worst case PEC_{SW} were also estimated for the sediment metabolite 4'-OH as 21.9 % of the PEC_{SW} calculated for the parent compound. The meeting of experts identified the need to recalculate PEC_{SED} for the parent compound for the uses different from oilseed rape, to take into account the accumulation of etofenprox after multiple applications and the PEC_{SED} of the metabolites α-CO and 4'-OH. The necessary $PEC_{SW\ /\ SED}$ values were provided by the rapporteur Member State in the addendum Volume 3 v3 after the meeting of experts.
Neither etofenprox nor its soil metabolite α-CO is expected to exceed the trigger of 0.1 µg / L for any of the representative uses and scenarios simulated. The environmental concentrations in air and transport through air of etofenrprox are considered negligible.

The risk assessment indicated low risk to birds and mammals for all intended uses. Refinements of the long-term risk assessment for mammals were, however, required for the uses in head cabbage, grape, peach and apple to meet the Annex VI trigger. The risk to fish-eating birds and mammals was considered to be low for all of the intended uses, as was the risk to earthworm-eating birds and mammals for the intended use in oilseed rape. Further refinements were still required to address the risk to earthworm-eating birds and mammals for the intended uses in head cabbage, grapevine, peach and apple. The acute risk to birds and mammals from consumption of contaminated drinking water from puddles was assessed as low for all intended uses of etofenprox. Etofenprox was not considered to biomagnify in the terrestrial food chain, and the risk from plant metabolites was assessed to be low. The risk to aquatic organisms was not addressed for any of the intended uses. The TER values for aquatic organisms, based on tier 1 effect data and FOCUS Step 3 and 4, failed to meet the Annex VI trigger value. The use of an endpoint from the available higher tier mesocosm study would require further supportive data. Member State experts suggested that single species tests on the most sensitive species from the mesocosm study should be provided to consolidate the confidence in the data from the mesocosm. The design of the single species tests should take into account the multi-application uses. Based on the additional studies, a relevant assessment factor should be reconsidered for a refined aquatic risk assessment. A fish full life cycle (FFLC) study was required by the Member State experts, which should be included in the aquatic risk assessment. The risk to sediment dwellers should be addressed for etofenprox and for the metabolites 4'-OH and α-CO. Also, the aquatic risk assessment for α-CO would have to be refined further for uses in head cabbage, grapevine, peach and

apple. In addition, the risk from biomagnification and potential endocrine disrupting effects on aquatic organisms should be addressed.

Hazard quotient (HQ) values indicated a high risk to bees from all intended uses. Member State experts concluded that the available field studies did not address the risk to bees, and they agreed that mitigation measures were needed for pre-flowering/flowering uses in oilseed rape, grapevine and apple to avoid exposure of bees. The Tier I risk assessment indicated a high in-field risk to *Aphidius rhopalosiphi* and *Typhlodromus pyri* for all intended uses. The off-field risk was considered to be low for *A. pyri* and *A. rhopalosiphi* for uses in oilseed rape and head cabbage, based on no-spray buffer zone of 1 and 5m, respectively. Higher tier risk assessment based on extended laboratory studies with *A. rhopalosiphi, T. pyri, Orius laevigatues* and *Chrysoperla carnea* still indicated a high in-field risk to non-target arthropods. The potential for in-field recovery was not addressed in the draft assessment report. The higher tier off-field risk assessment indicated a low risk to non-target arthropods for uses in oilseed rape and head cabbage, with no-spray buffer zones of 1 and 5m, respectively. For uses in grapevine, the assessment indicated a need for a no-spray buffer zone of 10m to identify a low risk. Further refinements were required to address the off-field risk to non-target arthropods for uses in peach and apple.

The risk to earthworms, non-target micro- and macro-soil organisms and non-target plants was assessed as low for all intended uses.

Key words: etofenprox, peer review, risk assessment, pesticide, insecticide

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, 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. Etofenprox is one of the 79 substances of the third stage, part A, covered by the 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 etofenprox, hereafter referred to as the draft assessment report, received by the EFSA on 15 July 2005. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report on 14 February 2007. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the revised version of the draft assessment report was distributed for consultation on 18 July 2007 to the Member States and the sole applicant Landis Kane Consulting 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 with Member States on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.
Taking into account the requested information received from the notifier, a scientific discussion took place in experts' meetings in October 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 November-December 2008 leading to the conclusions as laid down in this report.
During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

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

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

- the comments received;
- the resulting reporting table (revision 1-2, 17 July 2008)

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 (revision 2-1, 19 December 2008).

Given the importance of the draft assessment report including its addendum (compiled version of November 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

Etofenprox is the ISO common name for 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether (IUPAC).

Etofenprox belongs to the class of pyrethroid ether insecticides. It acts on the nervous system of insects disturbing the function of neurons by interaction with the sodium channel. Etofenprox has insecticide activity by contact and ingestion, has a broad spectrum of action on a wide variety of pests, with fast knockdown. Etofenprox is used in agriculture on oilseed rape, head cabbage, grape, peach and apple against sucking and biting insects including aphids, thrips, moths, leaf rollers and leafhoppers at adult and larval stage.

The representative formulated product for the evaluation was 'TREBON 30EC', an emulsifiable concentrate (EC) containing 287.5 g/L etofenprox, registered under different trade names in Europe.

Full details of the GAP can be found in appendix 1.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of etofenprox technical could not be concluded on, as the PRAPeR 56 meeting of experts (October 2008) did not accept the specification for the active substance. The minimum purity of the technical etofenprox in the existing FAO specification (471/TC(July 2007)) is 980 g/kg.

The PRAPeR 56 meeting of experts considered that the 5-batch data cannot be regarded as representative based on the evaluation for the FAO specification, and proposed a data gap for the applicant to provide a new representative 5-batch data and a specification of the technical active substance. The information regarding the confirmation of the identity of the impurities in the technical material was evaluated by the rapporteur Member State in an addendum, however in view of the restrictions concerning the acceptance of new (i.e. newly submitted) 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.

Since the minimum purity was not concluded on, the specification 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 etofenprox or the respective formulation. However, the following data gap was identified:

– surface tension of the neat formulation to confirm the need (or not) for the classification with phrase R65

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

Adequate analytical methods are available for the determination of etofenprox in the technical material and in the representative formulation (CIPAC methods 471/TC/M/3 and 471/EC/M/3, GC-FID), 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.

Residues of etofenprox and its metabolite α-CO[5] in food of plant origin can be monitored by GC-MS with LOQs of 0.01 mg/kg for both etofenprox and α-CO in oilseed rape, head cabbage, grape (bunches), peach and apple. The multi-residue method DFG S19 and also the (MRM) 1 are applicable for the determination of residues of etofenprox and its metabolite α-CO in food of plant origin.

Residues of etofenprox and its metabolite α-CO in food/feed of animal origin are determined by GC/MS with LOQ = 0.01 mg/kg for etofenprox and α-CO in meat and egg, and with LOQ = 0.01 mg/L for etofenprox and α-CO in milk.

Residues of etofenprox and α-CO in soil can be monitored by GC/MS with LOQ = 0.01 mg/kg, both for etofenprox and α-CO.

Adequate GC/MS methods are available to monitor residues of etofenprox and α-CO in water with LOQ = 0.05 µg/L in drinking and ground water, both for etofenprox and α-CO, and with LOQ = 0.01 µg/L in surface water, respectively.

GC-MS method is available to monitor etofenprox and α-CO residues in air with LOQ of 1 µg/m^3 for both compounds.

Analytical methods for the determination of residues in body fluids and tissues are not required as etofenprox is not classified as toxic or highly toxic.

2. Mammalian toxicology

Etofenprox was discussed at the PRAPeR 59 meeting of experts on mammalian toxicology in October 2008 on the basis of the draft assessment report (June 2005 and revised version of February 2007), the addendum 2 of May 2008 and the addendum 2, v2 of September 2008.

The technical specification of the active substance was not agreed by the PRAPeR 56 meeting on physical and chemical properties, however the experts at PRAPeR 59 concluded that the toxicological batches cover the specification as proposed in the addendum 2 to Volume 4 (May 2008). This will have to be confirmed when agreed specification is available.

[5] α-CO: 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate

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

Toxicokinetic properties of etofenprox were comprehensively evaluated in the rat using an approximate 1:1 mixture of [1-^{14}C-propyl]-etofenprox and [α-^{14}C-benzyl]-etofenprox. Further studies were performed in pregnant and lactating females to evaluate the placental and milk transfer of etofenprox on the metabolism in dogs, and an investigative study was also performed to determine if the plant metabolite α-CO was formed *in vivo* in rats.

The use of a mixture of two radiolabel positions rather than conducting separate studies was considered by the experts. They agreed that no general statement can be given on the approach in itself, but this could be considered on a case-by-case basis. For etofenprox, it was clear that the structure was not cleaved in the main metabolites; therefore no further data was required.

Oral absorption of etofenprox was rapid but limited based on the radioactivity found in the urine (2-3.3 % of the administered dose), bile (15.2 to 29.6 % of the administered dose) and carcass (2.8-5.9 % of the administered dose) after 48 hours; an average value between males and females of **30 %** was agreed by the meeting. It was noted that other assessments[6] concluded on a higher value for oral absorption of 65 %, based on the high amount of metabolites found in faeces that would represent an absorbed fraction of the substance. No justification was found to dismiss the data obtained from the bile excretion study, uncertainties remained on the rate of metabolism occurring in the gastrointestinal tract, and therefore the experts considered that oral absorption should be derived from the bile excretion study.

Maximum mean plasma concentrations occurred 3 to 5 hours post-treatment. Tissue distribution was extensive with higher concentrations found in fat, adrenal glands, liver, ovaries and thyroid. Etofenprox is transferred via the placenta to the foetus but placental and foetal concentrations were low relative to maternal plasma concentration. Unchanged etofenprox is actively secreted into the maternal milk. Tissue concentrations declined rapidly in all tissues, only fat presented a higher half-life of approximately 5 to 8.5 days. Excretion proceeded rapidly, predominantly via faeces and was almost complete within five days. Overall, faecal excretion amounted to 86.4 – 90.4 % whereas urinary elimination amounted to 6.3 – 10.7 %.

Metabolites represented the major components in faecal extracts (about 54 % of the administered dose); two major metabolites were identified as DE[7] (19.5-25.1 %) and 4'-OH[8] (7.2-13.8 %), resulted from O-deethylation of the ethoxyphenyl moiety and by ring hydroxylation of the phenoxybenzyl moiety. These metabolites were subsequently eliminated as glucuronide or sulphate conjugates. These metabolites were also found in bile and the liver; no parent compound was found in bile, but almost all radioactivity observed in fat corresponded to the parent compound. Most metabolites in urine samples could not be identified.

[6] Assessment report of etofenprox within the context of Directive 98/8/EC concerning the placing of biocidal products on the market – product-type 8 (wood preservatives), 13 September 2007; 1993 Joint FAO/WHO Meeting on Pesticide Residues Evaluation Part II, Toxicology, n. 863

[7] DE = desethyletofenprox: 3-phenoxybenzyl 2-(4-hydroxyphenyl)-2-methylpropyl ether

[8] 4'-OH = 4'-hydroxyetofenprox: 2-(4-ethoxyphenyl)-2-methylpropyl 3-(4-hydroxyphenoxy) benzyl ether

Metabolism in dogs was similar to the one observed in rats, however in dogs, unchanged etofenprox was the major component recovered in faeces.

2.2. ACUTE TOXICITY

A battery of acute toxicity tests in rat, mouse and dog were submitted, including oral, subcutaneous, intraperitoneal and percutaneous routes. Some tests were conducted before the adoption of GLP and/or specific guidelines; however recent guideline and GLP-compliant studies confirmed the conclusions obtained with older studies.

Etofenprox presented low acute toxicity, either by the oral, dermal or inhalation route; no skin or eye irritation was observed. No skin sensitisation effects were noted in a modified maximization test in guinea pig.

2.3. SHORT TERM TOXICITY

The oral short-term effects of etofenprox were investigated in a 90-day feeding study in rat and in mouse, and a 1-year feeding study in dog. Other routes were tested in a 28-day dermal and a 90-day inhalation toxicity studies in rat.

The liver and thyroid gland were the target organs in the rat upon oral administration at the dose level of 120 mg/kg bw/day and up. The hepatic response was characterised by hepatocyte enlargement and clinical evidence of liver dysfunction affecting fat metabolism and the synthesis of blood clotting factors. The effects on the thyroid was characterised by an increase in the number of thyroid microfollicles and reduced levels of circulating thyroxine. The NOAEL was the dose level of **20 mg/kg bw/day.**

The liver, kidneys and haemolymphoreticular system were identified as target organs in the mouse, but at a substantially higher dose level than in the rat (1975 mg/kg bw/day), which was shown to exceed the maximum tolerated dose. The NOAEL in mouse was 375 mg/kg bw/day.

In the dog, the liver was identified as a target organ as well, but hepatic effects were minimal and reversible, and occurred only at the high dose level of 339 mg/kg bw/day; the NOAEL was 32.2 mg/kg bw/day.

Similar histomorphological effects in the liver and thyroid were observed in rats upon inhalation of 0.21 mg etofenprox/L air, but there was no clinical evidence of effects on blood clotting time or circulating thyroxine levels. Additionally, inhalation of etofenprox affected the adrenal glands as shown by elevated adrenal weight and increased adrenal cortical thickness. The NOAEC was 0.042 mg/L air.

Dermal application of etofenprox did not produce any evidence of systemic toxicity up to 1000 mg/kg bw/day; however, minor local skin irritation occurred at all dose levels (from 400 mg/kg bw/day and up), which were reversible 14 days after cessation of dosing.

2.4. GENOTOXICITY

Etofenprox has been evaluated *in vitro* for point mutations in Ames test with *S. typhimurium*, for gene mutations in Chinese hamster V79 cells, for chromosomal aberrations in cultured human peripheral lymphocytes and for unscheduled DNA synthesis in human cells (cell line Hela S3), and *in vivo,* for clastogenicity on bone marrow erythrocytes in the micronucleus test. No potential for genotoxicity or clastogenicity was found.

2.5. LONG TERM TOXICITY

Long-term toxicity of etofenprox was examined in a 2-year study in rat (110 weeks) and in mouse (108 weeks).

No further target organs were identified in the long-term studies in rats and mice than the one identified in short-term studies. In the rat, the liver and thyroid were confirmed as target organs for non-neoplastic effects. The NOAEL was the dose level of **3.7 mg/kg bw/day** based on an increased incidence of eosinophilic hepatocytes at the next dose of 25.5 mg/kg bw/day. Additionally, reduced bodyweight gain, increased liver, kidney and thyroid weights, hepatocyte enlargement, increased thyroid cystic follicles and prolonged blood clotting times were observed at the highest dose of 186.7 mg/kg bw/day. This high dose level presented also an increased incidence of benign thyroid follicular cell adenomas. The aetiology of this effect was investigated in a mechanistic study (see below in point 2.8) and on this basis, the tumours were not considered relevant for human risk assessment.

In the mouse, the kidneys were identified as the main target organ. The NOAEL was the dose level of **3.1 mg/kg bw/day** based on an increased incidence of dilated/basophilic renal tubules at the next dose of 10.4 mg/kg bw/day and up. At higher dose renal lesions were characterised as increased incidence of cortical scarring and pale coloration, organ enlargement, dilated/cystic Bowman's capsules, dilated medullary tubules, focal loss of tubules, prominent interstitial papillary tissue and papillary mineralization. The severity of the renal lesions contributed to the increased mortality observed at the highest dose of 546.9 mg/kg bw/day.

The relevance of renal cortical tumours, observed only in males at the highest dose level, was discussed by the experts. Their incidence was only slightly above the level of significance, no renal tumours were seen in the rat, and the compound was not shown to be genotoxic. The meeting concluded that they were not relevant for humans and that no classification regarding carcinogenicity of etofenprox was required.

2.6. REPRODUCTIVE TOXICITY

Reproductive toxicity of etofenprox was tested in rat, in two multigeneration reproduction toxicity studies (one by gavage and one by dietary administration), a developmental/fertility toxicity study, and a further developmental study that included the rearing to maturation of the F_1 generation for assessment of behavioural development and reproductive capacity. Two developmental toxicity

studies were conducted in rabbits. A rat developmental neurotoxicity study was also submitted and is reported below under point 2.7.

Reproduction toxicity

No effect on reproductive parameters was observed in neither of the two-generation toxicity studies up to the highest dose tested of 246 mg/kg bw/day (when administered through the diet) or 5000 mg/kg bw/day (when administered by gavage). The NOAEL for parental and offspring's toxicity was the dose level of 4.3 mg/kg bw/day based on increased kidney and liver weights; higher dose level exhibited also reduced bodyweight/pre-weaning weight gain, minimally increased pup mortality during the lactation phase, increased thyroid weight and histopathological changes in the liver, kidneys and thyroid.

Developmental toxicity

No developmental effect was observed in neither of the two rat studies, therefore the developmental NOAEL was the highest dose tested of 5000 mg/kg bw/day. As this dose produced slightly reduced maternal bodyweight gain, the maternal NOAEL was 250 mg/kg bw/day.

In rabbits, maternal deaths and abortions were observed from the low dose level and up. The experts agreed that these effects were not dose-related at low doses and not reproducible in the second study up to 250 mg/kg bw/day. Therefore the NOAEL for both maternal and developmental toxicity was established at 100 mg/kg bw/day based on the occurrence of reduced maternal bodyweight gain and food consumption, abortions, mortality and slightly increased post-implantation loss and intrauterine growth retardation at the high dose of 300 mg/kg bw/day.

2.7. NEUROTOXICITY

Neurotoxicity was investigated in an acute study, a 13-week dietary study, and a developmental neurotoxicity study, all performed in rats.

In the acute neurotoxicity study, no adverse effect or sign of neurotoxicity including functional and neurohistopathological examinations was found up to the highest dose level of 2000 mg/kg bw.

No sign of neurotoxicity was observed in the 13-week study, increased liver weight at all dose levels was considered by the experts to represent an adaptive response to etofenprox treatment. The NOAEL was the dose level of 299 mg/kg bw/day, based on decreased bodyweight seen at the highest dose of 604 mg/kg bw/day.

In the developmental neurotoxicity study, maternal toxicity consisted of a transient decrease in weight gain at the mid-dose level of 79.2 mg/kg bw/day and up and, in the detailed functional observation battery (FOB) examination, a consistently higher rearing activity at the high dose of 238 mg/kg bw/day. Impaired pre-weaning survival and subcutaneous haemorrhagic lesions occurred in the offsprings at the high dose, while ocular lesions, possibly related to intraocular haemorrhage, were observed down to the mid-dose level. The NOAEL was the dose level of 28.4 mg/kg bw/day.

Considering the increased mortality seen in offprings exposed during weaning (exposed to etofenprox via the milk) in this study as well as in the multigeneration study (see point 2.6 above), the experts considered appropriate to propose classification with **R64 "May cause harm to breastfed babies".**
It was acknowledged that mixed exposure via the milk and treated diet could occur, however it could not be ruled out either, that this effect was not the result of exposure through milk.

2.8. FURTHER STUDIES

Metabolites

Supplementary studies were conducted on the plant metabolite α-CO.

α-CO

An absorption, distribution, metabolism and excretion study conducted with α-CO in rats showed the presence of the metabolites *m*-PB-acid[9] and 4'-OH-PB-acid[10], while no α-CO was recovered in urine. These metabolites were seen also in the metabolism study conducted with etofenprox as minor metabolites in urine; therefore it was taken as evidence that α-CO is a transient metabolite in the rat metabolism of etofenprox.

The oral LD_{50} of α-CO was higher than 5000 mg/kg bw in rat; the dermal LD_{50} was higher than 2000 mg/kg bw also in the rat.

A 4-week and a 13-week dietary toxicity studies with α-CO indicated the liver, kidneys and thyroid as target organs, although in the liver and thyroid, there were no histopathological changes. The effects were confined to minor changes in plasma protein and enzyme levels, and reduced circulating T_4[11] concentration. The effects of α-CO on the kidneys were characterised by increased organ weight and slight renal tubular hypertrophy, but without evidence of overt renal dysfunction. The NOAEL was the dose level of 54 mg/kg bw/day compared to the NOAEL of 20 mg/kg bw/day obtained in the 13-week study with etofenprox.

A bacterial reverse mutation assay in *Salmonella typhimurium* and *Escherichia coli*, a lethal DNA damage assay in *E. coli*, and an *in vitro* assessment of the clastogenic activity of α-CO in cultured human peripheral lymphocytes gave all negative results.

The experts noted that the chemical structure of α-CO is related to the parent etofenprox; no higher toxicity was evidenced from the data available in comparison to the parent compound, and therefore the meeting concluded that, if necessary, the reference values of etofenprox could be used also for the metabolite α-CO.

[9] m-PB-acid: 3-phenoxybenzoic acid
[10] 4'-OH-PB-acid: 3-(4-hydroxyphenoxy)benzoic acid
[11] T_4: thyroid hormone thyroxine

Mechanism studies

Thyroid function and hepatic microsomal enzyme induction

A 4-week dietary investigative study on the induction of specific hepatic microsomal enzymes and their influence on the pituitary-thyroid homeostasis, and thyroid morphology and cytology in rats was conducted with etofenprox. The intention was to elucidate the aetiology of the thyroid adenoma formation observed in the rat combined chronic toxicity/carcinogenicity study.

The liver was identified as the primary target organ, characterised by increased microsomal protein content, increased UDPGT[12] activity (the main hepatic enzyme responsible for the metabolism of thyroid hormones), and hepatic hypertrophy. Treatment-induced effects that were considered to be secondary to hepatic microsomal enzyme induction included a depression of circulating T_4 hormone, an increase in serum TSH[13] concentration, mild thyroid follicular cell proliferation and increased thyroid weight.

The NOAEL for the primary effect on the liver was 81.2 mg/kg bw/day based on the increased incidence of UDPGT activity at 316 mg/kg bw/day.

It is recognised that a sustained elevation in circulating TSH concentration can lead initially to hypertrophy of thyroid follicular cells, followed by hyperplasia and ultimately a greater risk of increased incidence of thyroid adenomas. This mechanism of action is also recognised as being a rat specific mode of action that is not relevant for humans.

General pharmacology

Etofenprox was tested for its general pharmacological properties on the central nervous system (CNS), on the respiratory and circulating systems, on smooth muscle, on the neuromuscular junction, on autonomic ganglia, on the urinary volume and components, and on blood coagulation. No biologically significant pharmacological activity was observed in none of these systems.

2.9. MEDICAL DATA

Comprehensive medical surveillance of workers continually involved in the manufacture of etofenprox for up to five years and three months demonstrated the absence of occupational adverse health effects. No clinical case or poisoning incident relating to etofenprox is known to the applicant.

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

ADI

In the draft assessment report, the rapporteur Member State proposed an ADI of 0.03 mg/kg bw/day based on the long-term mouse study presenting a NOAEL of 3.1 mg/kg bw/day and applying a safety factor of 100. This approach was agreed by the experts at the meeting, which is supported by the

[12] UDPGT : uridine diphosphoglucuronosyltransferase
[13] TSH : thyroid stimulating hormone

long-term rat study with a NOAEL of 3.7 mg/kg bw/day. The **ADI for etofenprox was established at 0.03 mg/kg bw/day**

AOEL

Initially in the draft assessment report, the rapporteur Member State proposed an AOEL of 0.2 mg/kg bw/day based on the 13-week oral rat study with a NOAEL of 20 mg/kg bw/day, a safety factor of 100 and no correction related to oral absorption. In the addendum 2 dated May 2008, the rapporteur Member State proposed to correct the AOEL taking into account a limited oral absorption of 35 %, resulting in an AOEL of 0.07 mg/kg bw/day. The rat was considered the most sensitive species; the findings observed in the multigeneration study were found to be in a similar range as those observed in the 13-week study, therefore the meeting agreed with the rapporteur Member State's approach. However, as oral absorption was set at 30 %, the resulting **AOEL is 0.06 mg/kg bw/day.**

ARfD

The rapporteur Member State proposed in the draft assessment report an ARfD of 0.2 mg/kg bw based on the same 13-week study in the rat (NOAEL of 20 mg/kg bw/day) and a safety factor of 100.
As etofenprox elicited low toxicity, is not a developmental or neurotoxic compound, the need to set an ARfD was discussed. Acute effects were however obtained in the developmental toxicity study in rabbit with a NOAEL of 100 mg/kg bw/day, therefore the meeting agreed to set the **ARfD at 1.0 mg/kg bw** based on this study and applying a safety factor of 100.

2.11. DERMAL ABSORPTION

An *in vivo* rat dermal absorption study was provided using the active substance rather than the representative formulation, an emulsifiable concentrate (EC). It resulted in a 33 % dermal absorption that is applicable only to the active substance. The meeting concluded that the results cannot be extrapolated to an EC formulation, therefore default value should be considered. Based on the molecular weight and log P_{ow}, the default value of 100 % would be applicable, but not realistic, however it could be corrected by the enteral absorption rate of 30 %.
The experts agreed that this **default value of 30 %** could be used according to the guidance document[14] on dermal absorption, leaving to the Member States to consider the need for an adequate study conducted with their respective representative formulations.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Estimations of operator, worker and bystander exposure were recalculated in the addendum to Volume 3 v3 of November 2008 based on the parameters agreed at the PRAPeR 59 meeting of experts.

[14] Guidance Document on Dermal Absorption, Sanco/222/2000 rev. 7, 19 March 2004

The representative plant protection product "TREBON 30EC" is an emulsifiable concentrate (EC) formulation containing 287.5 g etofenprox/L.
It is applied as foliar spray using vehicle mounted sprayers to oilseed rape, head cabbage, grapes, peaches and apples up to 0.21 kg etofenprox/ha.

Operator exposure

The operator exposure estimates were calculated using both the German[15] and the UK POEM[16] models. According to the German model, operator bodyweight is assumed to be 70 kg, 20 ha are treated per day when field crops are considered, 8 ha/day for high crops and 1 ha/day for hand-held equipment. According to the UK POEM, operator bodyweight is 60 kg, 50 ha are treated per day when field crops are considered, 15 ha/day for high crops and 1 ha/day for hand-held equipment. Packs of 10 L formulation and unspecified design were assumed, except for knapsack applications where 0.5 L bottles were assumed.

Estimated operator exposure presented as % of AOEL (0.06 mg/kg bw/day) according to the German model

German model	No PPE	With PPE during M/L	With PPE during M/L & application
Oil seed rape (0.060 kg ai/ha) FCTM	38.3	nc	nc
Head cabbage (0.150 kg ai/ha) FCTM	95	43.3	nc
Grapes (0.150 kg ai/ha) HCTM	120	99	15
Grapes (0.150 kg ai/ha) HCHH	263.3	46.6	nc
Peach & apple (0.210 kg ai/ha) HCTM	166	nc	21.6

PPE: gloves
M/L: mixing and loading
FCTM: field crop tractor mounted; HCTM: high crop tractor mounted; HCHH: high crop hand-held
nc: not calculated

[15] Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protections); Mitteilungen aus der Biologischen Bundesanstalt für Land- und Forstwirschaft, Berlin-Dahlem, n° 277, 1992
[16] Predictive Operator Exposure Model (POEM – UK MAFF, 1992)

Estimated operator exposure presented as % of AOEL (0.06 mg/kg bw/day) according to the UK POEM model

UK POEM	No PPE	With PPE
Oil seed rape (0.060 kg ai/ha, 400 L spray/ha) tractor mounted/trailed boom sprayer: hydraulic nozzles	1300	131.6
Head cabbage (0.150 kg ai/ha, 200 L spray/ha) tractor mounted/trailed boom sprayer: hydraulic nozzles	4011	416
Grapes (0.150 kg ai/ha, 1000 L spray/ha) tractor mounted broadcast air assisted sprayer	1401	210
Grapes (0.150 kg ai/ha, 1000 L spray/ha) knapsack sprayer*	152	63
Peach (0.210 kg ai/ha, 1500 L spray/ha) tractor mounted broadcast air assisted sprayer	2643	330
Apple (0.210 kg ai/ha, 1200 L spray/ha) tractor mounted broadcast air assisted sprayer	2713	368

PPE: gloves during mixing, loading & application
* as this model refers to field crops, it is not strictly relevant for grapevines

According to the UK POEM, estimated exposure of operators was above the AOEL even considering the use of personal protective equipment (gloves); according to the German model, the estimated exposure of operators was below the AOEL without PPE for field crop scenarios, and for high crop scenarios, if PPE were worn, as gloves during mixing/loading and application.

Worker exposure

Estimation of worker exposure was performed according to Krebs *et al.* 2000[17]. Transfer coefficient of 5000 [cm^2/person/h] was considered for field crops and worst-case (conservative) value of 30000 [cm^2/person/h] for the activities in vegetable fields, vineyards and orchard applications. Foliar dislodgeable residue default value of 1 [µg etofenprox/cm^2 per kg etofenprox/ha], 60 kg for worker bodyweight, and a working period of 8 hours/day were used.

[17] Krebs B, *et al*. "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.

Estimated worker exposure presented as % of AOEL (0.06 mg/kg bw/day)

Crop	No PPE	With PPE
Oil seed rape (0.060 kg ai/ha)	20	1
Head cabbage (0.150 kg ai/ha)	300	15
Grapes (0.150 kg ai/ha)	300	15
Peach (0.210 kg ai/ha)	420	21
Apple (0.175 kg ai/ha)	350	16.6

PPE: protective gloves, long-sleeved shirt and long trousers

The estimated exposure to etofenprox during re-entry operations does not exceed the AOEL, if PPE is worn.

EFSA note: The number of applications proposed in the GAP was not taken into consideration for the calculation of worker exposure, as the experts considered that this approach would be over conservative. Indeed, when the applications are foreseen in the early growth stage of the crop (pre-flowering, flowering, blossom or petals falling), these applications should not be added to the ones done pre-harvest. In some cases however, two applications are foreseen at 1 to 2 weeks interval before harvest, which could increase worker exposure to the active substance. In such cases, even if a worst case of twice the exposure is considered, the outcome would still be maintained, i.e. the estimated worker exposure would not exceed the AOEL, provided that PPE is worn.

Bystander exposure

Bystander exposure assessment was based on published studies (Lloyd and Bell, 1983[18] and Lloyd *et al*, 1987[19]), in which measurements of simulated bystander exposure were made during field crop spraying and broadcast air assisted applications for a bystander positioned at 8 m downwind from the edge of the treatment area. Assuming a bodyweight of 60 kg and no exposure reduction from clothing, the resulting level of exposure to etofenprox for unprotected bystanders represented between 0.15 to 5.5 % of the AOEL for the different representative scenarios.

The rapporteur Member State provided also a risk assessment for residential exposure to etofenprox in the addendum 2 v2. The meeting took note of it, however the experts considered that these models were not yet sufficiently recognized to be discussed and agreed.

[18] Lloyd G.A. and Bell G.J. (1983). Hydraulic nozzles: comparative spray drift study (UK MAFF/ADAS).
[19] Lloyd G.A., Bell G.J., Samuels S.W., Cross J.V. and Berrie A.M. (1987). Orchard Sprayers: Comparative operator exposure and spray drift study (UK MAFF/ADAS).

3. Residues

Etofenprox was discussed at the PRAPeR 60 meeting of experts for residues in October 2008 (round 12).

First, the experts discussed the unusual way the plant- and animal metabolism studies have been carried out. Studies were performed using applications of a 1:1 mixture of both labelled forms ([^{14}C-benzyl]-etofenprox and [^{14}C-propyl]-etofenprox) in a single experiment, instead of two distinct radioactive labels from two separate studies.

In the specific case of etofenprox, the meeting agreed that such practice could be accepted, since no extensive metabolism of the parent molecule was observed in plants and animals. The parent compound remained the major component of the residue and no extensive cleavage of the molecule was observed.

On the other hand and on a general point of view, in the case of an extensive metabolism and/or early cleavage of the parent compound, the recovered levels of the different metabolites may be underestimated when compared to the initial level of molecule (that takes into account the specific activity of both labels). In such a case, a specific part of the radioactivity might be missed by volatilization or incorporation in some matrices. Quantitatively, a metabolism study performed with a mixture of radioactive labels may be less reliable than two studies performed with two separate labels, even if such a practice may be acceptable on a qualitative point of view.

Finally, the experts were of the opinion that such metabolism studies performed with a mixture of different radioactive labels may only be accepted in the specific case, where no extensive cleavage of the parent molecule occurred. The meeting re-enforced its opinion that metabolism studies must be conducted separately according to the different labelling forms in order to depict the fate of each labelling portion of the molecule as completely as possible, and also to provide reliable quantitative information.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The metabolism of etofenprox has been investigated in three crop groups: oilseed/pulse crops (rapeseed), fruit crops (grape) and leafy crops (lettuce). Studies were performed using application of a 1:1 mixture of [^{14}C-benzyl]-etofenprox and [^{14}C-propyl]-etofenprox at dose rates representative of the supported uses (120 to 300 g a.s./ha) and at exaggerated dose rates of 1200 to 3000 g a.s./ha.

The metabolism in plants was limited and etofenprox was found to be the major compound of the residues, accounting for 62% of the TRR (0.02 mg/kg) in rape seeds, 85% (2.2-4.7 mg/kg) in grapes and 88% (2.1 mg/kg) in lettuce, considering the normal application rates. In a first step and to a limited extent, the metabolism starts with the oxidation of the benzylic carbon leading to the α-CO metabolite, the hydrolysis of ester links to yield the DE (desethyl-etofenprox) and DP (desphenyl-

etofenprox)[20], and finally an aromatic hydroxylation leading to the 4'-OH metabolite. These metabolites were detected in very low proportions, below 0.5%, except for the α-CO, which was observed in the range of 1% to 7% of the TRR. In a second step, further metabolism occurs by the cleavage of the first generation metabolites at the oxygen bound, resulting in the formation of the metabolites *m*-PB-acid, *m*-PB-alcohol[21], EPMP[22] and PENA[23], which were detected in low proportions, below 0.7% of the TRR (generally below 0.2%).

The meeting of experts discussed whether the grape metabolism study should be considered as sufficient to support the representative use on vineyard, since it was conducted with a single application instead of four as proposed in the intended uses. The experts agreed that four treatments with applications at earlier growth stages might change the proportions of the different metabolites. This was confirmed by the residue trials, where the ratio α-CO/parent was higher than the ratio calculated in the metabolism study (*c.a.* 22% and 5%, respectively). However and considering the limited metabolism of etofenprox in grape, the fact that all identified metabolites were recovered at a very low level (<1 % of the TRR), and that the most relevant metabolite (α-CO) was included in the residue definitions, the meeting concluded on the acceptability of the grape metabolism, even if it was performed with a single application.

Considering that the α-CO metabolite was observed in the grape, apple and peach supervised residue trials in proportions higher than 10% of the etofenprox levels, the meeting decided to define the residue for risk assessment as the "sum of etofenprox + α-CO expressed as etofenprox". For monitoring, the meeting discussed whether the residue definition could be limited to the parent compound only, taking into account that a conversion factor could be derived from the supervised residue trials where the α-CO residue levels were calculated to be about 12%, 14% and 22% of the etofenprox levels in peaches, apples and grapes, respectively. Finally and taking into account that the TMDI calculations were close to 100% of the ADI for some UK diets, the majority of the experts were of the opinion that the residue definition for monitoring should also include the metabolite α-CO, considering that it should be better to base further risk assessments on the measured residue levels, rather than to derive these levels by the use of a conversion factor.

Supervised residue trials were submitted to support representative uses on rape seed in Northern Europe only, and on cabbage, grapes, peach and apple in Southern Europe. Samples were analysed for the parent etofenprox and its metabolite α-CO, respectively, achieving a LOQ of 0.01 mg/kg for each individual compound (global LOQ 0.02 mg/kg). The meeting agreed that the requested use on "cabbage" has to be understood as "head cabbage", a minor crop in Southern EU. The highest values

[20] DP = desphenyl-etofenprox: 3-hydroxybenzyl 2-(4-ethoxyphenyl)-2-methylpropyl ether
[21] *m*-PB-alcohol: (3-phenoxyphenyl)methanol
[22] EPMP: 2-(4-ethoxyphenyl)-2-methylpropanoic acid
[23] PENA: 2-(4-ethoxyphenyl)-2-methylpropan-1-ol

of 0.14 mg/kg observed on cabbage in one trial was removed from the dataset, taking into account the applicant's explanation stating that the external wrapper leaves were not removed from the cabbage at harvest, as recommended in the sampling guidelines.

The storage stability studies demonstrated that residues of etofenprox and α-CO were stable under deep-freeze storage conditions for at least two years in rape seeds, cabbage and grapes. The additional storage stability data on peaches and apples, presented in the addendum I of March 2007, could not be considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007. However, the experts were of the opinion that these new results have to be considered as additional information only, since the initial study performed on cabbage and grapes is representative of the "high water content matrices group" that covers peach and apple matrices.

The standard hydrolytic study submitted during the peer review process in the addendum I of March 2007 could not be considered in the peer review, as laid down in Commission Regulation (EC) No 1095/2007, and the meeting of experts confirmed that such a study has to be provided. The explanation provided by the applicant, arguing that the results of the hydrolytic study presented under chapter B.2, are sufficient to predict that residues remain unchanged under hydrolytic conditions, was considered as not acceptable by the meeting.

Processing studies were provided for rape seeds, grapes, peaches and apples. Grapes were only processed to juice. No information was available for wine, as the additional data presented in the addendum I of March 2007 concerning the process to wine, could not be considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007. Thus, the experts confirmed the data gap initially identified for wine in the DAR, and one balance study and three follow-up studies for red wine and for raisin were requested. On the other hand, the new processing studies performed on apple and peach were taken into account in addition to the data initially presented in the DAR, the transfer in the processed fractions being higher in these new studies and therefore considered as adverse data. Finally and based on a total of four experiments, a mean transfer factor of 3.0 was derived for etofenprox and α-CO for the wet fruit pomaces. This pomace transfer factor was used in the animal burden calculation (see point 3.4).

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

A rotational crop study simulating a crop failure was provided. Etofenprox was applied once onto the bare soil as a 1:1 mixture of both labelled forms ([^{14}C-benzyl] and [^{14}C-propyl]-etofenprox) at a dose rate of 312 g a.s./ha (1X the cabbage dose rate). Lettuce, carrot and barley were sown four weeks

after application. The uptake of radioactivity was found to be limited, the maximum radioactive residue levels at harvest being 0.07 mg/kg in barley straw, 0.02 mg/kg in lettuce leaves and 0.007 mg/kg in carrot roots. Based on these results it was concluded that no significant residues of etofenprox and its metabolite α-CO are expected in rotational crop.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

As for plants, the goat and hen metabolism studies were performed using a 1:1 mixture of the two etofenprox labelled forms. The meeting discussed the validity of these studies as they were performed with the parent compound etofenprox only, whereas the α-CO metabolite was shown to be a significant constituent of the residues in plants (up to 12-22% of the etofenprox residue levels). Thus, the experts were of the opinion to request the applicant to provide information on the fate of this compound in the ruminant metabolism.

The metabolic fate of etofenprox was investigated in goat dosed for seven consecutive days at a rate of 1.5 and 13.5 mg/kg feed, the high dose rate being about an 8X and 23X dose rate for beef and dairy cattle, respectively. A large part of the radioactivity (*c.a.* 95%) was excreted in urine and faeces. 0.5-0.8% were recovered in milk and 2.9-3.7% in organs and tissues. The parent etofenprox was found to be the major residue in all goat matrices accounting for more than 95% of the TRR in milk, muscle and fat, and for 38 and 33% in liver and kidney, the highest residue level being observed in fat (0.72 mg/kg for the high dose). DE and *m*-PB-alcohol metabolites were also identified in liver (*c.a.* 10% TRR), and EPMP and *m*-PB-acid in kidney (*c.a.* 25%), but accounting for low absolute levels, below 0.025 mg/kg for the high dose group. The α-CO metabolite was not detected in the goat matrices but this compound was not fed to animals, and it cannot be concluded that α-CO is of no concern in ruminant matrices.

The hen metabolism study was carried out on animals dosed during 14 consecutive days at a level of 0.9 and 9.6 mg/kg feed. As for goat, a large part of the administered radioactivity (82-91%) was found in the excreta and 0.6% and *c.a.* 2.5% in eggs and organs/tissues, respectively. Etofenprox was always detected as the major residue accounting for more than 80% of the TRR in eggs, muscles and fat, except in liver, where the parent compound represented only 15% TRR. The other detected fractions were not identified, however they represented low proportions (<5% TRR) and low absolute levels. As for goat, the maximum residue level was found in fat (1.6 mg/kg in the high dose group).

Based on these studies and awaiting the additional information requested on the fate of the α-CO in ruminant metabolism, the meeting of experts concluded that the parent compound appears to be a valid maker of the residues in animal matrices, and proposed to provisionally define the residue in products of animal origin as “etofenprox parent compound only” for monitoring and risk assessment. The fat soluble property of the molecule was confirmed.

A livestock feeding study was provided on dairy cows, the animals being treated with etofenprox only, at dose rates of 10, 30 and 1000 mg/animal during 28 days, the median dose representing a 2.2X and 1.2X dose rate for dairy and beef cattle, respectively, taking into account animal burden calculated using the highest residue levels observed in cabbage, fruit pomace and oilseed cake. Based on this feeding study, MRLs were proposed for milk and ruminant matrices.

3.3. CONSUMER RISK ASSESSMENT

The consumer chronic- and acute risk assessments were performed using the EFSA model rev2, the UK PSD model, and the proposed MRLs for plant- and animal products as listed under point 3.4. According to the representative uses, the maximum TMDI is 32% of the ADI (0.03 mg/kg bw/day) for the DE child using the EFSA model, and 80% of the ADI for the UK toddler and UK vegetarian using the PSD consumer model. No acute risk is expected, the maximum IESTI (International Estimated Short Term Intake) being only 13% of the ARfD (1 mg/kg/day) for table grape and using both models.

The meeting pointed out that the consumer exposure was only considered through the representative uses of etofenprox as plant protection product on the representative uses presented in the DAR. However, this active substance has other area of uses (e.g. biocides) and a potential additional exposure might be expected.

3.4. PROPOSED MRLS

Based on the available supervised residue trial and the feeding study results, the following MRLs were proposed:

Plant products (residues defined as sum of etofenprox + α-CO)

- Apples	0.5 mg/kg	(based on Southern GAP only)
- Peach	0.5 mg/kg	(based on Southern GAP only)
- Table and wine grape	2.0 mg/kg	(based on Southern GAP only)
- Head cabbage	0.1 mg/kg	(based on Southern GAP only)
- Rapeseeds	0.02* mg/kg	(based on Northern GAP only)

Ruminant (residues provisionally defined as etofenprox)

- Meat	2.0 mg/kg	(on fat basis according Regulation (EC) No 396/2005[24])
- Fat	2.0 mg/kg	

[24] Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC

* MRL set at LOQ

- Milk 0.05* mg/kg
- Other ruminant products 0.05* mg/kg

These MRLs have to be considered as provisional, awaiting the additional information requested on the fate of the α-CO metabolite in ruminant metabolism.

4. Environmental fate and behaviour

Etofenprox was discussed at the PRAPeR 57 meeting of experts on fate and behaviour in the environment (October 2008) on basis of the DAR (June 2005), addendum I (March 2007), addendum II (May 2008) and addendum II v.2 (September 2008). After the meeting of experts the rapporteur Member State provided the addendum Volume 3 v3 to include further information requested during the meeting. If it is not otherwise indicated, the fate and behaviour studies were performed with [2-^{14}C]-propyl and [α-^{14}C]-benzyl labelled etofenprox.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of etofenprox in soil under dark aerobic conditions at 20 °C was investigated in a reliable study (Voelkl. S. 2001) with four soils (pH 6.8 – 7.4; OC 0.3 – 2.2 %, clay 8.0 – 29.1 %). Degradation occurred through oxidation at different parts of the molecule (mainly on the aromatic rings or in α-C position to the aromatic ring) followed by breaking down in smaller moieties. Unextracted radioactivity amounted to a maximum of 55.8 % AR after 55 days and mineralization (CO_2) up to a maximum of 45.6 % AR after 120 days. In a supplementary study (Tomoda K. 1985a), one of the metabolites **α-CO** (max 7 % AR after 1 week) was observed to exceed 5 % AR in one of the soils. This study was considered by the meeting of experts a reliable with respect to establishing the route of degradation, but not reliable to derive persistence endpoints and kinetic degradation parameters.

Degradation under anaerobic conditions was investigated in one soil (pH 5.8, OC 1.2 %, clay 29.1 %). Under these conditions metabolite 4'-OH was identified as a major metabolite (max 11.7 % AR after 90 days). Mineralization was negligible and unextractable residue in soil amounted to 9.5 % AR after 121 days.

Photolysis has been investigated in one soil with simulated sunlight (Xe arc lamp filtered for λ < 290 nm). Photolysis only slightly enhanced the degradation of etofenprox in soil. No metabolite exceeded 10 % AR at any data point. The main photodegradate was metabolite α-CO (max. 7.7 % AR after 20 days).

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

Reliable degradation rates in soil under aerobic conditions at 20 °C were calculated for etofenprox from data in the four soils of the study summarized in the route section (section 4.1.1). Under these conditions etofenprox may be considered to be low to moderately persistent (DT_{50} = 7 – 25 days). From data in the same study it was possible to calculate half-lives for the soil metabolite α-CO (DT_{50} = 12 – 45 days). In addendum II v2 the rapporteur Member State clarified that the kinetic analysis of this study was performed assuming SFO kinetic model.

An additional degradation study in four soils was available in the dossier (Lenz, 1996). During the peer review the applicant was requested to reanalyze the data from this study following the recommendations of FOCUS kinetics, because the study used the methods of Timme and Freehse[25] already considered inadequate by the SCP Opinion on the Guidance Document on Persistence in Soil (9188/VI/97 rev 8, 12.07.2000)[26]. Since this reanalysis was not available at the time the meeting of experts took place, the rapporteur Member State provided the new kinetic analysis after the meeting in addendum Volume 3 v3. Fitting with SFO was acceptable for one of the soils (DT_{50} = 12.4 days); however, for the other three soils acceptable fitting was obtained only with the FOMC model. In the latter cases, the RMS also calculated pseudo first order half-lives (DT_{90} / 3.3) in order to obtain kinetic parameters adequate for modelling (DT_{50} = 20.24 days – 57.7 days). The rapporteur Member State also normalized the values obtained for the soil moisture content; however, it should be taken into account that correction factors > 1 should not be used for moisture normalization.

Under dark anaerobic conditions etofenprox is highly persistent in soil (DT_{50} = 174 days). The applicant justified the waiving of addressing the anaerobic degradation of metabolite 4'-OH based on the availability of aerobic degradation rates in soil and water sediment studies, and on the unlikely occurrence of exposure to prolonged anaerobic conditions under normal agricultural practice for the representative uses proposed.

PEC soil were calculated for etofenprox based on the soil half-life (DT_{50} = 25 days) for all representative uses (see addendum II v.2.), assuming a single application for the total yearly amount applied (no degradation between applications). The meeting of experts agreed that these values could be used for the risk assessment. After the meeting the rapporteur Member State provided updated values in addendum Volume 3 v3, taking into account the pattern of applications and the degradation between them. During the revision of the draft conclusion it was noted that after the reanalysis of the soil degradation data the worst case soil half-life is 57.7 days. This latter value should be used to

[25] Timme G, Frehse H and Laska V (1986) statistical interpretation and graphic representation of the degradation behaviour of pesticide residues. II. *Pflanzenschutz-Nachr.* Bayer, 39, 187-203.

[26] Opinion of the Scientific Committee on Plants on the Draft Guidance Document on Persistence in Soil (DG VI - 9188/VI/97-Rev.5 of 20.12.1998) - (Opinion expressed by the Scientific Committee on Plants on 24 September 1999).

update the soil risk assessment and to assess other potential uses at national level. However, no effect on the risk assessment of the EU representative uses is expected.

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

Etofenprox batch adsorption / desorption experiments were performed in three soils (pH 6.0 – 7.1; OC 1.6 – 3.8 %; clay 5.1 – 19.4 %). According to the results of these experiments, etofenprox may be classified as immobile in soil (Koc = 8548 – 14923 mL / g). The meeting of experts identified a data gap for an additional batch soil adsorption / desorption study to fulfil the requirement of data for four soils. In order to cover the necessary range of soil properties, this study should be performed on an alkaline soil. However, taking into account the information already available, the meeting of experts agreed that this data gap was not essential to finalize the EU risk assessment. The adsorption coefficients of metabolites α-CO and 4'-OH were estimated with PCKOCWIN (EPA). The values estimated with this program were considered acceptable in this case, taking into consideration the resemblance of the metabolite with the parent compound. According to these simulations, these metabolites may be regarded as immobile in soil.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis of etofenprox was investigated in aqueous buffered solutions (pH: 4, 7 and 9) at 50 °C. Etofenprox was stable (< 10 % degradation) in all three experimental conditions. Therefore, chemical hydrolysis is not expected to contribute to the environmental degradation of etofenprox.

Aqueous photolysis of etofenprox under artificially simulated sunlight (Suntest CPS, Herareus, Xe lamp) was investigated in buffered solutions (pH 7) and in natural pond water at 25 °C. Photolysis of etofenprox is relatively rapid in both systems ($DT_{50\ buffered\ pH\ 7}$ = 4.7 days equivalent to $DT_{50\ 35\ °N}$ = 10.4 days; $DT_{50\ pond}$ = 7.9 days equivalent to $DT_{50\ 35\ °N}$ = 17.5 days). The equivalent half-lives were also calculated for latitudes 30, 40 and 50 °N for the four meteorological seasons. Major aqueous photolysis metabolites were **α-CO** (max 63.6 % at pH 7 and max. 37.8 % in pond water after 15 days, end of the study) and **PENA** (max. 12 % at pH 7 and max. 14.4 % in pond water after 15 days, end of study). Aqueous photolysis of metabolite α-CO was also investigated in a similar study, where it was stable to photolysis. Based on the results of the study performed with the parent compound and on theoretical grounds, metabolite PENA is not expected to be susceptible to aqueous photolysis. The metabolite α-CO was also found to reach up to 10 % of the parent's applied amount in the outdoor mesocosm study.

Ready biodegradation of etofenprox was investigated in two studies. The meeting of experts discussed the validity and the results of these studies and agreed that etofenprox should be considered as not ready biodegradable.

Dissipation/ degradation of etofenprox in water/sediment systems was investigated in two systems (pH_{water} = 6.1 – 7.8[27]; OC 5.1 – 7.3 %, clay 18.1 – 19.4 %). Rapid partition of etofenprox to the sediment occurs during the first seven days. The meeting of experts agreed on the half-lives calculated for etofenprox in the whole system ($DT_{50\ whole\ system}$ = 6.5 days – 20.1 days). Metabolite **4'-OH** was identified as a major metabolite (max. 12.2 – 21.4 %) in the sediment phase of both systems. This metabolite degraded in the whole water/sediment system with a half-life of 21.8 - 57 days.

The meeting of experts discussed the need to consider aqueous photolysis and photolysis metabolites for the EU risk assessment. From the results of the aqueous photolysis study and the mesocosm study the meeting concluded that photolysis could be a relevant process of etofenprox transformation in the environment. However, the results of the water/sediment study under light/dark cycles were considered inconclusive, possibly due to the strong sorption of the active substance to the sediment. The metabolite α-CO was found at levels of 37 – 63 % AR in the photolysis study, and at levels below 10 % of the applied dose in the mesocosm study. However, the details of the fate and behaviour of this metabolite in the mesocosm provided in the DAR were scarce (e.g. sampling scheme is not provided), and the meeting was not able to confirm the actual levels that may have been reached during the experiment. The meeting agreed that the risk assessment presented for this metabolite by the applicant on basis of the maximum level of 63 % of the parent on molar basis could be regarded as conservative. Further refinements could be considered if more information on the levels attained during the mesocosm study were available. No further quantitative details on the fate of α-CO metabolite in the mesocosm study were reported by the rapporteur Member State after the meeting.

PEC_{SW} were calculated with FOCUS SW modelling for the relevant scenarios based on the worst-case soil half-life and the mean water sediment system whole system half-life. Degradation in the water phase was assumed to occur with a half-life of 1000 days, and the mean whole system half-life (geometric mean $DT_{50\ whole\ system}$ = 18 d) was applied to the sediment phase. Step 3 and Step 4 (assuming 30 m spray drift buffer zone) were calculated for all representative uses, considering only one application. Due to the strong adsorption to the soil, it was considered that in this case a single application would represent a worst case PEC_{SW} with respect to multiple applications. PEC_{SW} of aqueous photolysis metabolite α-CO was estimated to be either 63.6 % or 10 % of the Step 3 PEC_{SW} of the parent compound, based on the maximum amount observed in the aqueous photolysis study or the mesocosm study, respectively. Worst case PEC_{SW} were also estimated for the sediment metabolite 4'-OH as 21.9 % of the Step 3 PEC_{SW} calculated for the parent compound. The meeting identified the need to recalculate PEC_{SED} for the parent compound for uses different to oilseed rape, to take into account the accumulation of etofenprox after multiple applications and the PEC_{SED} of metabolites α-CO and 4'-OH. For the metabolites α-CO and 4'-OH the meeting agreed that no new modelling was necessary, but that an estimation of PEC based on the maximum amount observed in the aqueous

[27] Values provided by the RMS after consultation of the original report, not reported in any previous peer review document.

photolysis study for α-CO (63.6 %) and water sediment study for 4-OH (21.9 %) could be used for the EU risk assessment. This is justified in this case due to the structural resemblance of the metabolites to the parent compound, and that only one route of entry / formation needs to be considered. The necessary $PEC_{SW / SED}$ values have been provided by the rapporteur Member State in the addendum Volume 3 v3 after the meeting of experts.

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

Potential contamination of ground water by etofenprox for the representative uses proposed was addressed following the FOCUS GW scheme with FOCUS PELMO (v 3.3.2) and FOCUS PEARL (v. 3.3.3). The resulting 80th percentile annual average leachate concentrations at 1m depth were below 0.001 µg / L in all the FOCUS scenarios for all representative uses simulated.

Potential contamination of ground water by the soil metabolite α-CO for the representative uses proposed was addressed following the FOCUS GW scheme with FOCUS PELMO (v 3.3.2) and FOCUS PEARL (v. 3.3.3). Values were recalculated after the meeting of experts assuming a maximum formation of 7 % (molar basis) in soil. The resulting 80th percentile annual average leachate concentrations at 1m depth were below 0.001 µg / L in all the FOCUS scenarios for all representative uses simulated. The applicant also provided FOCUS GW calculations for minor soil metabolites

4'-OH, DE and DP obtaining also levels below 0.001 µg / L for all of them. This metabolite does not need further groundwater assessment.

4.3. FATE AND BEHAVIOUR IN AIR

Due to the low potential for volatilization and the estimated rapid photochemical transformation of etofenprox (DT_{50} = 2.07 hours), the environmental concentrations in air and transport through air are considered negligible.

5. Ecotoxicology

Etofenprox was discussed at the PRAPeR 58 meeting of experts on ecotoxicology in October 2008, on the basis of the draft assessment report (June 2005), addendum 2 (May 2008), addendum 2 - version 2 (September 2008) and addendum Volume 3-version 3 (November 2008). New studies on fish, bees, non-target arthropods and non-target plants, which were not provided in the original DAR, were submitted in addendum 3 (May 2008). It was noted that in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, new studies could not be considered in the peer review.

Etofenprox is the active substance in the formulated insecticidal product "Trebon 30EC" (287.5 g/L). The representative field uses were as foliar spray in oilseed rape (North Europe, one application at 60 g a.s./ha), head cabbage (South Europe, two applications/14 days interval at 150 g a.s./ha), grapes (South Europe, four applications at 150 g a.s./ha), peach (South Europe, two applications/7 days interval at 210 g a.s./ha), and apple (South Europe, three applications at 210 g a.s./ha at first application and 150 g a.s./ha at two last applications).

The risk assessment was conducted according to the following guidance documents: Risk Assessment for Birds and Mammals, SANCO/4145/2000, September 2002; Aquatic Ecotoxicology, SANCO/3268/2001 rev.4 final, October 2002; Terrestrial Ecotoxicology, SANCO/10329/2002 rev.2 final, October 2002; Risk Assessment for non-target arthropods, ESCORT 2, March 2000, SETAC.

As the specification provided for etofenprox was not accepted by the PRAPeR 56 experts on physical/chemical properties, the meeting of ecotoxicological experts agreed that the applicant should provide an assessment of the equivalence of the specifications of the active substance with the batches used in the ecotoxicological effect studies.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The acute toxicity of the formulated product (Trebon 30EC) and etofenprox technical was investigated respectively in Japanese quail (*Colinus japanica*) and mallard duck (*Anas platyrhynchos*). Both endpoints were used in the acute risk assessment. The short-term toxicity of technical etofenprox was investigated in two bird species, bobwhite quail (*Colinus virginianus*) and mallard duck. The results of these studies indicated a low toxicity to birds. A study examining the reproductive effects on bobwhite quail was provided. The Tier I assessment provided TER values above the Annex VI trigger for the acute, short-term and long-term risk to medium herbivorous and insectivorous birds from all intended uses.

Acute oral studies were available for mouse and rat using both etofenprox technical and "Trebon 30EC". The studies available indicate a low acute toxicity to mammals, and no difference in toxicity could be concluded for etofenprox technical and "Trebon 30EC". A NOAEL endpoint from the mouse chronic carcinogenicity study was applied as the long-term toxicity endpoint in the Tier 1 risk assessment of the DAR. Acute TER values were above the Annex VI trigger for all intended uses. For the long-term risk assessment, only the TER calculations for oilseed rape meet the Annex VI requirement. For the uses in head cabbage, grapevine, peach and apple the risk assessment was refined by using the more ecotoxicologicaly relevant NOAEL from the rat two-generation reproduction study, and residue data from the residue decline studies (day 0). Refined long-term TER values were above the Annex VI trigger for all of the intended uses (see addendum II – ver. 2 (September, 2008)).

A log P_{ow} of 6.9 triggered a risk assessment of secondary poisoning. TER values for fish-eating birds were above the Annex VI trigger for all intended uses, as were the TER values for fish-eating mammals, based on the more ecotoxicologicaly relevant NOAEL from the rat two-generation reproduction study. The TER calculations were revised by EFSA after the peer-review, based on the updated FOCUS PECsw values provided in addendum Volume 3 ver.3 (November 2008). The updated TER values had no effect on the conclusion (see Appendix 1). The tier 1 risk assessment for earthworm-eating birds and mammals in the DAR indicated a need for further refinements for all intended uses. Revised 21-day twa PEC_{soil} values, provided in addendum II ver. 3 (September, 2008), gave TER values above the Annex VI trigger for the oilseed rape uses, whereas further refinements was still required for the additional multiple application uses in head cabbage, grapevine, peach and apple. It was noted during the meeting of member state experts that 21day twa PEC_{soil} values calculated for the multiple uses did not take into account degradation between spray applications. New TER values were provided in addendum Volume 3 ver.3 (November, 2008), for the multiple application uses. The revised risk assessment still indicated a need for further refinement to address the risk to earthworm-eating birds and mammals for the intended uses in head cabbage, grapevine, peach and apple. The suggested refinement of the risk assessment for earthworm-eating birds by considering a soil mixing depth of 15 cm instead of 5 cm was not supported by data and hence was rejected by Member State experts. Nor did Member State experts accept the proposed refinement of the risk assessment for earthworm-eating mammals by lowering the BCF value, based on open literature data, which compared experimentally derived BCF values for organic compounds with similar log P_{ow}. It was suggested by the Member State experts to base the refinements of the risk assessment on measured BCF values in earthworms.

The risk from bio-magnification was addressed in the DAR, based on ADME studies. The half-lives of elimination of etofenprox were less than 48 hours in rat and goat, and less than 24 hours in dog. Following multiple repeat exposures, tissue residues in goats, cows and hens were all significantly less than the concentrations in the food. These data indicated that etofenprox would not biomagnify in the terrestrial food chains.

The acute risk to birds and mammals from consumption of contaminated drinking water from puddles was considered to be low in the DAR for the intended uses of etofenprox. A recalculation of TERs for mammals was provided by EFSA after the peer-review, in accordance with the conclusion at PRAPeR 53. At PRAPeR 53 it was agreed, as a general approach, to base the Tier 1 risk assessment for birds and mammals on a 10g bird or mammal. The revised TER values did not change the conclusion of the risk assessment.

The risk to herbivorous birds and mammals from plant metabolites was considered in the DAR. Plant metabolism of etofenprox was examined in winter oilseed rape, grapes and lettuce. The only metabolite detected was α-CO reaching the maximum amount of 6.5% TRR in grape bunches.

Provided there is a low risk from the parent compound, the risk from plant metabolites was considered to be low.

In summary, the risk assessment from direct intake of etofenprox residues indicated a low risk to birds and mammals for all intended uses. Refinements of the long-term risk assessment for mammals were, however, required for uses in head cabbage, grape, peach and apple to meet the Annex VI trigger. (The risk was addressed based on available residue data in head cabbage, grapevine, peach and apple, respectively). The risk to fish-eating birds and mammals was considered to be low for all intended uses, as was the risk to earthworm-eating birds and mammals for the intended use in oilseed rape. Further refinements were required to address the risk from secondary poisoning to earthworm-eating birds and mammals for the intended uses in head cabbage, grapevine, peach and apple. The acute risk to birds and mammals from consumption of contaminated drinking water from puddles was calculated to be low for the intended uses of etofenprox. Etofenprox was not considered to biomagnify and the risk from plant metabolites was assessed to be low.

5.2. RISK TO AQUATIC ORGANISMS

The available acute toxicity data for etofenprox suggested a classification as very toxic to aquatic organisms, based on the acute toxicity to fish (LC_{50}=2.7 µg a.s./L), daphnia (LD_{50}=1.2 µg a.s./L) and algae (E_bC_{50}>150 µg a.s./L). The long-term toxicity to etofenprox was very high to *Daphnia magna* (NOEC=0.054 µg a.s./L). All the criteria for a Fish Full Life Cycle (FFLC) test were met, but no study was submitted in the dossier. Member State experts agreed that a FFLC study should be provided by the applicant. It was noted during the expert meeting that a Fish Early Life Stage (FELS) study had been provided to the rapporteur Member State and assessed in addendum III (May, 2008) after the DAR had been submitted. The FELS study could not be considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007. Based on the content of the active substance, the toxicity of the formulation "Trebon 30EC" was comparable to the toxicity of etofenprox technical. Acute and chronic studies with *Chironomides* were used for the aquatic risk assessment in the DAR. Member State experts, however, considered the studies inappropriate for a risk assessment as measured concentrations of the test dilution were missing (concentration was measured in application solution). A data gap was identified for the applicant to consider sediment dwellers (*Chironomids*) in a risk assessment. Consequently, the risk assessment for sediment dwellers has been removed from Appendix I. EFSA notes after the peer review that the risk assessment for sediment dwellers should be based on calculations for both PEC_{sw} and PEC_{sed}.

A summary of a mesocosm study from Cambridgeshire (UK) was provided in the DAR (Blake, 2004). Supplementary information was provided in addendum II-ver. 2 (September, 2008). 18 enclosures were established in an artificial pond, and exposed once to five different concentrations of etofenprox on the 11th of June 2002. The test solution was applied subsurface. Sampling of

zooplankton, benthic fauna, emerging insects and sediment-dwelling organisms were provided from 7 to 14 days before exposure to 112 days post-exposure. The concentration of etofenprox in the mesocosm was continuously decreasing and at day 14 the concentration was below the level of detection in the water phase at the highest exposure concentration (22 µg a.s./L). *Copepoda* was the most sensitive taxonomic group of zooplankton (the lowest observed NOEC at two consecutive sampling occasions was 0.05 µg a.s./L) compared to *Cladocera*, *Rotifera* and *Ostracoda* (lowest $NOEC_{community}$ was 2.0 µg a.s./L). From the benthic colonisers and emergent insects data it was evident that all significant effects were observed only on single sampling occasions and no dose-response effects were recorded for emergent insects. *Asellidae* were significantly affected (NOEC=0.05 µg a.s./L) and no recovery was detected during the study. The rapporteur Member State suggested a NOEC of 0.05 µg a.s./L with an assessment factor of 2. During the expert meeting it was considered that the mesocosm summary was lacking clear information on population recovery and data on effect classes. A suggestion by Member State experts to amend the summary in an addendum was not followed up by the rapporteur Member State after the expert meeting. The majority of Member State experts expressed concern about the effects on *Asellidae* as there was a high variability in the controls. They were not confident in the data and had concerns about the NOEC value of 0.050 µg/L. It was considered that a screening of laboratory studies with several invertebrate species would have been useful to consolidate the confidence in the data from the mesocosm. It was proposed in the expert meeting that the applicant should address the uncertainty of the study, particularly because of the variability within the controls, e.g. with single species studies on the most sensitive species identified in the mesocosm study, in order to derive a NOEC for the risk assessment. Based on that, the need for an additional assessment factor would have to be considered. EFSA notes that such single species studies on the most sensitive species should also take into account the multiple application for some of the intended uses.

Following comment during the peer review, the endpoint for several of the aquatic toxicity studies was recalculated, based on measured exposure concentrations. In addition, the use of time weighted average (twa) PEC values were avoided as no data were available to support such use. Revised TER calculations for the aquatic risk assessment were provided in addendum II-ver.2 (September, 2008). No complete FOCUS scenarios met the Annex VI trigger for any of the intended uses based on acute- and chronic endpoints for fish and invertebrates, and FOCUS Step 3 PEC_{sw} calculations. The risk assessment for the oilseed rape risk assessment was refined, based on FOCUS Step 4 PEC_{sw} calculations with a no-spray buffer zone of 30m in addendum Volume 3-ver. 3 (November, 2008). TERs for fish and algae were above the Annex VI for all scenarios. EFSA, however, noted that TERs for *Daphnia* based in the mesocosm endpoint, not supported by MS experts and the *Chironomus* endpoints, which were considered to be not reliable by MS experts, were included in the risk assessment. EFSA recalculated TERs for invertebrates, based on Tier 1 effect data and FOCUS Step 4 PEC_{sw} values with a no-spray buffer zone of 30m. All scenarios gave TERs below the Annex VI trigger, indicating a need for further refinements to address the risk to aquatic invertebrates (see

Appendix I). Furthermore, EFSA noted that a no-spray buffer zone of 30m would respect the maximum limitation of spray drift recommended in the FOCUS landscape and mitigation guidelines.

α-CO was found as a degradation product of etofenprox in the aqueous photolysis study and in the mesocosm study. The acute toxicity of α-CO was examined for fish, daphnia and algae. No effects were seen at the limit of solubility of α-CO (0.44-0.53 mg α-CO/L). No toxicity data were available for *Chironomids*. The rapporteur Member State suggested using the endpoint from the acute *Chironomus* toxicity study with etofenprox as a surrogate endpoint. This study was however not accepted by the Member State experts (see data gap in next paragraph). TER values for fish, daphnia and algae did meet the Annex VI trigger for use in oilseed rape, based on the worst case FOCUS Step 3 PEC_{sw} scenario (D2 Ditch). This was not the case for any of the other intended used. At FOCUS Step 3 two (R1 and R3) out of six scenarios met the Annex VI trigger for uses in head cabbage. For the grapevine, peach and apple uses all FOCUS Step 3 scenarios failed to meet the Annex VI trigger. It was concluded by the RMS in addendum Volume 3-ver.3 (November, 2008) that the aquatic risk assessment for α-CO would have to be refined further for uses in head cabbage, grapevine, peach and apple, taking into account mitigation measures at FOCUS Step 4 PEC_{sw}, e.g. no-spray buffer zones. An additional risk assessment was also provided for α-CO in the DAR, based on measured α-CO exposure values from the mesocosm study (Blake, 2004). EFSA notes that the use of such exposure data would however require further supporting information (see section 4.2).

It was recommended by fate experts that the risk from α-CO in sediment should be assessed as it was considered to adsorb strongly to sediment, and the multiple application should be taken into account. No data on the effects of α-CO (or etofenprox as mentioned above) were available for sediment dwellers. Member State experts noted that the acute toxicity studies available for fish, daphnia and algae indicated a lower toxicity than that of etofenprox. If a valid long-term *chrionomid* study would become available for etofenprox it was considered to cover the toxic effects of α-CO. The Member State experts agreed on a data gap for the applicant to address the risk to sediment dwellers from α-CO.

The metabolite 4'-OH had been identified in the water/sediment system after 7 days. The effects on sediment dwellers should therefore be covered by the chronic *Chironomus* toxicity study with etofenprox. It was commented by Member State experts, that chemical analysis to verify the presence of 4'-OH would have been relevant. As a data gap exists for the applicant to address the risk to sediment dwellers from etofenprox (see above), it should also be considered that the risk from 4'-OH should be addressed. An aquatic risk assessment was provided in the DAR for 4'-OH, based on modelled toxicity data (QSAR) for fish, daphnia and algae in addition to extrapolated toxicity data from etofenprox (1/10 of the toxicity). Acute toxicity data were available for *Chironomus*. The Member State experts did not consider the QSAR approach valid for substances with a specific mode of action like etofenprox. Furthermore, Member State experts noted that 4'-OH was not considered to

be a relevant metabolite in the water phase by fate experts. Consequently, the water-based aquatic risk assessment for 4'-OH has been removed from Appendix 1. Only the acute 4'-OH toxicity endpoint for *Chironomus* was left in Appendix 1.

A log P_{ow} of 6.9 triggered the assessment of bioaccumulation. BCF values of 1554, 7213 and 3951 were identified in edibles, non-edibles and whole fish, respectively. The clearance time (CT_{50}) was found to be 9-16 days (first-order kinetics). All triggers for the aquatic food chain assessment were met according to the aquatic guidance document and Member State experts considered that the risk from aquatic biomagnification should be addressed by the applicant.

Etofenprox was considered to have weak endocrine effects, but no further concerns were identified by the toxicologists. The potential for endocrine disruption was not addressed in the dossier and no elements were available for extrapolation to aquatic organisms. Member State experts agreed that the applicant should further address the endocrine disruption potential in aquatic organisms.

The risk to aquatic organisms was not addressed for any of the intended uses. TERs for aquatic organisms, based on Tier 1 effect data and FOCUS Step 3 and 4, failed to meet the Annex VI trigger. The use of an endpoint from the higher tier mesocosm study would require further supportive data. Member State experts suggested that single species tests on the most sensitive species from the mesocosm study should be provided to consolidate the confidence in the data from the mesocosm. The design of the single species test should take into account the multi-application uses. Based on the additional studies, a relevant assessment factor should be reconsidered for a refined aquatic risk assessment. A FFLC study was required by Member State experts, which should be included in the risk assessment. The risk to sediment dwellers should be addressed for etofenprox and the metabolites 4'-OH and α-CO. Also, the aquatic risk assessment for α-CO would have to be refined further for uses in head cabbage, grapevine, peach and apple. In addition, the risk from biomagnification and potential endocrine disrupting effects on aquatic organisms should be addressed.

5.3. RISK TO BEES

New oral and contact toxicity studies following EPPO guidelines were provided after submission of the DAR. The studies were assessed in addendum II-ver.2 (September, 2008)[28]. Oral and contact toxicity studies with the representative formulation (Trebon 30EC) were only available for an exposure duration of 24 hours, whereas studies with an exposure duration according to the guidelines were available for a slightly different formulation (Trebon 20EC). No new studies were required as field studies were available. The acute toxicity studies with etofenprox technical and the formulations indicated a similar high toxicity to bees (around 0.1 µg/bee). Hazard quotient (HQ) values calculated

[28] The studies could be taken into account considering the Commission Regulation (EC) No 1095/2007 as the study indicates a higher risk to bees.

for the oral and contact route indicated a high risk to bees for all intended uses. Two tunnel tests with bees were provided. In the first study (Muhlen *et al.*,1996) etofenprox was applied once at an application rate of 122 g a.s./ha, and in the second study (Anonymous, 1990) etofenprox was applied twice at an application rate of 40 g a.s./ha (8-22 days interval). A field test was additionally provided (Hurny, 1987). Spraying of mustard plants (*Sinapis alba*) in the flowering stage indicated that Trebon (30 EC) had a repellent effect, and a cage test under covered conditions indicated no adverse effects on colonies. Based on the studies the rapporteur Member State concluded that "Trebon 30EC" demonstrated a strong repellent effect and the low toxicity observed in these studies under semi-natural conditions suggested a classification as harmless to bees. The tunnel studies were discussed by Member State experts. Member State experts considered that the application rate only covered uses in oilseed rape. In one of the trials in the study by Muhlen *et al.* (1996), some mortality was observed but it was not clear if it was statistically significant as no statistics were performed. Consequently, the experts considered that effects could not be excluded, and mitigation measures should be set to avoid the exposure of bees also in oilseed rape during the flowering season. Based on the available data and the intended uses, Member State experts agreed that mitigation measures were needed for pre-flowering/flowering uses in oilseed rape, grapevine and apple to avoid exposure of bees. In addition, EFSA noted (after the peer review) that risk mitigation measures should be considered to avoid exposure of bees from pre-flowering/flowering weeds in the crops covered by the GAP. Risk mitigation measures may not be necessary, if the risk to bees was fully addressed, or the measures could potentially be limited by considering residual toxicity trials (from the applicant) to define the interval between treatment and flowering for these crops.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory tests were conducted with "Trebon 30EC" and the indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri*. LR_{50} values of 0.42 and 0.7 g a.s./ha were observed. Further laboratory tests were provided for *Diaeretiella rapae* and *Poecilus cupreus.* HQ values for all in-field uses were higher than the Annex VI trigger, indicating a need for further refinements. HQ values for the off-field risk assessment indicated a low risk to non-target arthropods with a no-spray buffer zone of 5 and 10m for the oilseed rape and head cabbage uses, respectively. For uses in grapevine, peach and apples, off-field HQ values were provided for no-spray buffer zones up to 20m, without meeting the Annex VI trigger requirements. Recalculated off-field HQ values for uses in head cabbage, grapevine, peach and apple provided by EFSA after the peer review did not change the conclusions for the off-field risk assessment. Four extended laboratory studies with *A. rhopalosiphi, T. pyri, Orius laevigatues* and *Chrysoperla carnea* exposed to "Trebon 30EC" were assessed in the DAR. The rapporteur Member State provided a refined risk assessment based on the extended laboratory studies and the HQ approach. The in-field risk assessment for all intended uses indicated effects >50% for all non-target arthropods tested in the higher tier tests. No data were provided in the DAR to address the potential for in-field recovery. An aged residue study was provided by the applicant after submission

of the DAR and it has been assessed by the rapporteur Member State in addendum III (May, 2008). The data could not be considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007. The expected field exposure did not exceed the LR_{50} in the off-field risk assessment for uses in oilseed rape and head cabbage, applying a no-spray buffer zone of 1m and 5m, respectively. The off-field assessment in grapevine indicated a need for a no-spray buffer zone of 10m to avoid exposure concentrations exceeding the LD_{50} for *O. laevigatus.* The risk to non-target arthropods was not addressed for uses in peach and apple based on no-spray buffer zones of 10m. Further mitigation measures would be required based on the available higher tier effect data.

5.5. RISK TO EARTHWORMS

The acute toxicity to earthworms was tested with technical and formulated etofenprox. The observed acute 14-day LC_{50} values were >23.6 and 51.35 mg a.s./kg soil (corrected by a factor of 2). A revised risk assessment was provided in addendum Volume 3 - ver.3 (November 2008), based on the highest PEC soil values for all intended uses, taking multiple applications into account where relevant. The acute TERs for all intended uses exceeded the Annex VI trigger of 10, indicating a low risk to earthworms. Based on the rapid degradation of etofenprox in soil, and the acceptable results of the assessment of the acute risk, a test to assess the sub-lethal effects on earthworms was deemed not necessary. The risk from the soil metabolite 4'-OH was considered to be covered by the risk assessment for etofenprox.

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

Based on the fact that etofenprox was considered to be not persistent and the low risk identified for earthworms, the risk to other soil non-target macro-organisms was considered to be addressed.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects of >25% on soil respiration and nitrification were observed in tests with etofenprox technical. The initial PEC soils are more than 6 times lower than the tested concentrations suggesting a low risk to soil micro-organisms for the representative uses evaluated.

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

Data on herbicidal effects (seedling growth test and vegetative vigour test) of the formulation "Trebon 30EC" on 10 non-target plants were provided in addendum III (May 2008), and a risk assessment was provided in addendum II – ver. 2 (September 2008). The ER_{50} values were >200 g a.s./ha. TER calculations were above the Annex VI trigger of 5 for intended uses in oilseed rape, head cabbage and grapes. For the intended uses in peach (TER = 4.9) and apple (TER = 4.3), the TERs

were just below the Annex VI trigger. Member State experts still considered the risk from the uses on peach and apple as being low, as the ER_{50} was a 'lower than' value.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No studies were provided to address the risk to biological methods of sewage treatment for any of the intended uses. The rapporteur Member State considered it unlikely that the use of etofenprox would result in significant contamination of sewage treatment plants, therefore no studies were required. This assessment was not commented during the peer review. EFSA did, however, consider this as a data gap to allow Member States to require the study if deemed relevant, in case of Annex I inclusion of etofenprox.

6. Residue definitions

Soil

Definition for risk assessment:	etofenprox
Definition for monitoring:	etofenprox

Water

Ground water

Definition for exposure assessment:	etofenprox, α-CO, 4'-OH (only under anaerobic conditions).
Definition for monitoring:	etofenprox

Surface water

Definition for risk assessment:	etofenprox, α-CO (photolysis metabolite).
Definition for monitoring:	etofenprox, α-CO (photolysis metabolite)

Air

Definition for risk assessment:	etofenprox
Definition for monitoring:	etofenprox

Food of plant origin

Definition for risk assessment:	sum etofenprox + α-CO expressed as etofenprox
Definition for monitoring:	sum etofenprox + α-CO expressed as etofenprox

Food of animal origin

Definition for risk assessment:	etofenprox (provisionally)
Definition for monitoring:	etofenprox (provisionally)

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

Soil

Compound (name and/or code)	Persistence	Ecotoxicology
etofenprox	low to moderately persistent (DT_{50} = 7 – 57.7 days)	The risk was assessed as low to soil living organisms for all intended uses

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
etofenprox	immobile in soil Koc = 9025 – 14923 mL / g	FOCUS: No, for the representative uses and scenarios simulated.	Yes	Yes	Yes
α-CO	Estimated to be immobile in soil	FOCUS: No, for the representative uses and scenarios simulated.	No	No (same toxicity as the parent, reference values of the parent are applicable to α-CO)	No
4'-OH (only under	Estimated to be	Estimated not to exceed 0.1 µg /	No	No data, data not required	No

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
anaerobic conditions)	immobile in soil	L, in case anaerobic conditions were relevant for the representative uses.			

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Etofenprox (water and sediment)	The risk to aquatic organisms was not addressed
α-CO (water and sediment)	The risk to sediment dwellers was not addressed
4-OH (sediment only)	The risk to sediment dwellers was not addressed

Air

Compound (name and/or code)	**Toxicology**
etofenprox	Rat LC_{50} inhalation > 5.88 mg/L air/4 h, whole-body, as a liquid aerosol, no classification proposed

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

- Representative 5-batch data and a specification of the technical active substance (relevant for all representative uses evaluated, data gap identified by PRAPeR 56 meeting of experts (October 2008), date of submission unknown; refer to chapter 1)
- Information regarding the confirmation of the identity of the impurities in the technical material (relevant for all representative uses evaluated, data gap identified by PRAPeR 56 meeting of experts (October 2008), data already submitted and evaluated in an addendum, not peer-reviewed in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, refer to chapter 1)
- Surface tension of the neat formulation to confirm the need (or not) for the classification with phrase R65 (relevant for all representative uses evaluated, data gap identified by PRAPeR 56 meeting of experts (October 2008), date of submission unknown; refer to chapter 1)
- To address a standard hydrolytic study in order to investigate the nature of the residues in processed commodities. This study was submitted by the applicant and presented in the addendum I of March 2007. However, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review (relevant for all representative uses evaluated, data gap identified by the rapporteur Member State and confirmed by the PRAPeR 60 meeting of experts, date of submission unknown; refer to chapter 3.1).
- To address one processing balance study for red wine and three follow-up studies for red wine and raisin. These studies were partly submitted by the applicant and presented in the addendum I of March 2007. However, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review (relevant for the representative use on grape, data gap identified by the rapporteur Member State and confirmed by the PRAPeR 60 meeting of experts, date of submission unknown; refer to chapter 3.1)
- To address information on the fate of the α-CO metabolite in the ruminant metabolism and to provide a statement on why this metabolite has to be considered or not in the animal residue definitions (relevant for the representative uses on rapeseeds, apples, peaches and cabbages, data gap identified by the PRAPeR 60 meeting of experts, date of submission unknown; refer to chapter 3.3)
- An additional batch soil adsorption / desorption study to fulfil the requirement of data for four soils. In order to cover the necessary range of soil properties this study should be performed

on an alkaline soil. (data gap identified by the PRAPeR 57 meeting of experts; the meeting of experts agreed that this data gap was not essential to finalize the EU risk assessment.; refer to point 4.1.3)

- To assess the equivalence of a new specification of the active substance with the batches used in the ecotoxicological effect studies (relevant for all representative uses evaluated; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5)
- To address the risk to earthworm-eating birds and mammals (relevant for uses in head cabbage, grapevine, peach and apple; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5.1)
- To address the risk to sediment-dwellers from etofenprox and the relevant metabolites 4'-OH and α-CO (relevant for all intended uses; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to point 5.2)
- To address the risk to aquatic invertebrates possibly by consolidating the confidence in the data from the mesocosm (Blake, 2004) (relevant for all intended uses; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5.2)
- To further refine the aquatic risk assessment for α-CO (relevant for intended uses in head cabbage, grapevine, peach and apple; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5.2)
- To provide a Fish Full Life Cycle study (relevant for all intended uses; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5.2)
- To address the endocrine disruption potential in aquatic organisms (relevant for all intended uses; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5.2)
- To address the risk from aquatic biomagnification (relevant for all intended uses; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to point 5.2)
- To consider toxicity trials to define the interval between treatment and flowering of oilseed rape, grapevine and apple (relevant for all intended uses; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5.3)
- To address the potential for in-field recovery for non-target arthropods (relevant for all intended uses; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5.4)
- To further address the off-field risk to non-target arthropods (relevant for intended uses in peach and apples; agreed at the PRAPeR 58 meeting of experts; proposed submission date unknown; refer to section 5.4)
- To provide a study on effects on biological methods of sewage treatment (relevant for all intended uses; identified by EFSA after the peer review; proposed submission date unknown; refer to section 5.9)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as insecticide as proposed by the applicant, which comprise foliar spraying to control *Meligethes aeneus* and *Ceutorhynchu assimilis* in oilseed rape in northern EU countries, and to control biting and sucking insects in head cabbage, grapes, peach and apples in southern EU countries, with application numbers and maximum application rates per treatment according to the endpoints.

The representative formulated product for the evaluation was 'TREBON 30EC', an emulsifiable concentrate (EC) containing 287.5 g/L etofenprox, registered under different trade names in Europe.

Since the minimum purity was not concluded on, the specification should be regarded as provisional for the moment.

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, however a data gap was identified for the surface tension of the neat formulation, as these data may lead to the need for additional classification.

Adequate methods are available to monitor all compounds given in the respective residue definitions in food/feed of plant and animal origin and environmental matrices.

In the mammalian metabolism studies, etofenprox was rapidly but partially absorbed after oral administration. It was uniformly distributed through the body, and transferred via placenta and via milk. There was no evidence of bioaccumulation; etofenprox was rapidly eliminated, mainly via faeces, a major part as metabolites.

The acute toxicity was low, either by the oral, dermal or inhalation route; no eye or skin irritation was observed, and no potential for skin sensitisation was found in a modified maximisation test. The main target organs of etofenprox were the liver and thyroid upon short-term or long-term exposure in the rat, which was the most sensitive species. The mouse presented also renal toxicity, but at much higher dose levels, and the dog was less sensitive showing effects only in the liver. The relevant NOAEL for short-term exposure was the dose level of 20 mg/kg bw/day from the 90-day rat feeding study; for long-term exposure, the NOAELs in rat and mouse were similar: 3.1 mg/kg bw/day in mouse and 3.7 mg/kg bw/day in rat. No potential for genotoxicity or neurotoxicity was observed. The aetiology of the formation of the thyroid adenomas observed in rats was elucidated in a mechanistic study and considered not relevant for human risk assessment. Marginally increased renal cortical tumours found only in male mice at high doses were also not considered relevant to humans. No effect on the reproduction, fertility or development was found, however considering the increased mortality of offsprings during the lactation phase, classification with **R64, "May cause harm to breastfed**

babies", was proposed. Further studies were provided on the plant metabolite α-CO, which showed that its toxicity is covered by the parent's toxicity studies.
The acceptable daily intake (ADI) of etofenprox was 0.03 mg/kg bw/day, the acceptable operator exposure level (AOEL) was 0.06 mg/kg bw/day, and the acute reference dose (ARfD) was set at 1.0 mg/kg bw. A default value of 30 % was agreed for dermal absorption.
The level of operator exposure calculated for the representative formulation "TREBON 30EC", at a maximum dose rate of 0.21 kg etofenprox/ha in high crops, was below the AOEL when the use of gloves was considered; in field crops, no personal protective equipment was needed to achieve an operator exposure estimate below the AOEL according to the German model. According to the UK POEM model, the estimated operator exposure was above the AOEL, even when the use of PPE was considered. Estimated exposure of workers entering crops treated with etofenprox was below the AOEL if PPE were worn. Bystander exposure was estimated to be below the AOEL.

Concerning the plant and animal metabolism studies, the meeting discussed the unusual way the experiments were conducted, using applications of a 1:1 mixture of both labelled forms in a single study, instead of two distinct radioactive labels from two separate studies. After discussion, the experts were of the opinion that such studies may only be accepted when no extensive cleavage of the parent molecule is observed. Thus, in the specific case of etofenprox, this practice could be accepted, as no extensive metabolism was observed in plants and animals. On the other hand, in the case of an extensive metabolism and/or early cleavage of the parent molecule, the recovered levels of the different metabolites may be underestimated when compared to the initial radioactive level of the parent molecule. In such a situation, the meeting re-enforced its opinion that metabolism studies must be conducted separately, according to the different labelling forms, in order to depict the fate of each labelling portion of the molecule as completely as possible, and to provide reliable quantitative information.

In plants, the metabolism of etofenprox has been investigated in rape seed, grape and lettuce. The metabolism was limited and etofenprox was found to be the major compound of the residues, the other metabolites being detected in very low proportions, up to 7% of the TRR for the α-CO metabolite. However, considering that the α-CO metabolite was observed in proportions higher than 10% of the etofenprox levels in the supervised residue trials, the meeting decided to define the residue for risk assessment and monitoring as the "sum of etofenprox and α-CO expressed as etofenprox". Sufficient supervised residue trials were submitted to propose MRLs on rape seed (Northern GAP) and on head cabbage, grape, peach and apple (Southern GAP). The storage stability studies demonstrated that etofenprox and α-CO residues were stable under freeze storage conditions for at least two years in oil and water-containing matrices. A standard hydrolytic study was identified as a data gap and additionally, one balance study and three follow-up studies were requested for red

wine and for raisin. Processing transfer factors could be calculated for some rape seed, apple and peach processed commodities.

For animals, the experts discussed the validity of the metabolism studies performed with the parent etofenprox only. Considering that the α-CO metabolite was shown to be a significant constituent of the residues in plants, the experts were of the opinion that information on the fate of this compound in the ruminant metabolism has to be requested. Parent etofenprox was found to be the major residue in all goat- and hen matrices, and the residue definition for monitoring and risk assessment was set provisionally as "etofenprox", awaiting the requested information on the α-CO metabolite. Based on the cow feeding study and the animal burden calculations, MRLs were proposed for milk and ruminant products.
The chronic and acute consumer risk assessments were performed using the EFSA and the UK PSD models. Using the MRLs proposed for plant- and animal products, the calculated theoretical maximum daily intakes and international estimated short term intakes were shown to be below the ADI and ARfD values.

Degradation of etofenprox in soil under dark aerobic conditions at 20 °C occurred through oxidation at different parts of the molecule followed by breaking down in smaller moieties (DT_{50} = 7 – 57.7 days). In one study, one of the metabolites, α-CO, was observed to exceed 5 % AR in one of the soils (DT_{50} = 12 – 45 days). Unextracted radioactivity amounted to a maximum of 55.8 % AR after 55 days, and mineralization (CO_2) up to a maximum of 45.6 % AR after 120 days. Under dark anaerobic conditions at 20 °C, etofenprox is highly persistent in soil (DT_{50} = 174 days). Under these conditions, metabolite 4'-OH was identified as a major metabolite. Mineralization was negligible and unextractable residue in soil amounted to 9.5 % AR after 121 days. Photolysis only slightly enhanced degradation of etofenprox in soil. PEC soil were calculated for etofenprox based on the soil half-life of 25 days for all representative uses. The meeting of experts agreed that these values could be used for the risk assessment.
According to the results of available soil batch adsorption/desorption experiments, etofenprox may be classified as immobile in soil (Koc = 8548 – 14923 mL / g). The meeting of experts identified a data gap for an additional batch soil adsorption/desorption study, but considered it not essential to finalize the EU risk assessment. The metabolites α-CO and 4'-OH were estimated to be immobile with PCKOCWIN (EPA).
Chemical hydrolysis is not expected to contribute to the environmental degradation of etofenprox. The photolysis of etofenprox is relatively rapid. The major aqueous photolysis metabolites were α-CO (max 63.6 %) and PENA (max. 14.4 %). The metabolite α-CO was also found to reach up to 10% of the parent's applied amount in the outdoor mesocosm study.
On the basis of the available studies, etofenprox should be considered not ready biodegradable.

In water/sediment systems, partition of etofenprox to the sediment occurs during the first seven days. The meeting of experts agreed on the half-lives calculated for etofenprox in the whole system ($DT_{50\ whole\ system}$ = 6.5 days – 20.1 days). The metabolite **4'-OH** was identified as a major metabolite in the sediment phase of both systems.

The meeting of experts discussed the need to consider aqueous photolysis and photolysis metabolites for the EU risk assessment, and agreed that the risk assessment presented for the metabolite α-CO by the applicant could be regarded as conservative.

PEC_{SW} were calculated with FOCUS SW modelling for the relevant scenarios based on the soil half-life of 25 days. Degradation in the water phase was assumed to occur with a half-life of 1000 days and the mean whole water/sediment system half-life was applied to the sediment phase. Step 3 and Step 4 (only oilseed rape; assuming 30m spray drift buffer zone) were calculated for the representative uses. PEC_{SW} of the aqueous photolysis metabolite, α-CO, was estimated to be 63.6 % of the PEC_{SW} of the parent compound. Worst case PEC_{SW} were also estimated for the sediment metabolite, 4'OH, as 21.9 % of the PEC_{SW} calculated for the parent compound. The meeting of experts identified the need to recalculate PEC_{SED} for the parent compound for the uses different to oilseed rape to take into account the accumulation of etofenprox after multiple applications, and the PEC_{SED} of the metabolites α-CO and 4-OH. The necessary $PEC_{SW\ /\ SED}$ values were provided by the rapporteur Member State in the addendum Volume 3 v3 after the meeting of experts.

Neither etofenprox nor its soil metabolite α-CO is expected to exceed the trigger of 0.1 µg / L for any of the representative uses and scenarios simulated. The environmental concentrations in air and transport through air of etofenprox are considered negligible.

The risk assessment indicated low risk to birds and mammals for all intended uses. Refinements of the long-term risk assessment for mammals were, however, required for the uses in head cabbage, grape, peach and apple to meet the Annex VI trigger. The risk to fish-eating birds and mammals was considered to be low for all of the intended uses, as was the risk to earthworm-eating birds and mammals for the intended use in oilseed rape. Further refinements were still required to address the risk to earthworm-eating birds and mammals for the intended uses in head cabbage, grapevine, peach and apple. The acute risk to birds and mammals from consumption of contaminated drinking water from puddles was assessed as low for all intended uses of etofenprox. Etofenprox was not considered to biomagnify in the terrestrial food chain and the risk from plant metabolites was assessed to be low.

The risk to aquatic organisms was not addressed for any of the intended uses. The TER values for aquatic organisms, based on tier 1 effect data and FOCUS Step 3 and 4, failed to meet the Annex VI trigger value. The use of an endpoint from the available higher tier mesocosm study would require further supportive data. Member State experts suggested that single species tests on the most sensitive species from the mesocosm study should be provided to consolidate the confidence in the data from the mesocosm. The design of the single species tests should take into account the multi-application uses. Based on the additional studies, a relevant assessment factor should be reconsidered for a

refined aquatic risk assessment. A fish full life cycle (FFLC) study was required by the Member State experts, which should be included in the aquatic risk assessment. The risk to sediment dwellers should be addressed for etofenprox and for the metabolites 4'-OH and α-CO. Also, the aquatic risk assessment for α-CO would have to be refined further for the uses in head cabbage, grapevine, peach and apple. In addition, the risk from biomagnification and potential endocrine disrupting effects on aquatic organisms should be addressed.

Hazard quotient (HQ) values indicated a high risk to bees from all intended uses. Member State experts concluded that the available field studies did not address the risk to bees, and they agreed that mitigation measures were needed for pre-flowering/flowering uses in oilseed rape, grapevine and apple to avoid exposure of bees. The Tier I risk assessment indicated a high in-field risk to *Aphidius rhopalosiphi* and *Typhlodromus pyri* for all intended uses. The off-field risk was considered to be low for *A. pyri* and *A. rhopalosiphi* for the uses in oilseed rape and head cabbage, based on no-spray buffer zone of 1 and 5m, respectively. Higher tier risk assessment based on extended laboratory studies with *A. rhopalosiphi, T. pyri, Orius laevigatues* and *Chrysoperla carnea* still indicated a high in-field risk to non-target arthropods. The potential for in-field recovery was not addressed in the draft assessment report. The higher tier off-field risk assessment indicated a low risk to non-target arthropods for uses in oilseed rape and head cabbage, with no-spray buffer zones of 1 and 5m, respectively. For the uses in grapevine, the assessment indicated a need for a no-spray buffer zone of 10m to identify a low risk. Further refinements were required to address the off-field risk to non-target arthropods for the uses in peach and apple.

The risk to earthworms, non-target micro- and macro-soil organisms and non-target plants was assessed as low for all intended uses.

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

- The estimated operator exposure was below the AOEL if personal protective equipment, as gloves during mixing, loading and application, is worn for high crop applications, according to the German model (refer to point 2.12).
- The estimated worker exposure was below the AOEL when PPE is worn, as protective gloves, long-sleeved shirt and long trousers (refer to point 2.12).
- Mitigation measures were needed for preflowering/flowering uses in oilseed rape, grapevine and apples to avoid exposure of bees. Additionally, mitigation measures should be considered to avoid exposure of bees from preflowering/flowering weeds for all intended uses.
- For uses in grapevine the higher tier off-field risk assessment on non-target arthropods indicated a need for mitigation measures, e.g. no-spry buffer zone of 10 m.

Critical areas of concern

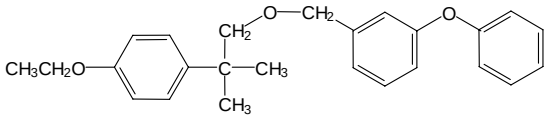
- The risk to earthworm-eating birds and mammals for the intended uses in head cabbage, grapevine, peach and apple was not addressed.
- The risk to aquatic organisms has not been addressed, including sediment dwellers, biomagnification and potential for effects from endocrine disruption.
- The risk to sediment dwellers from metabolites α-CO and 4'-OH has not been addressed.
- Further refinements are required to address the risk to non-target arthropods in-field for all uses, and off-field for uses in peach and apples.

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

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

Active substance (ISO Common Name)	Etofenprox
Function (*e.g.* fungicide)	insecticide
Rapporteur Member State	Italy

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether
Chemical name (CA)	1-[[2-(4-ethoxyphenyl)-2-methylpropoxy]methyl]-3-phenoxybenzene
CIPAC No	471
CAS No	[80844-07-1]
EEC No (EINECS or ELINCS)	407-980-2
FAO Specification (including year of publication)	471/TC(July 2007) min. 980 g/kg water: max 5 g/kg insolubles in acetone: max 1 g/kg
Minimum purity of the active substance as manufactured (g/kg)	open
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	No impurity of toxicological, environmental and/or other significance
Molecular formula	$C_{25}H_{28}O_3$
Molecular mass	376.5 g/mol
Structural formula	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity)	37.4 °C (purity > 99%, solid)
Boiling point (state purity)	not determinable due to decomposition at about 200°C
Temperature of decomposition	approximately 200 °C (purity > 99%, solid)
Appearance (state purity)	white crystalline powder (purity >99%)
Surface tension	68.12 mN/m (90% saturated aqueous solution, at 20.1 °C, solid)
Vapour pressure (in Pa, state temperature)	8.13 x 10^{-7} Pa at 25°C (purity > 99%, solid)
Henry's law constant (Pa m^3 mol^{-1})	0.0136 Pa m^3/mol at 25°C
Solubility in water (g/l or mg/l, state temperature)	pH 4: 0.0052 mg/l, at 20°C pH 7: 0.0225 mg/l, at 20°C pH 9: 0.012 mg/l, at 20°C (purity > 98% , solid)
Solubility in organic solvents (in g/l or mg/l, state temperature)	methanol: 49 g/l (at 20 °C) ethanol: 98 g/l (at 20 °C) acetone: 877 g/l (at 20 °C) ethylacetate: 837 g/l (at 20 °C) hexane: 667 g/l (at 20 °C) heptane: 621 g/l (at 20 °C) xylene: 856 g/l (at 20 °C) toluene: 862 g/l (at 20 °C) dichloromethane: 924 g/l (at 20 °C) (purity > 98% , solid)
Partition co-efficient (log P_{OW}) (state pH and temperature)	6.9 (HPLC method, at 20 °C) (purity > 99%, solid)
Hydrolytic stability (DT_{50}) (state pH and temperature)	pH 4: stable (at 50 °C) pH 7: stable (at 50 °C) pH 9: stable (at 50 °C) (purity > 98% , solid)
Dissociation constant	does not dissociate
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	maximum 273.5 nm in acidic and basic solution (acid methanol, pH 1 and basic methanol, pH 12) maximum 273.6 in neutral solution (methanol, pH 7)
Flammability	not highly flammable (purity 97.1% , solid)

Explosive properties	not explosive (purity 99.3% , solid)
Oxidising properties	Not oxidising (expert statement)

Details of intended uses (GAPs) for TREBON 30EC

Crop and/ or situation	**Member State Or Country**	**Product name**	**F G or I**	**Pests or Group of pests controlled**	**Formulation**		**Application**				**Application rate per treatment** (max)			**PHI** (days)	**Remarks**
(a)			(b)	(c)	Type (d-f)	Conc. of a.i. (i)	method kind (f-h)	growth stage & season (j)	number (max) (k)	timing	g a.i./hL	water L/ha	g a.i./ha	(l)	(m)
Oil seed rape	EU – N	Trebon 30EC	F	*Meligethes aeneus Ceutorhynchu assimilis*	EC	287.5 g/L	foliar spray	BBCH 64-65	1	Up to BBCH 65	15	400	60	n.a.	1) 3)
Head cabbage	EU – S	Trebon 30EC	F	biting and sucking insects	EC	287.5 g/L	foliar spray	BBCH 45-51	2	1) 21 days b.h 2) 7 days b.h.	50-75	200 - 300	150	7	1) 2)

Grapes	EU – S	Trebon 30EC	F	biting and sucking insects	EC	287.5 g/L	foliar spray	BBCH 57-88	4	1) blossom 2) petals falling 3) 28 days b.h. 4) 14 days b.h.	10-15	1000 - 1500	150	14	1) 2) 3)
Peach	EU – S	Trebon 30EC	F	biting and sucking insects	EC	287.5 g/L	foliar spray	BBCH 75-89	2	1) 14 days b.h. 2) 7 days b.h.	14	1500	210	7	1) 2)
Apple	EU – S.	Trebon 30EC	F	biting and sucking insects	EC	287.5 g/L	foliar spray	BBCH 51-88	3	1) pre-flowering 2) 14 days b.h. 3) 7 days b.h.	1 x 14-17.5 2 x 10-12.5	1200 - 1500	1 x 210 2 x 175	7	1) 2) 3)

1) Risk to aquatic organisms not addressed, including sediment dwellers, biomagnification and endocrine disruption; 2) risk to earthworm-eating birds and mammals was not addressed; 3) Risk to bees has not been addressed during pre-flowering/flowering.

Remarks:
(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) *e.g.* biting and sucking insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR) 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 plants, type of equipment used must be indicated
(i) g/kg or g/L
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions (e)

n.a. not applicable (since oilseed rape will be treated at flowering)

Chapter 2.2: Methods of Analysis

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

Technical as (principle of method)	CIPAC method 471/TC/M/3: Gas chromatography (GC) with flame ionisation detection (FID)
Impurities in technical as (principle of method)	GC with FID
Plant protection product (principle of method)	CIPAC method 471/EC/M/3: GC with FID

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Etofenprox and metabolite α-CO
Food of animal origin		Etofenprox
Soil		Etofenprox
Water	surface	Etofenprox and metabolite α-CO
	drinking/ground	Etofenprox
Air		Etofenprox

Monitoring/enforcement methods

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Crop samples are extracted with acetone. After filtration and evaporation of acetone, etofenprox and its metabolite α-CO are partitioned into hexane. The crude extract is cleaned up by Alumina (etofenprox) and by silica gel and florisil column chromatography (α-CO). Etofenprox and α-CO are determined by GC/MS. LOQ = 0.01 mg/kg, for etofenprox and α-CO in OSR, head cabbage, grape (bunches), peach and apple. DFG S19, (MRM) 1
Food/feed of animal origin (principle of method and LOQ for methods for monitoring	Ground meat and egg samples are extracted with acetone and methanol, respectively. After filtration, partitioning into hexane (or hexane:ethyl ether from milk samples) and

purposes)	purification by Alumina (etofenprox) or silica gel and florisil column chromatography (α-CO), etofenprox and α-CO are determined by GC/MS. LOQ = 0.01 mg/kg, for etofenprox and α-CO in meat (ruminant and chicken) and egg LOQ = 0.01 mg/l, for etofenprox and α-CO in milk
Soil (principle of method and LOQ)	Soil samples are extracted with acetone. After filtration, partitioning into hexane and purification by Alumina (etofenprox) or silica gel and florisil column chromatography (α-CO), etofenprox and α-CO are determined by GC/MS. LOQ = 0.01 mg/kg, for etofenprox and α-CO
Water (principle of method and LOQ)	Water samples are extracted with hexane. After evaporation of the solvent, purification by Alumina (etofenprox) or silica gel chromatography (α-CO), Etofenprox and α-CO are determined by GC/MS. LOQ = 0.05 µg/L, for etofenprox and α-CO in drinking and ground water LOQ = 0.01 µg/L, for etofenprox and α-CO in surface water
Air (principle of method and LOQ)	Air samples are collected by drawing air through an absorbent packed sampling tube. Etofenprox and α-CO are extracted with hexane:ethyl ether (1:1, v/v). Etofenprox and α-CO are determined by GC/MS. LOQ=1.00 µg/m^3, for etofenprox and α-CO
Body fluids and tissues (principle of method and LOQ)	Not required (justification given)

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

	RMS/peer review proposal
Active substance	No classification

Chapter 2.3: Impact on Human and Animal Health

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

Rate and extent of absorption:	Rapid but limited absorption: 30 % average both sexes based on urine and bile excretion.
Distribution:	Uniformly distributed with highest concentration found in fat, adrenals, liver, ovary, thyroid and GI tract. Transferred via placenta to the foetus but placental and foetal concentrations are low relative to maternal plasma concentration and foetal elimination is rapid. Actively secreted into maternal milk, but transfer decreases markedly on cessation of dosing.
Potential for accumulation:	No potential for accumulation
Rate and extent of excretion:	Rapid and extensive excretion, predominantly in the faeces (86.4 – 90.4 % of the administered dose). Urinary excretion 6.3 – 10.7 %, biliary excretion 15.2 – 29.6 % within 48 hours.
Metabolism in animals	≥ 63 % metabolized, based on urinary and faecal metabolites. Two major metabolites (DE, 19.5 – 25.1 % and 4'-OH, 7.2 – 13.8 %) formed by O-deethylation of ethoxyphenyl moiety and ring hydroxylation of phenoxybenzyl moiety, subsequently eliminated in bile and urine as glucuronide or sulphate conjugates.
Toxicologically relevant compounds ‡ (animals and plants)	Etofenprox and α-CO (toxicity of α-CO similar to parent's toxicity)
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	> 2000 mg/kg bw	
Rat LD_{50} dermal	> 2000 mg/kg bw	
Rat LC_{50} inhalation	> 5.88 mg/L air /4h by whole body exposure to a liquid aerosol.	
Skin irritation	Non-irritant	
Eye irritation	Non- irritant	
Skin sensitisation	Non-sensitising (maximisation test)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect	Rat: Liver (hepatocyte enlargement, liver fat metabolism dysfunction) and thyroid (↑ thyroid weight, ↓ T4) Mouse: Liver (haemolymphoreticular system, hepatocyte enlargement and liver dysfunction on fat metabolism) and kidneys (renal cortical scarring, tubular dilatation and basophilia). Dog: Liver (minimal hepatocyte enlargement and liver dysfunction on protein and fat metabolism).	
Relevant oral NOAEL ‡	Rat, 13-week: 20 mg/kg bw/day Mouse, 13-week : 375 mg/kg bw/day Dog, 52-week: 32.2 mg/kg bw/day	
Relevant dermal NOAEL ‡	Rabbit, 4-week : > 1000 mg/kg/day (systemic) < 400 mg/kg bw/day (local irritation)	
Relevant inhalation NOAEC ‡	Rat, 13-week: 0.04 mg/L air	

Genotoxicity ‡ (Annex IIA, point 5.4)

No genotoxic potential	

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

Target/critical effect	Rat: Liver (hepatocyte enlargement, eosinophilic hepatocytes) and thyroid (increased thyroid weight, thyroid cystic follicles, increased incidence of thyroid adenomas). Mouse: Kidney (↑ incidence of dilated/basophilic renal tubules). Also, renal cortical scarring/cysts, enlargement, dilated basophilic tubules, focal loss of tubules, dilated/cystic Bowman's capsule, papillary mineralisation at highest dose level.	
Relevant NOAEL ‡	Rat: 3.7 mg/kg bw/day Mouse: 3.1 mg/kg bw/day	
Carcinogenicity	No carcinogenic potential for human risk assessment	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: reduced body weight gain, organ weight changes	

	Reproduction: no findings Offspring: increased pup mortality during lactation phase	**R64**
Relevant parental NOAEL ‡	4.3 mg/kg bw/day	
Relevant reproductive NOAEL ‡	246 mg/kg bw/day	
Relevant offspring NOAEL ‡	4.3 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Rat : Maternal: reduced body weight gain Developmental: no findings Rabbit: Maternal: Reduced body weight gain Developmental: increased post implantation loss reduced foetal weight gain	
Relevant maternal NOAEL ‡	Rat: 250 mg/kg bw/day Rabbit: 100 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 5000 mg/kg bw/day Rabbit: 100 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Rat: NOAEL > 2000mg/kg bw	
Repeated neurotoxicity ‡	Rat, 13-week: NOAEL neurotoxicity 604 mg/kg bw/day NOAEL systemic 299 mg/kg bw/day based on decreased body weight gain	
Delayed neurotoxicity ‡	No data - not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Rat developmental neurotoxicity: NOAEL (functional development) 28.4 mg/kg bw/day based on FOB changes. Rat peri/post-natal study: NOAEL: 250 mg/kg bw/day based on ↑ pup mortality, tremor, haemorrhage, histopathological alterations in kidneys of F1 progeny General pharmacology:

	No biologically significant pharmacological activity on the CNS, somatic and autonomic nervous systems, respiratory and circulatory systems, smooth muscle, renal and hepatic function including blood coagulation. Rat 4-week investigative study: 1° target organ - liver: NOAEL (1° effect on liver) 81.2 mg/kg bw/day based on: ↑ hepatic UDPGT, ↑ liver weight, and also ↑ microsomal protein and liver hypertrophy at the highest dose level. 2° target organ - thyroid: ↑ serum TSH, ↓ serum T4, ↑ thyroid proliferation. Proposed mechanism leading to ↑ incidence of thyroid adenoma: ↑ hepatic UDPGT → ↓ serum T4 → ↑ serum TSH → ↑ thyroid proliferation → ↑ incidence of thyroid adenoma
Studies performed on metabolites or impurities	Metabolite α-CO: Rat oral LD_{50} > 5000 mg/kg bw Rat dermal LD_{50} > 2000 mg/kg bw Rat 4-week dietary study: NOAEL 156 mg/kg bw/day based on ↑ kidney weight. Rat, 13-week dietary study: NOAEL 54 mg/kg bw/day based on ↓ weight gain, ↓ plasma thyroxin and protein, ↑ plasma AP and GOT, ↑ liver and kidney weights, minor histopathology in the kidneys. Negative *in vitro* in a bacterial reverse mutation assay (*S. typhimurium and E. coli*). Negative *in vitro* in lethal DNA damage in *E. coli*. Negative *in vitro* clastogenicity in human lymphocytes.

Medical data ‡ (Annex IIA, point 5.9)

Medical surveillance of production workers: no pattern of abnormalities in production operatives suggestive of adverse health effects due to exposure to etofenprox. No clinical cases of poisoning incidents known to the registrant.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.03 mg/kg bw/day	Mouse, 2-year study; supported by rat, 2-year study	100

AOEL ‡	0.06 mg/kg bw/day	Rat, 13-week study	overall 333 (100 + 30 % for limited enteral resorption)
ARfD ‡	1.0 mg/kg bw	Rabbit, developmental study	100

Dermal absorption (Annex IIIA, point 7.3)

Formulation: Trebon 30 EC	33 % based *in vivo* rat performed with the a.s. 30 % (default value for the EC formulation)

Exposure scenarios (Annex IIIA, point 7.2)

Operator

	Without PPE	With gloves
German model (all values as % of AOEL)		
oil seed rape – 0.060 kg ai/ha	38.3 %	nc
head cabbage – 0.150 kg ai/ha	95 %	43.3 % (1)
grape – 0.150 kg ai/ha		
Boom sprayer	120 %	99 % (1) 15 % (2)
knapsack	263.3 %	46.6 % (1)
peach & apple– 0.210 kg ai/ha	166 %	21.6 % (2)
UK-POEM (all values as % of AOEL)		
oil seed rape – 0.060 kg ai/ha	1300 %	131.6 %(2)
head cabbage – 0.150 kg ai/ha	4011 %	416 % (2)
grape – 0.150 kg ai/ha		
boom sprayer	1401 %	210 % (2)
knapsack	152 %	63 % (2)
peach – 0.210 kg ai/ha	2643 %	330 % (2)
apple – 0.210 kg ai/ha	2713 %	368 % (2)

<table>
<tr><td rowspan="6">Workers</td><td colspan="3">nc not calculated
(1) Gloves worn during mixing and loading
(2) Gloves worn during mixing, loading and spraying</td></tr>
<tr><td colspan="3">Method of calculation: Krebs B. et. al.; 2000[29].
All values as % of AOEL (one application)</td></tr>
<tr><td></td><td>Without PPE</td><td>With PPE (1)</td></tr>
<tr><td>oil seed rape – 0.060 kg ai/ha</td><td>20 %</td><td>1 %</td></tr>
<tr><td>head cabbage & grape – 0.150 kg ai/ha</td><td>300 %</td><td>15 %</td></tr>
<tr><td>peach – 0.210 kg ai/ha
apple – 0.175 kg ai/ha</td><td>420 %
350 %</td><td>21 %
16.6 %</td></tr>
<tr><td>Bystanders</td><td colspan="3">(1) Gloves, long sleeved shirt and long trousers
Method of calculation according to Lloyd and Bell, 1983[30] and Lloyd et al, 1987[31]
Bystander exposure (unprotected): 0.15 % to 5.5 % of AOEL.</td></tr>
</table>

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

	RMS/peer review proposal
Substance classified: etofenprox	**R64** "May cause harm to breastfed babies"

[29] Krebs B, *et al*. "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.
[30] Lloyd G.A. and Bell G.J. (1983). Hydraulic nozzles: comparative spray drift study (UK MAFF/ADAS).
[31] Lloyd G.A., Bell G.J., Samuels S.W., Cross J.V. and Berrie A.M. (1987). Orchard Sprayers: Comparative operator exposure and spray drift study (UK MAFF/ADAS).

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	Fruit crops (grape), Leafy crops (lettuce), Pulses/Oilseeds crops (oil seed rape)
Rotational crops	lettuce, barley, root crop (carrots)
Plant residue definition for monitoring	parent compound plus α-CO, expressed as etofenprox
Plant residue definition for risk assessment	parent compound plus α-CO, expressed as etofenprox
Conversion factor (monitoring to risk assessment)	not applicable

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

Animals covered	lactating goat, laying hen
Animal residue definition for monitoring	Etofenprox (provisional awaiting information on the fate of the α-CO metabolite in ruminant metabolism)
Animal residue definition for risk assessment	Etofenprox (provisional as above)
Conversion factor (monitoring to risk assessment)	none
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes: log P_{OW} = 6.9 and maximum residue levels observed in ruminant fat and poultry fat

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

	Based on the results of a confined crop rotational study with ageing of treated soil for 30 days, it is concluded that a crop rotation study with ageing of the soil for 120 or 365

	days is not required and that the application of etofenprox will not give rise to significant residues in succeeding crops.

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

	Etofenprox and its metabolite α-CO stable at about -20°C for at least 2 years in oil seed rape (Oilseed), head cabbage, and grape (high water content matrices), Stable in apple and peach matrices in a study conducted over 6 months only

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

Intakes:	**Ruminant:**			**Poultry:**	**Pig**
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes Dairy cattle: 13 mg/animal (0.67 mg/kg DM/d) Beef cattle: 25 mg/animal (1.74 mg/kg DM/d)			No	No
Potential for accumulation (yes/no):	Yes (fat soluble)			Yes (fat soluble)	Not evaluated
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Yes			Yes	Not evaluated
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg				
	10	**30**	**1000 mg/animal/d**		
Muscle	<0.05	<0.05	0.18 mg/kg	not required	not required
Liver	<0.05	<0.05	0.41 mg/kg	not required	not required
Kidney	<0.05	<0.05	0.62 mg/kg	not required	not required
Fat (peritoneal)	0.39	1.24	9.82 mg/kg	not required	not required
Milk (max value)	<0.05	0.05	2.11 mg/kg	not relevant	not relevant
Eggs	not relevant			not required	not required

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

Crop	Northern/Southern Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL	STMR (b)	HR
MRL, STMR and HR are based on the sum of etofenprox and α-CO						
Winter rape	Northern	Etofenprox (α-CO): 8x <0.01 (<0.01),		0.02	0.02	0.02
Head cabbage	Southern	Etofenprox (α-CO): 4x <0.01 (<0.01), 2x 0.01 (<0.01), 0.04 (<0.01)	One trial [0.12 (0.02)] was disregarded by the PRAPeR 55. Database considered sufficient sine head cabbage is a minor crop in southern E.U.	0.1	0.015	0.05
Grapes	Southern	Etofenprox (α-CO): 0.29 (0.08), 0.35 (0.03), 0.38 (0.06), 0.39 (0.14), 0.39 (0.18), 0.53 (0.06), 0.96 (0.08),and 1.37 (0.31)		2	0.55	1.68
Peach	Southern	Etofenprox (α-CO): 0.01 (0.02), 0.08 (0.01), 0.14 (0.02), 0.18 (0.02), 0.20 (0.03), 0.23 (0.02), 0.37 (0.04)		0.5	0.22	0.41

Apple	Southern	Etofenprox (α-CO): 0.10 (0.01), 0.13 (0.02), 0.18 (003), 0.20 (0.03), 0.22 (0.04), 0.25 (0.04), 0.27 (0.03), 0.34 (0.02)		0.5	~~0.26~~ 0.25	0.36

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

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

ADI	0.03 mg/kg/day
TMDI (Highest calculated-UK and EFSA models)	**Highest TMDI** EFSA model: 32% ADI (DE Child) UK PSD model: 80% ADI (Toddler and vegetarian)
ARfD	1.00 mg/kg
Acute exposure (% ARfD)	**Highest IESTI** (using MRL values) EFSA model: 13% ARfD for table grapes (Children) UK PSD model: 12% ARfD for table grapes (Toddler)

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

Processing factors calculated for the sum etofenprox + α-CO

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Rape seeds / cake, crude oil and refined oil	1	not applicable (Residues below LOQ in RAC and processed fractions)	n.d.
Grape / juice	2	<0.02	n.d.
Peach, whole fruit / jam	4 (1 trial no taken into account since residues in RAC close to LOQ	0.24 (3 trials)	n.d.
whole fruit / juice		0.20 (3 trials)	n.d.
whole fruit / puree		0.89 (3 trials)	n.d.
whole fruit / wet pomace	1	4.20	n.d.
whole fruit / dry pomace	1	21.60	n.d.
Apple, whole fruit / puree	3	0.30	n.d.
whole fruit / juice	3	0.11	n.d.
whole fruit / washed fruit	1	0.62	n.d
whole fruit / press cake (wet pomace)	3	2.69	n.d

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

whole fruit / dry pomace	1	13.00	n.d
Apple + Peach whole fruit / wet pomace	4	3.0	n.d

* Calculated on the basis of distribution in the different portions or products as determined through balance studies,
n.d. not determined (no balance studies)

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

Plant Products

Apple	0.50 mg/kg (based on Southern GAP only)
Peach	0.50 mg/kg (based on Southern GAP only)
Table and wine grapes	2.0 mg/kg (based on Southern GAP only)
Head cabbage	0.10 mg/kg (based on Southern GAP only)
Rape seeds	0.02* mg/kg (based on Northern GAP only)

Products of animal origin

Ruminant	
Meat	2 mg/kg (**on fat basis**)
Fat	2 mg/kg
Offals	0.05 mg/kg
Milk	0.05* mg/kg

Chapter 2.5: Fate and Behaviour in the Environment

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

Mineralization after 120 days	39.1-45.6% after 120 days, (n=4) [α-^{14}C-benzyl] & [2-^{14}C-propyl] labels
Non-extractable residues after 120 days	42.9-52.8% after 120 days, (n=4) [α-^{14}C-benzyl] & [2-^{14}C-propyl] labels
Metabolites requiring further consideration - name and/or code, % of applied (range and maximum)	none

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

Anaerobic degradation	<u>Parent</u> Mineralisation: 1.9% after 121 days Non-extractable residues: 9.5% after 121 days

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

	Metabolites 4'-OH: 2.8-11.7% (max. after 90 days) other metabolites: each < 2.7% unknown: each < 2.9%
Soil photolysis	Parent Mineralisation: 7.4% after 30 days non-extractable residues 45% after 30 days Metabolites α-CO: 1.5-7.7 % (max. after 20 days) other metabolites: each < 2.6% unknown: each < 2.2%

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

Method of calculation	Laboratory: mainly 1st–order kinetics
Laboratory studies (range or median, with n value, with r^2 value)	Parent (see table below) Metabolites α-CO: DT_{50lab} (20°C ,aerobic) = 12-45 days. $DT_{50lab\ Norm\ pF2}$ = 9.72 – 36.9 Geometric mean $DT_{50lab\ Norm\ pF2}$ = 18.9 days (n=4, average r^2=0.95) 1st order 4'-OH: DT_{50lab} (20°C ,aerobic): 14-44 days. $DT_{50lab\ Norm\ pF2}$ = 11.3 – 36.1 Geometric mean $DT_{50lab\ Norm\ pF2}$ = 20.22 days (n=4, average r^2=0.884) 1st order
	Parent (see table below) Metabolites α-CO: DT_{90lab} (20°C ,aerobic): 39.6-148.5 days. 4'-OH: DT_{90lab} (20°C ,aerobic): 46-145 days (n=4, average r^2= 0.884) 1st order
	Parent DT_{50lab} (10°C, aerobic): 13 days (n=1, r^2=0.977) Metabolites 4'-OH: DT_{50lab} (10°C ,aerobic): 56 days (n=1, r^2=0.901) 1st order
	Parent DT_{50lab} (20°C, anaerobic): water phase: 3.1 days (n=1, r^2=0.967) total system: 174 days (n=1, r^2=0.942)
	degradation in the saturated zone: no data – not required
Field studies (state location, range	no data - not required

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

or median with n value)	
Soil accumulation and plateau concentration	no data - not required

Laboratory studies

Parent	**Aerobic conditions**				
Soil Type	pH	t. °C / % of MWHC	**DT_{50} / DT_{90} [days]**	**DT_{50}[days] Normalized (20°C and pF 2)**	**Method of calculation**
silt clay loam	6.7	20°C/40 %	7 / 22	5.7	SFO
loam	7.2	20°C/40 %	8 / 28	8	SFO
sandy loam	6.8	20°C/40 %	14 / 46	10.4	SFO
sandy loam	7.4	20°C/40 %	25 / 84	20.4	SFO
sand	5.9	20°C/40 %	12.4 / 16.9	12.4	SFO
loamy sand	5.6	20°C/40 %	57.74 / 191.7	57.74	PSEUDO SFO FMOC DT_{90} / 3.32
sandy loam	6.4	20°C/40 %	47.38 / 157.3	41.27	PSEUDO SFO FMOC DT_{90} / 3.32
loamy sand	6.6	20°C/40 %	20.24 / 67.2	20.24	PSEUDO SFO FMOC DT_{90} / 3.32
Geometric mean			**18.46 / 58.09**	**16.6**	
Median			**17.12 / 56.6**	**16.3**	

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_d (ml/g)	196 – 343 (median 234, n=3, soil to aqueous phase ratio of 1:5) 434 – 836 (median 519, n=3, soil to aqueous phase ratio of 1:25)
K_{oc} (ml/g)	8548 – 14923 (median 9025, n=3, soil to aqueous phase ratio of 1:5) 18968 – 33067 (median 22009, n=3, soil to aqueous phase ratio of 1:25)
pH dependence (yes / no) (if yes type of dependence)	not expected

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

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

Column leaching	n=3, radiolabelled material Leaching: distilled water, in amount of 3 to 5 folds of maximum water holding capacity of each soil in leachate: <0.1-4.0% of applied radioactivity in soil (0-5 cm): 73.8-90.5% of applied radioactivity in soil (5-10 cm): 1.0-1.6% of applied radioactivity Parent not detected in leachate
Aged residues leaching	ageing for 2 weeks at 25°C, n=3, radiolabelled material Leaching: distilled water, in amount of 3 to 5 folds of maximum water holding capacity of each soil in leachate: <0.1-3.4% of applied radioactivity in soil (0-5 cm): 44.6-66.5% of applied radioactivity in soil (5-10 cm): 0.3-2.1% of applied radioactivity Parent not detected in leachate
Lysimeter/ field leaching studies	no data - not required

PEC (soil) (Annex IIIA, point 9.1.3)

Method of calculation	DT_{50lab}: 25 days, 1st order kinetics
Application rate	***Oil seed rape*** Crop interception: 80% Number of applications: 1 Interval (days): 0 Application rate: 60 g as/ha

$PEC_{(s)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.016 (5 cm)	0.016 (5 cm)	Not relevant	Not relevant

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

Short term	0.016 (5 cm)	0.016 (5 cm)	Not relevant	Not relevant
24h	0.015 (5 cm)	0.016 (5 cm)		
2d	0.014 (5 cm)	0.015 (5 cm)		
4d				
Long term 7d	0.013 (5 cm)	0.015 (5 cm)	Not relevant	Not relevant
28d	0.007 (5 cm)	0.011 (5 cm)		
50d	0.004 (5 cm)	0.009 (5 cm)		
100d	0.001 (5 cm)	0.005 (5 cm)		

Application rate

Head cabbage
Crop interception: 70% (1st and 2nd application)
Number of applications: 2
Interval: 14 days between 1st and 2nd application
Application rates: 150 g as/ha

PEC$_{(s)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	Not relevant	Not relevant	0.101 (5 cm)	-
Short term	Not relevant	Not relevant	0.098 (5 cm)	0.099 (5 cm)
24h			0.095 (5 cm)	0.098 (5 cm)
2d			0.090 (5 cm)	0.095 (5 cm)
4d				
Long term 7d	Not relevant	Not relevant	0.083 (5 cm)	0.092 (5 cm)
28d			0.046 (5 cm)	0.070 (5 cm)
50d			0.025 (5 cm)	0.054 (5 cm)
100d			0.006 (5 cm)	0.034 (5 cm)

Application rate

Grape
Crop interception: 70% (1st and 2nd application), 85% (3rd and 4th application)

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

Number of applications: 4 Interval: 7 days interval between 1st and 2nd application, about 80 days interval between 2nd and 3rd application,14 days between 3rd and 4th application Application rates: 150 g as/ha

PEC$_{(s)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	Not relevant	Not relevant	0.109 (5 cm)	-
Short term	Not relevant	Not relevant	0.106 (5 cm)	0.108 (5 cm)
24h			0.104 (5 cm)	0.1063 (5 cm)
2d			0.098 (5 cm)	0.104 (5 cm)
4d				
Long term 7d	Not relevant	Not relevant	0.090 (5 cm)	0.099 (5 cm)
28d			0.050 (5 cm)	0.076 (5 cm)
50d			0.027 (5 cm)	0.059 (5 cm)
100d			0.007 (5 cm)	0.037 (5 cm)

Application rate

Peach Crop interception: 80% (1st and 2nd application) Number of applications: 2 Interval: 7 days between 1st and 2nd application Application rates: 210 g as/ha

PEC$_{(s)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	Not relevant	Not relevant	0.102 (5 cm)	-
Short term	Not relevant	Not relevant	0.099 (5 cm)	0.101 (5 cm)
24h			0.097 (5 cm)	0.099 (5 cm)
2d			0.091 (5 cm)	0.097 (5 cm)

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

4d				
Long term 7d	Not relevant	Not relevant	0.084 (5 cm)	0.093 (5 cm)
28d			0.047 (5 cm)	0.071 (5 cm)
50d			0.026 (5 cm)	0.055 (5 cm)
100d			0.006 (5 cm)	0.035 (5 cm)

Application rate	***Apple*** Crop interception: 50% (1st application), 80% (2nd and 3rd application) Number of applications: 3 Interval: about 100 days between 1st and 2nd application, 7 days between 2nd and 3rd application Application rates: 210 g as/ha (1st application) 175 g as/ha (2d and 3d applications)

PEC$_{(s)}$	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	Not relevant	Not relevant	0.140 (5 cm)	-
Short term	Not relevant	Not relevant	0.136 (5 cm)	0.138 (5 cm)
24h			0.132 (5 cm)	0.136 (5 cm)
2d			0.125 (5 cm)	0.133 (5 cm)
4d				
Long term 7d	Not relevant	Not relevant	0.115 (5 cm)	0.127 (5 cm)
28d			0.064 (5 cm)	0.097 (5 cm)
50d			0.035 (5 cm)	0.076 (5 cm)
100d			0.009 (5 cm)	0.047 (5 cm)

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

Hydrolysis of active substance and relevant	Etofenprox:

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

metabolites (DT_{50}) (state pH and temperature)	pH 4: stable (50 °C) pH 7: stable (50 °C) pH 9: stable (50 °C) Metabolite: [^{14}C]- α-CO pH 4 and 7: stable in acetonitrile solution (9:1, v/v) at 50°C pH 9: hydrolysed to PENA and m-PBAcid at 35°C and 45°C Calculated DT_{50}: 9.6 days at 35°C (1st order, r^2=0.977) and 2.4 days at 45°C (1st order, r^2=0.985) Predicted DT_{50}: 42.8 days at 25°C (Arrhenius equation)
Photolytic degradation of active substance and relevant metabolites	Etofenprox: Buffer solution pH 7, xenon arc lamp: DT_{50} 4.7 days (1st order) Natural pond water, xenon arc lamp: DT_{50} 7.9 days (1st order) Estimated DT_{50} at 40°N: 8.4 – 44.2 days Estimated DT_{50} at 50°N: 9.5 – 131 days Metabolites: α-CO: 37.8% (in natural pond water) and 63.6% (in buffer solution at pH 7), after 15 days PENA: 14.4% (in natural pond water) and 12% (in buffer solution at pH 7), after 15 days
Readily biodegradable (yes/no)	No

Degradation in water/sediment	
- DT_{50} water	Etofenprox:-not calculated
- DT_{90} water	Etofenprox: -not calculated
- DT_{50} whole system	Etofenprox: 6.5 – 20.1 days (n=2, r^2 >0.994) 4'-OH: 21.8 - 57 days
- DT_{90} whole system	Etofenprox: 23.8 - 143.0 days(n=2, r^2 >0.994) 4'-OH: 59.8 - 185 days
Mineralization	0.2 – 35.7% (n=2, after 100 days)
Non-extractable residues in sediment	0.1 – 30.8 % (n=2, after 0 - 99 days)
Distribution in water / sediment systems (active substance)	after 0 days, water phase: 22.3 - 32.1% (n=2) after 0 days, sediment phase: 63.1- 70.1% (n=2)

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

Distribution in water / sediment systems (metabolites)	after 99 days, water phase: not detected (n=2) after 99 days, sediment phase: 7.6-7.8% (n=2) water phase: max. 2.2% (4'-OH, after 14 days) other metabolites in water phase: each < 1.9% sediment phase: max. 21.4% (4'-OH after 7 days) other metabolites in sediment phase: each < 3.8%

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

Etofenprox - Oil seed rape

Method of calculation	FOCUS Step 4 $DT_{50\ sediment}$: 18 days (1st order, n=2) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days (1st order, n=4)*
Application rate	***Oil seed rape (winter)*** Number of applications: 1 Interval (days): 0 Application rate: 60 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift. Spray buffer strip of 30 m assumed as mitigation measure. No run off or drainage mitigation implemented.

* Geometric mean of 16.6 d to be used in future assessments

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D2	Ditch	0.019
D2	Stream	0.023
D3	Ditch	0.019
D4	Pond	0.004
D4	Stream	0.022
D5	Pond	0.004
D5	Stream	0.024
R1	Pond	0.004
R1	Stream	0.017
R3	Stream	0.024

Etofenprox - Head cabbage

Method of calculation	FOCUS Step 3

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

	$DT_{50\ sediment}$: 18 days (1st order, n=2) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days* (1st order, n=4)
Application rate	***Head cabbage*** Number of applications: 2 (but modeling for 1 application gives the higher PECsw than modeling for 2 applications) Interval: 14 days between 1st and 2nd applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift

* Geometric mean of 16.6 d to be used in future assessments

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D3	Ditch	0.935
D4	Pond	0.032
D4	Stream	0.760
D6	Ditch	0.936
R1	Pond	0.032
R1	Stream	0.620
R2	Stream	0.831
R3	Stream	0.873
R4	Stream	0.620

Etofenprox - Grape

Method of calculation	<u>FOCUS Step 3</u> $DT_{50\ sediment}$: 18 days (1st order, n=2) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days* (1st order, n=4)
Application rate	***Grapes (late applications)*** Number of applications: 4 Interval: 7 days interval between 1st and 2nd applications, about 80 days interval between 2nd and 3d applications,14 days between 3rd and 4th applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below

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

Main routes of entry	Spray drift

* Geometric mean of 16.6 d to be used in future assessments

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D6	Ditch	2.544
R1	Pond	0.090
R1	Stream	1.859
R2	Stream	2.501
R3	Stream	2.619
R4	Stream	1.865

Etofenprox - Peach

Method of calculation	FOCUS Step 3 $DT_{50\ sediment}$: 18 days (1st order, n=2) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days* (1st order, n=4)
Application rate	***Peaches (late applications)*** Number of applications: 2 Interval: about 7 days between 1st and 2nd applications Application rates: 210 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift

* Geometric mean of 16.6 d to be used in future assessments

D3	Ditch	7.365
D4	Pond	0.341
D4	Stream	7.390
D5	Pond	0.341
D5	Stream	8.269
R1	Pond	0.341
R1	Stream	5.861
R2	Stream	7.858
R3	Stream	8.263
R4	Stream	5.860
D3	Ditch	7.365

Etofenprox - Apple

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

Method of calculation	FOCUS Step 3 $DT_{50\ sediment}$: 18 days (1st order, n=2) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days* (1st order, n=4)
Application rate	***Apple (late applications)*** Number of applications: 3 Interval: about 100 days between 1st and 2nd applications, 7 days between 1st and 2nd applications Appplication rates: 210 g as/ha (1st application) 175 g as/ha (2d and 3d applications) Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift

* Geometric mean of 16.6 d to be used in future assessments

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D3	Ditch	7.598
D4	Pond	0.341
D4	Stream	7.173
D5	Pond	0.340
D5	Stream	6.843
R1	Pond	0.341
R1	Stream	5.856
R2	Stream	7.706
R3	Stream	8.191
R4	Stream	5.817

Metabolite α-CO – Oil seed rape**	
Method of calculation	FOCUS SW Step 3 Etofenprox $DT_{50\ sediment}$: 18 days (1st order, n=2) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days* (1st order, n=4) Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the PEC SW at FOCUS Step 3 for the parent. Worst case scenarios: maximum concentrations
Application rate	***Oil seed rape (winter)*** Number of applications: 1

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

	Interval (days): 0 Application rate: 60 g as/ha of parent Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift of etofrenprosx anad degradation in water.

* Geometric mean of 16.6 d to be used in future assessments
**Values calculated by EFSA on basis of the values provide by the RMS in Addendum 2 v2 and Addendum 3 for the parent etofenprox

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D2	Ditch	0.239
D2	Stream	0.213
D3	Ditch	0.238
D4	Pond	0.008
D4	Stream	0.204
D5	Pond	0.008
D5	Stream	0.220
R1	Pond	0.008
R1	Stream	0.156
R3	Stream	0.219

Metabolite α-CO – Oil seed rape	
Method of calculation	FOCUS Step 4 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Oil seed rape (winter)*** Number of applications: 1 Interval (days): 0 Application rate: 60 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water. Spray buffer strip of 30 m assumed as mitigation measure for the parent. No run off or drainage mitigation implemented.

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D2	Ditch	0.012

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

D2	Stream	0.015
D3	Ditch	0.012
D4	Pond	0.003
D4	Stream	0.014
D5	Pond	0.003
D5	Stream	0.015
R1	Pond	0.003
R1	Stream	0.011
R3	Stream	0.015

Metabolite α-CO – Head cabbage ~~**Metabolite α-CO – Oil seed rape**~~ Method of calculation	FOCUS Step 43 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Head cabbage*** Number of applications: 2 Interval (days): 0 Application rate: 150g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D3	Ditch	0.595
D4	Pond	0.020
D4	Stream	0.483
D6	Ditch	0.595
R1	Pond	0.020
R1	Stream	0.394
R2	Stream	0.529
R3	Stream	0.555
R4	Stream	0.394

Metabolite α-CO – Grape

Method of calculation	FOCUS Step 3 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion

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

	of the parent. Worst case scenarios: maximum concentrations
Application rate	***Grapes (late applications)*** Number of applications: 4 Interval: 7 days interval between 1st and 2nd applications, about 80 days interval between 2nd and 3d applications,14 days between 3rd and 4th applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D6	Ditch	1.618
R1	Pond	0.057
R1	Stream	1.182
R2	Stream	1.591
R3	Stream	1.666
R4	Stream	1.186

Metabolite α-CO – Peach

Method of calculation	FOCUS Step 3 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study) . Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Peaches (late applications)*** Number of applications: 2 Interval: about 7 days between 1st and 2nd applications Application rates: 210 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D3	Ditch	4.684
D4	Pond	0.217

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

D4	Stream	4.700
D5	Pond	0.217
D5	Stream	5.259
R1	Pond	0.217
R1	Stream	3.728
R2	Stream	4.998
R3	Stream	5.255
R4	Stream	3.727

Metabolite α-CO – Apple

Method of calculation	FOCUS Step 3 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Apple (late applications)*** Number of applications: 3 Interval: about 100 days between 1st and 2nd applications, 7 days between 1st and 2nd applications Application rates: 210 g as/ha (1st application) 175 g as/ha (2d and 3d applications) Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D3	Ditch	4.832
D4	Pond	0.217
D4	Stream	4.562
D5	Pond	0.216
D5	Stream	4.352
R1	Pond	0.217
R1	Stream	3.724
R2	Stream	4.901
R3	Stream	5.209
R4	Stream	3.700

Metabolite 4'-OH – Oil seed rape	FOCUS Step 4 Max. occurrence of 4'-OH: 21.9% TRR

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

Method of calculation	(water/sediment study) . Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Oil seed rape (winter)*** Number of applications: 1 Interval (days): 0 Application rate: 60 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water. Spray buffer strip of 30 m assumed as mitigation measure for the parent. No run off or drainage mitigation implemented.

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D2	Ditch	0.004
	Stream	0.005
D3	Ditch	0.004
D4	Pond	0.001
D4	Stream	0.005
D5	Pond	0.001
D5	Stream	0.005
R1	Pond	0.001
R1	Stream	0.004
R3	Stream	0.005

Metabolite 4'-OH – Head cabbage

Method of calculation	FOCUS Step 3 Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Head cabbage*** Number of applications: 2 Interval: 14 days between 1st and 2nd applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsw

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

		(µg/L)
D2	Ditch	0.205
	Stream	0.007
D3	Ditch	0.166
D4	Pond	0.205
D4	Stream	0.007
D5	Pond	0.136
D5	Stream	0.182
R1	Pond	0.191
R1	Stream	0.136

Metabolite 4'-OH – Grape

Method of calculation	FOCUS Step 3 Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Grapes (late applications)*** Number of applications: 4 Interval: 7 days interval between 1st and 2nd applications, about 80 days interval between 2nd and 3d applications,14 days between 3rd and 4th applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D6	Ditch	0.557
R1	Pond	0.020
R1	Stream	0.407
R2	Stream	0.548
R3	Stream	0.574
R4	Stream	0.408

Metabolite 4'-OH – Peach

Method of calculation	FOCUS Step 3

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

	Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Peaches (late applications)*** Number of applications: 2 Interval: about 7 days between 1st and 2nd applications Application rates: 210 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D3	Ditch	1.613
D4	Pond	0.075
D4	Stream	1.618
D5	Pond	0.075
D5	Stream	1.811
R1	Pond	0.075
R1	Stream	1.284
R2	Stream	1.721
R3	Stream	1.810
R4	Stream	1.283

Metabolite 4'-OH – Apple

Method of calculation	FOCUS Step 3 Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Apple (late applications)*** Number of applications: 3 Interval: about 100 days between 1st and 2nd applications, 7 days between 1st and 2nd applications Application rates: 210 g as/ha (1st application) 175 g as/ha (2d and 3d applications) Scenario/water body: all relevant FOCUS SW scenarios – see below

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

Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsw (µg/L)
D3	Ditch	1.664
D4	Pond	0.075
D4	Stream	1.571
D5	Pond	0.074
D5	Stream	1.499
R1	Pond	0.075
R1	Stream	1.282
R2	Stream	1.688
R3	Stream	1.794
R4	Stream	1.274

PEC (sediment)

Etofenprox - Oil seed rape	FOCUS Step 4 $DT_{50\ sediment}$: 18 days (1st order, n=2) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days (1st order, n=4)
Application rate	***Oil seed rape (winter)*** Number of applications: 1 Interval (days): 0 Application rate: 60 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D2	Ditch	0.073
D2	Stream	0.087
D3	Ditch	0.036
D4	Pond	0.030
D4	Stream	0.005
D5	Pond	0.028
D5	Stream	0.007
R1	Pond	0.027
R1	Stream	0.057
R3	Stream	2.842

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

Etofenprox - Head cabbage

Method of calculation	FOCUS Step 3 $DT_{50\ sediment}$: 18 (1st order, n=2) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days (1st order, n=4)
Application rate	***Head cabbage*** Number of applications: 2 Interval: 14 days between 1st and 2nd applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	Ditch	0.817
D4	Pond	0.470
D4	Stream	0.081
D6	Ditch	0.940
R1	Pond	0.685
R1	Stream	8.501
R2	Stream	17.28
R3	Stream	23.84
R4	Stream	29.98

Etofenprox - Grape

Method of calculation	FOCUS Step 3 $DT_{50\ sediment}$: 18 days (geometric mean, n=3) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days (1st order, n=4)
Application rate	***Grapes (late applications)*** Number of applications: 4 Interval: 7 days interval between 1st and 2nd applications, about 80 days interval between 2nd and 3d applications,14 days between 3rd and 4th applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift

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

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D6	Ditch	22.56
R1	Pond	1.950
R1	Stream	1.716
R2	Stream	0.571
R3	Stream	1.783
R4	Stream	0.851

Etofenprox - Peach

Method of calculation	FOCUS Step 3 $DT_{50\ sediment}$: 18 days (geometric mean, n=3) $DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days (1st order, n=4)
Application rate	***Peaches (late applications)*** Number of applications: 2 Interval: about 7 days between 1st and 2nd applications Application rates: 210 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	Ditch	11.51
D4	Pond	3.995
D4	Stream	1.071
D5	Pond	3.854
D5	Stream	3.646
R1	Pond	3.734
R1	Stream	1.460
R2	Stream	1.004
R3	Stream	3.519
R4	Stream	1.445

Etofenprox - Apple

Method of calculation	FOCUS Step 3 $DT_{50\ sediment}$: 18 days (geometric mean, n=3)

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

	$DT_{50\ water}$: 1000 days $DT_{50\ soil}$: 25 days (1st order, n=4)
Application rate	***Apple (late applications)*** Number of applications: 3 Interval: about 100 days between 1st and 2nd applications, 7 days between 1st and 2nd applications Application rates: 210 g as/ha (1st application) 175 g as/ha (2d and 3d applications) Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Spray drift

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	Ditch	9.026
D4	Pond	5.496
D4	Stream	0.824
D5	Pond	5.046
D5	Stream	0.312
R1	Pond	5.167
R1	Stream	1.678
R2	Stream	1.206
R3	Stream	3.037
R4	Stream	1.379

Metabolite α-CO – Oil seed rape	
Method of calculation	FOCUS Step 4 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Oil seed rape (winter)*** Number of applications: 1 Interval (days): 0 Application rate: 60 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water. Spray buffer strip of 30 m assumed as mitigation measure for the parent. No run off or drainage mitigation implemented.

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

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D2	Ditch	0.046
D2	Stream	0.055
D3	Ditch	0.023
D4	Pond	0.019
D4	Stream	0.003
D5	Pond	0.018
D5	Stream	0.004
R1	Pond	0.017
R1	Stream	0.036
R3	Stream	1.808

Metabolite α-CO – Head cabbage

Method of calculation	FOCUS Step 3 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Head cabbage*** Number of applications: 2 Interval: 14 days between 1st and 2nd applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	Ditch	0.520
D4	Pond	0.299
D4	Stream	0.052
D6	Ditch	0.598
R1	Pond	0.436
R1	Stream	5.407
R2	Stream	10.99
R3	Stream	15.16
R4	Stream	19.07

Metabolite α-CO – Grape

Method of calculation	FOCUS Step 3

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

	Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Grapes (late applications)*** Number of applications: 4 Interval: 7 days interval between 1st and 2nd applications, about 80 days interval between 2nd and 3d applications,14 days between 3rd and 4th applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D6	Ditch	14.35
R1	Pond	1.240
R1	Stream	1.091
R2	Stream	0.363
R3	Stream	1.134
R4	Stream	0.541

Metabolite α-CO – Peach

Method of calculation	FOCUS Step 3 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Peaches (late applications)*** Number of applications: 2 Interval: about 7 days between 1st and 2nd applications Application rates: 210 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	Ditch	7.320
D4	Pond	2.541

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

D4	**Stream**	**0.681**
D5	**Pond**	**2.451**
D5	**Stream**	**2.319**
R1	**Pond**	**2.375**
R1	**Stream**	**0.929**
R2	**Stream**	**0.639**
R3	**Stream**	**2.238**
R4	**Stream**	**0.919**

Metabolite α-CO – Apple

Method of calculation	FOCUS Step 3 Max. occurrence of α-CO: 63% TRR (aqueous photolysis study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Apple (late applications)*** Number of applications: 3 Interval: about 100 days between 1st and 2nd applications, 7 days between 1st and 2nd applications Application rates: 210 g as/ha (1st application) 175 g as/ha (2d and 3d applications) Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	**Ditch**	**5.741**
D4	**Pond**	**3.495**
D4	**Stream**	**0.524**
D5	**Pond**	**3.209**
D5	**Stream**	**0.198**
R1	**Pond**	**3.286**
R1	**Stream**	**1.067**
R2	**Stream**	**0.767**
R3	**Stream**	**1.932**
R4	**Stream**	**0.877**

Metabolite 4'-OH – Oil seed rape Method of calculation	FOCUS Step 4 Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations

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

Application rate	***Oil seed rape (winter)*** Number of applications: 1 Interval (days): 0 Application rate: 60 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water. Spray buffer strip of 30 m assumed as mitigation measure for the parent. No run off or drainage mitigation implemented.

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D2	Ditch	0.016
D2	Stream	0.019
D3	Ditch	0.008
D4	Pond	0.007
D4	Stream	0.001
D5	Pond	0.006
D5	Stream	0.002
R1	Pond	0.006
R1	Stream	0.0012
R3	Stream	0.622

Metabolite 4'-OH – Head cabbage

Method of calculation	FOCUS Step 3 Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Head cabbage*** Number of applications: 2 Interval: 14 days between 1st and 2nd applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	Ditch	0.179
D4	Pond	0.103
D4	Stream	0.018
D6	Ditch	0.206
R1	Pond	0.150

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

R1	**Stream**	**1.862**
R2	**Stream**	**3.784**
R3	**Stream**	**5.221**
R4	**Stream**	**6.566**

Metabolite 4'-OH – Grape

Method of calculation	FOCUS Step 3 Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Grapes (late applications)*** Number of applications: 4 Interval: 7 days interval between 1st and 2nd applications, about 80 days interval between 2nd and 3d applications,14 days between 3rd and 4th applications Application rates: 150 g as/ha Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D6	**Ditch**	**4.941**
R1	**Pond**	**0.427**
R1	**Stream**	**0.376**
R2	**Stream**	**0.125**
R3	**Stream**	**0.390**
R4	**Stream**	**0.186**

Metabolite 4'-OH – Peach

Method of calculation	FOCUS Step 3 Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Peaches (late applications)*** Number of applications: 2 Interval: about 7 days between 1st and 2nd applications Application rates: 210 g as/ha Scenario/water body: all relevant FOCUS SW

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

	scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	Ditch	2.521
D4	Pond	0.875
D4	Stream	0.235
D5	Pond	0.844
D5	Stream	0.798
R1	Pond	0.818
R1	Stream	0.320
R2	Stream	0.220
R3	Stream	0.771
R4	Stream	0.316

Metabolite 4'-OH – Apple

Method of calculation	FOCUS Step 3 Max. occurrence of 4'-OH: 21.9% TRR (water/sediment study). Calculated as the proportion of the parent. Worst case scenarios: maximum concentrations
Application rate	***Apple (late applications)*** Number of applications: 3 Interval: about 100 days between 1st and 2nd applications, 7 days between 1st and 2nd applications Application rates: 210 g as/ha (1st application) 175 g as/ha (2d and 3d applications) Scenario/water body: all relevant FOCUS SW scenarios – see below
Main routes of entry	Degradation of etofenprox in surface water

FOCUS scenario	Water body	Maximum PECsed (µg/Kg)
D3	Ditch	1.977
D4	Pond	1.204
D4	Stream	0.180
D5	Pond	1.105
D5	Stream	0.068
R1	Pond	1.132
R1	Stream	0.367
R2	Stream	0.264
R3	Stream	0.665
R4	Stream	0.302

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

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	Model calculations using Focus-Pelmo 3.3.2 and Focus-Pearl 3.3.3 Etofenprox DT_{50soil} = 11.1 d* K_{oc} = 10832 α-CO DT_{50soil} = 21.7 d** K_{oc} = 287900 (PCKOCWIN estimation) Max. 7 % was assumed to be applied as parent in the updated PEARL calculation*** 26 years run Scenari: Châteaudun, Hamburg, Kremsmünster, Jokioinen, Okehampton, Piacenza, Porto, Sevilla, Thiva Freundlich sorption exponent (1/n): 1 (the correct value for leaching modelling).
Application rate	**Winter rape** Single application Application/year: every year Application rate: 60 g as/ha

* Geometric mean of 16.6 d to be used in future assessments
** Geometric mean of 18.9 d to be used in future assessments
*** The PELMO calculation used a max of 3.5 % as surrogate of formation fraction and therefore is regarded as unreliable.

$PEC_{(gw)}$

Maximum concentration	Etofenprox: <0.001 µg/L α-CO, 4'-OH, DE and DP: <0.001 µg/L
Average annual concentration	Etofenprox: <0.001 µg/L α-CO, 4'-OH, DE and DP: <0.001 µg/L

Application rate	**Head cabbage** Two applications Application/year: every year Application rates: 150 g as/ha

$PEC_{(gw)}$

Maximum concentration	Etofenprox: <0.001 µg/L α-CO, 4'-OH, DE and DP: <0.001 µg/L
Average annual concentration	Etofenprox: <0.001 µg/L α-CO, 4'-OH, DE and DP: <0.001 µg/L

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

Application rate	**Grapevine** Four applications Application/year: every year Application ratess: 150 g as/ha
PEC$_{(gw)}$	
Maximum concentration	Etofenprox: <0.001 µg/L α-CO, 4'-OH, DE and DP: <0.001 µg/L
Average annual concentration	Etofenprox: <0.001 µg/L α-CO, 4'-OH, DE and DP: <0.001 µg/L
Application rate	**Peach** Two applications Application/year: every year Application rate: 210 g as/ha
PEC$_{(gw)}$	
Maximum concentration	Not simulated (see application to apple)
Average annual concentration	Not simulated (see application to apple)
Application rate	**Apple** Three applications Application/year: every year Application rates: 210 g as/ha (1st application) 175 g as/ha (2^{d} and 3^{d} applications)
PEC$_{(gw)}$	
Maximum concentration	Etofenprox: <0.001 µg/L α-CO, 4'-OH, DE and DP: <0.001 µg/L
Average annual concentration	Etofenprox: <0.001 µg/L α-CO, 4'-OH, DE and DP: <0.001 µg/L

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

Direct photolysis in air	guideline not yet available
Quantum yield of direct phototransformation	0.248 in buffer solution at pH 7 0.147 in natural pond water
Photochemical oxidative degradation in air	DT_{50} calculated=2.07 hours

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

Volatilization	Not expected (vapour pressure = 8.13×10^{-7} Pa and Henry's law constant = 0.0136 Pa m^3/mol)

PEC (air)

Method of calculation	guideline not yet available

$PEC_{(a)}$

Maximum concentration	guideline not yet available

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	Soil: parent compound Surface Water: parent compound and metabolites α-CO Sediment: parent compound and metabolites α-CO and 4'-OH Ground Water: parent compound etofenprox and metabolite α-CO. Metabolite 4'-OH only under anaerobic conditions. Air: parent compound

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

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

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

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

None

Chapter 2.6: Effects on Non-target Species

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

Acute toxicity to mammals	LD_{50} > 2000 mg as/kg bw (rat) (a.s.) LD_{50} > 5000 mg as/kg (dog) (a.s.) LD_{50} > 1500 mg as/kg (rat and mouse) (f.p.)
Acute toxicity to birds	LD_{50} > 2000 mg as/kg bw (mallard duck) (a.s.) LD_{50} > 630 mg as/kg bw (Japanese quail) (f.p.)
Dietary toxicity to birds	LC_{50} > 5000 mg as/kg diet (mallard duck and bobwhite quail) (a.s.), equivalent to: LC_{50} > 1284.40 mg as/kg bw/day (mallard duck) LC_{50} > 805.6 mg as/kg bw/day (bobwhite quail)
Chronic toxicity to mammals	NOEL (F0): 37~~-44~~ mg a.i./kg bw/day (rat) (a.s.)
Reproductive toxicity to birds	NOEL: 1000 mg as/kg diet (bobwhite quail) (a.s.), equivalent to: NOEL: 89.6 mg as/kg bw/day (bobwhite quail)

a.s.: tests with the active substance
f.p.: tests with the formulated product

(TREBON 30EC)

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
0.06	Oil seed rape	Medium herbivorous birds	acute	>504 >159*	10
0.06	Oil seed rape	Medium herbivorous birds	short-term	>442	10
0.06	Oil seed rape	Medium herbivorous birds	long-term	>93.3	5
0.06	Oil seed rape	Insectivorous birds	acute	>616 >266*	10
0.06	Oil seed rape	Insectivorous birds	short-term	>445	10
0.06	Oil seed rape	Insectivorous birds	long-term	>49.5	5
0.06	Oil seed rape	Medium herbivorous	acute	>1368 >1026*	10

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

		mammals			
0.06	Oil seed rape	Medium herbivorous mammals	long-term	8.7	5
0.06	Oil seed rape	Fish-eating bird	long-term	871**	5
0.06	Oil seed rape	Fish-eating mammal	long-term	581**	5
0.06	Oil seed rape	Earthworm-eating bird	long-term	18.3	5
0.06	Oil seed rape	Earthworm-eating mammal	long-term	5.94	5
0.06	Oil seed rape	Consumption of contaminated drinking water - bird	acute	>247***	10
0.06	Oil seed rape	Consumption of contaminated drinking water - bird	acute	>425*** *	10
0.15	Head cabbage	Medium herbivorous birds	acute	>168 >52.9*	10
0.15	Head cabbage	Medium herbivorous birds	short-term	>126	10
0.15	Head cabbage	Medium herbivorous birds	long-term	>26.6	5
0.15	Head cabbage	Insectivorous birds	acute	>247 >77.7*	10
0.15	Head cabbage	Insectivorous birds	short-term	>178.1	10
0.15	Head cabbage	Insectivorous birds	long-term	>19.8	5
0.15	Head cabbage	Medium herbivorous mammals	acute	>456 >342*	10
0.15	Head cabbage	Medium herbivorous mammals	long-term	4683	5
0.15	Head cabbage	Fish-eating bird	long-term	2571**	5
0.15	Head cabbage	Fish-eating mammal	long-term	1715**	5
0.15	Head cabbage	Earthworm-eating bird	long-term	**2.9**	5
0.15	Head cabbage	Earthworm-eating mammal	long-term	**0.94**	5
0.15	Head cabbage	Consumption of	acute	>49***	10

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

		contaminated drinking water - bird			
0.15	Head cabbage	Consumption of contaminated drinking water - bird	acute	>85****	10
0.15	Grapevines	Insectivorous birds	acute	>247 >77.7*	10
0.15	Grapevines	Insectivorous birds	short-term	>178.1	10
0.15	Grapevines	Insectivorous birds	long-term	>19.8	5
0.15	Grapevines	Small herbivorous mammals	acute	>80.6 >60.5*	10
0.15	Grapevines	Small herbivorous mammals	long-term	31	5
0.15	Grapevines	Fish-eating bird	long-term	152**	5
0.15	Grapevines	Fish-eating mammal	long-term	101**	5
0.15	Grapevines	Earthworm-eating bird	long-term	**2.7**	5
0.15	Grapevines	Earthworm-eating mammal	long-term	**0.87**	5
0.15	Grapevines	Consumption of contaminated drinking water - bird	acute	>247***	10
0.15	Grapevines	Consumption of contaminated drinking water - bird	acute	<425***	10
0.21	Peach	Insectivorous birds	acute	>176 >55.5*	10
0.21	Peach	Insectivorous birds	short-term	>127	10
0.21	Peach	Insectivorous birds	long-term	>14.1	5
0.21	Peach	Small herbivorous mammals	acute	>47.4 >35.6*	10
0.15	Peach	Small herbivorous mammals	long-term	82	5
0.15	Peach	Fish-eating bird	long-term	199**	5
0.15	Peach	Fish-eating mammal	long-term	132**	5
0.15	Peach	Earthworm-eating bird	long-term	**2.9**	5

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

0.15	Peach	Earthworm-eating mammal	long-term	**0.93**	5
0.15	Peach	Consumption of contaminated drinking water - bird	acute	>265***	10
0.15	Peach	Consumption of contaminated drinking water - bird	acute	>455****	10
0.21 x 1 0.15 x 2	Apple	Insectivorous birds	acute	>176 >55.5*	10
0.21 x 1 0.15 x 2	Apple	Insectivorous birds	short-term	>127	10
0.21 x 1 0.15 x 2	Apple	Insectivorous birds	long-term	>14.1	5
0.21 x 1 0.15 x 2	Apple	Small herbivorous mammals	acute	>47.4 >35.6*	10
0.21 x 1 0.15 x 2	Apple	Small herbivorous mammals	long-term	123	5
0.21 x 1 0.15 x 2	Apple	Fish-eating bird	long-term	318**	5
0.21 x 1 0.15 x 2	Apple	Fish-eating mammal	long-term	212**	5
0.21 x 1 0.15 x 2	Apple	Earthworm-eating bird	long-term	**2.1**	5
0.21 x 1 0.15 x 2	Apple	Earthworm-eating mammal	long-term	**0.68**	5
0.21 x 1 0.15 x 2	Apple	Consumption of contaminated drinking water - bird	acute	>212***	10
0.21 x 1 0.15 x 2	Apple	Consumption of contaminated drinking water - bird	acute	>364	10

All TERs based on the results of toxicity studies with the active ingredient etofenprox, except
*: based on the results of toxicity studies with the formulation TREBON 30EC.
**: TERs were recalculated by EFSA after the peer-review, based on maximum 21d twa FOCUS PECsw values revised by RMS in Addendum Vol. 3 ver. 3 (November, 2008).
***: Puddles scenario with a 10 g bird.
****: TERs were recalculated by EFSA after the peer-review for the puddles scenario with a 10g mammal, following the conclusion of member state experts for a Tier 1 risk assessment

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

for consumption of contaminated drinking water (PRAPeR 53, Round 10). The lower acute toxicity endpoint for the formulation was applied in the calculation.

‡ 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	Endpoint	Toxicity (mg/l)
Laboratory tests				
Fish				
Oncorhynchus mykiss	a.s. etofenprox	96 h, flow-through	Mortality, LC_{50}	0.0027 (2)
Oncorhynchus mykiss	a.s. etofenprox	21d, semi-static	Mortality and growth, NOEC	0.0021 (2)
Oncorhynchus mykiss	metabolite α-CO	96 h, flow-through	Mortality, LC_{50}	> 0.048 (2)
Oncorhynchus mykiss	Formulation TREBON 30EC	96 h, semi-static	Mortality, LC_{50}	0.0066(2)
Lepomis macrochirus	Formulation TREBON 30EC	96 h, semi-static	Mortality, LC_{50}	0.0066(2)
Aquatic invertebrate				
Daphnia magna	a.s. etofenprox	48 h, static renewal	Mortality, EC_{50}	0.0012 (2)
Daphnia magna	a.s. etofenprox	21 d, semi-static	Reproduction, NOEC	0.000054 (2)
Daphnia magna	metabolite α-CO	48 h, static	Mortality, EC_{50}	> 0.044 (2)
Daphnia magna	Formulation TREBON 30EC	48 h, static	Mortality, EC_{50}	0.00044(2)
Algae				
Pseudokirchneriella subcapitata	a.s. etofenprox	72 h, static	Biomass, E_bC_{50}	> 0.150 (1)
Pseudokirchneriella subcapitata	a.s. etofenprox	72 h, static	Biomass, NOEC	0.150 (1)
Pseudokirchneriella subcapitata	metabolite α-CO	96 h, static	Biomass, E_bC_{50}	> 0.053 (2)
Selenastrum capricornutum	Formulation TREBON 30EC	72 h, static	Biomass, E_bC_{50}	58 (1)
Selenastrum capricornutum	Formulation TREBON 30EC	72 h, static	Growth, NOEC	22 (1)
Sediment dwelling organisms				
Submitted toxicity studies on sediment dwellers exposed to etofenprox were not accepted in peer review. I.e. not studies available.				

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

Chironomus riparius	metabolite 4'-OH	48 h, static	Mortality, LC_{50}	0.0502 (2)
Microcosm or mesocosm tests				
A mesocosm study was provided (Blake, 2004). MS experts had concerns about the suggested mesocosm endpoint (NOEC of 0.00005 mg a.s./L for Asellidae) due to high viability in the control. It was considered that a screening of laboratory studies with several invertebrate species would have been useful to consolidate the confidence in the data from the mesocosm. The MS experts proposed that the applicant should address the uncertainty of the study, particularly because of the variability within the controls, e.g. with single species studies on the most sensitive species identified in the mesocosm study, in order to derive a NOEC for the risk assessment. Based on that, the need for an additional assessment factor would have to be considered.				

(1) based on nominal concentrations
(2) based on mean measured concentrations

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

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

FOCUS Step 3

Oil seed rape – 1 x 0.060 kg a.i./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i [(1)] (µg/L)	TER	Annex VI Trigger
a.s.	Fish	0.0027	Acute	0.380	**7.1**	100
a.s.	Fish	0.0021	Chronic	0.380	**5.5**	10
a.s.	Aquatic invertebrates	0.0012	Acute	0.380	**3.2**	100
a.s.	Aquatic invertebrates	0.000054	Chronic	0.380	**0.1**	10
a.s.	Algae	0.150	Chronic	0.380	394.7	10
Met. α-CO	Fish	0.048	Acute	0.242	198	100
Met. α-CO	Aquatic invertebrates	0.044	Acute	0.242	182	100
Met. α-CO	Algae	0.053	Chronic	0.242	219	10
Formulation TREBON 30EC	Fish	0.022	Acute	0.380	**17.4**	100
	Aquatic invertebrates	0.0015	Acute	0.380	**1.2**	100
	Algae	22	Chronic	0.380	48079	10

(1) For the FOCUS SW scenario giving the highest PECs values (D2, ditch for SW)

FOCUS Step 4 (30 m no-spray buffer zone)

Oil seed rape – 1 x 0.060 kg a.i./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i [(1)] (µg/L)	TER	Annex VI Trigger
a.s.	Fish	0.0027	Acute	0.024	112.5	100
a.s.	Fish	0.0021	Chronic	0.024	87.5	10
a.s.	Aquatic invertebrates	0.00044	Acute	0.024	**18.33**	100
a.s.	Aquatic invertebrates	0.000054	Chronic	0.024	**2.25**	10
a.s.	Algae	0.150	Chronic	0.024	6250	10
Met. α-CO	Fish	0.048	Acute	0.015	3200	100
Met. α-CO	Aquatic invertebrates	0.044	Acute	0.015	2933	100
Met. α-CO	Algae	0.053	Chronic	0.015	3533	10
Formulati	Fish	0.022	Acute	0.024	916.7	100

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

on TREBON 30EC	Algae	22 (1)	Chronic	0.024	$9.2x10^5$	10

(1) For the FOCUS SW scenario giving the highest PECs values (D5 stream)

FOCUS Step 4 (30 m no-spray buffer zone)

Oil seed rape – 1 x 0.060 kg a.i./ha. Acute and chronic risk assessment for aquatic invertebrates for all $FOCUS_{SW}$ scenarious.

Scenario	Water body type	Organism	Toxicity end point (µg/L)	Time scale	PEC_i (5) (µg/L)	TER	Annex VI Trigger
D2	Ditch	Aquatic invertebrates	0.44	Acute	0.019	**23.16**	100
D2	Ditch	Aquatic invertebrates	0.054	Chronic	0.019	**2.84**	10
D2	Stream	Aquatic invertebrates	0.44	Acute	0.023	**19.13**	100
D2	Stream	Aquatic invertebrates	0.054	Chronic	0.023	**2.35**	10
D3	Ditch	Aquatic invertebrates	0.44	Acute	0.019	**23.16**	100
D3	Ditch	Aquatic invertebrates	0.054	Chronic	0.019	**2.84**	10
D4	Pond	Aquatic invertebrates	0.44	Acute	0.004	110.00	100
D4	Pond	Aquatic invertebrates	0.054	Chronic	0.004	13.50	10
D4	Stream	Aquatic invertebrates	0.44	Acute	0.022	**20.00**	100
D4	Stream	Aquatic invertebrates	0.054	Chronic	0.022	**2.45**	10
D5	Pond	Aquatic invertebrates	0.44	Acute	0.004	110.00	100
D5	Pond	Aquatic invertebrates	0.054	Chronic	0.004	13.50	10
D5	Stream	Aquatic invertebrates	0.44	Acute	0.024	**18.33**	100
D5	Stream	Aquatic invertebrates	0.054	Chronic	0.024	**2.25**	10

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

R1	Pond	Aquatic invertebrates	0.44	Acute	0.004	110.00	100
R1	Pond	Aquatic invertebrates	0.054	Chronic	0.004	13.50	10
R1	Stream	Aquatic invertebrates	0.44	Acute	0.017	**25.88**	100
R1	Stream	Aquatic invertebrates	0.054	Chronic	0.017	**3.18**	10
R3	Stream	Aquatic invertebrates	0.44	Acute	0.024	**18.33**	100
R3	Stream	Aquatic invertebrates	0.054	Chronic	0.024	**2.25**	10

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

FOCUS Step 3

Head cabbage - 2 x 0.150 kg a.i./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i [(1)] (µg/L)	TER	Annex VI Trigger
a.s.	Fish	0.0027	Acute	0.936	**2.9**	100
a.s.	Fish	0.0021	Chronic	0.936	**2.2**	10
a.s.	Aquatic invertebrates	0.0012	Acute	0.936	**1.3**	100
a.s.	Aquatic invertebrates	0.000054	Chronic	0.936	**0.06**	10
a.s.	Algae	0.150	Chronic	0.936	160.3	10
Met. α-CO	Fish	0.048	Acute	0.595	**81**	100
Met. α-CO	Aquatic invertebrates	0.044	Acute	0.595	**74**	100
Met. α-CO	Algae	0.053	Chronic	0.595	89	10
Formulation TREBON 30EC	Fish	0.022	Acute	0.936	**7.1**	100
	Aquatic invertebrates	0.0015	Acute	0.936	**0.5**	100
	Algae	22	Chronic	0.936	19519	10

(1) For the FOCUS SW scenario giving the highest PECs values (D6, ditch for SW)

FOCUS Step 3

Grape - 4 x 0.150 kg a.i./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i [(1)] (µg/L)	TER	Annex VI Trigger
a.s.	Fish	0.0027	Acute	2.619	**1.03**	100
a.s.	Fish	0.0021	Chronic	2.619	**0.80**	10
a.s.	Aquatic invertebrates	0.0012	Acute	2.619	**0.46**	100
a.s.	Aquatic invertebrates	0.000054	Chronic	2.619	**0.02**	10
a.s.	Algae	0.150	Chronic	2.619	57.3	10
Met. α-CO	Fish	0.048	Acute	1.666	**29**	100
Met. α-CO	Aquatic invertebrates	0.044	Acute	1.666	**26**	100
Met. α-CO	Algae	0.053	Chronic	1.666	32	10
Formulation TREBON	Fish	0.022	Acute	2.619	**2.52**	100
	Aquatic invertebrates	0.0015	Acute	2.619	**0.17**	100

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

30EC	Algae	22	Chronic	2.619	6976	10

(1) For the FOCUS SW scenario giving the highest PECs values (R3, stream for SW)

FOCUS Step 3

Peach - 2 x 0.210 kg a.i./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (1) (µg/L)	TER	Annex VI Trigger
a.s.	Fish	0.0027	Acute	8.263	**0.33**	100
a.s.	Fish	0.0021	Chronic	8.263	**0.25**	10
a.s.	Aquatic invertebrates	0.0012	Acute	8.263	**0.15**	100
a.s.	Aquatic invertebrates	0.000054	Chronic	8.263	**0.01**	10
a.s.	Algae	0.150	Chronic	8.263	18.2	10
Met. α-CO	Fish	0.048	Acute	5.255	**9**	100
Met. α-CO	Aquatic invertebrates	0.044	Acute	5.255	**8**	100
Met. α-CO	Algae	0.053	Chronic	5.255	10	10
Formulation TREBON 30EC	Fish	0.022	Acute	8.263	**0.80**	100
	Aquatic invertebrates	0.0015	Acute	8.263	**0.05**	100
	Algae	22	Chronic	8.263	2211	10

(1) For the FOCUS SW scenario giving the highest PECs values (R3, stream for SW)

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

FOCUS Step 3

Apple - 1 x 0.210 and 2 x 175 kg a.i./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i [(1)] (µg/L)	TER	Annex VI Trigger
a.s.	Fish	0.0027	Acute	8.191	**0.33**	100
a.s.	Fish	0.0021	Chronic	8.191	**0.26**	10
a.s.	Aquatic invertebrates	0.0012	Acute	8.191	**0.15**	100
a.s.	Aquatic invertebrates	0.000054	Chronic	8.191	**0.01**	10
a.s.	Algae	0.150	Chronic	8.191	**18.3**	10
Met. α-CO	Fish	0.048	Acute	5.209	**9**	100
Met. α-CO	Aquatic invertebrates	0.044	Acute	5.209	**8**	100
Met. α-CO	Algae	0.053	Chronic	5.209	10	10
Formulation TREBON 30EC	Fish	0.022	Acute	8.191	**0.81**	100
	Aquatic invertebrates	0.0015	Acute	8.191	**0.05**	100
	Algae	22	Chronic	8.191	2230	10

(1) For the FOCUS SW scenario giving the highest PECs values (R3, stream for SW)

Bioconcentration

Log Pow	6.9
Bioconcentration factor (BCF)	in edibles, BCF=1554 in non-edibles, BCF=7213 in whole fish, BCF=3951
Annex VI Trigger for the bioconcentration factor	1000
Clearance time (CT_{50}) (CT_{90})	CT_{50} = 9-16 days (first-order kinetics) CT_{95} = 39-69 days (first-order kinetics)
Level of residues (%) in organisms after the 14 day depuration phase	34% - 67% (after 14 days depuration phase) 1.6% - 5.2% (after 62 days depuration phase)

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

Test substance	Acute oral toxicity LD_{50}	Acute contact toxicity LD_{50}

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

a.s.	0.024 µg a.s./bee (48 h)	0.015 µg a.s./bee (48 h)
Preparation	0.37 µg a.s./bee (48h)	0.04 µg a.s./bee (48 h)

Field or semi-field tests

Semi-field tests

Two tent tests were provided, indicating repellent effects on bee flight in flowering *Phacelia tanacetifolia* exposed to etofenprox. None of these studies were considered to be relevant by Member State experts to address the risk from the intended uses, either due to unexplained mortality (Muhlen *et al.*,1996) or due to inadequate exposure rate (Anonymous, 1990).

Field test (Hurny, 1987): Spraying of mustard plants (*Sinapis alba*) in flowering stage indicated that Trebon (30 EC) has a repellent effect. Cage test under field conditions in flowering mustard plants (*Sinapis alba*) under covered conditions indicated no adverse effects on colonies.

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

Oil seed rape, 1 x 60 g a.i./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	oral	2521	50
a.s.	contact	4138	50
Preparation	oral	164	50
Preparation	contact	1579	50

Head cabbage, 2 x 150 g a.i./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	oral	6303	50
a.s.	contact	10345	50
Preparation	oral	410	50
Preparation	contact	3947	50

Grape, 4 x 150 g a.i./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	oral	6303	50
a.s.	contact	10345	50
Preparation	oral	410	50
Preparation	contact	3947	50

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

Peach, 2 x 210 g a.i./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	oral	8824	50
a.s.	contact	14483	50
Preparation	oral	574	50
Preparation	contact	5526	50

Apple, 1 x 210 and 2 x 175 g a.i./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	oral	8824	50
a.s.	contact	14483	50
Preparation	oral	574	50
Preparation	contact	5526	50

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

Laboratory test with standard sensitive species, further laboratory and extended laboratory studies

Species	Stage	Test Substance	Endpoint	Effect
Laboratory tests				
Aphidius rhopalosiphi	Adult	TREBON 30EC	Mortality Reproductive capacity	LR_{50}: 0.42 g as/ha
Typhlodromus pyri	Protonymph	TREBON 30EC	Mortality Reproductive capacity	LR_{50}: 0.70 g as/ha
Diaeretiella rapae	Adult	TREBON 30EC	Mortality	100%[1]
Poecilus cupreus	Adult	TREBON 30EC	Mortality Food consumption	6.7 %[2] 79.7 % (relative to the control)

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

Extended laboratory tests				
Aphidius rhopalosiphi	Adult	TREBON 30EC	Mortality Reproductive capacity	LC_{50}: 23.9 g as/ha NOEC: 18.9 g as/ha
Typhlodromus pyri	Protonymph	TREBON 30EC	Mortality Reproductive capacity	LR_{50}: 4.8 g as/ha NOEC ≥ 1.0 g as/ha
Orius laevigatus	Second instar nymph	TREBON 30EC	Mortality Reproductive capacity	LR_{50}: 2.4 g as/ha NOEC ≥ 1.25 g as/ha
Chrysoperla carnea	First instar larvae	TREBON 30EC	Mortality Reproductive capacity	LR_{50}: 17.9 g as/ha NOEC ≥ 18.75 g as/ha

[1] 24 h, dose = 56.7 g a.s./ha
[2] 15 d, dose = 58.4 g a.s./ha

Hazard Quotients for *Aphidius rhopalosiphi* (LR_{50} = 0.70 g a.s./ha) and *Typhlodromus pyri* (LR_{50} = 0.42 g a.s./ha) *

Exposure	In-field	Off-field				
Buffer distance	–	1 m/3 m	5 m	10 m	15 m	20 m
OSR: 1 application at 60 g a.s./ha (Field crop, MAF = 1)						
Aphidius rhopalosiphi	**142.86**	**3.96**	0.81	0.41	0.29	0.21
Typhlodromus pyri	**85.71**	**2.37**	0.49	0.25	0.17	0.13
Cabbage: 2 applications at 150 g a.s./ha (Field crop, MAF = 1.7)						
Aphidius rhopalosiphi	**607.14**	**16.82**	**3.46**	1.76	1.21	0.91
Typhlodromus pyri	**364.29**	**10.09**	**2.08**	1.06	0.73	0.55
Grapevine: 4 applications at 150 g a.s./ha (Grapevine late, MAF = 2.7)						
Aphidius rhopalosiphi	**964.29**	**77.34**	**34.91**	**11.86**	**6.27**	**4.05**
Typhlodromus pyri	**578.57**	**46.40**	**20.94**	**7.12**	**3.76**	**2.43**
Peach: 2 applications at 210 g a.s./ha (Orchards late, MAF = 1.7)						
Aphidius rhopalosiphi	**850.00**	**133.71**	**71.49**	**30.60**	**15.39**	**9.27**
Typhlodromus pyri	**510.00**	**80.22**	**42.89**	**18.36**	**9.23**	**5.56**
Apple: 3 applications, first at 210 g a.s./ha, second/third at 175 g a.s./ha (Orchards late, MAF = 2.3)**						

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

Aphidius rhopalosiphi	**1150.00**	**180.90**	**96.72**	**41.40**	**20.82**	**12.54**
Typhlodromus pyri	**690.00**	**108.54**	**58.03**	**24.84**	**12.49**	**7.52**

* HQ values was recalculated by EFSA after the peer review

** The maximum single application rate, i.e. 210 g a.i./ha was used as a worst case scenario

Refined toxicity/exposure ratios for arthropods species: off-field scenario*

Species	Crop	AR (g as/ha)	MAF	Drift	vdf	CF	ARcorr (g as/ha)	Comparison with 50% effect rate
Aphidius rhopalosiphi	Oil seed rape	60	1	1 m: 2.77% 5 m: 0.57% 10 m: 0.29%	10	5	1 m: 0.83 5 m: 0.17 10 m: 0.09	< 23.9 < 23.9 < 23.9
	Head cabbage	150	1.7	1 m: 2.38% 5 m: 0.47% 10 m: 0.24%	10	5	1 m: 3.03 5 m: 0.60 10 m: 0.31	< 23.9 < 23.9 < 23.9
	Grape	150	2.7	3 m: 6.71% 5 m: 2.99% 10 m: 0.99%	10	5	3 m: 13.59 5 m: 6.05 10 m: 2.00	< 23.9 < 23.9 < 23.9
	Peach	210	1.7	3 m: 12.13% 5 m: 6.81% 10 m: 3.11%	10	5	3 m: 21.65 5 m: 12.16 10 m: 5.55	< 23.9 < 23.9 < 23.9
	Apple	210	2.3	3 m: 11.01% 5 m: 6.04% 10 m: 2.67%	10	5	3 m: 26.59 5 m: 14.59 10 m: 6.45	**> 23.9** **< 23.9** < 23.9
Typhlodromus pyri	Oil seed rape	60	1	1 m: 2.77% 5 m: 0.57% 10 m: 0.29%	10	5	1 m: 0.83 5 m: 0.17 10 m: 0.09	< 4.8 < 4.8 < 4.8
	Head cabbag	150	1.7	1 m: 2.38% 5 m: 0.47%	10	5	1 m: 3.03 5 m: 0.60	< 4.8 < 4.8

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

	e			10 m: 0.24%			10 m: 0.31	< 4.8
	Grape	150	2.7	3 m: 6.71% 5 m: 2.99% 10 m: 0.99%	10	5	3 m: 13.59 5 m: 6.05 10 m: 2.00	**> 4.8** **> 4.8** < 4.8
	Peach	210	1.7	3 m: 12.13% 5 m: 6.81% 10 m: 3.11%	10	5	3 m: 21.65 5 m: 12.16 10 m: 5.55	**> 4.8** **> 4.8** **> 4.8**
	Apple	210	2.3	3 m: 11.01% 5 m: 6.04% 10 m: 2.67%	10	5	3 m: 26.59 5 m: 14.59 10 m: 6.45	**> 4.8** **> 4.8** **> 4.8**
Orius laevigatus	Oil seed rape	60	1	1 m: 2.77% 5 m: 0.57% 10 m: 0.29%	10	5	1 m: 0.83 5 m: 0.17 10 m: 0.09	< 2.4 < 2.4 < 2.4
	Head cabbage	150	1.7	1 m: 2.38% 5 m: 0.47% 10 m: 0.24%	10	5	1 m: 3.03 5 m: 0.60 10 m: 0.31	**> 2.4** < 2.4 < 2.4
	Grape	150	2.7	3 m: 6.71% 5 m: 2.99% 10 m: 0.99%	10	5	3 m: 13.59 5 m: 6.05 10 m: 2.00	**> 2.4** **> 2.4** < 2.4
	Peach	210	1.7	3 m: 12.13% 5 m: 6.81% 10 m: 3.11%	10	5	3 m: 21.65 5 m: 12.16 10 m: 5.55	**> 2.4** **> 2.4** **> 2.4**
	Apple	210	2.3	3 m: 11.01% 5 m: 6.04% 10 m: 2.67%	10	5	3 m: 26.59 5 m: 14.59 10 m: 6.45	**> 2.4** **> 2.4** **> 2.4**

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

Chrysoperla carnea	Oil seed rape	60	1	1 m: 2.77% 5 m: 0.57% 10 m: 0.29%	10	5	1 m: 0.83 5 m: 0.17 10 m: 0.09	< 17.9 < 17.9 < 17.9
	Head cabbage	150	1.7	1 m: 2.38% 5 m: 0.47% 10 m: 0.24%	10	5	1 m: 3.03 5 m: 0.60 10 m: 0.31	< 17.9 < 17.9 < 17.9
	Grape	150	2.7	3 m: 6.71% 5 m: 2.99% 10 m: 0.99%	10	5	3 m: 13.59 5 m: 6.05 10 m: 2.00	< 17.9 < 17.9 < 17.9
	Peach	210	1.7	3 m: 12.13% 5 m: 6.81% 10 m: 3.11%	10	5	3 m: 21.65 5 m: 12.16 10 m: 5.55	**> 17.9** < 17.9 < 17.9
	Apple	210	2.3	3 m: 11.01% 5 m: 6.04% 10 m: 2.67%	10	5	3 m: 26.59 5 m: 14.59 10 m: 6.45	**> 17.9** < 17.9 < 17.9

* Higher tier risk assessment for non-target arthropods was converted to the Escort II format after the peer review.

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

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

Acute toxicity	Parent: LC_{50} > 47.2 mg as / kg soil LC_{50} corr > 23.6 mg as / kg soil TREBON 30EC: LC_{50} = 102.7 mg as / kg soil LC_{50} corr > 51.35 mg as / kg soil
Reproductive toxicity	Based on the rapid degradation of etofenprox in soil, and the acceptable results of the assessment of the acute risk, whether based on the toxicity tests with the active ingredient or with the 30% EC formulation, a test to assess the sublethal effects on earthworms is not necessary

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
0.060 x 1	OSR	14 d	1475 (a.s.)	10
			3209 (f.p.)	10
0.150 x 2	Head cabbage	14 d	234 (a.s.)	10
			510 (f.p.)	10
0.150 x 4	Grapevine	14 d	216 (a.s.)	10
			469 (f.p.)	10
0.210 x 2	Peach	14 d	231 (a.s.)	10
			503 (f.p.)	10
0.210 x 1 0.175 x 2	Apple	14 d	169 (a.s.)	10
			367 (f.p.)	10

a.s. active substance f.p.: formulated product (TREBON 30EC)

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

Nitrogen mineralization	No effects up to 0.67 kg as/ha
Dehydrogenase activity	No effects up to 0.67 kg as/ha

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

Preliminary screening date

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

Not required (see ER50 laboratory data)

Laboratory dose response tests

Most sensitive species	Test substance	ER50 (g a.i./ha) vegetative vigour	ER50 (g a.i./ha) emergence	Exposure [2] (g a.i./ha)	TER	Trigger
Oil seed rape						
10 species [1]	TREBON 30EC	>200	>200	1.66	120.5	5
Head cabbage						
10 species [1]	TREBON 30EC	>200	>200	5.0	40	5
Grape						
10 species [1]	TREBON 30EC	>200	>200	16.1	12.4	5
Peach						
10 species [1]	TREBON 30EC	>200	>200	40.8	4.9	5
Apple						
10 species [1]	TREBON 30EC	>200	>200	46.2	4.3	5

[1] Ten species tested and same ER50 values for all
[2] Based on the drift models produced by the BBA (Ganzelmeier et al., 1995; updated by Rautmann *et al.* 2001), without buffer zone (drift values at the edge of the field)

Classification and proposed labeling with regard to ecotoxicological data

N	Dangerous for the environment
R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment

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

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APPENDIX 2 – LIST OF ABBREVIATIONS

ADI	acceptable daily intake
ADME	absorption, distribution, metabolism, excretion
ai	active ingredient
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
a.s.	active substance
BCF	bioconcentration factor
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
CNS	central nervous system
d	day
DAR	draft assessment report
DM	dry matter
DNA	deoxyribonucleic acid
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	emulsifiable concentrate
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
F_1	filial generation, first
FAO	Food and Agriculture Organisation of the United Nations
FELS	fish early life stage
FFLC	fish full life cycle
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GC-FID	gas chromatography with flame ionisation detector

Appendix 2 – List of abbreviations

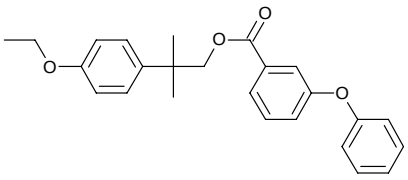
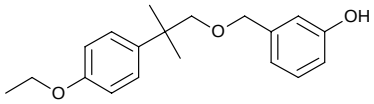
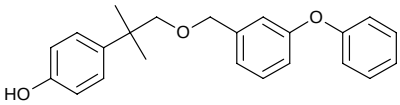
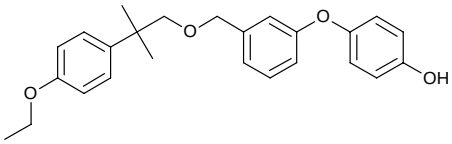
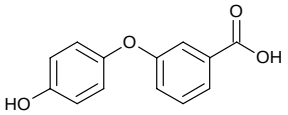
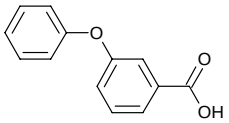
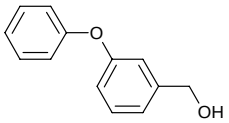
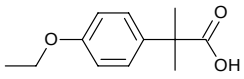
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GLP	good laboratory practice
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography
	or high performance liquid chromatography
HQ	hazard quotient
IESTI	International Estimated Short Term Intake
ISO	International 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
MRM	multi residue method
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OC	organic carbon content
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil

Appendix 2 – List of abbreviations

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
POEM	Predictive Operator Exposure Model
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RMS	rapporteur Member State
RPE	respiratory protective equipment
SFO	single first order
STMR	supervised trials median residue
T_4	thyroxine
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDPGT	uridine diphosphoglucuronosyltransferase
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

Appendix 3 – used compound code(s)

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
α-CO	2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzoate	
Desphenyl-etofenprox (DP)	3-hydroxybenzyl 2-(4-ethoxyphenyl)-2-methylpropyl ether	
Desethyletofenprox (DE)	3-phenoxybenzyl 2-(4-hydroxyphenyl)-2-methylpropyl ether	
4'-OH 4'hydroxyetofenprox	2-(4-ethoxyphenyl)-2-methylpropyl 3-(4-hydroxyphenoxy) benzyl ether	
4'-OH-PB-acid	3-(4-hydroxyphenoxy)benzoic acid	
m-PB-acid	3-phenoxybenzoic acid	
m-PB-alcohol	(3-phenoxyphenyl)methanol	
EPMP	2-(4-ethoxyphenyl)-2-methylpropanoic acid	
PENA	2-(4-ethoxyphenyl)-2-methylpropan-1-ol