CONCLUSION ON PESTICIDE PEER REVIEW

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

Issued on 29 September 2008

SUMMARY

Teflubenzuron is one of the 84 substances of the third stage Part B of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the EU-Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the EU-Commission.

The United Kingdom being the designated rapporteur Member State submitted the DAR on teflubenzuron in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 6 August 2007. The peer review was initiated on 26 November 2007 by dispatching the DAR for consultation of the Member States and the sole applicant BASF Agro BV. 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 June – July 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in September 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 apple and indoor tomatoes for the control of codling moth, leafminers, whiteflies and caterpillars. Full details of the GAP can be found in the attached list of end points.

[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 "Nomolt", a suspension concentrate (SC) containing 150 g/l teflubenzuron.
The minimum purity of teflubenzuron could not be concluded on as with the data available no specification could be set.
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.
There are methods available to monitor teflubenzuron residues in food/feed of plant and animal origin, soil and water, however data gaps were identified for confirmatory method(s) for the determination of teflubenzuron from plant matrices, from soil and from drinking and surface water. An analytical method to determine teflubenzuron residues in surface water with an LOQ of 0.0025 µg/l and a primary method for the determination of teflubenzuron from air with an LOQ of 1.8 µg/m^3 are missing.

In the mammalian metabolism studies, teflubenzuron was rapidly but only partially absorbed after oral administration. There was no evidence of bioaccumulation; teflubenzuron was eliminated mainly unchanged via faeces. The acute toxicity was low, either by the oral, dermal or inhalation route and no eye or skin irritation was observed. As the study on skin sensitisation was not considered acceptable by the experts, classification of teflubenzuron with R43, may cause sensitization by skin contact, was proposed. The main target organ of teflubenzuron was the liver upon short term or long term exposure in either the rat, mouse or dog species; the relevant NOAEL for short term exposure was the dose level of 8.0 mg/kg bw/day from the 90-day rat feeding study; only a LOAEL could be derived from the long term studies due to slight hepatotoxicity found at 2.1 mg/kg bw/day in the 18-month oncogenicity study in mouse. Benign hepatocellular adenomas observed only in this mouse study were not considered relevant for human exposure. There was no evidence for genotoxic or neurotoxic potential related to teflubenzuron administration; no effect on the reproduction, fertility or development was observed. The Acceptable Daily Intake (ADI) of teflubenzuron was 0.01 mg/kg bw/day based on the LOAEL from the 18-month study in mouse and applying a safety factor of 200; the Acceptable Operator Exposure Level (AOEL) was 0.016 mg/kg bw/day based on the oral 90-day rat study, a safety factor of 100 and a correction factor of 20 % for low oral absorption; no Acute Reference Dose (ARfD) was allocated. Dermal absorption was 2 % for the concentrate representative formulation and 20 % for the in-use spray dilution. The level of operator exposure calculated for the representative formulation Nomolt, at a maximum dose rate of 0.120 kg teflubenzuron/ha in apples and of 0.225 kg teflubenzuron/ha in protected tomatoes was below the AOEL, when the use of personal protective equipment (PPE) was considered. Estimated exposure of workers entering crops treated with teflubenzuron was below the AOEL, either if the dermal absorption assumption is based on the value obtained with the concentrate formulation or, alternatively, if PPE are worn. Bystander, residential and exposure of small children playing on a lawn contaminated with fallout from spray drift containing Nomolt were all estimated to be below the AOEL.

Concerning residues, the metabolism of teflubenzuron was investigated in apples, potatoes and a further study on spinach which was not regarded as acceptable by the PRAPeR meeting of experts. The major component in the crops at harvest was unmetabolised teflubenzuron. The experts requested new metabolism studies on rotational crops to support the use of teflubenzuron on tomatoes grown in glass houses on soil based systems, because the submitted studies were under dosed. Therefore, only a provisional residue definition could be proposed. Currently only the use of teflubenzuron on protected tomatoes is sufficiently supported by residue trials to set a provisional MRL. The PRAPeR meeting of experts followed the RMS's suggestion and set a data gap for residue trials on cherry tomatoes to cover fully the notified use on tomatoes. For the use on apples a data gap for further residue trials was identified. Sufficient processing studies on tomatoes were submitted to calculate transfer factors. Further processing studies are required for apples.
The metabolism study on goats and the animal transfer studies on dairy cattle require further investigation and the PRAPeR meeting of experts proposed a data gap for a new metabolism study and data on storage stability in animal products. Depending on the results of the metabolism study further studies on livestock might be required. Therefore, only provisional residue definitions for animal products were proposed. Intake calculations for livestock, which are required to support the notified use on apples, can only be carried out when the additional data on livestock and apple processing studies are available.
The consumer risk assessment and the MRL proposals cannot be finalised. On the basis of a provisional intake calculation for tomatoes only, the consumer exposure is expected to be below the ADI.

Teflubenzuron is moderate to high persistent in soil under dark aerobic conditions (DT_{50} = 30.4 – 151.5 d) and yields 3,5-dichloro-2,4-difluorophenylurea as a major metabolite. Another metabolite, 3,5-dichloro-2,4-difluoroaniline, exceeded 5 % in two non consecutive data points. After consultation with the experts on toxicology, a data gap to address ground water exposure for this metabolite has been identified.
Reliable kinetic parameters (formation and degradation rate constants) for the major metabolite 3,5-dichloro-2,4-dichlorophenylurea were not available and the PRAPeR meeting of experts identified a data gap for these parameters. The ground water exposure assessment may need to be subsequently updated.
Degradation was faster under anaerobic conditions than under aerobic ones in the experiment available where the rest of conditions are maintained. However, anaerobic conditions are not considered to be especially relevant for the representative uses (tomato and apple) evaluated at EU level. Photolysis does not significantly contribute to the environmental degradation of teflubenzuron in soil under EU realistic conditions.
Four field dissipation studies are available, which allow appropriately deriving the dissipation half lives for PEC soil calculations. However, the PRAPeR meeting of experts identified a new data gap

for a new kinetic evaluation of field dissipation study for its use in environmental modelling. This data gap was not considered essential to finalise the EU risk assessment.

PEC soil of teflubenzuron was calculated in the DAR for the use in apples (outdoor) based on the worst case field half live of 16.4 days. For the metabolites 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4-difluoroaniline the peak maximum PEC soil was calculated based on the maximum formations observed in the laboratory studies.

According to the available studies teflubenzuron may be considered immobile in soil (K_{OC} = 21 139 – 32 556 mL / g) and the metabolite 3,5-dichloro-2,4-difluorophenylurea may be considered to exhibit low mobility in soil (K_{OC} = 942 – 1720 mL / g).

In water teflubenzuron is stable at pH 5 and 7 and hydrolyses with a DT_{50} = 8.7 d at pH 9. The metabolite 3,5-dichloro-2,4-difluorophenylurea is expected to be stable to hydrolysis in the normal range of environmental conditions.

The RMS estimated an aqueous photolysis half-life of 13.7 days (40 ºN, continuous irradiation) on basis of the available study. RMS considered that photolysis would not contribute significantly to the environmental degradation of teflubenzuron under realistic conditions for the representative uses. Teflubenzuron was not readily biodegradable according the available study.

Dissipation / degradation of teflubenzuron was investigated in two dark aerobic water/sediment systems. In both systems, teflubenzuron partitioned to the sediment and degraded ($DT_{50whole\ system}$ = 11 – 21.4 d) to form the major metabolites 5-chloro-2,4-difluoroaniline (UNK 5 in the DAR), 3,5-dichloro-2,4-difluorophenyl-urea, 3,5-dichloro-2,4-difluoroaniline and 2,6-difluorobenzoic acid.

The applicant provided $PEC_{SW/SED}$ calculations based on FOCUS Step 1 and Step 2 for the metabolites 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4difluoroaniline, 2,6-difluorobenzoic acid and 5-chloro-2,4-difluoroaniline for the use in apples.

For the parent teflubenzuron $PEC_{SW/SED}$ values were calculated with FOCUS scheme up to Step 4 considering up to 100 m spray drift buffer zone for the use in apples. It is noted that this buffer zone represents a 99.6 % mitigation when compared with Step 3 (above the 95 % mitigation deemed as practicable by the FOCUS Landscape and Mitigation guidance document).

For the greenhouse use in tomatoes the RMS provided indicative parent PEC_{SW} value of 0.0225 mg/L based on 0.1 % losses to surface water (Dutch model). However, the RMS also indicated that from the ecotoxicology assessment the total loss from glasshouse should be 0.00001 % only. To attain this low level, glasshouses would have to operate with negligible emissions of teflubenzuron. With the available information, it is not possible to assess if measures that actually achieve these low levels of emission rates are practicable. Therefore, EFSA proposed a critical area of concern for the aquatic environment with respect to the uses in green house.

The PRAPeR meeting of experts considered for teflubenzuron that the trigger of 0.1 µg/L is not expected to be exceeded for the representative use in apples.

No PEC_{GW} calculations are available for metabolite 3,5-dichloro-2,4-difluoroaniline. The need to address the potential ground water contamination by this metabolite has been identified after consultation with the PRAPeR meeting of experts on toxicology. No groundwater assessment is

available for the greenhouse use. Therefore, the assessment presented is considered only to address situations were plants are grown on artificial substrate or on hydroponics.
On basis of its properties long term transport of teflubenzuron through the atmosphere is not expected to be of concern.

The acute and short term risk to birds and the acute and long term risk to mammals were concluded to be low in a first-tier assessment. No valid long term endpoint (reproductive toxicity) was available for birds and therefore, a data gap was identified for a suitable chronic study. The risk to earthworm and fish-eating mammals was considered low.
Teflubenzuron is highly toxic to aquatic organisms. A lower acute toxicity to fish was observed when formulated. Water/sediment metabolites were less toxic than the active substance and thus considered as not ecotoxicologically relevant. The most sensitive organisms tested were aquatic invertebrates. These effects were addressed by higher tier studies. A NOEC = 0.005 µg a.s./L from a mesocosm study and an assessment factor (AF) of 2 was agreed by the PRAPeR meeting of experts. The first-tier risk assessment indicated a potential high risk to aquatic organisms. For the outdoor use on apples, FOCUS step 4 scenarios only resulted in toxicity exposure ratios (TERs) above the trigger values for fish and algae if a no-spray buffer zone of 16 m was included in the calculations. None of the FOCUS step 4 scenarios resulted in TERs above the triggers for invertebrates, even including a no-spray buffer of 100 m and taking into account the higher tier study. For the application on greenhouse tomatoes, TERs based on the Dutch model PEC values were below the Annex VI triggers, except those related to the formulated product for fish (acute) and for algae. As mentioned above, a total loss percentage from glasshouses as low as 0.00001% would be needed to be achieve a low risk. Since during the peer review no mitigation measures were assessed which could allow the achievement of such negligible emissions, a potential high risk to aquatic organisms from greenhouse uses cannot be excluded. A data gap was suggested for further refinements.

A low risk to adult bees was identified. A potential high risk to hive development was not excluded, as clear effects on the bee population reduction were observed at tested rates lower than the GAP. Therefore, a data gap was suggested to further address the risk to bees for the outdoor use. For the glasshouse use the risk to bee population was expected to be low. However the risk to introduced pollinators might need to be managed. A high risk for non-target- arthropods was identified for the in-field exposure scenario and a no-spray buffer zone of 15 m would be needed to meet the trigger of 2 for the off-field scenario. The oral uptake was considered by the RMS a major route of exposure. The submitted data as well as the ESCORT2 approach did not address this route of exposure. A data gap was identified to further address the risk to non-target arthropods (i.e. a field study), considering the mode of action of the active substance and the potential for recovery.
Since teflubenzuron is a chitin synthesis inhibitor, a data gap was identified for a chronic study on earthworms, even if the acute risk was assessed as low and the DT_{50} in soil was lower than 100 d.

The risk to other soil macro-organisms, soil micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

Key words: teflubenzuron, 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 is one of the 84 substances of the third stage, part B, covered by the Regulation (EC) No 1490/2002 designating the United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, the United Kingdom submitted the report of its initial evaluation of the dossier on teflubenzuron, hereafter referred to as the draft assessment report, received by EFSA on 6 August 2007. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1095/2007 on 26 November 2007 to the Member States and the main applicant BASF Agro BV as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, EFSA identified and agreed on lacking information to be addressed by the 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 expert meetings in June - July 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 August 2008 leading to the conclusions as laid down in this report.

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

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

- the comments received,
- the resulting reporting table (rev 1-1 of 28 March 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 (rev.2-1 of 26 September 2008)

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

Teflubenzuron is the ISO common name for 1-(3,5-dichloro-2,4-difluorophenyl)-3-(2,6-difluorobenzoyl)urea (IUPAC).

Teflubenzuron belongs to the class of benzoylurea insecticides. It acts by inhibition of chitin synthesis and moulting, disrupting chitin deposition in the insect cuticle after ingestion. It may affect fertility of female insects after contact or ingestion. Teflubenzuron is used in agriculture to control codling moth, leafminers, whiteflies and caterpillars in fruit trees, vines, vegetables, potatoes, soybean, tobacco, cotton.

The representative formulated product for the evaluation was “Nomolt”, a suspension concentrate (SC) containing 150 g/l teflubenzuron, registered under different trade names in Europe.

The representative uses evaluated comprise field and greenhouse foliar spraying, when the first larvae are visible, to control codling moth *(Laspeyresia pomonella*), leafminers *(Leucoptera scitella, Phyllonorycter blancardella, Phyllonorycter coryfolella*) in apple and whiteflies *(Trialeurodes vaporariorum)* and caterpillars *(Lepidoptera, Spodoptera exigua*) in protected tomato, in all EU countries, at a maximum of 3 treatments per season, at maximum application rate per treatment of 120 g a.s./ha in apple and 225 g a.s./ha in tomato, with minimum 14, respective 7 days intervals between applications.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of teflubenzuron could not be concluded on. There is no FAO specification available.

The experts at the PRAPeR 51 meeting (June 2008) concluded that with the data available no specification can be set, as the 1991 and the 1995 batch data cannot be used, being considered not representative to the current production and non-GLP, respectively. The 2005 data were considered not representative for the production by the applicant. The 2007 data cannot be used in view of the restrictions concerning the acceptance of new (including newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007.
As a consequence a new data gap was identified by the experts at PRAPeR 51 meeting for a representative five batch analysis, and a specification for the technical material.

Besides the specification, 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 teflubenzuron or the respective formulation.
The main data regarding the identity of teflubenzuron and its physical and chemical properties are given in appendix 1.

Adequate analytical methods are available for the determination of teflubenzuron in the technical material and in the representative formulation (HPLC-UV) as well as for the determination of the respective impurities in the technical material (HPLC-UV). However, further data may be required depending on provision of new technical specification.
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.

There are methods available to monitor teflubenzuron residues in food/feed of plant and animal origin, soil and water, however data gaps were identified by the experts at PRAPeR 51 meeting for confirmatory method(s) for the determination of teflubenzuron from plant matrices, from soil and from drinking and surface water since HPLC-DAD was not considered sufficiently specific for teflubenzuron.
Residues of teflubenzuron in food of plant origin can be monitored by HPLC-UV with LOQ of 0.05 mg/kg (apple, tomato), however a data gap was set by the experts at PRAPeR 51 meeting for an independent laboratory validation for the use of the residue monitoring method in tomato. The multi-residue method DFG S19 with GC-ECD with a LOQ of 0.01 mg/kg in apple can also be used, however further validation data are required in terms of accuracy and precision.

Residues of teflubenzuron in food/feed of animal origin can be monitored by HPLC-UV with LOQ of 0.05 mg/kg in meat and 0.01 mg/kg in milk.
HPLC-UV method is available to monitor residues of teflubenzuron and its metabolite 2,4-difluoro-3,5-dichlorophenylurea in soil with LOQ of 0.01 mg/kg.
Residues of teflubenzuron in surface, ground and drinking water can be determined by HPLC-UV with LOQ of 0.1 µg/l, however the experts at PRAPeR 53 meeting concluded that the regulatory acceptable concentration for aquatic invertebrates is 0.0025 µg a.s./l. As a consequence a data gap was identified by EFSA for an analytical method to determine teflubenzuron residues in surface water with an LOQ of 0.0025 µg/l.
The residue definition for monitoring for ground water was not finalized. As a consequence data gaps may be set for the determination of the metabolites in ground water, pending on the final residue definition for monitoring.

The experts at PRAPeR 51 meeting set a data gap for a primary method for the determination of teflubenzuron from air with an LOQ of 1.8 µg/m^3, concentration derived from the AOEL.

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

2. Mammalian toxicology

Teflubenzuron was discussed at the PRAPeR expert's meeting on mammalian toxicology (PRAPeR 54) in July 2008 on basis of the Draft Assessment Report (July 2007) and the addendum 1 of May 2008.

No analysis of the impurity profile of the batches used in the toxicological studies is available due to the age of the toxicity studies, mainly performed between 1983 and 1987. A data gap was set for this information. EFSA note: considering the lack of technical specifications agreed by the meeting on physical and chemical properties (PRAPeR 51) because none of the batches from 1991, 1995 or 2005 were representative of the actual production, a critical area of concern was raised on the representativeness of the toxicological studies to characterise the active substance as currently produced.

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

In rat, teflubenzuron was absorbed rapidly but only partially from the gastrointestinal tract, absorption being dose-dependent and saturable. Based on 16 % biliary and 4 % urinary excretion within 48 hours, the extent of oral absorption was considered to be 20 % of the administered dose.
There was no evidence of bioaccumulation in organs and tissues; two days after a 7-day treatment, only the liver showed residues exceeding 0.05 %. Most of the radioactivity was excreted in faeces

(91-95 % of the administered dose) predominantly within 24 hours and only small quantities (< 1 %) were found in urine.

Teflubenzuron was eliminated largely unchanged via faeces, although a number of unidentified minor metabolites were found. In urine, hydroxylated metabolites of teflubenzuron were found in low amounts, as well as 3,5-dichloro-2,4-difluorophenylurea and its corresponding substituted aniline[2] indicating that cleavage of the benzoylurea moiety had occurred. Conjugates of these metabolites and the unconjugated 3,5-dichloro-2,4-difluorophenylurea were detected in bile.

2.2. ACUTE TOXICITY

Teflubenzuron presented low acute toxicity, either by the oral, dermal or inhalation route; no skin or eye irritation was observed. The Magnusson and Kligman skin sensitisation test showed certain limitations (a non-irritant concentration was used for induction, no positive control was available), therefore, the experts agreed that it should not be considered as acceptable and proposed a classification with **R43, may cause sensitisation by skin contact**, until an adequate study presents reliable results.

2.3. SHORT TERM TOXICITY

The oral short term effects of teflubenzuron were investigated in three 28-day dietary studies in rat and dog, which as range-finding or proof of oral absorption studies were all considered as supplementary studies; four 90-day feeding studies in rat, mice and dog, and a one-year feeding study in dog that were all considered as acceptable.

In rat, mouse and dog, teflubenzuron affected the liver with increased serum enzymes and increased liver weight; histopathological findings were found in mice and dogs. The **NOAEL was the dose level of 8.0 mg/kg bw/day in rat** and 11 mg/kg bw/day in mouse. In the 1-year, dog study, the rapporteur Member State proposed a NOAEL of 3.15 mg/kg bw/day based on increased liver weight, however this effect was considered an adaptive response at 17.3 mg/kg bw/day by the experts and therefore the overall NOAEL in dogs was set at this dose level taking into consideration dose spacing in the different dog studies.

2.4. GENOTOXICITY

Teflubenzuron was tested *in vitro* for reverse mutation in *Salmonella typhimurium*, point mutation at the hypoxanthine-guanine phosphoribosyl transferase (HPRT) locus of Chinese hamster V79 cell line, chromosome aberration in the same Chinese hamster V79 cell line and unscheduled DNA synthesis in rat hepatocytes; *in vivo* genotoxicity was performed in a mouse micronucleus test. The experts raised some concerns about the poor absorption of the substance and if it reached the bone marrow in the micronucleus test *in vivo*; the lack of testing the TA102 strain of *S. typhimurium* was also noted and the low solubility of the active substance that resulted in low concentrations in the cytogenetic assays.

[2] 3,5-dichloro-2,4-difluoroaniline

However all *in vitro* and *in vivo* tests gave negative results and no potential for carcinogenicity relevant for human exposure was found in long term studies, therefore the meeting agreed that no further genotoxicity testing was required and no genotoxic potential was attributed to teflubenzuron.

2.5. LONG TERM TOXICITY

Long term toxicity was examined in two 2-year studies in rat and an 18-months study in mouse.
As observed in short term toxicity studies, both species presented the liver as the target organ of teflubenzuron with increases in serum enzyme activities, in liver weight and in the incidence of non-neoplastic lesions in the liver. No carcinogenic potential was attributed to teflubenzuron in rat; in male mouse, benign liver adenomas were observed, that were not considered relevant for human exposure. The meeting confirmed the NOAEL proposed by the rapporteur Member State of 4.8 mg/kg bw/day in rat and the **LOAEL of 2.1 mg/kg bw/day in mouse** due to an increased incidence of slight hepatocellular hypertrophy, single cell necrosis and phagocytic cell foci observed at this low dose level, it was noted however, that no clear dose-response was evident.

2.6. REPRODUCTIVE TOXICITY

Reproductive toxicity of teflubenzuron was tested in a two-generation reproduction toxicity study in rat, two developmental toxicity studies in rat proceeded by a dose-range finding study and three developmental toxicity studies in rabbit.

Reproduction toxicity

No evidence of systemic toxicity was observed, no effect on the reproductive performance and parameters or on offspring's toxicity was found, and therefore the highest dose tested of 37 mg/kg bw/day was the NOAEL for all parameters tested of this study.

Developmental toxicity

In the developmental toxicity studies in rat, no effect was attributed to teflubenzuron administration and therefore the NOAELs for both maternal and developmental toxicity were the highest dose tested of 1000 mg/kg bw/day.
In rabbits, the only sign of maternal toxicity was an increased incidence of grossly granulated cut surfaces of the liver in dams treated with 1000 mg/kg bw/day; the maternal NOAEL was the 500 mg/kg bw/day dose level. As no effect was observed on the development of pups, the developmental NOAEL was again the highest dose tested of 1000 mg/kg bw/day.

2.7. NEUROTOXICITY

No study was provided. Teflubenzuron does not belong to a chemical group known to induce neurotoxicity, no concern was raised from the standard toxicity studies, and therefore no study was required.

2.8. FURTHER STUDIES

Mechanism studies

An investigation of the potential for covalent binding of teflubenzuron to mouse liver DNA was performed. There was no evidence that DNA binding could represent a potent mechanism of liver tumour induction by teflubenzuron.

Metabolites

Supplementary studies were conducted on two rat metabolites of teflubenzuron.

3,5-dichloro-2,4-difluoroaniline

The oral LD_{50} of this teflubenzuron metabolite was calculated to be 1759 mg/kg bw in males and females rat combined, 1986 mg/kg bw in males and 1552 mg/kg bw in females separately, indicating higher acute oral toxicity than the parent.

An Ames test gave negative results in several strains of *Salmonella typhimurium*.

This metabolite was reported to be present at levels below 1 % in rat's urine; therefore, insufficient toxicological information is available to conclude on its relevance for groundwater according to the guidance document on the assessment of the relevance of metabolites in groundwater[3] if it is estimated to occur in amounts above 0.1 µg/L in groundwater according to fate and behaviour environmental models.

3,5-dichloro-2,4-difluorophenylurea

The oral LD_{50} of this teflubenzuron metabolite was calculated to be 677 mg/kg bw in males and 703 mg/kg bw in female rat, indicating higher acute oral toxicity than the parent.

An Ames test gave negative results in several strains of *Salmonella typhimurium* and *Escherichia coli*.

This metabolite was also reported to be present at levels below 1 % in rat's urine. Based on the available information, it was considered by the experts as being potentially more toxic than the parent and therefore more toxicological information would be necessary in case reference values are to be set for 3,5-dichloro-2,4-difluorophenylurea.

2.9. MEDICAL DATA

On the basis of the consultation of a number of major databases, no occurrence of incidents of poisoning or epidemiological data was found.

[3] Sanco/221/2000 – rev.10 (25 February 2003): Guidance document on the assessment of the relevance of metabolites in groundwater of substances regulated under Council Directive 91/414/EEC.

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

ADI

The rapporteur Member State proposed in the draft assessment report an ADI of 0.01 mg/kg bw/day based on the 18-month carcinogenicity study in mouse presenting a LOAEL of 2.1 mg/kg bw/day based on minimal hepatic effects observed at this dose level that would require a safety factor of 200. The experts discussed whether a safety factor of 200 or 300 would be more appropriate, but the majority of the experts agreed with the rapporteur Member State. The **ADI for teflubenzuron was established at 0.01 mg/kg bw/day**

AOEL

Initially in the draft assessment report, the rapporteur Member State proposed an AOEL of 0.006 mg/kg bw/day base on the short term dog studies, a safety factor of 100 and a correction for low oral absorption of 20 %. As the overall NOAEL for short term dog studies was increased to 17.3 mg/kg bw/day during the meeting, the relevant NOAEL for short term studies became the dose level of 8.0 mg/kg bw/day from the 90-day rat study; applying the same safety factor of 100 and correction factor of 20 %, **the resulting AOEL was 0.016 mg/kg bw/day.**

ARfD

The rapporteur Member State proposed not to set an ARfD due to the low toxicity profile of the substance. The experts confirmed that no ARfD is necessary. **No ARfD was allocated.**

2.11. DERMAL ABSORPTION

Two *in vitro* percutaneous absorption studies were conducted with two concentrations of the representative formulation "Nomolt" through rat and human skin and one *in vivo* study in rat was also performed with two different concentrations of "Nomolt".

From the data presented in the *in vivo* study 24 hour after application (with the best recovery), the experts agreed that percutaneous absorption for both the concentrate and the dilution should be considered as 20 %, although the radioactivity found in the *Stratum corneum* was not included in the values obtained with the dilution considering the excreta pattern.

Due to the generally low recoveries in human *in vitro* data, no correction could be made for the dilution; for the concentrate a 1:10 correction was applied. The resulting dermal absorption was established at 2 % for the concentrate preparation and 20 % for the in-use field dilution.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product "Nomolt" is a suspension concentrate (SC) formulation containing 150 g teflubenzuron/L.

Estimations of operator, worker and bystander exposure were recalculated in the addendum 2 to volume 3 of August 2008 based on the parameters agreed at the PRAPeR expert meeting.
As a growth regulator insecticide, two representative uses have been supported, in apple orchards that are usually treated using air blast sprayers (tractor drawn air-assisted sprayers) and protected tomato plants that are sprayed manually, using knapsack equipment and spray lances.
According to the representative uses, the applied dose is 0.120 kg teflubenzuron/ha in apples and 0.225 kg teflubenzuron/ha in tomatoes; application volume is 2000 L spray/ha in apples and 1500 L spray/ha in tomatoes; the maximum number of applications per season is three, with a minimum interval between applications of 14 days in apples and 7 days in protected tomatoes.

Operator exposure

The operator exposure estimates were calculated using both the German[4] and the UK POEM[5] models for the use on apples, for the protected use on tomatoes selected data from the EUROPOEM[6] database were used.

Broadcast air-assisted sprayer in apples

According to the German model assumptions, the body weight of operators is 70 kg and the work rate is 8 ha/day. According to the UK POEM, body weight of operators is 60 kg and work rate is 15 ha/day; packaging of 5 L was assumed.

Estimated operator exposure presented as % of AOEL (0.016 mg/kg bw/day) in apples, application rate of 0.120 kg teflubenzuron/ha

Tractor-mounted (field crop)	No PPE	With PPE[(a)] during M/L	With PPE[(b)] during M/L & application
UK POEM	163	154	109
German model	203	199	31

[(a)] PPE: gloves; M/L: mixing and loading
[(b)] PPE: gloves when handling the concentrate and contaminated surfaces for the UK POEM; gloves (M/L & application), protective garment and sturdy footwear (application) for the German model

According to the UK POEM, estimated exposure of operators was above the AOEL even considering the use of personal protective equipment (PPE); according to the German model, the estimated exposure of operators was below the AOEL only if PPE are worn, as gloves during mixing/loading and application, and coverall and sturdy footwear during application.

[4] BBA (1992) "Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products"
[5] PSD (2003) "UK Predictive Operator Exposure Model (POEM)", version 3
[6] EUROPOEM Project Group (1996) "The development, maintenance and dissemination of a European predictive operator exposure model (EUROPOEM) database"

Greenhouse use in tomatoes

Estimation of operator exposure according to EUROPOEM was performed with 75th percentile data for the indoor use of hose-fed hand lance equipment and with 75th percentile data for the indoor use of hand-held equipment with UK POEM mixing and loading values for knapsack sprayers.

Estimated operator exposure presented as % of AOEL (0.016 mg/kg bw/day) in protected tomatoes, application rate of 0.225 kg teflubenzuron/ha

Scenario	No PPE	With PPE[(a)] during M/L & application	With PPE[(b)] during M/L & application
Hose-fed lance equipment	406	165	34
Knapsack sprayers	193	48	13

[(a)] PPE: gloves
[(b)] PPE: gloves and coveralls
M/L: mixing and loading

According to selected data from EUROPOEM, the estimated operator exposure was below the AOEL when protective coveralls and gloves are worn during mixing, loading and application.

Worker exposure

Estimation of worker exposure was performed according to an exposure model (Krieger, 1992[7], Krebs *et al.* 1996[8]) based on measured levels of dislodgeable foliar residues. As there is no agreed approach on which dermal absorption value should be used for worker exposure, the rapporteur Member State performed the calculations for both values, i.e. with 20% (for the dilution) and 2 % (for the concentrated formulation). The results of supervised residues trials in tomato in greenhouse were used to estimate the surface residues of teflubenzuron after the three sequential treatments of "Nomolt" assuming a 7-day interval between treatments and a 3-day pre-harvest interval. Trials data were also available for apple treatments assuming 14-day interval between the three sequential treatments; the Northern European dataset was used as representative of the worst case in apples.

For the orchard use (apples), transfer coefficient of 4500 [cm^2/person/h] was considered; foliar dislodgeable residue per 1 kg teflubenzuron/ha (FDR) of 0.686 [µg teflubenzuron/cm^2 per kg teflubenzuron/ha], default value of 60 kg for worker body weight, and a working period of 8 hours. For greenhouse's use in tomatoes, transfer coefficient of 4500 [cm^2/person/h] was considered and foliar dislodgeable residue per 1 kg teflubenzuron/ha (FDR) of 0.718 [µg teflubenzuron/cm^2 per kg teflubenzuron/ha].

[7] Krieger R.I., Ross J.H. and Thongsinthusak T. (1992) "Assessing human exposures to pesticides"
[8] Krebs B, *et al*. "Uniform principles for safeguarding the health of workers re-entering crop growing areas after application of plant protection products"

Estimated worker exposure presented as % of AOEL (0.016 mg/kg bw/day) assuming a dermal exposure of 2 % (concentrate formulation)

Worker exposure	**No PPE**	**With PPE [(a)]**
Apple (orchard)	51	5.1
Tomatoes (greenhouse)	54	5.4

[(a)] PPE: protective gloves, long sleeved shirt and long trousers – EFSA calculation with a reduction factor of 0.1 (10 %)

Estimated worker exposure presented as % of AOEL (0.016 mg/kg bw/day) assuming a dermal exposure of 20 % (diluted formulation)

Worker exposure	**No PPE**	**With PPE [(a)]**
Apple (orchard)	514	51.4
Tomatoes (greenhouse)	538	53.8

[(a)] PPE: protective gloves, long sleeved shirt and long trousers – EFSA calculation with a reduction factor of 0.1 (10 %)

Although the use of PPE is not considered a normal practice by the rapporteur Member State, it was agreed that the use of PPE lowers the exposure of workers to values below the AOEL.
Therefore, the estimated exposure to teflubenzuron during re-entry operations does not exceed the AOEL, if PPE is worn.

Bystander exposure

Bystander exposure assessment was based on direct measurements of simulated bystander exposure for orchard sprayers[9], for a bystander positioned at 8 m downwind from the edge of the treatment area. Assuming a body weight of 60 kg, 20 % dermal absorption for the spray solution, 100 % absorption of potential inhalation and no exposure reduction from clothing, the resulting level of exposure to teflubenzuron for unprotected bystanders was expected to represent **5 % of the AOEL**.

Residential exposure was assessed by the RMS on the basis of surrogate values derived from California Environmental Protection Agency studies[10] (with chlorpyrifos treated oranges). The highest potential exposure obtained (for children) was equivalent to **52 % of the AOEL**.

The level of systemic exposure for a small child playing on a lawn contaminated with fallout from spray drift containing "Nomolt" has been estimated using the spray drift fallout values for broadcast

[9] Lloyds G.A.; Bell G.J.; Samuels S.W.; Cross J.V.; Berrie A.M. (1987): "Orchard sprayers: comparative operator exposure and spray drift study" (MAFF/ADAS).
[10] California Environmental Protection Agency, Air resources Board (1998): "Report for the Application and Ambient Air Monitoring for Chlorpyrifos (and Oxon Analogues) in Tulare County During Spring/Summer 1996.

air-assisted sprayers used for and aquatic risk assessment[11] and US EPA values for residential exposure resulting from the contact with treated lawns[12]. Combining 15.6 % of the systemic AOEL for dermal exposure and 0.7 % of the AOEL not adjusted for low oral absorption for oral exposure, the resulting exposure was equivalent to **16 % of the AOELs** for teflubenzuron.

3. Residues

The active substance teflubenzuron was discussed at the PRAPeR experts meeting for residues (PRAPeR 55, round 11) in July 2008.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The nature of the residues in plants following the use of teflubenzuron was investigated in apples, spinach and potatoes. Apples were treated three times at intervals of three weeks with aniline ring ^{14}C-labelled teflubenzuron at a rate of 0.02 kg as/hl (3N) and application volumes of 0.1, 0.3 and 0.4 ml/apple (for the first, second and third application respectively). Samples of apples taken at different intervals after the first, second and third (final) treatment, contained average radioactive residues of 15, 68 and 130 µg, equivalent to 0.79-1.21, 0.50-0.87 and 0.92mg/kg. Approximately 98% of TRR was found in the peel, 2% in the pulp. Residues were almost completely extractable in organic solvents and identified by TLC and HPLC mainly as teflubenzuron.

Aniline ring ^{14}C-labelled teflubenzuron was applied to spinach grown under greenhouse conditions as foliar spray to run-off at a rate of 0.06 kg as/ha, 21 days after sowing. Samples taken at 0, 8 and 15 days after treatment contained radioactive residues of 6.9, 1.0 and 0.70 mg/kg. The radioactive residues were found mainly in the surface wash (99.0-99.2%); small amounts (0.8-1.0%) were extractable. Teflubenzuron was identified as the main component accounting for 95, 92 and 77% of TRR in 0 day, 8 day and 15 day samples respectively. The remaining 23% of the radioactivity was shown to consist of several components with a fraction of polar residues accounting for 8% of TRR.

In a study on potatoes aniline ring ^{14}C-labelled teflubenzuron was applied four times at a rate of 90 g as/ha at 2 week intervals either as foliar treatments or as soil treatment. Samples taken at maturity (63 days after the first application) contained TRR of <0.001 mg/kg in tubers and 8.31 mg/kg in tops for the foliar treatment and TRR of 0.002 mg/kg in tubers and 0.03 mg/kg in tops for soil treatment. Teflubenzuron accounted for >99% of TRR in the samples of tops after foliage treatment.

[11] Rautmann D.; Streloke M.; Winkler R. (2001): "New basic drift values in the authorization procedure for plant protection products".
[12] USA EPA (1998) "Occupational and residential exposure test guideline"; USA EPA (2001) "Recommended revisions to the standard operating procedures (SOPs) for residential exposure assessment; USA EPA (1999) "Overview of issues related to the standard operating procedures for residential exposure assessment".

The experts meeting discussed the acceptability of the metabolism studies in primary crops. The main issues of concern were 23% non characterised radioactive residues in one spinach sample and the fact that in all metabolism studies on primary crops only aniline ring labelled teflubenzuron was used. The experts concluded that due to the high proportion of teflubenzuron found in apples and tomatoes (98%), studies with labels in both rings are not required for the supported uses. However, further investigation of leaf metabolism with labelling in both rings is required in case of future uses on leafy crops. If cleavage of the teflubenzuron molecule is detected in these new metabolism studies and taking into account the toxicity of the found metabolites it may be necessary to perform metabolism studies in other crops.

On the basis of the results of the metabolism studies on primary crops the experts meeting concluded on a provisional residue definition for fruit and root crops for monitoring and risk assessment: teflubenzuron only. It might have to be revised when a new metabolism study on rotational crops requested by the meeting (see section 3.1.2) is available.

The notifier submitted eight residue trials each for apples in Southern and Northern Europe. The experts meeting concluded that 4 further residue trials are required on apples grown in Southern Europe and 4 further trials on apples grown in Northern Europe, treated with teflubenzuron according to the proposed critical GAP. Furthermore, validation data for the method RU 134/32/10 by Memmesheimer (1999) used in residue trials on apples is required.

Eight residue trials on protected tomatoes reflecting the notified critical GAP have been submitted. However, the RMS noted in the DAR that no trials were conducted with cherry tomatoes which represent a more critical situation for residues due to the smaller size. Therefore, the experts concluded that residue data on cherry tomatoes should be submitted to address the notified use on tomatoes. The meeting agreed that a general discussion is required regarding the residues in small and large varieties of crops.

A study on the effects of processing on the nature of the residues of teflubenzuron has not been submitted. However, it was shown that teflubenzuron remains intact when apple pomace was heated in an oven at 90°C for several hours. Teflubenzuron was also shown to be stable in peeled and canned tomatoes during sterilisation. The experts meeting concluded that these results are sufficient to demonstrate stability of the teflubenzuron under processing conditions.

On the basis of the results of a balance study and three follow-up studies performed with tomatoes, the following mean transfer factors were calculated: 0.45, 0.17, 1.78, 0.08, 7.73 and 0.07 for puree, juice, wet pomace, peeled tomato, peel and canned tomato.

In one processing study on apples the following processing factors were calculated: 1.58, 0.08, 0.25, 3.8 and 12 for washed fruit, juice, apple sauce and wet and dried pomace. The experts meeting concluded that the notifier has to provide a sufficient number of processing studies as required by Directive 91/414/EC to support the use on apples.

Storage stability studies show that teflubenzuron is stable in tomatoes for at least 18 months and in apples, pears, potatoes and cabbage for at least 36 months when stored under deep frozen conditions.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

The metabolism and distribution in rotational crops was investigated in studies with teflubenzuron ^{14}C-labelled at the aniline ring and the benzoyl ring respectively at a nominal rate of 500 g as/ha (0.75N compared to the cGAP for tomatoes). After ageing of the soil for 30, 121/120 and 360/365 days wheat and carrots were sown and pre-cultivated lettuce was planted. For crops grown in soil aged for 30 days TRR at harvest were 0.006 mg/kg in lettuce, 0.006 mg/kg in carrot tops, 0.003 mg/kg in carrot roots, 0.012 mg/kg in wheat grain and 0.032 in wheat straw in the study with benzoyl labelled teflubenzuron. In the study with aniline ring labelled teflubenzuron TRR were 0.007 mg/kg in lettuce, 0.026 mg/kg in carrot roots, 0.005 mg/kg in wheat grain and 0.244 mg/kg in wheat straw. Only the radioactive residues in straw samples (from the 30 and 120 day experiments) were further investigated. Neither teflubenzuron nor the two known soil metabolites 3,5-dichloro-2,4-difluorophenyl urea and 3,5-dichloro-2,4-difluoroanaline were detected in plants at levels >0.01 mg/kg.

The evaluation presented in the DAR is based on the use of compost, which had been used for growing protected tomatoes treated with teflubenzuron, on arable land. For this practice the application rate was calculated to be 15N and residues are unlikely to occur in rotational crops. However, the experts pointed out that lettuce or fruiting vegetables are grown in rotation after tomatoes in soil in glasshouses in some MS. The meeting concluded that the submitted studies were not acceptable for uses of teflubenzuron on tomatoes grown in soil systems because of the low application rate and insufficient identification of residues. Therefore, a new rotational crop study at the 1N rate and including a fruiting vegetable in addition to the standard crops is required.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The metabolism and distribution of residues in animals was investigated in goats and chicken, using aniline ring ^{14}C-labelled teflubenzuron.

For lactating goats dosed at 1 mg/kg bw/day (25 mg/kg diet) for 7.5 days the majority of the applied radioactivity was found in excreta (0.91% in urine, 91.95% in faeces and 9.98% in intestine contents) with less than 0.04% in milk and less than 0.3% in tissues. In milk a plateau was reached on day 5

(highest residue concentration of 0.013 mg/kg). Liver contained 0.486 mg/kg, kidney 0.034 mg/kg, muscle 0.010 mg/kg and fat 0.08 mg/kg TRR. Extractable residues accounted for 96% of TRR in faeces, 64% in milk and 58% in liver. On characterisation of extractable radioactivity in faeces the major component was identified as teflubenzuron (76.9 and 83.3%), besides smaller amounts of metabolite 3381[13] (3.6-3.8%) and further unidentified metabolites (6% and 2.1%). The main component in liver extracts was a polar non identified compound. Metabolite 3381 could be identified in liver extracts after enzyme treatment. In milk teflubenzuron and polar components were found.

For laying hens dosed at a rate of 1.25 mg/kg/day (25 mg/kg diet) for 7.5 days the majority of the radioactivity was recovered in excreta (93.9%), less than 0.01% in the eggs and less than 0.4% in the tissues. In liver, fat, skin and muscle TRR of 0.0075 mg/kg, 0.0015 mg/kg, 0.0002 mg/kg and 0.00004 mg/kg were found. Extractable residues accounted for 97% of TRR in faeces, 92% in eggs, 70% in liver and 94% in fat. In egg yolk the major component was identified as teflubenzuron (62.2% of TRR) besides unidentified compounds (4.8% and 6.6%). In liver teflubenzuron (30.2%) and unidentified compounds (12.7% and 8.5%) were found. Fat contained teflubenzuron (79.1%) and a further compound (8.7%). Kidney extracts contained teflubenzuron and trace amounts (0.02 mg/kg) of a material which co-chromatographed with E15[14].

After oral administration of teflubenzuron to goats or hens, residues are rapidly excreted. Only small amounts of residues are transferred into tissues, milk or eggs. Teflubenzuron and two metabolites (3381 and E15) have been identified, which were both also found in the metabolism of rats.

The experts meeting concluded that also livestock metabolism studies with teflubenzuron radio-labelled at the benzoyl ring are necessary to support uses on crops fed to animals (relevant to the representative use on apples) as some cleavage of the teflubenzuron molecule has been observed in the submitted studies. After evaluation of the new study, it should be further investigated if the goat metabolism study with the aniline ring label sufficiently addresses the nature of residues in matrices relevant to consumer exposure.

The PRAPeR meeting 54 on toxicology concluded that metabolite E15 is more acutely toxic as teflubenzuron. On the basis of evaluation in the DAR for the metabolites included in livestock tissues and assuming that the toxicological reference values of teflubenzuron could also be used for the metabolite, the PRAPeR meeting 55 proposed the following residue definitions for animal products: for monitoring: teflubenzuron only. For risk assessment: liver and kidney: sum of teflubenzuron and E15 expressed as teflubenzuron, other commodities: teflubenzuron only. EFSA notes that no data are available to establish conversion factors. During the preparation of the draft conclusion, EFSA noted

[13] 1-(3,5-dichloro-2,4-difluorophenyl)-3-(2,6-difluoro-3-hydroxybenzoyl)urea
[14] 3,5-dichloro-2,4-difluorophenylurea

that the available toxicological studies for E15 are not sufficient to set reference values. Therefore, EFSA states that the residue definition has to be regarded as provisional in relation to the uses on crops fed to animals and has to be re-addressed when further studies on livestock are available. On the basis of the results of these studies and of the dietary burden calculations it has to be decided if animal transfer studies are required and eventually if reference values for metabolites included in the residue definitions have to be set and if conversion factors have to be the established.

The PRAPeR meeting of experts stated that for completion of the data for apples (additional residue trials and processing studies) a livestock dietary burden calculation for intake of apple pomace is required.

Animal transfer studies were carried out on dairy cattle dosed at three different rates corresponding to 10, 30 and 100 mg/kg diet. Residues were below the LOQ (0.01 mg/kg) for all milk samples and most of the tissue samples with residues (all <0.05 mg/kg) found in some of the fat samples and a few liver and kidney samples. The study showed deficiencies concerning recovery data, for the residues analysed, and the dose levels used. The experts meeting decided that the acceptability of the study should be discussed after receipt of the outstanding data. EFSA states that the results of the new metabolism study and the livestock dietary burden calculation might trigger the requirement of an acceptable animal transfer study which should also include the analysis of relevant metabolites.

The experts meeting confirmed that data on the storage stability of residues prior to analysis for animal products is required to support the intended use on apples.

Animal transfer studies on poultry are not required to support the notified uses.

3.3. CONSUMER RISK ASSESSMENT

A calculation for the chronic intake carried out by the RMS on the basis of the provisionally proposed MRL for tomatoes (1 mg/kg) using the WHO Standard European Diet shows the highest result for cluster B (TMDI = 24% ADI).

A calculation carried out by EFSA using the EFSA model for the intake of tomatoes (provisionally proposed MRL: 1 mg/kg) showed that the WHO Cluster diet B (TMDI = 30.8% ADI) and the Italian model for children/toddlers (TMDI = 14.3% ADI) are the most critical models for the chronic intake.

The meeting concluded that the risk assessment for tomatoes is only provisional due to deficiencies in the rotational crop studies. It is noted that valid rotational crop studies are not required for crops grown on inert media/substrates or by nutrient film techniques only. EFSA notes that the risk assessment might also have to be revised following the assessment of additionally requested residue

trials on cherry tomatoes. To support the use on apples additionally the intake of apples and possibly also the intake of animal products after intake of pomace by livestock have to be taken into account when the additional data on apples and livestock are available.

3.4. PROPOSED MRLS

Based on data from eight residue trials in the DAR the RMS proposed a MRL of 1 mg/kg for tomatoes. EFSA notes that this MRL is provisional. The PRAPeR meeting of experts has identified a data gap for residue trials on cherry tomatoes and the MRL might have to be revised after the receipt of these studies. The expert meeting agreed that a general discussion is required regarding the residues in small and large varieties of crops. The number of residue trials on apples for Northern and Southern Europe is not sufficient to propose an MRL.

MRLs for animal products (required to support use on apples) can only be proposed after evaluation of outstanding data on apples and livestock.

4. Environmental fate and behaviour

Fate and behaviour of teflubenzuron in the environment was discussed in the PRAPeR 52 meeting of experts (subgroup 1, July 2008) on basis of the DAR prepared in July 2007 and the addendum 1 prepared in May 2008. Uses evaluated at EU level with respect to fate and behaviour in the environment, are apple (field) and tomato (greenhouse). The assessment presented only covers uses in greenhouse tomato when artificial subtract of hydroponic systems is used. Potential disposal of soil substrate after greenhouse use was addressed by the applicant and the PRAPeR meeting of experts agreed that this potential route of exposure would be covered by the uses already assessed in the DAR. Further groundwater assessment would be needed to consider the use on greenhouse tomatoes planted on natural soil.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of teflubenzuron in soil under dark aerobic conditions was investigated at 20 °C in two studies and two different soils (pH 5.8 – 8.1, OC 0.96 – 2.3 %; clay 23.6 – > 30 %) with the active substance ^{14}C labelled at the aniline and benzoyl rings respectively. The studies were considered to be conducted appropriately to current guidelines, with sufficient sampling points considering the degradation of the parent. In the study labelled at the aniline ring the metabolite **3,5-dichloro-2,4-difluorophenylurea** (max 10.4 % after 29 d) was identified as a major matabolite. Another metabolite: 3,5-dichloro-2,4-difluoroaniline (max 5.4 % after 29 d) exceeded 5 % in two non consecutive data points and was considered a minor metabolite by the RMS. The PRAPeR meeting of experts discussed the potential relevance of this metabolite and the fact that, even formally not reaching the trigger of ground water risk assessment, its occurrence above 4 .5 % AR from DAT 28

and 63 with a peak of 8.4 % AR at DAT 42 deserved further consideration. Considering the time spacing between the sampling, experts felt that there was a potential for this metabolite having exceeded 5 % in-between sampling occasions. Since there was no ground water assessment for this metabolite, the meeting required an assessment of its relevance by the toxicology experts. Toxicology assessment has found some indications that the metabolite could be more toxic than the parent, but there were not enough data available in the dossier to consider the assessment complete. Due to the fact that toxicological relevance of the metabolite may not be excluded, the indications on possible higher toxicity than the parent and the levels found in soil, a data gap has been identified to perform a ground water risk assessment for this metabolite.

Unextracted radioactivity amounted up to 34.4 % AR after 182 d. The mineralization of aniline ring is low and radioactivity found in the CO_2 traps reaches only a maximum of 6.5 % AR after 343 d. In the study performed with the active substance labelled at the benzoyl ring, no metabolite was found to account for more than 0. 1 % AR. Unextracted radioactivity amounted up to 28.8 % AR after 119 d and radioactivity found in the CO_2 trap amounted up to 51.9 % AR after 150 d.

Degradation of teflubenzuron under anaerobic conditions was also investigated under dark anaerobic conditions in the same studies and soils. The RMS considered that the anaerobic experiment performed with the benzoyl labelled substance was not scientifically reliable due to the low recoveries and the potential loss of not trapped volatiles. In the aniline labelled experiment the major metabolite 3,5-dichloro-2,4-difluorophenylurea accounted for a maximum of 28.2 % AR after 14 d under anaerobic conditions. However, anaerobic conditions are not considered to be especially relevant for the representative uses (tomato and apple) evaluated at EU level.

Teflubenzuron (aniline ^{14}C labelled) photolysis in soil was investigated in one study with artificially simulated sunlight (Xe arc lamp filtered for $\lambda < 290$ nm). Whereas photolysis is observed to some extent it was considered not to contribute to the environmental degradation of teflubenzuron under EU realistic conditions. No new metabolites where identified in the study for photolysis in soil.

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

Rate of degradation in soil under dark aerobic conditions at 20 °C was calculated for the route studies summarized above and with an additional study in three soils (pH 5.2 – 7.1; OC 0.9 – 2.6 %; clay 13.7 – 59.8 %). In these studies, teflubenzuron is moderate to high persistent in soil (DT_{50} = 30.4 – 151.5 d). The fitting of the degradation data was found not fully satisfactory by the RMS who proposed in the DAR the use of field studies for the risk assessment. However, the PRAPeR meeting of experts after the discussion of the additional information presented in addendum 1, including graphical representation of kinetic fittings, agreed that the laboratory degradation data was suitable and relevant for the EU risk assessment of the parent teflubenzuron. Degradation was faster under

anaerobic conditions than under aerobic conditions in the experiment available where the rest of conditions are maintained.

Data available in the dossier did not allow to obtain any reliable kinetic parameter (formation and degradation rate constants) for the major metabolite 3,5-dichloro-2,4-dichlorophenylurea. Therefore, the PRAPeR meeting of experts identified a data gap for half life and formation fraction of the 3,5-dichloro-2,4-dichlorophenylurea. Ground water exposure assessment may need to be subsequently updated.

Four field dissipation studies in four sites (Germany, Netherlands, Italy and S France) are available (pH 5.8 – 8.4; OC 1.3 – 3.1 %; clay 12.3 – 16.4 %; soil properties not reported for the German site). The RMS recalculated dissipation half lives by non linear regression based on first order kinetics (DT_{50} = 8.8 – 16. 4 d). The PRAPeR meeting of experts discussed the reliability of the field studies and noted that the quality of first order kinetic data fitting was not completely satisfactory. However, the experts considered that the derived dissipation half lives could be appropriate for PEC soil calculations. Also it was noted that in the field studies the product had been applied in autumn although the representative uses are for spring. The PRAPeR meeting of experts agreed that the dissipation observed in the field studies could be considered due mainly to degradation in soil since other dissipation / degradation processes such as volatilization, leaching and photolysis could be in principle excluded. However, the PRAPeR experts meeting considered it mandatory to normalize the available data for its use in modelling and identified a new data gap for a new kinetic evaluation of field dissipation studies, including normalisation of the data for temperature and moisture. This data gap was not considered essential to finalize the EU risk assessment.

PEC soil of teflubenzuron was calculated in the DAR for the use in apples (outdoor) based on the worst case field half live of 16.4 d. For the metabolites 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4-difluoroaniline the peak maximum PEC soil was calculated based on the maximum formations observed in laboratory studies.

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

Soil batch adsorption/desorption studies are available for teflubenzuron (four soils: pH 6.2 – 7.2; OC 0.8 – 3.8 %; clay 3.6 – 29.6 %) and its major soil metabolite 3,5-dichloro-2,4-difluorophenylurea (three soils: pH 5.6 – 7.1; OC 1.6 – 2.6 %; clay 26. 3 – 59.8 %). According the results of these studies, teflubenzuron may be considered immobile in soil (K_{OC} = 21 139 – 32 556 mL / g) and the metabolite 3,5-dichloro-2,4-difluorophenylurea may be considered low mobile in soil (K_{OC} = 942 – 1720 mL / g).

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Hydrolysis of teflubenzuron in buffered aqueous solutions (pH 5, 7 and 9) at 25 °C was investigated in one study. Teflubenzuron is stable at pH 5 and 7 and hydrolyses with a DT_{50} = 8.7 d at pH 9. Teflubenzuron hydrolyzed to 3,5-dichloro-2,4-difluorophenylurea (61 % AR), 3,5-dichloro-2,4-difluoroaniline (12 % AR), 2,6-diflurobenzoic acid (62 %) and difluorobenzamide (12 % AR). In these experiments a concomitant rearrangement reaction occurred that yield the transformation product *N*-(2,4-difluoro-3,5-dichlorobenzene)-5-fluoro[3*H*]-dihydroquinazoline-2,4-dione[15] (8 % AR).

Hydrolysis of major soil metabolite 3,5-dichloro-2,4-difluorophenylurea in buffered aqueous solutions (pH 4, 7 and 9) was investigated at 50 °C. The study showed that this metabolite is expected stable to hydrolysis in the normal range of environmental conditions.

Aqueous photolysis of teflubenzuron (^{14}C labelled in the aniline ring) under sterile conditions at pH 5 and 25 °C was investigated under artificially simulated sun light (Xe arc lamp filtered for $\lambda < 290$ nm). The applicant estimated an aqueous photolysis half life of 10 d. RMS recalculated a half life of 17.7 days by non linear regression based on first order kinetics. By analysis of the irradiance in the experiment, the RMS estimated a half life for latitudes 40 ºN of 13.7 days under continuous irradiation. The metabolite *N*-(2,4-difluoro-3,5-dicholorobenzene)-5-fluoro[3*H*]-dihydroquinazoline-2,4-dione was identified as major photodegradation product (max 32 % AR after 15 d, end of study). The applicant presented a reasoned justification for not having performed an aqueous photolysis study with the substance labelled at the benzoyl ring. The RMS considered that photolysis would not to contribute significantly to the environmental degradation of teflubenzuron under realistic conditions. The experts agreed that no further assessment of the photolysis metabolite was necessary.

Teflubenzuron was not readily biodegradable according the available study.

A study that investigates the dissipation/degradation of teflubenzuron (^{14}C labelled either at benzoyl or at the aniline ring) in two dark aerobic water/sediment systems (pH_{water} 6.1 – 8.1; pH_{sed} 5.5 – 7.1; OC 0.7 – 5.0 %; clay 3 – 44 %) is available. In both systems teflubenzuron partitioned to the sediment and degraded ($DT_{50whole\ system}$ = 11 – 21.4 d) to form the major metabolites **5-chloro-2,4-difluoroaniline** (UNK 5 in the DAR, aniline ^{14}C labelled: max 19.04 % AR after 30 d in water phase), **3,5-dichloro-2,4-difluorophenyl-urea** (CL-902374, aniline ^{14}C labelled: max 22,45 % AR after 14 d in water phase), **3,5-dichloro-2,4-difluoroaniline** (CL-902373**,** aniline ^{14}C labelled: max 26,42 % AR after 60 d in the sediment phase) and **2,6-difluorobenzoic acid** (CL-245508, benzoyl ^{14}C labelled: max 13,79 % AR after 14 d in the water phase). Mineralization was higher for the benzoyl moiety (CO_2 max = 14.06 % AR after 30 d) than for the aniline moiety (CO_2 max = 10.43 % AR after 120 d). In the experiments performed with the ^{14}C benzoyl labelled teflubenzuron a considerable amount of radioactivity was found in the volatiles trap (max 58.45 % AR after 60 d);

[15] 1-(3,5-dichloro-2,4-difluorophenyl)-5-fluoro-4a,8a-dihydroquinazoline-2,4(1*H*,3*H*)-dione

however, no characterization of this radioactivity is available. Unextracted radioactivity into the sediment at the end of the study (120 d) amounted to a maximum of 26.23 % AR for the benzoyl labelled teflubenzuron and up to 59.6 % AR for the aniline labelled one.

An additional study, following Dutch biocidal guidelines, was presented in the dossier. The RMS considered that the organic matter in the sediment of the systems used was above OECD 208 guideline recommendations and the results were not considered to be adequate for use in the EU risk assessment.

Furthermore a marine water sediment system was also presented by the applicant for teflubenzuron. This study was also not considered relevant for the EU risk assessment by the RMS. The PRAPeR meeting of the experts agreed that the end points of this study were not relevant for the continental surface water exposure assessment.

Applicant provided $PEC_{SW/SED}$ calculations based on FOCUS Step 1 and Step 2 for the metabolites 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4difluoro aniline, 2,6-difluorobenzoic acid and 5-chloro-2,4-difluoroaniline for the use in apples.

For the parent teflubenzuron $PEC_{SW/SED}$ were calculated with FOCUS scheme up to Step 4 by consideration of up to 100 m spray drift buffer zone for the use in apples. It is noted that this buffer zone represents a 99.6 % mitigation when compared with Step 3 (above the 95 % mitigation deemed as practicable by the FOCUS Landscape and Mitigation guidance document).

For the greenhouse use in tomatoes the RMS provided indicative parent PEC_{SW} value based on 0.1 % losses to surface water (Dutch model). Since the applicant was proposing a different value, the meeting of the experts required further clarifications to the RMS on the calculation presented in the DAR. These clarifications have been provided in addendum 2. The RMS confirms that the value obtained following the Dutch model (0.1 % of total amount applied to cover all losses) is 0.0225 mg/L. The RMS calculated this value as an estimate to cover total emissions from glasshouses (including for example losses via condensation and drainage) into a standard 30cm deep ditch based on the assumption that the indicative loss percentage of 0.1% for glasshouse uses based on the Dutch model should be applied to the total amount applied (e.g. 0.1% loss from 675g a.s. applied diluted into 30,000l of water). If the figure of 0.1% loss is taken to be equivalent to a spray drift loss alone the PEC_{SW} in a 30cm ditch would be 0.225 µg/l, as it was estimated by the applicant. It should be noted that a spray drift loss of 0.1% is equivalent to a loss of total mass of only 0.001%.

The regulatory acceptable concentration in surface water has been determined by the PRAPeR 53 experts meeting on ecotoxicology to be 0.0025µg/l. On this basis a total loss percentage from glasshouses of as low as 0.00001% would need to be maintained to ensure that concentrations in adjacent surface water bodies was acceptable. In the opinion of the RMS this level of loss percentage would effectively mean that glasshouses would have to be operated with zero emissions of teflubenzuron. The RMS considers that actual practices in glasshouses are likely to be highly variable across the EU and the likelihood of being able to maintain negligible emissions to surface water should therefore be considered carefully. No specific management measures to attain this have been proposed by the applicant. With the available information, it is not possible to assess if measures that

actually achieve these low levels of emission rates are practicable. Therefore, EFSA proposed a critical area of concern for the aquatic environment with respect to the uses in green house.

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

For the representative use in apples (outdoor), potential ground water contamination by teflubenzuron and its soil metabolite 3,5-dichloro-2,4-difluorophenylurea was addressed by the applicant with FOCUS PEC_{GW} calculations using FOCUS PEARL v.1.1.1. The applicant used input parameters derived from the laboratory studies. However, with respect to the parent compound, the meeting of experts did not agreed with the use of half lives obtained in the same soil (at 20 °C and 10 °C) as independent measurements and on the use of values derived from only 4 data experimental points. Consequently, the normalized geometric mean to be used for PEC_{GW} calculations is longer (DT_{50} = 92.1 d) than the one actually employed in the applicants calculation (DT_{50} = 66.6 d). The experts agreed that, taking into account the low mobility of the compound and the results of the modelling available, the trigger of 0.1 µg/L is not expected to be exceeded for the representative use in apples.
A data gap has been identified for reliable estimations formation fraction and half life in soil of the major soil metabolite 3,5-dichloro-2,4-difluorophenylurea. Therefore, ground water exposure assessment would need to be updated accordingly.
No PEC_{GW} calculations are available for metabolite 3,5-dichloro-2,4-difluoroaniline. The need to address potential ground water contamination by this metabolite has been identified after confirmation by meeting of experts on toxicology on its potential toxicological relevance (see point 4.1).
No groundwater assessment is available for the greenhouse use. Therefore, the assessment presented is considered only to address situations were plants are grown on artificial substrate or on hydroponics.

4.3. FATE AND BEHAVIOUR IN AIR

Teflubenzuron is not expected to be highly volatile on basis of the vapour pressure and Henry's Law constant. A volatilization study indicated that there is some potential volatilization of teflubenzuron from soil. Photochemical half life in air was calculated to be 1.7 d on basis of Atkinson model, below the trigger of 2 d. Therefore, long term transport of teflubenzuron is not expected to be of concern.

5. Ecotoxicology

Teflubenzuron was discussed at the PRAPeR meeting of experts for ecotoxicology (PRAPeR 53 – sub-group 1) in July 2008 on the basis of DAR and the addendum of May 2008.
Teflubenzuron is an Insecticide Growth Regulator (IGR). The representative uses evaluated were on tomatoes (greenhouse use) 3 applications (7 days interval) with an application rate of 0.225 kg a.s./ha

and on apples (outdoor use) 3 applications (14 days interval) with an application rate of 0.12 kg a.s./ha. The representative product evaluated was "Nomolt SC" with a concentration of 150 g a.s./L.
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, SETAC, March 2000.

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.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The submitted studies with teflubenzuron suggested low acute and short-term toxicity to birds. No mortality was observed up to the highest tested doses (acute LD_{50} >2000 mg a.s. /kg bw/day in mallard duck and >2250 mg a.s. /kg bw/day in bobwhite quail; short-term LC_{50} >1209 mg a.s. /kg bw/day in mallard duck and >1014 mg a.s. /kg bw/day in bobwhite quail). No suitable study was provided for the long-term (reproductive) toxicity. Neither of the submitted reproduction studies on bobwhite quail, reported in DAR allowed a NOEC to be established, despite the rates down to 80 ppm being tested. A new long term avian reproductive study was presented by the applicant, but it was not evaluated or peer reviewed and no assessment based on its results was conducted. Therefore a data gap was identified. On the basis of mammalian toxicity data (rat), teflubenzuron and the formulated product were of low acute toxicity to mammals: LD_{50} >5000 mg a.s. /kg bw/day (teflubenzuon) and >2000 mg /kg bw/day ("Nomolt"). The reproductive NOAEL was 40 mg a.s. /kg bw/day.

For the use on apples, toxicity exposure ratio (TER) values were calculated for insectivorous birds and small herbivorous mammals. The first-tier TERs were above the Annex VI triggers. No long term TERs were calculated for birds, as no valid endpoint was available.
The potential exposure via bioaccumulation along the food chain was assessed for earthworm-eating birds and mammals and for fish-eating birds and mammals. On the basis of first-tier TERs a low risk was identified to mammals. No TERs were calculated for birds (NOEC not available).
No risk assessment was conducted for the tomato greenhouse use, but as exposure was not expected, it was not considered necessary.

5.2. RISK TO AQUATIC ORGANISMS

Studies with teflubenzuron, the formulated product "Nomolt" and its metabolites 3,5-dichloro-2,4-phenyl-urea (CFPU) and 3,5-dichloro-2,4-difluoroaniline (CFA) were provided and peer reviewed. The studies showed that teflubenzuron is highly toxic to aquatic organisms. A lower acute toxicity of

the active substance to fish was observed when formulated. Both the active substance and the product were classified as R50/R53.

Invertebrates were the most sensitive organisms tested. The lowest endpoint was observed in a chronic study with teflubenzuron (*Daphnia magna*, 21-d EC_{50} = 0.000062 mg a.s./L). The acute 48-h EC_{50} was 0.0028 mg a.s./L (*Daphnia magna*). Effects on this group of organisms were also addressed by higher tier studies (indoor microcosm studies and outdoor mesocosm study).

A study conducted with teflubenzuron on *Chironomus riparius* gave a 28-d NOEC of 0.05 mg/kg sediment. The lowest 96-h LC_{50} for fish was >0.0065 mg a.s./L (*Lepomis macrochirus*) and the 28-d NOEC was 0.0186 mg a.s./L (*Oncorhynchus mykiss*). As for algae toxicity, the lowest 72-h EC_{50} was >0.02 mg a.s./L (*Selenastrum subspicatus*).

3,5-dichloro-2,4-phenyl-urea and 3,5-dichloro-2,4-difluoroaniline metabolites were less toxic than the parent. No studies were provided with the other two metabolites which occurred in the water sediment study (2,6-diflorobenzoic acid and the 5-chloro-2,4-difluoroaniline) (see section 4.2.1). However, the toxicity of these metabolites was also expected to be lower as for teflubenzuron, as argued by applicant in a position paper, which was discussed at the PRAPeR meeting of experts. The argumentation was based on the existing data for the 3,5-dichloro-2,4-phenyl-urea and 3,5-dichloro-2,4-difluoroaniline metabolites. In addition, the applicant assumed that all metabolites could be considered addressed by the higher tier study (i.e. 119-d mesocosm study), due to the short DT_{50} of teflubenzuron in water (see section 4.2.1). The experts agreed that all metabolites could be considered not ecotoxicologically relevant.

Aquatic risk assessment was conducted for teflubenzuron, metabolites and the formulated product on the basis of the $FOCUS_{SW}$ approach, for the outdoor use on apples.

At FOCUS Step 1, a potential high risk to the aquatic organisms was identified for the active substance since all TER values were below the Annex VI triggers.

As regards the formulated product “Nomolt”, a potential high acute risk to invertebrates and a potential high chronic risk to fish were identified, but the acute TER for fish was above the trigger. Since the toxicity value related to the active substance is a “greater than value” and the active substance was tested at its limit of solubility, the higher formulation endpoint was expected to give the more realistic results. Therefore the RMS considered the acute risk to fish with teflubenzuron addressed by the formulated product.

A low risk to all aquatic organisms was identified for the metabolites: all the TERs were above the trigger values.

FOCUS Step 2 and Step 3 calculations were performed for fish (chronic), invertebrates, algae and sediment-dwelling organisms with teflubenzuron and for invertebrates (acute) with the formulated product. The Annex VI triggers were not exceeded by any of the Step 2 TERs and by the most part of the Step 3 scenarios.

A Step 4 modelling was conducted. A low risk to fish, algae and sediment dwelling organisms was identified with mitigation measures equivalent to a 16 m non-spray buffer zone. However, this measure was not enough to mitigate the acute and chronic risk to invertebrates. For this group the risk was further refined by a mesocosm study. The experts discussed the endpoint and the assessment factor (AF) to be applied. The applicant proposed a NOEAC of 0.033 µg/L (addendum of May 2008). The RMS considered as more relevant a NOEC of 0.005 µg/L. Several points were identified at the meeting in favour of the RMS' proposal. The exposure regime in the study did not cover the GAP (2 applications in the study while 3 applications are foreseen in the GAP). The recovery was considered too long (direct effects on copepods and rotifers recovered 10 weeks after the last application). A general decline of the zooplankton population occurred at the end of the study. In conclusion, the experts agreed to use the NOEC of 0.005 µg/L and to apply an AF of 2 to address the uncertainty in the higher tier study.
TER values calculated with the NOEC of 0.005 µg/L, were still below the AF, even with a buffer zone of 100 meters. This represents a 99.6 % mitigation when compared to Step 3.

As regards the greenhouse use on tomatoes, risk assessment was conducted on the basis of the PEC_{sw} of 0.0025 mg/L calculated according to the Dutch model, which use 0.1% spay drift to predict environmental concentration in surface waters (no agreed EU model for surface water assessment for glasshouse uses is available). The TER values indicated a potential high risk to aquatic organisms, except those related to the formulated product for fish (acute) and for algae. As reported in the fate section (point 4.2.1) a total loss percentage from glasshouses as low as 0.00001% would be needed to achieve a low risk. During the peer review no mitigation measures were assessed, which could allow the achievement of such negligible emissions, therefore a potential high risk to aquatic organisms from greenhouse uses could not be excluded.

Overall, it was concluded that the risk to aquatic organisms is potentially high on the basis of the submitted data. For the outdoor application a high risk was identified with respect to aquatic invertebrates in a higher-tier assessment (mesocosm study even with a 100 m no-spray buffer zone).
For the greenhouse application the risk to all groups of organisms needed to be further refined. Therefore a data gap was proposed.

5.3. RISK TO BEES

Acute oral and contact toxicity studies were conducted with the technical and the formulated product "Nomolt" showing a similar toxicity of the a.s. when formulated (oral LD_{50} > 72 µg a.s./bee and >110 µg a.s./bee respectively, contact LD_{50} > 100 µg a.s./bee for both). The hazard quotient (HQ) values were below the Annex VI trigger of 50 indicating a low risk to adult bees from the representative uses evaluated. Since teflubenzuron is an IGR, a bee brood study was performed. Effects on egg laying and larval mortality were observed in this test, therefore several field studies and tunnel trials were conducted.

In the field studies the residue in pollen and the effects in field during flight following application of teflubenzuron were investigated. In the first study it was observed that the levels of teflubenzuron in pollen declined over the first week after the application. The second study showed an increase in bee mortality between days 13 and 17 after the application and a reduction of the average flight intensity between days 3 and 5, but overall the effects observed did not appear to be long lasting.

The tunnel tests were carried out at rates up to 100 g a.s./ha. At the lowest tested doses no effects on adult bees nor on hive development were observed. At the highest doses a clear reduction of population was observed (at 75 g a.s./ha 30% reduction, at 100 g a.s./ha 72% less bees than the control, study on *Phacelia*), even though a recovery was observed at the end of the test conducted on wheat.

All the field and tunnel tests were conducted with a single application of 120 g a.s. /ha, therefore they did not cover adequately the proposed GAP of teflubenzuron (120 g a.s. /ha × 3 applications).

Overall, on the basis of the submitted data a potential high risk to bees could not be excluded for the outdoor use on apples. Therefore, for the outdoor applications, EFSA suggests a data gap to further address the risk and to identify appropriate mitigation measures consequently.

The risk to bees was considered as low for the use on tomatoes in greenhouse, as no relevant exposure was expected. However, EFSA agrees with the RMS, who suggested to take into account at member state level the potential risk to the glasshouse pollinators.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory tests were conducted with formulated product "Nomolt" and the indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri*. A mortality of 22.5% and of 100% was observed, respectively at application rate of 180 g a.s. /ha. The HQ values could not be calculated for *T. pyri.* For *A. rhopalosiphi* the in-field HQ value was calculated as 1.533 and the off-field HQ was 0.169 indicating a low risk for this species. Further higher tier studies were submitted on *T. pyri*, *Drinio incospicua*, *Chrysoperla carnea* and *Orius laevigatus.* The lowest endpoint (LR_{50} = 0.73 g a.s./ha) was observed in the study with *Chrysoperla*, thus an aged residue study was conducted with this species. Significant effects were observed for the most sensitive stages (larvae/nymphs) at the tested rates lower than the proposed GAP.

The higher-tier HQ values indicated a high risk for both the in-field and the off-field population: mitigation measures (i.e. a buffer zone of 15 meters) were needed to meet the trigger of 2 for the off-field population. Moreover, the RMS underlined that the standard laboratory tests provided and the risk assessment performed did not completely cover the mode of action of teflubenzuron. Indeed, in addition to contact, teflubenzuron is active by ingestion of contaminated plant material while the submitted studies and the ESCORT2 approach covered only the contact exposure. The experts of the member states agreed with the RMS. Since teflubenzuron showed persistent effects on non-target arthropods it was concluded that the risk (in-field and off-field) should be further addressed considering the mode of action of the active substance (IGR) and the potential for recovery (data gap). To this purpose it might be useful to conduct a field study.

5.5. RISK TO EARTHWORMS

The acute toxicity to earthworms was tested with both technical teflubenzuron and the formulated product "Nomolt". For both a low toxicity was observed (LC_{50} >1000 mg a.s./kg soil). A 28-d NOEC of 8 mg/kg soil was observed in chronic study with a mixture of metabolite (3,5-dichloro-2,4-phenyl-urea and 3,5-dichloro-2,4-difluoroaniline). The RMS considered chronic testing with the active substance not necessary, because of the short half life of teflubenzuron in soil (field DT_{90} of 54.5 days < 100d) and because the high acute TER values. However the expert meeting considered this requirement criterion not applicable for teflubenzuron, since it is an IGR inhibiting chitin synthesis. Therefore a data gap was identified to provide a chronic study with earthworms, for the outdoor use.

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

Since DT_{90} was less than 100d, no data were required.

EFSA considered that it could become necessary to address the risk to soil non-target marco-organisms, depending on the outcome of the chronic risk to earthworms and the further data on non-target arthropods.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects of >25 % on soil respiration and nitrification were observed in tests with technical teflubenzuron up to concentration of 2 mg a.s./kg soil dw (soil PEC 0.089 mg a.s./kg) indicating a low risk to soil non-target micro-organisms for the representative uses evaluated.

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

Toxicity and inhibition of vegetative vigour, emergence, shoot growth and growth with the formulation "Nomolt" were investigated in tests with 6 plant species at an application rate of 120 g a.s. /ha. No effects were observed (ER_{50} >120). The TERs were > 6.36 on the basis of the exposure rate estimated from spray drift at 3m distance. According to the current guidance document SANCO 10329/2002, multiple applications were not taken into account in the risk assessment (i.e. multiple

application factor). The experts discussed the relevance of the consideration of a multiple application factor also for non target plant risk assessment. For teflubenzuron this was considered not relevant, however experts concluded that guidance is needed to address this issue.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Technical teflubenzuron did not inhibit the respiration of activated sewage sludge at a concentrations up to 1000 mg a.s./L, which was above the water solubility limit. In addition, no effects were observed at 0.028 mg a.s./L, which was in the range of water solubility. It was not expected that the concentrations of teflubenzuron in biological sewage treatment plants would reach a concentration of more than 1000 mg a.s./L if the product were to be applied according to the GAP and therefore the risk to biological methods of sewage treatment was considered to be low.

6. Residue definitions

Soil

Definition for risk assessment: teflubenzuron, 3,5-dichloro-2,4-difluorophenylurea.
Definition for monitoring: teflubenzuron

Water

Ground water

Definition for exposure assessment: teflubenzuron, 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4-difluoroaniline.
Definition for monitoring: teflubenzuron, 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4-difluoroaniline (pending finalization of exposure assessment for the metabolites.

Surface water

Definition for risk assessment: teflubenzuron, 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4-difluoroaniline, 2,6 difluorobenzoic acid, 5-chloro-2,4-difluoroaniline
Definition for monitoring: teflubenzuron

Air

Definition for risk assessment: teflubenzuron
Definitions for monitoring: teflubenzuron

Food of plant origin

Definition for risk assessment: teflubenzuron (fruit and root crops only, provisional)
Definition for monitoring: teflubenzuron (fruit and root crops only, provisional)

Food of animal origin

Definition for risk assessment:

Liver and kidney: sum of teflubenzuron and 3,5-dichloro-2,4-difluorophenyl urea expressed as teflubenzuron (provisional)

Other commodities of animal origin: teflubenzuron (provisional)

Definition for monitoring: teflubenzuron (provisional)

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
teflubenzuron	moderate to high persistent in soil (DT_{50} = 30.4 – 151.5 d)	The risk was assessed as low. A data gap was identified to address long-term effect on earthworm (due to teflubenzuron acting as a chitin synthesis inhibitor).
3,5-dichloro-2,4-difluorophenylurea	Information on formation fraction and half life in soil are not available, data gap identified.	Not relevant

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**
teflubenzuron	immobile (K_{OC} = 21 139 – 32 556 mL / g)	Trigger of 0.1 µg / L is not expected to be exceeded for the use in apples based on the available FOCUS GW		Yes	yes

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**
		calculations			
3,5-dichloro-2,4-difluorophenylurea	low mobile (K_{OC} = 942 – 1720 mL / g)	Data gap		Is a minor rat urine metabolite (< 1 %); the oral LD_{50} was 677 mg/kg bw in rat, indicating higher acute oral toxicity than the parent; an Ames test was negative. Insufficient data to conclude on its relevance.	no
3,5-dichloro-2,4-difluoroaniline	No data available, data gap identified.	No data available, data gap identified.		Is a minor rat urine metabolite (< 1 %); the oral LD_{50} was 1759 mg/kg bw in rat, indicating higher acute oral toxicity than the parent; an Ames test was negative. Insufficient data to conclude on its relevance.	no

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
teflubenzuron (water and sediment)	Very toxic to aquatic organisms, particularly to invertebrates. A potential high risk was not excluded.
3,5-dichloro-2,4-difluorophenylurea (water and sediment, from soils throught run off and drainage)	Not relevant
3,5-dichloro-2,4-difluoroaniline (water and sediment)	Not relevant
2,6 difluorobenzoic acid (water and sediment)	Not relevant
5-chloro-2,4-difluoroaniline (water and sediment)	Not relevant

Air

Compound (name and/or code)	Toxicology
teflubenzuron	Rat LC_{50} inhalation > 5.038 mg/L air/4 h, nose only, as a dust aerosol, no classification proposed

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

- A representative five batch analysis and a specification for the technical material (relevant for all representative uses evaluated, data gap identified by PRAPeR 51 meeting (June 2008), already submitted and presented in Addendum to vol. 4 (May 2008), however in view of the restrictions concerning the acceptance of new (including newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, could not be considered in the peer review; refer to chapter 1)
- Confirmatory method(s) for the determination of teflubenzuron from plant matrices, from soil and from drinking and surface water (relevant for all representative uses evaluated, data gap identified by PRAPeR 51 meeting (June 2008), date of submission unknown; refer to chapter 1)
- ILV for the use of the residue monitoring method in tomato (relevant for the uses in tomato, data gap identified by PRAPeR 51 meeting (June 2008), date of submission unknown; refer to chapter 1)
- Further validation data (accuracy and precision) for the multi-residue method DFG S19 with GC-ECD for the determination of residues in apple(relevant for the uses in apple, data gap identified by PRAPeR 51 meeting (June 2008), date of submission unknown; refer to chapter 1).
- ILV for the use of the residue monitoring method in tomato (relevant for the uses in tomato, data gap identified by PRAPeR 51 meeting (June 2008), date of submission unknown; refer to chapter 1)
- An analytical method to determine teflubenzuron residues in surface water with an LOQ of 0.0025 µg/l (relevant for all representative uses evaluated, data gap identified by EFSA after PRAPeR 53 meeting (July 2008), date of submission unknown; refer to chapter 1 and 5.2)
- Primary method for the determination of teflubenzuron from air with an LOQ of 1.8 µg/m^3 (relevant for all representative uses evaluated, data gap identified by PRAPeR 51 meeting (June 2008), date of submission unknown; refer to chapter 1)
- Information on the impurity profile of the batches used in key toxicological studies (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to chapter 2)
- A new rotational crop study at the 1N rate and including a fruiting vegetable in addition to the standard crops (relevant for the use on protected tomatoes grown on soil systems; data gap identified by PRAPeR 55 meeting (July 2008); date of submission unknown; refer to chapter 3).
- A livestock metabolism study with teflubenzuron radio-labelled in the benzoyl ring (relevant to support use on apples; data gap identified by PRAPeR 55 meeting (July 2008); date of submission unknown; refer to chapter 3).

- Four further residue trials on apples grown in Southern Europe and four further trials on apples grown in Northern Europe and treated with teflubenzuron according to the proposed critical GAP (relevant to support use on apples; data gap identified by PRAPeR 55 meeting (July 2008); date of submission unknown; refer to chapter 3).
- Validation data for the method RU 134/32/10 by Memmesheimer (1999) used in residue trials on apples (relevant to support use on apples; data gap identified by PRAPeR 55 meeting (July 2008); date of submission unknown; refer to chapter 3).
- Residue data on cherry tomatoes to fully cover the notified use on tomatoes (relevant for the use on tomatoes; data gap identified by PRAPeR 55 meeting (July 2008); date of submission unknown; refer to chapter 3).
- A sufficient number of processing studies on apples as required by Directive 91/414/EC. (relevant to support use on apples; data gap identified by PRAPeR 55 meeting (July 2008); date of submission unknown; refer to chapter 3).
- Data on the storage stability of residues prior to analysis for animal (relevant to support use on apples; data gap identified by PRAPeR 55 meeting (July 2008); date of submission unknown; refer to chapter 3).
- A data gap was identified for a study to derive half life and formation fraction of the major soil metabolite 3,5-dichloro-2,4-dichlorophenylurea, which may require a new ground water assessment (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to point 4.1).
- A data gap for the ground water exposure assessment of metabolite 3,5-dichloro-2,4-difluoroaniline, including the determination of the necessary input parameters (formation fraction, degradation rate, adsorption / desorption in soil) (relevant for all representative uses evaluated; no submission date proposed by the notifier; refer to chapter 4).
- A data gap was identified for a new kinetic evaluation of field dissipation studies, including normalisation of the data for temperature and moisture (this data gap was not considered essential to finalize the EU risk assessment; no submission date proposed by the notifier:; refer to point 4.1)
- A long term avian reproduction study with the concentration low enough to produce a NOEC (relevant to outdoor use on apples; study available but not peer reviewed, data gap identified by the PRAPeR 53 in July 2008; refer to pint 5.1).
- A refined risk assessment for aquatic organisms (relevant for the greenhouse tomatoes use evaluated; data gap identified by EFSA after PRAPeR 53 meeting in July 2008; refer to point 5.2).
- A refined risk assessment for bees (relevant for the outdoor use on apples; data gap identified by EFSA after PRAPeR 53 meeting in July 2008; refer to point 5.3).
- A refined risk assessment for non-target arthropods (i.e. field study) considering the mode of action of the substance and the potential for recovery (relevant for the outdoor use on apples; data gap identified by PRAPeR 53 in July 2008; refer to point 5.4).

- A chronic study on earthworms (relevant for the outdoor use on apples; data gap identified by PRAPeR 53 in July 2008; refer to point 5.4).

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 field and greenhouse foliar spraying, when the first larvae are visible, to control codling moth (*Laspeyresia pomonella*), leafminers (*Leucoptera scitella, Phyllonorycter blancardella, Phyllonorycter coryfolella*) in apple and whiteflies (*Trialeurodes vaporariorum)* and caterpillars (*Lepidoptera, Spodoptera exigua*) in protected tomato, in all EU countries, at a maximum of 3 treatments per season, at maximum application rate per treatment of 120 g a.s./ha in apple and 225 g a.s./ha in tomato, with minimum 14, respective 7 days interval between applications.

The representative formulated product for the evaluation was "Nomolt", a suspension concentrate (SC) containing 150 g/l teflubenzuron, registered under different trade names in Europe.

The minimum purity of teflubenzuron could not be concluded on as with the data available no specification could be set.

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 is possible. There are methods available to monitor teflubenzuron residues in food/feed of plant and animal origin, soil and water; however data gaps were identified for confirmatory method(s) for the determination of teflubenzuron from plant matrices, from soil and from drinking and surface water. An analytical method to determine teflubenzuron residues in surface water with an LOQ of 0.0025 µg/l and a primary method for the determination of teflubenzuron from air with an LOQ of 1.8 µg/m^3 are missing.

In the mammalian metabolism studies, teflubenzuron was rapidly but only partially absorbed after oral administration. There was no evidence of bioaccumulation; teflubenzuron was eliminated mainly unchanged via faeces. The acute toxicity was low, either by the oral, dermal or inhalation route and no eye or skin irritation was observed. As the study on skin sensitisation was not considered acceptable by the experts, and classification of teflubenzuron with R43, may cause sensitization by skin contact, was proposed. The main target organ of teflubenzuron was the liver at short term or long term exposure in either the rat, mouse or dog species; the relevant NOAEL for short term exposure was the dose level of 8.0 mg/kg bw/day from the 90-day rat feeding study; only a LOAEL could be derived from the long term studies due to slight hepatotoxicity found at 2.1 mg/kg bw/day in the 18-months oncogenicity study in mouse. Benign hepatocellular adenomas observed only in this mouse study were not considered relevant for human exposure. There was no evidence for genotoxic or

neurotoxic potential related to teflubenzuron administration; no effect on the reproduction, fertility or development was either observed. The Acceptable Daily Intake (ADI) of teflubenzuron was 0.01 mg/kg bw/day based on the LOAEL from the 18-month study in mouse and applying a safety factor of 200; the Acceptable Operator Exposure Level (AOEL) was 0.016 mg/kg bw/day based on the oral 90-day rat study, a safety factor of 100 and a correction factor of 20 % for low oral absorption; no Acute Reference Dose (ARfD) was allocated. Dermal absorption was 2 % for the concentrate representative formulation and 20 % for the in-use spray dilution. The level of operator exposure calculated for the representative formulation Nomolt, at a maximum dose rate of 0.120 kg teflubenzuron/ha in apples and of 0.225 kg teflubenzuron/ha in protected tomatoes was below the AOEL, when the use of personal protective equipment (PPE) was considered. Estimated exposure of workers entering crops treated with teflubenzuron was below the AOEL, either if the dermal absorption assumption is based on the value obtained with the concentrate formulation or, alternatively, if PPE are worn. Bystander, residential and exposure of small children playing on a lawn contaminated with fallout from spray drift containing Nomolt were all estimated to be below the AOEL.

Concerning residues, the metabolism of teflubenzuron was investigated in apples, potatoes and a further study on spinach which was not regarded as acceptable by the meeting of experts. The major component in the crops at harvest was unmetabolised teflubenzuron. New metabolism studies on rotational crops were requested by the experts to support the use of teflubenzuron on tomatoes grown in glass houses on soil based systems, because the submitted studies were under dosed. Therefore, only a provisional residue definition could be proposed. Currently only the use of teflubenzuron on protected tomatoes is supported by residue trials sufficiently to propose a provisional MRL. The PRAPeR meeting on expert followed the suggestion of the RMS formulated a data gap for residue trials on cherry tomatoes to fully cover the notified use on tomatoes. For the use on apples, a data gap for further residue trials was identified. Sufficient processing studies on tomatoes were submitted to calculate transfer factors. Further processing studies are required for apples.
The metabolism study on goats and the animal transfer studies on dairy cattle require further investigation and the meeting of experts formulated a data gap for a new metabolism study and data on storage stability in animal products. Depending on the results of the metabolism study further studies on livestock might be required. Therefore, only provisional residue definitions for animal products were proposed. Intake calculations for livestock, which are required to support the notified use on apples, can only be carried out when the additional data on livestock and apple processing studies are available.
The consumer risk assessment and the MRL proposals cannot be finalised. On the basis of a provisional intake calculation for tomatoes only, the consumer exposure is expected to be below the ADI.

Teflubenzuron is moderate to high persistent in soil under dark aerobic conditions (DT_{50} = 30.4 – 151.5 d) and yields 3,5-dichloro-2,4-difluorophenylurea as a major metabolite. Another metabolite: 3,5-dichloro-2,4-difluoroaniline exceeded 5 % in two non consecutive data points. After consultation with the experts on toxicology, a data gap to address ground water exposure for this metabolite has been identified.

Reliable kinetic parameter (formation and degradation rate constants) for the major metabolite 3,5-dichloro-2,4-dichlorophenylurea were not available and the meeting of experts identified a data gap for them. Ground water exposure assessment may need to be consequently updated.

Degradation was faster under anaerobic conditions than under aerobic ones in the experiment available where the rest of conditions are maintained. However, anaerobic conditions are not considered to be especially relevant for the representative uses (tomato and apple) evaluated at EU level. Photolysis does not significantly contribute to the environmental degradation of teflubenzuron in soil under EU realistic conditions.

Four field dissipation studies are available, which allow calculating dissipation half lives appropriate for PEC soil calculations. However, the experts' meeting identified a new data gap for a new kinetic evaluation of field dissipation studies for its use in environmental modelling. This data gap was not considered essential to finalize the EU risk assessment.

PEC soil of teflubenzuron was calculated in the DAR for the use in apples (outdoor) based on the worst case field half live of 16.4 d. For the metabolite For the metabolites 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4-difluoroaniline the peak maximum PEC soil was calculated based on the maximum formations observed in laboratory studies.

According the studies available, teflubenzuron may be considered immobile in soil (K_{OC} = 21 139 – 32 556 mL / g) and the metabolite 3,5-dichloro-2,4-difluorophenylurea may be considered to exhibit low mobility in soil (K_{OC} = 942 – 1720 mL / g).

In water, teflubenzuron is stable at pH 5 and 7 and hydrolyses with a DT_{50} = 8.7 d at pH 9. Metabolite 3,5-dichloro-2,4-difluorophenylurea is expected to be stable to hydrolysis in the normal range of environmental conditions.

The RMS estimated an aqueous photolysis half-life of 13.7 d (40 ºN, continuous irradiation) on basis of the available study. The RMS considered that photolysis would not contribute significantly to the environmental degradation of teflubenzuron under realistic conditions for the representative uses. Teflubenzuron was not readily biodegradable according the available study.

Dissipation/degradation of teflubenzuron was investigated in two dark aerobic water/sediment systems. In both systems, teflubenzuron partitioned to the sediment and degraded ($DT_{50whole\ system}$ = 11 – 21.4 d) to form the major metabolites 5-chloro-2,4-difluoroaniline (UNK 5 in the DAR), 3,5-dichloro-2,4-difluorophenyl-urea, 3,5-dichloro-2,4-difluoroaniline and 2,6-difluorobenzoic acid.

Applicant provided $PEC_{SW/SED}$ calculations based on FOCUS Step 1 and Step 2 for the metabolites 3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4difluoro aniline, 2,6-difluorobenzoic acid and 5-chloro-2,4-difluoroaniline for the use in apples.

For the parent teflubenzuron $PEC_{SW/SED}$ were calculated with FOCUS scheme up to Step 4 by consideration of up to 100 m spray drift buffer zone for the use in apples. It is noted that this buffer zone represents a 99.6 % mitigation when compared with Step 3 (above the 95 % mitigation deemed as practicable by the FOCUS Landscape and Mitigation guidance document).
For the greenhouse use in tomatoes the RMS provided indicative parent PEC_{SW} value of 0.0225 mg / L based on 0.1 % losses to surface water (Dutch model). However, the RMS also indicated that from the ecotoxicity assessment the total loss from glasshouse should be as low as 0.00001 %. To attain this low level, glasshouses would have to operate with negligible emissions of teflubenzuron. With the available information, it is not possible to assess if measures that actually achieve these low levels of emission rates are practicable. Therefore, EFSA proposed a critical area of concern for the aquatic environment with respect to the uses in green house.
The meeting of experts considered that the trigger of 0.1 µg/L is not expected to be exceeded by teflubenzuron for the representative use in apples.
A data gap has been identified for reliable kinetic formation and degradation parameters of the major soil metabolite 3,5-dichloro-2,4-difluorophenylurea. Therefore, ground water exposure assessment would need to be updated accordingly.
No PEC_{GW} calculations are available for metabolite 3,5-dichloro-2,4-difluoroaniline. The need to address potential ground water contamination by this metabolite has been identified after consultation with the meeting of experts on toxicology. No groundwater assessment is available for the greenhouse use. Therefore, the assessment presented is considered only to address situations were plants are grow on artificial substrate or on hydroponics.
On basis of its properties, long term transport of teflubenzuron through the atmosphere is not expected to be of concern.

The risk to birds and mammals was assessed as low except the long term risk to birds because no valid long term endpoint (reproductive) was available (data gap).
Teflubenzuron is highly toxic to aquatic organisms. A lower acute toxicity to fish was observed when formulated. Water/sediment metabolites were less toxic than the active substance and thus considered as not ecotoxicologically relevant. The most sensitive organisms tested were aquatic invertebrates. First-tier risk assessment indicated a potential high risk to aquatic organisms. FOCUS step 4 scenarios resulted in TERs above the triggers for fish and algae if a no-spray buffer zone of 16 m was included in the calculations but none of the FOCUS step 4 scenarios resulted safe for invertebrates, even including a no-spray buffer of 100 m and taking into account a higher tier study. A potential high risk to aquatic organisms was indentified also for the greenhouse use on tomatoes (TERs based on the Dutch model PEC were below the Annex VI triggers, except for the formulated product TERa fish and TER algae). As mentioned above, a total loss percentage from glasshouses as low as 0.00001% would be needed to be achieve a low risk. Since during the peer review no mitigation measures were assessed which could allow the achievement of such negligible emissions, a potential

high risk to aquatic organisms from greenhouse uses cannot be excluded. A data gap was suggested for further refinements.

A low risk to adult bees was identified. A potential high risk to hive development was not excluded, therefore, for the outdoor use, the risk to bees needs to be further addressed (data gap). For the glasshouse use the risk to bee population was expected to be low. However the risk to introduced pollinators might need to be managed. A high risk for non-target- arthropods was assessed for the in-field exposure scenario and a no-spray buffer zone of 15 m was needed to meet the trigger of 2 for the off-field scenario. The oral uptake was considered by RMS a major route of exposure. The submitted data as well as the ESCORT2 approach did not address this route of exposure. A data gap was identified to further address the risk to non-target arthropods, considering the mode of action of the active substance and the potential for recovery (i.e. a standard field study).

Since teflubenzuron is a chitin synthesis inhibitor, a chronic study on earthworms was requested (data gap), even if the acute risk was assessed as low and the DT_{50} in soil was lower than 100 d.

The risk to other soil macro-organisms, soil micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

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

- The estimated operator exposure was below the AOEL only if personal protective equipment (PPE) is worn (refer to point 2.12).
- The estimated worker exposure was below the AOEL only if PPE is worn (refer to point 2.12).
- Only root and fruit crops can currently be authorised (refer to point 3.1.1)
- Due to the incomplete ground water assessment, the fate and behaviour in the environment assessment presented are considered to only address uses in greenhouse tomato when artificial subtract of hydroponic systems are used.

Critical areas of concern

- No agreed technical specification
- No analytical method to monitor teflubenzuron residues in surface water and air
- No information on the impurity profile of the batches used in toxicological studies is available.
- Risk assessment for the consumer is not finalised due to data gaps identified in different areas of the residue section.
- For greenhouses use, aquatic risk assessment can only meet the triggers for all aquatic organisms if negligible emissions (i.e. 0.0001% of total emission) to surface water are assumed. Attainability of these low levels of exposure has not been demonstrated.

- For the outdoor application a high risk was identified with respect to aquatic invertebrates in a higher-tier assessment (mesocosm study even with a 100 m no-spray buffer zone).
- Long-term risk to birds, risk to bees and non-target arthropods was not finalised.

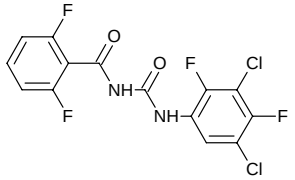
APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

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

Active substance (ISO Common Name) ‡	Teflubenzuron
Function (*e.g.* fungicide)	Insecticide
Rapporteur Member State	United Kingdom
Co-rapporteur Member State	Not applicable

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	1-(3,5-dichloro-2,4-difluorophenyl)-3-(2,6-difluorobenzoyl)urea
Chemical name (CA) ‡	*N*-[[(3,5-dichloro-2,4-diflurophenyl)amino]carbonyl]-2,6-difluorobenzamide
CIPAC No ‡	450
CAS No ‡	83121-18-0
EC No (EINECS or ELINCS) ‡	Not available
FAO Specification (including year of publication) ‡	Not available
Minimum purity of the active substance as manufactured ‡	Open
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Open (To be confirmed following submission of new five batch data)
Molecular formula ‡	$C_{14}H_6Cl_2F_4N_2O_2$
Molecular mass ‡	381.1 g/mol
Structural formula ‡	

Appendix 1 – list of endpoints

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	225-229 °C (99.5 % pure)
Boiling point (state purity) ‡	No data submitted – decomposition occurs before boiling point is reached
Temperature of decomposition (state purity)	225-229 °C (99.5 % pure)
Appearance (state purity) ‡	White crystalline solid (99.6 % technical)
Vapour pressure (state temperature, state purity) ‡	9.16×10^{-7} Pa at 20 °C (99.5 % pure)
Henry's law constant ‡	6.98×10^{-3} Pa $m^3.mol^{-1}$
Solubility in water (state temperature, state purity and pH) ‡	< 0.01 mg/L at 20 °C (pH 5) < 0.01 mg/L at 20 °C (pH 7) 0.11 mg/L at 20 °C (pH 9) (97.5 % pure)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20 °C in g/L (99.6 % technical) n-Heptane: 0.01 Toluene: 0.74 1,2-Dichloromethane: 1.51 Methanol: 1.06 Acetone: 8.85 Ethyl acetate: 6.28
Surface tension ‡ (state concentration and temperature, state purity)	No data submitted – teflubenzuron has a low water solubility
Partition co-efficient ‡ (state temperature, pH and purity)	Log P_{ow} = 4.98 at 20 °C (pH 5, 99.5 % pure) Log P_{ow} > 4.3 at 20 °C (pH 7, 99.3 % pure) Log P_{ow} at pH 9 not available
Dissociation constant (state purity) ‡	pKa = 9.2 in water/methanol 33/67 v/v pKa = 9.7 (extrapolated to water) (99.5 % pure)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	(99.5 % pure) Unbuffered (neutral) solution: λmax 249 nm; ε = 13543 Acidic solution (pH 1.5): λmax 251 nm, ε = 15153 Basic solution (pH 11.5): λmax 262 nm, ε = 21115 $L.mol^{-1}.cm^{-1}$

Appendix 1 – list of endpoints

Flammability ‡ (state purity)	not highly flammable (99.5 % technical)
Explosive properties ‡ (state purity)	not explosive (99.5 % technical)
Oxidising properties ‡ (state purity)	not oxidising (99.5 % technical)

Appendix 1 – list of endpoints

Summary of representative uses evaluated (Teflubenzuron)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	kg as/hL min – max (l)	water L/ha min – max	kg as/ha min – max (l)		
Tomato	Northern and Southern Europe	Nomolt	G	Insects: Whiteflies (*Trialeurodes vaporariorum*) & Caterpillars (*Lepidoptera, Spodoptera exigua*)	SC	150 g/L	Foliar spray	Application is pest related (At 1st flight of adults)	3	7	0.015	1500	0.225	3	(1), (3)
Apple	Northern and Southern Europe	Nomolt	F	Codling moth (*Laspeyresia pomonella*) Leafminers (*Leucoptera scitella; Phyllonorycter blancardella; P. coryfolella*	SC	150 g/L	Foliar spray	Application is pest related (At 1st flight of adults)	3	14	0.006	2000	0.12	14	(2), (4)

(1) Feasibility of risk management measures to ensure negligible exposure to surface water from greenhouses is needed for an acceptable environmental assessment.
(2) Outdoor use unacceptable ecotoxicology assessment
(3) Consumer risk assessment provisionally.
(4) Data gaps for apples in the section on residues.

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

Appendix 1 – list of endpoints

Methods of Analysis

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

Technical as (analytical technique)	HPLC-UV
Impurities in technical as (analytical technique)	Further data required depending on provision of new technical specification
Plant protection product (analytical technique)	HPLC-UV with detection at 230 nm

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Teflubenzuron (fruit and root crops only, provisional)
Food of animal origin		Teflubenzuron (provisional)
Soil		Teflubenzuron
Water	surface	Teflubenzuron
	drinking/ground	Teflubenzuron (not finalized)
Air		Teflubenzuron

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Single method HPLC-UV 0.05 mg/kg (apple, tomato) Multi-residue method DFG-S19 GC-ECD 0.01 mg/kg (apple) (Confirmatory methods and an ILV for tomato are outstanding)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-UV 0.05 mg/kg (meat), 0.01 mg/kg (milk)
Soil (analytical technique and LOQ)	HPLC-UV 0.01 mg/kg (Confirmatory methods are outstanding)

Appendix 1 – list of endpoints

Water (analytical technique and LOQ)	HPLC-UV 0.1 µg/L (drinking/surface/ground water) analytical method for surface water with an LOQ of 0.0025 µg/l is required (Confirmatory methods are outstanding)
Air (analytical technique and LOQ)	No method currently available
Body fluids and tissues (analytical technique and LOQ)	Not required [substance is not classified as toxic (T) or very toxic (T+)].

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

	RMS/peer review proposal
Active substance	Unclassified with regard to physical/chemical data

Appendix 1 – list of endpoints

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	In rats, teflubenzuron was absorbed only partially (approx. 20 % with 16 % in bile + 4 % in urine and carcass within 48 hours at 25 mg/kg bw) from the gastrointestinal tract, absorption being dose-dependent and saturable. Absorption was relatively rapid with peak plasma levels seen at *ca* 1 – 8 hours
Distribution ‡	Low levels (< 1 % in liver, muscle and fat at 6 hours)
Potential for accumulation ‡	There was no evidence of bioaccumulation in organs or tissues, plasma levels increased with the level of dosing in the rat 2-year study
Rate and extent of excretion ‡	Most of the radiolabel (91-95 % of the total dose) was excreted in the faeces, predominantly within 24 h, and only small quantities (< 1 %) were found in urine during eight days after treatment. Absorbed teflubenzuron was excreted mainly via the bile (*ca* 15 %), urinary excretion representing only a minor route (< 5 %).
Metabolism in animals ‡	Teflubenzuron was eliminated largely unchanged in faeces, although a number of unidentified minor metabolites (each < 1 %) were found.
Toxicologically relevant compounds ‡ (animals and plants)	Teflubenzuron, 3,5-dichloro-2,4-difluorophenyl urea
Toxicologically relevant compounds ‡ (environment)	Teflubenzuron, 3,5-dichloro-2,4-difluoroaniline

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5,000mg/kg	
Rat LD_{50} dermal ‡	> 2,000mg/kg	
Rat LC_{50} inhalation ‡	> 5.038mg/l (4-hour, nose-only exposure to dust aerosol)	
Skin irritation ‡	Not irritant	
Eye irritation ‡	Not irritant	
Skin sensitisation ‡	Negative in an inadequate study	**R43**

Appendix 1 – list of endpoints

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Hepatotoxicity	
Relevant oral NOAEL ‡	Rat (90-day): 8.0 mg/kg bw/day Dog (overall): 17.3 mg/kg bw/day Mouse (90-day): 11 mg/kg bw/day	
Relevant dermal NOAEL ‡	no study, not required	
Relevant inhalation NOAEL ‡	no study, not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

No genotoxic potential	

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

Target/critical effect ‡	Hepatotoxicity in rat and mouse	
Relevant NOAEL ‡	Rat: 4.8 mg/kg bw/day Mouse: LOAEL: 2.1 mg/kg bw/day	
Carcinogenicity ‡	liver adenomas in male mice only, not relevant to human exposures	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No effects on reproduction, parents and offspring	
Relevant parental NOAEL ‡	37 mg/kg bw/day (top dose)	
Relevant reproductive NOAEL ‡	37 mg/kg bw/day	
Relevant offspring NOAEL ‡	37 mg/kg bw/day	

Appendix 1 – list of endpoints

Developmental toxicity

Developmental target / critical effect ‡	Rat and rabbit: No developmental effects Rat: no adverse maternal effects Rabbit: maternal liver effects at the limit dose	
Relevant maternal NOAEL ‡	Rat: 1000 mg/kg bw/day (top dose) Rabbit: 500 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat and rabbit: 1000 mg/kg bw/day (top dose)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data, not required	
Repeated neurotoxicity ‡	No data, not required	
Delayed neurotoxicity ‡	No data, not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Investigation on the potential for covalent binding of teflubenzuron to mouse liver DNA: DNA binding do not represent a potent mechanism of liver tumour induction by teflubenzuron
Studies performed on metabolites or impurities ‡	3,5-dichloro-2,4-difluoroaniline: Rat oral LD_{50}: 1986/1552 mg/kg bw (males/females) Ames test: negative. 3,5-dichloro-2,4 difluorophenylurea: Rat oral LD_{50}: 677/703 mg/kg bw (males/females) Ames test: negative.-

Appendix 1 – list of endpoints

Medical data ‡ (Annex IIA, point 5.9)

Several databases were consulted and no occurrences of incidents of poisoning or epidemiological data were found

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/day	mouse carcinogenicity	200*
AOEL ‡	0.016 mg/kg bw/day	90-day rat study	500**
ARfD ‡	Not allocated		

* based on an LOAEL
** SF of 100 corrected for 20 % oral absorption

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Nomolt 150 SC)	2 % for the concentrate (rat *in vivo* + rat and human *in vitro* studies); 20 % for the dilution (rat *in vivo* study)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	**Orchard applications in apples** Tractor drawn air-assisted sprayers at max. dose rate of 0.120 kg teflubenzuron/ha UK POEM: % of AOEL No PPE 163 % With PPE (gloves during M/L) 154 % With PPE (gloves when handlong the concentrate and contaminated surfaces) 109 % German model: No PPE 203 % With PPE (gloves during M/L) 199 % With PPE (gloves during M/L & applic. and coverall & sturdy footwear during applic.) 31 % **Greenhouse applications in tomatoes** hand held at max. dose rate of 0.225 kg teflubenzuron/ha

Appendix 1 – list of endpoints

	Hose-fed lance equipment: % of AOEL No PPE 406 % With PPE (gloves during M/L & applic.) 165 % With PPE (gloves & coveralls during M/L & applic.) 34 % Knapsack sprayers: No PPE 193 % With PPE (gloves during M/L & applic.) 48 % With PPE (gloves & coveralls during M/L & applic.) 13 % M/L: mixing and loading; applic.: application
Workers	Assuming dermal absorption value derived from the concentrate formulation (2 %) : % of AOEL **Apples** No PPE 51 % With PPE (gloves, long sleeved shirt & long trousers) 5.1 % **Tomatoes** No PPE 54 % With PPE (gloves, long sleeved shirt & long trousers) 5.4 % Assuming dermal absorption value derived from the in-use spay dilution (20 %) : % of AOEL **Apples** No PPE 514 % With PPE (gloves, long sleeved shirt & long trousers) 51.4 % **Tomatoes** No PPE 538 % With PPE (gloves, long sleeved shirt & long trousers) 53.8 % According to exposure models (Krieger, 1992; Krebs *et al.* 1996) and supervised trials on residues after 3 sequential treatments in apples and tomatoes.

Appendix 1 – list of endpoints

Bystanders	According to the Lloyd & Bell, 1987, study (orchard sprayers), bystander exposure is estimated to represent 5 % of the AOEL. According to surrogate values derived from the Californian EPA studies, highest potential residential exposure is estimated to represent 52 % of the AOEL. According to spray drift fallout values used for an aquatic risk assessment and US EPA values for residential exposure resulting from contact with treated lawn (1998), the estimated exposure of children playing on a contaminated lawn represents 16 % of the AOEL.

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

	RMS/peer review proposal
Substance classified (teflubenzuron)	**Xi** "Irritant" **R43** "May cause sensitization by skin contact"

Appendix 1 – list of endpoints

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

Plant groups covered	Fruit (apple), and root (potato) crops Foliar treatment
Rotational crops	Valid rotational crop studies are outstanding.
Metabolism in rotational crops similar to metabolism in primary crops?	Not known
Processed commodities	No data submitted – justification accepted (Levels of teflubenzuron unchanged following high temperature drying and sterilisation on a weight/weight basis in processing studies)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Teflubenzuron (fruit and root crops only) (a)
Plant residue definition for risk assessment	Teflubenzuron (fruit and root crops only) (a)
Conversion factor (monitoring to risk assessment)	None

(a) Provisional, pending outstanding metabolism study on rotational crops.

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

Animals covered	Lactating goat and laying hen (aniline-labelled studies only)
Time needed to reach a plateau concentration in milk and eggs	5 days (milk), 9 days (eggs)
Animal residue definition for monitoring	Teflubenzuron (provisional)
Animal residue definition for risk assessment	Liver and kidney: sum of teflubenzuron and 3,5-dichloro-2,4-difluorophenyl urea expressed as teflubenzuron (provisional)) (a) Other commodities of animal origin: teflubenzuron (provisional) (a)
Conversion factor (monitoring to risk assessment)	(b)
Metabolism in rat and ruminant similar (yes/no)	(a)
Fat soluble residue: (yes/no)	yes

(a) Pending further data on livestock metabolism.
(b) Requirement to be evaluated when further data on livestock metabolism is available.

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

	Metabolism of rotational crops is not defined. No field studies are available.

Appendix 1 – list of endpoints

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

Teflubenzuron was stable for up to 36 months in the following crops: apple, pear, potato and cabbage. Teflubenzuron was stable for 18 months in tomatoes.
Data on storage stability of residues prior to analysis for animal products is required to support use on apples.

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	(a)	No	No
Potential for accumulation (yes/no):	n/a	n/a	n/a
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	n/a	n/a	n/a
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	(b)	Not required	Not required
Liver	(b)	Not required	Not required
Kidney	(b)	Not required	Not required
Fat	(b)	Not required	Not required
Milk	(b)		
Eggs		Not required	

(a) Expert meeting concluded that on completion of the data for apples (additional residue trials and processing studies) a livestock burden calculation for intake of apple pomace is required.
(b) Requirement to be evaluated after completion of data (residue trials and processing studies in apples, metabolism study on ruminant with bezoyl ring label).

Appendix 1 – list of endpoints

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

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Tomato	N & S Europe Glasshouse Foliar spray	3 x 0.07, 0.09, 0.32, 0.33, 0.35, 0.49	No trials on cherry tomato, therefore use restricted to non-cherry varieties.	1.0	0.49	0.21
Apple	N Europe Field Foliar spray	0.13, 0.19, 2 x 0.29	(d) Only 4 trials available at notified cGAP – 4 further trials required.			
Apple	S Europe Field Foliar spray	0.06, 0.07, 0.09, 0.10	Only 4 trials available at notified cGAP – 4 further trials required.			

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue
(d) Validation data for RU 134/32/10 by Memmesheimer (1999) used in residue trials on apples is required.

Appendix 1 – list of endpoints

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

ADI	0.01 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	24.34 % (worst case Cluster B)
TMDI (% ADI) according to national (to be specified) diets	n/a
IEDI (WHO European Diet) (% ADI)	n/a
NEDI (UK diet) (% ADI)	6 % (worst case toddler)
Factors included in IEDI and NEDI	n/a
ARfD	None specified, not considered to be acutely toxic
IESTI (% ARfD)	n/a
NESTI (% ARfD) according to national (to be specified) large portion consumption data	n/a
Factors included in IESTI and NESTI	n/a

(a) Risk assessment is provisional and based on intake of tomatoes only. To be reassessed when additional data on cherry tomatoes, apples and livestock are available.

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

Crop/ process/ processed product		Number of studies	Processing factors		Amount transferred (%) (Optional)
			Transfer factor	Yield factor	
Apple (a)					
Tomato	Pomace, wet	4	1.78	-	
	Juice	4	0.17	-	
	Puree	4	0.45	-	
	Peeled fruit	4	0.08	-	
	Peel	4	7.73	-	
	Canned tomato	4	0.07	-	

(a) To support the use on apples a sufficient number of processing studies on apples as required by Directive 91/414/EC has to be submitted.

Appendix 1 – list of endpoints

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

Tomato	1.0 mg/kg (provisional) (a)
Apples	(b)
Animal products	(b)

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

(a) Data gap for residue trials on cherry tomatoes identified.

(b) MRL proposal to be finalised upon submission of all data necessary to support the apple use

Appendix 1 – list of endpoints

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

Mineralization after 100 days ‡	2.2% after 98 d, [^{14}C-teflubenzuron]-aniline ring label (n= 1) 44% after 90 d, [^{14}C-teflubenzuron]-benzoyl ring label (n = 1)
Non-extractable residues after 100 days ‡	23.6% after 98 d, [^{14}C-teflubenzuron]-aniline ring label (n = 1) 28.3% after 90 d, [^{14}C-teflubenzuron]-benzoyl ring label (n = 1)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	3,5-dichloro-2,4-dichlorophenylurea: 10.4% at 29 d [^{14}C-teflubenzuron]-aniline ring label (n = 1) 3,5-dichloro-2,4-dichlorophenylurea: 2.64 - 10.71% at 14 d [^{14}C-teflubenzuron]-aniline ring label (n = 3) 3,5-dichloro-2,4-difluoroaniline: 5.4% at 29 d [^{14}C-teflubenzuron]-aniline ring label (n = 1) 3,5-dichloro-2,4-difluoroaniline: 2.13 - 8.43% at 42 d [^{14}C-teflubenzuron]-aniline ring label (n = 3)

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

Anaerobic degradation ‡

Mineralization after 100 days	Not recorded in [^{14}C-teflubenzuron]-aniline ring label study (n =1) 22.9% after 90 d (study end), [^{14}C-teflubenzuron]-benzoyl ring label (n = 1)
Non-extractable residues after 100 days	34.5% after 59 d (study end), [^{14}C-teflubenzuron]-aniline ring label (n =1) 34.1% after 90 d (study end), [^{14}C-teflubenzuron]-benzoyl ring label (n = 1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	3,5-dichloro-2,4-dichlorophenylurea: 28.2% at 14 d [^{14}C-teflubenzuron]-aniline ring label (n = 1)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None > 5% AR ([^{14}C-teflubenzuron]-aniline ring label (n = 1)).

Appendix 1 – list of endpoints

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

Laboratory

Soil	Original DT_{50} days	Study temp °C	Study moisture %	FOCUS pF2 moisture %	Normalised DT_{50} days
Speyer 2.1 (sand)	140.3	20	12.0	12.0	140.3
Speyer 3A (sandy silt loam)	72.8	20	20	25	62.2
Speyer 5M (sandy loam)	120.9	20	17.2	19	112.8
Sandy loam (Schlüter)	77.0[1]	22	11.175	14.9@0.33bar (actual value for soil)	73.2
GEOMEAN days (normalised)					**92.1**

[1]Although this value is actually an FOMC DT50 the RMS considers the inclusion of this value in the calculation of the geomean is the most appropriate way of handling this data point. The FOMC DT90 values were not supported by any of the other laboratory or field results and are likely to be an artefact of the laboratory study conditions.

Parent	Field studies							
Soil type (bare soil used in all studies)	Location (country or USA state).	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Silty loam	Germany	*	0 - 30	16.4	54.5	0.935		NLRFO#
Loess	Netherlands	6.5	0 - 30	16.0	53.2	0.984		NLRFO#
Sandy loam	Italy	5.8	0 - 30	8.8	29.2	0.982		NLRFO#
Sandy silt loam	S France	8.4	0 - 30	13.4	44.5	0.994		NLRFO#
Metabolites were not analysed for, as the max level of the single metabolite > 10% AR (3,5-dichloro-2,4-difluorophenylurea) was 10.71% and was combined with rapid laboratory degradation.								

*soil details not given for German site
#Non-linear regression first order kinetics

pH dependence ‡ (yes / no) (if yes type of dependence)	Not seen in field studies.
Soil accumulation and plateau concentration ‡	Not triggered.

Appendix 1 – list of endpoints

Laboratory studies ‡

Parent	Anaerobic conditions not anticipated under proposed GAP

Appendix 1 – list of endpoints

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sand	0.8	6.2		21139			N/A
Sandy loam	1.7	7.0		25711			N/A
Silt loam	1.8	7.1		32556			N/A
Clay loam	3.8	7.2		24842			N/A
Arithmetic mean				26062			
pH dependence, Yes or No			No				

Metabolite CFPU							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	2.3	5.6		942			1.04
Sandy silty loam	2.6	7.1		898			1.06
Silty sand	1.6	7.0		1720			1.22
Arithmetic mean/median					1187		
pH dependence (yes or no)			No				

Appendix 1 – list of endpoints

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

Column leaching (Metabolite CFPU)‡	Eluation (mm): 200 mm Time period (d): 2 d
	Leachate: 0.11 % total residues/radioactivity in leachate >88 % total residues/radioactivity retained in top 10 cm
Aged residues leaching (teflubenzuron)‡	Aged for (d): 30d Time period (d): 45 d Eluation (mm): 495 mm
	Analysis of soil residues post ageing (soil residues pre-leaching): 75.5 % teflubenzuron 5.6 % CFPU, 2.2 % CFA, 7.4% unknown. 80.5 % total residues/radioactivity retained in aged soil, 13.3 % total residues/radioactivity retained in top 5cm of column
	Leachate: <0.1 % total residues/radioactivity in leachate
Lysimeter/ field leaching studies ‡	Not required

Appendix 1 – list of endpoints

Lysimeter/ field leaching studies ‡	Not required

Appendix 1 – list of endpoints

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation Use on apple only considered – exposure from protected use on tomato likely to be minimal if applied on artificial substrate	DT_{50} (d): 16.4 days Kinetics: Non-linear, single first-order Field or Lab: worst-case from field study in Germany.
Application data	Crop: Apple Depth of soil layer: 5 cm Soil bulk density: 1.5 g/cm^3 % plant interception: 70% (foliage development) Number of applications: 3 Interval (d): 14 Application rate(s): 120 g as/ha

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.048	0.048	0.089	0.089
24h	0.046	0.047	0.086	0.087
2d	0.044	0.046	0.082	0.086
4d	0.041	0.044	0.075	0.082
7d	0.036	0.042	0.066	0.077
14d	0.027	0.036	0.049	0.067
28d	0.015	0.028	0.027	0.052
50d	0.006	0.020	0.011	0.037
100d	0.001	0.011	0.001	0.021

Plateau concentration	N/A

Appendix 1 – list of endpoints

Metabolite 1 3,5-dichloro-2,4-difluorophenylurea (CFPU)	Molecular weight relative to the parent: 0.632 No reliable estimate of degradation available. Max formation 10.7% (Laboratory - Baumann, J, 2003a)
Metabolite PEC calculated on a 'total load' approach based on 1 application of 360 g/ha of teflubenzuron	
Application data	Application rate assumed: 24.3 g as/ha; 70% crop interception
PEC_s (mg/kg)	0.010

Metabolite 2 3,5-dichloro-2,4-difluoroaniline (CFA) (does not occur >10%AR – but calculated for input to ecotox soil studies for completeness)	Molecular weight relative to the parent: 0.520 No reliable estimate of degradation available. Max formation 8.43% (Laboratory - Baumann, J, 2003)
Metabolite PEC calculated on a 'total load' approach based on 1 application of 360 g/ha of teflubenzuron	
Application data	Application rate assumed: 15.8 g as/ha; 70% crop interception
PEC_s (mg/kg)	0.006

Appendix 1 – list of endpoints

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

Hydrolytic degradation of the active substance (25ºC)	pH 5: stable
	pH 7: 95% AR remained as parent after 30 days
	pH 9: 8.7 days (1st order, r^2=0.975) CFPU: 61 %AR (30 d, aniline ring)) CFA 12 % AR (30 d, aniline ring) 2,6-difluorobenzoic acid 62% AR (30 d, benzoyl ring) 2,6-difluorobenzamide 12% AR (30 d, benzoyl ring)
Hydrolytic degradation of metabolite CFPU (50ºC)	Stable to hydrolysis at pH 4, 7 and 9
Photolytic degradation of active substance‡	DT_{50} : 10 days (equivalent to 13.7d 40°N, continuous irradiation) Artificial light, 820 W/m^2
Quantum yield of direct phototransformation in water at ☒ > 290 nm and pH5, 20°C	4.91 x 10^{-9} mol · Einstein $^{-1}$
Readily biodegradable ‡ (yes/no)	Not ready biodegradable.

Degradation in water / sediment

Parent	Distribution Sand system: max water 102.2 % after 0 d, max. sed 40.8 % after 7 d Clay system: max water 101.4 % after 0 d, max sed 36.1 % after 14 d							
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole system d.	St. (r^2)	DT_{50} water d	St. (r^2)	Method of calculation
Sand	6.1	5.5	20	11.4	0.966	4.9	0.960	SFO
Clay	8.1	7.1	20	21.4	0.987	9.7	0.976	SFO

Appendix 1 – list of endpoints

CFPU	Distribution Sand system: max water 22.5 % after 14 d, max. sed 3.8 % after 14 d Clay system: max water 10.5 % after 14 d, max sed 2.5 % after 14 d							
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	Method of calculation
Insufficient data points for reliable calculation								

CFA	Distribution Sand system: max water 26.4 % after 60 d, max. sed 11.2 % after 60 d Clay system: max water 7.1 % after 30 d, max sed 12.8 % after 60 d							
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	Method of calculation
Insufficient data points for reliable calculation								

2,6–difluorobenzoic acid	Distribution Sand system: max water 13.8 % after 14 d, ND in sed Clay system: max water 6.7 % after 7 d, ND in sed							
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	Method of calculation
Insufficient data points for reliable calculation								

5-chloro-2,4-difluoroaniline	Distribution Sand system: max water 19.1 % after 30 d, max. sed 10.4 % after 120 d Clay system: max water 15.0 % after 30 d, ND in sed							
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	Method of calculation
Insufficient data points for reliable calculation								

Appendix 1 – list of endpoints

Mineralization and non extractable residues				
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d (end of the study)
Sand	6.1	5.5	58.4 % 60 d (120 d)	59.6% 120 d (120 d)
Clay	8.1	7.1	58.1% 120 d (120 d)	34.0% 60 d (120 d)

Appendix 1 – list of endpoints

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

Parent Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: FOCUS 1.1; FOCUS SWASH 1.1; TOXSWA 2.0. Teflubenzuron: Molecular weight (g/mol): 381.1 Water solubility (mg/L): 0.01 K_{OC} (ml/g): 26062 DT_{50} soil (d): 66.6 days[16] (mean of 6 laboratory soils, normalised) DT_{50} water/sediment system (d): 57.1[17] DT_{50} water (d): 57.1 (2005 study); 21.5 (2006 study) DT_{50} sediment (d): 1000 (to reflect no degradation) 3,5-dichloro-2,4-difluorophenylurea: not included (see Table B.8.6.3) Crop interception (%): 70
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: MACRO 4.3; PRZM 3.22; FOCUS 1.1.3; TOXSWA 2.0. Vapour pressure: 1.3×10^{-8} Koc: 26062 1/n: 0.9
Application rate	Crop: Apples Crop interception %: 70 Number of applications: 3 for multiple application; single application also run. Interval (d): 14 Application rate(s): 120 g as/ha Application window: 58 days during July and October e.g. 10.07 – 06.09; 21.08 – 18.10.
	Glasshouse use considered below.

[16] Note that a value of 92.1 days (geomean of 4 laboratory soils, normalised) was derived following discussion at PRAPeR 52. Since the main route of entry of teflubenzuron to surface water is via spray drift the modelling has not been repeated using the revised geomean value as this will not affect the PECsw values at Step 3 and 4.

[17] PRAPeR 52 recommended that a whole system DT50 of 21.4 d be used for future risk assessments. Since this value will not affect the DT50 of metabolites up to Step 2 the modelling has not been repeated using the revised value.

Appendix 1 – list of endpoints

PECsw and PECsed values for teflubenzuron at FOCUS Steps 1 and 2

Scenario	PEC_{SWinit}(µg/L)	$PEC_{SEDinit}$ (µg/kg)
Step 1 N Europe	22.23	1000
Step 1 S Europe	22.23	1000
Step 2 N Europe	4.75	137.59
Step 2 S Europe	4.75	159.49

Maximum PECsw and PECsed values for teflubenzuron at FOCUS Step 3, single application

FOCUS STEP 3 Scenario	Water body	PECsw (µg/L)	PEC_{SED} (µg/kg)
D3 Vreedepeel	Ditch	4.261	13.090
D4 Skousbo	Pond	0.189	2.294
D4 Skousbo	Stream	4.277	7.335
D5 La Jallière	Pond	0.189	2.181
D5 La Jallière	Stream	4.616	8.699
R1 Weiherbach	Pond	0.189	2.155
R1 Weiherbach	Stream	3.269	5.343
R2 Porto	Stream	4.386	4.720
R3 Bologna	Stream	4.613	8.581
R4 Roujan	Stream	3.268	5.210

Appendix 1 – list of endpoints

Maximum PECsw and PECsed values for teflubenzuron at FOCUS Step 3, 3 applications

FOCUS STEP 4 Scenario	Water body	PECsw (µg/L)	PEC_{SED} (µg/kg)
D3 Vreedepeel	Ditch	3.056	17.045
D4 Skousbo	Pond	0.224	4.994
D4 Skousbo	Stream	3.049	6.134
D5 La Jallière	Pond	0.222	4.619
D5 La Jallière	Stream	3.291	7.894
R1 Weiherbach	Pond	0.209	4.749
R1 Weiherbach	Stream	2.330	4.798
R2 Porto	Stream	3.126	4.238
R3 Bologna	Stream	3.288	16.336
R4 Roujan	Stream	2.330	4.816

Maximum PECsw and PECsed values for teflubenzuron at FOCUS Step 4, single application, 16m buffer zone

FOCUS STEP 4 Scenario	Water body	PECsw (µg/L)	PEC_{SED} (µg/kg)
D3 Vreedepeel	Ditch	0.576	0.665
D4 Skousbo	Pond	0.070	0.831
D4 Skousbo	Stream	0.671	0.148
D5 La Jallière	Pond	0.070	0.765
D5 La Jallière	Stream	0.724	0.211
R1 Weiherbach	Pond	0.070	0.755
R1 Weiherbach	Stream	0.513	0.099
R2 Porto	Stream	0.688	0.153
R3 Bologna	Stream	0.724	0.506
R4 Roujan	Stream	0.513	0.188

Appendix 1 – list of endpoints

Maximum PECsw and PECsed values for teflubenzuron at FOCUS Step 4, 3 applications, 16m buffer zone

FOCUS STEP 4 Scenario	Water body	PECsw (µg/L)	PEC_{SED} (µg/kg)
D3 Vreedepeel	Ditch	0.422	1.569
D4 Skousbo	Pond	0.082	1.750
D4 Skousbo	Stream	0.490	0.268
D5 La Jallière	Pond	0.082	1.577
D5 La Jallière	Stream	0.529	0.404
R1 Weiherbach	Pond	0.074	1.638
R1 Weiherbach	Stream	0.374	0.207
R2 Porto	Stream	0.502	0.461
R3 Bologna	Stream	0.528	1.790
R4 Roujan	Stream	0.374	0.577

Maximum PECsw and PECsed values for teflubenzuron at FOCUS Step 4, single application, 18m buffer zone

FOCUS STEP 4 Scenario	Water body	PECsw (µg/L)	PEC_{SED} (µg/kg)
D3 Vreedepeel	Ditch	0.471	0.544
D4 Skousbo	Pond	0.062	0.732
D4 Skousbo	Stream	0.548	0.121
D5 La Jallière	Pond	0.062	0.673
D5 La Jallière	Stream	0.592	0.172
R1 Weiherbach	Pond	0.062	0.665
R1 Weiherbach	Stream	0.419	0.083
R2 Porto	Stream	0.562	0.149
R3 Bologna	Stream	0.591	0.480
R4 Roujan	Stream	0.419	0.068

Appendix 1 – list of endpoints

Maximum PECsw and PECsed of teflubenzuron at FOCUS Step 4, single application, various buffer zones

FOCUS STEP 4 Scenario	Water body	Buffer zone (m)	PECsw (µg/L)	PEC_{SED} (µg/kg)
D3 Vreedepeel	Ditch	45	0.471	0.544
D4 Skousbo	Pond	50	0.062	0.732
D4 Skousbo	Stream	50	0.548	0.121
D5 La Jallière	Pond	55	0.062	0.673
D5 La Jallière	Stream	55	0.592	0.172
R1 Weiherbach	Pond	45	0.062	0.665
R1 Weiherbach	Stream	45	0.419	0.083
R2 Porto	Stream	50	0.562	0.149
R3 Bologna	Stream	55	0.591	0.480
R4 Roujan	Stream	45	0.419	0.068

Maximum PECsw and PECsed values for teflubenzuron at FOCUS Step 4, 3 application, 75m buffer zone

FOCUS STEP 4 Scenario	Water body	PECsw (µg/L)	PEC_{SED} (µg/kg)
D3 Vreedepeel	Ditch	0.022	0.086
D4 Skousbo	Pond	0.008	0.170
D4 Skousbo	Stream	0.027	0.015
D5 La Jallière	Pond	0.008	0.152
D5 La Jallière	Stream	0.029	0.023
R1 Weiherbach	Pond	0.007	0.160
R1 Weiherbach	Stream	0.021	0.016
R2 Porto	Stream	0.028	0.047
R3 Bologna	Stream	0.031	0.199
R4 Roujan	Stream	0.021	0.069

Appendix 1 – list of endpoints

Maximum PECsw and PECsed values for teflubenzuron at FOCUS Step 4, single application, 100m buffer zone

FOCUS STEP 4 Scenario	Water body	PECsw (µg/L)	PEC_{SED} (µg/kg)
D3 Vreedepeel	Ditch	0.025	0.029
D4 Skousbo	Pond	0.006	0.067
D4 Skousbo	Stream	0.027	0.006
D5 La Jallière	Pond	0.006	0.061
D5 La Jallière	Stream	0.029	0.009
R1 Weiherbach	Pond	0.006	0.060
R1 Weiherbach	Stream	0.021	0.005
R2 Porto	Stream	0.028	0.015
R3 Bologna	Stream	0.029	0.050
R4 Roujan	Stream	0.021	0.021

Glasshouse use

Application rate	Crop: Tomatoes (glasshouse use only) Number of applications: 3 Interval (d): 7 Application rate(s): 225 g as/ha
PECsw: 22.5 µg/L	Assumptions: Based on total emissions into a standard 30 cm deep ditch and a total percentage loss of 0.1% from 675 g applied in 30000l water.
~~PECsw: 0.225 µg/L~~	~~Assumptions:~~ ~~Based on 0.1% loss equivalent to spray drift alone into a standard 30 cm deep ditch from 675 g applied in 30000l water. This is equivalent to a total mass loss of 0.001%.~~
Zero emissions	The regulatory acceptable concentration for aquatic organisms is 0.0000025 mg a.s./L (0.0025 µg/L). To achieve this the total loss percentage from the glasshouse would need to be as low as 0.00001%. This is considered to be effectively zero emissions. This would need to be considered by Member States in relation to their glasshouse practices.

Appendix 1 – list of endpoints

Metabolites

Spray drift is the main route of entry into surface waters. The rapporteur considers that it is valid to calculate PECsw for the 4 metabolites (3,5-dichloro-2,4-difluorophenylurea, 3,5-dichloro-2,4-difluoroaniline, 2,6-difluorobenzoic acid and 5-chloro-2,4-difluoroaniline) occurring in the water/sediment study (Oddy and Brett, 2006) from the active substance PECs using the maximum observed formations and their relative molecular weights compared to teflubenzuron at Steps 3 and 4. The relative molecular weight of 5-chloro-2,4-difluoroaniline is assumed to be the same as teflubenzuron in the absence of further information. Please see the table below for maximum observed occurrence and relative molecular weights of the metabolites.

Metabolite formation fractions and relative molecular weights

Substance	Relative molecular weight	Peak occurrence %
Teflubenzuron	381.1	-
3,5-dichloro-2,4-difluorophenylurea	241.0	22.5
3,5-dichloro-2,4-difluoroaniline	198.0	26.4
2,6-difluorobenzoic acid	158.1	13.8
5-chloro-2,4-difluoroaniline	381.1*	19.1

*Assumed same relative molecular weight as teflubenzuron

The estimated PECsw for the 4 metabolites at step 3 and 4 are as follows, calculated from the maximum PECsw for teflubenzuron at Step 3 (single application, D5 stream, 4.616 µg/L) and Step 4 (0.724 µg/L in D5/R3 stream, single application with 16m buffer zone):

Estimated PECsw for metabolites occurring in Oddy and Brett 2006

Substance	Step 3 PECsw (µg/L)	Step 4 PECsw (ug/L)
3,5-dichloro-2,4-difluorophenylurea	0.657	0.103
3,5-dichloro-2,4-difluoroaniline	0.633	0.099
2,6-difluorobenzoic acid	0.264	0.041
5-chloro-2,4-difluoroaniline	0.882*	0.138*

*Calculated on basis of same relative molecular weight as teflubenzuron

Appendix 1 – list of endpoints

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter) Use on apple only considered – exposure from protected use on tomato likely to be minimal if applied on artificial substrate	Model(s) used: PEARL V.1.1.1 Scenarios: Châteaudun; Hamburg; Jokioinen; Kremsmünster; Okehampton; Piacenza; Porto; Sevilla; Thiva. Crop: Apples Geometric mean or median parent DT_{50} field 16.6 d[18] K_{OC}: parent, arithmetic mean 26062 mL/g, $^1/_n$= 0.9 Metabolites: 3, 5-dichloro-2, 4-difluorophenylurea (soil metabolite > 10% AR: 100% formation rate assumed) Geometric mean or median DT_{50lab} 5.6 days (normalisation to 10kPa or pF2, 20 °C with Q10 of 2.2). K_{OC}: arithmetic mean 1187 mL/g, $^1/_n$ = 1.105.
Application rate	Application rate: 120 g a.s./ha. No. of applications: 3 Interception: 80% Time of application: June to October

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

	Scenario	Teflubenzuron (µg/L)	3,5-dichloro-2,4-difluorophenylurea (µg/L)
FOCUS PEARL V.1.1.1, APPLES	Châteaudun	<0.001	Data gap
	Hamburg	<0.001	Data gap
	Jokioinen	<0.001	Data gap
	Kremsmünster	<0.001	Data gap
	Okehampton	<0.001	Data gap
	Piacenza	<0.001	Data gap
	Porto	<0.001	Data gap
	Sevilla	<0.001	Data gap
	Thiva	<0.001	Data gap

[18] Note that a value of 92.1 days (geomean of 4 laboratory soils, normalised) was derived following discussion at PRAPeR 52. Since the groundwater leaching potential of teflubenzuron is considered to be negligible based on the very high Koc value the modelling has not been repeated using the revised geomean value. The PECgw would be expected to be <0.001µg/l.

Appendix 1 – list of endpoints

A data gap has been also identified for the groundwater exposure assessment of 3, 5-dichloro-2, 4-difluoroaniline.

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	No information
Photochemical oxidative degradation in air ‡	1.7 days (12 hour day, 1.5E6 OH/cm^3)
Volatilisation ‡	from plant surfaces (BBA guideline): <10 % after 24 hours
	from soil surfaces (BBA guideline): 18% after 1 day; 22% after 24 days
Metabolites	No information

PEC (air)

PEC$_{(a)}$

Maximum concentration	Negligible (due to DT50 < 2 days, 22% volatilisation after 24 days)

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: parent and 3,5-dichloro-2,4-difluoro phenylurea Surface Water: parent, 3,5-dichloro-2,4-difluoro phenylurea, 3,5-dichloro-2,4-difluoroaniline, 2,6-difluorobenzoic acid and 5-chloro-2,4-difluoroaniline. Sediment: parent Ground water:parent and 3,5-dichloro-2,4-difluoro phenylurea Air: parent

Appendix 1 – list of endpoints

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

Soil (indicate location and type of study)	
Surface water (indicate location and type of study)	
Ground water (indicate location and type of study)	
Air (indicate location and type of study)	

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

none proposed.

Appendix 1 – list of endpoints

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds				
Mallard Duck	teflubenzuron	Acute	LD_{50} >2,000	
Bobwhite Quail	teflubenzuron	Acute	LD_{50} >2,250	
Mallard Duck	teflubenzuron	Short-term	LDD_{50} >1,209	>5,000
Bobwhite Quail	teflubenzuron	Short-term	LDD_{50} >1,014	>5,000
		Long-term	NOEC not established	
Mammals				
Rat	teflubenzuron	Acute	>5000	
Rat	'Nomolt'	Acute	>2000	
Rat	teflubenzuron	Long-term	40	
Additional higher tier studies				
No data were submitted.				

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

Apples, 3 applications of 0.12 kg a.s./ha

Indicator species/Category[2]	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird	Acute	6.49	>308.17	10
Insectivorous bird	Short-term	3.62	280.17	10
Insectivorous bird	Long-term	3.62		5
Higher tier refinement (Birds)				
No data were submitted				

Appendix 1 – list of endpoints

Indicator species/Category[2]	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Mammals)				
	Acute	18.93	264.18	10
	Long-term	6.19	6.46	5
Higher tier refinement (Mammals)				
Not required				

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Bluegill sunfish *(Lepomis macrochirus)*	teflubenzuron	96 hr (flow-through)	Mortality, LC_{50}	> 0.0065 (mm)
Juvenile rainbow trout *(Oncorhynchus mykiss)*	teflubenzuron	28 d (flow-through)	Growth NOEC	0.0186 (mm)
Rainbow trout *(Oncorhynchus mykiss)*	'Nomolt'	96 hr (flow-through)	Mortality, LC_{50}	> 15.1 (mm) (> 114 mg formulation/l)
Rainbow trout *(Oncorhynchus mykiss)*	CFPU	96 hr (static)	Mortality, LC_{50}	> 7.8 (mm)
Rainbow trout *(Oncorhynchus mykiss)*	CFA	96 hr (static)	Mortality, LC_{50}	6.74 (mm)
Aquatic invertebrate				
Daphnia magna	teflubenzuron	48 h (static)	Immobilisation, EC_{50}	0.0028 (mm)
Daphnia magna	teflubenzuron	21 d (static-renewal)	NOEC	0.000062 (nom)
Daphnia magna	'Nomolt'	48 h (static)	Immobilisation, EC_{50}	0.00033 (nom) (0.0025 mg formulation/l)
Daphnia magna	'Nomolt'	21 d (static-renewal)	Reproduction, NOEC	0.000013 (nom) (0.0001 mg formulation/l)
Daphnia magna	CFPU	48 h (static)	Mortality, EC_{50}	15.1 (mm)
Daphnia magna	CFA	48 h (static)	Mortality, EC_{50}	1.48 (nom)
Sediment dwelling organisms				
Chironomus riparius	teflubenzuron	28 d (static)	NOEC	0.05 mg/kg sediment (dw)

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Algae				
Scenedesmus subspicatus	teflubenzuron	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	> 0.02 (nom) > 0.02 (nom)
Pseudokirchneriella subcapitata	CFPU	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	7.4 (mm) > 9.7 (mm)
Pseudokirchneriella subcapitata	CFA	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	1.26 (mm) 2.99 (mm)
Higher plant No data are required.				
Microcosm or mesocosm tests				
NOEC = 0.005 µg a.s./l. It was concluded at PRAPer 53 that a NOEAEC of 0.033 µg a.s./L was inappropriate and that the NOEC of 0.005 µg a.s./l (0.000005 mg a.s./L) should be used with an uncertainty factor of 2. Thus the regulatory acceptable concentration for aquatic invertebrates is 0.0025 µg a.s./l (0.0000025 mg a.s./L)				

[1] Based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$).

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

FOCUS Step1

Apples, 3 applications of 0.12 kg a.s./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg/L)	PEC_{twa}[2]	TER	Annex VI Trigger[1]
teflubenzuron	Fish	> 0.0065	Acute (LC50)	0.02223		**>0.292**	100
teflubenzuron	Fish	0.0186	Chronic (NOEC)	0.02223		**0.837**	10
teflubenzuron	Aquatic invertebrates	0.0028	Acute (EC50)	0.02223		**0.126**	100
teflubenzuron	Aquatic invertebrates	0.000062	Chronic (NOEC)	0.02223		**0.003**	10
teflubenzuron	Algae	> 0.02	Chronic (EC50)	0.02223		**>0.247**	10
teflubenzuron	Sediment-dwelling[1] organisms	0.05	Chronic (NOEC)	1		**0.050**	10
CFPU	Fish	>7.8	Acute (LC50)	0.00583		>1338	100
CFPU	Aquatic invertebrates	15.1	Acute (EC50)	0.00583		2590	100

Appendix 1 – list of endpoints

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg/L)	PEC_{twa}[2]	TER	Annex VI Trigger[1]
CFPU	Algae	7.4	Chronic (EC50)	0.00583		1269	10
'Nomolt'	Fish	15.1	Acute (LC50)	0.02223		679	100
'Nomolt'	Aquatic invertebrates	0.00033	Acute (EC50)	0.02223		**0.015**	100
'Nomolt'	Algae[3]	>133	Chronic (EC50)	0.02223		>5983	10

[1]PEC_{sed} has been used as the sediment dwelling organism study was a spiked sediment toxicity test. The units are mg/kg.
[2]Initial PECs were used in the chronic assessments at this stage, so the PEC_{twa} values are not listed.

FOCUS Step 2

Apples, 3 applications of 0.12 kg a.s./ha

Test substance	N/S[1]	Organism[2]	Toxicity end point (mg/L)	Time scale	PEC (mg/L)	TER	Annex VI Trigger[4]
teflubenzuron	N+S	Fish	0.0186	Chronic LC50	0.00475	**3.916**	10
teflubenzuron	N+S	Aquatic invertebrates	0.0028	Acute EC50	0.00475	**0.589**	100
teflubenzuron	N+S	Aquatic invertebrates	0.000062	Chronic NOEC	0.00475	**0.013**	10
teflubenzuron	N+S	Algae	> 0.02	Chronic EC50	0.00475	**>4.211**	10
teflubenzuron	S	Sediment-dwelling organisms[2]	0.05	Chronic (NOEC)	0.1595	**0.313**	10
'Nomolt'	N+S	Aquatic invertebrates	0.00033	Acute (EC50)	0.00475	**0.069**	100

[1] The PEC_{SW} is the same for Northern of Southern Europe. The PEC_{SED} is higher for Southern Europe, so has been chosen.
[2] The sediment dwelling organism study was a spiked sediment test, so the PEC_{SED} has been used in this case. The units are mg/kg.

Appendix 1 – list of endpoints

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Apples, 3 applications of 0.12 kg a.s./ha (worst case PEC from single or multiple applications)

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	PEC[1,2] (mg/L)	TER	Annex VI trigger[5]
teflubenzuron	D3[3]	Ditch	Fish	Chronic	0.0186	0.004261	4.37	10
teflubenzuron	D4[4]	Pond	Fish	Chronic	0.0186	0.000224	83.04	10
teflubenzuron	D4[3]	Stream	Fish	Chronic	0.0186	0.004277	4.35	10
teflubenzuron	D5[4]	Pond	Fish	Chronic	0.0186	0.000222	83.78	10
teflubenzuron	D5[3]	Stream	Fish	Chronic	0.0186	0.004616	4.03	10
teflubenzuron	R1[4]	Pond	Fish	Chronic	0.0186	0.000209	89.00	10
teflubenzuron	R1[3]	Stream	Fish	Chronic	0.0186	0.003269	5.69	10
teflubenzuron	R2[3]	Stream	Fish	Chronic	0.0186	0.004386	4.24	10
teflubenzuron	R3[3]	Stream	Fish	Chronic	0.0186	0.004613	4.03	10
teflubenzuron	R4[4]	Stream	Fish	Chronic	0.0186	0.003268	5.69	10
teflubenzuron	D3[3]	Ditch	Aquatic invertebrates	Acute	0.0028	0.004261	0.66	100
teflubenzuron	D4[4]	Pond	Aquatic invertebrates	Acute	0.0028	0.000224	12.50	100
teflubenzuron	D4[3]	Stream	Aquatic invertebrates	Acute	0.0028	0.004277	0.65	100
teflubenzuron	D5[4]	Pond	Aquatic invertebrates	Acute	0.0028	0.000222	12.61	100
teflubenzuron	D5[3]	Stream	Aquatic invertebrates	Acute	0.0028	0.004616	0.61	100
teflubenzuron	R1[4]	Pond	Aquatic invertebrates	Acute	0.0028	0.000209	13.40	100
teflubenzuron	R1[3]	Stream	Aquatic invertebrates	Acute	0.0028	0.003269	0.86	100
teflubenzuron	R2[3]	Stream	Aquatic invertebrates	Acute	0.0028	0.004386	0.64	100
teflubenzuron	R3[3]	Stream	Aquatic invertebrates	Acute	0.0028	0.004613	0.61	100
teflubenzuron	R4[4]	Stream	Aquatic invertebrates	Acute	0.0028	0.00233	1.20	100
teflubenzuron	D3[3]	Ditch	Aquatic invertebrates	Chronic	0.000062	0.004261	0.01	10
teflubenzuron	D4[4]	Pond	Aquatic invertebrates	Chronic	0.000062	0.000224	0.28	10
teflubenzuron	D4[3]	Stream	Aquatic invertebrates	Chronic	0.000062	0.004277	0.01	10
teflubenzuron	D5[4]	Pond	Aquatic invertebrates	Chronic	0.000062	0.000222	0.28	10
teflubenzuron	D5[3]	Stream	Aquatic	Chronic	0.000062	0.004616	0.01	10

Appendix 1 – list of endpoints

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	PEC[1,2] (mg/L)	TER	Annex VI trigger[5]
			invertebrates					
teflubenzuron	R1[4]	Pond	Aquatic invertebrates	Chronic	0.000062	0.000209	0.30	10
teflubenzuron	R1[3]	Stream	Aquatic invertebrates	Chronic	0.000062	0.003269	0.02	10
teflubenzuron	R2[3]	Stream	Aquatic invertebrates	Chronic	0.000062	0.004386	0.01	10
teflubenzuron	R3[3]	Stream	Aquatic invertebrates	Chronic	0.000062	0.004613	0.01	10
teflubenzuron	R4[4]	Stream	Aquatic invertebrates	Chronic	0.000062	0.00233	0.03	10
teflubenzuron	D3[3]	Ditch	Algae	Chronic	>0.02	0.004261	>4.69	10
teflubenzuron	D4[4]	Pond	Algae	Chronic	> 0.02	0.000224	>89.29	10
teflubenzuron	D4[3]	Stream	Algae	Chronic	>0.02	0.004277	>4.68	10
teflubenzuron	D5[4]	Pond	Algae	Chronic	> 0.02	0.000222	>90.09	10
teflubenzuron	D5[3]	Stream	Algae	Chronic	>0.02	0.004616	>4.33	10
teflubenzuron	R1[4]	Pond	Algae	Chronic	> 0.02	0.000209	>95.69	10
teflubenzuron	R1[3]	Stream	Algae	Chronic	>0.02	0.003269	>6.12	10
teflubenzuron	R2[3]	Stream	Algae	Chronic	>0.02	0.004386	>4.56	10
teflubenzuron	R3[3]	Stream	Algae	Chronic	> 0.02	0.004613	>4.34	10
teflubenzuron	R4[4]	Stream	Algae	Chronic	> 0.02	0.00233	>8.58	10
teflubenzuron	D3[3]	Ditch	Sediment dwellers[5]	Chronic	0.05	0.01745	2.87	10
teflubenzuron	D4[4]	Pond	Sediment dwellers[5]	Chronic	0.05	0.004994	10.01	10
teflubenzuron	D4[3]	Stream	Sediment dwellers[5]	Chronic	0.05	0.007335	6.82	10
teflubenzuron	D5[4]	Pond	Sediment dwellers[5]	Chronic	0.05	0.004619	10.82	10
teflubenzuron	D5[3]	Stream	Sediment dwellers	Chronic	0.05	0.008699	5.75	10
teflubenzuron	R1[4]	Pond	Sediment dwellers[5]	Chronic	0.05	0.00479	10.44	10
teflubenzuron	R1[3]	Stream	Sediment dwellers[5]	Chronic	0.05	0.005343	9.36	10
teflubenzuron	R2[3]	Stream	Sediment dwellers[5]	Chronic	0.05	0.00472	10.59	10
teflubenzuron	R3[3]	Stream	Sediment dwellers[5]	Chronic	0.05	0.016336	3.06	10
teflubenzuron	R4[4]	Stream	Sediment dwellers[5]	Chronic	0.05	0.005210	9.60	10

[1]PEC_{sw} (mg/l) used except for sediment dwelling organisms where the PEC_{sed} is used (the units are mg/kg). Maximum values have been used

Appendix 1 – list of endpoints

[2]The maximum PEC_{sw} from the worst case of single or multiple applications has been used
[3]Single application
[4]Multiple applications
[5] PEC_{SED} used for sediment dwelling organisms

FOCUS Step 4

Apples, 3 applications of 0.12 kg a.s./ha (worst case PEC from single or multiple applications)

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point[3] (mg/L)	Buffer zone distance[4]	PEC[5] (mg/L)	TER	Annex VI trigger[6]
D3	Ditch	Fish	Chronic	0.0186	16 m	0.000576	32.29	10
D4	Pond	Fish	Chronic	0.0186	16 m	0.000082	226.83	10
D4	Stream	Fish	Chronic	0.0186	16 m	0.000671	27.72	10
D5	Pond	Fish	Chronic	0.0186	16 m	0.000082	226.83	10
D5	Stream	Fish	Chronic	0.0186	16 m	0.000724	25.69	10
R1	Pond	Fish	Chronic	0.0186	16 m	0.000074	251.35	10
R1	Stream	Fish	Chronic	0.0186	16 m	0.000513	36.26	10
R2	Stream	Fish	Chronic	0.0186	16 m	0.000688	27.03	10
R3	Stream	Fish	Chronic	0.0186	16 m	0.000724	25.69	10
R4	Stream	Fish	Chronic	0.0186	16 m	0.000513	36.26	10
D3	Ditch	Sediment dwellers[7]	Chronic	0.05	16 m	0.001569	31.87	10
D4	Pond	Sediment dwellers[7]	Chronic	0.05	16 m	0.00175	28.57	10
D4	Stream	Sediment dwellers[7]	Chronic	0.05	16 m	0.000268	186.57	10
D5	Pond	Sediment dwellers[7]	Chronic	0.05	16 m	0.001577	31.71	10
D5	Stream	Sediment dwellers[7]	Chronic	0.05	16 m	0.000404	123.76	10
R1	Pond	Sediment dwellers[7]	Chronic	0.05	16 m	0.001638	30.53	10
R1	Stream	Sediment dwellers[7]	Chronic	0.05	16 m	0.000207	241.55	10
R2	Stream	Sediment dwellers[7]	Chronic	0.05	16 m	0.000461	108.46	10
R3	Stream	Sediment dwellers[7]	Chronic	0.05	16 m	0.00179	27.93	10
R4	Stream	Sediment dwellers[7]	Chronic	0.05	16 m	0.000577	86.66	10
D3	Ditch	Aquatic invertebrates (mesocosm end point)	Acute & chronic	0.000005	100m	0.000025	**0.20**	AF = 2
D4	Pond	Aquatic invertebrates	Acute &	0.000005	100m	0.000006	**0.83**	AF = 2

Appendix 1 – list of endpoints

Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point[3] (mg/L)	Buffer zone distance[4]	PEC[5] (mg/L)	TER	Annex VI trigger[6]
			chronic					
D4	Stream	Aquatic invertebrates	Acute & chronic	0.000005	100m	0.000027	**0.19**	AF = 2
D5	Pond	Aquatic invertebrates	Acute & chronic	0.000005	100m	0.000006	**0.83**	AF = 2
D5	Stream	Aquatic invertebrates	Acute & chronic	0.000005	100m	0.000029	**0.17**	AF = 2
R1	Pond	Aquatic invertebrates	Acute & chronic	0.000005	100m	0.000006	**0.83**	AF = 2
R1	Stream	Aquatic invertebrates	Acute & chronic	0.000005	100m	0.000021	**0.24**	AF = 2
R2	Stream	Aquatic invertebrates	Acute & chronic	0.000005	100m	0.000028	**0.18**	AF = 2
R3	Stream	Aquatic invertebrates	Acute & chronic	0.000005	100m	0.000029	**0.17**	AF = 2
R4	Stream	Aquatic invertebrates	Acute & chronic	0.000005	100m	0.000021	**0.24**	AF = 2
D3	Ditch	Algae	Chronic	> 0.02	16 m	0.000576	>34.72	10
D4	Pond	Algae	Chronic	> 0.02	16 m	0.000082	>243.90	10
D4	Stream	Algae	Chronic	> 0.02	16 m	0.000671	>29.81	10
D5	Pond	Algae	Chronic	> 0.02	16 m	0.000082	>243.90	10
D5	Stream	Algae	Chronic	> 0.02	16 m	0.000724	>27.62	10
R1	Pond	Algae	Chronic	> 0.02	16 m	0.000074	>270.27	10
R1	Stream	Algae	Chronic	> 0.02	16 m	0.000513	>38.99	10
R2	Stream	Algae	Chronic	> 0.02	16 m	0.000688	>29.07	10
R3	Stream	Algae	Chronic	> 0.02	16 m	0.000724	>27.62	10
R4	Stream	Algae	Chronic	> 0.02	16 m	0.000513	>38.99	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] Mesocosm endpoint is used for risk to invertebrates
[4] Modelling data was provided with buffer zone of 100 m for the single application and 75 m for multiple applications, but since an acceptable TER for both single and multiple applications is required the buffer zone distance is stated as 100 m in this case.
[5] The maximum PEC_{sw} from the worst case of single or multiple applications has been used
[6] Annex VI Trigger value has been adjusted for aquatic invertebrates because a mesocosm endpoint is used.

Appendix 1 – list of endpoints

[7] PEC_{SED} used for sediment dwelling organisms
[8]The mescocosm end point (NOEC) is to be used with an uncertainty factor (AF) of 2

Protected tomatoes is for up to 3 applications of 225 g a.s./ha

TERs for aquatic organisms assuming 0.1% loss from total in glasshouse (into a standard 30 cm deep ditch from 675 g applied in a water volume of 30000l)

Test substance	Organism	Toxicity end point (mg/l)	Time scale	PEC	TER	Annex VI Trigger [1]
teflubenzuron	Fish	0.0065	Acute	0.0225	**0.29**	100
teflubenzuron	Fish	0.0186	Chronic	0.0225	**0.83**	10
teflubenzuron	Aquatic invertebrates	0.0028	Acute	0.0225	**0.12**	100
teflubenzuron	Aquatic invertebrates	0.000062	Chronic	0.0225	**0.0028**	10
teflubenzuron	Algae	0.02	Chronic	0.0225	**0.89**	10
teflubenzuron	Sediment-dwelling organisms	0.05	Chronic	0.0225	**2.22**	10
Teflubenzuron/Nomolt	Aquatic invertebrates	0.000005	Acute + chronic	0.0225	**0.0002**	UF= 2[1]
'Nomolt'	Fish	15.1	Acute	0.0225	671.11	100
'Nomolt'	Aquatic invertebrates	0.00033	Acute	0.0225	**0.01**	100
'Nomolt'	Algae	133	Acute	0.0225	5911.11	10

[1]The mescocosm end point (NOEC) is to be used with an uncertainty factor (UF) of 2

The regulatory acceptable concentration for the most sensitive aquatic organism is 0.0000025 mg a.s./L. To achieve this concentration from glasshouse use total loss would need to be as low as 0.00001%. To achieve this level of loss glasshouses would need to operate with zero omissions of teflubenzuron. Member States would need to consider this in relation to glasshouse practices in their country.

Appendix 1 – list of endpoints

Bioconcentration		
	Active substance and metabolites	Active substance only
$logP_{O/W}$		5
Bioconcentration factor (BCF)	640	300
Annex VI Trigger for the bioconcentration factor	100	100
Clearance time (days) (CT_{50}) [12]	ct_{50}-α: 0.8 d ct_{50}-β: 9 d	
(CT_{90})	< 14 d	
Level and nature of residues (%) in organisms after the 14 day depuration phase	97% eliminated	

[1]Based on total ^{14}C
[2]The elimination of ^{14}C-residues was biphasic with a rapid reduction within days 0-3 of depuration period (>90% of the ^{14}C-residue were eliminated) and a longer phase elimination after 3 days

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

Test substance	Acute oral toxicity (LD_{50} µg a.s./bee)	Acute contact toxicity (LD_{50} µg a.s./bee)
teflubenzuron	72	100
'Nomolt'	110	100
Field or semi-field tests		
Bee Brood test Egg laying was reduced for about one week after application. Development of the larvae was reduced, as a consequence fewer pupae were built. However, development success of eggs and young larvae was also limited in the controls. Field test The application of 'Nomolt 150 g/l SC' at a rate of 120 g a.s./ha did not result in lasting effects on the honey bee colonies (*Apis mellifera* L.) when applied on a field with flowering *Phacelia*.		

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

Apples, 3 applications of 0.12 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
teflubenzuron	Contact	1.2	50
teflubenzuron	Oral	1.67	50
'Nomolt'	Contact	1.2	50
'Nomolt'	Oral	1.09	50

Appendix 1 – list of endpoints

It is important to note that teflubenzuron is an insect growth regulator and Escort 2 states in reference to such products that 'The HQ trigger values discussed above cannot be used to evaluate the data for special products since such products were not included in the validation exercise.'

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g a.s./ha)
Typhlodromus pyri	'Nomolt'	Mortality	100 % mortality at tested rate (180), so could not be calculated
Aphidius rhopalosiphi	'Nomolt'	Mortality	>180

Apples, 3 applications of 0.12 kg a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
'Nomolt'	*Typhlodromus pyri*	100 % mortality at tested rate, so could not be calculated	Could not be calculated but > 2	Could not be calculated	2
'Nomolt'	*Aphidius rhopalosiphi*	> 180	1.533	0.169	2

[1] MAF of 2.3 used, 3 applications with the default half life
[2] drift rate calculated at 3 m for an orchard application.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ha)[1]	End point	% effect[2]	Trigger value
Typhlodromus pyri	protonymph (max 24 h old)	'Nomolt' Detached apple leaves 14 days	6.775 17.01 42.69 107.1 268.9 675.0	LR_{50}	89.61	50 %
				Mortality	60.4% at 107.1	
				Fecundity	-34.1% at 42.69	
Typhlodromus pyri	freshly hatched	'Nomolt' *Phaseolus vulgaris* leaves 18 days	52.5	LR_{50}	> 52.5	50 %
				Mortality	-2%	
				Fecundity	-8%	
Drino inconspicua	10-11 days old	'Nomolt' Glass plate 28 days	22.5	LR_{50}	> 22.5	50 %
				Mortality	-7.9%	
				Parasitism	+16.3%	

Appendix 1 – list of endpoints

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ha)[1]	End point	% effect[2]	Trigger value
Chrysoperla carnea	larvae	'Nomolt' Detached apple leaves	0.065 0.175 0.437 1.277 3.447	LR_{50}	0.73	50 %
				Mortality	33.3% at 0.437 90% at 1.277	
				Fecundity	No effect up to 0.437	
Orius laevigatus	4 day old nymphs	'Nomolt' Detached apple leaves 18 days	1.95 5.47 15.31 42.85 120.0	LR_{50}	15.72	50 %
				Mortality	73.4% at 42.9	
				Fecundity	-62.3% at 5.47	
Chrysoperla carnea	2-3 day old larvae	'Nomolt' Detached apple leaves Aged residues – 7 day intervals after application	36.8 83.3 151.9 360	Mortality Day 0 Day 7-21 Day 63 Day 70 – 98 Fecundity Day 63 Day 70	 94-100% 88.6 – 100% 47.8% at 36.8 g a.s./ha 62 – 63% at 36.8 g a.s./ha Reduction at lowest rate. lowest rate similar to control	50 %

[1] initial residues unless specified
[2] For mortality positive percentages relate to adverse effects, for fecundity negative figures refer to reduction in fecundity (i.e. effects)

Field or semi-field tests
Summary data was submitted from a range of field studies, but this was not used in the risk assessment.

Appendix 1 – list of endpoints

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

Test organism	Test substance	Time scale	End point[1]
Earthworms			
Eisenia foetida	teflubenzuron	Acute 14 days	LC_{50} >1000 mg a.s./kg dw soil (>750 kg a.s/ha) $LC_{50\ CORR}$ >500 mg a.s./kg dw soil
Eisenia foetida	'Nomolt'	Acute 14 days	LC_{50} >1000 mg a.s./kg dw soil (>750 kg a.s/ha) $LC_{50\ CORR}$ >500 mg a.s./kg dw soil
Eisenia andrei	Mixture of metabolites (62.5% CFPU and 37.5% CFA)	Chronic	NOEC = 8.0 mg test item/kg dw soil (6000 g /ha)
Other soil macro-organisms			
No data were submitted			
Soil micro-organisms			
Nitrification	teflubenzuron	28 days	initial retardation at 2 mg a.s./kg soil no adverse effect up to 2 mg a.s./kg soil by day 56
Carbon mineralisation	teflubenzuron	28 days	no adverse effect up to 2 mg a.s./kg soil
Field studies			
Not required			

[1] corrected endpoint used in risk assessment due to log Pow >2.0 (LC_{50corr})

Appendix 1 – list of endpoints

Toxicity/exposure ratios for soil organisms

Apples, 3 applications of 0.12 kg a.s./ha

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Earthworms					
Eisenia foetida	teflubenzuron	Acute	0.089	5618	10
Eisenia foetida	'Nomolt'	Acute	0.089	5618	10
Eisenia andrei	CFPU[3]	Chronic	0.01	508	5
Eisenia andrei	CFA[3]	Chronic	0.006	500	5
Other soil macro-organisms					
Not required					

[1]mg a.s./kg dw soil
[2]PEC assumptions: Total load approach, 1 application of 360 g a.s/ha (section B.8.3)
[3]Assuming all the toxicity of the mixture came from that metabolite

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

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g a.s./ha) vegetative vigour	ER_{50} (g a.a./ha) emergence	Exposure[1] (g/ha)[2]	TER	Trigger
Allium cepa, *Avena sativ* , *Brassica napus*, *Cucumis sativus*, *Glycine max*, *Lycopersicon lycopersicum*	'Nomolt'	> 120	> 120	18.875	> 6.36	5
Allium cepa, *Avena sativ* , *Brassica napus*, *Cucumis sativus*, *Glycine max*, *Lycopersicon lycopersicum*	'Nomolt'	> 120		18.875	> 6.36	5

[1] Exposure has been estimated based on Ganzelmeier drift data

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

No data were submitted

Appendix 1 – list of endpoints

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

Test type/organism	end point
Activated sludge	EC_{50} (3 h) > 1000 mg a.s./l

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

Compartment	
soil	teflubenzuron, 3,5-dichloro-2,4-difluoroaniline (CFA), 3, 5-dichloro-2, 4-difluorophenylurea (CFPU)
water	teflubenzuron, 3,5-dichloro-2,4-difluoroaniline (CFA), 3, 5-dichloro-2, 4-difluorophenylurea (CFPU), 2,6-difluorobenzoic acid, Unknown 5
sediment	None
groundwater	None

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

	RMS/peer review proposal
Active substance	R50/R53

	RMS/peer review proposal
Preparation	R50/R53

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

(only entries marked yellow will be kept in final conclusion)

ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AR	applied radioactivity
ARfD	acute reference dose
a.s.	active substance
bw	body weight
°C	degree Celsius (centigrade)
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
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_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
G	glasshouse
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
H	Henry's Law constant (calculated as a unitless value) (see also K)
ha	hectare

Appendix 2 – abbreviations used in the list of endpoints

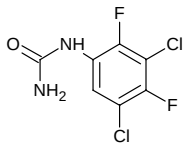
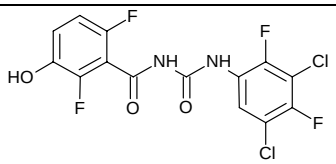
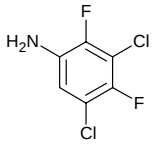
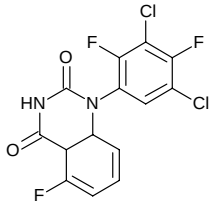
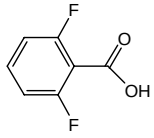
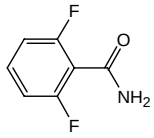
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
kg	kilogram
L	litre
LC	liquid chromatography
LC-MS	liquid 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)
m	metre
µg	microgram
mg	milligram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})

Appendix 2 – abbreviations used in the list of endpoints

ppp	plant protection product
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
SC	suspension concentrate
STMR	supervised trials median residue
TCD	thermal conductivity detector
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
wk	week
yr	year

Appendix 3 – used compound code(s)

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
CL 902374 E15 CFPU	3,5-dichloro-2,4-difluorophenylurea 1-(3,5-dichloro-2,4-difluorophenyl)urea	
3381	1-(3,5-dichloro-2,4-difluorophenyl)-3-(2,6-difluoro-3-hydroxybenzoyl)urea	
CL 902373 CFA	3,5-dichloro-2,4-difluoroaniline	
N-(2,4-difluoro-3,5-dichlorobenzene)-5-fluoro[3*H*]-dihydroquinazoline-2,4-dione	1-(3,5-dichloro-2,4-difluorophenyl)-5-fluoro-4a,8a-dihydroquinazoline-2,4(1*H*,3*H*)-dione	
2,6-diflurobenzoic acid	2,6-diflurobenzoic acid	
difluorobenzamide	2,6-difluorobenzamide	
5-chloro-2,4-difluoroaniline	5-chloro-2,4-difluoroaniline