European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance diflubenzuron[1]

(Question No EFSA-Q-2009-00240)

Issued on 16 July 2009

SUMMARY

Diflubenzuron is one of the 79 substances of the third stage part A of the review programme covered by Commission Regulation (EC) No 1490/2002[2].

Diflubenzuron was included in Annex I to Directive 91/414/EEC on 1 July 2008 pursuant to Article 11b of the Regulation (EC) No 1490/2002 (hereinafter referred to as 'the Regulation'). In accordance with Article 12a of the Regulation the European Food Safety Authority (EFSA) is required to deliver by 31 December 2010 its view on the draft review report submitted by the Commission of the European Communities (hereinafter referred to as 'the Commission') in accordance with Article 12(1) of the Regulation. This review report has been established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

Sweden being the designated rapporteur Member State submitted the DAR on diflubenzuron in accordance with the provisions of Article 10(1) of the Regulation, which was received by the EFSA on 16 November 2005. The peer review was initiated on 14 December 2005 by dispatching the DAR for consultation of the Member States and the sole notifier Chemtura Netherlands B.V. 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 the EFSA to identify the remaining issues which were agreed during a written procedure in July-August 2007. The identified issues as well as further information made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in January 2009.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in March 2009.

This conclusion was reached on the basis of the evaluation of the representative uses as an insecticide on apples, pears and mushrooms and in forestry. Full details of the GAP can be found in the list of end points attached in Appendix A.

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[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance diflubenzuron. *EFSA Scientific Report* (2009) 332, 1-111

[2] OJ L224, 21.08.2002, p.25, as amended by Regulation (EC) No 1095/2007 (OJ L246, 21.9.2007, p.19).

The representative formulated product for the evaluation was 'Dimilin WG 80', a water dispersible granule (WG).

Residues in apples and pears can be analysed by a HPLC method. The method for mushrooms is not validated for the residue definition. The LOQ for the surface water method is not low enough and a data gap has been identified.

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. However, data gaps have been identified for attrition, accelerated storage and shelf-life studies. The technical specification and batch data were not accepted and a data gap has been identified.

There is a lack of a peer reviewed specification and assessment of the equivalence of the batches tested in all the mammalian toxicity studies compared to the representative formulation. In mammals, diflubenzuron is not acutely toxic via oral, dermal or inhalation routes; it is not a skin or eye irritant nor a skin sensitizer. Diflubenzuron showed a consistent profile of toxicity after repeated oral administration to mice, dogs and rats, with the dog being the most sensitive species. The primary target of toxicity was erythrocytes, with secondary effects apparent in the spleen and in the liver (consistent with haemolytic anaemia). The relevant oral No Observed Adverse Effect Level (NOAEL) is 10 mg/kg bw/ day (1-year dog study). Diflubenzuron did not show any genotoxic potential. No evidence of carcinogenic potential was found in rats and mice. The relevant NOAEL from the long term toxicity and carcinogenicity studies is 6.4 mg/kg bw/day (mice study). No specific effect on the reproductive parameters was found in multigeneration studies with rats: the relevant parental NOAEL is lower than the LOAEL of 30 mg/kg bw/day, whereas the relevant reproductive and offspring NOAEL was 3200 mg/kg bw/day. Tested in developmental toxicity studies, diflubenzuron did not cause malformations in the rat or rabbit. The relevant maternal and developmental NOAEL is 1000 mg/kg bw/day (highest dose level tested, rat and rabbits). The Acceptable Daily Intake (ADI) of 0.1 mg/kg bw/day was derived from the 1 year dog study supported by the 91-week mouse study applying a SF of 100. The Acute Reference Dose (ARfD) is not allocated as it is not necessary. The Acceptable Operator Exposure Level (AOEL) of 0.033 mg/kg bw/day is based on the 1-year dog study with a correction for oral absorption of 33% and a SF of 100. The operator exposure is below the AOEL for the use on pome fruit, mushrooms (automatic sprayer) and in forestry (ground application) without the use of Personal Protective Equipment (PPE). Operator exposure is below the AOEL for hand-held application on mushrooms with the use of PPE. The operator exposure in forestry by aircraft application is inconclusive. The worker and bystander exposure was estimated to be below the AOEL for all scenarios considered.

Metabolism of diflubenzuron was investigated in apples and oranges after foliar application and in mushrooms after soil treatment. Whereas diflubenzuron only metabolised to a very small extent in fruits, metabolism in mushrooms was shown to be extensive. DFBA (2,6-difluorobenzoic acid) was the main component of radioactive residues, besides low concentrations of diflubenzuron, PCA (4-chloroaniline) and CPU (4-chlorophenylurea). Therefore, different residue definitions for fruits and mushrooms were proposed. As the toxicological evaluation of the metabolites has not yet been finalised, it was decided to include all metabolites in a provisional residue definition for risk assessment for mushrooms.

A sufficient number of residue trials on apples supporting the notified GAPs have been submitted to propose MRLs for apples and pears. The available residue trials on mushrooms have not been carried out in accordance with the residue definition and no MRL was proposed

for mushrooms. A data gap concerning a complete new data set has been identified. Whereas studies on the frozen storage stability showed satisfactory results for diflubenzuron and CPU, results for PCA were regarded as not conclusive. The notifier was asked to further investigate the storage stability of PCA. A data gap was identified concerning a hydrolysis study simulating pasteurisation to investigate the effect of processing on the nature of residues. Depending on the results of this study new processing studies on apples might be necessary. In the submitted studies, samples were only analysed for diflubenzuron.

Metabolism studies on dairy cattle and laying hens showed a low transfer of diflubenzuron residues into tissues, milk and eggs. Metabolism was extensive. Besides diflubenzuron, the following metabolites were identified: CPU, PCA and PCAA (4-chloroacetanilide). It was decided to include diflubenzuron and CPU in the risk assessment for monitoring in animal matrices, as they were regarded as suitable indicators for diflubenzuron residues. As the toxicological evaluation of the metabolites is not yet finalised, it was decided to include all metabolites identified in a provisional residue definition for risk assessment. In the absence of sufficient information on the effect of processing on the nature and level of residues, a provisional dietary burden calculation was carried out. It was decided that on the basis of this calculation either a feeding study on ruminants was necessary or a justification that no feeding study was necessary.

A provisional chronic dietary intake calculation showed that an exceedance of the ADI set by the toxicology meeting is not expected for intake of pome fruit and wild berries after applications of diflubenzuron according to the notified GAPs.

Diflubenzuron may be considered as low persistent in soil under dark aerobic conditions ($DT_{50\ norm}$ = 2.0 – 6.7 d). Upon degradation, it yields two major metabolites: DFBA (2,6-difluorobenzoic acid) and CPU (4-chlorophenylurea). DFBA exhibits low persistence in soil ($DT_{50\ 20\ °C}$ = 3.3 – 9.0 d) and CPU may be considered moderately persistent ($DT_{50\ 20\ °C}$ = 15.2 – 30.5 d). A flooded soil study under anaerobic conditions was presented by the notifier as a surrogate for the anaerobic degradation in soil. In this study degradation is slower than under aerobic conditions. No new metabolites were found in this study.

Photolysis does not contribute to the degradation of diflubenzuron in soil.

Batch adsorption / desorption studies indicate that diflubenzuron is immobile to slightly mobile (K_{Foc} = 1983 – 6918 mL/g) and CPU is medium mobile in soil (K_{Foc} = 209 – 291 mL/g). Due to the weak adsorption of DFBA, it was not possible to determine reliable adsorption parameters. During the peer review, it was agreed that simulations performed assuming a Koc = 0 could be used to finalize the EU exposure assessment.

Diflubenzuron is hydrolytically stable at pH 5 and 7 and hydrolyses to CPU and DFBA at pH 9. Metabolites CPU and DFBA are stable under these conditions.

Due to the fact that biological degradation is faster than aqueous photolysis it is considered that photodegradation will not contribute to the dissipation of diflubenzuron in the environment. Diflubenzuron is considered not readily biodegradable.

Diflubenzuron exhibited low persistence in water / sediment systems (DT_{50} whole system = 3.7 – 5.4 d). The major metabolites formed were DFBA (max. in water 7.3-13.1 % AR; max. in sediment 3.7 % AR after 4 d) and CPU (max. in water 31.1 % AR after 8 d or 16 d; max. in sediment 15.9-21.0 % AR after 16 d or 30d). Half-lives of the metabolites DFBA (DT_{50} whole system = 1.6 – 4.4 d) and CPU (DT_{50} whole system = 26.9 – 52.5 d) were calculated in the available study.

PEC $_{SW/SED}$ were calculated based on the uses of 'Dimilin WG 80' on pome fruit and in forestry.

For forestry (aerial and hand application) the RMS provided calculations of PEC_{SW} for parent and metabolites based only on the spray drift route of entry to surface waters assuming a drift of 33.2 % for aerial application and of 8.02% for hand application (vines application at > 50 cm is assumed to have the same drift as a hand application). The meeting of experts agreed with the PEC_{SW} for aerial application in forestry calculated by the RMS and presented in the addendum (December 2008). It was noted that PEC_{SED} were not calculated. The meeting of experts agreed that EFSA will highlight in the conclusion that when addressing the risk for aquatic insects, exposure via sediment needs to be addressed.

In a late stage clarification on the GAP, the notifier indicated that a hand-held sprayer could also be used in orchards and a tractor-mounted sprayer could be used in forests. These application practices have not been evaluated for the environment and a data gap was identified by the meeting of experts for these $PEC_{SW/SED}$.

Potential contamination of groundwater by diflubenzuron and its soil metabolites has been assessed with FOCUS PELMO v. 3.3.2. The 80th percentile at 1m depth for each of the compounds was below 0.002 µg/L for all the nine scenarios simulated. A data gap is identified since at least two different models need to be used. However, in this case, it may be concluded that contamination of ground water will not occur when the product is used according the proposed representative uses. Member States may require a calculation with a second model for confirmatory purposes.

New FOCUS GW (FOCUS PELMO v. 3.3.2 and FOCUS PEARL v. 3.3.3) modelling using a Koc = 0 for metabolite DFBA was requested during the peer review. The meeting of experts accepted the results of this modelling exercise, which indicates that the ground water limit of 0.1 µg/L was respected for the nine scenarios assessed for the use in orchards. However, a data gap was identified for the inclusion of the report in the updated dossier to be submitted to the Member States and EFSA.

A data gap for the full exposure assessment in soil, surface water and ground water for the representative use in protected mushrooms was identified by the meeting of experts.

According to the available information, long range transport and deposition of diflubenzuron may be considered negligible.

Diflubenzuron was very toxic to aquatic organisms. The acute EC_{50} for daphnids is 0.0026 mg a.s./L and the reproductive NOEC is 0.04 µg a.s./L. A mesocosm study (littoral enclosure study) was submitted to refine the risk assessment. A regulatory end point of 0.14 µg diflubenzuron/L was derived from the study. The regulatory end point can be used only in the risk assessment for zooplankton since the end point does not cover sensitive species with longer life cycles and a data gap was identified to address the risk to amphipods and univoltine insect species. The Annex VI trigger values were far below the trigger of 1 for zooplankton for the use in orchards even with a 30 m no-spray buffer zone. The TER was 2 for the use in forestry with a no-spray buffer zone of 20 m (hand application). Overall it was concluded that a high risk to aquatic organisms was indicated for the representative uses in orchards and forestry. Uncertainty remained with regard to the risk to bees since increased mortality of adult bees was observed in one of the field studies. It was not possible to exclude that the outdoor uses pose a high risk to bees on the basis of the peer reviewed data. Risk mitigation measures such as restriction of the use to non-flowering crops or specific growth stages are required to protect honey bees. Juvenile non-target arthropods were very sensitive

to diflubenzuron. Very large in-field no-spray buffer zones would be needed to protect non-target arthropods (75 m for the use in orchards). No higher-tier studies (aged residues studies, semi-field or field studies) were submitted to refine the risk assessment. It was concluded that the risk to non-target arthropods is high and that it needs to be demonstrated that recovery/recolonisation is possible within one year.

A conclusion on the risk to aquatic organisms from the use in mushrooms can only be drawn after a reliable estimation of exposure of surface water will be made available. The risk to all other groups of non-target organisms was considered to be low.

The risk to birds and mammals, earthworms, other soil non-target macro-organisms, soil micro-organisms and biological methods of sewage treatment was assessed as low for the representative uses in orchards and forestry.

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

TABLE OF CONTENTS

BACKGROUND

Commission Regulation (EC) No 1490/2002[3] laying down the detailed rules for the implementation of the third stage of the work programme 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 Report (DAR) provided by the designated rapporteur Member State.

Diflubenzuron is one of the 79 substances of the third stage part A of the review programme covered by Commission Regulation (EC) No 1490/2002.

Diflubenzuron was included in Annex I to Directive 91/414/EEC on 1 July 2008 pursuant to Article 11b of the Regulation (EC) No 1490/2002 (hereinafter referred to as 'the Regulation'). In accordance with Article 12a of the Regulation the European Food Safety Authority (EFSA) is required to deliver by 31 December 2010 its view on the draft review report submitted by the Commission of the European Communities (hereinafter referred to as 'the Commission') in accordance with Article 12(1) of the Regulation. This review report has been established as a result of the initial evaluation provided by the designated rapporteur Member State in the DAR. The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

In accordance with the provisions of Article 10(1) of the Regulation, Sweden submitted the DAR on diflubenzuron, which was received by the EFSA on 16 November 2005. Following an administrative evaluation, the DAR was distributed for consultation in accordance with Article 11(2) of the Regulation on 14 December 2005 to the Member States and to the sole notifier Chemtura Netherlands B.V., as identified by the rapporteur Member State.

The comments received on the DAR were evaluated and addressed by the rapporteur Member State. Based on this evaluation, the EFSA identified and agreed with Member States during a written procedure in July-August 2007 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 January 2009. 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 March 2009.

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

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 A.

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:

[3] OJ L224, 21.08.2002, p.25, as amended by Regulation (EC) No 1095/2007 (OJ L246, 21.9.2007, p.19).

- the comments received,
- the resulting reporting table (revision 1-2; 20 December 2007),

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

- the reports of the scientific expert consultation,
- the evaluation table (revision 2-1; 5 May 2009).

Given the importance of the draft assessment report including its addendum (compiled version of March 2009 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

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

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Diflubenzuron is the ISO common name for 1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea (IUPAC).

Diflubenzuron, belongs to the class of chitin synthesis inhibitors. It is a non-systemic insect growth regulator with contact and stomach action.

The representative formulated product for the evaluation was 'Dimilin WG 80', a water dispersible granule (WG).

The evaluated representative uses are as an insecticide on apples, pears and mushroom and in forestry.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

At the moment no minimum purity of diflubenzuron as manufactured can be given, because further clarification is needed. In addition, clarification is necessary with respect to the proposed maximum content of the significant impurities. The technical material contains a relevant impurity 4-chloroaniline (PCA) The maximum content of this impurity must not exceed 0.03 g/kg. At the moment no FAO specification exists for this Technical Material (TC).

Beside 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 diflubenzuron or the respective formulation. However, the following data gaps were identified:

- Accelerated storage and shelf-life studies with analysis of the relevant impurity.
- Attrition resistance in accordance with CIPAC MT 178.2
- A specification with supporting batch analysis and validated methods of analysis.
- Demonstration of the applicability of the existing CIPAC methods with chromatograms.

It should be noted that batch analysis data were submitted and are evaluated in the addendum to Vol. 4 dated December 2008. 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, these new studies could not be considered in the peer review.

It was noted during the evaluation process that the formulation has a tendency to produce persistent foam. This might be mitigated by label phrases at national level.

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of

diflubenzuron in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

The applicability of a multi-residue method is not concluded on. However, it should be noted that a study was submitted and is evaluated in the addendum to Vol.3, B5 dated December 2008 but it was not considered during the peer review process in accordance with Regulation 1095/2007. A method of analysis is available for watery matrices analysing for diflubenzuron. The method is HPLC-UV with MS confirmation and the LOQ is 0.1 mg/kg. There is no method available for the use on mushrooms where the residue definition is 2,6-difluorobenzoic acid (DFBA).

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

For environmental matrices a method is available for soil analysing for diflubenzuron, 4-chlorophenylurea (CPU) and 2,6-difluorobenzoic acid (DFBA). The method is LC-MS/MS with a LOQ of 0.005 mg/kg for diflubenzuron and 0.01 mg/kg for the metabolites. For water the method analyses for diflubenzuron, 4-chlorophenylurea (CPU) and 2,6-difluorobenzoic acid (DFBA). The method is LC-MS/MS with a LOQ of 0.1 µg/L. However, the method is not acceptable for surface water as a lower LOQ is required and a data gap has been identified. For air the method in the DAR was found not to be acceptable and this is also identified as a data gap. However, it is noted that an air method has already been supplied and is evaluated in the December 2008 addendum to Vol.3, B5 but it was not considered during the peer review process in accordance with Regulation 1095/2007.

A method of analysis for body fluids and tissues is not required as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

Diflubenzuron was discussed during the PRAPeR experts' meeting (PRAPeR 64) on mammalian toxicology in January 2009 on the basis of the DAR (May 2005), the revised DAR (December 2008) and the Addendum (December 2008). After the experts' meeting an Addendum 2 to the DAR (February 2009) was submitted by the RMS but not peer reviewed.

During the meeting the point was raised concerning the comparison of the current specification and the batches tested in the mammalian toxicity data package. An analysis of toxicological batches was not available and therefore a data gap was identified. Based on the available information, the impurity PCA was considered by the meeting as toxicologically relevant based on its carcinogenic properties (Carcinogen Cat 2; R 45, May cause cancer[4]). In

[4] Classification and labelling according to Directive 67/548/EEC (Annex I, Adaptation to the Technical Progress 24).

addition, toxicological information regarding the relevance of the impurity PCA submitted by the notifier was presented during the meeting but not evaluated by the RMS and a new open point for the RMS was identified in order to assess this.

EFSA note after the PRAPeR 64: In the Addendum 2 to the DAR (February 2009) the RMS confirmed that PCA has to be considered as an impurity of toxicological relevance since PCA has to be regarded as carcinogenic.

2.1. Absorption, distribution, excretion and metabolism (toxicokinetics)

The oral absorption of diflubenzuron is low, approximately 33% based on urinary excretion. It is uniformly distributed and shows no potential for bioaccumulation. The excretion is almost complete in 24 hours and takes place via bile and urine. The main pathway of metabolism is dechlorination, glucuronidation, sulphation and hydrolysis.

2.2. Acute toxicity

Diflubenzuron is not acutely toxic to rats via oral, dermal (LD_{50} higher than 4640 mg/kg bw and 2000 mg/kg bw, respectively) or inhalation (LC_{50} >2.5 mg/l of air - nose only/4h) routes; it is not a skin or eye irritant nor a skin sensitizer in the Guinea Pig Maximization Test (Magnusson &Kligman).

2.3. Short-term toxicity

Short-term toxicity has been studied with acceptable quality in four dietary studies in rats, two dietary studies in mice, two oral studies (by capsule) in dogs, two dermal and two inhalation studies in rats and rabbits. Diflubenzuron showed a consistent profile of toxicity after repeated oral administration to mice, dogs and rats being the dog the most sensitive species. The primary target of toxicity was erythrocytes, with secondary effects in the spleen and in the liver (consistent with haemolytic anaemia). The early effect was an increased concentration of methaemoglobin. The meeting concluded that methaemoglobinemia is a toxicologically relevant finding when considering the overall picture of haematological effects. The experts agreed that the relevant oral NOAEL is 10 mg/kg bw/day (instead of 2 mg/kg bw/day as initially proposed by the RMS) from the 1-year dog study based on haemotoxicity (liver pigmentation, liver and spleen weight changes and methaemoglobinemia) at 50 mg/kg bw/day. In addition it was agreed by the majority of the experts to not propose the classification as R48/22 (Harmful: danger of serious damage to health by prolonged exposure if swallowed) based on haemolytic anaemia.
The relevant dermal NOAEL is 322 mg/kg bw/day (highest dose level tested, 3-week rabbit study) and the relevant inhalation NOAEL is 0.1mg/L (highest dose level tested, 4-week rat study).

2.4. Genotoxicity

In a set of adequately conducted *in vitro* and *in vivo* genotoxicity assays diflubenzuron did not show any genotoxic potential.

2.5. Long-term toxicity and carcinogenicity

The long-term toxicity and carcinogenicity of diflubenzuron have been studied with acceptable quality in rats (2 years) and mice (91-weeks). Diflubenzuron showed the same toxicological profile after short-term and long-term exposure being the erythrocytes the primary target of toxicity (see section 2.3). No evidence of carcinogenic potential was found in rats and mice. The experts agreed that the relevant NOAELs from the long-term toxicity and carcinogenicity studies are 31 mg/kg bw/day and 6.4 mg/kg bw/day for rats and mice respectively.

It is noted that the composition of the batch tested for carcinogenic studies is unknown with regard to the presence of PCA.

2.6. Reproductive and developmental toxicity

In a two generation study in rats, diflubenzuron did not affect reproductive parameters; the relevant reproductive and offspring NOAEL is 3200 mg/kg bw/day (highest dose tested), whereas the relevant parental NOAEL is not identified since haematological effects (increased methaemoglobin formation, increased spleen and liver weights together with histopathological findings) were observed at the lowest dose level tested (30 mg/kg bw/day). Tested in acceptable developmental toxicity studies, diflubenzuron did not cause malformations in the rat or rabbit up to a dose level of 1000 mg/kg bw/day (highest dose level tested), representing the relevant maternal and developmental NOAEL.

2.7. Neurotoxicity

No signs on neurotoxicity occurred in the experimental tests. No data on delayed neurotoxicity are available but they are not required since diflubenzuron does not consist of chemical groups common to organophosphates.

2.8. Further studies

During the experts' meeting the toxicological relevance of metabolites 4-chloroaniline (PCA), 2,6-difluorobenzoic acid (DFBA), 2,6-difluorobenzamide (DFBAM) and 4-chlorophenylurea (CPU) was discussed. The meeting concluded that DFBA is expected to have the same toxicological profile as diflubenzuron since it occurs in the rat metabolism in high amounts and the same reference values of diflubenzuron could be used. With regard to CPU and DFBAM it was not possible to conclude on their toxicological relevance due to the lack of relevant data: for both metabolites a data gap was set for the notifier to address their toxicological relevance. (With regard to CPU and DFBAM, information was provided after the meeting but not considered during the peer review in accordance with regulation 1095/2007).

PCA was considered of toxicological relevance because of its carcinogenic properties; however, the setting of specific reference values was not possible, therefore, a data gap was set for the derivation of reference values.

After the meeting, the residue experts raised a further issue related to the metabolite 4-chloroacetanilide PCAA with regard to its possible relevance to consumers. No data are available to evaluate its toxicological relevance so a data gap was set.

EFSA note after the written procedure: the RMS informed EFSA that under the biocide application[5], diflubenzuron was discussed at the Biocide Technical Meeting held in Arona, March 2009 [6] According to the RMS, the database available was different from the one discussed in the PRAPeR 64. Based on that dataset, the RMS was of the opinion that it could not be excluded that PCA is formed in humans exposed to diflubenzuron, as PCA was found in animal species other than rodents, making the current absence of carcinogenic properties of diflubenzuron (based on rodent studies) uncertain with regard to human exposure. This was also briefly reported in the addendum 2 to the DAR submitted after the meeting. Should this information be confirmed, the clarification of the metabolism of diflubenzuron in humans should be further addressed.

2.9. Medical data

Reports indicating evidence of adverse effects to workers of manufacturing plants, agricultural workers and consumers have not been published. No cases of human intoxication by diflubenzuron have been reported.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

ADI

Initially the RMS proposed to use the NOAEL of 2 mg/kg bw/day from the 1 year dog study using a SF of 100 (DAR, May 2005). In the revised DAR (December 2008) and the addendum (December 2008) an ADI of 0.012 mg/kg bw/day was proposed (based on NOAEL of 1.2 mg/kg bw/day, 91-week mouse, SF 100,). During the meeting the relevant NOAEL to set the ADI was discussed. It was raised that in the DAR two long term toxicity studies in rats were available. The first study (1984) showed an NOAEL of 31.2 mg/kg bw/day based on haematological changes. The second long-term rat study (1976) was used by JMPR (2001) for setting the ADI of 0.02 mg/kg bw/day; however, the RMS considered the study not acceptable (very high mortality observed, several other limitations) where the only effect was an increase of methaemoglobin but well within the biological variation. The experts agreed that the ADI should be based on the 1-year dog study (revised NOAEL of 10 mg/kg bw/day, supported by 91-week mouse study, SF 100) and this results in an ADI of **0.1 mg/kg bw/day**.

AOEL

In the DAR an AOEL (based on an overall NOAEL of 10 from short term toxicity studies, SF 100, 33% oral absorption) was proposed of 0.033 mg/kg bw/day. In the revised DAR

[5] Evaluated under Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market

[6] Biocides Technical Meeting (TM I 09). Arona, Italy, 16-20 March 2009

(December 2008) and addendum (December 2008) it was proposed at 0.0066 mg/kg bw/day (based on the NOAEL of 2 mg/kg bw/day, 1 year dog, SF 100, 33% oral absorption). During the meeting the experts agreed that the AOEL should be based on the revised NOAEL of 10 mg/kg bw/day from the 1-year dog study supported by 13-week rat study (33% oral absorption and SF 100). The resulting AOEL is **0.033 mg/kg bw/day.**

ARfD

According to the toxicological picture of diflubenzuron, the setting of an ARfD was not considered necessary. The experts agreed.

EFSA note after the written procedure: The RMS informed EFSA that under the biocide application, more conservative reference values were established. Apparently, the database on which the decision was taken was not the same as the one available at the PRAPeR meeting in January 2009. However, no official document is yet available or peer reviewed.

2.11. Dermal absorption

The test substance in the summarised *in vivo* rat study was diflubenzuron and not the representative formulation Dimilin WG 80 (which contains 80% diflubenzuron). During the meeting the experts assumed that the co-formulants in the WG formulation would probably not increase the value. In the DAR a dermal absorption value of 0.5% for concentrate and dilution was proposed (not accounting for the amount in the skin), whereas in the revised DAR and addendum a value of 6% (including the amount stored in the skin) for concentrate and dilution was proposed. The experts agreed on 6% dermal absorption for both the concentrate and the dilution.

2.12. Exposure to operators, workers and bystanders

Dimilin WG 80 is a water dispersible granular (WG) formulation containing 800 g diflubenzuron/kg. The proposed use is as an insecticide on pome fruit, mushrooms and forestry, at the maximum application rate of 180 g as/ha, 1g as/m^2 and 48 g as/ha, respectively. Dimilin WG 80 is applied to pome fruit by tractor-mounted or hand-held spray equipment, to mushrooms by hand-held spray equipment or automatic sprayer, and to forestry by aerial and ground application.

During the meeting, a new AOEL was set and the input parameters applied to operator, worker and bystander were discussed and agreed on. Therefore, new calculations were provided after the meeting in the Addendum 2 to the DAR (February 2009). A summary is presented below.

Operators

Pome fruit:

Dimilin WG 80 is applied to pome fruit by tractor-mounted or hand-held spray equipment.

Estimated systemic exposure (mg/kg bw/day) was performed according to calculations with the German and UK POEM models. The default body weight of the operator is 70 kg in the German model and 60 kg in the UK POEM model. The treated area is 15 ha/day (UK

model), 8 ha/day (German model) for tractor-mounted sprayer and 1 ha for hand-held treatment (UK and German model).
The operator exposure estimates for tractor-mounted spraying in orchards showed that the exposure to diflubenzuron is below the AOEL without the use of PPE (52% AOEL, German model) and if gloves are used during mixing and loading and during spraying (66 % AOEL, UK model). The exposure during hand-held spraying is also below the AOEL without PPE (31% AOEL, German model) and if gloves are used during mixing and loading and during spraying (19 % AOEL, UK model).

Greenhouse using mushrooms grower.
Mushrooms are grown in insulated houses and planted in compost in wooden trays or aluminium shelves stacked in tiers on each side of a central aisle. Applications are made routinely to the casing media as a high volume low pressure spray drench. Applications are made automatically through the irrigation system in many modern greenhouses. Alternatively, applications are made using hand-held equipment.
The product is mixed and loaded prior to application in both methods but application by hand-held equipment involves a higher potential for exposure of operators. Estimations were calculated according to the German model. The treated area was 0.15 ha. It was noted during the experts' meeting that it is not a standard value, and also the scenario is particular and not represented in detail by any model. Based on the available information it was agreed as being representative. Since the operator does not need to be in the greenhouse during spraying, operator exposure during automatic spraying is considered negligible and the exposure during mixing/loading is 83 % of AOEL (without PPE). The operator exposure with hand-held sprayer is below the AOEL if gloves are used during mixing and loading and gloves together with coverall and sturdy footwear during spraying (46 % of AOEL).

Forestry
The proposed method of application in this scenario is through aircraft and with tractors or hand-held equipment.
The exposure of the operators to diflubenzuron during mixing/loading in the scenario of aircraft application was calculated by the RMS according to the German model. The treated area was 1000 ha. This results in 68% of the AOEL when gloves were used. Nevertheless, during the expert meeting these calculations were considered unreliable. Furthermore, there are no EU-models for estimating the exposure during application (aircraft). Therefore, aerial application in forestry was considered inconclusive and a data gap was set.
Ground application using either a tractor-mounted or a hand-held sprayer resulted in an exposure of 14 % and 8 % of the AOEL respectively, without the use of PPE according to the German model (without any modification of the standard input parameters).

Operator estimated exposure to Dimilin WG 80 presented as mg/kg bw/day and % of AOEL.

Field of use	Method of application	Model	PPE	Exposure mg kg^{-1} day^{-1}	% AOEL[3]
Pome fruit	Tractor-mounted sprayer	UK POEM	no	0.0415	>100
			yes[1]	0.0219	66
		German model	no	0.0172	52
	Hand-held sprayer	UK POEM	no	0.0401	>100
			yes[1]	0.0063	19
		German	no	0.0103	31
Forestry	Aerial application	Inconclusive			
	Ground application -Tractor-mounted sprayer	German Model	no	0.00459	14
	Ground application -Hand-held sprayer	German Model	no	0.00275	8
Mushrooms	Automatic sprayer	German Model (Mix/loading only)	no	0.0274	83
	Hand-held sprayer	German Model	no	0.0858	>100
			yes[2]	0.0150	46

[1] Gloves during Mixing, Loading and Application.
[2] Gloves during Mixing, Loading and Application; overall and sturdy footwear during Application.
[3] *AOEL= 0.033 mg $kg^{-1}day^{-1}$*

EFSA note after the written procedure: It is noted than even in the case of a lower AOEL (see EFSA note on point 2.10) (e.g. AOEL of 0.0066 mg/kg bw/day), a safe use would be

identified by increasing the use of PPE except for hand-held sprayer of mushrooms in greenhouse.

Workers

Pome fruits

Worker exposure to diflubenzuron during re-entering the application area in orchards for pruning operations has been estimated using the coefficients from EUROPOEM[7] resulting in 0.108 and 0.0108 mg/kg bw/day which is 327 and 33% of the AOEL without and with PPE (gloves).

Greenhouse using mushrooms grower.

A field study to measure the exposure of workers handling treated compost was considered as supportive of a worse case if re-entry exposure would occur in mushrooms greenhouses. Exposure estimates result in 0.0032 mg/kg bw/day which is 10% of the AOEL.

Forestry

Worker exposure to diflubenzuron during re-entering the application area in forest for scouting activities has been estimated using the coefficients from the EUROPOEM resulting in 0.027 mg/kg bw/day (without PPE) which is 81% of the AOEL.

EFSA note after the PRAPeR meeting: worker exposure estimates on Pome fruits and Forestry submitted in the Addendum 2 after the expert meeting were wrongly estimated since they did not have taken into account the application rate. The right values are 0.01944 and 0.001296 mg/kg bw/day for pome fruits and forestry respectively without the use of PPE. This represents 59 and 4 % of the AOEL for pome fruits and forestry respectively. If the workers wear gloves, the dermal absorption could be reduced and give an exposure of 0.001944 mg/kg bw/day (5.9% AOEL) and 0.0001296 mg/kg bw/day (0.4% AOEL) for pome fruits and forestry respectively. This assessment has not been peer reviewed.

EFSA note after the written procedure: It is noted than in the case of a lower AOEL (see EFSA note on point 2.10) (e.g. AOEL 0.0066 mg/kg bw/day), the values would be 294 and 30% of the AOELwithouth PPE for pome fruits and forestry respectively and 29.4 and 3% of the the AOEL with the use of gloves for pome fruits and forestry respectively.

Bystanders

Pome fruits and Forestry

For the estimation of bystander exposure, RMS used assumptions from Rautmann *et al*, 2001[8]. The maximum bystander exposure was estimated to be 0.001167 mg/kg bw/day

[7] EUROPOEM-the development, maintenance and dissemination of generic European databases and predictive exposure models to plant protection products. Final report December 2002

[8] Rautmann, D., Streloke, M., Winkler, R. (2001) New basic drift values in the authorisation procedure for plant protection products. In: Workshop on risk assessment and risk

which is 3.5% of AOEL for orchards and considered as worst case for forestry since the application rate in forestry is lower.

Greenhouse using mushrooms grower.
Bystanders are not expected to be present in mushroom houses during application.

3. Residues

The active substance diflubenzuron was discussed at the PRAPeR experts' meeting for residues 65, round 13 in January 2009.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The dossier on diflubenzuron has been submitted to support notified representative uses on apples, pears, mushrooms and in forestry.

The metabolism was studied on apples, oranges and mushrooms with diflubenzuron [14C] labelled in both phenyl groups.

After application of diflubenzuron on apples at a level of approximately 2 mg/kg (two times the proposed MRL) or oranges at a level of approximately 0.6 mg/kg (application rates [kg a.s./ha] were not calculated), TRR was found mainly in the surface wash of fruits harvested 9 weeks and 21 days after the application respectively. The majority (95-97%) of TRR was identified as diflubenzuron. Levels of possible metabolites (DFBA, CPU and PCA were used as reference standards) were below the limit of quantification.

After compost or casing treatment at an application rate of 5 g/m² (representing 5 times the notified cGAP) TRR in mushrooms varied from 0.1-0.3 mg/kg and 6-9 mg/kg respectively. After casing treatment (notified use) the majority of TRR was identified as DFBA (91%) besides low concentration of diflubenzuron (0.5%) and the metabolites CPU (0.8%) and PCA (0.6%). Whereas the procedural recoveries for DFBA and CPU were acceptable in this study, the procedural recoveries for PCA were low (31-61%). The notifier argued that the low recoveries could be explained by binding of PCA to plant components (lignin). The PRAPeR 65 meeting regarded this explanation as not conclusive as acceptable procedural recoveries for PCA were found in the storage stability study (see below). The specific metabolic profile observed is mushrooms is probably the fact of an uptake from the compost of the metabolites

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mitigation measures in the context of the authorisation of plant protection products (WORMM; Forster, R., Streloke, M. Eds.), 27-29 September, 1999, Heft 383, Biologischen Bundesanstalt für Land - und Fortwirtschaft, Berlin and Braunschweig, Germany.

DFBA and CPU resulting from the rapid degradation of diflubenzuron in the soil (see section 4).

The PRAPeR 64 meeting on toxicology concluded that the toxicological end points for diflubenzuron could be used for the metabolite DFBA. For PCA which is regarded as carcinogenic and for CPU the toxicological evaluation could not be finalised as the relevant information was only received during the meeting.

The PRAPeR 65 meeting discussed which of the metabolites should be included in the residue definitions for plant matrices. The meeting noted that only metabolism studies for fruit crops after foliar application and for mushrooms after compost or casing treatment were available and therefore no general residue definitions could be proposed.

As diflubenzuron accounted for 95-97% of the TRR in fruits and levels of PCA, CPU and DFBA were below the LOQ (0.001 mg/kg), the following residue definitions for fruits (after foliar application) were proposed for monitoring and risk assessment: diflubenzuron. The residue definition is provisional pending further information on the nature of processed fruits (see below).

The experts noted that diflubenzuron is not a suitable indicator for residues in mushrooms. The metabolism study showed that DFBA accounted for 91% of TRR and quantifiable residues of PCA and CPU were found in residue trials carried out in the USA and for CPU also in trials carried out in Northern Europe. Although DFBA is a common metabolite for several active substances, it was regarded as suitable indicator for diflubenzuron residues in mushrooms. Since no other active substance forming this metabolite is currently registered for uses on mushrooms, the experts decided to propose the following residue definitions for mushrooms:

- for monitoring: DFBA;
- for risk assessment: 1) DFBA
  and 2) sum of diflubenzuron, CPU and PCA expressed as PCA.

The residue definition for risk assessment is provisional. Following the finalisation of the toxicological evaluation of the metabolites CPU and PCA the residue definition should be reconsidered.

On apples, a total of eight residue trials were carried out in Northern Europe in 1993 and 2001, four of them as parallel trials comparing two different formulations of diflubenzuron. Eight residue trials were carried out in Southern Europe in 2001 and 2002. Samples were analysed for diflubenzuron. All residue trials were carried out with four instead of maximal two applications. However, the RMS argued in the DAR that the earlier applications contribute less to the residues than the later ones. It was noted that substantially longer intervals between the last two applications (up to 36 days) resulted in comparable residue levels as residue trials following the cGAP with intervals of approximately 14 days. This is in line with the finding that residues only decline slowly. Residue trials carried out in parallel with different formulations showed comparable residue levels.

On protected mushrooms, five residue trials were carried out in Northern Europe and two trials in the USA. Samples were analysed for diflubenzuron, PCA and CPU. Since the major metabolite DFBA was not analysed, no MRL was derived for mushrooms and the PRAPeR 65 meeting formulated a data gap concerning a complete residue data base on mushrooms in compliance with the residue definition for risk assessment. The notifier should assure that the analytical method for PCA used in these trials demonstrates acceptable recoveries and that the stability of PCA is taken into account (see storage stability of PCA, below).

The notifier does not support establishing MRLs for residues in wild berries and mushrooms after application of diflubenzuron in the forest. On request of the RMS the notifier submitted three residue trials on wild berries carried out in Northern Europe. EFSA notes that the application rate is missing in one of the trails and it is significantly higher than the notified GAP in the other studies. The results of the trials were used by the RMS to calculate a MRL of 0.5 mg/kg which was used for a tentative risk assessment (see section 3.3).

Submitted data on freezer storage stability showed that diflubenzuron residues are stable in apples for at least 12 months. Diflubenzuron and CPU are stable in mushrooms for at least 18 and 19 months respectively. However, recoveries for PCA were only 14-28% after storage for 1-18 months. The notifier argued that this can be explained through binding of PCA to the plant matrix. However, the PRAPeR 65 meeting noted inconsistent findings for procedural recoveries in different studies (see also metabolism studies on mushrooms) and therefore did not regard this explanation as conclusive. The notifier was asked to further investigate the stability of PCA during frozen storage.

Concerning studies on the effect of processing on the nature of residues, the RMS referred to the hydrolysis studies reported in section 3.1. The PRAPeR 65 meeting did not regard these studies as acceptable as they were carried out at room temperature. It was concluded that a hydrolysis study simulating the pasteurisation (relevant for processing of apples) is needed. However, for mushrooms, the meeting concluded that a study simulating pasteurisation is not needed, as DFBA is the main component and no further degradation through processing is expected for this compound.

EFSA noted after the PRAPeR 65 meeting that a model hydrolysis study simulating pasteurisation (90°C, pH 4, 20 min) was submitted and is included in the reference list of the DAR. However, it was not evaluated in the DAR and therefore was not discussed in the peer review. It is noted this study was carried out with non radio-labelled diflubenzuron.

Three studies on the level of residues in processed apple commodities were submitted. The samples were analysed for diflubenzuron only. Residues of diflubenzuron increased in pomace and decreased in juice and puree during processing. The PRAPeR 65 meeting noted that depending on the outcome of the study simulating pasteurisation, further data on the magnitude of residues in processed apples might be necessary.

Processing studies on mushrooms (canning) have been submitted. The samples were only analysed for diflubenzuron, PCA and CPU, but not for DFBA. EFSA notes that the necessity of processing studies on mushrooms in accordance with the residue definition should be

decided when new residue data on mushrooms and the consumer risk assessment for the consumption of mushroom are available.

3.1.2. Succeeding and rotational crops

In the peer review it was concluded that studies on residues in rotational and succeeding crops are not a requirement to support the notified uses.

However, the possible use of mushroom compost on agricultural land was discussed in the fate section (see section 4.). EFSA notes that if the further evaluation in the fate section shows that significant residues of diflubenzuron or its metabolites are expected in soil for this scenario, the possible occurrence of residues in crops grown on agricultural land where mushroom compost has been used has to be addressed also.

3.2. Nature and magnitude of residues in livestock

The intake of fruit pomace is relevant only for cattle. The notifier submitted metabolism studies on goats and poultry which were evaluated to propose residue definitions in animal matrices.

Lactating goats were dosed with diflubenzuron [14C] labelled in both phenyl rings at 0.2 and 5 mg/kg bw/day for three consecutive days. Information concerning the dose rate expressed as [mg/kg feed (DM)] is missing. The majority of the applied radioactivity was excreted. Transfer of radioactivity into milk and tissues was low. In the low dose group, TRR in milk was maximal 0.009 mg/kg, in liver 0.26 mg/kg, in kidney 0.02 mg/kg, in muscle 0.001 mg/kg and in fat 0.004 mg/kg. Only milk and fat were investigated for metabolite identification. The only identified metabolites in milk were CPU (max. 44%) and DFBAM (max. 6%). Liver contained CPU (max. 16%), diflubenzuron (max. 7%), DFBAM (max. 5%) and PCA (max. 0.06%). No metabolites could be identified in muscle, fat and kidney. The notifier argued that this was due to the low concentrations of TRR in these matrices. However, the PRAPeR 65 meeting noted that residues in the high dose group were only low in muscle whereas TRR levels up to 0.3 and 1 mg/kg were found in fat and kidney. It was concluded that the residue pattern in fat is presumable the same as in poultry fat (see below) as diflubenzuron is fat soluble in contrary to its metabolites. In addition, no information is available concerning metabolites in ruminant kidney.

Laying hens were dosed with diflubenzuron [14C] labelled in both phenyl rings at 1 and 10 mg/kg bw/day for 10 consecutive days. The majority of TRR was excreted, with less than 0.1% found in egg white, max. 0.4% in egg yolk and max. 5% in tissues. Highest residue levels were found in fat, liver and kidney, with TRR of 0.7, 0.4 and 1 mg/kg in the low dose group. Diflubenzuron was identified in all edible tissues at levels between 12% in liver and 99% in fat and also in eggs (max. 80% in egg yolk and 5% in egg white). CPU was found in tissues at levels between 1% (fat) and 28% (kidney) and in egg yolk at a level of 11%. PCAA was the main compound in egg white (37%) and was also found in low levels (0.3-3%) in fat and liver. PCA was identified in liver (max. 3%) and kidney (4%).

The PRAPeR 65 meeting concluded that diflubenzuron and metabolite CPU were suitable indicators for residues in animal matrices. Therefore, the following residue definition for monitoring for animal matrices was proposed: diflubenzuron and CPU, expressed as diflubenzuron. As the toxicological evaluation of the metabolites was not finalised, the experts proposed the following provisional residue definition for animal matrices for risk assessment: Sum of diflubenzuron, CPU, PCA and PCAA expressed as PCA. The residue definition for risk assessment for animal matrices should be readdressed when the toxicological evaluation of the metabolites of concern in animal matrices (CPU, PCA, DFBAM and PCAA) has been finalised.

The PRAPeR 65 meeting concluded that the dietary burden calculation could not be finalised, as the study on the effect of processing on the nature of residues (hydrolysis study simulating pasteurisation of apples) was outstanding and the residue definition for risk assessment for animal matrices was not finalised. The meeting carried out a provisional dietary burden calculation considering the intake of diflubenzuron only. For a STMR for apples of 0.41 mg/kg and a mean processing factor for apples to pomace of 3.2 the following intakes were calculated: 0.6 mg/kg feed (DM) for diary cattle and 1.7 mg/kg feed (DM) for beef cattle.

In the metabolism study on goats, information for the dose expressed as [mg/kg feed (DM)] is missing. The PRAPeR 65 meeting discussed if intake of feed per body weight for goats and cattle was different or if an extrapolation from the metabolism data on goats to cattle on the basis of intake per kg body weight was possible. A data gap was formulated. Either a feeding study on cattle is necessary or the notifier should show that it was not necessary.

No feeding studies are required for poultry.

Studies on the storage stability of diflubenzuron, 4-chlorophenylurea and 4-chloroaniline are available in the DAR as part of the metabolism study on livestock. EFSA notes that the presentation of the results in the DAR does not allow full evaluation of the validity of these studies and their results. If they are needed to support studies in livestock, full evaluation will be necessary.

EFSA notes that residues of diflubenzuron may also arise from its use as veterinary drug in fish or as biocide in livestock.

3.3. Consumer risk assessment

EFSA reconsidered the risk assessment initially proposed by the RMS and recalculated the chronic exposure (not peer reviewed) using the EFSA PRIMo rev.2 model and taking into account the ADI of 0.1 mg/kg bw/day and the proposed MRLs of 1 mg/kg for apple and pear and 0.5 mg/kg for wild berries (see section 3.1.1). As data for wild berries are not included in the model, the intake of the whole group “berries and small fruits” was taken into account as worst case estimate. Using these values, the highest TMDIs are 14% of the ADI for the German child and 7% of the ADI for the Dutch child. A refined calculation using the STMR for pome fruits (0.41 mg/kg) leads to a maximum IEDI of 6% ADI.

This risk assessment has to be considered as provisional, pending the finalisation of the residue definitions for plant and animal matrices and information on residues in processed

food and in animal matrices. In addition information on the toxicological relevance of some metabolites is not addressed and reference values for PCA regarded as carcinogenic are not available. However considering the low estimated intake (6% ADI), the fact that residue levels of PCA are expected to be low in apples, processed commodities and animal matrices, it is concluded that no exceedance of the ADI of 0.1 mg/kg bw/d is expected, although some uncertainties remain in the residue definitions and the toxicological end-points of some metabolites.

In addition, it must be noted that the intake of diflubenzuron and its metabolites through consumption of mushrooms was not taken into account in this risk assessment since no residue trials according to the residue definition were provided and no MRL could be derived for this commodity.

An ARfD was not set for diflubenzuron. Therefore, it was not necessary to carry out a consumer risk assessment for acute exposure.

EFSA notes that the RMS has informed EFSA after the drafting of the conclusion that under the biocide application an ADI of 0.012 mg/kg bw/day has been set (see section 2.10) and that it could not be excluded that PCA is formed in humans exposed to diflubenzuron (section 2.8). **Should these information be validated, a risk for the consumer could not be excluded in this case**.

3.4. Proposed MRLs

In accordance with the proposed residue definition for monitoring for fruit crops after foliar application (diflubenzuron alone) the following MRLs were proposed:
Apples and pears 1 mg/kg

As no residue trials on mushrooms in accordance with the proposed residue definition for monitoring of mushrooms (DFBA) are available a MRL for mushrooms cannot be proposed.

MRLs for wild mushrooms and wild berries resulting from the forestry application of diflubenzuron are not supported by the notifier. This issue should be dealt with at management level.

Due to a data gap (see section 3.2) it currently cannot be concluded on the need to propose MRLs in animal matrices.

4. Environmental fate and behaviour

Diflubenzuron was discussed in the meeting of experts on fate and behaviour (PRAPeR 62) on the basis of the DAR (May 2005), the revised DAR (December 2008) and the addendum (December 2008).
The meeting of experts discussed the need to address the environmental exposure derived from the use in protected mushrooms. The meeting agreed that the exposure from growing

mushrooms facilities cannot be automatically considered negligible. Additionally, it was noted that it is common practice in some Member States to spread used mushroom compost on agricultural land at the end of the mushroom growing cycle. Since the basis of the assessment presented by the notifier for this use was the assumption of negligible exposure, a data gap for the full exposure assessment in soil, surface water and ground water for the representative use in protected mushrooms was identified by the meeting of experts.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

Route of degradation of diflubenzuron under dark aerobic conditions was investigated in one study with three soils (pH = 6.5 – 7.4; OC = 1.1 – 2.5 %; clay = 6.2 – 37.2 %; 35- 40 % MWHC) at 20 ºC and one study with one soil (pH = 5.6; OC = 1.8 %; clay = 4.3 %; 10.5 % MWHC) at 24 ºC.

Degradation of diflubenzuron takes place by the breaking of its amide bond to yield the two major metabolites DFBA (max. 13.3 % AR after 3 d) and CPU (max. 30.8 % AR after 7d). Non extractable residues (NER) were formed in high quantities (max. 37.4-55 % AR at the end of the studies). CO_2 was formed in the range of 26.3 to 41.2 % AR at the end of the studies. The identity of the volatiles trapped in the alkaline trap was not justified in the DAR. The RMS clarified in the evaluation table and the meeting of experts that CO_2 was precipitated with barium hydroxide and that non-CO_2 radioactivity in the volatiles trap accounted for only 1.2 % AR. Whereas the maximum formation of the NER was not attained during the studies, since significant mineralization was observed, it is not expected that levels above 70 % would have been attained if the study had lasted longer.

Degradation under dark anaerobic conditions was investigated in one water sediment system at 24 ºC. This study was presented by the notifier as a surrogate for the anaerobic degradation in soil. No new metabolites were found in this study but there was a lower formation of NER, probably due to the slower degradation rate of parent and metabolites.

Photolysis of diflubenzuron in soil was investigated in a laboratory study with Xenon lamp (simulating noon light at mid-northern latitudes). No new major metabolites were identified in this study.

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

Persistence of diflubenzuron and its metabolites in soil under dark aerobic conditions was investigated in the same studies carried out to establish its degradation route. Diflubenzuron may be classified as low persistent ($DT_{50\ norm}$ = 2.0 – 6.7 d). Rate of degradation of metabolites was only investigated in the study performed with three soils. DFBA may be considered low persistent in soil ($DT_{50\ 20\ °C}$ = 3.3 – 9.0 d) and CPU moderately persistent ($DT_{50\ 20\ °C}$ = 15.2 – 30.5 d).

Under anaerobic conditions it is expected that the degradation would be slower ($DT_{50\ anaerobic\ water\ /\ sediment\ 20\ °C}$ = 31 – 34 d).

In the photolysis study, slower degradation was observed in the irradiated samples with respect to the dark ones, probably due to the lost of moisture. It may be concluded that photolysis does not contribute to the degradation of diflubenzuron in soil.
PEC soil were calculated assuming two applications of 180 g a.s./ha with 14 d interval. A crop interception of 50 % and worst case DT_{50} were assumed.
In reply to an ecotoxicology experts meeting issue, the experts in fate and behaviour indicated that since no field studies are available it is not possible to confirm that DT_{90} in field for the metabolite CPU will be less than 100 d. Current available laboratory information results in a DT_{90} between 55.7 - 111.8 d.

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

Batch adsorption / desorption studies are available for diflubenzuron and its metabolites CPU and DFBA. These studies indicate that diflubenzuron is immobile to slightly mobile (K_{Foc} = 1983 – 6918 mL/g) and CPU exhibits medium mobility (K_{Foc} = 209 – 291 mL/g). Due to the weak adsorption of DFBA it was not possible to determine reliable adsorption parameters. The notifier calculated adsorption of the DFBA in soil using the program EPA-PCKocWin v1.66 and log Pow data. The values obtained indicate that DFBA exhibits a very high mobility in soil (Koc [PCKocWin] = 39.6 mL/g; (Koc [log Pow] = 23.2 mL/g). However, as it is expected that DFBA will dissociate under environmental conditions the QSAR estimation was regarded as inappropriate by the meeting of experts in this case. It was agreed that simulations performed assuming a Koc = 0 could be used to finalize the EU exposure assessment.
Diflubenzuron column and aged column leaching experiments were performed in a study with three soils. Partition of the leachates with diethyl ether did not allow extracting the majority of the radioactivity. Therefore, the study is not further used in the risk assessment.
In the FOCUS GW modelling for diflubenzuron a Kf_{OC} of 9148 mL/g was used instead of the arithmetic mean of 4620 mL/g, although the meeting confirmed the arithmetic mean as agreed end point for subsequent assessments. The experts agreed that the results of the modelling presented were acceptable with respect to the EU risk assessment.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Diflubenzuron is hydrolytically stable at pH 5 and 7 and hydrolyses to CPU and DFBA at pH 9 (study summarized under physical chemical properties section of the DAR). Hydrolysis of CPU and DFBA was investigated in aqueous buffered solutions (pH 4, 7 and 9) at 50 ºC. Both metabolites are stable under these conditions.
Photolysis of diflubenzuron in water was investigated in one study summarized in the physical chemical properties section of the DAR. Photo degradation is relatively slow (DT_{50} = 40 d). Due to the fact that biological degradation is faster, it was agreed that photo degradation will not contribute to the dissipation of diflubenzuron in the environment.
A readily biodegradation study is available. The study was re-evaluated by the RMS in the revised DAR (December 2008). The meeting of experts discussed the results of the readily

biodegradation study and concluded that the study resulted in diflubenzuron being classified as not readily biodegradable under the conditions defined for the test.

The fate of diflubenzuron was investigated in one study with two dark aerobic water / sediment systems at 20 ºC. Diflubenzuron was low persistent in these systems (DT_{50} whole system = 3.7 – 5.4 d). Diflubenzuron partitions to the sediment to some extent (max. 20.7 – 24.4 % AR in the first 24 h). The major metabolites formed were DFBA (max. in water 7.3-13.1 % AR; max. in sediment 3.7 % AR after 4 d) and CPU (max. in water 31.1 % AR after 8 d or 16 d; max. in sediment 15.9-21.0 % AR after 16 d or 30d). Half-lives of metabolites DFBA (DT_{50} whole system = 1.6 – 4.4 d) and CPU (DT_{50} whole system = 26.9 – 52.5 d) were calculated with the data from this study. A multi-compartment model was used to fit the water / sediment data to obtain kinetic parameters from metabolite CPU. The RMS clarified that the water /sediment has been treated as a single compartment in order to obtain the whole system formation and degradation parameters for this metabolite. It was also clarified that the tool employed in this fitting exercise was MicroCal v. 3.5 using the Moore Fit approach.[9]

In a separate study, the fate of diflubenzuron applied as a suspension to WP 25 or WG 80 formulations was investigated in two water / sediment systems ($pH_{sediment}$ = 5.6 – 7.3) at 20 ºC. Incubation was carried out with a light regime of 12 h period. The half-lives obtained for the parent were in the same order than in the dark study indicating that photolytic breakdown will be of less importance compared to biological degradation. Some clarifications on this study have been provided by the RMS in the revised DAR (December 2007). The study is considered supplementary information and no EU end points have been derived from it.

Additional studies on the degradation of diflubenzuron in natural surface water and littoral enclosure water column were scientifically acceptable but not used in the EU risk assessment.

$PEC_{SW / SED}$ were calculated based on the uses of Dimilin WG 80 on pome fruit and forest. FOCUS SW scheme was used up to STEP 2 for the metabolites and up to STEP 4 for the parent compound in seven scenarios considered relevant for the representative use in orchards (pome fruit). STEP 4 calculations were conducted using TOXWA by implementing 10, 20 and 30 m buffer zones.

For forestry (aerial and hand application) the RMS provided calculations of PECsw for parent and metabolites based only on the spray drift route of entry to surface waters assuming a drift value of 33.2 % for aerial application and of 8.02% for hand application (vines application at > 50 cm is assumed to have the same drift as a hand application). PEC_{SW} for aerial application in forestry presented by the notifier were not agreed. However, the meeting agreed with the PEC_{SW} calculated by the RMS and presented in the addendum (December 2008). It was noted that PEC_{SED} were not calculated. The meeting agreed that EFSA will highlight in the conclusion that, when addressing the risk for aquatic insects, exposure via sediment needs to be addressed.

[9] Moore, J.W. and Pearson, R.G. (1981) "Kinetics and Mechanism" 3rd Edition, John wiley and son, NY.

In a late stage clarification on the GAP, the notifier indicated that a hand-held sprayer could also be used in orchards and a tractor mounted sprayer could be used in forests. These application practices have not been evaluated and no PEC_{SW} calculations are available for them. $PEC_{SW/SED}$ for the application with a tractor mounted spray in forests and hand held application in orchards need to be provided to finalize the EU risk assessment. A data gap was identified by the meeting of experts since no new calculations had been received by the RMS at the time of the meeting. The meeting proposed to use FOCUS SW pome / stone fruit scenarios to represent forestry in these calculations.

4.2.2. Potential for ground water contamination of the active substance, their metabolites, degradation or reaction products

Potential contamination of groundwater by diflubenzuron and its soil metabolites has been assessed with FOCUS-PELMO v. 3.3.2. Two applications in orchards of 180 g a.s./ha with 14 d interval were simulated for the relevant scenarios. Separate simulations were performed for diflubenzuron and its metabolites. Input parameters were chosen according to the FOCUS recommendations. The mean Koc of the two different estimations for DFBA was divided by two (Koc = 15.7 mL/g) to obtain a worst case for modelling. The 80th percentile at 1m depth for each of the compounds was below 0.002 µg/L for all the nine scenarios simulated. A data gap was identified since only modelling with FOCUS PELMO has been performed while EFSA asked for at least two different models to be used. However, since in this case variations of one order magnitude will not lead to a breach of the trigger concentration of 0.1 µg/L, it may be concluded that contamination of ground water will not occur when the product is used according the proposed representative uses. Member States may require a calculation with a second model for confirmatory purposes.
New FOCUS GW modelling using a Koc = 0 for metabolite DFBA was requested during the peer review. The RMS received the required modelling and summarized it in an addendum (December 2008). FOCUS PELMO v.3.3.2 and FOCUS PEARL v.3.3.3 were used to estimate the potential ground water contamination by metabolite DFBA resulting from the outdoor uses of diflubenzuron. The meeting of experts accepted the results of this modelling exercise, which indicates that the ground water limit of 0.1 µg/L was respected for the nine scenarios assessed for the use in orchards. However, since the report summarizing the modelling was only received by the RMS, a data gap was identified for the inclusion of the report in the updated dossier to be submitted to the Member States and EFSA.

4.3. Fate and behaviour in air

Diflubenzuron has a very low vapour pressure and a short half-life in atmosphere (DT_{50} = 3.1 h) due to reaction with hydroxyl radicals. Long range transport and deposition of diflubenzuron may be considered negligible.

5. Ecotoxicology

Diflubenzuron was discussed in the meeting of experts on ecotoxicology, PRAPeR 63 in January 2009 on the basis of the draft assessment report, addendum 1 (B8-9) (December 2008) and the revised DAR Vol 3 (B9) (December 2008). A not peer-reviewed addendum was submitted in February 2009. The representative uses evaluated are uses as an insecticide (insect growth regulator) in orchards (apples/pears) (2 x 180 g a.s./ha), mushrooms (1 x 1 g a.s./m^2) and forestry (1 x 48 g a.s./ha). The risk assessment was conducted according to the following guidance documents: Risk Assessment for Birds and Mammals, SANCO/4145/2000 September 2002; Aquatic Ecotoxicology, SANCO/3268/2001 rev.4 final, October 2002; Terrestrial Ecotoxicology, SANCO/10329/2002 rev.2 final, October 2002; Risk Assessment for non-target arthropods, ESCORT 2, March 2000, SETAC.

5.1. Risk to terrestrial vertebrates

Diflubenzuron was of low toxicity to birds and mammals. The first-tier TER values for birds and mammals exceeded the Annex VI trigger values for the uses in apples/pears and in forestry. No exposure of birds and mammals was expected from the indoor use in mushrooms.

Shortcomings were observed in the dietary studies with birds. Given the low toxicity to birds and the low acute and long-term risk it was assumed that the short-term risk to birds is low and no new dietary studies were required.

The risk to earthworm- and fish-eating birds and mammals from secondary poisoning was assessed as low for the use in orchards. The TERs for fish-eating birds and mammals exceeded the Annex VI trigger. The TERs for earthworm-eating birds and mammals was not calculated. Since the application rate in forests is lower than in orchards the risk was covered by the risk assessment for earthworm-eating birds and mammals for the orchard use.

The risk from uptake of contaminated drinking water was assessed as low (the first-tier TERs were above the Annex VI trigger values).
Overall it was concluded that the risk to birds and mammals was low for the representative uses evaluated.

5.2. Risk to aquatic organisms

Daphnids were the most sensitive organisms tested with an acute EC_{50} of 0.0026 mg a.s./L and a reproductive NOEC of 0.04 µg a.s./L. The TER values with FOCUS step2 PECsw were several orders of magnitude below the relevant Annex VI trigger values.

A NOEAEC of 0.7 µg diflubenzuron/L from an enclosure study based on effects on daphnids was suggested by the RMS. The notifier suggested an EAC (Environmentally Acceptable Concentration) of 13.6 µg diflubenzuron/L. The notifier submitted studies published in the literature in order to support the suggested EAC of 13.6 µg diflubenzuron/L. The studies provided some evidence that it is possible for daphnids to recover after exposure to diflubenzuron. However, the studies were either too short or no replicates were used. Therefore it was decided that the results of the enclosure study which was conducted to

modern test protocols cannot be overruled by these studies. No recovery of daphnids was observed in the enclosure studies because of the short duration of the study. However, recovery within 8 weeks was considered to be likely for daphnids taking into consideration the short reproductive cycles of daphnids. Impacts on amphipods were observed in the enclosure study at a concentration of 0.7 µg diflubenzuron/L and the power to detect effects on several other invertebrates (e.g. univoltine insect species) was low. It is very unlikely that amphipods and univoltine insect species could recover within a short period of time (8 weeks). Therefore the experts suggested that the end point of 0.7 µg diflubenzuron/L could only be used to assess the risk to zooplankton (daphnids) and that an assessment factor of 5 should be applied. The experts identified a data gap to address the risk to amphipods and aquatic insects. It need to be demonstrated that insects are less sensitive than daphnids and/or can recover within a short period of time (8 weeks).

The Annex VI trigger values were far below the trigger of 1 for daphnids based on the regulatory end point of 0.14 µg diflubenzuron/L (0.7 µg diflubenzuron/L divided by the assessment factor of 5) for the use in orchards even with a 30 m no-spray buffer zone (FOCUS step4 PECsw). The TER was 2 for the use in forestry with a no-spray buffer zone of 20 m (hand application). Therefore a high risk to aquatic organisms was indicated for the uses in orchards and forestry. In a late stage clarification on the GAP, the notifier indicated that hand-held sprayer could also be used for orchards and tractor mounted sprayer in forest. These application practices have not been evaluated and no PEC_{SW} calculations are available for them. A data gap was identified by the experts on fate and behaviour to calculate $PEC_{SW/SED}$ for the application with tractor mounted spray in forest and hand held application in orchards in order to finalize the EU risk assessment (see point 4.2.1.).

The risk to aquatic organisms from the use in mushrooms was considered to be low by the RMS assuming that the exposure of aquatic ecosystems is negligible. However a data gap was identified by the experts on fate and behaviour to provide an exposure assessment for the use in mushrooms. A conclusion on the risk to aquatic organisms from the use in mushrooms can only be drawn after a reliable estimation of exposure of surface water was made available.

The acute and long-term toxicity of the metabolites 4-chlorophenylurea (CPU) and 2,6-difluorobenzoic acid (DFBA) to aquatic organisms was assessed as low based on FOCUS step 2 PECsw values.

The BCF of diflubenzuron was estimated as 320. The risk of bio concentration and bioaccumulation in aquatic food chains was considered as low because of the rapid elimination from fish tissues (clearance time CT_{50} = 0.6 days) and the rapid dissipation of diflubenzuron from the water phase. The experts agreed that the risk of bio concentration/bioaccumulation in aquatic organisms was low.

Overall it was concluded that the risk to aquatic organisms is high for the uses in orchards and forestry.

5.3. Risk to bees

Because diflubenzuron acts as an insect growth regulator no studies on the oral and contact toxicity on adult bees were submitted. Semi-field and field tests were provided instead, in order to assess the long-term development of honey bee colonies. The two studies were conducted at a treatment rate of 200 g a.s./ha which was slightly higher than the highest representative use rate. One field study did not show effects on bee brood and development. However the study duration was too short to allow a scientifically sound assessment of the effects on honey bee brood and colony development. An increased mortality of adult bees which were exposed to diflubenzuron was observed in the second study. This effect was not observed until 4 weeks after treatment which indicated that a sufficiently long observation period was needed to detect possible effects following exposure to diflubenzuron. Some information based on a literature review was provided to demonstrate that the observed effects were not significant with respect to development of honey bee colonies. However, the published studies were either not conducted at a relevant application rate, only very briefly reported or the sensitive end point (adult mortality following exposure as a larvae) was not observed. Therefore it was concluded that the risk to honey bees is potentially high. A data gap was identified in the meeting of experts to address the risk to bees. Risk mitigation measures such as restriction of the use to non-flowering crops or growth stages are required. A new report from a field study was submitted by the notifier and evaluated by the RMS in the addendum (February 2009). The report was not taken into account in the peer review according to Commission Regulation (EC) No. 1095/2007.

5.4. Risk to other arthropod species

The HQ values calculated by the notifier for *Typhlodromus pyri* and *Aphidius rhopalosiphi* indicated that the risk to adult non-target arthropods was low. However, diflubenzuron is an insect growth regulator which acts as a chitin synthesis inhibitor. Therefore the risk assessment should be focused on the sensitive life stages. The tests with *Episyrphus balteus*, *Coccinella septempunctata* and *Chrysoperla carnea* were conducted with larvae and thus considered as more appropriate for the risk assessment. The LR_{50} of the three species were determined to be lower than the application rate in orchards. For the use in forestry the LR_{50} for *C. septempunctata* was higher than the application rate but not for the other two species. Therefore a potential high risk to non-target arthropods was indicated for both representative uses. The off-field dose rates were above the LR_{50} values for the most sensitive species (*C. carnea)* up to a distance of 40 m (orchard) and 10 m (forestry hand application) in the original risk assessment proposed by the RMS. No correction factor to account for differences in species sensitivity was used in the original risk assessment since the literature review submitted by the notifier provided some indication that the three tested species were among the most sensitive species. However no aged residues tests, semi-field or field studies were submitted to give an indication of the potential of recovery after an initial impact on arthropod populations. The most sensitive life stages (juveniles) were tested with 3 different arthropod species. The experts were of the opinion that the information was not sufficient to reduce the correction factor (uncertainty factor related to differences in species sensitivity) to

1 and proposed a correction factor of 5 which is recommended for higher tier risk assessment in the ESCORT 2 guidance document. This would result in the need of even larger in-field no-spray buffer zones (up to 75 m for the use in orchards). Such risk mitigation was considered as not realistic. A data gap was identified in the meeting of experts to demonstrate that recovery/recolonisation of the treated area is possible within 1 year.

Exposure of non-target arthropods from the greenhouse use in mushrooms was considered to be negligible.

Overall it was concluded that a high risk to non-target arthropods cannot be excluded for the use in orchards and forestry and the potential of recovery/recolonisation within one year needs to be demonstrated.

5.5. Risk to earthworms

The acute TER values were well above the Annex VI trigger of 10 for diflubenzuron and its major soil metabolites 4-chlorophenylurea (CPU) and 2,6-difluorobenzoic acid (DFBA) for the use in orchards and forestry. The laboratory DT_{90} values for CPU were in the range of 55.7 to 111.8 days but taking into account that the acute TER for CPU indicates a high margin of safety (more than two orders of magnitude higher than the Annex VI trigger) and given that the longest observed DT_{90} of CPU of 111 d was not extensively exceeding the trigger of 100 days and the maximum number of applications is only 2 per year, testing of reproductive effects was considered not necessary. The risk from the representative uses of diflubenzuron posed to earthworms was considered to be low.

5.6. Risk to other soil non-target macro-organisms

Because of the rapid degradation in soil ($DT90_f$ for diflubenzuron and 2,6-difluorobenzoic acid (DFBA) < 100 d) a separate testing with other soil non-target macro-organisms was considered as not necessary. The laboratory DT_{90} values for CPU were in the range of 55.7 to 111.8 days exceeding the trigger of 100 days. However differences in the acute toxicity to daphnids suggest that CPU has no insect growth regulating properties. The experts agreed that no studies with soil dwelling non-target arthropods were required.

5.7. Risk to soil non-target micro-organisms

Effects of > 25% on soil respiration and nitrification were observed in tests with the formulation Dimilin WG 80 at 28 d. A second study with a longer duration showed that no effects > 25% were observed one month after application. The maximum single application rate of Dimilin WG 80 of 180 g a.s./ha in orchards is lower than the rate of 750 g a.s./ha which was applied in the test. Given that the product is applied only two times in orchards and one time in forestry the risk to soil micro-organisms was considered to be low.

5.8. Risk to other non-target-organisms (flora and fauna)

No fungicidal or herbicidal effects were observed in screening tests. Therefore the risk to other non-target organisms was considered to be low for the representative uses in orchards and forestry.

5.9. Risk to biological methods of sewage treatment

The risk to biological methods of sewage treatment is considered to be low since no effects were observed up to a concentration of 1000 mg a.s./L.

6. Residue definitions

6.1. Soil

Definition for risk assessment: diflubenzuron, CPU, DFBA

Definition for monitoring: diflubenzuron

6.2. Water

6.2.1. Ground water

Definition for exposure assessment: diflubenzuron, CPU, DFBA

Definition for monitoring: diflubenzuron

6.2.2. Surface water

Definition for risk assessment

in surface water: diflubenzuron, CPU, DFBA

in sediment: diflubenzuron, CPU

Definition for monitoring: diflubenzuron

6.3. Air

Definition for risk assessment: diflubenzuron

Definition for monitoring: diflubenzuron

6.4. Food of plant origin

Fruit crops after foliar application:

Definition for risk assessment (**provisional**):

diflubenzuron; pending further information on the nature of processed fruits

Definition for monitoring: diflubenzuron

Mushrooms after soil treatment:

Definition for risk assessment (**provisional**):

(1) DFBA

(2) sum of diflubenzuron, CPU and PCA expressed as PCA; pending the finalisation of the toxicological evaluation of the metabolites

Definition for monitoring: DFBA

6.5. Food of animal origin

Definition for risk assessment (**provisional**):

Sum of diflubenzuron, CPU, PCA and PCAA expressed as PCA; pending the finalisation of the toxicological evaluation of the metabolites

Definition for monitoring: diflubenzuron and CPU, expressed as diflubenzuron.

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

6.6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
diflubenzuron	low persistent ($DT_{50\ norm}$ = 2.0 – 6.7 d)	The acute toxicity to earthworms was low (LC_{50} > 500 mg a.s./kg soil). The risk to earthworms and soil micro-organisms was assessed as low.
CPU	moderately persistent ($DT_{50\ 20\ °C}$ = 16.8 – 33.6 d)	The acute toxicity to earthworms was low (LC_{50} = 340 mg CPU/kg soil). The risk to earthworms and soil micro-organisms was assessed as low.
DFBA	low persistent ($DT_{50\ 20\ °C}$ = 3.6 – 9.0 d)	The acute toxicity to earthworms was low (LC_{50} > 500 mg DFBA/kg soil). The risk to earthworms and soil micro-organisms was assessed as low.

6.6.2. 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
diflubenzuron	immobile to slightly mobile (Koc = 1938 – 22826 mL/g)	FOCUS GW, No	Yes	Yes	Very toxic to aquatic organisms (daphnia acute EC_{50} = 0.0026 mg a.s./L and chronic NOEC = 0.04 µg a.s./L). The risk to aquatic organisms in surface water was assessed as high.
CPU	medium mobile (Koc = 209 – 291 mL/g)	FOCUS GW, No	No data available, no data needed	No data available to conclude, no data needed.	Low toxicity and low risk to aquatic organisms.
DFBA	Assumed to be very high mobile (Koc = 0 used in modelling)	FOCUS GW, No	No data available, no data needed	Yes (major rat metabolite, expected to have the same toxicological profile as diflubenzuron), no further data needed.	Low toxicity and low risk to aquatic organisms.

6.6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
diflubenzuron	Very toxic to aquatic organisms (daphnia acute EC_{50} = 0.0026 mg a.s./L and chronic NOEC = 0.04 µg a.s./L). No FOCUS step4 scenario exceeded the trigger of 1 with the regulatory end point of 0.14 µg diflubenzuron/L and no spray buffer zones of 30 m (orchards) and 20 m (forestry).
CPU	Low acute and long-term toxicity to aquatic organisms. The risk was assessed as low (TERs above the trigger with FOCUSsw step2)
DFBA	Low acute and long-term toxicity to aquatic organisms. The risk was assessed as low (TERs above the trigger with FOCUSsw step2)

6.6.4. Air

Compound (name and/or code)	Toxicology
diflubenzuron	Low acute toxicity by inhalation (LC_{50} > 2.5 mg/L, 4h).

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

- A revised specification (relevant for all uses evaluated, data gap identified by meeting of experts January 2009, proposed submission date unknown, refer to chapter 1).
- 5 batch analysis with validated methods of analysis (relevant for all uses evaluated, data gap identified by meeting of experts January 2009, data submitted and evaluated in the December 2008 addendum to Vol. 4, refer to chapter 1).
- Accelerated storage stability and shelf-life studies with analysis of the relevant impurity (relevant for all uses evaluated, data gap identified by meeting of experts January 2009, proposed submission date unknown, refer to chapter 1).
- Attrition test using CIPAC MT 178.2 (relevant for all uses evaluated, data gap identified by meeting of experts January 2009, proposed submission date unknown, refer to chapter 1).
- Applicability of the CIPAC methods for formulation analysis (relevant for all uses evaluated, data gap identified by meeting of experts January 2009, proposed submission date unknown, refer to chapter 1).
- Applicability of a multi-residue method (relevant for all uses evaluated, data gap identified by meeting of experts January 2009, data submitted and evaluated in the December 2008 addendum to Vol. 3, B5, refer to chapter 1).
- Method of analysis for 2,6-difluorobenzoic acid (DFBA) in mushrooms (relevant for the use on mushrooms, data gap identified by EFSA February 2009, proposed submission date unknown, refer to chapter 1).
- Method of analysis for surface water with an appropriate LOQ (relevant for all uses evaluated, data gap identified by meeting of experts January 2009, proposed submission date unknown, refer to chapter 1).
- Method of analysis for air (relevant for all uses evaluated, data gap identified in the DAR, data provided and evaluated in the December 2008 addendum to Vol. 3, B5, refer to chapter 1).
- Equivalence of the batches tested in the mammalian toxicology to the representative specification (relevant for all uses evaluated, data gap identified by the meeting of experts January 2009, proposed submission date unknown, refer to chapter 2).
- Toxicological relevance of metabolites CPU and DFBAM (relevant for all uses evaluated, data gap identified during the experts' meeting, data available and evaluated by the RMS in the addendum 2 (February 2009) but not peer-reviewed; refer to section 2.8).
- Toxicological reference values for consumers of the relevant metabolite PCA (relevant for all uses evaluated, data gap identified during the expert meeting; proposed submission date unknown, refer to section 2.8)
- Toxicological relevance of metabolite PCAA (relevant for all uses evaluated, data gap identified after the PRAPeR 64, date of submission unknown, refer to section 2.8)

- Operator exposure estimates during aircraft application (relevant for use in forestry; data gap identified by the meeting of experts January 2009, proposed submission date unknown, refer to section 2.12).
- Complete database of residue trials on mushrooms in compliance with the residue definition for risk assessment. The notifier should ensure that the analytical method for PCA used in these trials demonstrates acceptable recoveries and the storage stability of PCA should be taken into account. (relevant for the use on mushrooms; data gap identified by PRAPeR 65 meeting in January 2009, proposed submission date unknown, refer to section 3.1.1).
- Further investigation of the frozen storage stability of PCA (relevant for the use on mushrooms; data gap identified by PRAPeR 65 meeting in January 2009, proposed submission date unknown, refer to section 3.1.1).
- Study on the effect of processing on the nature of residues: Hydrolysis study simulating pasteurisation (relevant for uses on pome fruit, data gap identified by PRAPeR 65 meeting in January 2009, proposed submission date unknown, refer to section 3.1.1)
- Feeding study in ruminants or justification that feeding studies are not necessary (relevant for uses on pome fruit, data gap identified by PRAPeR 65 meeting in January 2009, proposed submission date unknown, refer to section 3.2)
- A data gap was identified during the peer review for a soil exposure assessment for the use in protected mushroom production (relevant for the protected mushroom representative use; proposed submission date unknown, refer to section 4.2.2)
- A data gap, needed to finalize the EU risk assessment, was identified during the peer review for FOCUS SW $PEC_{SW/SED}$ for the application with a tractor-mounted sprayer in forests (represented by pome / stone fruit FOCUS SW scenarios) and a hand held application in orchards (relevant for outdoor representative uses; proposed submission date unknown, refer to section 4.2)
- A data gap was identified during the peer review for a surface water exposure assessment for the use in protected mushroom production (relevant for protected mushroom representative use; no submission date proposed by the notifier; refer to section 4.2.1)
- A data gap was identified during the peer review for a ground water exposure assessment for the use in protected mushroom production (relevant for the protected mushroom representative use; proposed submission date unknown, refer to section 4.2.2)
- A data gap was identified for PEC GW calculations with a second model following the PPR opinion on FOCUS GW (the data gap is not considered essential to finalize the EU exposure assessment; proposed submission date unknown, refer to section 4.2.2)
- A formal data gap was identified for the study report with the FOCUS GW modelling of DFBA in the outdoor uses to be submitted to EFSA and the Member States (relevant for outdoor representative uses; data already available to RMS, refer to section 4.2.2)
- The risk to sensitive aquatic invertebrates with longer life cycles (amphipoda, univoltine insect species) needs to be addressed (relevant for the uses in orchards and

forestry; data gap identified in the meeting of experts on ecotoxicology (PRAPeR 63) in January 2009; proposed submission date unknown, refer to section 5.2.)

- A data gap was identified in the meeting of experts to address the risk to bees (relevant for the uses in orchards and forestry; data gap identified in the meeting of experts on ecotoxicology (PRAPeR 63) in January 2009; a new report from a field study was submitted by the notifier and evaluated by the RMS in the addendum; the study was not taken into account in the peer-review according to Commission Regulation (EC) No. 1095/2007); refer to section 5.3.)
- The potential of recolonisation/recovery of non-target arthropods within one year needs to be demonstrated (relevant for the uses in orchards and forestry; data gap identified in the meeting of experts on ecotoxicology (PRAPeR 63) in January 2009; proposed submission date unknown, refer to section 5.4.)

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

This conclusion was reached on the basis of the evaluation of the representative uses as an insecticide on apples, pears and mushrooms and in forestry. Full details of the GAP can be found in the list of end points attached in Appendix A.

The representative formulated product for the evaluation was 'Dimilin WG 80', a water dispersible granule (WG).

Residues in apples and pears can be analysed by a HPLC method. The method for mushrooms is not validated for the residue definition. The LOQ for the surface water method is not low enough and a data gap has been identified.

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. However, data gaps have been identified for attrition, accelerated storage and shelf-life studies. The technical specification and batch data were not accepted and a data gap has been identified.

There is a lack of a peer reviewed specification and assessment of the equivalence of the batches tested in all the mammalian toxicity studies compared to the representative formulation. In mammals, diflubenzuron is not acutely toxic via oral, dermal or inhalation routes; it is not a skin or eye irritant nor a skin sensitizer. Diflubenzuron showed a consistent profile of toxicity after repeated oral administration to mice, dogs and rats, with the dog being the most sensitive species. The primary target of toxicity was erythrocytes, with secondary effects apparent in the spleen and in the liver (consistent with haemolytic anaemia). The relevant oral No Observed Adverse Effect Level (NOAEL) is 10 mg/kg bw/ day (1-year dog study). Diflubenzuron did not show any genotoxic potential. No evidence of carcinogenic potential was found in rats and mice. The relevant NOAEL from the long term toxicity and carcinogenicity studies is 6.4 mg/kg bw/day (mice study). No specific effect on the reproductive parameters was found in multigeneration studies with rats: the relevant

parental NOAEL is lower than the LOAEL of 30 mg/kg bw/day, whereas the relevant reproductive and offspring NOAEL was 3200 mg/kg bw/day. Tested in developmental toxicity studies, diflubenzuron did not cause malformations in the rat or rabbit. The relevant maternal and developmental NOAEL is 1000 mg/kg bw/day (highest dose level tested, rat and rabbits). The Acceptable Daily Intake (ADI) of 0.1 mg/kg bw/day was derived from the 1 year dog study supported by the 91-week mouse study applying a SF of 100. The Acute Reference Dose (ARfD) is not allocated as it is not necessary. The Acceptable Operator Exposure Level (AOEL) of 0.033 mg/kg bw/day is based on the 1-year dog study with a correction for oral absorption of 33% and a SF of 100. The operator exposure is below the AOEL for the use on pome fruit, mushrooms (automatic sprayer) and in forestry (ground application) without the use of Personal Protective Equipment (PPE). Operator exposure is below the AOEL for hand-held application on mushrooms with the use of PPE. The operator exposure in forestry by aircraft application is inconclusive. The worker and bystander exposure was estimated to be below the AOEL for all scenarios considered.

A sufficient number of residue trials on apples supporting the notified GAPs have been submitted to propose MRLs for apples and pears. The available residue trials on mushrooms have not been carried out in accordance with the residue definition and no MRL was proposed for mushrooms. A data gap concerning a complete new data set has been identified. Whereas studies on the frozen storage stability showed satisfactory results for diflubenzuron and CPU, results for PCA were regarded as not conclusive. The notifier was asked to further investigate the storage stability of PCA. A data gap was identified concerning a hydrolysis study simulating pasteurisation to investigate the effect of processing on the nature of residues. Depending on the results of this study new processing studies on apples might be necessary. In the submitted studies, samples were only analysed for diflubenzuron.

Metabolism studies on dairy cattle and laying hens showed a low transfer of diflubenzuron residues into tissues, milk and eggs. Metabolism was extensive. Besides diflubenzuron, the following metabolites were identified: CPU, PCA and PCAA. It was decided to include diflubenzuron and CPU in the risk assessment for monitoring in animal matrices, as they were regarded as suitable indicators for diflubenzuron residues. As the toxicological evaluation of the metabolites is not yet finalised, it was decided to include all metabolites identified in a provisional residue definition for risk assessment. In the absence of sufficient information on the effect of processing on the nature and level of residues, a provisional dietary burden calculation was carried out. It was decided that on the basis of this calculation either a feeding study on ruminants was necessary or a justification that no feeding study was necessary.

A provisional chronic dietary intake calculation showed that an exceedance of the ADI set by the toxicology meeting is not expected for intake of pome fruit and wild berries after applications of diflubenzuron according to the notified GAPs.

Diflubenzuron may be considered as low persistent in soil under dark aerobic conditions ($DT_{50\ norm}$ = 2.0 – 6.7 d). Upon degradation, it yields two major metabolites: DFBA and CPU. DFBA exhibits low persistence in soil ($DT_{50\ 20\ °C}$ = 3.3 – 9.0 d) and CPU may be considered moderately persistent ($DT_{50\ 20\ °C}$ = 15.2 – 30.6 d). A flooded soil study under anaerobic

conditions was presented by the notifier as a surrogate for the anaerobic degradation in soil. In this study degradation is slower than under aerobic conditions. No new metabolites were found in this study.

Photolysis does not contribute to the degradation of diflubenzuron in soil.

Batch adsorption / desorption studies indicate that diflubenzuron is immobile to slightly mobile (K_{Foc} = 1983 – 6918 mL/g) and CPU is medium mobile in soil (K_{Foc} = 209 – 291 mL/g). Due to the weak adsorption of DFBA, it was not possible to determine reliable adsorption parameters. During the peer review, it was agreed that simulations performed assuming a Koc = 0 could be used to finalize the EU exposure assessment.

Diflubenzuron is hydrolytically stable at pH 5 and 7 and hydrolyses to CPU and DFBA at pH 9. Metabolites CPU and DFBA are stable under these conditions.

Due to the fact that biological degradation is faster than aqueous photolysis it is considered that photodegradation will not contribute to the dissipation of diflubenzuron in the environment. Diflubenzuron is considered not readily biodegradable.

Diflubenzuron exhibited low persistence in water / sediment systems (DT50 whole system = 3.7 – 5.4 d). The major metabolites formed were DFBA (max. in water 7.3-13.1 % AR; max. in sediment 3.7 % AR after 4 d) and CPU (max. in water 31.1 % AR after 8 d or 16 d; max. in sediment 15.9-21.0 % AR after 16 d or 30d). Half-lives of the metabolites DFBA (DT_{50} whole system = 1.6 – 4.4 d) and CPU (DT_{50} whole system = 26.9 – 52.5 d) were calculated in the available study.

$PEC_{SW/SED}$ were calculated based on the uses of 'Dimilin WG 80' on pome fruit and in forestry.

For forestry (aerial and hand application) the RMS provided calculations of PEC_{SW} for parent and metabolites based only on the spray drift route of entry to surface waters assuming a drift value of 33.2 % for aerial application and of 8.02% for hand application (vines application at > 50 cm is assumed to have the same drift as a hand application). The meeting of experts agreed with the PEC_{SW} for aerial application in forestry calculated by the RMS and presented in the addendum (December 2008). It was noted that PEC_{SED} were not calculated. The meeting of experts agreed that EFSA will highlight in the conclusion that when addressing the risk for aquatic insects, exposure via sediment needs to be addressed.

In a late stage clarification on the GAP, the notifier indicated that a hand-held sprayer could also be used in orchards and a tractor mounted sprayer could be used in forests. These application practices have not been evaluated and a data gap was identified by the meeting of experts for these $PEC_{SW/SED}$.

Potential contamination of groundwater by diflubenzuron and its soil metabolites has been assessed with FOCUS PELMO v. 3.3.2. The 80th percentile at 1m depth for each of the compounds was below 0.002 µg/L for all the nine scenarios simulated. A data gap is identified since at least two different models need to be used. However, in this case, it may be concluded that contamination of ground water will not occur when the product is used

according the proposed representative uses. Member States may require a calculation with a second model for confirmatory purposes.

New FOCUS GW (FOCUS PELMO v. 3.3.2 and FOCUS PEARL v. 3.3.3) modelling using a Koc = 0 for metabolite DFBA was requested during the peer review. The meeting of experts accepted the results of this modelling exercise, which indicates that the ground water limit of 0.1 µg/L was respected for the nine scenarios assessed for the use in orchards. However, a data gap was identified for the inclusion of the report in the updated dossier to be submitted to the Member States and EFSA.

A data gap for the full exposure assessment in soil, surface water and ground water for the representative use in protected mushrooms was identified by the meeting of experts.

According to the available information, long range transport and deposition of diflubenzuron may be considered negligible.

Diflubenzuron was very toxic to aquatic invertebrates. No-spray buffer zones of 30 m and 20 m were not sufficient to achieve TERs above the trigger. Furthermore the risk to amphipods and other sensitive arthropods with longer life cycles (univoltine insect species) needs to be addressed. Uncertainty remained with regard to the risk to bees since increased mortality of adult bees was observed in one of the field studies. It was not possible to exclude that the outdoor uses pose a high risk to bees on the basis of the peer reviewed data. Risk mitigation measures such as restriction of the use to non-flowering crops or specific growth stages are required to protect honey bees. Juvenile non-target arthropods were very sensitive to diflubenzuron. Very large in-field no-spray buffer zones would be needed to protect non-target arthropods (more than 75 m for the use in orchards). No higher-tier studies (aged residues studies, semi-field or field studies) were submitted to refine the risk assessment. It was concluded that the risk to non-target arthropods is high and that it needs to be demonstrated that recovery/recolonisation is possible within one year.

A conclusion on the risk to aquatic organisms from the use in mushrooms can only be drawn after a reliable estimation of exposure of surface water will be made available. The risk to all other groups of non-target organisms was considered to be low.

The risk to birds and mammals, earthworms, other soil non-target macro-organisms, soil micro-organisms and biological methods of sewage treatment was assessed as low for the representative uses in orchards and forestry.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- Diflubenzuron should not be applied during flowering of the crop in order to protect bees (see section 5.3).

ISSUES THAT COULD NOT BE FINALISED

- Use on protected mushrooms is not covered by the environmental risk assessment peer reviewed at EU level due to the lack of data (see chapter 4).

CRITICAL AREAS OF CONCERN

- Lack of peer reviewed specification and assessment of the equivalence of the batches tested in all the mammalian toxicity studies compared to the representative specification. This is particularly important because of the unknown concentration of the carcinogenic impurity PCA in the batches tested in the carcinogenicity studies.
- The risk to aquatic organisms (the refined TERs for zooplankton were below the trigger even with no-spray buffer zones of 20-30 m, in addition a data gap was identified to address the risk to aquatic organisms with longer life cycles like amphipoda and univoltine insect species).
- The risk to bees (increased mortality of bees was observed after exposure as larvae in one of the field studies, this needs to be addressed further, in the meantime risk mitigation measures are suggested in order to protect bees).
- The risk to non-target arthropods (In-field no-spray buffer zones up to 75 m would be needed for a safe use in orchards. Therefore a data gap was identified to demonstrate that recovery/recolonisation would be possible within 1 year.).

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APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

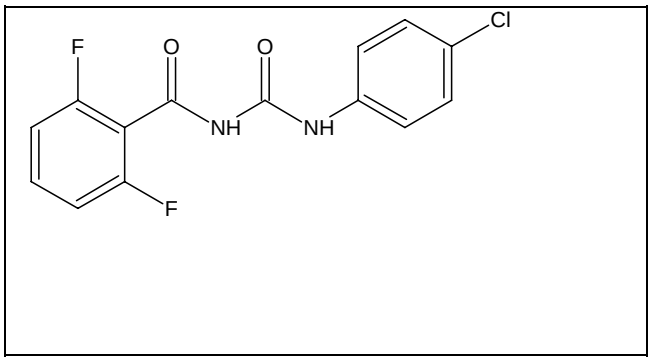
Active substance (ISO Common Name) ‡	diflubenzuron
Function (e.g. fungicide)	insecticide

Rapporteur Member State	Sweden
Co-rapporteur Member State	Not relevant

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea
Chemical name (CA) ‡	N-[[(4-chlorophenyl)amino]carbonyl]-2,6-difluorobenzamide
CIPAC No ‡	339
CAS No ‡	35367-38-5
EC No (EINECS or ELINCS) ‡	252-529-3
FAO Specification (including year of publication) ‡	None for TC
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	4-chloroaniline (PCA), CAS No.: 106-47-8, EEC No.: 203-401-0: max 0.03 g/kg
Molecular formula ‡	$C_{14}H_9ClF_2N_2O_2$
Molecular mass ‡	310.7

Structural formula ‡



Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	227.6 °C ± 0.3 °C, purity >99.5%
Boiling point (state purity) ‡	257 °C ± 0.5 °C at 40 kPa, purity 99.1%
Temperature of decomposition (state purity)	Not applicable, since no decomposition occurs at the melting point or the boiling point
Appearance (state purity) ‡	Physical state and colour: White (Munsell Notation N 9.5/) crystalline solid consisting of very fine needle-like crystals, purity 99.1% and 99.9% Odour: Faint, characteristic of aromatic compounds, at room temperature, purity 99.1%
Vapour pressure (state temperature, state purity) ‡	≤ 1.2 x 10^{-7} Pa at 25 °C, purity >99.5%
Henry's law constant ‡	≤ 4.7 x 10^{-4} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	purity >99.5% pH 4: 10 x 10 -5 g/L at 25 °C pH 7: 8 x 10 -5 g/L at 25 °C pH 10: 32 x 10-5 g/L at 25 °C
Solubility in organic solvents ‡ (state temperature, state purity)	purity 99.1->99.5% n-hexane: 0.063; toluene: 0.29; dichloromethane: 1.8; methanol: 1.1; acetone: 6.98; ethyl acetate: 0.48 (g/L at 20 ± 0.5 °C)
Surface tension ‡ (state concentration and temperature, state purity)	Not applicable, since the solubility in water is less than 1 mg/L

Partition co-efficient ‡ (state temperature, pH and purity)	At pH 3 and 22 °C ± 0.1°C Diflubenzuron: log P_{ow} = 3.89, purity 97.6% CPU: log P_{ow} =1.14 DFBA: log P_{ow} =-0.02
Dissociation constant (state purity) ‡	No data available-justification accepted
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	In acetonitrile, purity 99.9% λ_{max}: 257 nm; ε: 15148 l x mol^{-1} x cm^{-1} at 290 nm; ε: 10500 l x mol^{-1} x cm^{-1}
Flammability ‡ (state purity)	Not highly flammable and does not self-ignite, purity 99.1%
Explosive properties ‡ (state purity)	Not explosive, purity 99.1%
Oxidising properties ‡ (state purity)	Not oxidizing, purity 99.1%

Summary of representative uses evaluated (diflubenzuron)*

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preperation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					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	water L/ha min max	kg as/ha min max		
Apples and pears	EU	Dimilin WG-80	F	Apple rust mite, Codling moth, Leafminers, Leafrollers, Pear suckers	WG	800 g/kg	Tractor-mounted and Hand-held sprayer*	Spring or autumn application depending on the pest to be controlled	max. 2	14-28 days	0.012	1500	0.18	14 days	Major crop The environmental risk assessment could not be concluded due to data gaps
Mushrooms	EU	Dimilin WG-80	I	Sciarid flies	WG	800 g/kg	Automatic and Hand-held sprayer	Course spray: Immediate after casing	1 per crop cycle	N.A.	0.1	1-1.5 L/m^2	1 g a.s./m^2	N.A.	Minor crop Environmental risk assessment not concluded due to data gaps The consumer risk assessment could not be concluded due to data gaps.
Forestry	EU	Dimilin WG-80	F	Various Lepidopterous and non-Lepidopterous	WG	800 g/kg	Aerial application, including ULV and	Dependent on pest to be controlled	max. 1	N.A.			0.048	N.A.	The environmental risk assessment could not be concluded due to data gaps

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Preperation		Application				Application rate per treatment			PHI (days)	Remarks:
(a)			(b)	(c)	Type	Conc. of as	method kind	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max	(l)	(m)
					(d-f)	(i)	(f-h)								
				forest pests			LV				1.6 0.16	3-5 30-50			[2]
							Ground application with tractor mounted** or hand-held spray				0.008	600			

*Exposure assessment to surface water for the application with hand held sprayer is not finalized.
**Exposure assessment to surface water for the application with the tractor mounted sprayer is not finalized.
[1] A high risk and/or data gaps were identified in section 5 (ecotoxicology)
[2] The environmental risk assessment could not be finalised because no exposure assessment was available (data gap identified in section 4, fate and behaviour)..

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)	HPLC-UV
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Fruit crops foliar application: diflubenzuron Mushrooms soil application: DFBA
Food of animal origin	Diflubenzuron and CPU expressed as diflubenzuron.
Soil	diflubenzuron
Water surface	diflubenzuron
drinking/ground	diflubenzuron
Air	diflubenzuron

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	<u>Apples:</u> HPLC-UV (HPLC-MS for confirmation); LOQ: 0.1 mg/kg (diflubenzuron) Open for mushrooms (method does not cover proposed residue definition for monitoring)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Open as it is not yet clear if MRLs will be needed

Soil (analytical technique and LOQ)	LC-MS/MS; LOQ: 0.005 mg/kg (diflubenzuron) and 0.01 mg/kg (4-chlorphenylurea and 2,6-difluorobenzoic acid)
Water (analytical technique and LOQ)	LC-MS/MS (surface water); LOQ: 0.100 µg/L (diflubenzuron, 4-chlorphenylurea and 2,6-difluorobenzoic acid) Method acceptable for drinking water; surface water open due to insufficient LOQ
Air (analytical technique and LOQ)	Open
Body fluids and tissues (analytical technique and LOQ)	not required

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

	RMS/peer review proposal
Active substance	None

Impact on Human and Animal Health

EFSA note after the written procedure: the RMS informed EFSA that under the biocide application[10], diflubenzuron was discussed at the Biocide Technical Meeting held in Arona, March 2009 [11] According to the RMS, the database available was different from the one discussed in the PRAPeR 64. Based on that dataset, the metabolism and the reference values for diflubenzuron might be different. The issue has been highlighted to the Commission for consideration.

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

Rate and extent of oral absorption ‡	Oral absorption approx. 33%, based on urinary excretion
Distribution ‡	Uniformly distributed
Potential for accumulation ‡	No evidence of accumulation
Rate and extent of excretion ‡	Excretion almost complete in 24 hours
Metabolism in animals ‡	Extensively metabolised (approx.40% by dechlorination, glucuronidation, sulphation and hydrolysis).
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound, PCA and metabolites
Toxicologically relevant compounds ‡ (environment)	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 4640 mg/kg bw	
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 2.5 mg/L, 4h (nose-only, dust)	
Skin irritation ‡	Non-irritant	

[10] Evaluated under Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market

[11] Biocides Technical Meeting (TM I 09). Arona, Italy, 16-20 March 2009

Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Non-sensitizer (Magnusson &Kligman)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Haemolytic anaemia	
Relevant oral NOAEL ‡	Rat (90-day): 11 mg/kg bw/d Mouse (90-day): 9.7 mg/kg bw/d Dog (1-year): 10 mg/kg bw/d	
Relevant dermal NOAEL ‡	Rat (21-day): 1000 mg/kg bw/d (highest dose level tested). Rabbit (3-weeks): 322 mg/kg bw/d (highest dose level tested).	
Relevant inhalation NOAEL ‡	Rat (4-weeks): 0.1 mg/L (highest dose level tested). Rabbit (3-weeks): 1.9 mg/L (highest dose level tested).	

Genotoxicity ‡ (Annex IIA, point 5.4)

……	No genotoxic potential	

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

Target/critical effect ‡	Haemolytic anaemia	
Relevant NOAEL ‡	Rat (2-years): 31 mg/kg bw/d Mouse (91-weeks): 6.4 mg/kg bw/d	
Carcinogenicity ‡	No carcinogenic potential	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No effect on reproduction Parental: Haemolytic anaemia No effects on the offspring	
Relevant parental NOAEL ‡	LOAEL: 30 mg/kg bw day^{-1} (lowest dose level tested)	
Relevant reproductive NOAEL ‡	3200 mg $kg^{-1}day^{-1}$ (highest dose level tested)	
Relevant offspring NOAEL ‡	3200 mg $kg^{-1}day^{-1}$ (highest dose level tested)	

Developmental toxicity

Developmental target / critical effect ‡	No developmental, no maternal effects	
Relevant maternal NOAEL ‡	Rat & rabbit NOAEL: 1000 mg $kg^{-1}day^{-1}$ (highest dose level tested)	
Relevant developmental NOAEL ‡	Rat & rabbit NOAEL: 1000 mg $kg^{-1}day^{-1}$ (highest dose level tested)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data, no study required	
Repeated neurotoxicity ‡	No data, no study required	
Delayed neurotoxicity ‡	No data, no study required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data, no study required

Studies performed on metabolites or impurities ‡	Limited information available, further information / evaluation required for CPU, PCA (Carc. Cat.2) and DFBAM

Medical data ‡ (Annex IIA, point 5.9)

…… ……..	No evidence of adverse effects to workers of manufacturing plants, agricultural worker and consumers

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.1 mg $kg^{-1}day^{-1}$	1 year dog	100
AOEL ‡	0.033 mg $kg^{-1}day^{-1}$	1year dog	100 (33 % oral abs)
ARfD ‡	Not allocated- not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (Dimilin WG-80)	Active substance tested considered to be representative for the formulation. Concentrate and spray dilution: 6% Rat *in vivo* study

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Pome fruit: Tractor-mounted sprayer UK POEM: 66% of AOEL with gloves during mixing and loading and during application. German model: 52% of AOEL without PPE. Hand-held sprayer UK POEM: 19% of AOEL with gloves during mixing and loading and during application. German model: 31% of AOEL without PPE Forestry: German model Ground application - tractor mounted sprayer 14 % of AOEL without PPE Ground application – hand held sprayer 8 % of AOEL without PPE Aircraft Application: inconclusive. Mushrooms German model Automatic sprayer 83 % of AOEL without PPE Hand-held sprayer 46 % of AOEL with gloves during mixing and loading and gloves, coverall and sturdy footwear during spraying
Workers	Pome fruit: 59% of AOEL Forestry: 4% of AOEL Mushrooms: 10 % of AOEL
Bystanders	Pome fruit: 3.5 % of AOEL Forestry: ≤3.5 % of AOEL Mushrooms: Not relevant

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

	RMS/peer review proposal
Substance (name)	RMS: No classification

Residues

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

Plant groups covered	Fruit group (apples and oranges) after foliar treatment, and fruit group (mushrooms) after soil treatment (growth medium/casing).
Rotational crops	Not applicable (a)
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable (a)
Processed commodities	A data gap concerning a hydrolysis study simulating pasteurization (relevant for apples) has been formulated. Concerning mushrooms it was decided that the main component in mushrooms DFBA is not expected to metabolize further during processing. Therefore, it was decided that no study on the effect of processing on the nature of residues (hydrolysis study simulating pasteurization) is necessary.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No information on the effect of processing on the nature of residues for apples is available (data gap). The main component in mushrooms DFBA is not expected to metabolize further during processing.
Plant residue definition for monitoring	For fruit crops after foliar application: diflubenzuron, For mushrooms after soil application: 2,6-difluorobenzoic acid

Plant residue definition for risk assessment	For fruit crops after foliar application (provisional): diflubenzuron; pending further information on the nature of the residues in processed fruit (data gap). For mushrooms after soil application (provisional): (1) 2,6-difluorobenzoic acid (2) Sum of diflubenzuron + 4-chlorophenylurea + 4-chloroaniline expressed as 4-chloroaniline; pending the finalisation of the toxicological evaluation of the metabolites.
Conversion factor (monitoring to risk assessment)	None

(a) EFSA notes that if the further evaluation in the fate section shows that significant residues of diflubenzuron or its metabolites are expected on agricultural land where mushroom compost has been used, the possible occurrence of residues in crops grown on such agricultural land has to be addressed also.

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

Animals covered	Poultry (laying hen) and ruminants (lactating goat)
Time needed to reach a plateau concentration in milk and eggs	Milk: The metabolism study was carried out for 3 days only. It is not possible to conclude if a plateau was reached during this time. Egg white: 2.5 days Egg yolk: 7.5 days
Animal residue definition for monitoring	Diflubenzuron and 4-chlorophenylurea expressed as diflubenzuron
Animal residue definition for risk assessment	Provisional**:** Sum of diflubenzuron + 4-chlorophenylurea + 4-chloroaniline + 4-chloroacetanilide expressed as 4-chloroaniline pending the finalisation of the toxicological evaluation of the metabolites
Conversion factor (monitoring to risk assessment)	None

Metabolism in rat and ruminant similar (yes/no)	Yes.
Fat soluble residue: (yes/no)	Yes.

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

……	Not applicable (a)

(a) EFSA notes that if the further evaluation in the fate section shows that significant residues of diflubenzuron or its metabolites are expected on agricultural land where mushroom compost has been used, the possible occurrence of residues in crops grown on such agricultural land has to be addressed also.

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

	Apples: Diflubenzuron was stable for 12 months at –18 °C. Mushrooms: Diflubenzuron was stable for 18 months at – 18 °C 4-chlorophenylurea was stable for 19 months at –18 °C, 4-chloroaniline was not stable under theses conditions: Notifier to investigate the stability of 4-chloroaniline during frozen storage (data gap). Studies on the storage stability of diflubenzuron, 4-chlorophenylurea and 4-chloroaniline are available in the DAR as part of the metabolism study on livestock. EFSA notes that the presentation of the results in the DAR does not allow full evaluation of the validity of these studies and their results. If they are needed to support feeding studies in livestock, full evaluation will be necessary.

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

The dietary burden calculation could not be finalised, as the study on the effect of processing on the nature of residues (hydrolysis study simulating pasteurisation of apples) was outstanding and the residue definition for risk assessment for animal matrices was not finalised. The meeting carried out a provisional dietary burden calculation considering the intake of diflubenzuron only. For a STMR for apples of 0.41 mg/kg and a mean processing factor for apples to pomace of 3.2 the following intake was calculated: 0.6 mg/kg feed (DM) for diary cattle and 1.7 mg/kg feed (DM) for beef cattle.

Data gap: Notifier to provide either a feeding study in ruminants or a justification on the basis of the metabolism study showing that a feeding study is not required.

	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)			
Potential for accumulation (yes/no):			
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)			
	Feeding studies Residue levels in matrices : Mean (max) mg/kg		
Muscle			
Liver			
Kidney			
Fat			
Milk			
Eggs			

Summary of residues data according to the representative uses on raw agricultural commodities and feeding stuffs (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)
Apple	Northern	0.10, 2 x 0.16, 0.20, 0.32, 0.39, 0.43, 0.44, 0.45, 0.50, 2 x 0.52	Only four of the trials were performed with Dimilin WG 80, the other was performed with Dimilin 25 WP. However bridging studies in whole fruit and processed fruit did not show any significant difference in residues between the 2 formulations. EFSA notes that four of the trials were carried out as parallel trials comparing two different formulations of diflubenzuron. However, deletion of the lower results of each of the parallel trials would not significantly change the overall results.	1.0	0.52	0.41

Apples	Southern	0.24, 0.35, 0.35, 0,35, 0.37, 0.41, 0.46, 0.55	All trials were performed with Dimilin 25 WP	1.0	0.55	0.36
Mushrooms	Green houses indoor		The submitted trials were not carried out in accordance with the proposed residue definition. Data gap: A complete data base of residue trials on mushrooms in compliance with the residue definition for risk assessment is necessary.			

(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

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

EFSA notes that the RMS has informed EFSA after the drafting of the conclusion that under the biocide application an ADI of 0.012 mg/kg bw/day has been set (see section 2.10) and that it could not be excluded that PCA is formed in humans exposed to diflubenzuron (section 2.8). **Should these information be validated, a risk for the consumer could not be excluded in this case**.

ADI	0.1 mg kg^{-1} day^{-1}
TMDI (% ADI) according to WHO European diet	-
TMDI (% ADI) according to EFSA PRIMO rev.2 model diets	Maximum TMDI DE Child: **13,7%** NL Child: **7,4%**
IEDI (WHO European Diet) (% ADI)	-
NEDI (specify diet) (% ADI)	Not applicable since TMDI calculations demonstrate that the ADI will no be exceeded
Factors included in IEDI and NEDI	
ARfD	No ARfD is established
IESTI (% ARfD)	Not applicable
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not applicable
Factors included in IESTI and NESTI	Not applicable

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 wet pomace	3	3.2 (a)		
Apple juice	3	<0.2 (a)		
Apple raw Juice	3	<0.2 (a)		
Apples puree	3	<0.2 (a)		

Mushrooms	(b)			

(a) Provisional: depending on the results of the hydrolysis study simulating pasteurisation (data gap) new processing studies may be necessary.

(b) The submitted studies have not been carried out in accordance with the proposed residue definition in mushrooms. EFSA notes that the necessity of processing studies on mushrooms in accordance with the residue definition should be decided when new residue data on mushrooms and the consumer risk assessment for the consumption of mushroom are available.

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

Apple	1.0 mg/kg

Fate and Behaviour in the Environment

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

Mineralization after 100 days ‡	39.5-41.2 % after 59 d (n=3); 26.3 % after 21 d (n=1), labelled in both phenyl groups
Non-extractable residues after 100 days ‡	48.3-55 % (after 59 d, n=3); 37.4 % after 21 d (n=1)
Metabolites requiring further consideration‡ - name and/or code, % of applied (range and maximum)	2,6-difluorobenzoic acid (DFBA) 7.1-13.3 % at day 3-13 (n=3), 4-chlorophenylurea (CPU) 19.2-30.1% at day 13 (n=3)

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

Anaerobic degradation ‡

Mineralization after 100 days	2.77 % mineralisation after 90 d;
Non-extractable residues after 100 days	35 %
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	2,6-difluorobenzoic acid (DFBA) 44.7 % at day 90 (n=1), 4-chlorophenylura (CPU) 32.2% at day 90 (n=1)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	9 % mineralisation after 16 d; main metabolites CPU. This is a minor route in the overall soil degradation process

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

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X[12]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		5.6	24 / 10.5	2.2 / 7.4	2.0	0.99	SFO
Sandy loam		7.2	20 / 40	6.7 / 22.2	6.7	0.99	SFO
Clay/silty loam		6.5	20 / 35	2.6 / 8.6	2.3	0.99	SFO
Clay loam		7.4	20 / 40	3.6 / 12	3.3	0.9	SFO
Geometric mean					3.2		
CPU (4-chlorophenylurea)	Aerobic conditions						
Sandy loam		7.2	20 / 40	19.3/64.2	19.3	0.99	SFO
Clay/silty loam		6.5	20 / 35	16.8/55.7	15.2	0.99	SFO
Clay loam		7.4	20 / 40	33.6/111.8	30.5	0.9	SFO
Geometric mean					20.7		
DFBA (2,6-difluorobenzoic acid)	Aerobic conditions						
Sandy loam		7.2	20 / 40	9/30	9.0	0.99	SFO
Clay/silty loam		6.5	20 / 35	7.9/26.3	7.1	0.99	SFO
Clay loam		7.4	20 / 40	3.6/11.9	3.3	0.9	SFO
Geometric mean					5.9		

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

pH dependence ‡ (yes / no) (if yes type of dependence)	no
Soil accumulation and plateau concentration ‡	Not required

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	X[13]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Silty loam		7.4	24 / -	32 / 107		0.97	SFO

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
Sandy clay soil	1.41	6.8	-	-	97.7	6918	1.22
Silty clay loam soil	1.35	6.0	-	-	92.0	6801	1.21
Sand	1.2	6.2	-	-	34.2	2780	0.97
Sandy clay	1.9	6.7	-	-	36.8	1983	0.99
Arithmetic mean/median						4620	
pH dependence, Yes or No			no				

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

Metabolite CPU (4-chlorophenylurea)‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sand soil	0.4	6.0	-	-	1.2	291	0.74
Sand soil	2.5	5.5	-	-	6.0	237	0.79
Sandy loam soil	0.9	6.6	-	-	2.3	244	0.79
Loam soil	1.5	7..5	-	-	3.2	209	0.79
Arithmetic mean/median						245	
pH dependence (yes or no)			no				
Metabolite DFBA (2,6-difluorobenzoic acid)							
Data not available and not required when a default of 0 mL/g can be used in exposure assessment							

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

Column leaching ‡	Not required
Aged residues leaching ‡	Not required
Lysimeter/ field leaching studies ‡	Not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	The worst case laboratory DT_{50} of 6.7 days was used (first order kinetics).
Application data	Crop: Pome fruit Crop interception: 50 % Number of applications: 2: Interval (d): 14 Application rate:180 g/ha (max. application rate for the proposed use in orchards)

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application TWA	Two applications Actual	Two applications TWA
Initial	0.12		0.15	
Short term				
24h	0.108	0.11	0.13	0.14
2d	0.098	0.11	0.12	0.13
4d	0.079	0.098	0.098	0.12
Long term				
7d	0.058	0.085	0.072	0.11
28d	0.0066	0.039	0.008	0.048
45d	0.001	0.026	0.001	0.032
100d	0.000	0.023	0.000	0.014

Metabolite 4-chlorophenylurea (CPU	Molecular weight relative to the parent: degradation to 4-chlorophenylurea (CPU) was assumed to be a complete and instantaneous process in order to provide a simplified 'worst-case' scenario where each molecule of diflubenzuron was assumed to be converted into one molecule of CPU, i.e. each gram of diflubenzuron applied would be converted to 0.55 gram of CPU.
Method of calculation	DT_{50} (d): 33.6 days Kinetics: SFO Field or Lab: representative worst case from field studies.
Application data	Application rate assumed: See parent

PEC$_{(s)}$ (mg/kg fw)	Single application Actual	Single application TWA	Multiple application Actual	Multiple application TWA
Initial	0.066		0.115	
Short term				
24h	0.065	0.065	0.113	0.114
2d	0.063	0.065	0.111	0.113
4d	0.061	0.063	0.106	0.111
Long term				
7d	0.057	0.061	0.100	0.107
28d	0.037	0.050	0.065	0.088
50d	0.026	0.043	0.046	0.075
100d	0.008	0.028	0.015	0.049

Metabolite 2,6-difluorobenzoic acid (DFBA) Method of calculation	Molecular weight relative to the parent. Degradation to 2,6-difluorobenzoic acid (DFBA) was assumed to be a complete and instantaneous process in order to provide a simplified 'worst-case' scenario where each molecule of diflubenzuron was assumed to be converted into one molecule of DFBA, i.e. each gram of diflubenzuron applied would be converted to 0.51 gram of DFBA. DT_{50} (d): 9 days Kinetics: SFO Field or Lab: representative worst case from field studies.
Application data	Application rate assumed: See parent

PEC$_{(s)}$ (mg/kg fw)	Single application Actual	Single application TWA	Multiple application Actual	Multiple application TWA
Initial	0.061		0.082	
Short term				
24h	0.057	0.059	0.076	0.079
2d	0.052	0.057	0.070	0.076
4d	0.045	0.053	0.060	0.071
Long term				
7d	0.036	0.047	0.048	0.063
28d	0.007	0.025	0.009	0.034
50d	0.002	0.017	0.003	0.023
100d	0.000	0.008	0.000	0.011

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	No degradation at pH 5 or 7. Degradation to 4-chlorophenylurea (CPU) and 2,6-difluorobenzoic acid (DFBA) at pH 9. Major metabolites CPU and DFBA both have DT_{50} of greater than one year at pH 4, 7 and 9 (25°C).
Photolytic degradation of active substance and metabolites above 10 % ‡	Minor route of degradation
Quantum yield of direct photo transformation in water at Σ > 290 nm	4.7×10^{-5} mol/Einstein
Readily biodegradable ‡ (yes/no)	No

Degradation in water / sediment

Parent	Distribution (max 72% in water after 0 d. Max. sed 24.4 x % after 4 d)									
Water/sediment system	**pH w**	**pH sed**	**t. °C**	**DT50 / DT90 whole**	**St. (r^2)**	**DT50 /DT90 water**	**St. (r^2)**	**DT50-DT90 sed**	**St. (r^2)**	**Method of calculation**
River system	6.5	7.05	20	5.4/17.8	0.99	3.2/10.6	0.99	-	-	SFO
Pond system	6.97	6.77	20	3.7/12.3	0.99	2.8/9.4	0.99	-	-	SFO
Geometric mean				4.5/14.8		3.0/10.0		-		
CPU (4-chlorophenylurea)	Distribution (max in water 31% after 16 d., in sed 21 % after 30 d, in whole syst. 48 % after 16 d))									
River system	6.5	7.05	20	26.9/89.4	0.99	18.1/60.3	0.99	-	-	SFO
Pond system	6.9	6.77	20	52.5/174.4	0.99	31.8/105.6	0.97	-	-	SFO
Geometric mean				37.6/124.9		24.0/79.8		-		
DFBA (2,6-difluorobenzoic acid)	Distribution (max in water 13% after 4 d., max. sed 3.7 % after 4 d, in whole syst. 17 % after 4 d)									
River system	6.5	7.05	20	1.6/5.2	0.99	1.5/5.0	0.98			SFO
Pond system	6.97	6.77	20	4.4/14.7	0.99	4.2/14.0	0.98			SFO
Geometric mean				2.7/8.7		2.5/8.4				

Mineralisation and non extractable residues					
Water / sediment system	pH w	pH sed	Mineralisation	Non-extractable residues in sed.	Non-extractable residues in sed.
			% after 104 d (end of the study)		
River system	6.5	7.05	33.1	36.4	36.4
Pond system	6.97	6.77	37.5	44.4	44.4

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

Method of calculation	Focus surface water simulations for the use in orchards For the use in forestry PEC was calculated assuming spray drift (Rautmann 1999) over a 30 cm deep water body.

PECsw Parent - Orchard

Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 310.7 Water solubility (mg/L): 0.08 Koc/Kom (L/kg): 4609 DT_{50} soil (d): 3.7 days DT_{50} water/sediment system (geometric mean): DT_{50} water (d): 4.5 (DT_{50} for total system) DT_{50} sediment (d): 4.5 (DT_{50} for total system)
Parameters used in FOCUSsw step 3 (if performed)	Vapour pressure: Koc/Kom: 4609*/2673 1/n: 1.1 DT_{50} soil (at pF2): 3.2
Application rate	Crop: pome fruit Crop interception: 20% Number of applications: 2 Interval (d): 14 d Application rate(s): 180 g as/ha Application window: 01 Apr- 20 May; 18 Mar-06 May; 01 Mar-19 Apr depending on scenario

*The correct value that should have been used is the arithmetic mean of 4629 mL/g. However experts at the PRAPeR 62 agreed that no new simulation is needed since this difference is not likely to have a significant influence on the outcome of the modelling.

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	Initial	15.6664		86.7006	
	24 hours	5.9006	10.7835	77.9501	82.3254
	2 days	3.2079	7.6689	66.8223	77.3558
	4 days	2.537	5.1264	49.1055	67.4896
	7 days	1.2429	3.6481	30.9345	55.4514
	14 days	0.4228	2.2051	10.5238	37.2093
	21 days	0.1438	1.5565	3.5802	26.9571
	28 days	0.0489	1.1894	1.218	20.7666
	42 days	0.0057	0.7996	0.141	14.0112
Southern EU	Initial	15.6664		118.0954	
	24 hours	5.9006	10.7835	104.8631	111.4792
	2 days	3.2079	7.6689	89.8933	104.4287
	4 days	3.2181	5.2115	66.0596	90.9736
	7 days	1.672	3.931	41.615	74.7008
	14 days	0.5688	2.478	14.1573	50.1083
	21 days	0.1935	1.7683	4.8163	36.299
	28 days	0.0658	1.3559	1.6385	27.9625
	42 days	0.0076	0.9129	0.1896	18.8661

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D3	ditch	0	11.989		-	-
		24	5.199	8.989	-	-
		2d	0.659	5.702	-	-
		4d	0.069	2.955	-	-
		7d	0.023	1.706	-	-
		14d	0.004	0.858	-	-
		21d	0.001	1.112	-	-
		28d	0.000	0.839	-	-
		42d	0.000	0.560	-	-
D4	pond	0	0.976		-	-
		24	0.881	0.926	-	-
		2d	0.800	0.883	-	-
		4d	0.666	0.806	-	-
		7d	0.512	0.712	-	-
		14d	0.284	0.549	-	-
		21d	0.160	0.516	-	-
		28d	0.088	0.511	-	-
		42d	0.020	0.413	-	-
D4	stream	0	11.400		-	-
		24	0.000	0.650	-	-

		2d	0.000	0.325	-	-
		4d	0.000	0.163	-	-
		7d	0.000	0.093	-	-
		14d	0.000	0.047	-	-
		21d	0.000	0.058	-	-
		28d	0.000	0.043	-	-
		42d	0.000	0.029	-	-
D5	pond	0	0.989		-	-
		24	0.905	0.945	-	-
		2d	0.832	0.906	-	-
		4d	0.709	0.837	-	-
		7d	0.565	0.750	-	-
		14d	0.287	0.585	-	-
		21d	0.140	0.543	-	-
		28d	0.069	0.512	-	-
		42d	0.016	0.392	-	-
D5	stream	0	12.494		-	-
		24	0.000	0.836	-	-
		2d	0.000	0.418	-	-
		4d	0.000	0.209	-	-
		7d	0.000	0.120	-	-
		14d	0.000	0.060	-	-
		21d	0.000	0.061	-	-
		28d	0.000	0.046	-	-
		42d	0.000	0.030	-	-
R1	pond	0	0.915		-	-
		24	0.836	0.873	-	-
		2d	0.768	0.837	-	-
		4d	0.654	0.772	-	-
		7d	0.498	0.688	-	-
		14d	0.263	0.528	-	-
		21d	0.141	0.431	-	-
		28d	0.076	0.462	-	-
		42d	0.019	0.387	-	-

R1	stream	0	9.629		-	-
		24	0.003	1.655	-	-
		2d	0.002	0.829	-	-
		4d	0.001	0.415	-	-
		7d	0.000	0.237	-	-
		14d	0.000	0.119	-	-
		21d	0.000	0.158	-	-
		28d	0.000	0.119	-	-
		42d	0.000	0.079	-	-
R2	stream	0	12.756		-	-
		24	0.001	1.080	-	-
		2d	0.001	0.540	-	-
		4d	0.000	0.270	-	-
		7d	0.000	0.155	-	-
		14d	0.058	0.079	-	-
		21d	0.000	0.054	-	-
		28d	0.000	0.077	-	-
		42d	0.000	0.053	-	-
R3	stream	0	13.622		-	-
		24	0.031	4.330	-	-
		2d	0.012	2.174	-	-
		4d	0.005	1.091	-	-
		7d	0.002	0.625	-	-
		14d	0.001	0.336	-	-
		21d	0.000	0.385	-	-
		28d	0.000	0.301	-	-
		42d	0.000	0.200	-	-
R4	stream	0	0.000	0.168	-	-
		24	0.000	0.084	-	-
		2d	0.002	0.974	-	-
		4d	0.001	0.488	-	-
		7d	0.000	0.279	-	-
		14d	0.000	0.147	-	-
		21d	0.000	0.098	-	-

		28d	0.000	0.075	-	-
		42d	0.000	0.086	-	-

FOCUS STEP 4 Scenario 20 m buffer zone	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D3	ditch	0	1.415		-	-
		24	0.616	1.062	-	-
		2d	0.080	0.675	-	-
		4d	0.008	0.350	-	-
		7d	0.002	0.202	-	-
		14d	0.000	0.101	-	-
		21d	0.000	0.132	-	-
		28d	0.000	0.099	-	-
		42d	0.000	0.066	-	-
D4	pond	0	0.188		-	-
		24	0.170	0.179	-	-
		2d	0.155	0.170	-	-
		4d	0.129	0.156	-	-
		7d	0.099	0.138	-	-
		14d	0.055	0.106	-	-
		21d	0.031	0.100	-	-
		28d	0.017	0.099	-	-
		42d	0.004	0.080	-	-
D4	stream	0	1.481		-	-
		24	0.000	0.085	-	-
		2d	0.000	0.042	-	-
		4d	0.000	0.021	-	-
		7d	0.000	0.012	-	-
		14d	0.000	0.006	-	-
		21d	0.000	0.007	-	-
		28d	0.000	0.006	-	-
		42d	0.000	0.004	-	-
D5	pond	0	0.191		-	-
		24	0.175	0.182	-	-
		2d	0.161	0.175	-	-
		4d	0.137	0.162	-	-
		7d	0.110	0.145	-	-
		14d	0.056	0.113	-	-
		21d	0.027	0.105	-	-
		28d	0.013	0.099	-	-
		42d	0.003	0.076	-	-
D5	stream	0	1.624		-	-
		24	0.000	0.109	-	-
		2d	0.000	0.054	-	-

		4d	0.000	0.027	-	-
		7d	0.000	0.016	-	-
		14d	0.000	0.008	-	-
		21d	0.000	0.008	-	-
		28d	0.000	0.006	-	-
		42d	0.000	0.004	-	-
R1	pond	0	0.176		-	-
		24	0.161	0.168	-	-
		2d	0.148	0.161	-	-
		4d	0.126	0.149	-	-
		7d	0.097	0.133	-	-
		14d	0.051	0.102	-	-
		21d	0.027	0.083	-	-
		28d	0.015	0.089	-	-
		42d	0.004	0.075	-	-
R1	stream	0	1.251		-	-
		24	0.000	0.215	-	-
		2d	0.000	0.108	-	-
		4d	0.000	0.054	-	-
		7d	0.000	0.031	-	-
		14d	0.000	0.015	-	-
		21d	0.000	0.021	-	-
		28d	0.000	0.015	-	-
		42d	0.000	0.010	-	-
R2	stream	0	1.658		-	-
		24	0.000	0.140	-	-
		2d	0.000	0.070	-	-
		4d	0.000	0.035	-	-
		7d	0.000	0.020	-	-
		14d	0.058	0.011	-	-
		21d	0.000	0.009	-	-
		28d	0.000	0.010	-	-
		42d	0.000	0.008	-	-
R3	stream	0	1.770		-	-
		24	0.004	0.563	-	-
		2d	0.002	0.283	-	-
		4d	0.001	0.142	-	-
		7d	0.000	0.081	-	-
		14d	0.000	0.064	-	-
		21d	0.000	0.050	-	-
		28d	0.000	0.049	-	-
		42d	0.000	0.033	-	-
R4	stream	0	1.259		-	-
		24	0.001	0.253	-	-
		2d	0.000	0.127	-	-
		4d	0.000	0.063	-	-
		7d	0.000	0.036	-	-
		14d	0.000	0.026	-	-

		21d	0.000	0.017	-	-
		28d	0.000	0.014	-	-
		42d	0.000	0.011	-	-

FOCUS STEP 4 Scenario 30 m buffer zone	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D3	ditch	0	0.486		-	-
		24	0.212	0.365	-	-
		2d	0.028	0.232	-	-
		4d	0.003	0.120	-	-
		7d	0.001	0.069	-	-
		14d	0.000	0.035	-	-
		21d	0.000	0.045	-	-
		28d	0.000	0.034	-	-
		42d	0.000	0.023	-	-
D4	pond	0	0.083		-	-
		24	0.075	0.079	-	-
		2d	0.068	0.075	-	-
		4d	0.057	0.069	-	-
		7d	0.044	0.061	-	-
		14d	0.024	0.047	-	-
		21d	0.014	0.044	-	-
		28d	0.008	0.044	-	-
		42d	0.002	0.035	-	-
D4	stream	0	0.510		-	-
		24	0.000	0.029	-	-
		2d	0.000	0.015	-	-
		4d	0.000	0.007	-	-
		7d	0.000	0.004	-	-
		14d	0.000	0.002	-	-
		21d	0.000	0.003	-	-
		28d	0.000	0.002	-	-
		42d	0.000	0.001	-	-
D5	pond	0	0.084		-	-
		24	0.077	0.080	-	-
		2d	0.071	0.077	-	-
		4d	0.061	0.071	-	-
		7d	0.048	0.064	-	-
		14d	0.025	0.050	-	-
		21d	0.012	0.046	-	-
		28d	0.006	0.044	-	-
		42d	0.001	0.034	-	-

D5	stream	0	0.559		-	-
		24	0.000	0.037	-	-
		2d	0.000	0.019	-	-
		4d	0.000	0.009	-	-
		7d	0.000	0.005	-	-
		14d	0.000	0.003	-	-
		21d	0.000	0.003	-	-
		28d	0.000	0.002	-	-
		42d	0.000	0.001	-	-
R1	pond	0	0.078		-	-
		24	0.071	0.074	-	-
		2d	0.065	0.071	-	-
		4d	0.056	0.066	-	-
		7d	0.043	0.059	-	-
		14d	0.023	0.045	-	-
		21d	0.012	0.037	-	-
		28d	0.007	0.039	-	-
		42d	0.002	0.033	-	-
R1	stream	0	0.431		-	-
		24	0.000	0.074	-	-
		2d	0.000	0.037	-	-
		4d	0.000	0.019	-	-
		7d	0.000	0.011	-	-
		14d	0.000	0.005	-	-
		21d	0.000	0.007	-	-
		28d	0.000	0.005	-	-
		42d	0.000	0.004	-	-
R2	stream	0	0.571		-	-
		24	0.000	0.049	-	-
		2d	0.000	0.025	-	-
		4d	0.000	0.012	-	-
		7d	0.000	0.007	-	-
		14d	0.058	0.005	-	-
		21d	0.000	0.005	-	-
		28d	0.000	0.004	-	-
		42d	0.000	0.004	-	-
R3	stream	0	0.610		-	-
		24	0.002	0.296	-	-
		2d	0.001	0.159	-	-
		4d	0.000	0.080	-	-
		7d	0.000	0.046	-	-
		14d	0.000	0.037	-	-
		21d	0.000	0.025	-	-
		28d	0.000	0.024	-	-
		42d	0.000	0.016	-	-
R4	stream	0	0.433		-	-
		24	0.000	0.105	-	-
		2d	0.000	0.053	-	-

		4d	0.000	0.026	-	-
		7d	0.000	0.015	-	-
		14d	0.000	0.014	-	-
		21d	0.000	0.009	-	-
		28d	0.000	0.008	-	-
		42d	0.000	0.006	-	-

PECsw Parent - forestry

Method of calculation	Dis-DT_{50} 3 days (first order kinetics, average from laboratory studies)
Application rate	48 g a.s./ha
Main routes of entry	Spray drift over a 30 cm deep water body. For aerial application spray drift of 33.2% and for hand application 8.02 % (default buffer zones) was used.

$PEC_{(sw)}$ (µg / l) Aerial application	Single application Actual	Single application TWA	Multiple application Actual	Multiple application TWA
Initial	5.31		-	-
Short term				
24h	4.22	4.74		
2d	3.35	4.25	-	-
4d	2.11	3.47		
Long term				
7d	1.05	2.63		
14d	0.21	1.58		
21d	0.04	1.09	-	-
28d	0.01	0.82		
42d	0.00	0.55		

$PEC_{(sw)}$ (µg / l) Hand application	Single application Actual	Single application TWA
Initial	1.28	-
Short term	1.031	1.151
24h	0.830	1.039

2d 4d	0.538	0.856
Long term 7d 14d 21d 28d 42d	 0.281 0.062 0.014 0.003 0.000	 0.659 0.402 0.278 0.211 0.141

PEC$_{(sw)}$ (µg / l) Hand application	Single application actual	Single application actual	Single application actual	Single application actual	Single application actual
Bufferzone	5 m	10 m	15 m	20 m	30 m
Initial	0.58	0.20	0.10	0.07	0.04

PECsw Metabolite - Orchard

Metabolite 2,6-difluorobenzoic acid (DFBA) Parameters used in FOCUSsw step 1 and 2	Molecular weight: 158.1 Water solubility (mg/L): 3063 Soil and water metabolite Koc/Kom (L/kg): 15.7/9.1 DT50 soil (d): 6.3 days DT50 water/sediment system (d): DT50 water (d): 2.7 (whole system) DT50 sediment (d): 2.7 (whole system) Maximum occurrence observed (% molar basis with respect to the parent) Water/sediment: 16.9 % (Whole system), 13.1 (water), 3.7 (sediment) Soil: 13.3 %
Parameters used in FOCUSsw step 3 (if performed)	Vapour pressure: 0.235 Kom/Koc: 15.7/9.1 1/n: 0.9 (default) Formation fraction in soil (kdp/kf): 13.3%

Application rate	Crop: pome fruit Number of applications:2 Interval (d):14

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0	1.353		0.1282	
	24	1.0328	1.1929	0.1181	0.1231
	2d	0.7989	1.0544	0.0914	0.1139
	4d	0.9757	0.9035	0.0547	0.0929
	7d	0.4502	0.8087	0.0253	0.0695
	14d	0.0746	0.5094	0.0042	0.0407
	21d	0.0124	0.3512	0.0007	0.0278
	28d	0.0021	0.2649	0.0001	0.0209
	42d	0.0001	0.1768	0	0.0139
Southern EU	0	1.4733		0.2063	
	24	1.1372	1.3053	0.1785	0.1924
	2d	0.8797	1.1569	0.1381	0.1754
	4d	0.5265	0.9244	0.0827	0.142
	7d	0.2437	0.6864	0.0383	0.106
	14d	0.0404	0.4001	0.0063	0.0619
	21d	0.0067	0.273	0.0011	0.0423
	28d	0.0011	0.2055	0.0002	0.0318
	42d	0	0.1371	0	0.0212

Metabolite 4-chlorophenylurea (CPU) Parameters used in FOCUSsw step 1 and 2	Molecular weight: 170.6 Water solubility (mg/L): 1773 Soil and water metabolite Koc/Kom (L/kg): 245/142.1 DT50 soil (d): 22.2 days DT50 water/sediment system (d): DT50 water (d): 37.6 (whole system) DT50 sediment (d): 37.6 (whole system) Maximum occurrence observed (% molar basis with respect to the parent) Water/sediment system: 47.7 % (whole system), 31.8 % (water), 21 % (sediment) Soil: 30.8 %
Parameters used in FOCUSsw step 3 (if performed)	Vapour pressure: 0.022 1/n: 0.9 (default)

Application rate	Formation fraction in soil (kdp/kf): 30.8% Crop: pome fruit Number of applications:2 Interval (d):14

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0	7.2024		16.2527	
	1d	6.6337	6.9181	15.9558	16.1042
	2d	6.5126	6.7456	15.6643	15.9571
	4d	6.2768	6.5699	15.0973	15.6683
	7d	5.9391	6.3713	14.285	15.2481
	14d	5.2201	5.9717	12.5556	14.3251
	21d	4.5881	5.6136	11.0356	13.4766
	28d	4.0327	5.2863	9.6996	12.6959
	42d	3.1154	4.709	7.4932	11.3136
Southern EU	0	8.9801		20.5285	
	1d	8.379	8.6796	20.1535	20.341
	2d	8.2259	8.491	19.7854	20.1552
	4d	7.9282	8.2837	19.0692	19.7904
	7d	7.5016	8.0392	18.0432	19.2597
	14d	6.5934	7.5386	15.8588	18.0939
	21d	5.7952	7.0877	13.9389	17.0221
	28d	5.0936	6.675	12.2514	16.0359
	42d	3.935	5.9465	9.4646	14.2901

PECsw Metabolite - forestry

Metabolite 2,6-difluorobenzoic acid (DFBA)	Spray drift (Rautmann 1999) over a 30 cm deep water body and instantaneous degradation to metabolites.
Method of calculation	
Maximum formation	16.9 %.
DT50	2.7 d
Application rate	4.14 g a.s./ha assuming DFBA is formed at a maximum of 16.9 % (whole system)
Main routes of entry	Spray drift and transformation of a.s.

PEC(sw) (µg / l) Aerial application	Single application Actual	Single application TWA	Multiple application Actual	Multiple application TWA
Initial	0.458		-	-
Short term 24h 2d 4d	0.359 0.281 0.173	0.406 0.363 0.293	-	-
Long term 7d 14d 21d 28d 42d	0.083 0.015 0.003 0.001 0.000	0.220 0.130 0.089 0.067 0.045	-	-

PEC(sw) (µg / l) Hand application	Single application Actual	Single application TWA
Initial	0.110	-
Short term 24h 2d 4d	0.094 0.079 0.057	0.102 0.094 0.081
Long term 7d 14d 21d 28d 42d	0.035 0.011 0.003 0.001 0.000	0.065 0.043 0.031 0.024 0.016

Metabolite 4-chlorophenylurea (CPU)	
Method of calculation	Spray drift (Rautmann 1999) over a 30 cm deep water body and instantaneous degradation to metabolites.
Maximum formation	47.7 % (whole system)
DT50	24.95 d
Application rate	11.7 g/ha (assumed that CPU is formed at a maximum of 47.7 %)
Main routes of entry	Spray drift and transformation of a.s.

PEC(sw) (µg / l) Aerial application	Single application Actual	Single application TWA	Multiple application Actual	Multiple application TWA
Initial	1.29		-	-
Short term 24h 2d 4d	 1.26 1.22 1.16	 1.27 1.26 1.22	-	-
Long term 7d 14d 21d 28d 42d	 1.06 0.88 0.72 0.59 0.40	 1.17 1.07 0.98 0.90 0.76	-	-

PEC(sw) (µg / l) Hand application	Single application Actual	Single application TWA
Initial	0.311	-
Short term 24h 2d 4d	 0.304 0.298 0.285	 0.308 0.305 0.298
Long term 7d 14d 21d 28d 42d	 0.267 0.229 0.197 0.169 0.125	 0.289 0.268 0.250 0.233 0.204

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

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)	FOCUS groundwater scenarios with PELMO model (FOCUS ver 3.3.2, July 2002), according to FOCUS guidelines. Scenarios: Chateaudun, Hamburg, Jokioinen, Kremsmunster, Okehampton, Piacenza, Porto, Sevilla and Thiva. Crop: Pome fruit DT50: Diflubenzuron 3.4 d (average from 4 soils, the geometric mean is 3.7 d, but since all scenarios resulted in a PEC <0.001 µg DFB/L the RMS believes that this inconsistency will not affect the final outcome of the risk assessment); CPU 21.9 d (average from 3 soils); DFBA 7.9 d (average from 3 soils) Koc: Diflubenzuron 9148* ml/g (average of initially submitted studies); CPU 245ml/g: DFBA 0 mL/g used as a default in the absence of data
Application rate	2 x 180 g a.s./ha in orchards with a 14 days interval.

*The correct value that should have been used is the arithmetic mean of 4629 mL/g. However experts at the PRAPeR 62 agreed that no new simulation is needed since this difference are not likely to have a significant influence on the outcome of the modelling.

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

	Scenario	Parent (µg/L)	Metabolite (µg/L)		
			DFBA		CPU
		PELMO	PELMO	PEARL	PELMO
Pome fruit, orchards	Chateaudun	<0.001	0.011	0.017	<0.001
	Hamburg	<0.001	0.003	0.034	<0.001
	Jokioinen	<0.001	0.020	0.071	<0.001
	Kremsmunster	<0.001	0.006	0.015	<0.001
	Okehampton	<0.001	0.005	0.020	<0.001
	Piacenza	<0.001	0.007	0.016	<0.001
	Porto	<0.001	0.000	0.000	<0.001
	Sevilla	<0.001	0.000	0.006	<0.001
	Thiva	<0.001	0.000	0.000	<0.001

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

Direct photolysis in air ‡	Non-volatile. No data required
Quantum yield of direct phototransformation	4.7 x 10^{-5} mol/Einstein
Photochemical oxidative degradation in air ‡	DT_{50} 3.08 h
Volatilisation ‡	from plant surfaces: Negligible
	from soil: Negligible
Metabolites	

PEC (air)

Method of calculation	Not applicable

$PEC_{(a)}$

Maximum concentration	The vapour pressure of diflubenzuron is very low (2 x 10-7 Pa at 25°C) and the half-life of diflubenzuron in air is rapid (3.08 hours). Consequently, losses of diflubenzuron through evaporation will not be significant and concentrations of diflubenzuron in air will be negligible.

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: Diflubenzuron, CPU and DFBA Surface water: Diflubenzuron, CPU and DFBA Air: Diflubenzuron Groundwater: Diflubenzuron, CPU and DFBA

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

Soil (indicate location and type of study)	No data provided – none required
Surface water (indicate location and type of study)	No data provided – none required
Ground water (indicate location and type of study)	No data provided – none required
Air (indicate location and type of study)	No data provided – none required

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

Non biodegradable R53

Effects on non-target Species

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 and bobwhite quail	a.s.	Acute	LD_{50} >5000 mg/kg bw	
bobwhite quail	a.s.	Short-term	LD_{50} >1206 mg/kg bw d	
bob white quail	a.s.	Long-term	NOEC 42.7 mg/kg bw d	
Mammals ‡				
Mice and rat	a.s.	Acute	> 4 640 mg/kg	
	a.s.	Long-term	NOEL 3 678 mg/kg bw/day	

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

Crop and application rate: Orchards; 0.18 kg as/ha

Indicator species/Category	**Time scale**	**ETE**	**TER**	**Annex VI Trigger**
Tier 1 (Birds)				
Insectivorous bird	Acute	9.73	>514	10
Insectivorous bird	Short-term	5.43	222	10
Insectivorous bird	Long-term	5.43	7.9	5
Drinking water (surface water)	Acute	0.00423	1182033	10

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Drinking water(surface water)	Long-term	0.00423	10000	5
Earthworm eating bird	Long-term	0.053	809	5
Fish eating bird	Long-term	0.12	360	5
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	17.8	>261	10
Small herbivorous mammal	Long-term	5.6	651	5
Drinking water (surface water)	Acute	0.00246	1886178	10
Drinking water (surface water)	Long-term	0.00246	1495000	5
Earthworm eating mammal	Long-term	0.067	54895	5
Fish eating mammal	Long-term	0.074	49702	5

Forest; 0.048 kg as/ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird	Acute	2.6	>1923	10
Insectivorous bird	Short-term	1.45	832	10
Insectivorous bird	Long-term	1.45	29.4	5
Drinking water (surface water aerial application)	Acute	0.0014	3571428	10
Drinking water(surface water aerial application)	Long-term	0.0014	30500	5

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Drinking water (surface water hand held application)	Acute	0.0003	16666667	10
Drinking water(surface water hand held application)	Long-term	0.0003	142333	5
Drinking water (puddles hand held application)	Acute	4.32	1157	10
Drinking water(puddles hand held application)	Long-term	4.32	9.9	5
Fish eating bird	Long-term	0.36	119	5
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	4.74	> 979	10
Small herbivorous mammal	Long-term	1.34	2741	5
Drinking water (surface water, aerial application)	Acute	0.00085	5461393	10
Drinking water (surface water, aerial application)	Long-term	0.00085	4329096	5
Drinking water (surface water, hand held application)	Acute	0.00021	22656250	10
Drinking water (surface water, hand held application)	Long-term	0.00021	17958984	5
Drinking water (puddles)	Acute	2.56	1812	10
Drinking water (puddles)	Long-term	2.56	1436	5
Fish eating mammal (aerial application which is protective for hand held)	Long-term	0.22	16718	5

* the risk to earthworm-eating birds and mammals for the use in forestry was covered by the assessment for orchards which resulted in higher PECsoil values.

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	End point	Toxicity (mg/L)
Laboratory tests				
Fish *Cyprinodon variegatus*	diflubenzuron	96 h, static	LC50	> 0.13
Fish *Brachydanio rerio*	4-chlorophenylurea	96 h, static	LC50	70
Fish *Brachydanio rerio*	2,6-difluorobenzoic acid	96 h, static	LC50	> 100
Fish *Oncorhynchus mykiss*	Dimilin WG-80	96 h, static	LC50	> 102
Fish *Oncorhynchus mykiss*	diflubenzuron	21 d, semi-static	Mortality NOEC	0.2
Aquatic invertebrate *Daphnia magna*	diflubenzuron	48 h, static	Mortality EC50	0.0026 (95- %CI: 0.0017-0.0038) a.s. mg/L
Aquatic invertebrate *Daphnia magna*	4-chlorophenylurea	48 h, static	Mortality EC50	116
Aquatic invertebrate *Daphnia magna*	2,6-difluorobenzoic acid	48 h, static	Mortality EC50	>60
Aquatic invertebrate *Daphnia magna*	Dimilin WG-80	48 h, static	Mortality EC50	0.0026
Aquatic invertebrate *Daphnia magna*	diflubenzuron	21 d, flow-through	Mortality-reproduction NOEC	0.00004
Algae *Selenastrum capricornutum*	diflubenzuron	72 h, static	Cell density EC50	20
Algae *Selenastrum capricornutum*	4-chlorophenylurea	72 h, static	ECb50 ECr50	30 90

Algae *Selenastrum capricornutum*	2,6-difluorobenzoic acid	72 h, static	ECb50 ECr50	> 100 > 100
Algae *Selenastrum capricornutum*	Dimilin WG-80	72 h, static	ECr50	>80
Aquatic macrophyte *Lemna gibba*	4-chlorophenylurea	14 d, static	EC50	> 0.19
Microcosm or mesocosm tests				
A NOAEC (0.7 µg/L) for the zooplankton community can be derived from the littoral enclosure study supported by the literature data submitted by the notifier during the evaluation process. It was considered by the PRAPeR 63 that the risk to zooplankton could be addressed by this end point (0.7 µg/L) together with an AF of 5. However, for the insect community no NOAEC could be determined in the littoral enclosure study. The experts were of the opinion that the risk to insects (and amphipods) needs to be addressed by further data, to demonstrate that they are less sensitive or that a recovery can take place in an acceptable time after the exposure event.				

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

FOCUS Step2

Crop and application rate: Pome fruit; 2 applications at 180 g /ha, 14 days interval.

Test substance	N/S	Test organism	Time scale	Toxicity end point (µg/L)	$PEC_{initial,sw}$ µg a.s./L	TER	Annex VI trigger
a.s.	N & S	*D. magna*	48 h	2.6	15.67	0.17	100
CPU	S	*D. magna*	48 h	116000	8.98	1292	100
DFBA	S	*D. magna*	48 h	> 60000	1.47	40816	100
a.s.	N & S	*D. magna*	21 d	0.04	15.67	0.0026	10

Crop and application rate: Forest; 0.048 kg a.s./ha. Test substance: a.s.

Application rate (kg as/ha)	**Crop**	**Organism**	**Time scale**	**Toxicity end point (µg/L)**	**$PEC_{initial,sw}$* µg a.s./L**	**Distance (m)**	**TER**	**Annex VI Trigger**
0.048	Forest, aerial application	*D. magna*	21 d	0.04	5.31	3 m	0.008	10
0.048	Forest, hand application	*D. magna*	21 d	0.04	1.28	3 m	0.03	10

0.048	Forest, aerial application	NOEAEC zooplankton**	-	0.14	5.31	3 m	0.026	1
0.048	Forest, hand application	NOEAEC zooplankton **	-	0.14	1.28	3 m	0.109	1
0.048	Forest, hand application	NOEAEC zooplankton**	-	0.14	0.2	10	0.7	1
0.048	Forest, hand application	NOEAEC zooplankton**	-	0.14	0.07	20	2	1

* PEC based on spray drift over a static 30-cm deep waterbody. Distance x m from treated area, drift rates according to "Focus surface water scenarios in the EU evaluation process under 91/414/EEC (SANCO/4802/2001-rev-1)".
** the risk to insects (and amphipods) needs to be addressed by further data

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Crop and application rate: Pome fruit; 2 applications at 180 g /ha, 14 days interval. Test substance: a.s.

Scenario[1]	**Water body type[2]**	**Test organism[3]**	**Time scale**	**Toxicity end point (µg/L)**	**$PEC_{initial,sw}$ µg a.s./L**	**TER**	**Annex VI trigger**
D3	ditch	D. magna	21 d	0.04	11.989	0.003	10
D4	pond	D. magna	21 d	0.04	0.976	0.041	10
D4	stream	D. magna	21 d	0.04	11.400	0.004	10
D5	pond	D. magna	21 d	0.04	0.989	0.040	10
D5	stream	D. magna	21 d	0.04	12.494	0.003	10
R1	pond	D. magna	21 d	0.04	0.915	0.044	10
R1	stream	D. magna	21 d	0.04	9.629	0.004	10
R2	stream	D. magna	21 d	0.04	12.756	0.003	10
R3	stream	D. magna	21 d	0.04	13.622	0.003	10
R4	stream	D. magna	21 d	0.04	9.686	0.004	10
D3	ditch	NOEAEC zooplankton**	-	0.14	11.989	0.012	1
D4	pond	NOEAEC zooplankton **	-	0.14	0.976	0.144	1
D4	stream	NOEAEC zooplankton**	-	0.14	11.400	0.012	1
D5	pond	NOEAEC zooplankton**	-	0.14	0.989	0.071	1
D5	stream	NOEAEC zooplankton**	-	0.14	12.494	0.012	1

R1	pond	NOEAEC zooplankton **	-	0.14	0.915	0.154	1
R1	stream	NOEAEC zooplankton**	-	0.14	9.629	0.014	1
R2	stream	NOEAEC zooplankton**	-	0.14	12.756	0.01	1
R3	stream	NOEAEC zooplankton**	-	0.14	13.622	0.01	1
R4	stream	NOEAEC zooplankton **	-	0.14	9.686	0.014	1

** the risk to insects (and amphipods) needs to be addressed by further data

FOCUS Step 4

Crop and application rate: Pome fruit; 2 applications at 180 g /ha. Test substance: a.s.

Scenario[1]	**Water body type[2]**	**Test organism[3]**	**Time scale**	**Toxicity end point (mg/L)**	**Buffer zone distance**	**$PEC_{initial,sw}$ µg a.s./L**	**TER**	**Annex VI trigger**
D3	ditch	NOEAEC zooplankton**	-	0.14	20 m	1.42	0.098	1
D4	pond	NOEAEC zooplankton**	-	0.14	20 m	0.19	0.736	1
D4	stream	NOEAEC zooplankton**	-	0.14	20 m	1.48	0.094	1
D5	pond	NOEAEC zooplankton**	-	0.14	20 m	0.19	0.74	1
D5	stream	NOEAEC zooplankton**	-	0.14	20 m	1.62	0.86	1
R1	pond	NOEAEC zooplankton**	-	0.14	20 m	0.18	0.8	1
R1	stream	NOEAEC zooplankton**	-	0.14	20 m	1.25	0.115	1
R2	stream	NOEAEC zooplankton**	-	0.14	20 m	1.66	0.084	1
R3	stream	NOEAEC zooplankton**	-	0.14	20 m	1.77	0.080	1
R4	stream	NOEAEC zooplankton	-	0.14	20 m	1.26	0.112	1

		**						
D3	ditch	NOEAEC zooplankton**	-	0.14	30 m	0.49	0.07	1
D4	pond	NOEAEC zooplankton**	-	0.14	30 m	0.08	1.68	1
D4	stream	NOEAEC zooplankton**	-	0.14	30 m	0.51	0.28	1
D5	pond	NOEAEC zooplankton**	-	0.14	30 m	0.08	1.66	1
D5	stream	NOEAEC zooplankton**	-	0.14	30 m	0.56	0.26	1
R1	pond	NOEAEC zooplankton**	-	0.14	30 m	0.08	1.80	1
R1	stream	NOEAEC zooplankton**	-	0.14	30 m	0.43	0.32	1
R2	stream	NOEAEC zooplankton**	-	0.14	30 m	0.57	0.24	1
R3	stream	NOEAEC zooplankton**	-	0.14	30 m	0.61	0.24	1
R4	stream	NOEAEC zooplankton**	-	0.14	30 m	0.43	0.32	1

** the risk to insects (and amphipods) needs to be addressed by further data

Bioconcentration				
	Active substance	**DFBA**	**CPU**	
$logP_{O/W}$	3.89	-0.02	1.14	
Bioconcentration factor (BCF) ‡	320*			
Annex VI Trigger for the bioconcentration factor	100**			
Clearance time (days) (CT_{50})	0.6			

Bioconcentration				
Level and nature of residues (%) in organisms after the 14 day depuration phase	0.1 %			

*although the study was not considered fully valid it indicated a low potential for bioconcentration

** data requirements triggered due to bioconcentration:

- direct long-term effects in fish. However since the diflubenzuron EC_{50} > 0.1mg/L no further data for long term effects in fish are needed
- Secondary poisoning of birds and mammals: for bird is provided see above.
- Biomagnification in aquatic food-chains: is not needed since the BCF< 1000 and DT_{90}< 100 days

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

Test substance	**Acute oral toxicity (LD_{50} µg/bee)**	**Acute contact toxicity (LD_{50} µg/bee)**
Toxicity to adult bee a.s. ‡	Literature data > 25 µg/bee*	Literature data > 30 µg/bee*
Toxicity to larvae a.s. ‡	Literature data 0.4 mg/ L*	Literature data 0.05 µg/larvae*
Field or semi-field tests New field study evaluated in addendum, however the study was not considered by PRAPeR 63		

* Based on data for the Preparation Dimilin WP25

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

No hazard quotients were calculated. The mode of action of diflubenzuron indicates that it is more severly toxic to honey bee brood than to adults, and hence risk assessment is based on the results from the field study.

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

Diflubenzuron is more toxic to larvae (insect growth regulator) than to adults, therefore standard risk assessment using HQ is not possible. Instead it is proposed to use a 50% effect as a trigger value for both lethal and sub-lethal end points as an indication of hazard (for both in- and off-field scenarios).

Laboratory tests with standard sensitive species ‡

Species	Stage	Test Substance	Dose (kg as/ha)	End point	Effect	Annex VI Trigger
Aphidius rhopalosiphi	(adult)	Dimilin WG-80	0.144	survival and fecundity	No significant effect on survival, no interpretation of effects on fecundity could be made	50 %
Typhlodromus pyri	Proto nymph	Dimilin WG-80	0.144	survival and fecundity	No significant effect	50 %
Aleochara bilineata	Life-cycle	Dimilin WG-80	0.180	Adult survival and ability to produce eggs	not affected. Fecundity test not considered valid since only 10 % emerged in controls	50 %

Extended laboratory studies and semi-field test ‡

Species	Stage	Test Substance	Dose (kg as/ha)	End point	Effect	Annex VI Trigger
Episyrphus balteus	Life-cycle	Dimilin WG-80	0.120	mortality	97.5 % Fecundity test not considered valid.	50 %
Coccinella septempunctata	Life-cycle	Dimilin WG-80	0.040-0.320 g	LR50	168 g a.s./ha (i.e. 210 g product/ha), 95 % CI 48.3-256 g a.s./ha (i.e 60-318 g product/ha).	Not applicable
Chrysoperla carnea	Life-cycle	Dimilin WG-80	0.0004 - 0.0064	LR50	nominally 1.3 g a.s./ha (i.e. 1.6 g product/ha), 95 % CI 0.9-1.7 g a.s./ha (i.e. 1.2-2.1 g product/ha.)	Not applicable

OFF-crop risk assessment for non-target arthropods

Application rate	Crop	Organism	Distance from edge	Drift rate early application * (g a.s./ha)	Drift rate late application * (g a.s./ha)	LR50
180 g/ha	Pome fruit	*C. carnea*	3	390	185	1.3
	Pome fruit	*C. carnea*	5	260	105	1.3
	Pome fruit	*C. carnea*	10	145	50	1.3
	Pome fruit	*C. carnea*	15	85	25	1.3
	Pome fruit	*C. carnea*	20	40	15	1.3
	Pome fruit	*C. carnea*	30	24	5	1.3
	Pome fruit	*C. carnea*	40	5	3.5	1.3
	Pome fruit	C. carnea	50	3.5	2.5	1.3
	Pome fruit	*C. carnea*	**75**	1	1	1.3
	Pome fruit	*C. carnea*	**100**	**0.5**	**0.5**	1.3

Application rate	Crop	Organism	Distance from edge	Drift rate * (g a.s./ha)	LR50
48 g a.s./ha	Forest, hand application	C. carnea	3	19.2	1.3
	Forest, hand application	C. carnea	5	8.5	1.3
	Forest, hand application	C. carnea	10	2.95	1.3
	Forest, hand application	C. carnea	15	1.55	1.3
	Forest, hand application	C. carnea	20	1	1.3
	Forest, aerial application	C. carnea	3	79	1.3

* For the calculation of the drift rate a correction factor of 5 has been used according to the recommendations for higher tier risk assessment in ESCORT 2.

Field or semi-field tests:
Additional data was submitted in the form of a literature review, summarized in the DAR. The overall conclusion from all available information is that the risk to non target arthropods in-field is not acceptable; the in-field recovery/recolonisation needs to be further addressed. In order to protect off-crop non-target arthropods buffer zones is needed (for the use in orchards 75 m is needed.).

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			
	diflubenzuron	Acute 14 days	LC_{50} > 500*mg a.s./kg d.w.soil
	diflubenzuron	Chronic	Not required
	Dimilin WG 80	Acute	LC_{50} > 397* mg a.s./kg d.w.soil
	4-chlorophenylurea**	Acute	340* mg a.s./kg d.w.soil
	2,6-difluorobenzoic acid	Acute	> 500* mg a.s./kg d.w.soil
Soil micro-organisms			
Nitrogen mineralisation	diflubenzuron	Short and Long-term	Short term effects but no effects on nitrate formation after > 1 months at 750 g a.s/ha
Carbon mineralisation	diflubenzuron	Short-term	< 25 % effect at 750 g a.s/ha
Field studies: not required			

**end point has been corrected due to log Pow >2.0 (e.g. $LC50_{corr}$)*
*** IGR mode of action not present in CPU metabolite and PRAPeR 63 did not considerd testing with soil non-target macro-organism as necessary.*

Toxicity/exposure ratios for soil organisms

Crop and application rate: Orchards 180 g a.s./ha (2 applications, 14 d interval), Forest 48 g a.s/ha

Test organism	Test substance	End point	Crop	Soil PEC i (mg a.s./kg soil)	TER	Trigger
Earthworms	diflubenzuron	Acute (14 days)	Orchards	0.148	>2630	10

Earthworms	diflubenzuron	Acute (14 days)	Forestry	0.040	>9750	10
Earthworms	4-chlorophenylurea	Acute (14 days)	Orchards	0.115	2956	10
Earthworms	4-chlorophenylurea	Acute (14 days)	Forestry	0.031	10981	10
Earthworms	2,6-difluorobenzoic acid	Acute (14 days)	Orchards	0.099	>5050	10
Earthworms	2,6-difluorobenzoic acid	Acute (14 days)	Forestry	0.027	>18518	10

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

Preliminary screening data

No effect on any species tested at 10 kg/ha

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

Test type/organism	End point
Activated sludge	No effect at 1000 mg a.s./L

Ecotoxicologically relevant compounds

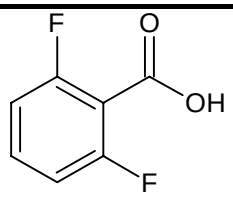
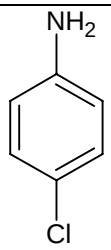
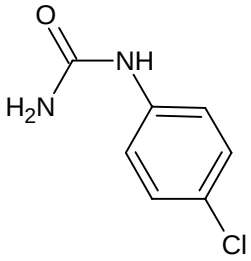
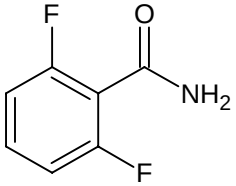
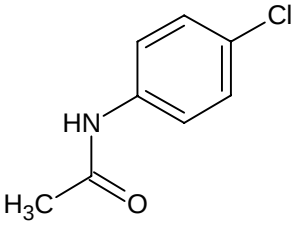
Compartment	Ecologically relevant residue
soil	a.s.
water	a.s.
sediment	a.s.
groundwater	none
air	a.s.

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	R 50 R53

	RMS/peer review proposal
Preparation	R 50 R53

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name	Structural formula
DFBA	2,6-difluorobenzoic acid	
PCA	4-chloroaniline	
CPU	4-chlorophenylurea	
DFBAM	2,6-difluorobenzamide	
PCAA	4-chloroacetanilide	

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
CT	clearance time
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT50	period required for 50 percent disappearance (define method of estimation)
DT90	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EAC	Environmentally Acceptable Concentration
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union

EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram
G	glasshouse
GAP	good agricultural practice
GC	gas chromatography
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
H	Henry's Law coefficient (calculated as a unitless value) (see also K)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
IGR	insect growth regulator
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor

MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
NER	Non Extractable Residues
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEAEC	no observed environmental adverse effect concentraion
NOEC	no observed effect concentration
NOEL	no observed effect level
OC	organic carbon content
OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pKa	negative logarithm (to the base 10) of the dissociation constant
Pow	partition coefficient between n-octanol and water
PPE	personal protective equipment
ppm	parts per million (10-6)
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RMS	rapporteur Member State
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SF	safety factor

SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TC	technical material
TER	toxicity exposure ratio
TERA	toxicity exposure ratio for acute exposure
TERLT	toxicity exposure ratio following chronic exposure
TERST	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year