European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

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

Issued on 4 June 2009

SUMMARY

Clofentezine 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].

Clofentezine 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.

The United Kingdom being the designated rapporteur Member State submitted the DAR on clofentezine in accordance with the provisions of Article 10(1) of the Regulation, which was received by the EFSA on 22 August 2005. The peer review was initiated on 17 February 2006 by dispatching the DAR for consultation of the Member States and the sole applicant Makhteshim Agan International Coordination Centre. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues which were agreed during a written procedure in August-September 2007. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in 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.

The conclusion was reached on the basis of the evaluation of the representative uses as acaricide as proposed by the notifier, which comprise foliar spraying in pome fruit, stone fruit, grapes, strawberries and ornamentals for the control of mites. Full details of the GAP can be found in the attached list of end points.

[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance clofentezine. *EFSA Scientific Report* (2009) 269, 1-113

[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 'Apollo 50 SC', a suspension concentrate (SC) containing 500 g/L clofentezine, registered under different trade names in Europe.

The minimum purity of clofentezine technical could not be concluded on, as the original manufacturing site was no longer in use, and the data on the new source could not be considered in the peer review.

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

Adequate methods are available to monitor clofentezine residues in food/feed of plant origin and environmental matrices, however a data gap was identified for a confirmatory method for determination of clofentezine in commodities with high water content. Furthermore, pending on the final residue definition for products of animal origin, a data gap was identified for a fully validated method for the determination of the compounds in the residue definition.

In mammals, clofentezine is of low acute oral, dermal and inhalational toxicity; it is not a skin or eye irritant, nor a skin sensitiser. The main toxicological effect after repeated oral administration to mice, rats, and dogs was liver enlargement. The relevant short-term No Observed Adverse Effect Levels (NOAELs) are 2.65 mg/kg bw/day in rats, 151.4 mg/kg bw/day in mice and 1.7 mg/kg bw/day in dogs, whereas the relevant long-term NOAELs in rats and mice are 2 mg/kg bw/day and 5 mg/kg bw/day, respectively. Clofentezine does not have a genotoxic or carcinogenic potential. Clofentezine does not affect fertility or reproductive performance. Relevant maternal and offspring NOAELs are 4 mg/kg bw/day, based on increased liver weight and reduced body weight in parents and decreased pup weight in offspring, whereas the relevant reproductive toxicity NOAEL is 27.8 mg/kg bw/day. Clofentezine does not show any teratogenic effects in rats or rabbits: the relevant maternal NOAELs are 250 mg/kg bw/day (rabbit) and 320 mg/kg bw/day (rat), whereas the developmental NOAELs are 1000 mg/kg bw/day and 3200 mg/kg bw/day, in rabbits and rats, respectively. The Acceptable Daily Intake (ADI) of 0.02 mg/kg bw/day was based on the long-term toxicity NOAEL from the 2-year rat study, with a safety factor of 100. The overall toxicological picture of clofentezine did not justify setting an Acute Reference Dose (ARfD). The Acceptable Operator Exposure Level (AOEL) of 0.01 mg/kg bw/day was based on the NOAEL from the 90-day study in rat, with a safety factor of 100 and corrected by 50 % oral absorption. In all scenarios proposed for the operator applying 'Apollo 50 SC' exposure levels are below the AOEL (mainly with the use of personal protective equipment - PPE) as well as for bystanders; worker exposure estimates shows levels below the AOEL, except for re-entry in treated pome and stone fruit crops (107 % of the AOEL, no PPE considered).

The metabolism of clofentezine has been investigated in the fruit plant group only, on apple, lemon, peach and grape. The parent clofentezine was shown to be the major compound accounting for 55 % to 87 % of the total radioactive residue (TRR). The metabolic pathway runs through the cleavage of the tetrazine ring to form 2-chlorobenzonitrile (AE F023666), which is further oxidised to 2-chlorobenzamide (AE F092117), 2-chlorobenzyl alcohol and 2-chlorobenzoic acid (AE C500233, NC233). **This degradation pathway is specific to plants, since no metabolites resulting from the cleavage of the parent compound were found in rat metabolism**. Based on these studies, the plant residue definition for monitoring

was limited to the parent clofentezine only. However, for risk assessment, the experts were of the opinion to include the metabolite 2-chlorobenzonitrile (AE F023666) in the residue definition, awaiting additional information on its toxicity and its toxicological relevance.

The residue trials were sufficient to propose an MRL for strawberries grown outdoor. For the other crops, the residue database was considered not relevant and incomplete, as the residue trials were mainly performed with application rates in excess of 50 % to the representative GAPs. A new residue data set in compliance with the critical GAPs was requested for plums, grapes and apples. Clofentezine residues were shown to be stable over 2 years in high water containing matrices.

In a standard hydrolytic study, clofentezine was totally degraded at 120°C to form the metabolites hydrazide-hydrazone (AE C593600, FBC 93600)[3], 2-chlorobenzamide (AE F092117) and 2-chlorobenzonitrile (AE F023666). These metabolites are not covered by the rodent metabolism, and no information was provided on their toxicological relevance and their possible residue levels in the processed fractions. Therefore, no residue definition was proposed, and a new processing data set taking into account the parent clofentezine and its breakdown metabolites was requested in addition to clarification concerning their toxicity and their residue levels in the processed fractions. Transfer factors (TF) taking into account the parent clofentezine only were proposed for apple juice, apple wet and dry pomace, apple sauce, pasteurised canned strawberries and raisin. Transfer in grape juice and wine was identified as a data gap.

No standard rotational crop study was submitted, but considering the DT_{90} value up to 640 days in the aerobic field studies and the fact that outdoor strawberry crops may be rotated, the EFSA is of the opinion that a standard rotational crop study has to be requested.

The discussion concerning the metabolism of clofentezine in animals was not conclusive. No residue definition was proposed, even if there was clear evidence that the residue definition for animal products should at least include the parent clofentezine and the metabolite 4-hydroxy-clofentezine[4]. Moreover, considering that the dietary intake by animals is mainly based on a processed commodity (apple pomace), it was concluded that information on the nature of the residues in the processed feed is needed prior to propose a reliable residue definition for animal products. Nevertheless, and considering the residues resulting from the representative uses, no residues above the LOQ (limit of quantification) are expected in animal matrices and there is no need to set a residue definition for animal products at the moment.

Using to the EFSA PRIMo rev2 model, the MRL of 2.0 mg/kg is proposed for strawberries, the highest TMDI (theoretical maximum daily intake) is 7 % of the ADI.

According to the available studies, clofentezine is moderate to high persistent in soil (DT_{50} = 16.8 – 109 days) under dark aerobic conditions. Under these conditions clofentezine yields two major metabolites: **hydrazide-hydrazone** (AE C593600, FBC 93600) (maximum of 13 % AR after 30 days in one soil) and **2-chlorobenzoic acid** (AE C500233, NC233) (maximum of 13.6 % based on theoretical molar basis). The rapporteur Member State calculated the half-life of the metabolite hydrazide-hydrazone (AE C593600, FBC 93600) based on data in one soil (Cottenham) (DT_{50} = 43 days). This value was derived from the decline phase of the metabolite, ignoring the concomitant formation. The assessment presented by the rapporteur

[3] hydrazide-hydrazone (AE C593600, FBC 93600): 2-chloro-*N*'-[(2-chlorophenyl)methylidene] benzohydrazide
[4] 4-hydroxy-clofentezine: 3-chloro-4-[6-(2-chlorophenyl)-1,2,4,5-tetrazin-3-yl]phenol

Member State may be regarded as a conservative estimate, since this half-life is used associated to a formation fraction of 1. A data gap for two additional half-lives has been identified in order to complete the minimum data set required. This data gap is not considered essential to finalize the EU risk assessment, however, the data may be needed by Member States when evaluating other potential uses of clofentezine. An additional data gap was identified for ground water and surface water exposure assessments for the metabolite 2-chlorobenzoic acid (AE C500233, NC233). Bound residue comprised up to 32.3 % AR and CO_2 up to 40.7 % AR after 120 days.

The degradation seems to be enhanced under anaerobic conditions, with higher levels of bound residue (43.5 % AR after 90 days) and lower levels of CO_2 (19 % AR after 90 days), than under aerobic conditions. However, no major metabolites were observed under the anaerobic test conditions.

Photolysis may contribute to the degradation of clofentezine in the environment. The only metabolite identified was 2-chlorobenzonitrile (AE F023666) that reached a maximum of 5.5 % AR at the end of the study (30 days). This metabolite should be assessed for potential ground water contamination.

Field soil dissipation trials from different locations of Germany, the United Kingdom and Italy are available and summarized in the DAR. Maximum plateau residue of 16 - 26 % of the initial applied concentration (on molar basis) of clofentezine was calculated to be reached after 3-5 years.

No batch soil adsorption/desorption studies are available for clofentezine because of the low solubility (3 μg/L). According to an estimation (based on the octanol/water partition coefficient) clofentezine was considered to be low mobile in soil (K_{oc} = 1064 mL/g). The result was confirmed by available soil column leaching- and soil TLC (thin layer chromatography) experiments. A batch soil adsorption/desorption study was conducted with the soil metabolite hydrazide-hydrazone (AE C593600, FBC 93600) in three soils. This metabolite showed low mobility in soil (K_{foc} = 742 - 1084 mL/g). A possible pH-dependence was indicated by this study with lower sorption at higher pH.

The hydrolysis of clofentezine was pH-dependent (pH 5: DT_{50} = 10.4 days; pH 7: DT_{50} = 26.4 hours – 34.4 hours; pH 9: DT_{50} = 4.3 hours at 22 ºC). The main hydrolysis product was hydrazide-hydrazone (AE C593600, FBC 93600) (maximum of 45 % AR at pH 9 and 22 ºC), that was further degraded to the minor metabolites 2-chlorobenzonitrile (AE F023666) and 2-chlorobenzamide (AE F092117).

According to the information available, photolysis may contribute to the environmental degradation of clofentezine. A major aqueous photolysis metabolite was identified: 2-chlorobenzonitrile (AE F023666; maximum of 79 % AR). The meeting of experts concluded that this metabolite needs to be assessed for its fate and effects on the aquatic environment. Clofentezine is not readily biodegradable.

The degradation of clofentezine was investigated in one study in two water sediment systems. Clofentezine dissipated from the water phase via either partition to the sediment or degradation to metabolite hydrazide-hydrazone (AE C593600, FBC 93600). Clofentezine whole system half-lives of 7.1 days – 13.1 days were observed.

The Step 4 FOCUS PEC_{SW} used in the risk assessment presented in the DAR were considered not appropriate for the EU risk assessment. The PRAPeR 63 meeting of experts on ecotoxicology did not agree with the acceptable concentration proposed by the rapporteur Member State in Addendum 2. With the agreed ecotoxicological end point, mitigation would

be needed to demonstrate an acceptable use with respect to the aquatic environment. No new Step 4 FOCUS PEC_{SW} calculations are available, and therefore the aquatic risk assessment remains open. It should be noted that the ecotoxicological end point is also pending on the evaluation of a study that cannot be considered at this stage in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007.

The meeting of experts agreed that $PEC_{SW/SED}$ values for the aqueous photolysis metabolite 2-chlorobenzonitrile (AE F023666) are needed to finalize the EU risk assessment. No new calculations have been performed after the meeting of experts. The rapporteur Member State proposed in the list of end points to use the FOCUS Step 1 $PEC_{SW,}$ calculated for the parent compound as a worst case surrogate for this metabolite in the EU risk assessment.

The potential ground water contamination by clofentezine and its soil metabolite hydrazide-hydrazone (AE C593600, FBC 93600) was assessed for the representative uses in apples (fruit/stone fruit), grapevines and strawberries. The calculated concentrations were all below 0.001 µg/L. Whereas the EFSA Opinion on FOCUS GW models[5] requires that the calculations should be done with an additional model, it is not likely that in this case the trigger of 0.1 µg/L would be breached.

During the peer review the need to assess the potential ground water contamination by the soil aerobic metabolite 2-chlorobenzoic acid (AE C500233, NC233) and the soil photolysis metabolite 2-chlorobenzonitrile (AE F023666) was identified. Therefore, new data gaps have been identified for the corresponding studies and calculations.

Clofentezine may be considered slightly volatile. On the basis of the estimated atmospheric half-life of 5.1 days clofentezine would be considered relatively stable in air. The experts agreed that even when the volatilization from water and soil and plant surfaces is expected to be low, long-range transport in the atmosphere may occur due to the formation of aerosols when the substance is sprayed.

The acute and short-term dietary risk to birds was low, but a high long-term risk to insectivorous birds cannot be excluded for the uses in pome/stone fruit, vineyards, strawberries and ornamentals. The risk to mammals was assessed as low for all representative uses. The risk to aquatic organisms was assessed as low except for the long-term risk to fish. No full FOCUS Step 3 scenario resulted in a TER greater than 10. However, the long-term risk assessment for fish was based on a NOEC value from an early life stage study where only one concentration was tested. A new study was made available where more concentrations were tested. The new study was not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007 and should be considered at Member State level.

The in-field hazard quotient (HQ) value was <2 for *Typhlodromus pyri* but not for *Aphidius rhopalosiphi.* No effects of >50 % were observed in standard laboratory studies with *Trichogramma cacoeciae*, *Chrysoperla carnea, Phytoselius persimilis* and *Poecilus cupreus.* Concerns remained with regard to the risk to sensitive life stages of non-target arthropods. The applicant submitted new studies to address the risk to sensitive life stages of non-target arthropods. The studies were evaluated by the rapporteur Member State in Addendum 1, but

[5] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models. The EFSA Journal (2004) 93, 1-20

were not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007. A litter bag study was triggered but not included in the original dossier. A litter bag study was submitted by the applicant and evaluated by the rapporteur Member State in Addendum 1, but the study was not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007.

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

Key words: clofentezine, peer review, risk assessment, pesticide, acaricide

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BACKGROUND

Commission Regulation (EC) No 1490/2002[6] 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.

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

Clofentezine 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.

In accordance with the provisions of Article 10(1) of the Regulation, the United Kingdom submitted the DAR on clofentezine which was received by the EFSA on 22 August 2005. Following an administrative evaluation, the DAR was distributed for consultation in accordance with Article 11(2) of the Regulation on 17 February 2006 to the Member States and to the sole notifier Makhteshim Agan International Coordination Centre, 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 August-September 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 draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Protection Products and their Residues (PPR).

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:

[6] 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; 3 January 2008),

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

- the reports of the scientific expert consultation,
- the evaluation table (revision 2-1; 22 April 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.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Clofentezine is the ISO common name for 3,6-bis(2-chlorophenyl)-1,2,4,5-tetrazine (IUPAC).

Clofentezine belongs to the class of tetrazine acaricides, mite growth regulators. It is a contact acaricide which acts on the eggs or newly hatched larvae. It has no activity against adult mites. Clofentezine interferes with cell growth and differentiation during the final stages of embryonic and early larval development. It is used for the control of spider mites in a wide variety of different crops.

The representative formulated product for the evaluation was 'Apollo 50 SC', a suspension concentrate (SC) containing 500 g/L clofentezine, registered under different trade names in Europe.

The representative uses evaluated comprise foliar spraying:
to control *Panonychus ulmi*, *Tetranychus urticae* (and related species) on pome fruit and stone fruit, at growth stages of BBCH 08-56 and BBCH 08-75, respectively, in all EU countries, at a single application, at maximum application rate of 200 g a.s./ha,

to control *Panonychus ulmi* and *Tetranychus urticae* on grapes, at growth stages of BBCH 11-75, in all EU countries, at a single application, at maximum application rate of 150 g a.s./ha,

to control *Panonychus ulmi* and *Tetranychus spp.* on strawberries grown outdoor and indoor, at the occurrence of infestation up to growth stage of BBCH 85, in all EU countries, at a single application, at maximum application rate of 200 g a.s./ha, and

to control Tetranychus *spp.* on ornamentals grown outdoor and under glass, in all EU countries, at a single application, at maximum application rate of 200 g a.s./ha.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of clofentezine technical could not be concluded on, as the original manufacturing site was no longer in use, and the data on the new source could not be considered 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. It should be noted that the new five-batch data were already submitted and presented in an addendum to Volume 4 (June 2007), however were not peer-reviewed. As a consequence, the PRAPeR 61 meeting of experts (January 2009) proposed a new data gap for formal reason for the applicant to provide the technical specification and the supporting 5-batch data.

The minimum purity of the technical clofentezine in the existing FAO specification (418/TC (April 2007)) is 980 g/kg.

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 clofentezine or the respective formulation.

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

Adequate analytical methods are available for the determination of clofentezine in the technical material and in the representative formulation (HPLC-UV), as well as for the

determination of the respective impurities in the technical material (HPLC-UV). CIPAC methods also exist for the determination of the active substance in the technical material and in the formulation (418/TC/M/3 and 418/SC/M/3).

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

Only single methods for the determination of residues are available. Residues of clofentezine in food of plant origin can be monitored by HPLC-UV with LOQs of 0.01 mg/kg in apples, pears, grapes, peaches and strawberries, however, a lack of an acceptable confirmatory method has been identified for determination of clofentezine in commodities with high water content. It should be noted that data on a confirmatory method have been evaluated in an addendum to Volume 3 (December 2008), however, could not be considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007.

Pending on the final residue definition, a fully validated method, including a confirmatory method and an ILV for the determination of the compounds in the residue definition for animal tissues and products (milk, eggs, muscle, liver, kidney and fat) might be identified as a data gap. It should be mentioned that a method for residues of clofentezine and 4-hydroxy-clofentezine[7] in animal tissues and products has been submitted and evaluated in an addendum to Volume 3 (June 2007), however was not peer reviewed in view of the restrictions as laid down in Commission Regulation (EC) No 1095/2007. The PRAPeR 61 meeting of experts (January 2009) agreed with the rapporteur Member State's view that the environmental method (HPLC-MS/MS) could be validated for these matrices, too.

Residues of clofentezine in soil can be monitored with HPLC-MS/MS with a LOQ of 0.02 mg/kg. Adequate HPLC-MS/MS methods are available to monitor residues of clofentezine in surface water and drinking water, with LOQs of 0.05 µg/L. During the finalization of the conclusion, EFSA set a provisional residue definition for ground water as clofentezine, 2-chlorobenzoic acid (AE C500233, NC233) and 2-chlorobenzonitrile (AE F023666) (see point 6.2.1). A GC-MS method is available to monitor residues of 2-chlorobenzonitrile (AE F023666) with a LOQ of 0.1 µg/l, however, pending on the final residue definition, a data gap might be needed for a method for the determination of residues of 2-chlorobenzoic acid (AE C500233, NC233).

HPLC-MS/MS method is available to monitor clofentezine residues in air with a LOQ of 0.6 $\mu g/m^3$.

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

2. Mammalian toxicity

Clofentezine was discussed at the PRAPeR 64 meeting of experts held in Parma in January 2009.

[7] 4-hydroxy-clofentezine: 3-chloro-4-[6-(2-chlorophenyl)-1,2,4,5-tetrazin-3-yl]phenol

The equivalence of the batches used in the mammalian toxicity studies compared to the proposed specification was discussed in the meeting. The originally proposed source was considered not valid as it is no longer produced. The new source could not be considered in the peer review in view of the restrictions of Commission Regulation No 1095/2007. All toxicological studies were performed with the old source. It could not be clarified whether the method of manufacture changed. The meeting could not draw a conclusion.

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

After oral administration in rats, clofentezine was excreted predominantly in the faeces. The data were not conclusive as to the systemic bioavailability, however a comparison of oral and intravenous dosing suggested that absorption by the oral route is high. The issue was discussed during the meeting. Studies in 5 species were available, but without data on bile excretion. The rapporteur Member State applied a very conservative approach and recommended 50 % oral absorption. The amount excreted via urine and faeces did not seem to differ after oral or intravenous application. The experts decided that the oral absorption is at least 50 %, although it is regarded as a very conservative approach.

Distribution in organs and tissues is low. The levels in plasma reached a maximum 4 to 6 hours after an oral dose. The highest residues were found in the liver.

Metabolism data show that after oral dosing unchanged clofentezine was the major component in faeces, whereas the material excreted in rat urine consisted mainly of metabolites. The two major pathways were hydroxylation of clofentezine and formation of a monochlorosulfur derivative. In the faeces 50 % was excreted unchanged; the rest was metabolised to more that 20 minor metabolites. Bioaccumulation was discussed during the meeting: the overall picture from the study analysed was not consistent; however, it was clear that clofentezine is not bioaccumulating.

2.2. Acute toxicity

Clofentezine is of low acute oral (LD_{50} > 5200 mg/kg bw), dermal (LD_{50} > 2100 mg/kg bw) and inhalational toxicity (LC_{50} > 1.51 mg a.s./L). Clofentezine was found not to be a skin or eye irritant. Skin sensitisation was discussed during the PRAPeR 64 meeting: the experts agreed that clofentezine is not a skin sensitiser, although the negative Magnusson & Kligman test showed some limitations.

2.3. Short-term toxicity

The main toxicological effect after short-term oral administration to mice, rats and dogs was liver enlargement. In rats, decreased haemoglobin was observed at high-dose levels, as well as effects on biochemical parameters. Histopathological liver changes were associated with liver enlargement and liver enzyme induction. The relevant NOAELs were 2.65 mg/kg bw/day in rats, 151.4 mg/kg bw/day in mice, and 1.7 mg/kg bw/day in dogs.

2.4. Genotoxicity

At the time of drafting the DAR, the rapporteur Member State set a data gap for the applicant to submit a new Ames test. The new Ames test was presented in the addendum to the DAR, but it was submitted after the Commission deadline (according to Commission Regulation No. 1095/2007). The experts re-discussed the available mutagenicity data package of clofentezine and agreed that clofentezine does not have a genotoxic potential. It was also

considered that the new Ames test is not expected to change the overall genotoxic picture of clofentezine.

2.5. Long-term toxicity

Similarly to the short-term studies, the liver was the target organ of clofentezine toxicity also in the long-term toxicity studies. Increased weight in rats and mice was accompanied by centrilobular hepatocyte enlargement as well as focal cystic degeneration, fatty change and telangiectasis of hepatocytes in rats, and focal altered hepatocytes in mice. In rats a slight increase in thyroid follicular cell tumours was observed. In mice a non-significant increase in benign liver tumours was found in females. Neither effect was considered to be a clear indication of carcinogenicity. The relevant NOAELs in rats and mice are 2 mg/kg bw/day and 5 mg/kg bw/day, respectively.

2.6. Reproductive toxicity

In a two-generation study clofentezine did not affect fertility or reproductive performance. Maternal effects (decreased growth, liver enlargement) were seen in all generations at 400 ppm. The relevant maternal and offspring NOAELs are 4 mg/kg bw/day, based on increased liver weight and reduced body weight in parents and decreased pup weight in offsprings, whereas the relevant reproductive toxicity NOAEL is 27.8 mg/kw bw/day. There were no indications of teratogenic effects in rats or rabbits: the relevant maternal NOAELs are 250 mg/kg bw/day (rabbit) and 320 mg/kg bw/day (rat), whereas the developmental NOAELs are 1000 mg/kg bw/day and 3200 mg/kg bw/day, in rabbits and rats, respectively.

2.7. Neurotoxicity

The available data from a variety of species did not indicate that clofentezine has any neurotoxic potential.

2.8. Further studies

Clofentezine has been shown to increase hepatic uptake, conjugation and metabolism of thyroid hormones. The increased removal of the thyroid hormone from the systemic circulation results in prolonged TSH stimulation of the thyroid, which, in rats, results in increased glandular activity and in neoplasia.

During the PRAPeR 64 meeting the toxicological relevance of clofentezine metabolites 2-chlorobenzoic acid (AE C500233, NC233), 2-chlorobenzonitrile (AE F023666), and 2-chlorobenzamide (AE F092117) was discussed. Limited toxicological information was reported in Addendum 2 to Volume 3 of the DAR (December 2008), which was considered not sufficient to conclude on the toxicological relevance of the metabolites, as well as on specific trigger values.

2.9. Medical data

Occupational hygiene monitoring results in the representative production plant have shown that exposure during packing is limited; there were no adverse health effects attributable to clofentezine detected during medical surveillance of manufacturing plant personnel. There are no reported cases of human poisoning or adverse systemic reactions to clofentezine. No epidemiological studies have been conducted.

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

Acceptable Daily Intake (ADI):

The **ADI of 0.02 mg/kg bw/day** was based on the long-term toxicity NOAEL from the 2-year rat study, with a safety factor of 100.

Acute Reference Dose (ARfD):

The overall toxicological picture of clofentezine did not justify setting an ARfD.

Acceptable Operator Exposure Level (AOEL):

The **AOEL of 0.01 mg/kg bw/day** was based on the NOAEL from the 90-day study in rats, with a safety factor of 100 and corrected by 50 % oral absorption.

2.11. Dermal absorption

Dermal penetration of clofentezine representative formulation 'Apollo 50 SC' was tested in *in vivo* rat studies in rats and resulted in 2 %, 5 % and 10 % for the three concentrations tested 5, 0.5 and 0.05 g a.s./L respectively.

2.12. Exposure to operators, workers and bystanders

'Apollo 50 SC' is intended to be used in orchards (apples, stone fruits), grapevines, strawberries and ornamentals (both outdoor and indoor use) at a maximum application rate of 200 g a.s./ha.

Operator

Model	Crop	Application method	Systemic exposure (mg/kg bw/day)	% of systemic AOEL
Pome and stone fruits	German model	tractor-mounted/trailed broadcast air-assisted sprayers	0.0024	24*
	German model	hand-held equipment	0.0069	69°
	UK POEM	tractor-mounted/trailed broadcast air-assisted sprayers	0.0384	384^
	UK POEM in conjunction with 75th percentile spraying values from the German model	hand-held equipment	0.0091	91*
Grapes	German model	tractor-mounted/trailed broadcast air-assisted sprayers	0.0096	96^
	UK POEM	tractor-mounted/trailed broadcast air-assisted sprayers	0.0384	384^

	EUROPOEM 75th percentile data for grapevine spraying with UK POEM mixing and loading values for broadcast air-assisted sprayers	tractor-mounted/trailed broadcast air-assisted sprayers	0.0098	98^
	German model	hand-held equipment	0.0052	52°
	UK POEM in conjunction with 75th percentile spraying values from the German model	hand-held equipment	0.0068	68*
Outdoor strawberries and ornamentals	German model	Field crop sprayers	0.0087	87
	UK POEM	Field crop sprayers	0.0034	34^
	UK POEM	Knapsack sprayers on low crops	0.0093	93*
Protected strawberries and ornamentals	EUROPOEM 75th percentile data	hand-held equipment	0.0062	62^
	EUROPOEM 75th percentile data for the indoor use of hand-held equipment with UK POEM mixing and loading values for knapsack sprayers	hand-held equipment	0.0085	85^

* gloves when handling the concentrate, and coveralls and protective gloves during application
° gloves when handling the concentrate
^ gloves when handling the concentrate and during application

The use of 'Apollo 50 SC' in all scenarios proposed shows exposure levels below the AOEL with the use of PPE, except for the application of UK POEM to assess exposure for tractor spraying in grapes and pome/stone fruits (estimated exposure 384 % of the AOEL, even with the use of PPE). Exposure estimates for spraying activities on outdoor strawberries and ornamentals, assessed with the German model (no PPE considered), were also below the AOEL.

Worker

Worker exposure estimates based on the German worker re-entry model and using published transfer coefficient data indicate that the levels of systemic exposure to clofentezine is below the AOEL, except for pome and stone fruits (no use of PPE):

Ornamentals: 24 % of the AOEL

Strawberries: 32 % of the AOEL

Grapes: 80 % of the AOEL

Pome and stone fruit: 107 % of the AOEL

EFSA notes that the exposure during re-entry activities in pome and stone fruits can be further refined and be below the AOEL, as the reported levels are estimated based on dislodgeable foliar residues shortly after application (worst case), as well as no use of personal protective equipment was considered.

Bystander

Bystander exposure estimates based on published field study measurements indicated that exposure to clofentezine represents 16 % and 1 % of the proposed systemic AOEL, for tractor-mounted/trailed broadcast air-assisted sprayers and field crop sprayers, respectively. The use of hand-held equipment outdoors was expected to result in lower levels of exposure than those estimated for tractor-mounted/trailed equipment. Bystanders are not expected to be present when a pesticide is used on protected crops.

3. Residues

The active substance was discussed at the PRAPeR 65 meeting of experts on residues in January 2009.

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

The metabolism of clofentezine has been investigated in apple (foliage and fruit), lemon (foliage), peach (fruit) and grapes, using [^{14}C]-clofentezine labelled on the tetrazine ring. These studies reflect the proposed representative use pattern of the compound, the application rates representing 0.5 to 2.5 times the normal rate, some experiments being conducted with an exaggerated dose in order to facilitate the metabolite identification (up to 38N). Samples were taken at PHIs ranging from 0 day up to 103 days after treatment. The metabolic pattern was shown to be similar, with the parent clofentezine being the major compound of the extractable residues, accounting for 55 % to 87 % of the TRR in fruit or leaf samples collected 25 to 103 days after application. All the other identified compounds were less than 10 % of the TRR. The metabolic pathway runs through cleavage of the tetrazine ring to form 2-chlorobenzonitrile (AE F023666), which is further oxidised to 2-chlorobenzamide (AE F092117), 2-chlorobenzyl alcohol and 2-chlorobenzoic acid (AE C500233, NC233). In addition, the metabolite di-hydro-clofentezine (NC 22505)[8] was identified on apple leaves in one study up to 11 % of the TRR. However, and taking into account the argumentation provided by the applicant, the meeting of experts concluded that this compound has not to be considered as a plant metabolite, but as an artefact of the TLC analytical method. **This degradation pathway is specific to plants, since no metabolites resulting from the cleavage of the parent compound were found in the rat metabolism,** where mainly hydroxy metabolites were identified.

Based on these metabolism studies, the meeting of experts confirmed the plant residue definition for monitoring proposed by the rapporteur Member State as the parent clofentezine

[8] Di-hydro-clofentezine (NC 22505): 3,6-bis(2-chlorophenyl)-1,2-dihydro-1,2,4,5-tetrazine

only. However, for risk assessment, the experts expressed their concern regarding the metabolite 2-chlorobenzonitrile (AE F023666) recovered in proportions of *c.a.* 8 % of the TRR in the lemon and peach studies. Considering that:

- this metabolite and its further degradation products were not observed in the rat metabolism and therefore not covered by the toxicological studies,
- this metabolite and its further metabolites were observed in non-negligible proportions in the standard hydrolytic processing study,
- the available studies were considered not sufficient to give an opinion on the toxicological relevance of this metabolite by the PRAPeR 64 meeting of experts on mammalian toxicology,
- 2-chlorobenzonitrile (AE F023666) seems to be of higher acute toxicity than clofentezine (LD_{50} > 300 mg/kg bw, clofentezine LD_{50} > 5200 mg/kg bw) and is classified (Xn R21/22[9], Xi R36[10]),

the meeting of experts was of the opinion that 2-chlorobenzonitrile (AE F023666) has to be included in the residue definition for risk assessment and that the applicant should address additional information on its toxicity and its toxicological relevance.

Considering that 2-chlorobenzonitrile (AE F023666) is expected to be present at *c.a.* 10 % of the clofentezine level, the rapporteur Member State proposed in the Addendum 3 of February 2009 a conversion factor of 1.1 for the risk assessment. This value was not discussed, nor peer reviewed. The EFSA is of the opinion that this conversion factor has to be considered as a provisional default value, since 2-chlorobenzonitrile (AE F023666) was not observed in the rat metabolism and no data were provided to confirm whether its toxicity is covered by the ADI proposed for the parent compound. Moreover, new residue trials, where both the parent compound and the metabolite 2-chlorobenzonitrile (AE F023666) are analysed, are necessary in order to propose a more accurate conversion factor (see point above).

Residue trials were submitted to support the representative uses on pome fruits, plums, grapes and strawberries. The samples were analysed for the parent clofentezine only, and no information was provided on the potential residue levels for 2-chlorobenzonitrile (AE F023666). The residue database was considered sufficient to propose an MRL for strawberries grown outdoor only, and the applicant was requested to provide the full data package to support the indoor uses on strawberries.

For the other crops, the residue database was considered not relevant and incomplete, since most of the trials were overdosed, using application rates of *c.a.* 300 g a.s./ha instead of 200 g a.s./ha, and with two applications instead of one. Moreover, on apples, some studies were not reported with enough details to confirm the application rates and many replicate values from a single residue trial (same location, variety, application date…) were considered in the DAR as individual trial. Therefore, the meeting of experts concluded that new residue trials performed in compliance with the critical GAPs have to be requested on plums, grapes and apples, with the samples being analysed for both clofentezine and its metabolite 2-chlorobenzonitrile (AE F023666) included in the residue definition for risk assessment.

In conclusion, no MRLs could be defined for apples, plums and grapes with regard to the intended GAPs, and the MRLs proposed for these crops in the DAR by the rapporteur Member State have to be considered as an overestimation derived from overdosed trials.

[9] Xn R21/22: ‘ Harmful if swallowed’; ‘Harmful in contact with skin’
[10] Xi R36: ‘Irritating to eyes’

Nevertheless, the results from these overdosed studies (STMR, HR…) were used as a worst case by the meeting of experts for the calculation of the animal burden (see point 3.3).

The storage stability studies were performed on peaches, almond hulls and nutmeats using the parent clofentezine only. For peaches, low recoveries (61 %) were observed at one time point (after 246 days), whereas recoveries were higher than 70 % for the other sampling dates up to 2 years. After discussion, the experts concluded that clofentezine residues have to be considered stable over two years in high water containing matrices when stored frozen. The storage period for fruits sampled in the residue trials was less than 100 days and the results are then fully covered by the stability study performed on peaches. More variable results were observed in nutmeat where low recoveries (39-61 %) were observed after 3 months and 2 years, respectively. Such a discrepancy could not be explained by taking into account the procedural recoveries provided by the rapporteur Member State in the evaluation table. Finally, and considering that the study was not relevant for the supported uses, the meeting of experts concluded that the stability in oily matrices has to be reconsidered if further uses are envisaged on such a crop group.

The effect of processing on the nature of the residues was investigated through a standard hydrolysis study simulating sterilisation, baking/boiling and pasteurisation. Clofentezine was totally degraded at 120°C (pH 6) to form the metabolites hydrazide-hydrazone (AE C593600, FBC 93600)[11] (78 % TRR), 2-chlorobenzamide (AE F0092117) (17 % TRR) and 2-chlorobenzonitrile (AE F023666) (5 % TRR). No degradation was observed at 90°C and clofentezine was slightly degraded to hydrazide-hydrazone (AE C593600, FBC 93600) at 100°C (12 % TRR).

None of these metabolites were detected in the rodent metabolism and based on the limited toxicological data reported in the DAR, the PRAPeR 64 meeting of experts on mammalian toxicology was unable to conclude on their toxicological relevance. In addition, no information was provided on their possible residue levels in the processed fractions, since, except for one study, only the parent clofentezine was analysed for in the studies performed on apples, grapes and strawberries. However, significant levels might be expected since there is some evidence of degradation during the process, the residue levels of clofentezine being in some experiments lower in dry fractions than in the wet fractions. Considering the points above, the meeting of experts concluded that further clarification concerning the toxicity of these metabolites and their possible residue levels in the processed commodities are needed in order to finalize a residue definition. Provisionally, the experts were of the opinion that the residue definition for monitoring in processed commodities should at least include the parent clofentezine and its metabolite 2-chlorobenzonitrile (AE F023666).

Transfer factors (TF) taking into account the parent clofentezine only were calculated for apple juice, apple wet and dry pomace, apple sauce and pasteurised canned strawberries. On grapes, a transfer factor was derived for raisins, but no data was submitted for juice and wine. After discussion, the meeting of experts concluded that a new processing data set taking into account the residues of the parent clofentezine and the breakdown metabolites identified in the standard hydrolysis study have to be provided for all the supported crops. These new studies should include a heating step (at least 90°C if relevant) in order to provide reliable information, since it was seen that the degradation of the parent compound increases with temperature.

[11] hydrazide-hydrazone (AE C593600, FBC 93600): 2-chloro-*N*'-[(2-chlorophenyl)methylidene]benzohydrazide

3.1.2. Succeeding and rotational crops

No standard rotational crop studies were submitted. Limited information was provided on the TRR levels in orange fruits, orange leaves and apple seedlings following two soil applications of [^{14}C]-clofentezine at a rate of 600 or 1200 g a.s./ha. Apples, pears, plums and grapes are perennial crops and therefore studies investigating the transfer from soil to succeeding and rotational crops are not relevant. However, the rotation of strawberry crops is a possible scenario. This point was not discussed during the meeting, but considering a DT_{90} value up to 640 days in the aerobic field studies, the EFSA is of the opinion that a standard rotational crop study has to be requested in order to cover the possible rotation for strawberries grown outdoor.

3.2. Nature and magnitude of residues in livestock

The discussion concerning the metabolism of clofentezine in animals was not conclusive. The experts were unable to get a clear picture of the metabolites effectively detected in ruminant matrices, since the studies concerning the identification of the metabolites were reported in different sections of the DAR. The rapporteur Member State was requested to submit a complete assessment taking into account all the information available in the toxicology and residue sections of the DAR. The rapporteur Member State provided this full evaluation in Addendum 3 of February 2009, but this new assessment was not discussed, nor peer reviewed.

On dairy cattle and in lactating goat the metabolism studies were conducted using [^{14}C]-clofentezine labelled on the tetrazine ring. The cattle were dosed at a rate of 2.2 mg/kg bw/day during three consecutive days (*c.a.* 40N the calculated intake for beef cattle). Maximum radioactive residues were found in liver (0.76 mg/kg), kidney (0.36 mg/kg) and renal fat (0.26 mg/kg), the residue level in muscle being limited to 0.016 mg/kg. Most of the radioactivity was extractable (83-93 %) and the vast majority of the residues in milk, liver, kidneys and renal fat was identified as 4-hydroxy-clofentezine, representing 74 % to 90 % of the TRR. The 4-hydroxy-clofentezine was also shown to be a major metabolite in milk (80 % TRR) in a goat study, where the animal was dosed at a rate of 2.2 mg/kg bw/day over 7 days. However, in an additional study performed on a goat and a calf, where the animals were given a single dose of 20 mg/kg bw/day, the metabolites in liver were identified as hydroxylated clofentezine (mainly 3-hydroxy-clofentezine[12] and 4-hydroxy-clofentezine with small amount of
5-hydroxy-clofentezine[13]) but not exclusively as 4-hydroxy-clofentezine. The parent clofentezine was never detected in ruminant matrices, except in one study, where it accounted for 8 % of the TRR in calf liver.

On poultry, a metabolism study was provided although poultry is not exposed to clofentezine residues based on the representative uses. The metabolic fate of clofentezine was investigated in laying hens dosed for three consecutive days at a rate of 17 mg/kg bw/day with [^{14}C]-clofentezine. The highest radioactive residues were found in fat (3.04 mg/kg), skin (0.87 mg/kg) and liver (0.70 mg/kg). In contrast to ruminants, the parent compound was by far identified as the dominant compound in all tissues accounting for 34 % to 89 % of the TRR, with lower amounts of 4-hydroxy and 3-hydroxyclofentezine (6 % to 30 % TRR).

[12] 3-hydroxy-clofentezine: 2-chloro-3-[6-(2-chlorophenyl)-1,2,4,5-tetrazin-3-yl]phenol
[13] 5-hydroxy-clofentezine: 4-chloro-3-[6-(2-chlorophenyl)-1,2,4,5-tetrazin-3-yl]phenol

A livestock feeding study was conducted on dairy cattle using three dose levels of clofentezine; 0.6, 1.7 and 5.7 mg/kg bw/day over 28 consecutive days. The clofentezine theoretical dietary intake by livestock was estimated by the meeting of experts to be 0.015 mg/kg bw/day and 0.052 mg/kg bw/day, for the dairy and beef cattle respectively, based on a STMR value of 0.16 mg/kg for apple and a transfer factor of 5.8 in wet pomace. Thus, the lower dose rate of 0.6 mg/kg bw/day in the feeding study can be considered to be approximately 11 times the maximum intake estimated on the representative uses. The samples were analysed using a common moiety method analysing clofentezine and all the metabolites containing the 2-chlorobenzoyl moiety. This method was considered as sufficiently validated and appropriate in the framework of this peer review, since its scope includes the parent compound and all the hydroxy-metabolites. At the lower dose level, residues were below the limit of quantification (<0.05 mg/kg) in all matrices except in liver (0.26 mg/kg). Based on these results, it was concluded that no residues of clofentezine and its hydroxy-metabolites are expected above 0.02 mg/kg in ruminant matrices.

No residue definition was proposed by the meeting of experts, but there is clear evidence from the studies above that the residue definition for animal products should at least include the parent clofentezine and 4-hydroxy-clofentezine. Other hydroxy metabolites (3-hydroxy and
5-hydroxy) were identified, probably in lower amounts, but their exact proportions were not given. Nevertheless, and considering the residue resulting from the representative uses (apple pomace), no residues above the LOQ are expected in animal matrices and there is no need to set a residue definition for animal products at the moment.

In addition, and considering that the dietary intake by animals is mainly based on a processed commodity (apple pomace) that may contain significant levels of breakdown metabolites formed during the process, the experts were of the opinion that information on the possible residue level of these metabolites in the processed feed is needed as well as clarification on their toxicological relevance, before proposing a reliable residue definition for animal products.

3.3. Consumer risk assessment

The chronic dietary exposure assessment has been carried out using to the EFSA PRIMo rev2 model. Considering the MRL of 2 mg/kg defined for strawberries and the provisional conversion factor of 1.1 proposed by the rapporteur Member State in order to take into account the 2-chlorobenzonitrile (AE F023666) residues, the highest TMDI is 7 % of the ADI (0.02 mg/kg bw/day) for the FR toddler. No Acute Reference Dose was defined for clofentezine.

3.4. Proposed MRLs

As mentioned in section 3.1.1, MRL was proposed for strawberries grown outdoor only, since for the other crops the residue data set was considered not relevant, as the residue trials were performed with application rates in excess of 50 % to the representative GAPs.

Strawberries: 2 mg/kg (outdoor uses only)

No residue (clofentezine+hydroxy-metabolites) above the LOQ and resulting from the representative uses are expected in products of animal origin.

4. Environmental fate and behaviour

The environmental fate and behaviour of clofentezine was discussed at the PRAPeR 62 meeting of experts (January 2009) on basis of the DAR (August 2005) and the Addendum 2 (December 2008). After the meeting the rapporteur Member State presented the Addendum 3 (February 2009) and an updated list of end points (February 2009).

Some of the environmental fate and behaviour studies were performed in aqueous media, at concentrations significantly above the measured aqueous solubility. The reliability of these studies was discussed by the meeting of experts. It was found that in all these studies a small portion of co-solvents (eg. acetone) had been used to prepare the test solutions. In general, the experts found this approach reasonable and considered that it was not expected to have a negative impact on the results of these studies. However, for the same reason, the absence of a proper soil adsorption/desorption study for clofentezine was not found as fully justified.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

The route of degradation of clofentezine in soil under dark aerobic conditions was investigated in two studies with a total of three soils (pH 6.2 – 6.6, OM 1.9 – 14.7 %, clay 1.4 – 49.2 %, MWHC % 48 – 114; Leake and Arnold, 1983a, Leake and Arnold, 1983b). The first of these studies, where only two of the soils were used and last only 67 days, was considered only as supplementary information by the rapporteur Member State. In the second study the three soils were used to investigate the degradation of clofentezine ^{14}C labelled in the tetrazine ring at 25 °C. Two major metabolites were identified in this study: **hydrazide-hydrazone**
(AE C593600, FBC 93600, maximum of 13 % AR after 30 days in one soil) and an **unidentified metabolite** (maximum of 10.8 % AR after 21 days). There was an attempt to identify this product by repeating the study three years later in the same soil (Newby and Arnold, 1986). The high levels of the unidentified compound were not reproduced and the metabolite remained unidentified. The meeting of experts agreed that also the metabolite **2-chlorobenzoic acid** (AE C500233, NC233) should be considered to exceed the trigger of 10 % on the molar basis even when the observed radioactivity is below 10 % AR (due to the symmetry of the parent molecule and the labelling in the product used in the experiment, maximum of 13.6 % on theoretical molar basis). A data gap was identified for ground water and surface water exposure assessments for this metabolite. Further studies may also be required to derive the parameters needed for these assessments. Bound residue comprised up to 32.3 % AR and CO_2 up to 40.7 % AR after 120 days.

The degradation under dark anaerobic conditions was investigated in the same study with the same soils. Anaerobic conditions were established by flooding selected samples after 30 days of aerobic incubation and purging with N_2. The degradation seems to be enhanced under anaerobic conditions, with higher levels of bound residue (43.5 % AR after 90 days) and lower levels of CO_2 (19 % AR after 90 days) than under aerobic conditions. However, no major metabolites were observed under the test conditions.

The photolysis in soil was investigated under natural summer sunlight conditions in Essex, UK (52 °N), at temperatures that varied between 6.8 – 28.4 °C. Photolysis may contribute to the degradation of clofentezine in the environment. The only metabolite identified was 2-chlorobenzonitrile (AE F023666) that reached 5.5 % AR at the end of the study (30 days). The meeting of experts agreed that this metabolite should be assessed for potential ground

water contamination in case it is considered toxicologically relevant by the PRAPeR 64 meeting of experts on mammalian toxicology. Due to the lack of data, the experts on mammalian toxicology were unable to conclude on the toxicological non-relevance of this metabolite and, therefore, it needs to be addressed for potential ground water contamination and the data gap identified at the PRAPeR 62 meeting is confirmed.

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

The rate of degradation of clofentezine in soil under dark aerobic conditions at 22 °C was investigated in two soils (pH 6.2 – 7.8, OM 1.9 – 4.5 % AR, clay 5.3 – 10.8 %, MWHC 38 – 41.3 %), with non-labelled clofentezine, at an application rate equivalent to 2 kg/ha (Snowdon, 1982b). The rapporteur Member State performed a new kinetic analysis of these experiments based on first order kinetics and following FOCUS guidance. This new assessment was summarized in Addendum 2 and was discussed by the meeting of experts. According to these results, clofentezine is moderate to medium persistent in soil (DT_{50} = 16.8 – 82.1 days). The meeting of experts discussed the reliability of the half-lives derived from the experiments performed in the studies for route of degradation. It was agreed that since the two soils used in the first study are also used in the second one, the experiment results should be combined. In these experiments, clofentezine was moderate to high persistent in soil (DT_{50} = 16.8 – 109 d).

In the above experiments, a faster degradation was observed in the alkaline soils. This is in line with the results of the aquatic hydrolysis study, and may indicate that chemical hydrolysis contributes to the degradation of clofentezine in soil. In the studies for route of degradation no significant differences were observed between the sterile and non-sterile experiments. Therefore, the degradation of clofentezine in soil seems to be rather more chemical than microbiological. The potential effect of the pH on the rate of degradation was discussed during the meeting of experts. However, it was agreed that with the available data the pH-dependence could not be completely confirmed, and the experts considered appropriate to use the geometric mean half-life of all reliable data for environmental modelling.

The rapporteur Member State calculated the half-life of the metabolite hydrazide-hydrazone (AE C593600, FBC 93600) based on data in one soil (Cottenham) from the study on route of degradation (DT_{50} = 43 days). This value was derived from the decline phase of the metabolite, ignoring the concomitant formation, and the assessment presented by the rapporteur Member State may be regarded as a conservative estimate, since this half-life is used associated to a formation fraction of 1. A data gap for two additional half-lives has been identified at the time of writing the conclusion, in order to complete the minimum data set required. This data gap is not considered essential to finalize the EU risk assessment but the data may be required by Member States when evaluating other potential uses of clofentezine.

Field soil dissipation trials in different locations of Germany, the UK and Italy are available and summarized in the DAR. Only dissipation half-lives for PEC soil calculations have been used further in the assessment from these trials. Field accumulation studies did not show accumulation after three years of continuous application at rates of 1 and 2 kg/ha in the only site tested (Shelford, UK).

Long-term predicted plateau was calculated based on a kinetic fitting (first-order of biexponential) of the three German sites, where residues > 10 % remained after one year

(DT_{90} = 435. 4 – 640.5 days) (Jenne 2000c). Maximum plateau residue of 16 - 26 % of the initial applied concentration (on a molar basis) of clofentezine was reached after 3-5 years.

Short-term PEC soil were calculated assuming an annual application at a maximum rate of 100 to 200 g a.s. / ha to either pome fruit, stone fruit, grapes, strawberries or ornamentals, with the minimum interception factor according to $FOCUS_{SW}$ or $FOCUS_{GW}$. Field worst-case half-life (DT_{50} = 131.1 days, Germany) for the parent clofentezine and peak formation of 13 % of applied substance and a half-life of 43 days for the metabolite hydrazide-hydrazone (AE C593600, FBC 93600). The risk assessment is based on the worst-case representative use of 200 g a.s./ha in orchards (BBCH 08-19). For the metabolite 2-chlorobenzoic acid (AE C500233, NC233) the meeting of experts estimated a maximum PEC soil of 0.268 mg/kg to be used in the environmental risk assessment.

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

No batch soil adsorption/desorption studies are available for clofentezine because of the low solubility (2.52 µg/L). Mobility was estimated from the octanol/water partition coefficient (log P_{ow} = 4.09) based on the equation proposed by Briggs (1981).[14] According to this estimation clofentezine was considered to be low mobile in soil (K_{oc} = 1064 mL/g). The result was confirmed by available soil column leaching- and soil TLC experiments. The meeting of experts discussed the need for an experimental batch adsorption/desorption study in soil for clofentezine. Whereas the case presented by the applicant was not found fully justified, the absence of this study was accepted in this case on the basis of the low solubility, the non-ionisable molecular structure and supplementary information available.

A batch soil adsorption/desorption study was conducted with the soil metabolite hydrazide-hydrazone (AE C593600, FBC 93600) in three soils (pH 5.7 – 8.3, OC 2.0 – 2.9 %; clay 6.7 – 23.6 %). Partial degradation was observed in all samples with levels of the hydrolysis product 2-chlorobenzamide (AE F092117, maximum of 10-15 % AR in the supernatant). However, the study was adequate to establish that this metabolite was low mobile in soil (K_{foc} = 742 - 1084 mL/g). A possible pH-dependence was indicated by this study with lower sorption at higher pH.

Three soil column-, an aged soil column-, and a thin layer soil chromatography studies were available. Only qualitative information can be derived from these studies that overall confirms the low mobility of clofentezine in soil. Some unidentified radioactivity (up to 2.05 % AR) was found in the leachate of the soil column studies.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

The hydrolysis of clofentezine was investigated in buffer aqueous solutions in one study at pH ≈ 5, 7 and 9 and temperatures of 10, 22 and 38 ºC, and in a second study at pH 7 and 25 ºC or 35 ºC. The hydrolysis of clofentezine was pH-dependent (pH 5: DT_{50} = 10.4 days; pH 7: DT_{50} = 26.4 hours – 34.4 hours; pH 9: DT_{50} = 4.3 hours at 22 ºC). The main hydrolysis product was hydrazide-hydrazone (AE C593600, FBC 93600; maximum of 45 % AR at pH 9 and 22 ºC), that was further degraded to the minor metabolites 2-chlorobenzonitrile (AE

[14] Briggs, G.G. 1981. *J. Agric. Food Chem.* 29. p 1050-1059 (1981).

F023666) and 2-chlorobenzamide (AE F092117).

The photolysis in water was investigated in one study under outdoor conditions (t = 6.8 – 28 ºC) and natural sunlight in Essex, UK (52 ºN). During the peer review the acceptability of this study was questioned due to the high concentration employed (250 µg/L *versus* a measured solubility < 3 µg/L), and the lack of control on the experimental conditions. According to this study photolysis may contribute to the environmental degradation of clofentezine. A major aqueous photolysis metabolite was identified: 2-chlorobenzonitrile (AE F023666; maximum of 79 % AR). The meeting of experts concluded that this metabolite needs to be assessed for its fate and effects on the aquatic environment. At the time of the experts meeting the applicant had submitted a new photolysis study in water performed according to current study guidelines. However, this study could not be taken into consideration in view of the restrictions of Commission Regulation (EC) No 1095/2007. Since the reliability of the available study is doubtful and does not allow the calculation of the quantum yield, the meeting of experts identified a formal data gap for a new photolysis study in water. This data gap was not considered essential to finalize the EU assessment.

A ready biodegradation study is available, clofentezine is not readily biodegradable.

The degradation of clofentezine was investigated in one study in two water sediment systems (pH sediment: 6.6 – 6.8; pH water: 8.2 – 8.3). Clarifications on the low recovery observed for some data points and other drawbacks identified by the rapporteur Member State and/or during the peer review were submitted by the applicant and summarized by the RMS in Addendum 2. Overall, the meeting of experts considered acceptable the clarifications provided, and agreed with the rapporteur Member State on the acceptability of the end points derived from this study. However, the meeting of experts noted that the aqueous phase of both systems was alkaline. Since the vast majority of the EU surface water is alkaline, it was considered that a data gap at EU level was not appropriate in this case. The EFSA was however requested to note in the conclusion that Member States may need to require further information, including new studies, to address acidic surface water bodies. Clofentezine dissipated from the water phase via either partitioning to the sediment or degradation to the metabolite hydrazide-hydrazone (AE C593600, FBC 93600). Volatiles trapped in the ethanolamine trap were assumed to be CO_2. Mineralization in the water/sediment system reached a peak of 32 % AR after 42 days. Bound residue to the sediment reached a maximum level of 26.3 % AR after 14 days.

Multicompartmental modelling with the program TopFit was used to derive kinetic parameters for use in FOCUS SW. The model is complex with a large number of parameters fitted in comparison with the experimental data points available. The experts had reservations with respect to the separated degradation half-lives derived for water and sediment phases. The meeting of experts agreed on whole system half-lives of 7.1 days – 13.1 days as the only peer reviewed end points for the environmental risk assessment. After the meeting the rapporteur Member State presented a new calculation of the water phase dissipation half-lives based on FOCUS kinetics guidance in Addendum 3. These values are not required for the EU risk assessment and are not peer reviewed. However, Member States may wish to use them in their specific national assessment schemes.

Step 4 FOCUS PEC_{SW} used in the risk assessment presented in the DAR were considered not appropriate for the EU risk assessment by the rapporteur Member State and by the meeting of experts. A new risk assessment was presented in Addendum 2, establishing two key acceptable concentrations.

- 25 µg/L when exposure is the result of a single spray drift event (acute exposure)
- 5 µg/L when exposure results from multiple run-off, drainage or spray drift events (chronic exposure).

In the DAR only Step 3 results for the scenarios that gave the maximum Step 3 PEC SW calculations for the pome fruit use were reported. In Addendum 2 the rapporteur Member State provided additional FOCUS Step 3 PEC_{SW} results for all the representative uses and pertinent scenarios. The scenarios presented maximum concentrations below 5 µg/L for grapevine, strawberry and ornamentals. For apple, pear and plum 5 µg/L was exceeded for some scenarios, but none of the scenarios resulted in PEC_{SW} above 25 µg/L. The rapporteur Member State also presented the case that in most of the cases the maximum exposure is due to single exposure event. Therefore, the change in the input parameters agreed by the experts in the meeting would have no impact in most of the cases. The meeting of experts agreed that no new FOCUS SW calculations would be needed, if the acceptable concentrations were accepted by the meeting of experts on ecotoxicology. However, the PRAPeR 63 meeting of experts on ecotoxicology did not agree with the acceptable concentration proposed by the rapporteur Member State in Addendum 2, and agreed that the end point driving the risk assessment had to be 7 µg/L based on the information available in the dossier (resulting in an acceptable concentration of 0.7 µg/L). With this end point, mitigation would most likely be needed to demonstrate any acceptable use with respect to the aquatic environment. No new calculations are available and therefore the aquatic risk assessment remains open. It should be noted that the ecotoxicological end point is also pending on the evaluation of a study that cannot be considered at this stage in view of the restrictions of Commission Regulation (EC) No 1095/2007.

The meeting of experts agreed that $PEC_{SW/SED}$ for the aqueous photolysis metabolite 2-chlorobenzonitrile (AE F023666) are needed to finalize the EU risk assessment. No new calculations have been performed after the meeting of experts, but the rapporteur Member State proposed in the list of end points to use FOCUS Step 1 PEC_{SW} calculated for the parent compound as a worst case surrogate for this metabolite in the EU risk assessment.

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

The potential ground water contamination by clofentezine and its soil metabolite hydrazide-hydrazone (AE C593600, FBC 93600) was assessed based on the 1m depth 80th percentile annuals average concentrations calculated by FOCUS PELMO (V.3.3.2) for the representative uses in apples (fruit/stone fruit), grapevines and strawberries. Geometric mean of normalised half-lives were obtained from the laboratory degradation studies ($DT_{50\ norm}$ = 71.3 days). For the soil metabolite hydrazide-hydrazone (AE C593600, FBC 93600) normalized half-life calculated by the rapporteur Member State was used (DT_{50} = 62.4 days). The calculated concentrations were all below 0.001 µg/L. Whereas the EFSA Opinion on FOCUS GW models[15] requires that the calculations should be done with an additional model, it is not likely that in this case the trigger of 0.1 µg/L would be breached.

During the peer review the need to assess the potential ground water contamination by the soil aerobic metabolite 2-chlorobenzoic acid (AE C500233, NC233) and by the soil

[15] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models. The EFSA Journal (2004) 93, 1-20

photolysis metabolite 2-chlorobenzonitrile (AE F023666) was identified. Therefore, new data gaps for the corresponding studies and calculations have been identified.

4.3. Fate and behaviour in air

Clofentezine has a vapour pressure of 6.0 x 10^{-7} Pa at 20 °C and Henry's law constant of 0.168 Pa m^3/mol. Therefore clofentezine may be considered slightly volatile. According to the study available, over a period of 24 hours only 1.1 – 1.8 % and 0.8 % - 1.7 % volatilised from plant- and soil surfaces, respectively. On the basis of the estimated atmospheric half-life of 5.1 days, clofentezine would be considered relatively stable in air. The meeting of experts discussed the potential for long-range transport of clofentezine through the atmosphere. During the peer review it was noted that substances with similar Henry's law constant are included in monitoring programs for long-range transport. In this particular case the experts noted that the high Henry's law constant was mainly due to the low solubility and that, under normal environmental conditions, it is expected that clofentezine will be partitioned to solid materials, reducing the potential of volatilization form the water bodies. However, the experts agreed that even when the volatilization from water and soil and plant surfaces is expected to be low, long-range transport in the atmosphere may occur due to the formation of aerosols when the substance is sprayed.

5. Ecotoxicology

Clofentezine was discussed at the PRAPeR 63 meeting of experts on ecotoxicology (January 2009) on the basis of the Draft Assessment Report, Addendum 1 (B9) from June 2007, Addendum 2 (B9) from December 2008. A non peer-reviewed addendum was submitted in February 2009. The representative uses evaluated are uses as an acaricide in orchards, grapes, strawberries and roses at application rates of up to 200 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

The acute and short-term risk to birds was assessed as low for all representative uses. The first-tier long-term TER values of 1.26, 1.69 and 1.26 indicated a potential high long-term risk to birds for the uses in pome fruit/stone fruit, grapes and strawberries, respectively. The refinement steps suggested in the original dossier were not sufficiently supported by data. The following key issues were identified by the rapporteur Member State and in the peer review in relation to the refined risk assessment:

1. Pome/stone fruit in northern and southern Member States: further justification was needed for the refinement of PD (including the proportion of invertebrates taken from the ground) and for using of radiotracking data from blue tit (*Cyanistes caeruleus)* in the risk assessment for great tit (*Parus major)*.
2. Vineyard: further justification is needed regarding prevalence or frequency of yellowhammer *Emberiza citrinella* in northern EU vineyards and cirl bunting *Emberiza cirlus* and crested lark *Galerida cristata* in southern EU vineyards. The

proposed PD refinement was accepted for yellowhammer but for cirl bunting concerns remained due to the fact that the data on PD were not from vineyards. For PD refinement for crested lark no information was provided where the data was collected. Uncertainty remained regarding insectivorous birds that feed from insects on the vine itself.

3. Strawberries: Yellow wagtail (*Motacilla flava*) as focal species needs to be supported by data on the prevalence or frequency of this species. The PD refinement was of limited value since data are from birds that fed on a meadow. PT refinement needs to be justified.
4. Ornamentals: The risk assessment for blackbird (*Turdus merula*) assuming a diet consisting of earthworms and large arthropods had numerous flaws. However, the risk to earthworm-eating birds was sufficiently addressed. The risk to insectivorous birds feeding on invertebrates on ornamentals was not addressed.

New information including field studies were submitted by the applicant and evaluated by the rapporteur Member State in Addendum 1 and Addendum 2. However, in view of the restrictions of Commission Regulation (EC) No 1095/2007 the new data were not taken into account in the peer review. Data gaps to address the long-term risk to birds remain for all representative uses evaluated.

The risk to small herbivorous mammals was assessed for the uses in pome/stone fruit and ornamentals (rose) and grapes. For the use in strawberries an insectivorous mammal was chosen for the risk assessment based on the assumption that strawberry foliage is not specifically attractive to herbivorous mammals. All first-tier TER values exceeded the Annex VI trigger values of 10 and 5, indicating a low acute and long-term risk to mammals from the representative uses.

The risk to birds and mammals from the uptake of contaminated drinking water was assessed as low by the rapporteur Member State in Addendum 2. The experts agreed to the assessment.

Overall it was concluded that the acute and short-term dietary risk to birds is low but a high long-term risk to insectivorous birds cannot be excluded for the uses in pome/stone fruit, vineyards, strawberries and ornamentals. The risk to mammals was assessed as low for all representative uses.

5.2. Risk to aquatic organisms

Clofentezine has low water solubility (0.025 mg/L). The end points observed in studies with technical clofentezine were determined by the solubility of the test substance. Higher test concentrations were achieved with formulated clofentezine. The end points observed for formulated clofentezine were used in the risk assessment. The acute risk assessment was based on a worst case FOCUS Step 1 PECsw of 0.047 mg clofentezine/L for the early use in orchards. The resulting TER values were well above the Annex VI trigger value of 100 indicating a low acute risk to aquatic organisms.

The lowest 21 day NOEC for *Daphnia magna* was observed in a test with the technical a.s. (0.025 mg a.s./L). However this was the only concentration tested. A second study (21 days) with the formulation 'Apollo 50 SC' resulted in a NOEC of 0.05 mg a.s./L. A 21-day test with the formulation 'Apollo 50 SC' was conducted under the presence of sediment. A NOEC of 0.25 mg a.s./L (nominal concentration) was observed in this study with sediment. The experts agreed that the NOEC of 0.25 mg a.s./L can be used in the risk assessment in

combination with total load PEC_{SW} values from FOCUS Step 1 and Step 2. The end point of 0.05 mg a.s./L should be used with FOCUS Step 3 PEC_{SW} values. The worst case FOCUS Step 3 scenario R3 stream (PEC of 0.00177 mg a.s./L) gave a TER of 28 indicating a low long-term risk to daphnids.

The risk to sediment-dwelling organisms was assessed as low, since the TER values for sediment exceeded the trigger of 10 with FOCUS Step 2 PEC_{SW} values.

Two long-term studies with fish were made available in the original dossier. A NOEC of 12.5 mg clofentezine/L was observed in a fish juvenile growth test with the formulation.

An early life stage test was conducted with technical clofentezine with a single concentration of 0.007 mg clofentezine/L. No adverse effects were observed. The NOEC from this study was 0.007 mg clofentezine/L since it was the only concentration tested. A new early life stage test with more than one concentration tested was submitted by the applicant and evaluated by the rapporteur Member State in Addendum 1. However, in view of the restrictions of Commission Regulation (EC) No 1095/2007 the new study could not be taken into account in the peer review, and the end point of 0.007 mg clofentezine/L became the end point which was driving the aquatic risk assessment. No full FOCUS Step 3 scenario resulted in a TER greater than 10. The trigger of 10 was exceeded only in the part scenarios R1 (pond) for the use in grapes and D4 (pond) for the use in strawberries and grapes. A final conclusion on the aquatic risk assessment can be drawn after the assessment of the new early life stage study with fish.

Metabolites:

Hydrazide-hydrazone (AE C593600, FBC 93600) is a major metabolite in sediment (maximum of 22.2 % of AR). It was assumed that hydrazide-hydrazone (AE C593600, FBC 93600) was present in the test with *Chironomus ripariu* and that the formation of the metabolite hydrazide-hydrazone in the test system was similar as in the water sediment study, since the degradation to hydrazide-hydrazone is via hydrolysis and not reliant on microbial activity. Therefore, the risk to sediment-dwelling organisms was considered to be addressed by the risk assessment for clofentezine.

No risk assessment was conducted for the metabolite 2-chlorobenzonitrile (AE F023666). The metabolite is formed via photolysis up to 74.6 % of AR. Solar irradiation could promote the formation of 2-chlorobenzonitrile (AE F023666) under natural conditions. Therefore a risk assessment was considered necessary by the experts. Acute studies with 2-chlorobenzonitrile (AE F023666) and fish, daphnids and algae were available. The TER values were calculated on the basis of the maximum initial PECsw for clofentezine from FOCUS Step 1, assuming that the parent compound is immediately converted to the metabolite. The TERs exceeded the trigger values of 100 and 10 indicating a low risk.

The BCF for clofentezine was determined as 248 for the whole fish. Although the Annex VI trigger for the bioconcentration factor is 100 for not readily biodegradable substances, the risk to aquatic organisms from bioaccumulation was considered to be low since the substance is excreted rapidly (CT_{90} = 3 days).

Overall, it was concluded that a high long-term risk to fish cannot be excluded for all representative uses, since no full FOCUS Step 3 scenario resulted in a TER greater than 10. However, the long-term risk assessment for fish is based on the NOEC value from an early life stage study where only one concentration was tested. A new study was made available where more concentrations were tested. This study was not taken into account in the peer

review in view of the restrictions of Commission Regulation (EC) No 1095/2007 and should be considered at Member State level.

5.3. Risk to bees

The acute oral and contact toxicity to bees was tested with the formulation 'Apollo 50 SC'. The LD_{50} values were >252.6 µg clofentezine/bee and >84.5 µg clofentezine/bee. Since the substance has no systemic properties, bee brood is considered not to be exposed via pollen or nectar. The HQ values for oral and contact toxicity were calculated as 0.8 and 2.4, indicating a low risk to bees.

5.4. Risk to other arthropod species

The toxicity of the formulation 'Apollo 50 SC' was tested with *Aphidius rhopalosiphi*, *Typhlodromus pyri*, *Trichogramma cacoeciae*, *Chrysoperla carnea, Phytoselius persimilis* and *Poecilus cupreus* in standard laboratory tests. No effects of >50 % were observed at the tested dose of 300 g clofentezine/ha. The HQ values for *T. pyri* (based on an LR_{50} of > 300 g a.s./ha) were in the range of 0.01-0.67, indicating a low risk for all representative uses. The in-field HQ values for *A. rhopalosiphi* were above the trigger of 2 for all representative uses. However, the standard laboratory studies with *T. pyri* do not cover the first life stages, which are potentially more sensitive to clofentezine. Reduction in reproduction of up to 37 % was observed in a higher tier study with *A. rhopalosiphi* at a treatment rate of 300 g clofentezine/ha. Since the effect was < 50 % at a treatment rate higher than the suggested 200 g clofentezine/ha, the risk was considered to be low.

Only brief summaries of field studies with *T. pyri* in English language were submitted by the applicant. No study details were given in these summaries. Therefore it was not possible for the rapporteur Member State to judge the reliability of the study results. The studies could not be used in the risk assessment. The applicant submitted new studies with *Coccinella septempunctata* and *Aleochara bilineata* to address the risk to early life stages of insects including eggs. The rapporteur Member State evaluated the studies in Addendum 1, however, the studies could not be taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007. Therefore, it was concluded that a high risk to sensitive stages of non-target arthropods cannot be excluded on the basis of the peer reviewed data and a data gap was identified by the meeting of experts to address the risk to sensitive life stages of non-target arthropods.

5.5. Risk to earthworms

The acute toxicity of formulated clofentezine to earthworms was low and the acute TER was calculated as >800 based on the maximum accumulated (peak plateau) PEC soil of 0.268 mg clofentezine/kg d.wt.soil. Clofentezine is persistent in soil and therefore a chronic risk assessment was conducted. The chronic NOEC was determined as 2 mg clofentezine/kg d.wt.soil. Because of the logPow of > 2 the NOEC was divided by 2. By comparing the end point of 1mg clofentezine/kg with the peak plateau soil concentration of 0.268 mg clofentezine/kg d.wt.soil the resulting TER value was 3.7. No effects were seen in a second study at the tested treatment rate of 5.5 kg clofentezine/ha. If this is corrected by 2 and the resulting NOEC of 2.75 kg clofentezine/ha is compared to the peak plateau PECsoil expressed at an application rate of 0.252 kg clofentezine/ha (the peak plateau PEC soil was achieved by an application rate of 1.26 x 0.2 kg a.s./ha), the long-term TER was 11.

However, only one concentration was tested in this study and the number of offspring was reduced by about 19 %.

The rapporteur Member State recalculated the NOEC from the first study in Addendum 1 as 2.656 mg a.s./kg d.wt.soil. The resulting TER of 9.9 exceeded the trigger of 5 indicating a low risk to earthworms.

An earthworm field study was submitted which was conducted at treatment levels of 186 g clofentezine/ha and 372 g clofentezine/ha. No adverse effects were observed until the end of the study after 6 months.

No studies with earthworms were conducted with the major soil metabolite hydrazide-hydrazone (AE C593600, FBC93600). The toxicity to earthworms was assumed to be similar to the parent clofentezine because of structural similarity. The initial (maximum) PEC soil for hydrazide-hydrazone was calculated as 0.027 mg/kg soil. The toxicity of hydrazide-hydrazone would have to be more than 100 times more toxic than the parent clofentezine in order to breach the Annex VI trigger values. Such an increase in toxicity was considered very unlikely, and therefore the experts agreed that the risk from hydrazide-hydrazone to earthworms can be considered as low.

The risk from the soil metabolite 2-chlorobenzoic acid (AE C500233, NC233) was assessed as low. The acute and long-term TER values were greater than the trigger values of 10 and 5, with a soil PEC of 0.019 mg 2-chlorobenzoic acid/kg d.wt.soil and an assumed 10 times increased toxicity compared to clofentezine.

Overall, it was concluded that the risk to earthworms was low for the representative uses evaluated.

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

No effects on mortality and reproduction of *Folsomia candida* were observed in a study with the formulation 'Apollo 50 SC' up to a concentration of 160 mg clofentezin/kg d.wt.soil (NOEC). The NOEC was divided by two to take into account the organic matter in the artificial soil and the logPow of >2. If the NOEC of 80 mg clofentezine/kg d.wt.soil is compared to the maximum estimated soil concentration of 0.268 mg clofentezine/kg, the resulting TER is 299. Therefore it was concluded that the risk from the representative uses to collembola was low.

No litter bag study was submitted to address the potential effects on organic matter breakdown. Such a study is triggered since the field DT_{90} in some of the field studies was > 365 days. A litter bag study was submitted by the applicant and evaluated by the rapporteur Member State in Addendum 1. The study was not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007 and a data gap remains for the submission of a litter bag study.

5.7. Risk to soil non-target micro-organisms

No effects on soil respiration and nitrification were observed within 28 days at a treatment rate of 200 g clofentezine/ha. Since no effects were observed at a rate 10 times higher than the proposed maximum use rate, the risk to soil micro–organisms is considered to be low.

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

No phytotoxic effects (visual effects and growth) were observed in a test with the formulation 'Apollo 50 SC' and two monocotyledon and four dicotyledon plant species, at a rate of 300 g clofentezine/ha. Therefore the risk to non-target flora is considered to be low.

5.9. Risk to biological methods of sewage treatment

The EC_{50} for inhibition of respiration of activated sewage sludge was determined as > 1000 mg clofentezine/L. Therefore the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

6.1. Soil

Definition for risk assessment:	clofentezine; hydrazide-hydrazone (AE C593600, FBC 93600); 2-chlorobenzoic acid (AE C500233, NC233)
Definition for monitoring:	clofentezine (assessment for soil metabolite 2-chlorobenzoic acid (AE C500233, NC233) needs to be finalized).

6.2. Water

6.2.1. Ground water

Definition for exposure assessment:	clofentezine; hydrazide-hydrazone (AE C593600, FBC 93600); 2-chlorobenzoic acid (AE C500233, NC233); 2-chlorobenzonitrile (AE F023666)
Definition for monitoring:	clofentezine (provisional, since assessment of 2-chlorobenzoic acid (AE C500233, NC233) and 2-chlorobenzonitrile (AE F023666) needs to be finalized).

6.2.2. Surface water

Definition for risk assessment

in surface water:	clofentezine; hydrazide-hydrazone (AE C593600, FBC 93600); 2-chlorobenzoic acid (AE C500233, NC233; from soil via run-off and drainage); 2-chlorobenzonitrile (AE F023666)
in sediment:	clofentezine; hydrazide-hydrazone (AE C593600, FBC 93600)

Definition for monitoring:	clofentezine (assessment for soil metabolite 2-chlorobenzoic acid needs to be finalized)

6.3. Air

Definition for risk assessment:	clofentezine
Definition for monitoring:	clofentezine

6.4. Food of plant origin

Definition for risk assessment:	clofentezine + 2-chlorobenzonitrile (AE F023666) expressed as clofentezine (provisional)
Definition for monitoring:	clofentezine

6.5. Food of animal origin

Definition for risk assessment:	Open (not necessary to support the intended uses)
Definition for monitoring:	Open (not necessary to support the intended uses)

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
clofentezine	moderate to high persistent (DT_{50} = 16.8 – 109 d)	The risk to earthworms, collembola and soil micro-organisms was assessed as low.
hydrazide-hydrazone (AE C593600, FBC 93600)	Moderate persistent (DT_{50} = 43 d)	No studies with soil-dwelling organisms were made available. The risk to earthworms was assessed as low, since the toxicity to earthworms would need to be 100 times greater than the toxicity of clofentezine to breach the TER trigger of 10. Such an increase of toxicity was considered unlikely.
2-chlorobenzoic acid (AE C500233, NC233)	Data gap identified	No studies with soil-dwelling organisms were made available. The risk to earthworms was assessed as low assuming a 10 times greater toxicity as the parent clofentezine.

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
clofentezine	Estimated to be low mobile in soil (K_{oc} = 1064 mL/g)	No, FOCUS GW	Yes	Yes	Harmful to aquatic organisms (R52). Exposure via groundwater is negligible.

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
hydrazide-hydrazone (AE C593600, FBC 93600)	low mobile in soil (K_{foc} = 742 - 1084 mL/g)	No, FOCUS GW	No data submitted. No data needed	No data, not needed	No data available. No data needed.
2-chlorobenzoic acid (AE C500233, NC233)	Data gap identified	Data gap identified	No data submitted, depending on the environmental fate and behavior assessment.	No data, pending further environmental fate and behavior assessment.	No data submitted, depending on the environmental fate and behavior assessment.
2-chlorobenzonitrile (AE F023666) (photolysis metabolite)	Data gap identified	Data gap identified	No data submitted, depending on the environmental fate and behavior assessment.	No data, pending further environmental fate and behavior assessment	No data submitted, depending on the environmental fate and behavior assessment.

6.6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Clofentezine (water and sediment)	Harmful to aquatic organisms (R52), The acute risk to aquatic organisms was assessed as low but no TER was above the trigger of 10 for the long-term risk to fish. However, the long-term risk assessment for fish was based on a NOEC value from an early life stage study where only one concentration was tested. A new study was made available where more concentrations were tested. The new study was not taken into account in the peer review according to Commission Regulation (EC) No 1095/2007.
hydrazide-hydrazone (AE C593600, FBC 93600; water and sediment)	No studies with aquatic organisms available. However, the toxicity would need to be more than 100 times greater compared to the parent clofentezine to breach the Annex VI trigger values. This was considered very unlikely.
2-chlorobenzoic acid (AE C500233, NC233; soil metabolite)	No studies were made available. The risk to aquatic organisms needs to be addressed (Data gap).
2-chlorobenzonitrile (AE F023666) (photolysis metabolite)	Harmful to aquatic organisms (daphnids EC_{50} = 13 mg a.s./L). The risk to aquatic organisms was assessed as low.

6.6.4. Air

Compound (name and/or code)	Toxicology
Clofentezine	Not acutely toxic via inhalation

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

- Representative 5-batch data and a specification of the technical active substance (relevant for all representative uses evaluated, data gap identified by PRAPeR 61 meeting of experts (January 2009), data already submitted and presented in an addendum to Volume 4 (June 2007), however not peer reviewed in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007; refer to chapter 1)
- Confirmatory method for determination of clofentezine in commodities with high water content (relevant for commodities with high water content, data gap identified by PRAPeR 61 meeting of experts (January 2009), data already submitted and evaluated in an addendum to Volume 3 (December, 2008), however, not peer reviewed in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007; refer to chapter 1)
- Pending on the final residue definition for products of animal origin a fully validated method, including a confirmatory method and an ILV for the determination of the compounds in the residue definition for animal tissues and products (relevant for pome fruit, data gap identified by the rapporteur Member State, confirmed by PRAPeR 61 meeting of experts (January 2009), date of submission unknown, however, data for the determination of clofentezine and 4-hydroxy-clofentezine were already submitted and evaluated in an addendum to Volume 3 (June, 2007) but not peer reviewed in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007; refer to chapter 1)
- Equivalence of the batches tested in the mammalian toxicity studies compared to the representative specification (relevant for all uses, data gap identified by the rapporteur Member State, confirmed by PRAPeR 64 meeting of experts; date of submission unknown; refer to chapter 2)
- Data to address the toxicological relevance of the metabolite 2-chlorobenzonitrile (AE F023666) identified in the plant metabolism and in the standard hydrolytic study (relevant for all notified uses; data gap identified by PRAPeR 65 meeting of experts (January 2009), no submission date proposed by the notifier; refer to chapter 3.1.1)
- A complete set of residue trials supporting the notified representative uses on strawberries grown indoor, the samples being analysed for clofentezine and the metabolite 2-chlorobenzonitrile (AE F023666) (relevant for the notified use on strawberries under greenhouse; data gap identified by PRAPeR 65 meeting of experts (January 2009), no submission date proposed by the notifier; refer to chapter 3.1.1)
- A complete set of residue trials supporting the notified representative uses on pome fruits, plums and grapes, in compliance with the critical GAPs, the samples being analysed for clofentezine and the metabolite 2-chlorobenzonitrile (AE F023666) (relevant for the notified uses on apples, plums and grapes; data gap identified by PRAPeR 65 meeting of experts (January 2009), no submission date proposed by the notifier; refer to chapter 3.1.1).

- Data to address the toxicological relevance of the metabolites hydrazide-hydrazone (AE C593600, FBC 93600) and 2-chlorobenzamide (AE F092117) identified in the standard hydrolytic study (relevant for all notified uses; data gap identified by PRAPeR 65 meeting of experts (January 2009), no submission date proposed by the notifier; refer to chapter 3.1.1)
- A complete set of processing studies on pome fruits, plums, strawberries and grapes. The process should include a heating step, at least 90°C if relevant (juice and canned fruit pasteurisation/sterilisation, heated wine process…) and the samples analysed for clofentezine and the metabolites identified in the standard hydrolytic study (relevant for all the notified uses; data gap identified by PRAPeR 65 meeting of experts (January 2009), no submission date proposed by the notifier; refer to chapter 3.1.1).
- A rotational crop study (relevant for the notified use on outdoor strawberries; data gap identified by the EFSA after the PRAPeR 65 meeting of experts, no submission date proposed by the notifier; refer to chapter 3.1.2)
- A data gap has been identified for studies to derive two additional half-lives for the major soil aerobic metabolite hydrazide-hydrazone (AE C593600, FBC 93600) to complete the minimum data set required (this data gap is not considered essential to finalize the EU risk assessment; no submission date proposed by the notifier; refer to chapter 4.1.2) .
- Potential ground water contamination by the metabolite 2-clorobenzonitrile, produced by photolysis in soil, needs to be assessed. Further studies may also be required to derive the parameters needed for this assessment (relevant for all representative uses evaluated, data gap identified by PRAPeR 62 meeting of experts and confirmed by the results of PRAPeR 64 meeting of experts, date of submission unknown; refer to chapter 4).
- A data gap has been identified for a new photolysis study in water (considered not essential to finalize EU risk assessment, data gap identified by PRAPeR 62 meeting of experts; a new study is already available, neither assessed nor peer-reviewed in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007; refer to chapter 4).
- A data gap has been identified for ground water and surface water exposure assessments for the aerobic soil metabolite 2-chlorobenzoic acid (AE C500233, NC233). Further studies may also be required to derive the parameters needed for these assessments (e.g. formation and degradation rates and adsorption/desorption in soil), the risk to aquatic organisms also needs to be addressed (relevant for all representative uses evaluated, data gap identified by PRAPeR 62 meeting of experts, date of submission unknown; refer to chapter 4).
- The long-term risk to birds needs to be addressed further (relevant for all representative uses evaluated; data gap identified by PRAPeR 63 meeting of experts (January 2009); higher tier data were submitted by the applicant and evaluated by the rapporteur Member State but not taken into account in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007; refer to chapter 5.1.)
- A new early life stage study with fish. (relevant for all representative uses evaluated; data gap identified by PRAPeR 63 meeting of experts (January 2009); the study was submitted by the applicant and evaluated by the rapporteur Member State but not taken into account

in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007; refer to chapter 5.2.)

- The risk to sensitive life stages of non-target arthropods needs to be addressed (relevant for all representative uses evaluated; data gap identified by PRAPeR 63 meeting of experts (January 2009); studies were submitted by the applicant and evaluated in Addendum 1 but not taken into account in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007; refer to chapter 5.4.)
- A litter bag study (relevant for all representative uses evaluated; data gap identified by PRAPeR 63 meeting of experts (January 2009); a litter bag study was submitted by the applicant and evaluated in Addendum 1 but not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007; refer to chapter 5.6.)

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The conclusion was reached on the basis of the evaluation of the representative uses as an acaricide as proposed by the applicant which comprise foliar spraying to control *Panonychus ulmi*, *Tetranychus urticae* (and related species) on pome fruit and stone fruit, *Panonychus ulmi* and *Tetranychus urticae* on grapes, *Panonychus ulmi* and *Tetranychus spp.* on strawberries grown outdoor and indoor, and *Tetranychus spp.* on ornamentals grown outdoor and under glass, in all EU countries, with the number of applications and maximum application rates per treatment according to the end points.

The representative formulated product for the evaluation was 'Apollo 50 SC', a suspension concentrate (SC) containing 500 g/L clofentezine, registered under different trade names in Europe.

The minimum purity of clofentezine technical could not be concluded on, as the original manufacturing site was no longer in use and the data on the new source could not be considered in the peer review.

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

Adequate methods are available to monitor clofentezine residues in food/feed of plant origin and environmental matrices, however, pending on the final residue definition in ground water, a data gap for a method for one metabolite might be identified. Data gaps were identified for a confirmatory method for the determination of clofentezine in commodities with high water content and, pending on the final residue definition in animal tissues and products, for a fully validated method, including a confirmatory method and an ILV for the determination of the compounds in the residue definition.

In mammals, clofentezine is of low acute oral, dermal and inhalational toxicity; it is not a skin or eye irritant, nor a skin sensitiser. The main toxicological effect after repeated oral administration to mice, rats, and dogs was liver enlargement. The relevant short-term

NOAELs are 2.65 mg/kg bw/day in rats, 151.4 mg/kg bw/day in mice, and 1.7 mg/kg bw/day in dogs, whereas the relevant long-term NOAELs in rats and mice are 2 mg/kg bw/day and 5 mg/kg bw/day, respectively. Clofentezine does not have a genotoxic or carcinogenic potential. Clofentezine does not affect fertility or reproductive performance. Relevant maternal and offspring NOAELs are 4 mg/kg bw/day, based on increased liver weight and reduced body weight in parents and decreased pup weight in offspring, whereas the relevant reproductive toxicity NOAEL is 27.8 mg/kg bw/day. Clofentezine does not show any teratogenic effects in rats or rabbits: the relevant maternal NOAELs are 250 mg/kg bw/day (rabbit) and 320 mg/kg bw/day (rat), whereas the developmental NOAELs are 1000 mg/kg bw/day and 3200 mg/kg bw/day, in rabbits and rats, respectively. The ADI of 0.02 mg/kg bw/day was based on the long-term toxicity NOAEL from the 2-year rat study, with a safety factor of 100. The overall toxicological picture of clofentezine did not justify setting an Acute Reference Dose (ARfD). The AOEL of 0.01 mg/kg bw/day was based on the NOAEL from the 90-day study in rats, with a safety factor of 100 and corrected by 50 % oral absorption. In all scenarios proposed for the operator applying 'Apollo 50 SC' exposure levels are below the AOEL (mainly with the use of PPE) as well as for bystanders; worker exposure estimates show levels below the AOEL, except for re-entry in treated pome and stone fruit crops (107 % of the AOEL, no PPE considered).

The metabolism of clofentezine has been investigated in the fruit plant group only, on apple, lemon, peach and grape. The parent clofentezine was shown to be the major compound accounting for 55 % to 87 % of the TRR. The metabolic pathway runs through the cleavage of the tetrazine ring to form 2-chlorobenzonitrile (AE F023666), which is further oxidised to 2-chlorobenzamide (AE F092117), 2-chlorobenzyl alcohol and 2-chlorobenzoic acid (AE C500233, NC233). **This degradation pathway is specific to plants, since no metabolites resulting from the cleavage of the parent compound were found in rat metabolism**. Based on these studies, the plant residue definition for monitoring was limited to the parent clofentezine only. However, for risk assessment, the experts were of the opinion to include the metabolite 2-chlorobenzonitrile (AE F023666) in the residue definition, awaiting additional information on its toxicity and its toxicological relevance.

The residue trials were sufficient to propose an MRL for strawberries grown outdoor. For the other crops, the residue database was considered not relevant and incomplete, as the residue trials were mainly performed with application rates in excess of 50 % to the representative GAPs. A new residue data set in compliance with the critical GAPs was requested for plums, grapes and apples. Clofentezine residues were shown to be stable over 2 years in high water containing matrices.

In a standard hydrolytic study, clofentezine was totally degraded at 120°C to form the metabolites hydrazide-hydrazone (AE C593600, FBC 93600), 2-chlorobenzamide (AE F092117) and 2-chlorobenzonitrile (AE F023666). These metabolites are not covered by the rodent metabolism, and no information was provided on their toxicological relevance and their possible residue levels in the processed fractions. Therefore, no residue definition was proposed, and a new processing data set taking into account the parent clofentezine and its breakdown metabolites was requested in addition to clarification concerning their toxicity and their residue levels in the processed fractions. Transfer factors taking into account the parent clofentezine only were proposed for apple juice, apple wet and dry pomace, apple sauce, pasteurised canned strawberries and raisin. The transfer in grape juice and wine was identified as a data gap.

No standard rotational crop study was submitted, but considering the DT_{90} value up to 640 days in the aerobic field studies and the fact that outdoor strawberry crops may be rotated, the EFSA is of the opinion that a standard rotational crop study has to be requested.

The discussion concerning the metabolism of clofentezine in animals was not conclusive. No residue definition was proposed, even if there was clear evidence that the residue definition for animal products should at least include the parent clofentezine and the metabolite 4-hydroxy-clofentezine. Moreover, considering that the dietary intake by animals is mainly based on a processed commodity (apple pomace), it was concluded that information on the nature of the residues in the processed feed is needed prior to propose a reliable residue definition for animal products. Nevertheless, and considering the residues resulting from the representative uses, no residues above the LOQ are expected in animal matrices and there is no need to set a residue definition for animal products at the moment.

Using to the EFSA PRIMo rev2 model, the MRL of 2.0 mg/kg is proposed for strawberries, the highest TMDI is 7 % of the ADI.

According to the available studies, clofentezine is moderate to high persistent in soil (DT_{50} = 16.8 – 109 days) under dark aerobic conditions. Under these conditions clofentezine yields two major metabolites: **hydrazide-hydrazone** (AE C593600, FBC 93600) (maximum of 13 % AR after 30 days in one soil) and **2-chlorobenzoic acid** (AE C500233, NC233) (maximum of 13.6 % based on theoretical molar basis). The rapporteur Member State calculated the half-life of the metabolite hydrazide-hydrazone (AE C593600, FBC 93600) based on data in one soil (Cottenham) (DT_{50} = 43 days). This value was derived from the decline phase of the metabolite, ignoring the concomitant formation. The assessment presented by the rapporteur Member State may be regarded as a conservative estimate, since this half-life is used associated to a formation fraction of 1. A data gap for two additional half-lives has been identified in order to complete the minimum data set required. This data gap is not considered essential to finalize the EU risk assessment, however, the data may be needed by Member States when evaluating other potential uses of clofentezine. A data gap was identified for ground water and surface water exposure assessments for the metabolite 2-chlorobenzoic acid (AE C500233, NC233). Bound residue comprised up to 32.3 % AR and CO_2 up to 40.7 % AR after 120 days.

The degradation seems to be enhanced under anaerobic conditions, with higher levels of bound residue (43.5 % AR after 90 days) and lower levels of CO_2 (19 % AR after 90 days) than under aerobic conditions. However, no major metabolites were observed under the anaerobic test conditions.

Photolysis may contribute to the degradation of clofentezine in the environment. The only metabolite identified was 2-chlorobenzonitrile (AE F023666) that reached a maximum of 5.5 % AR at the end of the study (30 days). This metabolite should be assessed for potential ground water contamination.

Field soil dissipation trials from different locations of Germany, the United Kingdom and Italy are available and summarized in the DAR. Maximum plateau residue of 16 - 26 % of the initial applied concentration (on molar basis) of clofentezine was calculated to be reached after 3-5 years.

No batch soil adsorption/desorption studies are available for clofentezine because of the low solubility (3 µg/L). According to an estimation (based on the octanol/water partition coefficient) clofentezine was considered to be low mobile in soil (K_{oc} = 1064 mL/g). The result was confirmed by available soil column leaching- and soil TLC experiments. A batch

soil adsorption/desorption study was conducted with the soil metabolite hydrazide-hydrazone (AE C593600, FBC 93600) in three soils. This metabolite showed low mobility in soil (K_{foc} = 742 - 1084 mL/g). A possible pH-dependence was indicated by this study with lower sorption at higher pH.

The hydrolysis of clofentezine was pH-dependent (pH 5: DT_{50} = 10.4 days; pH 7: DT_{50} = 26.4 hours – 34.4 hours; pH 9: DT_{50} = 4.3 hours at 22 ºC). The main hydrolysis product was hydrazide-hydrazone (AE C593600, FBC 93600) (maximum of 45 % AR at pH 9 and 22 ºC), that was further degraded to the minor metabolites 2-chlorobenzonitrile (AE F023666) and 2-chlorobenzamide (AE F092117).

According to the information available, photolysis may contribute to the environmental degradation of clofentezine. A major aqueous photolysis metabolite was identified: 2-chlorobenzonitrile (AE F023666; maximum of 79 % AR). The meeting of experts concluded that this metabolite needs to be assessed for its fate and effects on the aquatic environment. Clofentezine is not readily biodegradable.

The degradation of clofentezine was investigated in one study in two water sediment systems. Clofentezine dissipated from the water phase via either partition to the sediment or degradation to metabolite hydrazide-hydrazone (AE C593600, FBC 93600). Clofentezine whole system half-lives of 7.1 days – 13.1 days were observed.

The Step 4 FOCUS PEC_{SW} used in the risk assessment presented in the DAR were considered not appropriate for the EU risk assessment. The PRAPeR 63 meeting of experts on ecotoxicology did not agree with the acceptable concentration proposed by the rapporteur Member State in Addendum 2. With the agreed ecotoxicological end point, mitigation would be needed to demonstrate any acceptable use with respect to the aquatic environment. No new Step 4 FOCUS PEC_{SW} calculations are available, and therefore the aquatic risk assessment remains open. It should be noted that the ecotoxicological end point is also pending on the evaluation of a study that cannot be considered at this stage in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007.

The meeting of experts agreed that $PEC_{SW/SED}$ values for the aqueous photolysis metabolite 2-chlorobenzonitrile (AE F023666) are needed to finalize the EU risk assessment. No new calculations have been performed after the meeting of experts. The rapporteur Member State proposed in the list of end points to use the FOCUS Step 1 $PEC_{SW,}$ calculated for the parent compound as a worst case surrogate for this metabolite in the EU risk assessment.

The potential ground water contamination by clofentezine and its soil metabolite hydrazide-hydrazone (AE C593600, FBC 93600) was assessed for the representative uses in apples (fruit/stone fruit), grapevines and strawberries. The calculated concentrations were all below 0.001 µg/L. Whereas the EFSA Opinion on FOCUS GW models requires that the calculations should be done with an additional model, it is not likely that in this case the trigger of 0.1 µg/L would be breached.

During the peer review the need to assess the potential ground water contamination by the soil aerobic metabolite 2-chlorobenzoic acid (AE C500233, NC233) and the soil photolysis metabolite 2-chlorobenzonitrile (AE F023666) was identified. Therefore, new data gaps have been identified for the corresponding studies and calculations.

Clofentezine may be considered slightly volatile. On the basis of the estimated atmospheric half-life of 5.1 days clofentezine would be considered relatively stable in air. The experts

agreed that even when the volatilization from water and soil and plant surfaces is expected to be low, long-range transport in the atmosphere may occur due to the formation of aerosols when the substance is sprayed.

The acute and short-term dietary risk to birds was low, but a high long-term risk to insectivorous birds cannot be excluded for the uses in pome/stone fruit, vineyards, strawberries and ornamentals. The risk to mammals was assessed as low for all representative uses. The risk to aquatic organisms was assessed as low except for the long-term risk to fish. No full FOCUS Step 3 scenario resulted in a TER greater than 10. However, the long-term risk assessment for fish was based on a NOEC value from an early life stage study where only one concentration was tested. A new study was made available where more concentrations were tested. The new study was not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007 and should be considered at Member State level.

The in-field HQ value was <2 for *Typhlodromus pyri* but not for *Aphidius rhopalosiphi.* No effects of >50 % were observed in standard laboratory studies with *Trichogramma cacoeciae*, *Chrysoperla carnea, Phytoselius persimilis* and *Poecilus cupreus.* Concerns remained with regard to the risk to sensitive life stages of non-target arthropods. The applicant submitted new studies to address the risk to sensitive life stages of non-target arthropods. The studies were evaluated by the rapporteur Member State in Addendum 1, but were not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007. A litter bag study was triggered but not included in the original dossier. A litter bag study was submitted by the applicant and evaluated by the rapporteur Member State in Addendum 1, but the study was not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007.

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

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

- For the operator applying 'Apollo 50 SC': use of PPE in all scenarios except for tractor-mounted spraying activities on outdoor strawberries and ornamentals (German model), where no PPE is needed.
- For re-entry workers in pome and stone fruit crops: the use of PPE would reduce the estimated exposure below the AOEL.

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.
- Ground water exposure assessment not finalized for the major soil aerobic metabolite 2-chlorobenzoic acid (AE C500233, NC233) and for the soil photolysis metabolite 2-chlorobenzonitrile (AE F023666). With the available data it was not possible to exclude the toxicological relevance of these metabolites.
- Clofentezine has potential for long-range transport through the atmosphere.

- The long-term risk to birds (The first-tier long-term TERs were 1.26 for the uses in orchards, vineyards, ornamentals and 1.69 for the use in strawberries. The suggested refinements of PD and PT were not sufficiently justified by data).
- The long-term risk to fish (No full FOCUS Step 3 scenario resulted in a TER greater than 10. However, the long-term risk assessment is based on the NOEC value from an early life stage study where only one concentration was tested. A new study was made available where more concentrations were tested. This study was not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007 and should be considered at Member State level).
- The risk to sensitive life stages of non-target arthropods (The in-field HQ was >2 for *A. rhopalosiphi*. The effects observed in standard laboratory tests were <50 % at an application rate of 300 g a.s./ha, however, the most sensitive life stages were not covered by the tests. New studies were submitted by the applicant but not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007 and should be considered at Member State level).
- The risk to organic matter breakdown (A litter bag study was triggered because of the persistence of clofentezine in soil. A litter bag study was submitted by the applicant and evaluated by the rapporteur Member State in Addendum 1, but the study was not taken into account in the peer review in view of the restrictions of Commission Regulation (EC) No 1095/2007.)

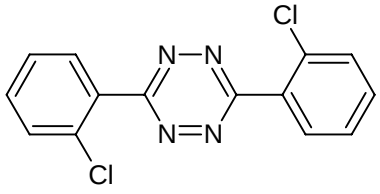
APPENDICES

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) ‡	clofentezine
Function (*e.g.* fungicide)	Acaricide
Rapporteur Member State	United Kingdom
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	3,6-bis (2-chlorophenyl)-1,2,4,5-tetrazine
Chemical name (CA) ‡	3,6-bis (2-chlorophenyl)-1,2,4,5-tetrazine
CIPAC No ‡	418
CAS No ‡	74115-24-5
EC No (EINECS or ELINCS) ‡	277-728-2
FAO Specification (including year of publication) ‡	418/TC (April 2007), min. 980 g/kg
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	None
Molecular formula ‡	$C_{14}H_8Cl_2N_4$
Molecular mass ‡	303.1 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	182-183°C (purity 99.3-99.7%)
Boiling point (state purity) ‡	Not determined – substance decomposes before boiling point is reached.
Temperature of decomposition (state purity)	190-250 °C (99.7%)
Appearance (state purity) ‡	Magenta crystalline solid (purity not specified)
Vapour pressure (state temperature, state purity) ‡	6.0 x 10^{-7} Pa at 20°C (99.7%)
Henry's law constant ‡	0.168 Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	At pH5, solubility = 2.52 µg/l (98.2%) at 22°C At pH7, solubility = < 2µg/l (98.2%) at 22°C At pH9, solubility = < 2µg/l (98.2%) at 22°C
Solubility in organic solvents ‡ (state temperature, state purity)	Ethylacetate: 5.67 g/l at 20°C (99.7%) n-Heptane: 0.11 g/l at 20°C (99.7%) Acetone: 9.3 g/l at 25°C (>99%) Dichloromethane: 37.4 g/l at 20°C (>99%) Ethanol: 0.49 g/l at 20°C (>99%) Xylene: 5.0 g/l at 20°C (>99%) DMSO 11.8 g/l at 20°C (>99%)
Surface tension ‡ (state concentration and temperature, state purity)	Not required as solubility of clofentezine is < 1 mg/l at various pH values.
Partition co-efficient ‡ (state temperature, pH and purity)	log P_{OW} = 3.1 at 20°C log P_{OW} = 4.09 at 25°C Log P_{OW} is independent of pH
Dissociation constant (state purity) ‡	Not calculated – clofentezine is unstable at high pH where dissociation will occur therefore dissociation constant may not be calculated experimentally

UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	UV/Vis, IR, MS and ^{1}H NMR spectra (99.9%) were submitted. Molar absorption coefficients were calculated for neutral, acid and basic solutions of the material in methanol. Solutions were acidified or made alkali as required by the addition of HCl and KOH respectively. Acidic (526.3nm) = 636 L mol^{-1} cm^{-1}, Maximum absorbance at 538 nm Neutral (534.5nm) = 465 L mol^{-1} cm^{-1}. Maximum absorbance at 538 nm Basic (536.2nm) = 220 L mol^{-1} cm^{-1}. Maximum absorbance at 544 nm The molar coefficients at 290 nm: Neutral solution – 11308 l/mol cm Acid solution – 13372 l/mol cm Basic solution – 3800 l/mol cm
Flammability ‡ (state purity)	Not highly flammable (technical material, purity not stated)
Explosive properties ‡ (state purity)	Non-explosive (96%)
Oxidising properties ‡ (state purity)	Non-oxidising (case)

Summary of representative uses evaluated (*Clofentezine*)*

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	Kg as/hL min – max (l)	water L/ha min – max	Kg as/ha min – max (l)		
Pome fruit Apples-Pears	B, E, EL, F, I, NL, POR, UK	Apollo 50 SC	F	Tetranychus ssp., Panonychus ssp., P.ulmi	SC	500 g/L	Foliar, air assisted & hydrolic	08 – 56	1	NR	0.007 – 0.05	400-1500	0.1-0.2	35	[1] [2] [3]
Stone fruit: Plums	E, F, UK	Apollo 50 SC	F	Tetranychus ssp., Panonychus ssp., P.ulmi	SC	500 g/L	Foliar, air assisted & hydrolic	08 - 75	1	NR	0.007 – 0.05	400-1500	0.1-0.2	35	[1] [2] [3]
Grapes	E, F, I	Apollo 50 SC	F	Tetranychus ssp., Panonychus ssp., P.ulmi	SC	500 g/L	Foliar, air assisted & hydrolic	11 – 75	1	NR	0.01 – 0.05	300-1000	0.1-0.15	30	[1] [2] [3]
Strawberries	B, E, F, I, NL	Apollo 50 SC	F / G	Tetranychus ssp., P.ulmi	SC	500 g/L	Foliar, hydrolic	At occurrence - 85	1	NR	0.007 - -0.04	500-1500	0.1-0.2	3	[1] [2] [3]
Roses (Ornamentals)	B, F, I, NL	Apollo 50 SC	F / G	Tetranychus ssp.	SC	500 g/L	Foliar, hydrolic	At occurrence	1	NR	0.006 – 0.04	500-2500	0.15-0.2	n.a.	[1] [2] [3]

[1] data gaps were identified in section 5 (ecotoxicology).

[2] data gaps and issues in section 4 (fate and behaviour in the environment including ground water)

[3] data gap identified in section 3 (residues).

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

Methods of Analysis

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

Technical as (analytical technique)	Technical material dissolved in acetonitrile, then analysed via HPLC with UV detection at 230nm (C18 column).
Impurities in technical as (analytical technique)	Technical material dissolved in dimethylformamide, then analysed via HPLC with UV detection at 235nm (C18 column)
Plant protection product (analytical technique)	Plant Protection Product dissolved in acetone, then analysed by HPLC with UV detection at 243nm. Mobile phase methanol/tetrahyrofuran/deionised water.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	clofentezine
Food of animal origin	Open (not necessary to support the intended uses)
Soil	clofentezine (assessment for soil metabolite 2-chlorobenzoic acid needs to be finalized).
Water	surface water: clofentezine (assessment for soil metabolite 2-chlorobenzoic acid needs to be finalized) ground water: clofentezine (provisional, since assessment of 2-chlorobenzoic acid and 2-chlorobenzonitrile needs to be finalized).
Air	clofentezine

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Maceration with acetone, prior to clean up with water and washing with hexane. Further clean up via Sep-pak cartridge, elution with dichloromethane and hexane. Analysis via HPLC/UV with detection at 268nm. LOQ = 0.01mg/kg (clofentezine) Validated for watery crops only A confirmatory method is required

Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Open Clofentezine Derivitisation method to 2-chlorobenzoic acid. Hydrolysis with HBr. Extraction with diethyl ether. Derivatisation with MSTFA. Analysis by GC/MS (monitoring for m/z = 111, 139 and 213), using an Optima-5-MS column, LOQ = 0.05 mg/kg liver, 0.02 mg/kg muscle and fat and 0.01 mg/kg milk and eggs. The data submitted by the applicant to address the outstanding data required, was correct with regard to the approach taken, however, as pointed out in Addendum 1 there are a number of issues associated with the acceptance of the method for the purpose of enforcement and with the associated validation data. Therefore, the RMS recommends that a HPLC-MS/MS is developed (along the lines of the environment methods) and validated for clofentezine and its metabolite 4-hydroxy-clofentezine (including ILV data) for animal products (milk, eggs, muscle, liver, kidney and fat).
Soil (analytical technique and LOQ)	Extraction with acetonitrile/ water. Analysis by HPLC/MS-MS. Parent ion of 303 with daughter ion of 305. LOQ = 0.02 mg/kg (clofentezine)
Water (analytical technique and LOQ)	Clean up by SPE tube, analysis via HPLC-MS/MS. Parent ion 303, daughter ion 305. LOQ = 0.05µg/l. (clofentezine) (surface water and drinking water) (analytical method for 2-chlorobenzoic acid might be needed pending on the final residue definition)

Air (analytical technique and LOQ)	Adsorption using Tenax sampling cartridge – analysis via reverse phase HPLC with UV detection at 268nm or MS/MS, using parent ion 303, daughter ion 305. LOQ = 0.60 µg/m^3 (clofentezine)
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

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

Rate and extent of oral absorption ‡	Comparative i.v and oral studies suggest 50% conservative estimate for enteral absorption
Distribution ‡	Well distributed with highest concentration in liver
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	80-90% in 48 hours almost complete by 96 hours
Metabolism in animals ‡	Similar in all species rat, mouse, rabbit, and dog, baboon, apparently most extensive in the rat Main pathway: methyl thiolation and than hydroxylation
Toxicologically relevant compounds ‡ (animals and plants)	Parent
Toxicologically relevant compounds ‡ (environment)	-

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	Rat/mouse >5200 mg/kg bw	
Rat LD_{50} dermal ‡	Rat >2100 mg/kg bw	
Rat LC_{50} inhalation ‡	LC50 >1.51 mg a.i/litre (4h, nose only)	
Skin irritation ‡	Very slight (no classification needed)	
Eye irritation ‡	Mild (no classification needed)	
Skin sensitisation ‡	Negative in Magnusson & Kligman assay.	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Liver and blood (reduced haemoglobin levels)

Relevant oral NOAEL ‡	90 day rat study: 2.65 mg/kg bw/day 90 day mouse study: 151.4 mg/kg bw/day 1 year dog: 1.7 mg/kg bw/day
Relevant dermal NOAEL ‡	No data, not required
Relevant inhalation NOAEL ‡	No data, not required

Genotoxicity ‡ (Annex IIA, point 5.4)

Overall no genotoxic potential

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

Target/critical effect ‡	liver and thyroid
Relevant NOAEL ‡	2 year rat study: 2 mg/kg bw/day 2 year mouse: 5 mg/kg bw/day
Carcinogenicity ‡	In the rat study with relatively low dose levels a slight increase of thyroid follicular cell tumours was observed. In mice a non-significant increase in benign liver tumours was found in females. Neither effect was considered to be a clear indication of carcinogenicity.

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	• Parental:increased liver weight and reduced body weight • Offspring: decreased pup weight • There were no specific effects on reproduction.
Relevant parental NOAEL ‡	• 4 mg/kg bw/day
Relevant reproductive NOAEL ‡	• 27.8 mg/kg bw/day
Relevant offspring NOAEL ‡	• 4 mg/kg bw/day

Developmental toxicity

Developmental target / critical effect ‡	**Maternal toxicity**: liver effects (rat) reduced bodyweight gain (rabbit) **Developmental toxicity**: rat (none) reduced foetal weight (rabbit) There was no evidence of teratogenic effects
Relevant maternal NOAEL ‡	**Maternal**: 250 mg/kg bw/day (rabbit) 320 mg/kg bw/day (rat)
Relevant developmental NOAEL ‡	**developmental**: 1000 mg/kg bw/day (rabbit) 3200 mg/kg bw/day (rat)

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	The available data from a variety of mammalian and other species do not indicate that clofentezine has any neurotoxic potential. No neurohistopathological changes have been observed in subacute, subchronic or chronic toxicological studies. In addition, clofentezine has shown no cholinesterase inhibiting activity.
Repeated neurotoxicity ‡	see above
Delayed neurotoxicity ‡	see above

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Clofentezine has been shown to increase hepatic uptake, conjugation and metabolism of thyroid hormone. Biliary excretion of the thyroid hormones therefore rises with increased bile flow and increased hormone excretion into the bile, but only at high dose irrelevant to carcinogenicity.
Studies performed on metabolites or impurities ‡	None

Medical data ‡ (Annex IIA, point 5.9)

All manufacturing personnel, including formulators, packers and maintenance workers, are medically examined by a company physician before commencing employment. Additionally, periodic medical examinations are undertaken e.g. annually or in the event of an adverse work-related health effect being reported. There have been no adverse health effects attributable to Clofentezine detected during medical surveillance of manufacturing plant personnel

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.02 mg/kg bw/day	2 year rat, supported by 1 year dog	100
AOEL ‡	0.01 mg/kg bw/day	90 day rat study	100 (correction for oral absorption of 0.5)
ARfD ‡	Not allocated, not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation ("Apollo 50 SC")	2% for the concentrate and 5% and 10% for the dilutions based on the *in vivo* rat studies

Exposure scenarios (Annex IIIA, point 7.2)

Operator	**Pome and stone fruit through tractor-mounted/trailed broadcast air-assisted sprayers**: 24% of the AOEL=(German model;= protective gloves when handling the concentrate, and coveralls and protective gloves during application) 384 % of the AOEL (UK POEM; gloves when handling the concentrate and during application

Pome and stone fruit through hand-held equipment:

69% of the AOEL (German model; protective gloves when handling the concentrate)

91% of the AOEL (mixing and loading values from the UK POEM in conjunction with 75th percentile spraying values from the German model; protective gloves when handling the concentrate, and coveralls and protective gloves during application)

Grapes through tractor-mounted/trailed broadcast air-assisted sprayers:

96% of the AOEL (German model; protective gloves when handling the concentrate and during application.

98% of the AOEL (EUROPOEM data in conjunction with mixing and loading data from the UK POEM; protective gloves when handling the concentrate and during application

Grapes through hand-held equipment:

52% of the proposed systemic AOEL (German model; protective gloves when handling the concentrate).

68% of the AOEL (mixing and loading values from the UK POEM in conjunction with 75th percentile spraying values from the German model; protective gloves when handling the concentrate, and coveralls and protective gloves during application).

Strawberry and ornamentals through tractor-mounted/trailed field crop sprayers:

87% of the AOEL (German model, no PPE).

34% of the AOEL (UK POEM; protective gloves when handling the concentrate and when handling contaminated surfaces

	Outdoor strawberry and ornamentals through hand-held equipment: 93% of the AOEL (UK POEM; protective gloves when handling the concentrate, and coveralls and protective gloves during application). **Protected strawberry and ornamentals through hose-fed hand lance:** 62% of the proposed systemic AOEL (EUROPOEM data, protective gloves when handling the concentrate and during application). **Protected strawberry and ornamentals through knapsack sprayers:** 85% of the proposed systemic AOEL (EUROPOEM data in conjunction with UK POEM mixing and loading values; protective gloves when handling the concentrate and during application).
Workers	Ornamentals: 24% of the AOEL Strawberries: 32% of the AOEL Grapes: 80% of the AOEL Pome and stone fruit: 107% of the AOEL (no PPE considered)
Bystanders	16% and 1% of the proposed systemic AOEL, tractor-mounted/trailed broadcast air-assisted sprayers and field crop sprayers respectively The use of hand-held equipment outdoors is likely to result in lower levels of bystander exposure than those estimated for tractor-mounted/trailed equipment. Bystanders are not likely to be present when a pesticide is used on protected crops.

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

	RMS/peer review proposal
Substance classified (name)	None

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

Plant groups covered	Fruiting Crops (apple, lemon, peach and grape)
Rotational crops	Open
Metabolism in rotational crops similar to metabolism in primary crops?	Open
Processed commodities	Open: additional information requested to propose residue definition for processed commodities.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No: Metabolite hydrazide-hydrazone accounting for 78% TRR (under sterilisation conditions) not detected in plant metabolism.
Plant residue definition for monitoring	Parent clofentezine
Plant residue definition for risk assessment	Parent clofentezine and 2-chlorobenzonitrile expressed as clofentezine (provisional)
Conversion factor (monitoring to risk assessment)	1.1: clofentezine to parent+2-chlorobenzonitrile (provisional: awaiting information on toxicilogical relevance of 2-chlorobenzonitrile and possible residue levels in treated crops)

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

Animals covered	Ruminant (cattle, goat), poultry (hen)
Time needed to reach a plateau concentration in milk and eggs	Milk = 3 days Eggs = no plateau reach, only 3 day study
Animal residue definition for monitoring	Open
Animal residue definition for risk assessment	Open
Conversion factor (monitoring to risk assessment)	Open
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes: Clofentezine (log P_{ow} = 4.1) and 4-HO-clofentezine (log P_{ow} = 3.6, by calculation)

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

Study (*c.a.* 3N rate with regard to apple GAP) showed minimal uptake in apple seedlings and orange fruit/foliage.

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

No significant decline residues at ≤ -18°C: - after 12 months in apple fruit - after 2 years in peach

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

	Ruminant:	**Poultry:**	**Pig:**
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (yes/no - If yes, specify the level) **Provisional:** Intakes based on a median residue level in apples of 0.16 mg/kg and a processing factor of 5.8. Intakes of the metabolites observed on processing may have to be taken into account.	Yes Clofentezine Dairy = 0.4 Beef = 1.2 mg/kg DM	No	No
Potential for accumulation (yes/no):	Yes		
Metabolism studies indicate potential level of residues ≥0.01 mg/kg in edible tissues (yes/no)	Yes		
Feeding study conducted on dairy cattle using clofentezine only. A further feeding study maybe required once the residue definition for processed commodities and animals has been finalised.	Feeding studies (Specify the feeding rate in cattle and poultry considered as relevant) Residue levels in matrices: Mean (max) mg/kg **Feeding rate : 0.4 mg/kg bw/d** (**Residues given as sum of all compounds containing the 2-chlorobenzoyl moiety expressed as clofentezine**)		
Muscle	<0.05	-	-
Liver	0.26	-	-
Kidney	<0.05	-	-
Fat	<0.05	-	-
Milk	<0.05		
Eggs		-	

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

Crop	Northern/ Southern field or glasshouse,	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Apples	N	0.11, 0.07, 0.17	Further residue trials required	Open		
	S	0.04	Further residue trials required	Open		
Plums	N	0	Residue trials provided not compliant with cGAPs. A complete residue data set according the proposed GAPs is required	Open		
	S	0		Open		
Grapes	N	0	Residue trials provided not compliant with cGAPs. A complete residue data set according the proposed GAPs is required	Open		
	S	0		Open		

Strawberries	N (outdoor)	2x 0.09, 0.16, 0.19, 0.23, 0.24	MRL of 2,0 mg/kg for strawberries grown outdoor based on the southern residue trials only.	**2.0**	0.24	0.18
	S (outdoor)	0.13, 0.50, 0.56, 0.60, 0.70, 0.72, 0.73, 0.75, 0.81, 1.10			1.1	0.71
	(Indoor)		A complete residue data set required	Open		

(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)

ADI	0.02 mg/kg/bw/day
TMDI according to WHO European diet	
TMDI according to EFSA PRIMo rev2	Highest TMDI: 7% ADI (FR toddler)
IEDI (WHO European Diet) (% ADI)	-
NEDI (specify diet) (% ADI)	-
Factors included in IEDI and NEDI	-
ARfD	Not required
IESTI (% ARfD)	-
NESTI (% ARfD) according to national (to be specified) large portion consumption data	-
Factors included in IESTI and NESTI	-

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	
Apples/ Juice	5	0.14		
Apples/ Dry Pomace	5	15.1#		
Apples/ Wet Pomace	5	5.8#		
Apples/ Apple Sauce	2	0.025		
Grapes/ Juice (Must)	2	0.03		
Grapes/ Wine	1	0.17		
Grapes/ Raisins	10	1.20		
Grapes/ Dry Pomace	4	1.90		
Grapes/ Wet Pomace	3	1.72		
Strawberries/ Canning	2	0.235		

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

 # Due to the fluctuation in transfer factors, the worst case transfer factor is used in this case

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

Strawberries	2 mg/kg

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

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

Mineralization after 100 days ‡	15.7-37.5% after 90 d, [^{14}C-tetrazine]-label (n= 3) Sterile conditions: ≤0.1% after 30 d (n= 3)
Non-extractable residues after 100 days ‡	28.2-35.5% after 90 d, [^{14}C-tetrazine]-label (n= 3) Sterile conditions: 7.6-30.0% after 30 d (n= 3)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	AE C593600 (hydrazide-hydrazone) - 13% at 30 d (n = 3) 2-chlorobenzoic acid potentially formed at greater than 10% (theoretical maximum of 13.6% AR) Unidentified metabolite – 10.8% at 21 d (n = 3) [^{14}C-tetrazine] label

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

Anaerobic degradation ‡

Mineralization after 100 days	10.1-20.2% after 60 d
Non-extractable residues after 100 days	38.7-58.5% after 60 d
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	None (2-chlorobenzonitrile reached a maximum occurrence of 5.5% at the end of the study, 31 d) [^{14}C-tetrazine] label

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	O.M. %	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Cottenham, loamy sand	1.9	6.5	15 / 50% MWHC	104.1	70.8	0.95	SFO
Bottisham, clay loam	14.7	6.2	15/ 50% MWHC	70.8	48.1	0.94	SFO
Cottenham, loamy sand	1.9	6.5	25 / 50% MWHC	115.7	168.0	0.99	SFO
Bottisham, clay loam	14.7	6.2	25/ 50% MWHC	131.9	191.5	0.90	SFO
Speyer 2.3, sandy loam	1.9	7.8	22/ 40% MWHC	16.9	16.8	0.99	SFO
Speyer 2.2, Sandy loam	4.5	6.2	22/ 40% MWHC	82.1	86.5	9.3 (chi^2)	SFO
Geometric mean/median					62.5[a]	-	

[a]: geometric mean calculated from 4 data points after individual geometric mean values for the two results for the Cottenham soils (i.e. geomean of 70.8 and 168 = 109.1 d) and the two results for the Bottisham soils (i.e. geomean of 48.1 and 191.5 = 96.0 d) were calculated

AE C593600	Aerobic conditions							
Soil type	O.M. %	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/ k_f	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Cottenham, loamy sand	1.9	6.5	25 / 50% MWHC	43	-	62.4	0.998	SFO from peak
Geometric mean/median						62.4		

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	OM %	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Loamy sand (bare soil)	Wunstorf-Liethe, Germany	3.6	5.6	0-10	28	280	0.95	-	TopFit 2-comp. model
Loamy sand (bare soil)	Niederkirchen, Germany	1.8	7.5	0-10	28	93	0.95	-	TopFit 2-comp. model
Loamy sand (bare soil)	Rheinheim, Germany	1.5	5.4	0-10	77	256	0.89	-	TopFit 1-comp. model
Loamy sand (bare soil)	Rheinheim, Germany	1.5	5.4	0-10	48.8	640.5	0.93	-	Bi-exponential model equivalent to DFOP
Clayey loam (bare soil)	Orsingen-Nenzingen, Germany	2.4	7.9	0-10	20	66	0.98	-	TopFit 1-comp. model
Humic loam (bare soil)	Schwichteler, Germany	2.75	5.8	0-10	30	512	0.98	-	TopFit 2-comp. model
Humic loam (bare soil)	Schwichteler, Germany	2.75	5.8	0-10	29	478.7	0.98	-	Bi-exponential model equivalent to DFOP
Sandy loam (bare soil)	Hilgermissen, Germany	2.8	4.6	0-10	72	241	0.93	-	TopFit 1-comp. model
Sand (bare soil)	Weeze-Wemb Germany	n.r.	n.r.	0-10	131.1	435.4	0.98	-	SFO

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	OM %	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Humus sand (bare soil)	Langförden-Lohe, Germany	11.0	6.4	0-10	77	400	-	-	TopFit 2-comp. model
Sandy loam/loam (bare soil)	Nittenau-Thann, Germany	2.6	7.1	0-10	6.7	22	-	-	TopFit 1-comp. model
Sandy loam (bare soil)	Goch-Nierswalde, Germany	6.4	6.3	0-10	33	110	-	-	TopFit 1-comp. model
Sandy loam (bare soil)	Shelford, UK	2.3	7.8	0-10	49	163	0.93	-	SFO
Sandy loam (bare soil)	Shelford, UK	2.3	7.8	0-10	36 73	120 243	0.96 0.97	-	SFO – results for each plot
Sandy loam (bare soil)	Shelford, UK	2.3	7.8	0-10	54 72	179 239	0.95 0.95	-	SFO – results for each plot
Sandy loam (bare soil)	Shelford, UK	2.3	7.8	0-10	39 51	130 169	0.98 0.94	-	SFO – results for each plot
Sandy loam (bare soil)	Shelford, UK	2.3	7.8	0-10	33 40	110 133	0.99 0.99	-	SFO – results for each plot
Sandy loam (bare soil)	Shelford, UK	2.3	7.8	0-10	31 33	103 110	0.96 0.93	-	SFO – results for each plot

Field studies ‡

Parent	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	OM %	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Sandy loam (bare soil)	Shelford, UK	2.3	7.8	0-10	58 46	192 153	0.98 0.99	-	SFO – results for each plot
Sandy loam (bare soil)	Shelford, UK	2.3	7.8	0-10	50 53	166 176	0.95 0.99	-	SFO – results for each plot
Geometric mean/median					-	-			

n.r. not reported

pH dependence ‡ (yes / no) (if yes type of dependence)	DT_{50} of active substance possibly decreased with increasing pH
Soil accumulation and plateau concentration ‡	Plateau concentration of 0.268 mg/kg reached after 4-5 years application of 200 g/ha per annum with 20% interception by the crop (calculated value).

Laboratory studies ‡

Parent	Anaerobic conditions: Not determined

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡
K_{oc} estimated to be 1064 ml/g based on a log K_{ow} value of 4.09 and the equation of Briggs (1981)

AE C593600 ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	2.0	5.7	-	-	21.7	1084	0.92
Sandy loam	2.9	6.7	-	-	24.7	851	0.93
Loamy sand	2.1	8.3	-	-	15.6	742	0.99

Arithmetic mean/median		892	0.92
pH dependence (yes or no)	Possible dependence for the metabolite AE C593600: stronger sorption at lower pH		

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

Column leaching ‡	Guideline: BBA Merkblatt No. 37, 1980 Precipitation : 400 ml Time period (d): 2 d Leachate: <0.02 µg a.i./ml in leachate 97-101% applied clofentezine retained in top 0-5cm Guideline: BBA Merkblatt No. 37, 1980 Precipitation : 393 ml Time period (d): 2 d Leachate: 0.49-0.99% AR in leachate (majority present as 2-chlorobenzoic acid). NB 2.05% AR was lost from 1 soil when water was used as the mobile phase rather than 0.01M $CaCl_2$). Guideline: none Precipitation : 1027 ml Time period (d): 30 d Leachate: ≤0.27% AR in leachate >90% AR (with >90% remaining as clofentezine) retained in top 0-2.5cm
Aged residues leaching ‡	Guideline: none Aged for (d): 31 d Time period (d): 45 d Precipitation : 0.49 ml/hr Leachate: 0% AR in leachate (no LOD reported) 45-61% AR retained in top 0-5cm

Lysimeter/ field leaching studies ‡	None submitted, none required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent	DT_{50} (d): 131.1 days
Method of calculation	Kinetics: 1st order Field or Lab: representative worst case from field studies.
Application data	Crop: Orchard (apples and pears) % plant interception: 20% (based on FOCUSsurface water guidance) Number of applications: 1 Application rate(s): 200 g as/ha

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average
Initial	0.213	
Short term	0.212	0.213
2d	0.211	0.212
4d	0.209	0.211
Long term	0.206	0.209
28d	0.184	0.198
50d	0.164	0.187
100d	0.126	0.166
Plateau concentration	0.268 mg/kg after 4-5 yr (based on a worst case field study with a DT_{90} of 640.5d derived from a 2-compartment model)	

Metabolite AE C593600 Method of calculation	DT_{50} (d): 43 days (25°C) Kinetics: 1st order, calculated from peak of formation Field or Lab: representative worst case from lab studies.
Application data	Crop: Orchard (apples and pears) % plant interception: 20% (based on FOCUSsurface water guidance) Number of applications: 1 Application rate(s): 25.2 g/ha (based on peak formation of 13% in laboratory study and relative molecular weights of parent and metabolite of 303.2 and 293.2 respectively).

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.027			
Short term	0.026	0.027		
2d	0.026	0.026		
4d	0.025	0.026		
Long term	0.024	0.025		
28d	0.017	0.022		
50d	0.012	0.018		
100d	0.005	0.013		

Metabolite 2-chlorobenzoic acid Method of calculation	Peak PECsoil calculated based on peak parent PECsoil of 0.268 mg/kg (after accumulations) and assuming a peak theoretical formation of 13.6 % on a molar basis and correcting for parent and metabolite molecular weights of 303 and 156 g/mol respectively. Peak PECsoil = 0.268 * 13.6% * 156/303.1 = 0.019mg/kg

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 4.95: 22°C DT_{50} 248.8 hours (1^{st} order)[a]
	pH 6.98: 22°C DT_{50} 34.4 hours (1st order)[a] pH 7: 25°C DT_{50} 1.1 d (1^{st} order); 35°C DT_{50} 0.6 d (1^{st} order)[b]
	pH 9.18: 22°C DT_{50} 4.3 hours (1^{st} order)[a] AE C593600: peak of 45.1% AR, further hydrolysed to stable metabolites AE F023666 (2-chlorobenzonitrile) and AE F092117 (2-chlorobenzamide)
Photolytic degradation of active substance and metabolites above 10 % ‡	Natural light, 52°N; DT_{50} <7 days AE F023666: 74.6% AR (31 d) Estimated DT_{50} at 50°N (summer) 0.8 days
Quantum yield of direct phototransformation in water at Σ > 290 nm	θ of 3.0×10^{-4}
Readily biodegradable ‡ (yes/no)	No

[a]: clofentezine concentration tested ranged from 14 to 26µg/l
[b]: clofentezine concentration tested was approximately 2.1µg/l

Degradation in water / sediment

Parent	Distribution (Max. sed 27.5-38.7 % after 2 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (chi^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Sandy clay loam	8.3	6.8	20	13.1	10.1					SFO
Clay loam	8.2	6.6	20	7.1	25.4			-		

Geometric mean/median	-	9.6				-		

AE C593600	Distribution (max in water 4.4-7.5% after 7 d. Max. sed 14.8-22.2 % after 7-21 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	r^2	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Sandy clay loam	8.3	6.8	20					10.3	0.97	Pseudo SFO
Clay loam	8.2	6.6	20			6.3	0.7	14.1	0.90	Pseudo SFO
Geometric mean/median						-		12.1		

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. max x % after n d	Non-extractable residues in sed. x % after n d (end of the study)
Sandy clay loam	8.3	6.8	29.9% (42 d)	16.9 % (42 d)	16.9 % (42 d)
Clay loam	8.2	6.6	32.0 % (42 d)	26.3 % (14 d)	24.8 % (42 d)

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

Parent	1st order DT_{50} in soil: 71.3 d
Parameters used in FOCUSsw step 1 and 2	1st order DT_{50} in whole water / sediment system (Step 1): 7 d 1st order DT_{50} in water (Step 2): 2.4 d 1st order DT_{50} in sediment (Step 2): 53.3 d K_{OC}: 1064 ml/g Mol. Wt. 303.1 Field or Lab: representative worst case from laboratory studies
Parameters used in FOCUSsw step 3 (if performed)	DT_{50} and Koc as per Step 2 1/n: 0.9 Vapour pressure 6 x 10^{-7} Pa
Application rate	Crop: pome fruit/ stone fruit Number of applications: 1 (Step 2 assumptions:- early application in Southern Europe, Mar – May; No interception assumed at Step 1 or 2) Application rate(s): 200 g as/ha Depth of water body: 30 cm (FOCUS Step 1 and 2)

FOCUS STEP 1 **Pome fruit/stone fruit: Early, 200 g a.s./ha**	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	47.03		293.27	
	24 h	32.25	39.64	343.18	318.23
	2 d	29.21	35.17	310.83	322.48
	4 d	23.96	30.84	254.98	302.23
	7 d	17.81	26.51	189.45	267.25
	14 d	8.90	19.68	94.73	201.95
	21 d	4.45	15.26	47.36	157.41
	28 d	2.23	12.25	23.68	126.60
	42 d	0.56	8.57	5.92	88.67

Total load PECsw at Step 1 (Pome fruit/stone fruit: Early, 200 g a.s./ha) = 86.13µg/l

FOCUS STEP 2 **Pome fruit/stone fruit: Early in Southern Europe (Mar-May), 200 g a.s./ha**	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	19.46		158.48	
	24 h	8.88	14.17	157.71	158.09
	2 d	6.38	10.90	140.15	153.51
	4 d	15.19	9.48	110.69	139.25
	7 d	8.88	10.17	77.70	119.57
	14 d	3.89	8.11	34.02	86.26
	21 d	1.70	6.29	14.89	65.23
	28 d	0.75	5.01	6.52	51.46
	42 d	0.14	3.46	1.25	35.37

Total load PECsw at Step 2 (Pome fruit/stone fruit: Early, 200 g a.s./ha) = 45.1µg/l

Total load PECsw at Step 2 (Pome fruit/stone fruit: Late, 200 g a.s./ha) = 18.18µg/l

Total load PECsw at Step 2 (Grapevine: Early, 150 g a.s./ha) = 20.59µg/l

Total load PECsw at Step 2 (Grapevine: Late, 150 g a.s./ha) = 11.23µg/l

Total load PECsw at Step 2 (Strawberries: minimal crop cover, 200 g a.s./ha) = 22.36µg/l

Total load PECsw at Step 2 (Ornamentals: minimal crop cover, 200 g a.s./ha) = 25.87µg/l

Step 3 full summary results:-

Step 3 Scenario	**Apples, pears and plums (early)**	
	Water body	**Global Maximum (µg/l)**
D3	Ditch	15.5
D4	Pond	0.94
	Stream	15.5
D5	Pond	0.94
	Stream	14.8
R1	Pond	0.94
	Stream	12.6
R2	Stream	16.6
R3	Stream	17.7
R4	Stream	12.5

Step3 Scenario	Apples, pears and plums (late)	
	Water body	Global Maximum (µg/l)
D3	Ditch	7.3
D4	Pond	0.33
	Stream	7.1
D5	Pond	0.33
	Stream	8.0
R1	Pond	0.33
	Stream	5.6
R2	Stream	7.6
R3	Stream	7.9
R4	Stream	5.8

Step 3 Scenario	Grapes (early)	
	Water body	Global Maximum (µg/l)
D6	Ditch	0.85
R1	Pond	0.03
	Stream	0.62
R2	Stream	0.82
R3	Stream	0.87
R4	Stream	0.62

Step 3 Scenario	Grapes (late)	
	Water body	Global Maximum (µg/l)
D6	Ditch	2.57
R1	Pond	0.09
	Stream	1.88
R2	Stream	2.53
R3	Stream	2.65
R4	Stream	1.89

Step 3 Scenario	Strawberries and ornamentals (early)	
	Water body	Global Maximum (µg/l)
D3	Ditch	1.26
D4	Pond	0.04
	Stream	1.02
D6	Ditch	1.26
R1	Pond	0.13
	Stream	1.39
R2	Stream	1.11
R3	Stream	1.66
R4	Stream	2.55

Step 3 Scenario	Strawberries and ornamentals (late)	
	Water body	Global Maximum (µg/l)
D3	Ditch	1.26
D4	Pond	0.04
	Stream	0.98
D6	Ditch	1.28
R1	Pond	0.15
	Stream	0.84
R2	Stream	1.12
R3	Stream	1.22
R4	Stream	2.05

Step 3 full results for worst case scenarios:-

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)	
			Actual	TWA
early application of 200 g a.i./ha on pome fruit (apples and pears) in scenario D3/ditch		0 h	15.50	
		24 h	5.83	11.13
		2 d	0.64	6.85
		4 d	0.07	3.53
		7 d	0.03	2.04
		14 d	0.01	1.03
		21d	0.00	0.69
		28 d	0.00	0.51
		42 d	0.00	0.34
early application of 200 g a.i./ha on pome		0 h	0.94	
		24 h	0.84	

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)	
			Actual	TWA
fruit (apples and pears) in scenario D4/pond		2 d	0.75	
		4 d	0.61	
		7 d	0.45	
		14 d	0.22	
		21 d	0.08	
		28 d	0.04	
		42 d	0.01	
early application of 200 g a.i./ha on pome fruit (apples and pears) in scenario R3/stream		0 h	17.66	
		24 h	0.02	
		2 d	0.01	
		4 d	0.01	
		7 d	0.00	
		14 d	0.00	
		21 d	0.00	
		28 d	0.00	
		42 d		

Metabolite AE C593600 Parameters used in FOCUSsw step 1 and 2	1st order DT_{50} in soil: 62.4 d 1st order DT_{50} in whole water / sediment system (Step 1): 14.1 d 1st order DT_{50} in water (Step 2): 14.1 d 1st order DT_{50} in sediment (Step 2): 14.1 d K_{OC}: 892 ml/g Mol. Wt. 293 Peak occurrence in soil: 13% Peak occurrence in water/sediment: 22% Field or Lab: worst case sediment DT_{50} value of 14.1 d selected for all phases for AE C593600
Parameters used in FOCUSsw step 3 (if performed)	Not required
Application rate	Crop: pome fruit/ stone fruit Number of applications: 1 (Step 2 assumptions:- early application in Southern Europe, Mar – May; No interception assumed at Step 1 or 2) Application rate(s): 200 g as/ha
Main routes of entry	29.2% drift from 3 meter; 10% runoff/drainage (Step 1); 4% runoff/drainage (Step 2)

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Pome fruit/stone fruit: Early, 200 g a.s./ha	0h	7.96		34.12	
	24h	5.44	6.70	48.54	41.33
	2d	5.18	6.01	46.21	44.35
	4d	4.70	5.47	41.88	44.18
	7d	4.05	5.00	36.14	41.93
	14d	2.87	4.21	25.62	36.26
	21d	2.04	3.62	18.16	31.39
	28d	1.44	3.14	12.87	27.39
	42d	0.73	2.44	6.47	21.36

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Pome fruit/stone fruit: Early in Southern Europe (Mar-May), 200 g a.s./ha	0 h	4.14		25.62	
	24 h	2.51	3.33	24.39	25.00
	2 d	2.15	2.83	23.22	24.40
	4 d	3.33	2.60	21.04	23.26
	7 d	2.58	2.70	18.16	21.68
	14 d	1.83	2.44	12.87	18.52
	21 d	1.30	2.14	9.12	15.98
	28 d	0.92	1.88	6.47	13.91
	42 d	0.46	1.48	3.25	10.83

Metabolite 2-chlorobenzonitrile	Worst case parent FOCUSsw Step 1 PECsw value of 47.03µg/l taken as a surrogate value for this major aqueous and soil photolytic metabolite

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PELMO (v. 3.3.2) Scenarios (list of names): Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Seville, Thiva Crop(s): Apple, Strawberry, Grapevine Geometric mean parent DT_{50lab} 71.3 d (normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). K_{oc}: parent, 1064 ml/g (single value), $^1/_n$= 0.9 (default) Mol. Wt. = 303.2 Metabolite AE C593600 Single DT_{50lab} value of 62.4 d (normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). K_{foc}: mean, 892 ml/g, $^1/_n$= 0.92 Mol. Wt. = 293.2
Application rate	Application rate: Apple, 200 g a.s./ha (plus 50% interception); Grapevine, early, 100 g a.s./ha (plus 50% interception); Grapevine, late, 150 g a.s./ha (plus 70% interception); Strawberry, 200 g a.s./ha (plus 30% interception for early apps; 60% interception for late apps). No. of applications: 1 Time of application (month or season): Apple, Strawberry (early) and Grapevine (early) = Spring; Strawberry (late) = Spring/Summer; Grapevine (late) = Summer/Autumn

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

Model /Crop	Scenario	Parent (µg/L)	Metabolite (µg/L) AE C593600
	Chateaudun	<0.001	<0.001
	Hamburg	<0.001	<0.001
	Jokioinen	<0.001	<0.001
	Kremsmunster	<0.001	<0.001
	Okehampton	<0.001	<0.001
	Piacenza	<0.001	<0.001
	Porto	<0.001	<0.001
	Sevilla	<0.001	<0.001
	Thiva	<0.001	<0.001

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

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	active substance: 3.0 x 10^{-4} (mean over 280-800nm)
Photochemical oxidative degradation in air ‡	DT_{50} of 5.1 d on a 12h basis derived by the Atkinson method of calculation
Volatilisation ‡	from plant surfaces (BBA guideline): 1.1
	from soil (BBA guideline): -0.8-1.7% after 24h (within the analytical precision of the radioactivity measurements)
Metabolites	None

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	Not quantified

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil: clofentezine; AE C593600 (hydrazide-hydrazone); 2-chlorobenzoic acid (AE C500233) Surface Water: clofentezine; AE C593600 (hydrazide-hydrazone); 2-chlorobenzoic acid (AE C500233) via run-off and drainage; 2-chlorobenzonitrile (AE F023666) Sediment: clofentezine; AE C593600 (hydrazide-hydrazone) Groundwater: clofentezine; AE C593600 (hydrazide-hydrazone); 2-chlorobenzoic acid (AE C500233); 2-chlorobenzonitrile (AE F023666) Air: clofentezine

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

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

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

Candidate for R53

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	a.s.	Acute	>3000	
Bobwhite quail	a.s.	Short-term	>4000	>20000
Bobwhite quail	a.s.	Long-term	7.62	90
Mammals ‡				
Rat	a.s.	Acute	>5200	
Rat	a.s.	Long-term	40	
Additional higher tier studies ‡				
None				

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

Pome, stone fruit and rose, ornamental uses – 200 g a.s./ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird	Acute (diet)	10.82	>277	10
Insectivorous bird[1]	Acute (dw)	53.9	>55.6	10
Insectivorous bird	Short-term	6.03	>663	10
Insectivorous bird	Long-term	6.03	**1.26**	5
Tier 1 (Mammals)				
Small herbivorous mammal	Acute (diet)	23.6	>220	10
Small herbivorous mammal[1]	Acute (dw)	53.9	>165.7	10
Small herbivorous mammal	Long-term	6.8	5.9	5

Grape use – 150 g a.s./ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird	Acute	8.11	>370	10
Insectivorous bird	Short-term	4.52	>885	10
Insectivorous bird	Long-term	4.52	**1.69**	5
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	17.72	>293	10
Small herbivorous mammal	Long-term	5.08	7.9	5

Strawberry use – 200 g a.s./ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird	Acute	10.82	>277	10
Insectivorous bird	Short-term	6.03	>663	10
Insectivorous bird	Long-term	6.03	**1.26**	5
Tier 1 (Mammals)				
Small herbivorous mammal	Acute	1.76	>2954	10
Small herbivorous mammal	Long-term	0.6	67	5

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg a.s./L)
Laboratory tests				
Fish				
Rainbow trout	a.s.	96 hr (flow-through)	Mortality, EC_{50}	>0.0146 (m)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg a.s./L)
Bluegill sunfish	a.s.	96 hr (flow-through)	Mortality, EC_{50}	>0.25 (m)
Bluegill sunfish	Apollo 50SC	96 hr (flow-through)	Mortality, EC_{50}	>100 (n)
Rainbow trout	Apollo 50SC	96-hr (flow-through)	Mortality, EC_{50}	**>10 (n)**
Rainbow trout	a.s.	97-day ELS	NOEC	0.007 (mm)
Rainbow trout	Apollo 50SC	21-day Prolonged toxicity	NOEC	12.5 (n)
Rainbow trout	2-chloro-benzonitrile	96-hr (semi-static)	Mortality, EC50	22 (n)
Aquatic invertebrate				
Daphnia magna	a.s.	48 hr (static)	Mortality, EC_{50}	>0.00084 (m)
Daphnia magna	a.s.	21 d (static)	Reproduction, NOEC	0.025 (n)
Daphnia magna	Apollo 50SC	21 d (static)	Reproduction, NOEC	**0.05 (n)**
Daphnia magna	Apollo 50SC	21 d (static) modified with sediment	Reproduction, NOEC	**0.25 (n)**
Daphnia magna	Apollo 50SC	48 hr (static)	Mortality, EC_{50}	**>100 (n)**
Daphnia magna	2-chloro-benzonitrile	48 hr (static)	Mortality, EC50	13 (n)
Sediment dwelling organisms				
Chironomus riparus	Apollo 50SC	28 d (static)	NOEC	**0.5 (n)**

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg a.s./L)
Algae				
Scenedesmus pannonicuss‡	a.s.	72 h (static)	EC_{50}	Not stated – however, claimed to be greater than the water solubility of clofentezine
Pseudokirchneriella subcapitata	Apollo 50SC	72 h (static)	EbC50 and ErC50	**>40 (m)**
Pseudokirchneriella subcapitata	2-chloro-benzonitrile	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	16 (n) 47 (n)
Microcosm or mesocosm tests				
None submitted				

(n) = nominal

(m) = measured

[1]The water solubility of clofentezine is 0.00252 mg/L or 2.52 µg/L. Due to the low water solubility, difficulties were experienced in carrying out some of the above toxicity studies. Various approaches were used to try to get the active substance in to solution, however, it is proposed to focus the acute risk assessment on the formulation studies which, for this active substance, are considered to provide a more realistic and hence useful indication of the potential acute toxicity of the active substance. Figures used in the following assessment are in **bold**. As regards the chronic or long-term risk for *Daphnia magna*, studies have been carried out and it is proposed that one of two end points are used depending upon the main route of exposure – for those where spray drift is the major route, it is proposed to use the end point based on the formulation (i.e. 0.25 mg/L), whereas when the route of exposure is due to either drainflow or run-off , an end point based on the active substance will be used (i.e. 0.05 mg a.s./L). Figures used in the following assessment are in **bold**.

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

FOCUS Step1

Pome fruit, stone fruit (early) – 200 g a.s./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg a.s./L)	PEC_{twa}	TER	Annex VI Trigger [1]
Apollo 50SC	Rainbow trout	>10	Acute	0.047	n.a.	212	100
a.s.	Rainbow trout	0.007	Chronic	0.047	n.a.	0.15	10
Apollo 50SC	*Daphnia magna*	>100	Acute	0.047	n.a.	2127	100
Apollo 50SC	*Daphnia magna*	0.25 In the presence of sediment	Chronic	0.086[2]	n.a.	**2.9**	10
Apollo 50SC	*Daphnia magna*	0.05	Chronic	0.047	n.a.	**1.1**	10
Apollo 50SC	*Pseudokirchneriella subcapitata*	>40	Chronic	0.047	n.a.	851	10
Apollo 50SC	Sediment-dwelling[1] organisms	0.5	Chronic	0.086[2]	n.a.	**5.8**	10
2-chloro-benzonitrile	Rainbow trout	22	Acute	0.047[3]	n.a.	468	100
2-chloro-benzonitrile	*Daphnia magna*	13	Acute	0.047[3]	n.a.	277	100
2-chloro-benzonitrile	*Pseudokirchneriella subcapitata*	16	Acute	0.047[3]	n.a.	340	10

[1] Water spiked study – hence PEC_{sw} is required.
[2] Total load PEC used as study used a sediment water design.
[3] This PEC is based on the PEC for the active substance and hence is a worst case.

FOCUS Step1

Grape use (late) – 150 g a.s./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg a.s./L)	PEC_{twa}	TER	Annex VI Trigger[1]
Apollo 50SC	Rainbow trout	>10	Acute	0.025	n.a.	400	100
a.s.	Rainbow trout	0.007	Chronic	0.025	n.a.	0.28	10
Apollo 50SC	*Daphnia magna*	>100	Acute	0.025	n.a.	4000	100
Apollo 50SC	*Daphnia magna*	0.25 In the presence of sediment	Chronic	0.086[2]	n.a.	**2.9**	10
Apollo 50SC	*Daphnia magna*	0.05	Chronic	0.025	n.a.	**2**	10
Apollo 50SC	*Pseudokirchneriella subcapitata*	>40	Chronic	0.025	n.a.	1600	10
Apollo 50SC	Sediment-dwelling[1] organisms	0.5	Chronic	0.086[2]	n.a.	**5.8**	10

[1] Water spiked study – hence PEC_{sw} is required.
[2] Worst case total load PEC for early applications to pome and stone fruit has been used.

FOCUS Step1

Strawberry use – 200 g a.s./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i (mg a.s./L)	PEC_{twa}	TER	Annex VI Trigger[1]
Apollo 50SC	Rainbow trout	>10	Acute	0.029	n.a.	345	100
a.s.	Rainbow trout	0.007	Chronic	0.029	n.a.	0.24	10
Apollo 50SC	*Daphnia magna*	>100	Acute	0.029	n.a.	3448	100
Apollo 50SC	*Daphnia magna*	0.25 In the presence of sediment	Chronic	0.086[2]	n.a.	**2.9**	10
Apollo 50SC	*Daphnia magna*	0.05	Chronic	0.029	n.a.	**1.7**	10
Apollo 50SC	*Pseudokirchneriella subcapitata*	>40	Chronic	0.029	n.a.	1379	10
Apollo 50SC	Sediment-dwelling[1] organisms	0.5	Chronic	0.086[2]	n.a.	**5.8**	10

[1] Water spiked study – hence PEC_{sw} is required.
[2] Worst case total load PEC for early applications to pome and stone fruit has been used.

Ornamental use – 200 g a.s./ha

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger[1]
Apollo 50SC	Rainbow trout	>10	Acute	0.032	n.a.	312	100
a.s.	Rainbow trout	0.007	Chronic	0.032	n.a.	0.22	10
Apollo 50SC	*Daphnia magna*	>100	Acute	0.032	n.a.	3125	100
Apollo 50SC	*Daphnia magna*	0.25 In the presence of sediment	Chronic	0.086[2]	n.a.	**2.9**	10
Apollo 50SC	*Daphnia magna*	0.05	Chronic	0.032	n.a.	**1.6**	10
Apollo 50SC	*Pseudokirchneriella subcapitata*	>40	Chronic	0.032	n.a.	1250	10
Apollo 50SC	Sediment-dwelling[1] organisms	0.5	Chronic	0.086[2]	n.a.	**5.8**	10

[1] Water spiked study – hence PEC_{sw} is required.
[2] Worst case total load PEC for early applications to pome and stone fruit has been used.

FOCUS Step 2

Pome fruit, stone fruit (early) – 200 g a.s./ha

Test substance	N/S	Organism[1]	Toxicity end point (mg/L)	Time scale	PEC[2]	TER	Annex VI Trigger
a.s.	S	Rainbow trout	0.007	Chronic	0.045[3]	**0.15**	10
Apollo 50SC	S	*Daphnia magna*	0.25 In the presence of sediment	Chronic	0.045[3]	**5.5**	10
Apollo 50SC	S	*Daphnia magna*	0.05	Chronic	0.019	**2.6**	10

Test substance	N/S	Organism[1]	Toxicity end point (mg/L)	Time scale	PEC[2]	TER	Annex VI Trigger
Apollo 50SC	S	Sediment-dwelling[1] organisms	0.5	Chronic	0.045[3]	11.1	10

[1] critical groups which fail at Step 1 are only included.
[2] maximum values have been used.
[3] Total load PEC surface water

Grape use (early) – 150 g a.s./ha

Test substance	N/S	Organism[1]	Toxicity end point (mg/L)	Time scale	PEC[2]	TER	Annex VI Trigger
a.s.	S	Rainbow trout	0.007	Chronic	0.021[3]	**0.33**	10
Apollo 50SC	S	*Daphnia magna*	0.25 In the presence of sediment	Chronic	0.021[3]	11.9	10
Apollo 50SC	S	*Daphnia magna*	0.05	Chronic	0.008	**6.25**	10
Apollo 50SC	S	Sediment-dwelling[1] organisms	0.5	Chronic	0.021[3]	23.8	10

[1] critical groups which fail at Step 1 are only included.
[2] maximum values have been used.
[3] Total load PEC surface water

Strawberry use – 200 g a.s./ha

Test substance	N/S	Organism[1]	Toxicity end point (mg/L)	Time scale	PEC[2]	TER	Annex VI Trigger[4]
a.s.	S	Rainbow trout	0.007	Chronic	0.022[3]	**0.32**	10
Apollo 50SC	S	*Daphnia magna*	0.25 In the presence of sediment	Chronic	0.022[3]	11.3	10
Apollo 50SC	S	*Daphnia magna*	0.05	Chronic	0.0089	**5.6**	10
Apollo 50SC	S	Sediment-dwelling[1] organisms	0.5	Chronic	0.022[3]	22.7	10

[1] critical groups which fail at Step 1 are only included.
[2] maximum values have been used.
[3] Total load PEC surface water

Ornamental use – 200 g a.s./ha

Test substance	N/S	Organism[1]	Toxicity end point (mg/L)	Time scale	PEC[2]	TER	Annex VI Trigger[4]
a.s.	S	Rainbow trout	0.007	Chronic	0.026[3]	**0.27**	10
Apollo 50SC	S	*Daphnia magna*	0.25 In the presence of sediment	Chronic	0.026[3]	**9.6**	10
Apollo 50SC	S	*Daphnia magna*	0.05	Chronic	0.0097	**5.2**	10
Apollo 50SC	S	Sediment-dwelling[1] organisms	0.5	Chronic	0.026[3]	19	10

[1] critical groups which fail at Step 1 are only included.
[2] maximum values have been used.
[3] Total load PEC surface water

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

From the above risk assessment, it can be seen that the chronic risk to fish is driving the risk assessment, i.e. the 'regulatory acceptable concentration' is 0.0007 mg/L for fish (i.e. 0.007/10), compared to 0.025 or 0.005 mg a.s./L for *Daphnia magna* and 0.05 mg a.s./l for sediment-dwelling organisms. Due to this, it is proposed to focus the following risk assessment on the chronic risk to fish with the assumption that if the risk to fish is addressed then the risk to aquatic invertebrates will also be addressed.

Pome and stone fruit – 200 g a.s./ha

It should be noted that only **early** applications are shown as these represent a worst case relative to late applications.

Test substance	Scenario [1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	PEC[4]	TER	Annex VI trigger [5]
a.s.	D3	Ditch	Rainbow trout	Chronic	0.007	0.0155	0.45	10
	D4	Pond	Rainbow trout	Chronic	0.007	0.00094	7.4	10
		Stream	Rainbow trout	Chronic	0.007	0.0155	0.45	10
	D5	Pond	Rainbow trout	Chronic	0.007	0.00094	7.4	10
		Stream	Rainbow trout	Chronic	0.007	0.0148	0.47	10
	R1	Pond	Rainbow trout	Chronic	0.007	0.00094	7.4	10
		Stream	Rainbow trout	Chronic	0.007	0.0126	0.56	10
	R2	Stream	Rainbow trout	Chronic	0.007	0.0166	0.42	10
	R3	Stream	Rainbow trout	Chronic	0.007	0.0177	0.39	10
	R4	Stream	Rainbow trout	Chronic	0.007	0.0125	0.56	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.
[4] global maximum PEC have been used for the comparison

Grapes (late) – 150 g a.s./ha

It should be noted that only **late** applications are shown as these represent a worst case relative to early applications.

Test substance	Scenario [1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	PEC[4]	TER	Annex VI trigger [5]
a.s.	D6	Ditch	Rainbow trout	Chronic	0.007	0.0026	2.7	10
	R1	Pond	Rainbow trout	Chronic	0.007	0.00009	77.8	10
		Stream	Rainbow trout	Chronic	0.007	0.0019	3.7	10
	R2	Stream	Rainbow trout	Chronic	0.007	0.0025	2.8	10
	R3	Stream	Rainbow trout	Chronic	0.007	0.0026	2.7	10
	R4	Stream	Rainbow trout	Chronic	0.007	0.0019	3.7	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.
[4] global maximum PEC have been used for the comparison

Strawberries and ornamentals (late) – 200 g a.s./ha

It should be noted that only **late** applications are shown as these represent a worst case relative to early applications.

According to the fate assessment exposure to the aquatic environment is due to a combination of spray drift and/or drainflow or spray drift and/or run-off. Therefore, it is proposed to use the end point of 0.05 mg a.s./L in the following risk assessment.

Test substance	Scenario [1]	Water body type [2]	Test organism [3]	Time scale	Toxicity end point (mg/L)	PEC [4]	TER	Annex VI trigger [5]
a.s.	D3	Ditch	Rainbow trout	Chronic	0.007	0.0013	5.4	10
	D4	Pond	Rainbow trout	Chronic	0.007	0.00004	175	10
		Stream	Rainbow trout	Chronic	0.007	0.00102	6.9	10
	D6	Ditch	Rainbow trout	Chronic	0.007	0.00136	5.1	10
	R1	Pond	Rainbow trout	Chronic	0.007	0.00013	53.8	10
		Stream	Rainbow trout	Chronic	0.007	0.0014	5	10
	R2	Stream	Rainbow trout	Chronic	0.07	0.00111	6.3	10
	R3	Stream	Rainbow trout	Chronic	0.007	0.0017	4.1	10
	R4	Stream	Rainbow trout	Chronic	0.007	0.0026	2.7	10

[1] drainage (D1-D6) and run-off (R1-R4)
[2] ditch/stream/pond
[3] include critical groups which fail at Step 2.
[4] global maximum PEC have been used for the comparison

Bioconcentration	
	Active substance
$logP_{O/W}$	>3
Bioconcentration factor (BCF) [1] ‡	248
Annex VI Trigger for the bioconcentration factor	100
Clearance time (days) (CT_{50})	Not calculated
(CT_{90})	3 days
Level and nature of residues (%) in organisms after the 14 day depuration phase	Not determined.

[1] only required if log $P_{O/W}$ >3.
* based on total ^{14}C or on specific compounds

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)
a.s.	> 252.6 µg a.s./bee	> 84.5 µg a.s./bee
Preparation[1]	>587.41 µg form/bee	>196.5 µg form/bee

[1] for preparations endpoint is expressed in units of preparation

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

Pome, stone fruit and rose, ornamental uses, strawberry – 200 g a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	2.4	50
a.s.	oral	0.8	50
Apollo 50SC	Contact	2.4	50
Apollo 50SC	oral	0.8	50

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g a.s./ha)
Typhlodromus pyri ‡	Apollo 50SC	Mortality	>300
Aphidius rhopalosiphi ‡	Apollo 50SC	Mortality	36.2

Pome, stone and ornamental rose use at 200 g a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
Apollo 50SC	*Typhlodromus pyri*	>300	0.67	0.10 - 0.19	2
	Aphidius rhopalosiphi	36.2	**5.52**	0.87 - 0.67	2

[1] Please note that the range of hazard quotient is due to early and late applications. Default distance of 3 m used.

Grape use at 150 g a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
Apollo 50SC	*Typhlodromus pyri*	>300	0.5	0.01-0.08	2
	Aphidius rhopalosiphi	36.2	**4.14**	0.11-0.65	2

[1] Please note that the range of hazard quotient is due to early and late applications. Default distance of 3 m used.

Strawberry use at 200 g a.s./ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
Apollo 50SC	*Typhlodromus pyri*	>300	0.67	0.02	2
	Aphidius rhopalosiphi	36.2	5.52	0.15	2

[1] spray drift distance is 1 m.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)[1]	End point	% effect[2]	Trigger value
T. pyri‡	Adult	Apollo 50SC	300	Mortality	0%	50 %
Trichogramma cacoeciae‡	Adult	Apollo 50SC applied to glass plate	300	Mortality Fecundity	2.1% 18.9%	50 %
Chysoperla carnae‡	Adult	Apollo 50SC applied to glass plate	300	Mortality Reprod-uction	0% 0%	50 %
Poecilus cupreus‡	Adult	Apollo 50SC applied to damp sand	300	Mortality Feeding rate	0% 1%	50 %
Aphidius rhopalosiphi‡	Adult	Organisms exposed to dry residues of Apollo 50SC applied to leaves	300	Mortality Reprod-uction	25% 37% decrease in reprod-uction	50 %

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)[1]	End point	% effect[2]	Trigger value
Trichogramma cacoeciae	Adult	Organisms were exposed to dried residues of Apollo 50SC applied to leaves	200	Mortality	20.2% compared to 16.2% in the control, considered to be non-significant.	50 %
Phytoselius persimilis	Nym-pal stages of mixed age	Organisms were exposed to residues of Apollo 50SC applied to leaves	200	Mortality Eggs laid	No significant effects on either endpoint	50 %
Field study						
Several studies submitted on *T pyri*, however they added little to the overall assessment and were lacking in details.						

[1] Application rate refers to g a.s./ha
[2] positive percentages relate to positive effects

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
Earthworms			
Eisenia foetida	Apollo 50SC	Acute	LC50 corr = 215 mg a.s./kg
	2-chlorobenzoic acid	Acute	LC50 corr = 21.5 mg a.s./kg d.wt. soil (calc assuming 10x more toxic that a.s.)
	Apollo 50SC	Chronic	NOECcorr = 1.5 kg a.s./ha NOECcorr = 2.656 mg a.s./kg d.wt. soil
	2-chlorobenzoic acid	Chronic	NOECcorr = 0.1 mg a.s./kg d.wt. soil NOECcorr = 0.25 kg a.s./ha (calc assuming 10x more toxic that a.s.)
Other soil macro-organisms			
Folsomia candida	Apollo 50SC ‡	Reproduction	NOEC = 160 mg a.s./kg soil
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡		4.0 L form/ha resulted in a -1.2% deviation from the control on day 28.
Carbon mineralisation	a.s. ‡		4.0 L form/ha resulted in a +5.6% deviation from the control on day 28.
Field studies			
Study submitted but not taken into account in the peer-review in view of the restrictions of Commission Regulation (EC) No 1095/2007.			

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Folsomia candida					
	Apollo 50SC	Reproduction	0.268 mg a.s./kg	597	10
Earthworms					
	Preparation	Acute	0.268 mg a.s./kg	800	10
	2-chlorobenzoic acid	Acute	0.019 mg a.s./kg[3]	1132	10
	Preparation	Chronic	0.268 mg a.s./kg[1]	9.9	5
	2-chlorobenzoic acid	Chronic	0.019 mg a.s./kg[3]	5.3	5

[1] PEC was considered to be worst case in that no interception was considered. It should be noted that 25% interception would give a TER of >5 for the

[2] according to Section B.8.3, the plateau concentration in terms of application rate would be 1.26 times the application rate therefore the application rate would be equivalent to 252 g a.s./ha.

[3] Soil PEC of 2-chlorobenzoic acid is determined to be 0.019 mg/kg (i.e. 0.268mg/kg x 0.136 x 156/303).

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

Not required for herbicides as ER_{50} tests should be provided

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha)[2] vegetative vigour	ER_{50} (g/ha)[2] emergence	Exposure[1] (g/ha)[2]	TER	Trigger
All species tested	Apollo 50SC	>300 g a.s./ha	>300 g a.s./ha	60	5	5

[1] based on 30% drift at 3 m for stone, pome fruit and ornamentals.

[2] for preparations indicate whether dose is expressed in units of a.s. or preparation

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

Not required.

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

Test type/organism	end point
Activated sludge	NOEC = 1000 mg/L

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

Compartment	
soil	Clofentezine
water	Clofentezine
sediment	Clofentezine
groundwater	Clofentezine

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	R52, R53, S60 and S61

	RMS/peer review proposal
Preparation	R52, R53, S35 and S57 (or S60 and S61)

APPENDIX B – LIST OF ABBREVIATIONS

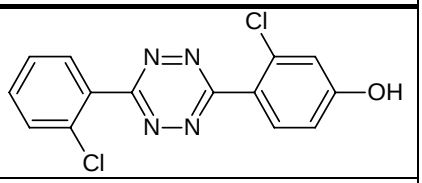
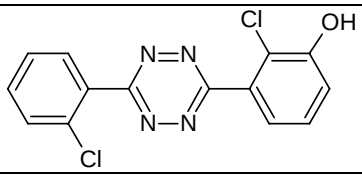
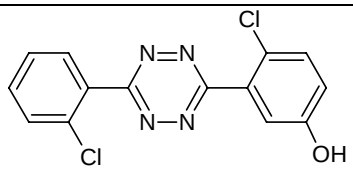
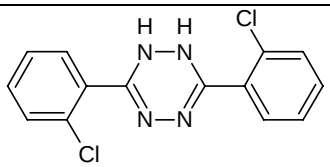
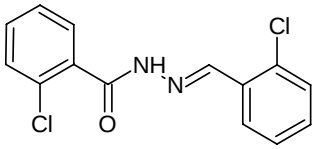
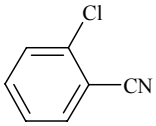
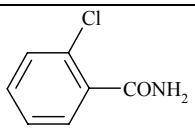
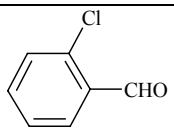
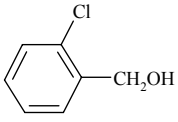
1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
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
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
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
GAP	good agricultural practice
GC	gas chromatography
GC-MS	gas chromatography-mass spectrometry
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
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
ILV	inter laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
iv	intravenous
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)
LR	lethal rate
m	metre
M/L	mixing and loading
MAF	multiple application factor
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
NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
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
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	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
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure

TER_{ST}	toxicity exposure ratio following repeated exposure
TF	transfer factor
TK	technical concentrate
TLC	thin layer chromatography
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

APPENDIX C – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name	Structural formula
4-hydroxy-clofentezine	3-chloro-4-[6-(2-chlorophenyl)-1,2,4,5-tetrazin-3-yl]phenol	
3-hydroxy-clofentezine	2-chloro-3-[6-(2-chlorophenyl)-1,2,4,5-tetrazin-3-yl]phenol	
5-hydroxy-clofentezine	4-chloro-3-[6-(2-chlorophenyl)-1,2,4,5-tetrazin-3-yl]phenol	
Di-hydro-clofentezine NC 22505	3,6-bis(2-chlorophenyl)-1,2-dihydro-1,2,4,5-tetrazine	
Hydrazide-hydrazone AE C593600 FBC 93600	2-chloro-*N*'-[(2-chlorophenyl)methylidene] benzohydrazide	
2-chlorobenzonitrile AE F023666	2-chlorobenzonitrile	
2-chlorobenzamide AE F092117	2-chlorobenzamide	
2-chlorobenzaldehyde AE 0035831	2-chlorobenzaldehyde	
2-chlorobenzyl alcohol	2-chlorobenzyl alcohol (2-chlorophenyl)methanol	
2-chlorobenzoic acid AE C500233 NC233	2-chlorobenzoic acid