CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance cyflumetofen[1]

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Cyflumetofen is a new active substance for which in accordance with Article 6 (2) of Council Directive 91/414/EEC[3] the Netherlands received an application from Otsuka AgriTechno Co. Ltd for inclusion in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision of 26 April 2010 (2010/244/EU)[4].

Following the agreement between the European Commission and the European Food Safety Authority (EFSA) for the EFSA to organise a peer review of those new active substances for which the decision on the completeness of the dossier had been published after June 2002, the designated rapporteur Member State the Netherlands (RMS) provided its initial evaluation of the dossier on cyflumetofen in the Draft Assessment Report (DAR), which was received by the EFSA on 12 November 2010.

The peer review was initiated on 26 January 2011 by dispatching the DAR for consultation of the Member States and the applicant Otsuka AgriTechno Co. Ltd. Following consideration of the comments received on the DAR, it was concluded that EFSA should conduct a focused peer review in the areas of mammalian toxicology, environmental fate and behaviour and ecotoxicology and deliver its conclusions on cyflumetofen.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of cyflumetofen as an acaricide on ornamental crops, nursery trees, perennial ornamentals and public greens, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

In the area of identity, physical/chemical/technical properties and methods of analysis, only a data gap for an analytical method for metabolite B-2 in surface water was identified.

Data gaps were identified in the mammalian toxicology section to clarify the positive result in the *in vitro* mammalian gene mutation assay on the groundwater metabolite B-3 and pending on the fulfilment of this data gap by demonstrating that the B-3 metabolite is not relevant *in vivo*, to provide sufficient toxicological information to allow the setting of reference values for B-3. Furthermore, the

[1] On request from the European Commission, Question No EFSA-Q-2011-00394, approved on 16 December 2011.
[2] Correspondence: pesticides.peerreview@efsa.europa.eu
[3] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19 and by L309, 24.11.2009, p.1
[4] OJ No L 107, 29.4.2010, p. 22-23

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relevance of most of the impurities has to be assessed. Regarding applications on public greens, the exposure assessment for children has not been performed.

No data gap was identified in the residues section. The residue definition for fruit crops is limited to 'cyflumetofen (sum of isomers)' for monitoring and set provisionally as 'sum of cyflumetofen (sum of isomers) and metabolite B-1 expressed as cyflumetofen' for risk assessment. As the representative uses refer to plants not used as food or feed items, residue trials were not provided and no consumer risk assessment through dietary intake was conducted. A negligible exposure of the consumers to residues of metabolite B-1 is expected when groundwater is used as drinking water (1% of the ADI).

The data available on environmental fate and behaviour are sufficient to carry out the required environmental exposure assessments at the EU level for the representative uses of cyflumetofen, with the exception of a groundwater exposure assessment for the critical GAP on tree nursery, perennial ornamentals and public greens. For the representative use on ornamentals, a high potential for groundwater contamination >0.1 µg/L over significant areas of the EU by the metabolite B-3 was identified. On the basis of the available mammalian toxicology data it was concluded that metabolite B-3 is toxicologically relevant and a risk was identified.

The risk to birds and mammals, honeybees and non-target arthropods, earthworms and non-target soil macro- and micro-organisms, biological methods for sewage treatment and non-target terrestrial plants for the representative uses of cyflumetofen was considered to be low. Two data gaps were identified regarding the assessments for aquatic organisms.

KEY WORDS

Cyflumetofen, peer review, risk assessment, pesticide, acaricide

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BACKGROUND

In accordance with Article 6 (2) of Council Directive 91/414/EEC[5] the Netherlands received an application from Otsuka AgriTechno Co. Ltd for inclusion of the active substance cyflumetofen in Annex I to Directive 91/414/EEC. Complying with Article 6 of Directive 91/414/EEC, the completeness of the dossier was evaluated and confirmed by Commission Decision of 26 April 2010 (2010/244/EU).

Following the agreement between the European Commission and the EFSA for the EFSA to organise a peer review of those new active substances for which the completeness of the dossier had been officially confirmed after June 2002, the RMS the Netherlands provided its initial evaluation of the dossier on cyflumetofen in the DAR, which was received by the EFSA on 12 November 2010 (The Netherlands, 2010).

The peer review was initiated on 26 January 2011 by dispatching the DAR to Member States and the applicant Otsuka AgriTechno Co. Ltd for consultation and comments. In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table. The comments were evaluated by the RMS in column 3 of the Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

The scope of the peer review and the necessity for additional information, to be submitted by the applicant in accordance with Article 8(3) of Commission Regulation (EC) No 188/2011, was considered in a telephone conference between the EFSA, the RMS, and the European Commission on 10 May 2011. On the basis of the comments received, the applicant's response to the comments and the RMS' evaluation thereof it was concluded that the EFSA should organise a consultation with Member State experts in the areas of mammalian toxicology, environmental fate and behaviour and ecotoxicology, and that further information should be requested from the applicant in the areas of physical, chemical properties, mammalian toxicology, environmental fate and behaviour and ecotoxicology.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in consultation with Member State experts, and the additional information to be submitted by the applicant, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in November – December 2011.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as an acaricide on ornamental crops, nursery trees, perennial ornamentals and public greens, as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues

[5] OJ No L 230, 19.8.1991, p. 1. Directive as last amended by L 20, 22.1.2005, p.19 and by L309, 24.11.2009, p.1

raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2011) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the DAR,
- the Reporting Table (10 May 2011),
- the Evaluation Table (12 December 2011),
- the report(s) of the scientific consultation with Member State experts,
- the comments received on the assessment of the additional information,
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its addendum (compiled version of October 2011 containing all individually submitted addenda (The Netherlands, 2011)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Cyflumetofen is the ISO common name for 2-methoxyethyl (*RS*)-2-(4-tert-butylphenyl)-2-cyano-3-oxo-3-(α,α,α-trifluoro-o-tolyl)propionate (IUPAC).

The representative formulated product for the evaluation is 'OK-5101' a suspension concentrate (SC) containing 200 g/l cyflumetofen.

The representative uses evaluated comprise both indoor and outdoor spray application to ornamental crops, nursery trees, perennial ornamentals and to public greens for the control of *Tetranychyus urticae* (red spider mite). Full details of the GAP can be found in the list of end points in Appendix A.

It must be noted that cyflumetofen is a racemic mixture, but the possible preferential metabolism/degradation of each enantiomer in animals and the environment was not investigated in the studies submitted in the dossier and was therefore not considered during the peer review. Moreover, the analytical methods used in the studies reported through all sections were not stereo-selective, and all values mentioned as "cyflumetofen" have to be considered as "sum of isomers". The possible impact of each individual enantiomer on the toxicity and the environment was not evaluated. A general data gap, applicable for sections 4 and 5, was therefore identified to address the impact of the isomeric composition of the substance.

CONCLUSIONS OF THE EVALUATION

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

The following guidance documents were followed in the production of this conclusion: SANCO/3030/99 rev. 4 (European Commission, 2000) and SANCO/825/00 rev. 7 (European Commission, 2004a).

The minimum purity of the active substance as manufactured is 975 g/kg. There is no FAO specification for this substance.

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

Methods of analysis for products of plant and animal origin are not required as there are no edible crop uses. The residue definition for environmental matrices is 'cyflumetofen' for soil and air, 'cyflumetofen and B-2' for surface water and 'cyflumetofen and B-3' for ground water. Soil, air and water can be analysed by LC-MS/MS methods. However, a method for B-2 in surface water is identified as a data gap. A method of analysis for body fluids and tissues is not required as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

The following guidance documents were followed in the production of this conclusion: SANCO/221/2000 rev. 10 - final (European Commission, 2003), SANCO/222/2000 rev. 7 (European Commission, 2004b) and SANCO/10597/2003 rev. 8.1 (European Commission, 2009).

Cyflumetofen was discussed at the Pesticides Peer Review Expert Meeting 88 in September 2011.

The batches used in the toxicological studies support the agreed technical specification; however the relevance of most of the impurities was not addressed.

Low acute toxicity has been observed when cyflumetofen was administered by the oral, dermal or inhalation routes. No skin or eye irritation was observed but cyflumetofen produced skin sensitisation in a Magnusson and Kligman test.

The main target organs of cyflumetofen upon short-term and long-term exposure were the adrenals with vacuolation and hypertrophy of the adrenal cortical cells in rats and mice and vacuolation and degeneration of the adrenal cortex in dogs. The mechanism of toxicity was shown to involve interference with cholesterol metabolism resulting in cholesterol deposition in the adrenal gland and presumably also in the ovary through reduction in hormone-sensitive lipase. Both short-term and long-term relevant NOAELs were 16.5 mg/kg bw/day as observed in the 90-day and 2-year rat studies. Cyflumetofen did not present carcinogenic or genotoxic potential *in vivo*.

In a reproductive toxicity study, a delay in sexual development was observed in the presence of parental toxicity and possibly associated with hormonal effects in females, but not in males; this finding did not result in an impairment of the reproductive or fertility parameters. The parental, offspring and reproductive NOAELs were identified at 10.4 mg/kg bw/day dose level, taking into consideration dose spacing. This was not considered a critical NOAEL compared to the short-term and long-term NOAELs. Delayed or incomplete ossification was observed in the developmental studies in rats and rabbits in the presence of maternal toxicity. Both the maternal and developmental NOAELs in rat were 50 mg/kg bw/day; in rabbit, the developmental NOAEL was established at 250 mg/kg bw/day.

No indication of neurotoxicity was observed after a single administration of cyflumetofen.

Toxicological studies were provided on two metabolites found in groundwater at levels exceeding 0.75 µg/L according to environmental fate and behaviour models (see section 4). **B-1** was identified as a major metabolite after oral administration of cyflumetofen to rats. It is of low acute oral toxicity in rat and did not present a genotoxic potential *in vivo*. B-1 was found to be non-relevant from the toxicological point of view according to the guidance document on the assessment of groundwater metabolites (European Commission, 2003) and the reference values of the parent cyflumetofen are applicable to this metabolite. **B-3** was not found in the rat metabolism studies performed with cyflumetofen. It appeared to be more toxic than the parent as observed in a dose-range finding study to the UDS assay where mortality was seen at 500 mg/kg bw. Positive results were observed in the strain TA100 of the *S. typhimurium* reverse mutation assay and in a mammalian cell gene mutation test without metabolic activation. During the Pesticide Peer Review Expert Meeting, the majority of the experts considered that the positive results in the gene mutation assay were not satisfactorily outweighed by the negative results found in the rat hepatocyte UDS test *in vivo*. The RMS disagreed with this conclusion, considering that it isn't clear which genotoxicity test would be suitable to address this concern. A data gap was identified for further evidence showing that B-3 is not a mutagenic compound. The metabolite was found relevant according to the guidance document on the assessment of groundwater metabolites (European Commission, 2003); no reference values could be set from the available data. Pending on the demonstration that the metabolite is not relevant, a consumer exposure risk assessment would be needed for this metabolite derived from the groundwater exposure, and a data gap was identified for toxicological information allowing to set reference values for B-3.

The acceptable daily intake (ADI) of cyflumetofen is 0.17 mg/kg bw/day, based on the NOAEL of 16.5 mg/kg bw/day from the 90-day and 2-year rat studies, applying the standard safety factor of 100. The acceptable operator exposure level (AOEL) is 0.11 mg/kg bw/day, based on the same NOAELs of 16.5 mg/kg bw/day from the 90-day and 2-year rat studies, a 100 safety factor applied and correction for limited oral absorption of 68 %. No acute reference dose (ARfD) is allocated to cyflumetofen.

The estimated operator exposure level is below the AOEL when the use of personal protective equipment (PPE) – such as gloves during mixing and loading (M/L) and/or coveralls - is considered in

the worst cases (manual spraying and indoor uses) according to the UK POEM and Dutch models. For outdoor uses, only downward applications have been considered. Estimated worker exposure after one application of cyflumetofen was below the AOEL when no PPE are worn; when considering the four possible applications and assuming that there is no decay in the residues between applications, it is likely that worker exposure would exceed the AOEL without PPE but the use of PPE would lower worker exposure below the AOEL. Estimated bystander exposure outdoor is below the AOEL; in applications on public greens, no exposure risk assessment has been performed for children playing in these areas and this was identified as a data gap. Bystander exposure is not relevant to indoor applications.

3. Residues

The assessment in the residue section is based on the guidance documents listed in the document SANCO/1607/VI/97 rev. 2 (European Commission, 1999), and the JMPR recommendations on livestock burden calculations stated in the 2004 and 2007 JMPR reports (JMPR, 2004 and 2007).

Metabolism studies on fruit crops (mandarin, apple and eggplant) were submitted and residue definitions for monitoring and risk assessment were derived, although not required when considering the representative uses on ornamentals, tree nurseries and public greens. The studies were conducted with a single foliar application of ^{14}C-cyflumetofen, either labelled on the *t*-butyl phenyl ring (label A) or the trifluoromethyl phenyl ring (label B) at a dose of 600 g a.s./ha.

The metabolism was seen to be limited. The major part of the radioactive residues remained on the surface of fruits and leaves and was easily removed by solvent rinses (56% to 97% TRR). The parent cyflumetofen was identified as the major component of the total radioactive residues, accounting for 67% to 87% TRR on fruits and leaves 7 days after application, and 44% to 81% TRR after 30 days. Degradation compounds were recovered at a level lower than 10% TRR, except for the metabolite B-1 resulting from the cleavage of the parent molecule and representing up to 11% TRR in mandarin (0.06 mg/kg) and 15% TRR in eggplant (0.06 mg/kg). In addition B-1 conjugates (metabolites U1 and U2) were detected up to 16% TRR in eggplant fruits at PHI 14 days.

Based on these studies, it is proposed to limit the residue definition for monitoring to 'cyflumetofen (sum of isomers)' only, as the parent compound appears to be a significant marker of the total residues in fruits. For risk assessment, considering the conclusion of the Pesticides Peer Review Expert Meeting 88 on toxicology stating that the toxicological reference values set for the parent are also applicable to the metabolite B-1, and considering that B-1 (free and conjugated) was detected in eggplant fruit at similar levels and proportions as cyflumetofen, it is proposed to define the residue as 'sum of cyflumetofen (sum of isomers) and B-1, expressed as cyflumetofen'. This residue definition for risk assessment is restricted to fruit crops and should be reconsidered for other representative uses, pending on the submission of residue trials and, if relevant, of processing studies on fruit crops.

As the representative uses refer to plants not used as food or feed items, residue trials were not provided and no consumer risk assessment through dietary intake was conducted.

It is noted that the metabolite B-1 is estimated to leach to groundwater at significant levels. The 0.75 µg/L trigger was exceeded in the majority of the pertinent FOCUS scenarios with a maximum concentration of 12.629 µg/L estimated for winter cereals, late application in the FOCUS Jokioinen scenario (see section 4). A negligible exposure of the consumers can be expected when groundwater is used as drinking water (1% of the ADI).

4. Environmental fate and behaviour

In soil laboratory incubations under aerobic conditions in the dark, cyflumetofen exhibited low to high persistence, forming the major (>10% applied radioactivity (AR)) metabolite **AB-1** (max. 21.6 % AR, considering also the cis/trans isomers across the double bond of the enol form of AB-1; AB-1 alone max. 8.3% AR), which exhibited moderate to high persistence, metabolites **B-1** (max. 63 % AR) and **B-3** (max. 23 % AR) , which exhibited low to moderate persistence. Mineralisation to carbon dioxide accounted for 1.7-36.7 % AR with cyflumetofen B-labelled and 31.2% AR with A-labelled after 120 to 121 days. The formation of unextractable radioactivity accounted for 30.1-40.1 % AR (B-label, 90-120 days) and 37.8% AR (A-label, 90 days). Studies on degradation in soil under anaerobic conditions were not provided as exposure to anaerobic conditions is not expected for the representative uses applied for. However, it should be noted that these data might be considered necessary at Member State level where anaerobic conditions are envisaged to be relevant. Photolytic degradation on soil surfaces is not expected to play a role in the overall fate of cyflumetofen residues in soil. Cyflumetofen and metabolite AB-1 were essentially immobile in soil. Metabolites B-1 and B-3 exhibited very high mobility.

Cyflumetofen is susceptible to aquatic photolysis in aqueous buffer solution (pH 5). Specific photolytic degradation products exceeding 10% AR were **AB-15** (max 54.7% AR) and **AB-7** (max 10.8% AR). In laboratory incubations in dark aerobic natural sediment-water systems, cyflumetofen partitioned from the water phase to the sediment and exhibited very low to moderate persistence in the whole system. Several relevant degradation products (> 10% of applied radioactivity) were formed in both compartments (**AB-11**, water max 10.0% AR and sediment max 10.1%; **B-1**, water max 65% AR and sediment max 21.5% AR) or in the water compartment only (**A-2** max 18.4% AR; **Met-1** max 10.7% AR; **Met-8** max 19.5% AR) or in the sediment compartment only (AB-1 max 14.6%; Met-4 max 10.7%). Metabolite Met-5 was formed in the water/sediment study with B-radiolabelled cyflumetofen with a maximum level of 28% AR in the sediment. This metabolite matched with AB-1 and **B-2** but, as a conservative approach, it was considered equal to B-2 only. The exposure assessment of B-2 was discussed at the Pesticides Peer Review Teleconference TC 58 in September 2011. New FOCUS surface water modelling (following FOCUS, 2001 guidance) up to Step 4 for metabolite B-2 was provided by the RMS (The Netherlands, 2011). The new PEC (predicted environmental concentration) in surface water and sediment are calculated from combined emission routes: via soil from the metabolite B-1 and via in-situ formation in the water/sediment system. For cyflumetofen and the metabolites AB-1, AB-11, AB-15, B-1, B-3 and A-2 surface water and sediment concentrations were calculated using FOCUS Step 1 and Step 2 models. For AB-11, AB-15, B-2 and A-2, run-off/drainage was set at zero as these metabolites were not formed in soil. During the peer review predicted environmental concentration (PEC) in water and sediment were updated also for cyflumetofen, metabolite AB-1 and the aqueous photolysis metabolite AB-15 (The Netherlands, 2011). It is agreed that these PECs as presented in Appendix A are appropriate for use in risk assessment. No aquatic exposure assessment was considered necessary for the photolytic aquatic metabolite AB-7. With respect to Met-1 and Met-8 no PECsw/sed calculations were provided. These metabolites are qualitatively assessed in the ecotox section. Satisfactory information to address Met-4 was provided in the revised DAR and no further assessment is required.

In the original DAR groundwater exposure assessments were carried out using FOCUS (FOCUS, 2000) scenarios and the models PEARL 3.3.3[6] for the active substance cyflumetofen and the soil metabolites AB-1, B-1 and B-3 in three separate runs (parent-metabolite combinations) based on worst-case formation fractions of 1 for each metabolite. As no FOCUS crop exists for ornamentals, winter cereals was selected as representative crop. Following the commenting phase on the DAR, new PECgw were estimated also with a second FOCUS model (FOCUS PELMO 3.3.2), with an additional representative crop (vines FOCUS scenarios), a crop interception value of 60% and, for the parent

[6] Simulations complied with the EFSA opinion (EFSA, 2004) and correctly utilised the agreed Q10 of 2.58 (following EFSA, 2007) and Walker equation coefficient of 0.7

cyflumetofen, considering the revised geometric mean soil DT_{50} of 8.8 days[7]. This modelling indicates that annual average concentrations of cyflumetofen and metabolite AB-1 in leachate leaving the top 1 m soil column would be less than the parametric drinking water limit of 0.1 µg/L in all pertinent FOCUS groundwater scenarios. This was however not the case for the soil metabolites B-1 and B-3. PECgw for B-1 breaches the 0.1 µg/L limit for late applications in all scenarios (both PEARL and PELMO) and > 0.75 µg/L for all scenarios except for Sevilla scenario for the combinations PELMO/winter cereals and PEARL/vines (range of calculated values 0.357 to 12.629 µg/L for winter cereals and 0.646 to 9.911 µg/L for vines). For the same metabolite, for early application, PECgw ranged from 0.001 to 1.685 µg/L for winter cereals and from 0.018 to 1.430 µg/L for vines. The modelling for metabolite B-3 shows that at almost all scenarios for the early applications and at all scenarios for the late applications the parametric drinking water limit of 0.1 µg/L was exceeded (range of calculated values < 0.001 to 3.540 µg/L for winter cereals and 0.002 to 3.881 µg/L for vines). Based on the information available, metabolite B-3 is considered toxicologically relevant (see section 2) and a risk was identified. As no PEC_{gw} calculations are available for the representative uses with an application rate lower than the maximum recommended label rate, it is concluded that the assessment of the potential for groundwater exposure for the critical GAP on tree nursery, perennial ornamentals and public greens is not finalised.

The regulatory dossier provides no information on the environmental behaviour of each individual enantiomer of metabolites AB-1, AB-7 and AB-11 which contain chiral carbon atoms. It is not known if one isomer is degraded more quickly than the other or if any other conversion between isomers occurs. References made to these metabolites therefore relate to the sum of isomers of unknown ratio. However, it is considered that the margins of safety on the available risk assessments are large enough that the uncertainty on the relative toxicity and contributions to the total residues levels of the isomers of these metabolites do not change the conclusion of low aquatic risk.

Cyflumetofen has a low potential for volatilization with an estimated atmospheric half-life shorter than 2 days. Therefore long-range transport through the atmosphere is not expected.

5. Ecotoxicology

The following documents were considered for the risk assessments: European Commission (2002a, 2002b, 2002c) and SETAC (2001).

The risk to **birds** and to **non-target terrestrial vertebrates** other than birds for the parent cyflumetofen and for the relevant metabolites was assessed as low.

In most cases, due to the low solubility in water, the exact toxicity of cyflumetofen or the tested metabolites could not be established from the studies on aquatic organisms. The acute and long-term risk to **aquatic organisms** based on these data was assessed as low for the parent cyflumetofen. It is noted however that cyflumetofen might be regarded as a potential endocrine disruptor and this issue was not regarded to be covered by the available information for aquatic vertebrates. Therefore a data gap was agreed for further assessments that cover the full life-cycle.

Considerations for ten metabolites of cyflumetofen were necessary for aquatic organisms however toxicity data for water column living organisms were only available for three of them (AB-11, B-1, B-2). These data covered only acute toxicity for daphnids and algae. Based on these data, low risk was identified for metabolites AB-11 and B-1. However a high acute risk was identified for aquatic invertebrates for the metabolite B-2. Therefore a data gap was identified for further assessments for aquatic organisms for this metabolite. Regarding the other cases where risk assessments were

[7] The appropriate geomean soil DT_{50} for cyflumetofen should be 30.6 days (normalised to 20°C and pF2 soil moisture). The use of this correct value would not change the final risk assessment for cyflumetofen and its degradation products (see details in the Evaluation table under Data requirement 4.1).

necessary, but no toxicological endpoints were available, the pragmatic approach assuming that the metabolite is ten times more toxic than the parent molecule was used as a first tier evaluation. Using this approach, low risk was concluded for some metabolites in the long-term scale, but high risk was identified for others. All acute TER values were below the relevant trigger for aquatic invertebrates. Also high acute risk was identified for some metabolites for fish.

For second tier assessments, estimation of the toxicological profile of the metabolites and the parent by QSAR approach was provided (only acute endpoints were generated). These QSAR data were compared with the available measured endpoints and qualitative assessments were conducted for the metabolites where no measured endpoints were available. In some cases the expected fate and behaviour of the metabolite in natural waters (see section 4) was also taken into consideration in these assessments. Considering these and also the margins of safety where the risk characterization was quantitative, low risk was concluded for the metabolites in question. It is noted however that these assessments contain some uncertainty particularly for the risk to aquatic invertebrates regarding metabolite 1 and the unidentified metabolite 8. For the long-term risk assessments, the evaluations for the acute scale and also the expected fate and behaviour of the metabolites in natural waters were considered. The long-term risk for the metabolites was considered as low by the Pesticides Peer Review Expert Teleconference 58 even if cyflumetofen can be used up to four times in a season.

To support the risk assessment for the sediment-dwellers, only toxicological data for the parent and for one of the relevant metabolites were available. Based on these data, low risk was identified for sediment-dwellers. Regarding the other metabolites, qualitative assessments were conducted that indicated low risk. In these assessments the QSAR estimations that were mentioned above, and in some cases the expected fate and behaviour of the metabolites in natural water bodies or in the available laboratory tests, were considered.

Based on the logPow values, assessments for bioaccumulation were triggered for the parent molecule and for several metabolites. A fish bio-concentration study was only available for the parent cyflumetofen. Regarding the relevant metabolites, qualitative assessments were conducted considering the available study on the parent, QSAR estimations and in some case the expected fate and behaviour of the metabolite in natural water bodies. Considering these assessments, the risk for bio-concentration in fish was considered as low.

The risk to **honeybees** and **non-target arthropods** other than bees for the representative uses of cyflumetofen was considered to be low. It is noted that cyflumetofen is effective against phytophagous mites, acting on all life-stages. This indicates potential effects on the reproduction. The available first tier risk assessments for non-target arthropods and for bees were, however, based on toxicity data on mortality only.

The risk to **earthworms** and **non-target soil macro- and micro-organisms** for the parent cyflumetofen and for the major soil metabolites was assessed as low. Because of the lack of toxicity data, the evaluation for the metabolite B-3 was based on only qualitative assessments.

The risk to the **biological methods for sewage treatment** and **non-target terrestrial plants** for the representative uses of cyflumetofen was considered to be low.

6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Cyflumetofen	Low to high persistence ($DT_{50\ lab}$ = 1.54-153.4 d, 20°C, pF2 (-10kPa), DFOP or FOMC kinetics)	The risk to soil organisms was assessed as low.
B-1	Low to moderate persistence ($DT_{50\ lab}$ = 6.3-16.8 d, 20°C, pF2 (-10kPa), SFO kinetics)	The risk to soil organisms was assessed as low.
B-3	Low to moderate persistence ($DT_{50\ lab}$ = 5.9-15.1 d, 20°C, pF2 (-10kPa), SFO kinetics)	The risk to soil organisms was assessed as low.

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**
Cyflumetofen	Immobile (HPLC method K_{oc} = 131826 mL/g)	No	Yes	Yes	Data gap for further risk assessments for long-term scale for aquatic vertebrates.
AB-1	Immobile (K_{doc} = 6200-450000 mL/g)	No	Less active against the target than the parent.	No data, data not required	The risk to aquatic organisms was assessed as low.
SHL10b (trans isomer of AB-1)	QSARs KOCWIN estimate >9950 L/kg[(b)]	No data, data not required[(b)]	No data, data not required	No data, data not required	No data, data not required

B-1	Very high mobility (Column leaching study K_{oc} = 3.7-6.56 mL/g)	modelling (FOCUS PEARL and PELMO)[(a)]: Winter cereals > 0.75 µg/L at 9/9 FOCUS scenarios for late applications and at 5/9 FOCUS scenarios for early applications (6/9 scenarios > 0.1 µg/L); concentrations up to 12.629 µg/L Vines > 0.75 µg/L at 8/8 FOCUS scenarios for late applications and at 4/8 FOCUS scenarios for early applications (6/8 scenarios > 0.1 µg/L); concentrations up to 9.911 µg/L	No (significantly less active against the target than the parent)	No Rat LD_{50} oral > 2000 mg/kg bw Gene mutation test *in vitro* positive in absence of metabolic activation; Ames test, chromosome aberration test *in vitro* and *in vivo* UDS test negative Reference values of cyflumetofen are applicable to B-1	The risk to aquatic organisms was assessed as low.

B-3	Very high mobility (K_{Foc} = 11.7-16.9 mL/g)	modelling (FOCUS PEARL and PELMO)[(a)]: Winter cereals > 0.75 µg/L at 9/9 FOCUS scenarios for late applications; > 0.1 µg/L at 5/9 FOCUS scenarios for early applications; concentrations up to 3.540 µg/L Vines cereals > 0.75 µg/L at 4/8 FOCUS scenarios for late applications; > 0.1 µg/L at 4/8 FOCUS scenarios for early applications; concentrations up to 3.540 µg/L	No (significantly less active against the target than the parent)	Yes Mortality at 500 mg/kg bw (rat) Gene mutation test *in vitro* in absence of metabolic activation and Ames test in strain TA100 positive; Negative chromosome aberration *in vitro* and *in vivo* UDS test	The risk to aquatic organisms was assessed as low.

(a): The critical GAP for cyflumetofen on ornamental is 4 applications of 300 g a.s./ha with an interval of 7 days. No FOCUS crop exists for ornamentals, therefore winter cereals and vines were selected as representative crops. Calculations were performed for early applications in March and late applications in September for all FOCUS scenarios.
(b): Refer to Reporting Table 4(2).

6.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Cyflumetofen	Data gap for further risk assessments for long-term scale for aquatic vertebrates.
AB-1 (sediment only)	The risk to aquatic organisms was assessed as low.
B-1	The risk to aquatic organisms was assessed as low.
AB-11	The risk to aquatic organisms was assessed as low.

B-3	The risk to aquatic organisms was assessed as low.
A-2 (water only)	The risk to aquatic organisms was assessed as low.
B-2	High acute risk was identified for aquatic invertebrates. Data gap for further assessments.
AB-15 (aqueous photolysis metabolite)	The risk to aquatic organisms was assessed as low.
Met-1 (water only)	The risk to aquatic organisms was assessed as low.
Met-8 (water only)	The risk to aquatic organisms was assessed as low.

6.4. Air

Compound (name and/or code)	**Toxicology**
Cyflumetofen	Rat LC_{50} oral > 2.65 mg/L air/ 4h (nose only; maximum attainable concentration), no classification proposed

7. List of studies to be generated, still ongoing or available but not peer reviewed

This is a complete list of the data gaps identified during the peer review process, including those areas where a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 7 of Directive 91/414/EEC concerning information on potentially harmful effects).

- Cyflumetofen is a racemic mixture. The preferential metabolism/degradation of each enantiomer in animals and the environment, as well as the possible impact on the toxicity and the environment needs to be addressed (relevant for all representative uses evaluated; data gap identified by EFSA during drafting of the conclusion; submission date proposed by the applicant: unknown; see sections 4 and 5).

- Method of analysis for B-2 in surface water (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)

- Assessment of the relevance of most impurities (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 2)

- Further evidence to clarify the positive result in the *in vitro* mammalian gene mutation assay on the groundwater metabolite B-3 and pending on the demonstration that the metabolite is not relevant, toxicological information allowing to derive reference values for this metabolite (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 2)

- Exposure risk assessment for children playing on public greens (relevant for use on public greens; submission date proposed by the applicant: unknown; see section 2)

- Groundwater exposure assessment for the representative uses on tree nursery, perennial ornamentals and public greens (submission date proposed by the applicant: unknown; see section 4)

- Further ecotoxicological studies and assessments for aquatic vertebrates that cover the full life-cycle for the parent cyflumetofen (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5)

- Further assessments for aquatic organisms (especially aquatic invertebrates) for metabolite B-2 (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5)

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

- Operators should use PPE in some worst case scenarios (manual spraying and indoor uses) to lower the exposure below the AOEL (see section 2).

- Workers should use PPE when considering the 4 possible applications to lower exposure below the AOEL (see section 2).

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

1. The assessment of the potential for groundwater exposure for the representative uses (tree nursery, perennial ornamentals and public greens) with an application rate lower than the maximum label rate considered in the critical GAP (ornamental crops, 300 g a.s./ha).

2. The risk assessment for long-term scale for cyflumetofen for aquatic vertebrates could not be finalized

3. An exposure risk assessment for children playing on public greens has not been performed.

9.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

- none

9.3. Overview of the concerns for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 8, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

Representative use		Ornamental crops	Tree nursery	Perennial ornamentals	Public greens
Operator risk	Risk identified				
	Assessment not finalised				
Worker risk	Risk identified				
	Assessment not finalised				
Bystander risk	Risk identified				
	Assessment not finalised				X[3]
Consumer risk	Risk identified				
	Assessment not finalised				
Risk to wild non target terrestrial vertebrates	Risk identified				
	Assessment not finalised				
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified				
	Assessment not finalised				
Risk to aquatic organisms	Risk identified				
	Assessment not finalised	X[2]	X[2]	X[2]	X[2]
Groundwater exposure active substance	Legal parametric value breached				
	Assessment not finalised				
Groundwater exposure metabolites	Legal parametric value breached	X 9/9 scenarios			
	Parametric value of 10µg/L[(a)] breached				
	Assessment not finalised		X[1]	X[1]	X[1]
Comments/Remarks					

The superscript numbers in this table relate to the numbered points indicated within sections 9.1 and 9.2. Where there is no superscript number, see sections 2 to 6 for further information. A column is greyed out if there is a concern for that specific use

(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

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APPENDICES

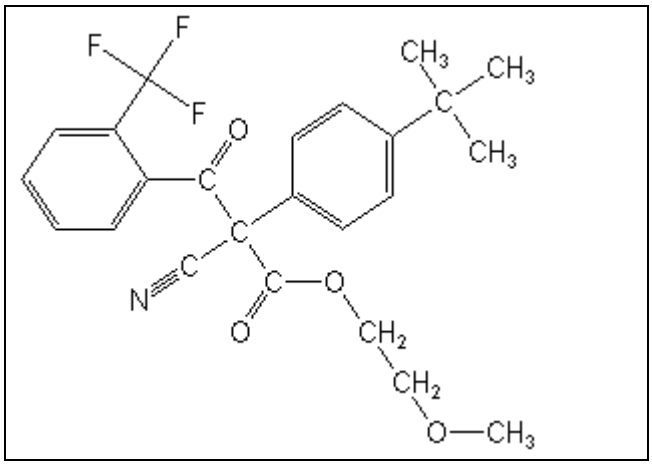
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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

Active substance (ISO Common Name)	Cyflumetofen (ISO approved)
Function (*e.g.* fungicide)	acaricide
Rapporteur Member State	The Netherlands

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	2-methoxyethyl (*RS*)-2-(4-*tert*-butylphenyl)-2-cyano-3-oxo-3-(α,α,α-trifluoro-*o*-tolyl)propionate
Chemical name (CA)	2-methoxyethyl α-cyano-α-[4-(1,1-dimethylethyl)phenyl]-β-oxo-2-(trifluoromethyl)benzenepropanoate
CIPAC No	721
CAS No	400882-07-7
EEC No (EINECS or ELINCS)	Not allocated
FAO Specification (including year of publication)	Not allocated
Minimum purity of the active substance as manufactured (g/kg)	975 g/kg (racemic , commercial scale production)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	Open
Molecular formula	$C_{24}H_{24}F_3NO_4$
Molecular mass	447.45

Structural formula	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity)	77.9 – 81.7 °C (98.46%)
Boiling point (state purity)	293°C (98.46%)
Temperature of decomposition (state purity)	> 293 °C (98.46%)
Appearance (state purity)	White odourless solid (98.46% PAI) Yellow solid with no characteristic odour (98.4% TGAI)
Vapour pressure (state temperature, state purity)	< 5.9×10^{-6} Pa at 25 °C (98.4%)
Henry's law constant	< 9.4×10^{-2} $Pa.m^3.mol^{-1}$
Solubility in water (state temperature, state purity and pH)	28 µg/L at 20 °C and pH 7 No pH dependence.
Solubility in organic solvents (state temperature, state purity)	acetone > 500 g/L solvent dichloromethane > 500 g/L solvent ethyl acetate > 500 g/L solvent n-hexane 5.16 g/L solution methanol 98.7 g/L solution toluene > 500 g/L solvent All at 20 °C (98.46%)
Surface tension (state concentration and temperature, state purity)	Not required (solubility < 1 mg/L)
Partition co-efficient (state temperature, pH and purity)	Log Pow = 4.3 at 25 °C (98.46%) No pH dependence
Dissociation constant (state purity)	No dissociation expected in a relevant pH range.
UV / VIS absorption (max.) incl ε (state purity, pH)	At 25 °C (98.46%): No maximum above 290 nm, but significant absorption does occur (ε > 10 $L.mol^{-1}.cm^{-1}$) at

	acidic and neutral conditions. At alkaline conditions cyflumetofen is insufficiently stable to conclude if absorption is of breakdown products or of cyflumetofen.
Flammability (state purity)	Not highly flammable (98.0% TGAI) Auto-ignition at 320 °C (98.0% TGAI)
Explosive properties (state purity)	Not explosive (98.0% TGAI)
Oxidising properties (state purity)	Not oxidising (98.0% TGAI)

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical and chemical data	No classification is required.

List of representative uses evaluated (cyflumetofen)

Crop and/or situation (a)	Member State or Country	Product name	FG or I (b)	Pests or Group of pests controlled (c)	Formulation		Application					Application rate per treatment						PHI (days) (l)	Remarks (m)
					Type (d-f)	Conc. of as (PAI g/kg) (i)	method kind (f-h)	growth stage & season (j)	Number (k) min	Number (k) Max	Interval between applications (min)	g as/hl min	g as/hl max	water L/ha min	water L/ha max	kg as/ha min	kg as/ha max		
Ornamental crops (NNNZZ)	NL	OK-5101	G	*Tetranychus urticae* (TETRUR)	SC	200	spray	All pest stages Jan - Dec	1	4	7 days	20.0	20.0	500	1500	0.10	0.30	n.a.	-
Ornamental crops (NNNZZ)	NL	OK-5101	F	*Tetranychus urticae* (TETRUR)	SC	200	spray	All pest stages March - Sept	1	4	7 days	20.0	20.0	300	1000	0.06	0.20	n.a.	-
Tree nursery (NNNBA)	NL	OK-5101	G	*Tetranychus urticae* (TETRUR)	SC	200	spray	All pest stages Jan - Dec	1	4	7 days	20.0	20.0	500	1000	0.10	0.20	n.a.	-
Tree nursery (NNNBA)	NL	OK-5101	F	*Tetranychus urticae* (TETRUR)	SC	200	spray	All pest stages March - Sept	1	4	7 days	20.0	20.0	300	1200	0.06	0.24	n.a.	Restricted to downward spraying
Perennial ornamentals (BBBPE)	NL	OK-5101	G	*Tetranychus urticae* (TETRUR)	SC	200	spray	All pest stages Jan - Dec	1	4	7 days	20.0	20.0	500	1000	0.10	0.20	n.a.	-
Perennial ornamentals (BBBPE)	NL	OK-5101	F	*Tetranychus urticae* (TETRUR)	SC	200	spray	All pest stages March - Sept	1	4	7 days	20.0	20.0	300	1000	0.06	0.20	n.a.	Restricted to downward spraying
Public green	NL	OK-5101	F	*Tetranychus urticae* (TETRUR)	SC	200	spray	All pest stages March - Sept	1	4	7 days	20.0	20.0	1000	1000	0.20	0.20	n.a.	Restricted to downward spraying

Proposed resistance management strategy for cyflumetofen: To prevent resistance development in ornamentals, perennial plants and tree nursery, do not use this product more often than 2 programs (blocs) per year (a program (bloc) is one or 2 treatments at a 7 days interval).

Remarks

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)

(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)

(i) g/kg the active cyflumetofen is a racemate

(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

(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 plants - type of equipment used must be indicated

Footnote: SC = Suspensible Concentrate
NA = not applicable

of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

Methods of Analysis

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

Technical as (principle of method)	HPLC-UV at 220 nm
Impurities in technical as (principle of method)	HPLC-UV at 220 nm GC-FID Confirmation of identity using LC-UV and GC-MS
Plant protection product (principle of method)	HPLC-UV (285 nm)

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Cyflumetofen (sum of isomers) – Fruit crops only.
Food of animal origin		Not applicable as representative uses do not lead to residues in food/feed of animal origin.
Soil		Cyflumetofen (sum of isomers)
Water	surface	Cyflumetofen (sum of isomers), B-2
	drinking/ground	Cyflumetofen (sum of isomers), B-3
Air		Cyflumetofen (sum of isomers)

Monitoring/ Enforcement methods

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not applicable as representative uses do not lead to residues in food/feed of plant origin.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not applicable as representative uses do not lead to residues in food/feed of animal origin.
Soil (principle of method and LOQ)	LC-MS/MS Cyflumetofen LOQ 0.05 mg/kg
Water (principle of method and LOQ)	LC-MS/MS Cyflumetofen, B-3 LOQ 0.1 µg/L (drinking, ground and surface water) Open for B-2 in surface water.
Air (principle of method and LOQ)	LC-MS/MS Cyflumetofen LOQ 2.76 µg/m^3
Body fluids and tissues (principle of method and LOQ)	Not required as cyflumetofen is not classified as (very) toxic.

Impact on Human and Animal Health

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

Rate and extent of oral absorption	68 % based on the radioactivity recovered from urine (29 %), bile (37 %), tissues and residual carcass (2.4 %), within 48 hours.
Distribution	Widely distributed. The highest concentrations were found in the liver, followed by kidney.
Potential for accumulation	No evidence for accumulation
Rate and extent of excretion	The majority of the radioactivity (> 90 %) was excreted in the urine and feces by 72 hr. Urine: 58 – 67%, Feces: 25 – 33% of the administered dose.
Metabolism in animals	Extensively metabolised by molecular cleavage, hydrolysis and conjugation.
Toxicologically relevant compounds (animals and plants)	Cyflumetofen
Toxicologically relevant compounds (environment)	Cyflumetofen and B-3

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral	> 2000 mg/kg bw	
Rat LD_{50} dermal	> 5000 mg/kg bw	
Rat LC_{50} inhalation	> 2.65 mg/L air/ 4h (nose only; maximum attainable concentration)	
Skin irritation	Non-irritant	
Eye irritation	Non-irritant	
Skin sensitisation	Sensitising (M & K)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect	Rat & mouse: vacuolation and hypertrophy of adrenal cortical cells. Dog: vacuolation and degeneration adrenal cortex.	
Relevant oral NOAEL	90-day rat: 16.5 mg/kg bw/day 90-day mouse: 117 mg/kg bw/day 1-year dog: LOAEL 30 mg/kg bw/day	
Relevant dermal NOAEL	No data – not required	
Relevant inhalation NOAEL	No data – not required	

Genotoxicity (Annex IIA, point 5.4)

	Positive *in vitro* gene mutation assay; Cyflumetofen unlikely to be genotoxic *in vivo.*	

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

Target/critical effect	Rat: increased adrenal weight, vacuolation and hypertrophy of adrenal cortical cells, vacuolation of ovarian interstitial cells. Mouse: vacuolation of adrenal cortical cells.	
Relevant NOAEL	16.5 mg/kg bw/day (2-year, rat) 144 mg/kg bw/day (18-month, mouse)	
Carcinogenicity	Cyflumetofen has no carcinogenic potential	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect	Parental & offspring: increased adrenal weights and hypertrophy of adrenal cortical cells. Reproductive: delay in sexual development possibly related to hormonal effects in females.	
Relevant parental NOAEL	10.4 mg/kg bw/day	
Relevant reproductive NOAEL	10.4 mg/kg bw/day	
Relevant offspring NOAEL	10.4 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect	Rat: Maternal: increased adrenal weight and increased incidence of vacuolation of adrenal cortical cells. Developmental: delayed ossification of sternal centra. Rabbit: Maternal: decreased body weight gain. Developmental: incomplete ossification, hyoid changes and reduced foetal weight. No teratogenic effects	
Relevant maternal NOAEL	Rat: 50 mg/kg bw/day	

	Rabbit: 50 mg/kg bw/day	
Relevant developmental NOAEL	Rat: 50 mg/kg bw/day Rabbit: 250 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity	No indications for neurotoxicity after single dose of 2000 mg/kg bw.	
Repeated neurotoxicity	No data available - not required. No concern from other studies.	
Delayed neurotoxicity	No data - not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies	To elucidate the mechanism(s) for the effects on adrenal gland and ovary, a 28-day mechanistic study was performed in rats. Quantitative analysis of gene expression in the adrenal gland revealed a significant decrease in HSL (hormone-sensitive lipase) at 5000 mg/kg food of both sexes. Since HSL is a major enzyme involved in cholesterol metabolism and regulates cholesterol hydrolysis in the adrenal gland, the decrease in HSL might result in inhibition of hydrolysis, leading to cholesterol deposition in adrenals, which would be consistent with the lipid deposition observed. A similar mechanism is probably present in ovaries. The threshold for the described mechanism lies between 100 and 5000 mg/kg food (i.e. between 7.44 and 378 mg/kg bw/d for males and 7.59 and 347 for females). In conclusion, the vacuolation of adrenal cortical cells and vacuolation of interstitial ovary cells after repeated exposure to cyflumetofen is probably due to cholesterol deposition as a result of a reduction in hormone-sensitive lipase.

Studies performed on metabolites or impurities	Metabolite B-1: - Rat LD_{50} oral >2000 mg/kg bw - Ames test: negative - Chromosome aberration test: negative - Gene mutation test (TK): positive in absence of metabolic activation - *In vivo* DNA repair assay (UDS): negative - QSAR: no structural alerts Metabolite B-3: - Mortality observed at 500 mg/kg bw in a dose-range finding study to the UDS assay in rat - Ames test: positive in TA 100, negative in TA 1535, TA 1537 and TA 98 - Chromosome aberration test: negative - Gene mutation test (TK): positive in absence of metabolic activation - *In vivo* DNA repair assay (UDS): negative - QSAR: no structural alerts

Medical data (Annex IIA, point 5.9)

Limited information – new compound; no adverse health effects observed in workers from manufacturing plant

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI	0.17 mg/kg bw/day	90-day and 2-year rat studies	100
AOEL	0.11 mg/kg bw/day	90-day-and 2-year rat	100 * (overall 147)
ARfD	Not allocated, not necessary		

*correction for oral absorption of 68 %

Dermal absorption (Annex IIIA, point 7.3)

Cyflumetofen dissolved in acetonitrile	concentrate: 28 % spray dilution: 21 % *In vitro* human skin

Exposure scenarios (Annex IIIA, point 7.2)

Operator

Mechanical downward spraying (field) on ornamentals, tree nursery, perennial ornamentals and public green (application rate 0.24 kg cyflumetofen/ha)

UK-POEM:	% of AOEL
Without PPE	536 %
With PPE (gloves during M/L)	52 %
German model:	% of AOEL
Without PPE	69 %
With PPE (gloves during M/L)	27 %

Manual downward spraying (field) on tree nursery and public green (application rate 0.24 kg cyflumetofen/ha)

UK-POEM:	% of AOEL
Without PPE	294 %
With PPE (gloves during M/L)	77 %

Manual spraying (indoors) on ornamentals (application rate 0.30 kg cyflumetofen/ha)

Dutch model:	% of AOEL
Without PPE	222 %
With PPE (gloves and coverall during M/L and application)	26 %

Manual spraying (indoors) on tree nursery and perennial ornamentals (application rate 0.20 kg cyflumetofen/ha)

Dutch model:	% of AOEL
Without PPE	148 %
With PPE (gloves and coverall during M/L and application)	17 %

Workers	Re-entry activities in ornamentals, tree nursery and perennial ornamentals (field) (application rate 0.24 kg cyflumetofen/ha after 1 application) EUROPOEM II: % of AOEL Without PPE 79 % With PPE (gloves and coverall) 8 % Considering a max. of 4 applications and assuming no decay in residues between applications, exposure remains below the AOEL when PPE are worn. Re-entry activities in ornamentals, tree nursery and perennial ornamentals in the greenhouse (application rate 0.30 kg cyflumetofen/ha after 1 application) EUROPOEM II: % of AOEL Without PPE 98 % With PPE (gloves and coverall) 10 % Considering a max. of 4 applications and assuming no decay in residues between applications, exposure remains below the AOEL when PPE are worn.
Bystanders	Spraying (field) on ornamentals, tree nursery, perennial crops and public green (application rate 0.24 kg cyflumetofen/ha) EUROPOEM II: 1 % of AOEL Risk assessment for children playing on public green has not been performed. Indoor: Not applicable (greenhouse applications)

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

	RMS/peer review proposal
Cyflumetofen	*Under Council Directive 67/548/EEC:* **Xi** "irritant" **R43** "may cause sensitisation by skin contact" *Under Regulation EC 1272/2008:* Skin Sens. 1: **H317** "May cause an allergic skin reaction"

Residues

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

Plant groups covered	Fruit crops (mandarin, eggplant, apple)
Rotational crops	Not requested, having regard to the DT_{90} values calculated for different types of soils in laboratory studies, for Cyflumetofen and its main soil metabolites B-1, AB-1 and B-3 (almost all below 100 days).
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable
Processed commodities	Not provided and not required having regard to the representatives uses
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Cyflumetofen, sum of isomers (fruit crop only)
Plant residue definition for risk assessment	Sum of cyflumetofen (sum of isomers) and metabolite B-1 expressed as cyflumetofen (provisional, fruit crops only)
Conversion factor (monitoring to risk assessment)	Not relevant considering the representative uses

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

Animals covered	Not provided and not required having regard to the representatives uses
Time needed to reach a plateau concentration in milk and eggs	Not applicable
Animal residue definition for monitoring	Not applicable
Animal residue definition for risk assessment	Not applicable
Conversion factor (monitoring to risk assessment)	Not applicable
Metabolism in rat and ruminant similar (yes/no)	Not applicable
Fat soluble residue: (yes/no)	Not applicable

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

Not applicable

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

Not provided and not required having regard to the representatives uses

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

	Ruminant:	**Poultry:**	**Pig:**
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Not applicable	Not applicable	Not applicable
Potential for accumulation (yes/no):	Not applicable	Not applicable	Not applicable
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	-	-	-
	Feeding studies Residue levels in matrices : Mean (max) mg/kg		
Muscle	-	-	-
Liver	-	-	-
Kidney	-	-	-
Fat	-	-	-
Milk	-		
Eggs		-	

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

Crop	Northern Southern Region, field or glasshouse	Trials results relevant to the representative uses (a)	Recommendation/ comments	**MRL** estimated from trials according to representative use	**HR** (c)	**STMR** (b)
		Not applicable				

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

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

ADI	0.17 mg/kg bw/day
TMDI (PRIMo Model rev.2, % ADI)	Not applicable, uses on non-edible crops.
IEDI (WHO European Diet) (% ADI)	Not relevant
Factors included in IEDI and NEDI	Not relevant
ARfD	Not allocated, not necessary
IESTI (% ARfD)	Not applicable
Factors included in IESTI and NESTI	Not applicable

The highest consumer exposure resulting from the possible presence of B-1 in groundwater used as drinking water was estimated to be 1% of the ADI only (Infant, 5 kg bw, consuming 0.75 L water per day).

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%)
		Transfer Factor	Yield factor	
Not provided and not required				

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

No MRLs proposed	representative uses on non-edible crops.

Fate and behaviour in the environment

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

Mineralization after 100 days	31.2% after 121 d, [^{14}C-A]-label (n=1) 1.7-36.7 % after 120-121 d, [^{14}C-B]-label (n=4) Sterile conditions: <0.1% after 30 d [^{14}C-A]-label (n=1) Sterile conditions: 4.1% after 30 d [^{14}C-B]-label (n=1)
Non-extractable residues after 100 days	37.8% after 90 d, [^{14}C-A]-label (n=1) 30.1-40.1% after 90-120 d, [^{14}C-B]-label (n=4) Sterile conditions: 42.7% after 30 d [^{14}C-A]-label (n=1) Sterile conditions: 19.7% after 30 d [^{14}C-B]-label (n=1)
Metabolites requiring further consideration - name and/or code, % of applied (range and maximum)	Significant metabolites (exceeding 10% AR or 2x 5% at two consecutive time points) were: AB-1 (including dimers/isomers of AB-1): max 19.9-21.6% at 10-59 d (n=2). Max 21.6% at 10 d. AB-1 alone reached a maximum level of 8.3% (day 59) [14C-A] & [14C-B] labels B-1: max 22.9-63.0 % at 6-90 d (n=4) [14C-B] label. Max 63% at day 90 B-3: max 4.8-23% at 6-21 d (n=3) [14C-B] label. Max 23% at day 21.

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

Anaerobic degradation

Mineralization after 100 days	No data, not required
Non-extractable residues after 100 days	No data, not required
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data, not required

Soil photolysis

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	In general, metabolite levels are similar in irradiated and dark incubations. B-1 is found as a major (photolysis) metabolite (max 47.6% AR and 37.7% AR in irradiated and dark soil respectively)

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	**parameter for**	**Kinetics**	**Optimised model parameters**	**St. (r^2)**	**DT_{50}/DT_{90} (d)**	**DT_{50} (d) 20°C pF2/10kPa** [1]
Wolston (A-label) Sandy loam[2] pH 6.5	Persistence	DFOP	g = 0.93 ± 0.03 k_1 = 0.43 ± 0.05 d^{-1} k_2 = 0.01 ± 0.01 d^{-1} M_0 = 102.58 ± 3.69	0.991	1.81 / 7.72	-
	Modelling	FOMC	α = 3.05 ± 2.58 β = 7.13 ± 7.50 M_0 = 102.45 ± 4.73	0.984	1.82 / 8.04	3.80[3]
Wolston (B-label) Sandy loam[2] pH 6.5	Persistence	DFOP	g = 0.95 ± 0.02 k_1 = 0.34 ± 0.02 d^{-1} k_2 = 0.01 ± 0.01 d^{-1} M_0 = 104.81 ± 2.04	0.997	2.29 / 8.63	-
	Modelling	SFO	M_0 = 103.61 ± 3. k = 0.30 ± 0.02 d^{-}	0.991	2.34 / 7.78	3.67
Wolston Sandy loam[2] (mean)						**3.73**
Speyer 2.2 Sandy loam[4] pH 5.6	Persistence	DFOP	g = 0.91 ± 0.06 k_1 = 0.20 ± 0.04 d^{-1} k_2 = 0.0003 ± 0.0097 d^{-1} M_0 = 106.98 ± 6.14	0.964	4.33/23.10	-
	Modelling	FOMC	α = 1.63 ± 1.03 β = 7.13 ± 6.56 M_0 = 107.43 ± 8.20	0.940	3.79/22.25	**6.70**[3] **(#)**
Speyer 2.3 Sandy loam[4] pH 6.2	Persistence and modelling	DFOP	g = 0.83 ± 0.03 k_1 = 0.31 ± 0.03 d^{-1} k_2 = 0.004 ± 0.003 d^{-1} M_0 = 99.49 ± 3.05	0.989	3.13/134.1	**153.4**[5]

Speyer 6S Clay[4] pH 7.0	Persistence	DFOP	g = 0.96 ± 0.01 k_1 = 0.33 ± 0.02 d^{-1} k_2 = 0.0 ± 0.006 d^{-1} M_0 = 99.83 ± 2.06	0.996	2.20/8.40	-
	Modelling	FOMC	α =2.32 ± 0.91 β = 5.76 ± 3.08 M_0 = 101.69 ± 3.53	0.988	2.01/9.80	**1.54**[3]
Geometric mean						**8.8 (#)**

[1] Normalised to 20°C based on a Q10 factor of 2.58
[2] Incubation at 25°C and pF2 soil moisture
[3] DT_{90}/3.32
[4] Incubation at 20°C and 45% of the MWHC
[5] Calculated from the slow phase (k_2) of the DFOP model.
 # The DFOP slow phase DT_{50} of 1000 d from Speyer 2.2 soil should be considered valid for modelling purposes; the resulting overall geomean DT_{50} for cyflumetofen is 30.6 d, normalised to reference conditions (refer to the Evaluation table under Data requirement 4.1).

B-1	Aerobic conditions (study dosed with B-1)							
Soil type	X[1]	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
Loamy sand	-	5.4	20 °C / 40 %	6.3 /21.0	-	6.30	0.993	SFO (persistence & modelling)
Sandy loam	-	6.2	20 °C / 40 %	16.7 / 55.5	-	12.80	0.988	SFO (persistence & modelling)
Clay	-	7.2	20 °C / 40 %	36.3 / 121	-	16.82	0.959	SFO (persistence & modelling)
Geometric mean/median						11.07		

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

AB-1	Aerobic conditions (study dosed with AB-1)							
Soil type	X[1]	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

Sand	-	5.1	20 °C / 40 %	0.07 / 90.8	-	138.63[2]	0.998	DFOP (persistence) Slow phase DFOP (modelling) k_1 = 12.40 ± 1.13 k_2 = 0.005 ± 0.001 g = 0.847 ± 0.007 M_0= 95.0 ± 1.2
Loamy sand	-	5.4	20 °C / 40 %	0.08 / 69.3	-	115.52[2]	0.999	DFOP (persistence) Slow phase DFOP (modelling) k_1 = 10.75 ± 0.50 k_2 = 0.006 ± 0.001 g = 0.846 ± 0.004 M_0= 88.0 ± 0.7
Clay	-	7.2	20 °C / 40 %	0.11 / 15.7	-	35.69[2]	0.999	DFOP (persistence) Slow phase DFOP (modelling) k_1 = 7.81 ± 0.22 k_2 = 0.009 ± 0.001 g = 0.885 ± 0.004 M_0= 90.0 ± 0.7
Geometric mean/median						82.99		

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

[2] Based on slow phase DFOP

B-3	Aerobic conditions (study dosed with B-3)							
Soil type	X[1]	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
Loamy sand	-	5.4	20 °C / 40 %	15.1 / 50.1	-	15.10	0.990	SFO (persistence & modelling)
Sandy loam	-	6.4	20 °C / 40 %	11.0 / 36.5	-	8.88	0.988	SFO (persistence & modelling)
Clay	-	7.2	20 °C / 40 %	12.7 / 42.2	-	5.89	0.989	SFO (persistence & modelling)
Geometric mean/median						9.24		

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

Field studies

Parent	No data, not required.

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

Laboratory studies ‡

Parent	Anaerobic conditions: no data, not required

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Cyflumetofen (parent): HPLC method Koc = 131826 mL/g. For modelling a 1/n of 1.0 was used. Due to instability of the compound, batch adsorption studies could not be performed.

Metabolite AB-1							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand (average of 2 replicates)	2.29	5.7	1.55E3	65500	-	-	1 (default)
Sandy loam (average of 2 replicates)	1.02	6.3	4.6E3	450000	-	-	1 (default)
Sandy clay (average of 2 replicates)	1.90	6.9	0.12E3	6200	-	-	1 (default)
Arithmetic mean/median							
pH dependence (yes or no)			No				

Metabolite B-3							
Soil Type	OC %	Soil pH ($CaCl_2$)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	2.36	5.6	-	-	0.277	11.73	0.874
Sandy loam	1.02	6.3	-	-	0.172	16.86	1.039
Sandy clay	1.89	7.0	-	-	0.214	12.20	0.959
Arithmetic mean					0.221	13.60	0.957
pH dependence (yes or no)			No				

Metabolite B-2

EPIWIN estimation: Koc = 22180 L/kg. For FOCUS Step 4 PECsw modeling a 1/n of 1.0 was used.

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

Column leaching with metabolite B-1	Eluation (mm): 200 mm Time period (d): 48 hours
	Study with unlabeled B-1 Koc = 3.7 – 6.56 mL/g (n=3). Mean Koc = 4.83 mL/g. For modelling a default 1/n = 1.0 was used.
Aged residues leaching	No data. Not required.
Lysimeter/ field leaching studies	No data. Not required.

$PEC_{(soil)}$ (OECD data point IIIA 9.4)

Method of calculation	EU 7617/VI/96 and Sanco/10058/2005 vs. 1 March 2005 "FOCUS degradation kinetics". **Cyflumetofen** Worst-case degradation pattern: DFOP with DT_{50}/DT_{90} 3.13/134.1 days[#] g = 0.828597, k_1 = 0.30511135, k_2 = 0.004197616 **AB-1** Worst-case degradation pattern: DFOP with DT_{50}/DT_{90} 0.07/90.8 days g = 0.847, k_1 = 12.4018, k_2 = 0.0046659 **B-1** Worst-case degradation pattern: SFO with DT_{50} 36.3d **B-3** Worst-case degradation pattern: SFO with DT_{50} 15.1d *[#]The worst-case soil DT_{50} for cyflumetofen should be DFOP with DT50/DT90 4.33/23.10 days with g = 0.91 ± 0.06; k_1 = 0.20 ± 0.04 d^{-1}; k_2 = 0.0003 ± 0.0097 d^{-1}. The resulting maximum concentration in soil for cyflumetofen over 5.0cm considering accumulation is **0.5084 mg/kg**. The use of this PECsoil to calculate the TER for soil organisms does not affect the final results of the risk assessment.*
Application data	**Cyflumetofen** cGAP: 4 x 300 g a.s./ha; interval 7 days; crop interception 50%* **AB-1** cGAP: 4 x 300 g a.s./ha; interval 7 days; crop interception 50%*; corrections for MW (345.3/447.45) and max% of formation (21.6%) **B-1** cGAP: 4 x 300 g a.s./ha; interval 7 days; crop interception 50%*; corrections for MW (190.12/447.45) and max% of formation (63%) **B-3** cGAP: 4 x 300 g a.s./ha; interval 7 days; crop interception 50%*; corrections for MW (189.14/447.45) and max% of formation (23%) ** in the revised DAR an interception value of 60% was defended (as infestation is on well-developed leaves only) and used for PECgw and PECsw/sed. PECsoil calculations are not revised and remain based on the extreme worst-case assumption of 50 % crop interception.*

$PEC_{(s)}$ Cyflumetofen		Single application Actual (mg/kg)	Single application Time weighted average (mg/kg)	Multiple application Actual	Multiple application Time weighted average
Initial		-	-	0.319	-
Short term	24h	-	-	0.269	0.294
	2d	-	-	0.232	0.272
	4d	-	-	0.185	0.240
Long term	7d	-	-	0.150	0.209
	14d	-	-	0.126	0.174
	21d	-	-	0.121	0.157
	28d	-	-	0.117	0.147
	50d	-	-	0.106	0.132
	100d	-	-	0.086	0.114

$PEC_{(s)}$ AB-1		Single application Actual (mg/kg)	Single application Time weighted average (mg/kg)	Multiple application Actual	Multiple application Time weighted average
Initial		-	-	0.048	-
Short term	24h	-	-	0.019	0.034
	2d	-	-	0.019	0.026
	4d	-	-	0.019	0.023
Long term	7d	-	-	0.019	0.021
	14d	-	-	0.018	0.020
	21d	-	-	0.018	0.019
	28d	-	-	0.017	0.019
	50d	-	-	0.015	0.018
	100d	-	-	0.012	0.016

$PEC_{(s)}$ B-1		Single application Actual (mg/kg)	Single application Time weighted average (mg/kg)	Multiple application Actual	Multiple application Time weighted average
Initial		-	-	0.177	-
Short term	24h	-	-	0.174	0.176
	2d	-	-	0.171	0.174
	4d	-	-	0.164	0.171
Long term	7d	-	-	0.155	0.166

14d	-	-	0.136	0.155
21d	-	-	0.119	0.146
28d	-	-	0.104	0.137
50d	-	-	0.068	0.114
100d	-	-	0.026	0.079

$PEC_{(s)}$ B-3		Single application Actual (mg/kg)	Single application Time weighted average (mg/kg)	Multiple application Actual	Multiple application Time weighted average
Initial		-	-	0.051	-
Short term	24h	-	-	0.049	0.050
	2d	-	-	0.047	0.049
	4d	-	-	0.043	0.047
Long term	7d	-	-	0.037	0.044
	14d	-	-	0.027	0.038
	21d	-	-	0.020	0.033
	28d	-	-	0.014	0.029
	50d	-	-	0.005	0.020
	100d	-	-	0.001	0.011

Route and rate of degradation in water (OECD data point IIA 2.9 and IIA 7.5 to IIA 7.9)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 4: DT_{50} = 7.7 days (25°C) (SFO, r^2 = 0.998-0.999) A-1: max 26.9% AR (21 d) A-2: max 14.6% AR (30 d) A-18: max 12.6% AR (30 d) AB-1: max 34.8% AR (30 d) B-1: max 48.4% AR (30 d) All other metabolites <10% AR
	pH 5: DT_{50} = 6.0 days (25°C) (SFO, r^2 = 0.999-0.999) A-1: max 10.0% AR (7 d) A-2: max 14.1% AR (21 d) AB-1: max 23.7% AR (14 d) AU16: max 15.8% AR (30 d) AU17: max 21.1% AR (30 d) B-1: max 52.6% AR (30 d) BU14: max 11.4% AR (14 d) All other metabolites <10% AR

	pH 7: DT_{50} = 9.8 hours (25°C) (SFO, r^2 = 0.998-1.000) A-1: max 14.4% AR (8 hours) A-2: max 19.1% AR (120 hours)/24.3% (at 240 h)/44.12% (at 720 h)* A-18: max 36.2% AR (120 hours) AB-1: max 44.5% AR (120 hours) B-1: max 53.2% AR (48 hours) All other metabolites <10% AR ** during peer review it was discussed that the levels of A1/A2 at 240 and 720 h consist of A2*
	pH 9: DT_{50} = 10.3 min (25°C) (SFO, r^2 = 0.943-0.992) A-1: max 28.3% AR (15 minutes) A-2: max 15.1% AR (90 minutes) A-18: max 48.8% AR (1440 minutes) AB-1: max 45.7% AR (1440 minutes) B-1: max 50.3% AR (1440 minutes) All other metabolites <10% AR
Photolytic degradation of active substance and relevant metabolites	Cyflumetofen: pH 5: DT_{50} = 1.28 hours (25°C) (20 W/m^2, 300-400 nm) Simulated DT50 in Tokyo 35°N (April-June) = 0.14 d natural water: DT_{50} = 1.07 hours (25°C) (20 W/m^2, 300-400 nm)
	In buffer pH 5 solutions, aquatic photolytic metabolites products exceeding 10% of AR: B-1 (max 11.88% AR) AB-7 (max 10.82% AR) AB-15 (max 54.67% AR) No other degradation products above 10% AR were observed. B-1 was also a significant degradation product under dark conditions (max 13.27 % AR). Hence, the only specific photolytic degradation products of cyflumetofen are AB-15 and AB-7.
Readily biodegradable (yes/no)	No data submitted.

Degradation in water / sediment

Cyflumetofen	Distribution (Max. sed 28.3-66.8% after 0.1-5 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys. (d)	χ^2	DT_{50}-DT_{90} Water (d)[3]	χ^2	DT_{50}-DT_{90} Sed (d)[3]	χ^2	Method of calculation
Goorven (A-label)	6.2	Mean 5.1 (4.56-5.13)	20	9.9-48.7 10.8-35.8	6.61 7.14	0.7-7.5	9.96	12.0-50.6	9.35	HS/FOMC/FOMC[1] SFO[2]
Goorven (B-label)	6.2	Mean 5.1 (4.56-5.54)	20	14-47 14-47	5.44 5.44	0.1-2.0	3.86	15-50	8.62	SFO/FOMC/SFO[1] SFO[2]
Mean of labels				12.4						
Schoonrewoerd-sewiel (A-label)	4.9	Mean 7.2 (7.17-7.23)	20	0.2-2.2 0.2-0.7	5.83 16.34	0.1-0.5	2.40	2.1-7.0	13.38	HS/FOMC/SFO[1] SFO[2]
Schoonrewoerd-sewiel (B-label)	4.9	Mean 7.2 (7.17-7.36)	20	0.08-0.4 0.08-0.3	6.89 11.73	0.05-0.15	8.50	1.6-5.2	2.78	DFOP/SFO/SFO[1] SFO[2]
Mean of labels				0.14		-		-		
Geometric mean (DT50)				**1.32**		-		-		

[1] best fit models
[2] acceptable fit for modelling
[3] DT_{50} for dissipation (includes adsorption/desorption)

B-2 (Met-5)

Distribution sediment max 28% (2 d) and water max 15.4% (0.7 d)

Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys. (d)	χ^2	DT_{50}-DT_{90} Water (d)	χ^2	DT_{50}-DT_{90} Sed (d)	χ^2	Method of calculation
Goorven (B-label)	6.2	Mean 5.1 (4.56-5.54)	20	0.77-2.55	33.33	n.c.	-	n.c.	-	SFO (2-103 days)
Schoonrewoerd-sewiel (B-label)	4.9	Mean 7.2 (7.17-7.36)	20	40.0-131	3.40	n.c.	-	n.c.	-	SFO (12-102 days)
Geometric mean (DT50)				**5.5**		-		-		

Distribution in water/sediment systems (metabolites)	A-label study (metabolites >10% AR and compartment) Met-1: water max 10.7% (59 d) Met-4*: sediment max 10.7% (29 d) A-2: water max 18.4% (0.7 d) AB-1: sediment max 14.6% (29 d) Met-8: water max 19.5% (5 d) AB-11: water max 10.0% (0.7 d) and sediment max 10.1% (12 d) B-label study (metabolites >10% AR and compartment) B-1: sediment max 21.5% (29 d) and water max 65% (5 d) B-2/AB-1 (Met 5#): sediment max 28% (2 d) and water max 15.4% (0.7 d) *A qualitative assessment to address the environmental exposure of Met 4 was provided during the peer review. It was concluded that no further assessment for this metabolite is required. #Met 5 matched with AB-1 and B-2 based on retention time. The presence of B-2 was confirmed by GC-MS. In the exposure assessment it is assumed that Met-5 equals to B-2.

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. Max x % after n d (end of the study)
Goorven (A-label)	6.2	5.1	20% at 98 d	Max 33% at 98 d	33% at 98 d
Goorven (B-label)	6.2	5.1	2.8% at 103 d	Max 19% at 62 d	9.7% at 103 d
Schoonre-woerdsewiel (A-label)	4.9	7.2	2% at 57 d	Max 17% at 57 d	17% at 57 d
Schoonre-woerdsewiel (B-label)	4.9	7.2	3.2% at 103 d	Max 13% at 103 d	13% at 103 d

PEC (surface water) (OECD data point IIIA 9.7)

Method of calculation	For all simulations described below, multiple and single application scenarios were calculated In Volume 3 B.8.6.1. In the LoEP, only values used for aquatic risk assessment are presented. **Cyflumetofen** FOCUS STEP1 and STEP2 Worst-case scenario: grass, Southern Europe (March-May), intermediate crop cover DT_{50} wat/sed: 1.32 d (geomean) **B-1** FOCUS STEP1 and STEP2 Worst-case scenario: Winter cereals, Southern Europe (March-May), intermediate crop cover DT50 wat/sed: 1000 d (used for water and sediment compartment) **AB-11, A-2, AB-15** FOCUS STEP1 and STEP2 Worst-case scenario: Winter cereals, no run-off/drainage, intermediate crop cover DT_{50} wat/sed: 1000 d (used for water and sediment compartment) **B-3** FOCUS STEP1 and STEP2 Worst-case scenario: Winter cereals, Southern Europe (March-May), intermediate crop cover. Only entry through run-off/drainage. DT_{50} wat/sed: 1000 d (used for water and sediment compartment) **B-2** FOCUS STEP1 and STEP2 Worst-case scenario: Winter cereals, no run-off/drainage, intermediate crop cover DT_{50} wat/sed: 1000 d (used for water and sediment compartment)

	B-2 (continued) FOCUS STEP4 for in situ formed B-2 Worst-case scenario: Cereals (spring and winter), no run-off/drainage, intermediate crop cover DT_{50} water: 1000 d; DT_{50} sediment: 5.5 d Koc 22180 L/kg, 1/n 1.0. This STEP 4 is combined with a FOCUS STEP 3 run for B-1 (soil metabolite, precursor of B-2) accounting for 25 % conversion to B-2 to account for the potential formation of B-2 via drainage or run-off of B-1 from soil. The corrected dose B-1 that could be formed into B-2 is calculated as: dose rate of parent (240 g a.s./ha) x formation of B-1 (63%) x 0.4 (assuming 0.6 interception) x rel molar weight B-1/parent (190.12/447.45=0.425) x mean estimated formation of B-2 from B-1 (0.25, see above section) x rel molar weight of B-2/B-1 and a stoechiometric factor* (362.23/2x190.12=0.95). The loading of B-1 in STEP 3 run hence amounts to 240 x 0.63 x 0.4 x 0.425 x 0.25 x 0.95= **6.1** gram/ha ** needed since 1 mole of B-2 can only be formed by 2 moles of B-1.* In this run the following B-1 properties are used: DT_{50} soil 11.07 d (20°, moisture corrected) Koc 4.83 L/kg (Kom = 2.80), 1.0 (worst-case, no 1/n available) DT50 wat/sed: 1000 d (used for water and sediment compartment)
Application rate	cGAP: 4 x 240 g a.s./ha, interval 7 days, intermediate crop cover
Main routes of entry	Cyflumetofen: drift, runoff/drainage B-1: run-off/drainage (max 63% in soil), in situ formation (max 84.4% in total wat/sed system) AB-11: in situ formation (max 13.7% in total wat/sed system) B-2: -in situ formation (max 28% in total wat/sed system) combined with -emission via drainage/run-off of B-1 assuming a formation of B-2 from B-1 of 25% (see Addendum 1) B-3: run-off/drainage (max 23% in soil) A-2: in situ formation (max 22.7% in total wat/sed system) AB-15: in situ formation through photolysis (max 35% in total wat/sed system)

$PEC_{(sw)}$
Cyflumetofen

FOCUS STEP 1	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
Initial	2.6598	-	596.6057	-
Short term 24h	0.2751	1.4674	362.6221	479.6139
2d	0.1627	0.8407	214.4871	380.8579
4d	0.0569	0.4707	75.0404	256.8181
Long term 7d	0.0118	0.2813	15.5287	162.9434
14d	0.0003	0.1422	0.3933	83.5305
21d	0.0000	0.0948	0.0100	55.7218
28d	0.0000	0.0711	0.0003	41.7920
42d	0.0000	0.0474	0.0000	27.8613
50d	0.0000	0.0398	0.0000	23.4035
100d	0.0000	0.0199	0.0000	11.7018

$PEC_{(sw/sed)}$
Cyflumetofen

FOCUS STEP 2	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
(single appl.)	Actual	TWA	Actual	TWA
Initial	2.21	-	71.57	---
Short term 24h	0.4401	1.3237	42.3497	56.9591
2d	0.0906	0.7945	25.0494	45.3294
4d	0.0583	0.4210	8.7638	30.5954
Long term 7d	0.0112	0.2528	1.8136	19.4172
14d	0.0003	0.1279	0.0459	9.9545
21d	0.0000	0.0853	0.0012	6.6405
28d	0.0000	0.0640	0.0000	4.9805
42d	0.0000	0.0427	0.0000	3.3203
50d	0.0000	0.0358	0.0000	2.7891
100d	0.0000	0.0179	0.0000	1.3945

FOCUS STEP 2	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
(multiple appl.)	Actual	TWA	Actual	TWA
Initial	1.4899	---	147.2203	-

Short term 24h	0.2972	0.8936	87.0913	117.1558
2d	0.0613	0.5364	51.5136	93.2291
4d	0.1144	0.2936	18.0225	62.9240
Long term 7d	0.0231	0.1926	3.7296	39.9339
14d	0.0006	0.0994	0.0945	20.4727
21d	0.0000	0.0664	0.0024	13.6570
28d	0.0000	0.0498	0.0001	10.2429
42d	0.0000	0.0332	0.0000	6.8286
50d	0.0000	0.0279	0.0000	5.7360
100d	0.0000	0.0139	0.0000	2.8680

$PEC_{(sw)}$ AB-1

During the peer review it was considered that AB-1 is not a major soil metabolite and the route via drainage/run-off does not need to be considered. Therefore, an alternative approach was followed for major sediment metabolite AB-1. Based on correction of the parent values (STEP 1-2) the following PECsed are calculated for AB-1:

STEP 1: 596.6057 (PECsed OK-5101) x 14.6% (maximum observed% AB-1) x 345.37/447.45 (relative molecular weight)= **67.23 µg/kg**
STEP 2: 147.2203 x 14.6% x 345.37/447.45 = **16.59 µg/kg**

$PEC_{(sw/sed)}$ B-1

FOCUS STEP 1	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
Initial	88.2772	-	4.1109	-
Short term 24h	88.1958	88.2365	4.2599	4.1854
2d	88.1346	88.2008	4.2569	4.2219
4d	88.0125	88.1372	4.2510	4.2379
Long term 7d	87.8297	88.0446	4.2422	4.2416
14d	87.4046	87.8308	4.2216	4.2368
21d	86.9815	87.6182	4.2012	4.2283
28d	86.5605	87.4063	4.1809	4.2190
42d	85.7246	86.9848	4.1405	4.1995
50d	85.2506	86.7453	4.1176	4.1883
100d	82.3466	85.2677	3.9773	4.1177

$PEC_{(sw/sed)}$ AB-11

FOCUS STEP 1	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
Initial	1.1663	-	0.0000	-
Short term 24h	0.0104	0.5884	8.6631	4.3316
2d	0.0104	0.2994	8.6571	6.4959
4d	0.0104	0.1549	8.6451	7.5735
Long term 7d	0.0104	0.0930	8.6272	8.0289
14d	0.0103	0.0517	8.5854	8.3176
21d	0.0103	0.0379	8.5439	8.3999
28d	0.0102	0.0310	8.5025	8.4308
42d	0.0101	0.0240	8.4204	8.4410
50d	0.0101	0.0218	8.3738	8.4340
100d	0.0097	0.0159	8.0886	8.3322

$PEC_{(sw)}$ B-2 combined emission routes

FOCUS STEP 4	August-September (single application)			
	PIECsw (µg/L)	TWA 4 (µg/L)	TWA 21 (µg/L)	TWA 28 (µg/L)
D1 ditch	0.336	0.112	0.0231	0.0173
D1 stream	0.245	0.0403	0.00770	0.00578
D2 ditch	0.337	0.118	0.0256	0.0195
D2 stream	0.249	0.0875	0.0190	0.0145
D3 ditch	**0.354 (maximum value)**	0.0712	0.0319	0.0294
D4 pond	0.0214	0.0209	0.0181	0.0166
D4 stream	0.239	0.0423	0.0380	0.0352
D5 pond	0.0641	0.0621	0.0407	0.0338
D5 stream	0.258	0.0715	0.0538	0.0470
D6 ditch	0.335	0.122	0.0269	0.0212
R1 pond	0.0113	0.00878	0.00438	0.00350
R1 stream	0.181	0.0157	0.00452	0.00340
R3 stream	0.352	0.0531	0.0124	0.00928
R4 stream	0.183	0.00932	0.00178	0.00133

$PEC_{(sed)}$ B-2 combined emission routes

FOCUS STEP 4	August-September (multiple application)			
	PIECsw (µg/L)	TWA 4 (µg/L)	TWA 21 (µg/L)	TWA 28 (µg/L)
D1 ditch	0.471	0.469	0.446	0.434
D1 stream	0.428	0.427	0.411	0.397
D2 ditch	0.446	0.434	0.349	0.319
D2 stream	0.328	0.319	0.257	0.235
D3 ditch	1.224	1.219	1.193	1.181
D4 pond	1.016	1.014	0.966	0.934
D4 stream	2.044	2.040	1.949	1.895
D5 pond	0.260	0.259	0.248	0.243
D5 stream	0.536	0.536	0.533	0.530
D6 ditch	0.107	0.0946	0.0715	0.0667
R1 pond	0.0282	0.0279	0.0248	0.0238
R1 stream	0.0327	0.0286	0.0213	0.0210
R3 stream	0.0819	0.0736	0.0460	0.0388
R4 stream	0.0994	0.0894	0.0484	0.0404

-$PEC_{(sw/sed)}$ A-2

FOCUS STEP 1	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
Initial	0.7762	-	0.0000	-
Short term 24h	0.2849	0.5306	3.6809	1.8404
2d	0.2847	0.4077	3.6783	2.7600
4d	0.2843	0.3461	3.6732	3.2179
Long term 7d	0.2837	0.3195	3.6656	3.4114
14d	0.2823	0.3013	3.6478	3.5340
21d	0.2810	0.2947	3.6302	3.5690
28d	0.2796	0.2911	3.6126	3.5821
42d	0.2769	0.2868	3.5777	3.5865
50d	0.2754	0.2851	3.5579	3.5835
100d	0.2660	0.2779	3.4367	3.5402

$PEC_{(sw/sed)}$ AB-15

FOCUS STEP 1	PECsw (µg/L) **based on Koc of 0 L/kg**		PECsed (µg/kg dry sediment) **based on Koc of 3180 L/kg**	
	Actual	TWA	Actual	TWA
Initial	4.8559	-	0.0000	-
Short term 24h	4.8526	4.8543	29.4489	14.7244
2d	4.8492	4.8526	29.4285	22.0816
4d	4.8425	4.8492	29.3877	25.7448
Long term 7d	4.8324	4.8442	29.3267	27.2930
14d	4.8091	4.8325	29.1847	28.2743
21d	4.7858	4.8208	29.0435	28.5542
28d	4.7626	4.8091	28.9029	28.6589
42d	4.7166	4.7859	28.6238	28.6937
50d	4.6905	4.7728	28.4655	28.6698
100d	4.5308	4.6915	27.4958	28.3238

FOCUS STEP 2 Single application	PECsw (µg/L) **based on Koc of 0 L/kg**		PECsed (µg/kg dry sediment) **based on Koc of 3180 L/kg**	
	Actual	TWA	Actual	TWA
Initial	1.21	---	6.70	---
Short term 24h	1.2131	1.2136	6.6923	6.6937
2d	1.2123	1.2131	6.6882	6.6920
4d	1.2106	1.2123	6.6791	6.6878
Long term 7d	1.2081	1.2110	6.6652	6.6811
14d	1.2023	1.2081	6.6330	6.6651
21d	1.1964	1.2052	6.6009	6.6490
28d	1.1907	1.2023	6.5689	6.6330
42d	1.1792	1.1965	6.5055	6.6011
50d	1.1726	1.1932	6.4695	6.5829
100d	1.1327	1.1729	6.2491	6.4708

FOCUS STEP 2 Multiple application	PECsw (µg/L) **based on Koc of 0 L/kg**		PECsed (µg/kg dry sediment) **based on Koc of 3180 L/kg**	
	Actual	TWA	Actual	TWA
Initial	3.2535	---	17.9557	-
Short term 24h	3.2512	3.2523	17.9479	17.9518

2d	3.2490	3.2512	17.9368	17.9471
4d	3.2445	3.2490	17.9124	17.9359
Long term 7d	3.2377	3.2456	17.8752	17.9178
14d	3.2221	3.2377	17.7887	17.8749
21d	3.2065	3.2299	17.7026	17.8318
28d	3.1909	3.2221	17.6169	17.7887
42d	3.1601	3.2066	17.4467	17.7031
50d	3.1427	3.1977	17.3503	17.6543
100d	3.0356	3.1433	16.7593	17.3537

$PEC_{(sw/sed)}$ B-3

FOCUS STEP 1	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
Initial	30.5571	-	4.1558	-
Short term 24h	30.5359	30.5465	4.1529	4.1543
2d	30.5148	30.5359	4.1500	4.1529
4d	30.4725	30.5148	4.1443	4.1500
Long term 7d	30.4092	30.4831	4.1356	4.1457
14d	30.2620	30.4093	4.1156	4.1357
21d	30.1155	30.3358	4.0957	4.1257
28d	29.9698	30.2625	4.0759	4.1157
42d	29.6803	30.1166	4.0365	4.0959
50d	29.5162	30.0336	4.0142	4.0846
100d	28.5108	29.5221	3.8775	4.0150

FOCUS STEP 2 Single application	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
Initial	1.13	-	0.15	-
Short term 24h	1.1310	1.1314	0.1538	0.1539
2d	1.1302	1.1310	0.1537	0.1538
4d	1.1287	1.1302	0.1535	0.1537
Long term 7d	1.1263	1.1290	0.1532	0.1536
14d	1.1209	1.1263	0.1524	0.1532
21d	1.1154	1.1236	0.1517	0.1528

28d	1.1100	1.1209	0.1510	0.1524
42d	1.0993	1.1155	0.1495	0.1517
50d	1.0932	1.1124	0.1487	0.1513
100d	1.0560	1.0935	0.1436	0.1487

FOCUS STEP 2 Multiple application	PECsw (µg/L)		PECsed (µg/kg dry sediment)	
	Actual	TWA	Actual	TWA
Initial	2.4314	-	0.3307	-
Short term 24h	2.4297	2.4306	0.3304	0.3306
2d	2.4280	2.4297	0.3302	0.3304
4d	2.4247	2.4280	0.3298	0.3302
Long term 7d	2.4196	2.4255	0.3291	0.3299
14d	2.4079	2.4197	0.3275	0.3291
21d	2.3963	2.4138	0.3259	0.3283
28d	2.3847	2.4080	0.3243	0.3275
42d	2.3616	2.3964	0.3212	0.3259
50d	2.3486	2.3898	0.3194	0.3250
100d	2.2686	2.3491	0.3085	0.3195

PEC (sediment)

Method of calculation	See PEC surface water
Application rate	See PEC surface water

PEC$_{(sed)}$	See tables PEC Surface water

PEC (ground water) (OECD data point IIIA 9.6)

Method of calculation and type of study (e.g. Modelling, monitoring, lysimeter)	Modelling (FOCUS-PEARL 3.3.3 and FOCUS-PELMO 3.3.2) PECgw are estimated for cyflumetofen and the soil metabolites AB-1, B-1 and B-3 in three separate runs (parent-metabolite combinations) based on worst-case formation fractions of 1 for each metabolite.

Application rate	cGAP: 4 x 300 g a.s./ha; 2 blocks of 2 applications, interval of 7 days within block and of ~3 weeks between two blocks. Application dates: Early: 01 and 08 March + 01 and 08 April Late: 23 and 30 August + 23 and 30 September Crop interception: 60% Scenario: winter cereals/vines x relevant FOCUS locations (as surrogates for ornamentals) Cyflumetofen: DT50 8.77 d, Koc 131826 L/kg, 1/n = 1 AB-1: DT50 82.99 d, Koc 6200 L/kg, 1/n = 1, ffM =1 B-1: DT50 11.07 d, Koc 4.83 L/kg, 1/n = 1, ffM=1 B-3: DT50 9.24 d, Koc 13.60 L/kg, 1/n = 0.957, ffM=1

$PEC_{(gw)}$ cyflumetofen

FOCUS model	**PEARL 3.3.3**		**PELMO 3.3.2**	
FOCUS Scenario	**early application (µg/L)**	**late application (µg/L)**	**early application (µg/L)**	**late application (µg/L)**
Winter cereals				
Chateaudun	<0.001	<0.001	<0.001	<0.001
Hamburg	<0.001	<0.001	<0.001	<0.001
Kremsmuenster	<0.001	<0.001	<0.001	<0.001
Jokioinen	<0.001	<0.001	<0.001	<0.001
Okehampton	<0.001	<0.001	<0.001	<0.001
Piacenza	<0.001	<0.001	<0.001	<0.001
Porto	<0.001	<0.001	<0.001	<0.001
Sevilla	<0.001	<0.001	<0.001	<0.001
Thiva	<0.001	<0.001	<0.001	<0.001
Vines				
Chateaudun	<0.001	<0.001	<0.001	<0.001
Hamburg	<0.001	<0.001	<0.001	<0.001
Kremsmuenster	<0.001	<0.001	<0.001	<0.001
Piacenza	<0.001	<0.001	<0.001	<0.001
Porto	<0.001	<0.001	<0.001	<0.001
Sevilla	<0.001	<0.001	<0.001	<0.001

Thiva	<0.001	<0.001	<0.001	<0.001

$PEC_{(gw)}$ AB-1

FOCUS model	**PEARL 3.3.3**		**PELMO 3.3.2**	
FOCUS Scenario	**early application (µg/L)**	**late application (µg/L)**	**early application (µg/L)**	**late application (µg/L)**
Winter cereals				
Chateaudun	<0.001	<0.001	<0.001	<0.001
Hamburg	<0.001	<0.001	<0.001	<0.001
Kremsmuenster	<0.001	<0.001	<0.001	<0.001
Jokioinen	<0.001	<0.001	<0.001	<0.001
Okehampton	<0.001	<0.001	<0.001	<0.001
Piacenza	<0.001	<0.001	<0.001	<0.001
Porto	<0.001	<0.001	<0.001	<0.001
Sevilla	<0.001	<0.001	<0.001	<0.001
Thiva	<0.001	<0.001	<0.001	<0.001
Vines				
Chateaudun	<0.001	<0.001	<0.001	<0.001
Hamburg	<0.001	<0.001	<0.001	<0.001
Kremsmuenster	<0.001	<0.001	<0.001	<0.001
Piacenza	<0.001	<0.001	<0.001	<0.001
Porto	<0.001	<0.001	<0.001	<0.001
Sevilla	<0.001	<0.001	<0.001	<0.001
Thiva	<0.001	<0.001	<0.001	<0.001

$PEC_{(gw)}$ B-1

FOCUS model	**PEARL 3.3.3**		**PELMO 3.3.2**	
FOCUS Scenario	**early application (µg/L)**	**late application (µg/L)**	**early application (µg/L)**	**late application (µg/L)**
Winter cereals				
Chateaudun	0.153	2.466	0.090	1.498
Hamburg	1.495	8.432	0.761	10.108
Kremsmuenster	1.120	3.113	0.714	3.287
Jokioinen	1.685	10.536	1.314	**12.629**
Okehampton	1.354	5.101	0.879	5.823

Piacenza	0.580	4.482	0.605	6.307
Porto	0.074	1.588	0.048	1.995
Sevilla	0.002	1.051	0.001	0.357
Thiva	0.006	2.038	0.001	1.192

Vines

Chateaudun	1.294	2.429	1.311	2.273
Hamburg	1.309	7.925	0.989	9.911
Kremsmuenster	1.162	3.232	1.238	4.457
Piacenza	1.430	3.202	1.188	4.301
Porto	0.056	1.502	0.096	2.411
Sevilla	0.397	0.646	0.018	0.974
Thiva	0.218	0.895	0.075	1.666

$PEC_{(gw)}$ B-3

FOCUS model	**PEARL 3.3.3**		**PELMO 3.3.2**	
FOCUS Scenario	**early application (µg/L)**	**late application (µg/L)**	**early application (µg/L)**	**late application (µg/L)**
Winter cereals				
Chateaudun	0.023	0.479	0.013	0.300
Hamburg	0.261	2.524	0.148	3.540
Kremsmuenster	0.192	1.004	0.145	0.713
Jokioinen	0.247	1.828	0.227	2.876
Okehampton	0.353	1.875	0.226	2.442
Piacenza	0.155	1.828	0.207	3.080
Porto	0.002	0.380	0.004	0.477
Sevilla	<0.001	0.357	<0.001	0.077
Thiva	<0.001	1.042	<0.001	0.314
Vines				
Chateaudun	0.294	0.700	0.352	0.737
Hamburg	0.227	2.682	0.219	**3.881**
Kremsmuenster	0.189	1.033	0.247	1.238
Piacenza	0.488	1.594	0.442	2.251
Porto	0.002	0.429	0.009	0.800
Sevilla	0.083	0.225	0.002	0.270
Thiva	0.041	0.334	0.013	0.616

Fate and behaviour in air (OECD data points IIA 7.10 and IIIA 9.9)

Direct photolysis in air	Cyflumetofen: DT_{50} in air = 12.7 hours. (AOPWIN v 1.91 software; part of US-EPA's EPI suite vs 3.12 of 2000)
Quantum yield of direct phototransformation	Not required.
Photochemical oxidative degradation in air	Cyflumetofen: DT_{50} in air = 8.2 hours (0.34 day) based on a 12-h OH-radical concentration of 1.5 $*10^6$ molecules cm^{-3}. (AOPWIN v 1.91 software; part of US-EPA's EPI suite vs 3.12 of 2000)
Volatilization	Not required. Not expected to be significant based on low vapour pressure.

$PEC_{(air)}$

Method of calculation	Not required.

$PEC_{(a)}$

Maximum concentration	Not required.

Definition of the Residue (OECD data point IIA 7.11)

Relevant to the environment (for further risk assessment)	Soil: Cyflumetofen (sum of isomers), B-1 and B-3 Groundwater: Cyflumetofen (sum of isomers), B-1, B-3 and AB-1. Surface water: Cyflumetofen (sum of isomers), AB-11, AB-15 (aqueous photolysis metabolite), B-1, B-2, B-3 (via soil), A-2, Met1 and Met8. Sediment: Cyflumetofen (sum of isomers), AB-1, AB-11, B-1, B-2, B-3 (via soil). Air: parent cyflumetofen (sum of isomers) by default

Monitoring data, if available (OECD data point IIA 7.12)

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water indicate location and type of study)	Not available

Air (indicate location and type of study)	Not available

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data
Candidate for R53 (no data submitted on ready biodegradability)

Ecotoxicology

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

Species	Test substance	Time scale	End point [1] (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Bobwhite quail	cyflumetofen	Acute	LD_{50} **>2000** mg a.s./kg bw	
Mallard duck	cyflumetofen	Acute	LD_{50} >2250 mg a.s./kg bw	
Bobwhite quail	cyflumetofen	Short-term	LC_{50} **>1411** mg a.s./kg bw/d	>5000 mg a.s./kg feed
Mallard duck	cyflumetofen	Short-term	LC_{50} >2380 mg a.s./kg bw/d	>5620 mg a.s./kg feed
Bobwhite quail	cyflumetofen	Long-term	NOEC ≥ **84.4** mg a.s./kg bw/day (males)	≥ 1000 mg a.s./kg feed
Mammals ‡				
Rat	cyflumetofen	Acute	LD_{50} **>2000** mg a.s./kg	
Rat	Metabolite B-1	Acute	LD_{50} >2000 mg/kg bw	
Rat	cyflumetofen	Long-term	NOAEL **34.6** mg a.s./kg bw[2]	500 mg a.s./kg feed

[1] **Bold:** endpoints used for risk assessment

[2] Ecologically relevant NOEC from the two-generation study in rats, based on the lack of effects on population relevant parameters.

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

Crop and application rate

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Unprotected tree nursery, 4 x 240 g a.s./ha or as a worst case 2 x 480 g a.s./ha				
Tier 1 – uptake via diet (herbivorous birds)				
	Acute	38	>53	10
	Short-term	18	>81	10
	Long-term	9.3	≥ 9	5
Tier 1 – uptake via diet (insectivorous birds)				
	Acute	13	>154	10
	Short-term	7.2	>195	10
	Long-term	7.2	≥ 12	5

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1– uptake via drinking water (Birds)				
Puddles/leaf axils	Acute	10.8	>185	10
Surface water	Acute	0.0007	>3E+06	10
Tier 1 – secondary poisoning (Birds)				
Earthworm-eating bird	Long-term	0.013	≥ 63E+02	5
Fish-eating bird	Long-term	0.0033	≥ 26E+03	5
Tier 1– uptake via diet (Herbivorous mammals)				
	Acute	14	>143	10
	Long-term	3.4	10	5
Tier 1– uptake via drinking water (Mammals)				
Puddles/leaf axils	Acute	6.4	>313	10
Surface water	Acute	0.0004	>5E+06	10
Tier 1 – secondary poisoning (Mammals)				
Earthworm-eating mammals	Long-term	0.017	21E+02	5
Fish-eating mammals	Long-term	0.0021	17E+03	5

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

Laboratory tests				
Test substance	Organism	Time-scale (test type)	Endpoint	Toxicity [1] (mg a.s./L)
Fish				
cyflumetofen	*Oncorhynchys mykiss* (rainbow trout)	96h (flow-through)	Survival, LC_{50}	>0.63 (mm)
cyflumetofen	*Cyprinus carpio* (carp)	96h (flow-through)	Survival, LC_{50}	>0.54 (mm)
cyflumetofen	*Pimephales promelas* (fathead minnow)	8d (flow-through)	Survival/hatching, NOEC	≥ 0.145 (mm)
cyflumetofen	*Cyprinus carpio* (carp)	28d (flow-through)	Survival/growth, NOEC	0.072 (mm)
SCELTA 20SC	*Oncorhynchus mykiss* (rainbow trout)	96h (static)	Survival, LC_{50}	>0.89 (>4.45 mg form/L) (mm)
Aquatic invertebrate				
cyflumetofen	*Daphnia magna*	48h (flow-through)	Immobility, EC_{50}	>0.063 (mm)
cyflumetofen	*Daphnia magna*	21d (flow-	Mortality, NOEC	0.065 (mm)[2]

		through)		
SCELTA 20SC	*Daphnia magna*	48h (static)	Immobility, EC_{50}	>1.0 (>5.0 mg form/L) (nom) or >0.7 (>3.5 mg form./L) (mm)
AB-11	*Daphnia magna*	48h (static)	Immobility, EC_{50}	>0.5 (nom) or >0.476 (mm)
B-1	*Daphnia magna*	48h (static)	Immobility, EC_{50}	>180 (nom)
B-2	*Daphnia magna*	48h (static)	Immobility, EC_{50}	>0.039 (im) or >0.0062 (mm)
Sediment dwelling organisms				
cyflumetofen	*Chironomus riparius*	28d (static)	Emergence/development (water spiked) , NOEC	≥ 0.064 (im)
AB-1	*Chironomus riparius*	28d (static)	Emergence/development (sediment spiked) , NOEC	59.6 mg/kg (im)
Algae				
cyflumetofen	*Selenastrum capricornutum*	72h (static)	Biomass/growth rate, EC_{50}	>0.30 (im) or >0.0396 (mm)
SCELTA 20SC	*Selenastrum capricornutum*	72h (static)	Biomass/growth rate, EC_{50}	>1.0 (>5.0 mg form/L) (nom) or >0.279 (>1.4 mg form./L) (mm)
AB-11	*Pseudokirchneriella subcapitata*	72h (static)	Biomass/growth rate, EC_{50}	>0.5 (nom) or >0.157 (mm)
B-1	*Pseudokirchneriella subcapitata*	96h (static)	Biomass/growth rate, EC_{50}	>100 (nom)
B-2	*Pseudokirchneriella subcapitata*	72h (static)	Biomass/growth rate, EC_{50}	>0.073 (im) or >0.0101 (mm)
Microcosm or mesocosm tests:				
Not required				

[1] nominal: (nom), initially measured: (im) or mean measured concentrations: (mm)

[2] This study is less reliable due to high mortality in the control. However, the experts in the Pesticides Peer Review Expert Meeting considered that a new chronic study with daphnids for cyflometofen is not required based on the following arguments: in the study, no effects were seen on reproduction (thus: NOECreproduction ≥151 µg a.s./L); the chronic NOEC for daphnids of 65 µg a.s./L is based on mortality which is a worst case approach; the NOEC of 65 µg a.s./L is comparable to the acute NOEC for daphnids and to the chronic NOEC for *Chironomus*; for *Chironomus*, there is still a margin of safety (TERlt 24 based on FOCUS Step 1).

Toxicity/exposure ratios for aquatic organisms (OECD data point IIIA 10.2)

Unprotected tree nursery, 4x240 g a.s./ha

Active substance

Scenario	PECsw (µg L)	fish acute	fish prolonged	Daphnia acute	Daphnia prolonged	Algae	Sed. dweller prolonged
		C.carpio	*C.carpio*	*Daphnia magna*	*Daphnia magna*	*S. subspicatus*	*C. riparius*
		LC_{50}	NOEC	EC_{50}	NOEC	EC_{50}	NOEC
		>540 µg/L	72 µg/L	>63 µg/L[1] >700 µg/L[2]	65 µg/L	>39.6 µg/L	≥ 64 µg/L
FOCUS Step 1							
	2.6598	>203	27	**>24**	24	>15	≥ 24
FOCUS Step 2							
	2.21			**>29**[1] >263[2]			
Annex VI trigger		100	10	100	10	10	10

[1] Based on test with a.s.

[2] Based on test with formulated product (use of this endpoint supported by a second study with the a.s., see DAR)

Metabolites

	Metabolite AB-11		
Scenario	**PECsw (µg L)**	**Daphnia acute**	**Algae**
		Daphnia magna	***S. subspicatus***
		EC_{50}	EC_{50}
		>476 µg/L	>157 µg/L
FOCUS Step 1			
	1.166	>408	>135
Annex VI trigger		100	10

	Metabolite B-1		
Scenario	**PECsw (µg L)**	**Daphnia acute**	**Algae**
		Daphnia magna	***S. subspicatus***
		EC_{50}	EC_{50}
		>180000 µg/L	>100000 µg/L
FOCUS Step 1			
	88.2772	>2039	>1133
Annex VI trigger		100	10

	Metabolite B-2		
Scenario	**PECsw (µg L)**	**Daphnia acute**	**Algae**
		Daphnia magna	***S. subspicatus***
		EC_{50}	E_bC_{50}
		>6.2 µg/L	>10.1 µg/L
FOCUS Step 1			
	2.001	**>3.1**	**>5.0**
FOCUS Step 2			
	0.500	**>12**	>20
FOCUS Step 4 D3 / ditch, August-September, single application[1]	0.354	>**18**	
Annex VI trigger		100	10

[1] scenario with highest PECsw

	Metabolite AB-1	
Scenario	**PECsed (µg/kg)**	**Sed. dweller prolonged**
		C. riparius
		NOEC
		59600 µg/kg
FOCUS Step 1		
	67.23	887
Annex VI trigger		10

Bioconcentration			
	Active substance	AB-15	A-2
$logP_{O/W}$	4.3	5.05 / 5.87[1]	3.47 / 3.14[1]
Bioconcentration factor (BCF)	170 (for total radioactivity) < 100 (for a.s., as cyflumetofen was not detected in any fish sample)	170[2]	178[3]
Annex VI Trigger for the bioconcentration factor	100		
Clearance time (days) (CT_{50})	2.2-2.5 days (total radioactivity; whole fish)		

Bioconcentration			
(CT_{90})	7.4-8.3 days (total radioactivity; whole fish)		
Level and nature of residues (%) in organisms after the 29 day depuration phase	8		

[1] estimated with EPA Epi Suite software / estimated with ACD-Labs-LogP
[2] estimated value (from study with parent)
[3] calculated value according to logBCF=0.85*logPow-0.7

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)
cyflumetofen	not available	>102 µg a.s./bee
SCELTA 20SC	>116 µg a.s./bee	> 100 µg a.s./bee
Field or semi-field tests		
Not required		

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

Protected ornamental crops, 4x300 g a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
cyflumetofen	Contact	<2.9	50
cyflumetofen	Oral	not available	50
Preparation	Contact	<3.0	50
Preparation	Oral	<2.6	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} kg a.s./ha)
Typhlodromus pyri	SCELTA 20SC	Mortality	>1.4 kg a.s./ha
Aphidius rhopalosiphi	SCELTA 20SC	Mortality	>1.4 kg a.s./ha

Hazard quotients for non-target arthropods (Annex IIIA, point 10.5)

Laboratory tests								
Test substance	Use pattern	Species	Endpoint (LR_{50}, g a.s./ha)(A)	Exposure (g a.s./ha)		HQ		Trigger
				in-field	off-field	in-field	off-field	
SCELTA 20SC	Protected ornamental crops, 4x300 g a.s./ha	*T. pyri*	>1400	1020	-	<0.7	-	2
		A. rhopalosiphi	>1400	1020	-	<0.7	-	2
	Unprotected tree nursery, 4x240 g a.s./ha	*T. pyri*	>1400	816	1.9	<0.6	<0.01	2
		A. rhopalosiphi	>1400	816	1.9	<0.6	<0.01	2

(A) From laboratory exposure on glass plates

Field or semi-field tests
Not required

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4, 8.5 and 8.10. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point
Earthworms			
	cyflumetofen	Acute 14 days	LC_{50} >1000 mg a.s./kg soil dw
	SCELTA 20SC	Acute	LC_{50} >1050 mg a.s./kg soil dw
	cyflumetofen	Chronic	NOEC ≥ 1000 mg a.s./kg soil dw
	AB-1	Acute	LC_{50} >1000 mg/kg soil dw
	B-1	Acute	LC_{50} >1000 mg/kg soil dw
Soil micro-organisms			
Nitrogen mineralisation	cyflumetofen	28 days	NOEC ≥ 1.36 mg a.s./kg soil dw (1000 g a.s./ha)
Carbon mineralisation	cyflumetofen	28 days	NOEC ≥1.36 mg a.s./kg soil dw (1000 g a.s./ha)
Field studies			
Not required			

Toxicity/exposure ratios for soil organisms
Protected ornamentals, 4x300 g a.s./ha

Test organism	Test substance	Time-scale	Endpoint (LC_{50} or NOEC, mg a.s./kg soil)	Soil PEC [2] (mg a.s./kg soil)	TER	Trigger
Earthworms						
	cyflumetofen	Acute	>500 [1]	0.319	>1567	10
	cyflumetofen	Chronic	≥ 500 [1]	0.319	≥ 1567	5
	AB-1	Acute	>500 [1]	0.048	>10417	10
	B-1	Acute	>500 [1]	0.177	>2825	10

[1] Corrected value as logPow of the test substance is >2
[2] initial PEC soil was used

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

Preliminary screening data

Tested pre- and post-emergence on common chickweed (*Stellaria media*), indian jointvetch (*Aeschynomene indica*), southern crabgrass (*Digitaria ciliaris*) and early watergrass (*Echinochloa oryzicola*). Tested via the water on *Monochoria vaginalis*, small flower umbrella sedge (*Cyperus difformis*), early watergrass (*Echinochloa oryzicola*) and Japanese bulrush (*Scirpus juncoides*). Results: cyflumetofen is not herbicidal at a dose of 2 kg a.s./ha.

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

Test type/organism	end point
Activated sludge	EC_{50} >100 mg a.s./L

Ecotoxicologically relevant compounds

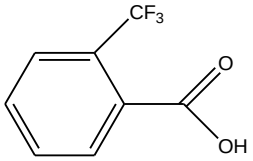
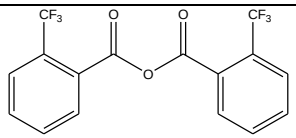
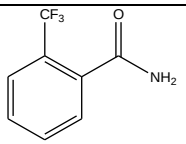
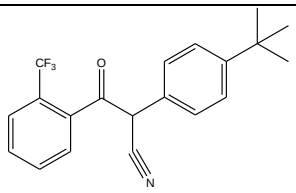
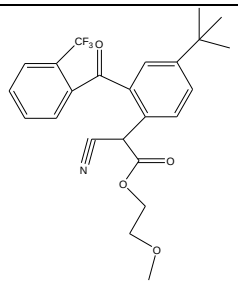
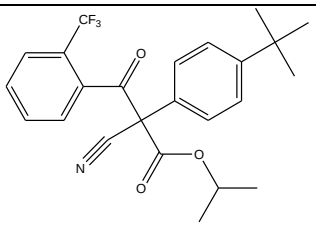
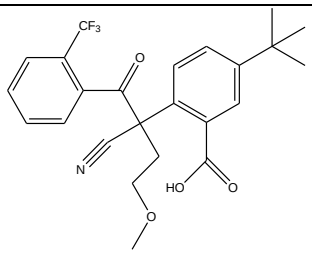
Compartment	
soil	Cyflumetofen
water	Cyflumetofen, B-2
sediment	Cyflumetofen
groundwater	Cyflumetofen

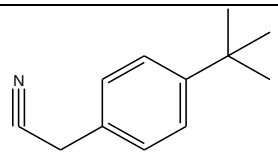
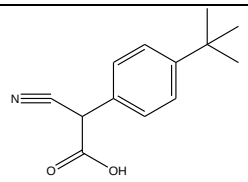
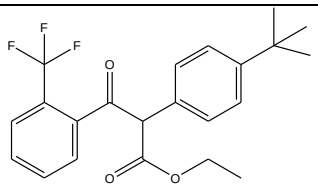
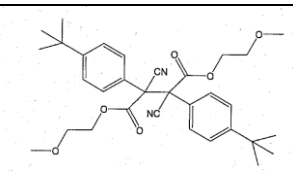
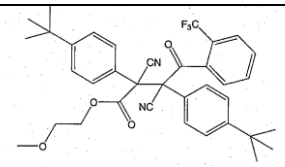
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

RMS/peer review proposal

Active substance	No classification is proposed.

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name*	Structural formula*
B-1	α,α,α-trifluoro-o-toluic acid	
B-2	α,α,α-trifluoro-o-toluic anhydride	
B-3	2-(trifluoromethyl) benzamide	
AB-1	*RS*)-2-(4-*tert*-butylphenyl)-3-oxo-3-(*α,α,α*-trifluoro-*o*-tolyl)proprionontrile	
AB-7	2-methoxyethyl *(RS)* – [4-*tert*-butyl-2-(α,α,α-trifluoro-*o*-toluoyl)phenyl] cyanoacetate	
AB-11	isopropyl (*RS*)-2-(4-*tert*-butylphenyl)-2-cyano-3-oxo-3-(*α,α,α*-trifluoro-*o*-tolyl)proprionate	
AB-15	5-tert-butyl-2-(2-cyano-1-(2-(trifluoromethyl)phenyl)-4-methoxy-1-oxobutan-2-yl)benzoic acid	

A-2	(4-tert-butylphenyl) acetonitrile	
A-18	4-*tert*-butylphenyl) cyanoacetic acid	
Metabolite 1 (Met-1)	ethyl 2-(4-*tert*-butylphenyl)-3-oxo-3-[2-(trifluoromethyl) phenyl]propanoate	
AU16		
AU17 (BU17)		
BU14	Unidentified	Unidentified
Metabolite 4 (Met-4)	Unidentified	Unidentified
Metabolite 5 (Met-5)	Unidentified	Unidentified
Metabolite 8 (Met-8)	Unidentified	Unidentified
U-1 and U-2	Conjugates of metabolite B-1	None

* ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

1/n	slope of Freundlich isotherm
λ	wavelength
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 Abstracts Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DFOP	double first order in parallel
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
ELINCS	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
FOMC	first order multi-compartment
g	gram
GAP	good agricultural practice
GC	gas chromatography
GC-FID	gas chromatography, flame ionisation detection
GC-MS	gas chromatography, mass spectrometry detection
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
HPLC-UV	high pressure liquid chromatography – ultraviolet
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography - mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC-UV	liquid chromatography - ultraviolet
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
mN	milli-newton

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
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content
Pa	pascal
PAI	pure active ingredient
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
PIEC	predicted initial environmental concentration
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
REACH	Registration, Evaluation, Authorisation of CHemicals
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
TGAI	technical grade of active ingredient
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake

TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UK POEM	United Kingdom Predictive Operator Exposure Model
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