CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion regarding the peer review of the pesticide risk assessment of the active substance zeta-cypermethrin

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SUMMARY

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

Belgium being the designated rapporteur Member State submitted the DAR on zeta-cypermethrin in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 10 July 2006. The peer review was initiated on 6 October 2006 by dispatching the DAR for consultation of the Member States and the applicant FMC Chemical sprl. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by EFSA to identify the remaining issues which were agreed during a written procedure in October 2007. The identified issues as well as further information made available by the applicant upon request were evaluated in a series of scientific meetings with Member State experts in May-June 2008.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in August 2008 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide as proposed by the notifier. Full details of the GAP can be found in the attached list of endpoints.

The representative formulated product for the evaluation was “Fury 10 EW (NP Free)”, an emulsion, oil in water (EW) containing 100 g/L (96.9 g/kg) zeta-cypermethrin.

[1] OJ No L 224, 21.08.2002, p. 25, as amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

The technical specification for the active substance was based on pilot scale production and was only partially accepted by the PRAPeR meeting of experts (May 2008).
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. Adequate methods are available to monitor all compounds given in the respective residue definitions in food/feed of plant and animal origin, environmental matrices and body fluids and tissues.

As for mammalian toxicology, the dossier submitted contained studies on both zeta-cypermethrin and cypermethrin. Considering the ratio of the most potent isomers between zeta-cypermethrin and cypermethrin and focusing on neurotoxicity (difference using the NOAELs and LOAELs of rat studies), a factor of 2 could be established showing that zeta-cypermethrin is more toxic than cypermethrin. When orally administered, zeta-cypermethrin is toxic (proposed to be classified T, R25 – "toxic if swallowed"). It is harmful for inhalation (Xn, R20). No toxic effects were observed after dermal exposure. It is not irritating to eyes or skin but is a skin sensitizer in a Buehler test (Xi, R43 – "irritant; may cause sensitisation by skin contact"). Neurotoxicity is the target effect of zeta-cypermethrin for short term exposures. The relevant NOAEL of 7.5 mg/kg bw/day is from the 2-year feeding study in dogs. The classification as R48/22 ("danger of serious damage to health by prolonged exposure, if swallowed") was proposed based on mortality in several studies. Overall, it was concluded that zeta-cypermethrin is neither genotoxic nor carcinogenic under experimental conditions (carcinogenicity was tested with cypermethrin). The relevant long term toxicity and carcinogenicity NOAEL of 7.5 mg/kg bw/day is from the 2-year rat study. The relevant parental and offspring NOAEL in multigeneration studies is 5.9 mg/kg bw/day, while the reproductive NOAEL is 22 mg/kg bw/day. Zeta-cypermethrin was negative for developmental toxicity when tested in rats. The relevant maternal NOAEL in rat and rabbit are 12.5 and ≥120 mg/kg bw/day, respectively; the relevant developmental NOAEL are 35 mg/kg bw/day in rat, and ≥120 mg/kg bw/day in rabbit. Zeta-cypermethrin is a neurotoxic agent (acute and subchronic NOAELs 10 mg/kg bw and 5 mg/kg bw/day, respectively). The acceptable daily intake (ADI) is 0.04 mg/kg bw/day, based on the overall cypermethrin NOAEL for dogs of 7.5 mg/kg bw/day and a 100-fold safety factor with an additional factor of 2 for the higher toxicity of zeta-cypermethrin vs. cypermethrin. The acute reference dose (ARfD) is 0.125 mg/kg bw based on the developmental toxicity study in rats supported by the acute neurotoxicity with zeta-cypermethrin, applying a safety factor (SF) of 100. An acceptable operator exposure level (AOEL) of 0.02 mg/kg bw/day was based on the overall cypermethrin NOAEL for dogs of 7.5 mg/kg bw/day using a 100-fold safety factor with an additional factor of 2 for the higher toxicity of zeta-cypermethrin and correcting for 50% oral absorption. The estimated operator, worker and bystander exposure is below the AOEL even without the use of personal protective equipment (PPE).
In order to support the uses of zeta-cypermethrin the applicant submitted plant metabolism studies performed with cypermethrin. Several groups of plants were investigated; root crops (sugar beet),

cereals (maize), pulses/oilseeds (cotton), fruit crops (apples) and leafy crops (lettuce). The major degradation pathway of cypermethrin starts with the cleavage of the parent molecule to yield *cis/trans* DCVA[2] and the *m*PBAldehyde[3], this latter metabolite being further oxidised or reduced to the corresponding *m*PBAcid[4] or *m*PBAlcohol[5] followed by conjugations. In most of the plant matrices investigated, unchanged cypermethrin was the predominant residue accounting for more than *c.a.* 50% of the TRR. The meeting discussed whether the plant metabolism studies performed with cypermethrin were relevant for zeta-cypermethrin and if a preferential metabolism may be suspected for some isomers with a special impact on toxicology. A bridging study on maize detailing the respective metabolism of both cypermethrin and zeta-cypermethrin was provided by the applicant, however, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new studies could not be considered in the peer review. However, and taking into account the no residue situation resulting from the intended uses on cereals, maize and peas, the meeting was of the opinion that the possible isomeric conversion from less to more toxic isomers would not be significant and concluded that a residue definition can be proposed based on the metabolism studies performed with cypermethrin. Finally, it was concluded that a global residue definition has to be proposed in order to take into account the various mixtures of cypermethrin isomers available on the market. Thus, for plants, the residue for monitoring and risk assessment was defined as "cypermethrin, including other mixtures of constituent isomers (sum of isomers)".

Numerous supervised residue trials performed with zeta-cypermethrin were submitted to propose MRLs. Nevertheless, some of them were rejected since growth stages at application were not in compliance with the critical GAP and/or analytical methods were not sufficiently validated. Finally, MRLs were defined for wheat, triticale and pea without pods and, awaiting the evaluation of additional data provided by the applicant that were not considered during the meeting with regard to Commission Regulation (EC) No 1095/2007, provisional MRLs were proposed for maize, barley, oat, pea with pods and pulses. No degradation of residues was observed for zeta-cypermethrin in different plant- and animal matrices when stored under frozen conditions for up to 18 months. Some instability was observed at some time points for the metabolites *m*PBAcid and *cis*-DCVA in some animal matrices, but globally, the results were considered acceptable. No processing studies were provided since no significant residues were observed in any commodities supporting the representative uses. However, the EFSA noted that the cypermethrin hydrolysis breakdown product, *m*PBAldehyde, was found in a tomato processing study, and this compound is suspected of endocrine activity. This concern was considered to be not relevant for the intended uses supported in the DAR but the meeting noted that this point has to be re-considered if additional uses are envisaged.

[2] *cis*/*trans* DCVA: *cis*/*trans* (*RS*)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid
[3] *m*PBAldehyde: 3-phenoxybenzaldehyde
[4] *m*PBAcid: 3-phenoxybenzoic acid
[5] *m*PBAcohol (3-phenoxyphenyl)methanol

Lactating cow and laying hen metabolism studies performed with cypermethrin were evaluated. The major route of degradation consisted of the hydrolysis of ester linkage to generate the *cis* and *trans* DCVA moiety and the *m*PBAldehyde that undergoes further oxidation and/or reduction to the corresponding acid (*m*PBAcid) or alcohol (*m*PBAlcohol) and their hydroxy products. The metabolism of the cyclopropyl moiety was considered as insufficiently investigated in the ruminant metabolism study as in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the additional data from literature presented in the addendum of May 2008, could not be considered in the peer review. This point remains open and has to be reconsidered. Nevertheless, and taking into account the complete metabolic pathway in poultry, and the data from the rat metabolism study indicating a similar pathway, the meeting of experts concluded that there was enough evidence to propose the residue for monitoring and risk assessment for animal products as "cypermethrin, including other mixtures of constituent isomers (sum of isomers)". Considering the potential livestock exposure to zeta-cypermethrin residues through consumption of treated feed items (maize, cereals, pea and pulses), feeding studies indicate that no measurable residues may be present above the LOQ in the different animal-products and the MRLs for animal commodities were proposed at LOQ values.

Considering the representative uses and the toxicological endpoints set for zeta-cypermethrin, no chronic or acute concerns were observed, the theoretical maximum daily intake (TMDI) being less than 2% of the ADI and the maximum national estimated short term intake (NESTI) less than 1% of ARfD. In addition, the meeting concluded on the need for a global risk assessment taking into account the other sources of exposure resulting from the uses of all other cyprermethrin isomer mixtures available on the market and their respective toxicological reference values.

In soil under aerobic conditions zeta-cypermethrin exhibits low to medium persistence forming the soil metabolites DCVA[6] (accounting for up to 24% of applied radioactivity (AR)) which exhibits low persistence and *m*PBAcid (accounting for up to 8.4 % AR in the available guideline study or 29.5% AR in a study with limited sampling intervals) which also exhibits low persistence. Mineralisation of both the cyclopropyl- and benzyl rings to carbon dioxide accounted for 25-27% AR after 91 days. The formation of unextractable residues was a significant sink, accounting for 12-26 % AR after 91 days. Isomers of cypermethrin are immobile in soil, DCVA exhibits very high mobility in soil and *m*PBAcid exhibits high to medium mobility. There was no indication that the soil adsorption of isomers of cypermethrin was pH dependent. There was no clear evidence that the soil adsorption of DCVA or *m*PBAcid was pH dependant. A data gap was identified for a satisfactory aerobic soil laboratory route of degradation study dosed with zeta-cypermethrin, which is necessary to ensure that

[6] information on isomer ratio not reported in the DAR / addendum to the DAR

all potential soil metabolites that might reach levels that trigger a groundwater exposure assessment have been identified. The available route of degradation study that used cypermethrin as the test substance was considered insufficient to address the presence of zeta-cypermethrin metabolites at the 5% AR trigger for leaching assessment level as prescribed in agreed EU guidance.

In dark natural sediment water systems zeta-cypermethrin partitioned rapidly from water to sediment where it degraded exhibiting low persistence to the metabolites *m*PBAcid and DCVA, which were present predominantly in the water phase where they exhibited medium to high persistence. The terminal metabolite, CO_2, accounted for a maximum of 22 % AR (cyclopropyl label) and 58% AR (phenyl label) at 99 days (study end). Unextracted sediment residues were a significant sink representing 16-27 % AR at study end. The necessary surface water and sediment exposure assessments were appropriately carried out using the agreed FOCUS scenarios approach for component isomers of the active substance at step 1. Step 3 and 4 calculations are also available (but only for surface water and not sediment), with spray drift mitigation being applied at step 4. However, these calculations did not adhere to the FOCUS surface water guidance, so a data gap is identified for more appropriate calculations, therefore only relatively crude estimates of surface water exposure are available for the aquatic risk assessment. For the metabolites *m*PBAcid and DCVA appropriate FOCUS step 1 exposure assessments were agreed by the peer review. These values are the basis for the risk assessment discussed in this conclusion.
The potential for groundwater exposure from the applied for intended uses by component isomers of the active substance, *m*PBAcid and *trans*-DCVA above the parametric drinking water limit of 0.1 µg/L, was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios. However the groundwater exposure assessment for metabolites cannot be finalised until the data gap identified for a satisfactory soil route of degradation study is filled.

The risk to mammals and the acute and short-term risk to birds were assessed as low but a potential high long-term risk to insectivorous birds cannot be excluded for all representative uses evaluated. A data gap was identified for further refinement of the risk assessment for insectivorous birds. Zeta-cypermethrin is very toxic to fish and aquatic invertebrates. The aquatic risk assessment was based on preliminary FOCUS step 4 PECsw values which included a 20m no-spray buffer zone. The acute TERs for fish exceeded the Annex VI trigger of 100 in all scenarios for the use in cereals and in all scenarios except R3 and R4 for the use in peas. However no full scenario resulted in a TER of >100 for the use in maize and the long-term TERs were significantly below the Annex VI trigger of 10 in all scenarios even with a no-spray buffer zone of 20m. A data gap was identified for further refinement of the aquatic risk assessment. Two mesocosm studies with zeta-cypermethrin were submitted by the applicant, however, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new studies could not be considered in the peer review. The risk to aquatic organisms from the metabolites *cis*-DCVA, *trans*-DCVA and 3-phenoxybenzoic acid

(*m*PBAcid) was assessed as low. Zeta-cypermethrin is very toxic to bees. A potential high risk was indicated in the first-tier risk assessment. The mortality of adult bees was increased in higher tier tests during the first 1-4 days after treatment. No impact on bee brood development was observed but it was noted that no reserves were accumulated in the bee hives. This observation may be explained by the repellent effect of zeta-cypermethrin. The experts considered the risk to bees as low for the use in cereals which are considered as not attractive for bees. Risk mitigation measures such as no application during flowering were proposed for the use in peas. The higher tier studies did not cover the application rate in maize and a data gap was identified to address the risk to bees further. A high in-field risk to non-target arthropods was indicated from the standard laboratory and the extended laboratory tests. The applied doses in the field tests were too low for the representative uses and a data gap was identified to address further the in-field and the off-field risk to non-target arthropods for all representative uses. Although formally not triggered, the experts considered it necessary to address the risk to soil dwelling mites and collembola because of the potential high risk to arthropods. It was suggested that investigation of soil dwelling mites and collembola should be included in a field study with non-target arthropods. The study on effects on respiration of activated sewage sludge was assessed as not valid. A new study was submitted by the applicant but in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new studies could not be considered in the peer review.
The risk to earthworms, soil non-target micro-organisms and non-target plants was assessed as low.

Key words zeta-cypermethrin, cypermethrin, peer review, risk assessment, pesticide, insecticide

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, as amended by Commission Regulation (EC) No 1095/2007 regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Zeta-cypermethrin is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 designating Belgium as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Belgium submitted the report of its initial evaluation of the dossier on zeta-cypermethrin, hereafter referred to as the draft assessment report, received by EFSA on 10 July 2006. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1490/2002 on 6 October 2006 to the Member States and the main applicant FMC Chemical sprl. as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, EFSA identified and agreed with Member States during a written procedure in October 2007 on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in experts' meetings in May-June 2008. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in August 2008 leading to the conclusions as laid down in this report.

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

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

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

- the comments received;
- the resulting reporting table (revision 1-1 of 19 December 2007)

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

- the reports of the scientific expert consultation;
- the evaluation table (revision 2-1 of 19 September 2008).

Given the importance of the draft assessment report including its addendum (compiled version of September 2008 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

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

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Zeta-cypermethrin is the ISO common name for mixture of the stereoisomers (*S*)-α-cyano-3-phenoxybenzyl (1*RS*,3*RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate where the ratio of the (*S*);(1*RS*,3*RS*) isomeric pair to the (*S*);(1*RS*,3*SR*) isomeric pair lies in the ratio range 45-55 to 55-45, respectively (IUPAC).
Zeta-cypermethrin belongs to the class of pyrethroid ester insecticides. It acts by contact and by ingestion. Zeta-cypermethrin acts on the central and peripheral nervous system of target insects, disturbs the function of neurons by interaction with the sodium channel by modulating the opening and the closing of the channels, leading to synaptic discharge, repetitive discharge, depolarisation and ultimately death. Zeta-cypermethrin is used in agriculture against a broad range of foliar insects.

The representative formulated product for the evaluation was "Fury 10 EW (NP Free)", an emulsion, oil in water (EW) containing 100 g/L (96.9 g/kg) zeta-cypermethrin, registered under different trade names in Europe.

The representative uses evaluated comprise: foliar spraying to control European cornborer (*Ostrinia nubilalis*) and pink stalk borer (*Sesamia nonagrioides*) in maize, in all EU countries, at single application, at maximum application rate per treatment of 37.5 g a.s./ha;

- foliar spraying to control leaf, flag and ear aphids in cereals, up to growth stage of BBCH 69, in all EU countries, at a maximum of 2 treatments, at maximum application rate per treatment of 15 g a.s./ha, interval between applications of 2-4 weeks, and
- foliar spraying to control pea aphids, pea moth (*Cydia nigricana*) pea weevil (*Bruchus pisorum*) and *Thrips ssp* in peas, in all EU countries, at a maximum of 2 treatments, at maximum application rate per treatment of 15 g a.s./ha, interval between applications of 2-4 weeks.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of zeta-cypermethrin is 850 g/kg (pilot scale production). *Cis/trans*-ratio should be in range of 55/45 – 45/55. There is no FAO specification available.

The revised technical specification for the active substance based on pilot scale production was only partially accepted by the PRAPeR 46 meeting of experts (May 2008) and a data gap was proposed for the applicant to provide a new specification removing the impurities not detected in the batch analysis.

Toluene and tar residues were considered relevant impurities by the PRAPeR 49 meeting of experts (June 2008), but the levels proposed in the current specification are of no toxicological concern.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of zeta-cypermethrin or the respective formulation, however the following data gaps were identified by the PRAPeR 46 meeting of experts:

- further information or indications available to ensure that none of mentioned unknown compounds are present at a concentration higher than 1 g/kg.
- a 5-batch analysis for the actual industrial scale production
- an alternative method as replacement for the non-specific method for the determination of impurities (APG 428A) and data on the specificity of the methods used for the determination of significant impurities
- shelf-life study of the NPE-free formulation
- to address the stability of dilute emulsions and preparations which are emulsions
- to address the resistance of the packaging material to “Fury 10 EW (NP Free)”

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

Adequate analytical methods are available for the determination of zeta-cypermethrin in the technical material and in the representative formulation (HPLC-UV) as well as for the determination of the respective impurities in the technical material (HPLC-UV, GC-FID, GPC-Light Scattering). The total cypermethrin content can be determined by HPLC-UV and the ratio of enantiomers and zeta-cypermethrin content by HPLC-UV on a chiral column. The existing CIPAC methods (332/TC/M/3 and 332/EC/M/3.2) can be used for the determination of the total cypermethrin content in the technical material and formulation.

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

The residue definition for monitoring purposes for all compartments was set to sum of component isomers of cypermethrin.

Adequate methods are available to monitor cypermethrin residues in food/feed of plant- and animal origin. Residues of cypermethrin in food of plant origin can be monitored by the multi method DFG S19 with GC-ECD with LOQ of 0.01 mg/kg (tomatoes, oranges, wheat) and also by GC-MSD with LOQ of 0.02 mg/kg (maize). Residues of cypermethrin in food/feed of animal origin can be monitored by the multi method DFG S19 with GC-ECD with LOQ of 0.01 mg/kg in milk and with LOQ of 0.05 mg/kg in egg, muscle and fat, respectively.
GC-ECD methods are available to monitor residues of cypermethrin in soil with LOQ of 0.005 mg/kg, in water with LOQ of 0.05 µg/L (drinking and ground water) and LOQ = 0.001 µg/L (surface water) and in air with LOQ = 1.7 µg/m³.
Cypermethrin residues in body fluids and tissues can be monitored by GC-ECD, with LOQ of 0.05 mg/kg (liver, kidney and blood).

2. Mammalian toxicology

Zeta-cypermethrin was discussed in the PRAPeR 49 meeting of experts in June 2008.
The dossier submitted contained study on both zeta-cypermethrin and cypermethrin. Thus during the meeting of experts the relative toxicity of zeta-cypermethrin and cypermethrin as well as the "bridging" concept were discussed.
The RMS provided in the addendum the differences in toxicity between cypermethrin and zeta-cypermethrin. Focusing on neurotoxicity a factor of 2 (difference using the NOAELs and LOAELs of rat studies) could be established showing that zeta-cypermethrin is more toxic than cypermethrin.

Furthermore, zeta-cypermethrin contains 44% of the most potent isomers compared to cypermethrin which contains these isomers at 22%. This represents a factor of 2.
The meeting agreed on the bridging approach with a factor of 2 as proposed in the DAR and in the addendum.
The dossier comprised studies performed with both zeta-cypermethrin and cypermethrin (as it is specified in the list of endpoints).

The compliance of batches tested in mammalian toxicology to the proposed specification was also discussed. Only the pilot plant is supported by the section on identity, physical and chemical properties.
Higher levels of several impurities were proposed in the current specification compared to the batches tested for mammalian toxicity. Clarification regarding those impurities was provided by the applicant and/or the RMS.
The PRAPeR meeting of experts agreed that impurity 6 and toluene are relevant but the levels proposed in the current specification are of no toxicological concern.
All other impurities were at comparable or higher levels in the batches tested for mammalian toxicity than in the current specification.

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

Overall, oral absorption of zeta-cypermethrin is approximately 50% based on urinary excretion within 24 hours; faecal excretion represented a mean of 22% of the dose. It is widely distributed, with the majority of residues in fat and skin after 8 days. In humans, similarly to other mammals, ester cleavage and elimination of the cyclopropane carboxylic acid and phenoxybenzyl moieties are the major route of metabolism. Marked differences in the urinary metabolite profile were seen after dermal exposure.

The PRAPeR meeting of experts concluded that “danger of cumulative effects” (R33) was not applicable to zeta-cypermethrin. The RMS noted that it was usually applied for heavy metals, etc.

2.2. ACUTE TOXICITY

When zeta-cypermethrin is orally administered undiluted, it is toxic and therefore should be classified T, R25 (“toxic if swallowed”) (LD50=86 mg/kg bw). Cypermethrin should be classified as “harmful for inhalation” (Xn, R20) and this would apply also to zeta cypermethrin (LC50=1.26 mg/L).
No toxic effects were observed after dermal exposure to zeta-cypermethrin.
Zeta-cypermethrin was not irritating to eyes or skin but is a skin sensitizer in a Buehler test (Xi, R43 – “irritant; may cause sensitisation by skin contact”).

2.3. SHORT TERM TOXICITY

Oral administration of cypermethrin causes neurotoxic effects in rats and dogs: ataxia, splayed hindlimbs, unthriftiness, decreased activity, dehydration, abdomino-genital staining were observed in rats at doses near the MTD (70 mg/kg bw/day for zeta-cypermethrin). Dogs exhibited varying degrees of tremor activity and irregular gait, some animals were ataxic.

Dogs appeared to be more sensitive to neurotoxic effects of cypermethrin. When the 90-day dietary studies of rat and dog are compared, no signs of neurotoxicity were evident in rats at doses of 1500 ppm (150 mg/kg bw/d), while in dogs, neurotoxicity was evident at doses of 800 ppm (30 mg/kg bw/day) (dietary 90-day dog study). The relevant NOAEL of 7.5 mg/kg bw/day is derived from the 2-year feeding study in dogs (with cypermethrin).

During the meeting the rationale for proposing R48/22 ("danger of serious damage to health by prolonged exposure, if swallowed") was discussed: in several studies some mortalities were observed besides neurotoxic effects. In particular:

- 28-day rat study: neurotoxicity at 69 mg/kg bw/day and mortality at 102 mg/kg bw/day;
- 90-day rat study: mortality and neurotoxicity at 68 mg/kg bw/day;
- 2-generation rat study: mortality and clinical signs of neurotoxicity at 43 mg/kg bw/day.

2.4. GENOTOXICITY

Zeta-cypermethrin was tested in 4 *in vitro* and 1 *in vivo* study.

A slight increased mutation rate was seen in the Ames test in tester strain *TA 100* at 3333 and 10000 µg/plate with a maximum increase of 2-fold in mean revertants/plate at 10000 µg/plate (without metabolic activation). Chromosomal aberrations were not observed, zeta-cypermethrin did not cause a significant increase in the UDS DNA synthesis and did not induce *in vivo* chromosomal aberrations. Overall, it can be concluded that zeta-cypermethrin is not genotoxic.

2.5. LONG TERM TOXICITY

Only cypermethrin was tested in long term toxicity and carcinogenicity studies in rats and mice (2-year and 18- month studies, respectively).

The relevant NOAEL of 7.5 mg/kg bw/day is derived from the rat study, based on clinical signs of neurotoxicity as well as a decreased bodyweight gain accompanied by lower food consumption and less efficient food utilization.

Cypermethrin is not carcinogenic under experimental conditions.

2.6. REPRODUCTIVE TOXICITY

Zeta-cypermethrin was investigated in a 2-generation study in rats, at doses ranging from 7.5 to 750 ppm. The relevant parental and offspring NOAEL is 5.9 mg/kg bw/day (reduced pup bodyweights in

both generations during the lactation periods and pup mortality were reported at maternal toxic doses), while the reproductive NOAEL is 22 mg/kg bw/day.
Zeta-cypermethrin was tested in rats for developmental toxicity. While clear maternal toxicity occurred at 35 mg/kg bw/day, no foetotoxicity or developmental effects were observed in foetuses. In rabbits, cypermethrin was tested up to 120 mg/kg bw/day without producing maternal or developmental toxicity.
Relevant maternal NOAEL in rat and rabbit are 12.5 and ≥120 mg/kg bw/day, respectively; the relevant developmental NOAEL are 35 mg/kg bw/day in rat and ≥120 mg/kg bw/day in rabbit.

2.7. NEUROTOXICITY

Acute neurotoxicity was tested in rats, showing clinical signs and FOB effects at 50 mg/kg bw for zeta-cypermethrin (NOAEL 10 mg/kg bw) and at 100 mg/kg bw for cypermethrin (NOAEL 30 mg/kg bw). Subchronic toxicity NOAEL of zeta-cypermethrin was 5 mg/kg bw/day, based on increased landing foot splay and reduced motor activity in rats at 26 mg/kg bw/day, whereas for cypermethrin the NOAEL was set at 25 mg/kg bw/day for the occurrence of FOB effects in female rats at 65 mg/kg bw/day.

2.8. FURTHER STUDIES

No studies on metabolites were submitted.

A developmental neurotoxicity study in rats was summarised in the DAR showing a maternal and developmental toxicity NOAEL of 9 mg/kg bw/day based on reduced bodyweight gain. Zeta-cypermethrin did not show any developmental neurotoxic potential.

Placental and lactational transfer was investigated after dietary exposure of dams. Zeta-cypermethrin was identified in milk following dietary administration indicating that a transfer occurred from food to milk and that exposure of pups occurred via milk.
The proposal for classification of zeta-cypermethrin as R64 (“may cause harm to breastfed babies”) was discussed in a meeting of experts. The RMS summarized the arguments for classification with R64 in an addendum. The proposal for classification is based on supplementary studies, where clear maternal toxicity was observed at 47.7 mg/kg bw/day. At this dose level, 7.8-11.55 ppm zeta-cypermethrin was measured in milk and toxic effects were noted in pups. At the lower dose of 17 mg/kg bw/day, there is no evidence of maternal toxicity, but there is a slight decrease of litter weight (not statistically significant) starting from PND11 to PND17. At this dose level, zeta-cypermethrin reaches 0.58-3.9 ppm in milk.
It was noted that the effects occurred when the pups began to eat treated diet and not very early during the lactation period. The RMS pointed out that this might be due to an accumulation of the

substance. However, there were no neurotoxic effects in the pups, just reduced bodyweight, even if the substance was found in the milk.
The meeting decided that classification with R64 is not warranted (to be confirmed by EChA).

2.9. MEDICAL DATA

According to the existing medical records from the manufacturing plant, none of the employees have experienced any detectable health effects apart from occasional and temporary paresthesia resulting from skin contact.
All recorded cases of poisoning involved mild symptoms of vertigo, nystagmus, drowsiness, emesis, hypertonia, nausea, headache, lassitude, anorexia, redness of the face, pyrexia, swelling of lymph nodes, slight conjunctivitis, cauterization of the eyes, slight effects on skin and ears and labored breathing. Severely poisoned patients may have convulsions, coma and pulmonary edema. Death may occur from respiratory paralysis. The prognosis is good with appropriate medical treatment with full recovery even in severely poisoned patients.

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

ADI

During the meeting of experts, the value of 0.04 mg/kg bw/day was agreed for the ADI, based on the overall cypermethrin NOAEL for dogs of 7.5 mg/kg bw/day and a 100-fold safety factor with an additional factor of 2 for the higher toxicity of zeta-cypermethrin vs. cypermethrin.

ARfD

The ARfD of 0.125 mg/kg bw as proposed in the DAR was confirmed by the experts. The value was based on the developmental toxicity study in rats (NOAEL 12.5 mg/kg bw/day) supported by the acute neurotoxicity with zeta-cypermethrin, applying a SF of 100.

AOEL

During the meeting, the experts discussed the most suitable study to be considered for setting the AOEL: the question was raised if the 1-year dog study should be used for the AOEL instead of the 90-day dog study because of a lower NOAEL. It was noted that also for cypermethrin and alpha-cypermethrin the 90-day study was used. It was concluded that the 1- and 2-year studies were more appropriate, with 7.5 mg/kg bw/day considered as the relevant overall NOAEL for subchronic dog studies.
An AOEL of 0.02 mg/kg bw/day was based on the overall cypermethrin NOAEL for dogs of 7.5 mg/kg bw/day using a 100-fold safety factor with an additional factor of 2 for the higher toxicity of zeta-cypermethrin and correcting for 50% oral absorption. This is supported by a read-across

through a 13-week neurotoxicity- and multigeneration study with zeta-cypermethrin with a NOAEL of 5.9 mg/kg bw/day.

2.11. DERMAL ABSORPTION

No specific studies were submitted. Based on the physico-chemical properties of zeta-cypermethrin (log Pow=5-6 and MW=416) a default value of 10% was proposed to be used for the operator exposure estimates to "Fury 10 EW". This was agreed in the PRAPeR meeting of experts.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Zeta-cypermethrin is formulated as an emulsion (100 g/L). It is proposed for applications in maize (maximum individual rate of 37.5 g a.s./ha) and in cereals and peas (maximum individual rate of 15 g a.s./ha).

Application in field crops occurs by tractor-mounted/trailed boom sprayer and application in high crops by tractor mounted /trailed broadcast air-assisted sprayer.

Operator

Operator exposure was estimated according to the UK POEM model and the German model.

Model	**Application method (crop)**	**Systemic exposure (mg/kg bw/day)**		**% of systemic AOEL**	
		No PPE	**PPE**	**No PPE**	**PPE***
UK POEM	Field crop	0.02422	0.01822	121	91
UK POEM	High crop	0.02236	0.02086	112	104
German	Field crop	0.00477	0.00182	24	9.1
German	High crop	0.00241	0.00188	12	9.4

*Gloves during mixing/loading and during the application

Worker

After the meeting the RMS has presented revised calculation of worker exposure in an addendum.

The total absorbed dose by a worker was recalculated using a DFR of 3 µg/cm²/kg a.s./ha, an inspection duration of 2 hours, and a bodyweight of 60 kg and compared with the revised AOEL=0.02 mg/kg bw/day.

$D = DFR \times TF \times AR \times P$,

where:

- DFR is the dislodgeable foliar residue (0.003 mg a.s./cm² - EUROPOEM agreed value),
- TF is the transfer factor (5000 cm²/person/h)
- WR is the working rate (2h/d (scouting task)
- AR is the application rate, which is maximally 0.0375 kg a.s./ha
- P is the penetration factor (100% if no PPE is used, 5% when PPE is used)
- Skin absorption of 10%

D= 0.0019 mg a.s./kg bw/day

The estimated exposure for re-entry workers not wearing PPE is 9.5% of the AOEL.
The estimated exposure for re-entry workers wearing PPE is 0.47% of the AOEL.

Bystander
After the meeting the RMS has presented revised calculation of bystander exposure in an addendum considering either Lloyd and Bell[7] or Ganzelmeier[8] models.
A surface area of 2 m^2 was used for calculation.

With the Lloyd and Bell model, using a bodyweight of 60 kg, the total systemic absorbed dose would be 0.000123 mg/kg bw/day, which would then represent 0.615% of the AOEL.

With the Ganzelmeier model, 2 m^2 surface area was considered, predicting a total exposure of 0.00004 mg/kg bw/day, which would account for 0.2% of the proposed AOEL.

3. Residues

Zeta-cypermethrin was discussed at the PRAPeR meeting of experts for residues (PRAPeR 50, subgroups 1 and 2, round 10) in June 2008.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

No metabolism studies using ^{14}C-labelled zeta-cypermethrin were provided. In order to support the intended uses of zeta-cypermethrin on maize, cereals and peas, the applicant has submitted plant metabolism studies performed with ^{14}C-cypermethrin labelled either on the benzyl ring or the

[7] Lloyd GA, Bell GJ (1983). Hydraulic nozzles: Comparative spray drift study. AHU report n°122
[8] Ganzelmeier H, Rautmann D, Spangenberg R, Streloke M, Herrmann M, Wenzelburger H-J, Walter HF Studies on the spray drift of plant protection products. Mitteilungen aus der Biologischen Bundensanstalt für Land- und Forstwirtschaft Berlin-Dahlem. Heft 305, 1995. Updated: BBA (2000:1).

cyclopropyl moiety. Several groups of plants were investigated: root crops (sugar beet), cereals (maize), pulses/oilseeds (cotton), fruit crops (apples) and leafy crops (lettuce).

A metabolic pathway could be drawn for cypermethrin in the different crop categories and a residue definition could be established in plant matrices. The major degradation pathway of cypermethrin starts with the hydrolytic cleavage of the ester linkage of the parent molecule that yields *cis/trans* DCVA[9] under its free form and the *m*PBAldehyde[10], this latter metabolite being further oxidised or reduced to the corresponding *m*PBAcid[11] or *m*PBAlcohol[12] followed by glycoside conjugation. The *cis/trans* DCVA, *m*PBAlcohol, *m*PBAcid and their hydroxy derivates are further conjugated mainly with sugars to form the glycosides, sulphate glycosides or malonyl glycosides. In a lower extent, a minor way identified was the initial hydroxylation of the parent cypermethrin with further hydrolysis, oxidation and reduction reactions. In all cases, unchanged cypermethrin was the predominant residue accounting for *c.a.* more than 50% of the TRR in beetroot foliage and roots, maize fodder and silage, apple peel and pulp and lettuce leaves. Cypermethrin was therefore considered as a valid indicator of the level of contamination of commodities. Every metabolite formed in plant was also observed in the rat metabolism.

In an addendum the RMS pointed out the respective characteristics of cypermethrin and zeta-cypermethrin. Cypermethrin is an ester pyrethroid having three chiral carbons:

1. At the third carbon of the cyclopropane ring giving the *cis/trans* isomers. The *trans*-isomer is much more readily hydrolysed by esterases, contributing to a lower toxic potential than the *cis*-isomer,
2. At the first carbon of cyclopropane ring leading to the 1R and 1S isomers,
3. At the cyano-carbon bearing group, leading to the αS/αR isomers. In mammals, as in insects, the αS configuration greatly enhanced the acute neurotoxicity while the R epimer (αR) is not toxic (public literature: Soderlund et al., 2002).

Both cypermethrin and zeta-cypermethrin are mixtures of the 8 different isomers (comprising 4 pairs of diastereoisomers) having a *cis*/*trans* isomeric ratio of c.a. 50/50. The difference in the two active substances is that cypermethrin has a 50/50 *α*S/*α*R ratio, whereas zeta-cypermethrin is enriched in the αS–enantiomer, which is the most toxic isomer with a ratio of *c.a.* 88/12.

The meeting of experts discussed whether the plant metabolism studies performed with cypermethrin are relevant for zeta-cypermethrin, and especially if a preferential metabolism may be suspected for

[9] cis/*trans* DCVA: (1*R*,3*RS*)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid
[10] mPBAldehyde: 3-phenoxybenzaldehyde
[11] mPBAcid: 3-phenoxybenzoic acid
[12] mPBAcohol (3-phenoxyphenyl)methanol

some isomers with a special impact on toxicology, taking into account the toxicological potency of each individual isomer. Experts were informed that the applicant provided by early 2008 a bridging study on maize to detail the respective metabolism of both cypermethrin and zeta-cypermethrin, and to clarify the ratios of *cis/trans* isomers and αS/αR enantiomers in the plant residues. However, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, this study could not be considered in the peer review.

Little information was available in the DAR concerning a possible isomeric conversion for cypermethrin, except in the metabolism study performed on apple where the *cis/trans* isomer ratio was followed. In this study an isomeric conversion from the *cis*- to the *trans*-isomer was observed in peel and leaves at a rate of 12% and 25%, respectively; so from the more toxic to the less toxic isomers. At the opposite, no data were available on the possible evolution of the αS/αR ratio. Nevertheless, taking into account the αS/αR ratio of 88/12% in zeta-cypermethrin, the meeting was of the opinion that the increase of the toxicity level of the residues would not be significant if a total conversion from the less toxic isomers (αR) to the more toxic isomers (αS) is envisaged. Moreover, the residue levels observed in the representative crops (cereals, maize and pea) account finally for a small portion of the ADI and ARfD values and the possible increase of toxicity due to an isomeric conversion would not cause a concern for the consumer.

Finally, the meeting was of the opinion that the possible isomeric conversion from the less toxic to the more toxic isomers would not be significant for the considered uses on cereals, maize and peas and that a residue definition can be proposed based on the metabolism studies performed with cypermethrin. Nevertheless, if future additional uses lead to a potential increase of the residues by consumers, the bridging metabolism study performed on maize and submitted early 2008 would have to be considered.

Taking into account the various cypermethrins available on the world market (alpha-cypermethrin, zeta-cypemethrin, theta-cypermethrin, etc.), the meeting of experts concluded that a global residue should be the most suitable for plant commodities and proposed for both monitoring and risk assessment to set the residue definition as **cypermethrin, including other mixtures of constituent isomers (sum of isomers)**.

Numerous supervised residue trials conducted with zeta-cypermethtrin on maize, winter wheat, winter barley, triticale, oat and pea were submitted. Clarifications were provided in the addendum of May 2008 on the criteria used to retain or to exclude some trials. In particular, trials have been rejected since growth stages at last application were not in compliance with the critical GAP and/or the analytical methods were not sufficiently validated. It was agreed that for cereals, the growth stage is a better control point for the selection than the PHI since an application at a later stage than the

requested one leads to higher residues in straw and by means, to an overestimation of the residue intake by animals. Concerning the analytical methods, the applicant submitted additional validation data, however, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new studies could not be considered in the peer review. After the meeting the RMS updated the initial addendum (July 2008), giving clear indications on the selected trials retained for the MRL setting.

The meeting of experts discussed the validity of the storage stability studies with regard to the revised data provided by the RMS in the May 2008 addendum, where residue levels at the different sampling times from the original DAR were presented uncorrected for average procedural recoveries. On plant, no degradation was observed for zeta-cypermethrin in pea and cereal matrices for a storage period up to 15 months. In addition, storage stability studies performed with cypermethrin using field-incurred samples (lettuce, tomato and cottonseed) or spiked samples (apple, cabbage) indicated that residues were stable over 12 and 18 months, respectively, when stored at –18°C. The meeting agreed that there was no degradation for plant matrices and that residue trials were analysed within this time period. For livestock matrices, storage studies were conducted to determine the stability of cypermethrin and its metabolites *cis*-DCVA, *trans*-DCVA and *m*PBAcid. Some instability was seen in eggs for *m*PBAcid (recovery 64%) and in poultry muscle and liver for *cis*-DCVA (56-58 %) within three and six months but this was not seen in the ruminant tissues. However, the experts agreed that this slight degradation observed at some time points was not an issue and that the results are globally acceptable.

No processing studies were provided, considering that no significant residues were observed in any commodities supporting the representative uses. Nevertheless, the EFSA noted that the cypermethrin hydrolysis breakdown product, *m*PBAldehyde, was found in a tomato processing study, and this compound is suspected of endocrine activity. The meeting noted that from literature there are evidences that *m*PBAldehyde has oestrogenic properties but this concern is not relevant for the intended uses supported by the applicant. This point should be re-considered when additional uses become relevant.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

A rotational crop study including wheat, sugar beet, lettuce and cotton was conducted with cypermethrin at the excessive application rate of 1000 g/ha (27X). The meeting discussed whether this rotational crop study should be considered acceptable with regard to the high application rate and the fact that non-negligible amounts of radioactivity were also detected in the control plants. The experts agreed that despite the high application rate, the total radioactivity at harvest remained limited with a maximum level of 0.06-0.07 mg/kg in wheat grain, wheat chaff and wheat straw and for the shorter plant-back interval. **This suggests that following normal agricultural practices, cypermethrin**

residue levels in the edible parts of the rotational crops will be below 0.01 mg/kg. Moreover, and considering the highest DT_{90} of 93 days observed for cypermethrin (median DT_{90f} 59 days for zeta-cypermethrin), the meeting was of the opinion that no further rotational crop study should be required.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

As for plants, the applicant submitted animal metabolism studies performed with ^{14}C-cypermethrin in order to support the uses of zeta-cypermethrin. The metabolism has been investigated in lactating cows and laying hens using both labelling on cyclopropyl- and benzyl moiety. These studies demonstrated that following oral administration, the total radioactivity was rapidly eliminated in urine and faeces. In lactating cow, less than 0.2%-0.5% of the administered dose was recovered in milk and less than 0.05% in edible tissues. In laying hen, the majority of the administered radioactivity was recovered in the excreta (up to 99 %), against 0.1-0.3 % in the eggs and 0.7-1.8 % in the edible tissues.

No metabolite identification was performed in cow milk, muscle and fat due to the levels of total radioactivity (maximum TRR: 0.029 mg/kg in milk, <0.04 mg/kg in muscle). Parent cypermethrin was recovered at a low level in liver and kidney, the main compound in these organs being the *m*PBAcid and its amino acids conjugates with the glutamic acid and glycine. In the laying hen study, parent compound was recovered as the predominant residue in fat (up to 70% TRR) and egg yolk (up to 29% TRR), *m*PBAcid and its conjugates being major in liver.

Based on these studies a metabolic pathway was proposed for cypermethrin in animals. The major route of degradation consisted of ester linkage through hydrolysis to generate the *cis* and *trans* DCVA moiety (although not demonstrated in ruminants as no residue characterisation was performed in the study performed with the ^{14}C-cyclopropyl label) and the *m*PBAldehyde which undergoes further oxidation and/or reduction to the corresponding acid (*m*PBAcid) or alcohol (*m*PBAlcohol) and their hydroxy products. All the identified metabolites were also recovered in the rat metabolism.

The meeting of experts discussed whether the metabolism of the cyclopropyl moiety has been sufficiently investigated in ruminants. The additional data from literature concerning this moiety presented in the addendum of May 2008 were not considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007. This point remains open and has to be re-considered. Nevertheless, taking into account the complete metabolic pathway in poultry, and the data from the rat study indicating a similar pathway, the meeting of experts considered that there was enough evidence to propose the following residue definition for monitoring and risk assessment for animal products “cypermethrin, including other mixtures of constituent isomers (sum of isomers)”.

Feeding studies on dairy cattle and poultry were performed using cypermethrin. The livestock dietary burden calculation was updated in the addendum of July 2008 and the RMS confirmed after the meeting that the dosages applied in the feeding study on ruminants were effectively those initially stated in the DAR, and that the values discussed during the meeting were correct. Samples were analysed for parent and for the metabolites *cis*-DCVA, *trans*-DCVA and *m*PBAcid. For dairy cattle, at the lower dose rate investigated of 5 mg/kg diet, corresponding to *c.a.* 30 times the estimated animal burden for dairy cattle, the highest cypermethrin residue levels were 0.012 mg/kg in liver, 0.018 mg/kg in milk, 0.031 mg/kg in muscle, 0.103 in milk cream and 0.182 mg/kg in peritoneal fat. No metabolites were detected except *cis*-DCVA in peritoneal fat and milk cream (0.029 and 0017 mg/kg, respectively) and *trans*-DCVA in kidney and in peritoneal fat (0.026 mg/kg). In the poultry study, no residues of parent or of any metabolite were detected above the LOQ in eggs and poultry tissues at the minimum dose level of 2 mg/kg diet, corresponding to more than 50 times the estimated dietary burden. Therefore it was concluded that no measurable residues are expected above the LOQ in the different animal products through consumption of treated feed items (cereal grains, maize and pulses) and MRLs were proposed at LOQ values.

3.3. CONSUMER RISK ASSESSMENT

The meeting agreed that for zeta-cypermethrin a consumer risk assessment has to be conducted using the toxicological reference values set for this active substance and the representative uses supported in the DAR. Nevertheless, considering the various mixtures of cypermethrin isomers available on the world market (alpha-cypermethrin, zeta-cypemethrin, theta-cypermethrin, etc.), **the meeting of experts concluded on the need of a global risk assessment taking into account the other sources of exposure resulting from the uses of all other possible isomer mixtures** and the different toxicological reference values set for the different isomeric mixtures of cypermethrin.

For zeta-cypermethrin, considering the representative uses on maize, cereals, peas and pulses and the ADI value of 0.04 mg/kg bw/day, no chronic concern was observed, the theoretical maximum daily intake (TMDI) being less than 2% of the ADI, irrespective of the model used (WHO, German or UK). The acute exposure estimates based on UK consumption indicates that the maximum national estimated short term intake (NESTI) is less than 1% of ARfD for wheat.

3.4. PROPOSED MRLS

The additional residues trial data and validation data provided by the applicant early 2008 were not considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007. Therefore some MRL proposals have to be considered as provisional awaiting the full evaluation of these data. The supervised residue trials were performed using zeta-cypermethrin and the residue was analysed and determined as total cypermethrin (sum of isomers).

- **On maize,** a provisional MRL of 0.02* mg/kg was proposed based on Northern European trials and pending the results of further trials supporting the critical dose rate of 37.5 g a.s./ha with an application at the critical growth stage (BBCH 63-65; 50% male flowering) and using a validated analytical method. Moreover, residue trials are requested in Northern and Southern Europe on maize forage.

- **On cereals,** the residue database was considered sufficient to propose an MRL of 0.02* mg/kg on winter wheat (and triticale by extrapolation) and, pending further residue trials and validation data, a provisional MRL of 0.05 mg/kg on winter barley (and oats by extrapolation).

- **On peas** the residue database was considered sufficient to propose an MRL of 0.02* mg/kg on pea without pods and a provisional MRL of 0.02* mg/kg on pea with pods, pending the validation of the analytical method for pea with pods.

- **On pulses**, a provisional MRL of 0.02* mg/kg is proposed awaiting additional trials in Northern EU.

4. Environmental fate and behaviour

Zeta-cypermethrin was discussed at the PRAPeR experts' meeting for environmental fate and behaviour PRAPeR 47 in May 2008. Cypermethrins contain 8 enantiomers. When analysed using non-chiral chromatography techniques 4 peaks can be resolved. Zeta-cypermethrin contains predominantly 4 isomers (the 1S *cis* S, 1R *cis* S, 1S *trans* S and 1R *trans* S isomers), with the other 4 being defined as impurities so are present at low levels. It should also be noted that the methods of analysis used in the fate and behaviour studies with the exception of the sterile aqueous hydrolysis study were not stereo-selective. Therefore the regulatory dossier provides no information on the behaviour of individual enantiomers in the environment. Whilst in the non-chiral analyses information on the potentially resolvable diastereoisomers are potentially available, the results for individual diastereoisomers were not reported in the DAR. Therefore all active substance residues reported in this conclusion are for the sum of whichever of the 8 enantiomers were present in a sample. Therefore, based on the available information, it is unclear if any isomers are degraded preferentially compared to the others in the environmental matrices studied or if epimerisation may occur (as was observed under sterile alkaline aqueous hydrolysis conditions, see section 4.2.1, which were the only conditions where this was investigated).

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

A soil route of degradation study carried out with zeta-cypermethrin as dosing material is not available. The most pertinent information in the applicant's dossier (agreed as being relied on for regulatory assessment) were experiments in a single soil (USDA[13] sandy loam, pH6.9, organic carbon (oc) 1.04%) where cypermethrin labelled in either the cyclopropyl or benzyl rings was dosed. These experiments were carried out under aerobic conditions in the laboratory (25°C and 75% 1/3 bar moisture holding capacity (MHC) in the dark). The formation of residues not Soxhlet extracted by acetonitrile/water were a sink that accounted for 12 and 26 % of the different applied radiolabels (AR) respectively after 91 days. Mineralisation to carbon dioxide accounted for 25 and 27 % AR respectively after 91 days. The only metabolites identified were DCVA[14] (max. 24 % AR after 62 days) and *m*PBAcid (max. 8.4 % AR after 30 days).

The experts from the member states discussed the case made by the applicant that was evaluated by the RMS in the addendum to the DAR B.8 dated July 2008 (section B.8.1.1), on why it would be appropriate to extrapolate the route of soil degradation evident from this study dosed with cypermethrin, to support the assessment of the route of soil degradation of zeta-cypermethrin. The experts confirmed that, based on the RMS evaluation presented in the DAR, this study as described above appeared to be an acceptable study for supporting the assessment of the route of degradation of cypermethrin and is probably also representative for the route of degradation of zeta-cypermethrin with regard to the main metabolites that will be formed. I.e. they agreed that the degradation pathway identified in the study will probably be representative of the degradation pathway of zeta-cypermetrhin. However, the level of potential breakdown products that may be formed from zeta-cypermethrin could be different to that observed in the available study dosed with cypermethrin. The experts considered that, based on the evidence of the cypermethrin study, zeta-cypermethrin metabolites above 5% AR may well occur over relatively prolonged periods (unidentified fractions in chromatography from the cypermethrin study were in the range of 3-6% AR; i.e. potentially equivalent to up to 6-12%AR had zeta-cypermethrin been dosed). The experts also noted that this potential concern is confounded by the fact that for the available cyclopropyl radiolabel experiment, recoveries were poor over the period from days 60 to 150. The experts therefore concluded that there was a data gap and that a new aerobic soil laboratory route of degradation study dosed with zeta-cypermethrin was necessary to enable an appropriate environmental exposure assessment to be completed (confirm if additional metabolites >5% AR that would trigger an assessment of leaching to groundwater are present). As a new study was considered necessary, the experts indicated that any new study carried out in the future should be carried out using chiral analytical methods, at least for some representative sampling times.

[13] United States Department of Agriculture soil classification
[14] information on isomer ratio not reported in the DAR / addendum to the DAR

The experts also discussed the studies Harvey (1991), Standen (1976) and Standen (1978), as results from these references were an integral part of the argumentation put forward by the applicant (see addendum to the DAR B.8 dated July 2008, final addendum pages 129 to 132) why further data on the route of degradation of zeta-cypermethrin were not necessary. The experts agreed that these studies should not be relied on for regulation due to the deficiencies already highlighted by the RMS in the DAR. However, in one of these studies (Standen, 1976, where the deficiencies identified were that the material balance was not available, as volatiles were not trapped and samples were only taken at 4 intervals) the metabolite *m*PBAcid was reported to have been present at up to 29% AR after 112 days. Consequently, experts agreed that *m*PBAcid had to be considered as a major metabolite. Whilst it was agreed that the study Sakata (1986) could be considered to provide useful supporting information (conclusion of the RMS in the DAR), there is little other reliable information the results from this study can support. As a consequence, whilst the applicant's argumentation as presented in the addendum regarding the relative degradation rates of the *cis* and *trans* isomers of zeta-cypermethrin being equivalent to that seen for cypermethrin is plausible, the experimental data for cypermethrin assessed were considered insufficient to be relied on as a basis to extrapolate to the likely behaviour of *cis* and *trans* isomers of zeta-cypermethrin.

There was no reliable information on the soil degradation of cypermethrin or zeta-cypermethrin under anaerobic laboratory conditions provided by the applicant. The experts from member states discussed if anaerobic conditions could be excluded for the applied for intended uses being assessed at EU level (this was the position of the RMS). The experts agreed that soil residues were unlikely to encounter anaerobic soil conditions considering the degradation rate of zeta-cypermethrin in soil under aerobic conditions (see section 4.1.2) when considering the timing of application associated with the uses requested on peas and maize. However, it was concluded that this could not be excluded completely for the uses on cereals (specifically the potential autumn applications to winter cereals for virus vector control) in all EU territories. Therefore, a data gap was identified for a laboratory anaerobic soil degradation study, but these data are only necessary to support the applied for intended use of autumn application to winter cereals or any other use that may be requested with autumn applications, in territories where anaerobic soil conditions cannot be excluded.

A laboratory natural light soil photolysis study dosed with cypermethrin was agreed by the experts from member states to indicate that degradation by photolysis would not be expected to be a process that significantly influences the dissipation of zeta-cypermethrin in the environment (see addendum to the DAR B.8 dated July 2008 pages 137 to 139 of the final addendum, where the RMS re-evaluation of this study (Estigoy *et. al*, 1991) can be found). The study Swales (2003) summarised on final addendum pages 139 to 143 was not considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007.

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

In the single satisfactory route of degradation study described at section 4.1.1 above, where cypermethrin was dosed a single first order linear regression DT_{50} of 60 days was estimated (25°C and 75% 1/3 bar MHC). When normalised to FOCUS reference conditions[15] (20°C using a Q10 of 2.2 and -10kPa soil moisture) this DT_{50} is 89 days. The conclusion of the peer review was that no other reliable laboratory soil DT_{50} were available (including cypermethrin dosed studies) in the applicant's dossier, as already discussed in section 4.1.1 above. However, contrary to the RMS' proposal in the DAR, the member state experts considered that additional laboratory soil degradation studies where zeta-cypermethrin was dosed were not necessary, as DT_{50} for the active substance derived from the available field studies where zeta-cypermethrin was dosed were sufficient to finalise the environmental exposure assessment for the active substance.

For the identified major soil metabolites *cis*-DCVA, *trans*-DCVA and *m*PBAcid, satisfactory laboratory soil degradation studies (20°C and 42-50% maximum water holding capacity (MWHC)) were available in 3 soils where these materials were applied as test substances. In the DCVA dosed studies single first order linear regression DT_{50} were 2.7 to 11 days (FOCUS reference condition values 2.4 to 9.5 days, geometric mean 4.2 days). For *m*PBAcid in 2 of the soils biphasic fitting was carried out. The range of single first order linear regression DT_{50} for *m*PBAcid were 3 to 7 days (slower second phase values for the 2 soils where a biphasic fit was employed, FOCUS reference condition values 2.7 to 7 days, geometric mean 4.3 days). Further details regarding the kinetic fitting for these metabolite values can be found in the addendum to the DAR B.8 dated July 2008 on pages 177 to 182 of the final addendum.

Satisfactory field soil dissipation studies (bare soil) were provided from six sites, four of which were located in Germany, 1 in southern France and 1 in Italy where applications were made in May and June, where zeta-cypermethrin was applied as the test substance. At the German field trial sites only residues of component isomers of the active substance were analysed for. At the French and Italian trial sites, in addition to analysis for residues of component isomers of the active substance, the methods used also determined residues of *m*PBAcid and isomers of DCVA. At the 4 German sites, residues were determined over the 0-5cm soil layer (though sampled to 30cm residues were not detected (> 0.001mg/kg) below 5cm). At these trial sites DT_{50} for the sum of the component isomers of the active substance were estimated to be 6 to 24 days with the associated DT_{90} being 42 to 80 days (best fit kinetics using linear regression and with the exception of the Rodenbach trial site, the pattern of decline did not conform to a first order curve). At the southern French and Italian sites, residues were determined over the 0-5cm soil layer (though sampled to 100cm, residues were not detected (> 0.003mg/kg) below 5cm). At these trial sites non linear regression single first order DT_{50} for the

[15] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

sum of the component isomers of the active substance were estimated to be 21 and 11 days (DT_{90} 71 and 37 days, kinetic fits presented in the addendum to the DAR B.8 dated July 2008 on pages 185 to 186 of the final addendum). For *m*PBAcid, single first order DT_{50} of 4.8 and 5.9 days were estimated (associated kinetic formation fractions 0.033 and 0.068, respectively; see addendum to the DAR B.8 dated July 2008, pages 187 and 189 of the final addendum). At the Italian site only, a single first order DT_{50} of 2.9 days was estimated for *trans*-DCVA (associated kinetic formation fractions 0.062; see addendum to the DAR B.8 dated July 2008, page 188 of the final addendum). *Cis*-DCVA was not detected in the samples taken at either trial site. *Trans*-DCVA was not detected in the samples taken at the French trial site.

The peer review agreed that the field dissipation studies evaluated in the DAR that were carried out in the USA were not useful to support the EU assessment.

The member state experts agreed the kinetic assessment of the six European field studies that was carried out for residues of component isomers of the active substance that follows the time step normalisation approach to FOCUS reference conditions (20°C using a Q10 of 2.2 and -10kPa soil moisture using a Walker equation coefficient of 0.7) and followed FOCUS kinetics guidance. This agreed assessment is set out in the addendum to the DAR B.8 dated July 2008, section B.8.1.3.1. This assessment results in reference condition single first order DT_{50} of 8.6, 9.3 and 12.8 days (from the 3 German sites excluding Christinenthal). For the other three trial sites the first order multi compartment model better described the residue decline and the DT_{50} were 7.8[16], 8.4[17] and 11[18] days (associated DT_{90} 50.5, 89.2 and 93.3 days respectively). To calculate a geometric mean single first order value for use in FOCUS modelling the FOMC DT_{90} were divided by 3.32 to provide an appropriate estimate of a normalised first order DT_{50} to represent these three trial sites (the resulting values are 15.2, 26.9 and 28.1 days). The resulting FOCUS reference condition geometric mean single first order DT_{50} for residues of component isomers of the active substance is 15.1 days.

The experts agreed that for PEC soil for zeta-cypermethrin it was appropriate to use the longest not normalised field first order DT_{50} of 24 days in calculations (as the DT_{90} at this site (80 days) was also the longest value). For the metabolites it was agreed that the longest not normalised first order DT_{50} values (laboratory values) would be the appropriate values to use (DCVA 11 days and *m*PBAcid 7 days), though for the applied for intended uses in the EU level assessment it was sufficient to just use the initial PEC for the maize use to cover the applied for intended uses. The PEC soil of the metabolites were calculated assuming 100% formation from the active substance due to uncertainties in the reliability of the measured formation fractions in the available laboratory studies dosed with

[16] α= 1.41678 ß= 12.3728
[17] α= 0.881522 ß=7.0614
[18] α= 1.05707 ß= 11.9102

cypermethrin (that with one exception had employed limited numbers of sampling intervals). The values agreed are in appendix 1.

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

The adsorption/desorption of cypermethrin (results reported as sum of isomers) was investigated in 4 soils in satisfactory batch adsorption experiments. Calculated adsorption $K_f$oc values varied from 72405 to 285652 mL/g, (arithmetic mean 121786 mL/g) (1/n 1.15 – 1.47, mean 1.3). There was no evidence of a correlation of adsorption with pH.

The adsorption/desorption of *m*PBAcid was investigated in 3 soils in satisfactory batch adsorption experiments. Calculated adsorption $K_f$oc values varied from 118 to 215 mL/g, (arithmetic mean 152 mL/g) (1/n 0.65 – 0.67, mean 0.66). There was no clear evidence of a correlation of adsorption with pH, though no alkaline soils were investigated.

The adsorption/desorption of *trans*-DCVA was investigated in 3 soils in satisfactory batch adsorption experiments. Calculated adsorption $K_f$oc values varied from 18 to 48 mL/g, (arithmetic mean 28 mL/g) (1/n 0.56 – 0.81, mean 0.64). There was no clear evidence of a correlation of adsorption with pH, though no alkaline soils were investigated, all adsorption values are low.

No information was provided on the soil adsorption of *cis*-DCVA. (*Note*: whilst this metabolite was not detected (>0.003mg/kg) in the European field dissipation studies, it was detected in the not relied on USA field studies when cypermethrin was applied as test substance at up to 0.04mg/kg (see appendix 1 section B.8 of the DAR)). The data gap identified in section 4.1.1 for a satisfactory aerobic laboratory soil route of degradation study where zeta-cypermethrin is dosed, needs to be filled to allow further consideration of whether information on the soil adsorption of *cis*-DCVA might be necessary to complete the soil mobility assessment.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Zeta-cypermethrin was stable under sterile hydrolysis conditions at 50°C at pH 4. At pH 7 at 25°C a first order DT_{50} of 25 days was estimated (calculated as sum of the component isomers); at this temperature at pH 9 zeta-cypermethrin was very labile. In the pH 9 experiment analysis by chiral chromatography indicated that epimerisation occurred in a way that all 8 isomers were in equilibrium (12.5% of each isomer). This analysis was not done at pH 7. The hydrolytic breakdown products of zeta-cypermethrin were not identified (test substance was not radiolabelled). The metabolites *m*PBAcid, *m*PBAlcohol, *cis*-DCVA and *trans*-DCVA were shown to be stable to aqueous hydrolysis (evidence from pH 4, 7 and 9, 50°C experiments).

In a laboratory study where the direct aqueous photolysis of zeta-cypermethrin as test substance under sterile conditions was investigated, a rate of degradation (single first order DT_{50}) of 3.05 test system days (calculated as sum of the component isomers) continuous illumination for a light path length of 1cm was determined (dark control value 6.7 days). When equated to Central European May sunlight for the 1cm light path length this value is 1.5 days, for a 1m light path length the value is 14 days. The photolytic breakdown products of zeta-cypermethrin were not identified (the test substance was not radiolabelled). In a laboratory study where the direct aqueous photolysis of *m*PBAcid as test substance under sterile conditions was investigated at pH 4, 7 and 9, the rates of degradation (single first order DT_{50}) of 1.07, 2.83 and 4.07 days continuous illumination respectively for a light path length of 1cm were determined. When equated to Central European May sunlight for the 1cm light path length these values as calculated by the applicant are 77, 120 and 170 days, respectively. For a 1m light path length the values are 900, 1800 and 1600 days, respectively.

Though hydrolysis and photolysis metabolites were not identified, the EFSA considers that exceptionally in this case the exposure assessment can be completed without these data utilising the results of the dark aerobic sediment water study as a good indication of the expected breakdown products in natural aquatic systems, as the expected rapid partitioning of the active substance to sediment (active substance has very high adsorption values, see section 4.1.3) will limit the potential for aqueous photolysis.

A data gap exists for a ready biodegradability test. In the absence of a peer reviewed ready biodegradability study zeta-cypermethrin must be considered not readily biodegradable. The study Dengler (2007) summarised in section B.8.4.3 of the addendum to the DAR B.8 dated July 2008 could not be considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007.

In water-sediment studies (2 systems studied at 20°C in the laboratory, sediment pH 7.6 and 8.1, water pH 8.6 and 8.4) the applied zeta-cypermethrin (labelled in either the cyclopropyl or benzyl rings) partitioned very rapidly from the water phase to sediment where it consequently degraded with low persistence (biphasic pattern of decline, DT_{50} 1.5 to 2.5 days, DT_{90} 16 to 26 days). The metabolites formed: *m*PBAcid, *cis*-DCVA and *trans*-DCVA were then found predominantly in the water phase (max. 33 to 38 % AR, 16 to 20 % AR and 35 to 47 % AR in water, respectively, but only max. 5 to 6 % AR, 2 to 3 % AR and 5 to 8 % AR in sediment, respectively). Whole system DT_{50} estimated for the three metabolites from the maximum observed occurrence considered by EFSA to represent graphical estimates, were 13 to 145 days, 63 to 79 days and 95 to 117 days respectively. The formation of sediment residues not Soxhlet extracted by acetonitrile/water were a sink that accounted for 16 to 22% AR and 26 to 27 % AR of the different radiolabels, respectively after 99

days. Mineralisation to carbon dioxide accounted for 16 to 21 % AR and 52 to 58 % AR, respectively after 99 days.

The experts agreed that for step 3 and 4 FOCUSsw calculations, sum of the component isomers of the active substance, a surface water DT_{50} of 1000 days (default) and sediment single first order DT_{50} of 6.12 days (geometric mean whole system value, estimated by dividing the biphasic DT_{90} of 16 and 26 days by 3.32) were the most appropriate values to use as input in FOCUS scenario modelling. The other component isomers of the active substance properties agreed as the most appropriate for step 3 and 4 calculations were: the geometric mean single first order soil DT_{50} of 15.1 days and the arithmetic mean K_{foc} of 121786 mL/g (1/n 1.3). For the metabolites, when using the FOCUSsw step 1 and 2 calculator, the substance input parameters as set out on pages 8-71 and 8-72 of the DAR were agreed as appropriate (close enough to the correct parameters). However, it was noted that the step 2 calculations were not correct as the run-off percentages assumed were not appropriate for the applied for intended uses. Of greater concern was the issue that in the further step 3 and 4 simulations provided before the meeting of member state experts, an inappropriate water dissipation single first order DT_{50} of 0.1 days had still been used (as clarified in addendum to the DAR B.8 as revised in July 2008, pages 173 to 174 of the final addendum). This was done even though this had been identified as inappropriate in the comments provided by member states on the step 3 simulations that had been presented in the original DAR. Therefore, the time weighted average values from these step 3 and 4 simulations as reported in the addendum must not be used for risk assessment (and are not included in appendix 1). It was clear, that for a substance with a K_{foc} of 121786 mL/g, spray drift will usually be the dominant route of entry to surface water, so in these FOCUS step 3 and 4 calculations the 90th percentile spray drift values from a single application should have been simulated for the applied for intended uses on cereals and peas to give global maximum surface water concentrations for the risk assessment. This was not done, the lower spray drift assumptions resulting from 2 applications (82nd percentiles) were used in the simulations. Therefore, the only global maximum PEC in surface water available generated in accordance with the agreed FOCUS surface water guidance in relation to drift parameterisation are those for the applied for intended use on maize (where only a single application was applied for). The results of the 2 application simulations for peas and cereals would have been appropriate to generate the PEC in sediment for these applied for intended uses. However, the simulated sediment concentrations were not provided in the report of the modelling. Therefore, a data gap is identified for FOCUS surface water step 4 simulations for component isomers of cypermethrin that utilise appropriate DT_{50} values, simulate single applications as well as multiple applications and report results for sediment concentrations as well as surface water concentrations. In the absence of these calculations the EFSA considers that risk managers should take as the best characterisation of exposure concentrations for use in aquatic risk assessment the following maximum surface water values. These are SWASH drift calculator estimates for cereals, peas and 25m for maize but the global maximum PEC at baseline distance and 20m from addendum B.8 as revised in

July 2008 for maize and the R4 stream scenario result for peas, where a run-off event must have contributed to the PECsw estimated:

	FOCUS baseline distance PECsw (µg/L)		20m no spray drift buffer zone PECsw (µg/L)		25m[19] no spray drift buffer zone PECsw (µg/L)
	Ditch or stream	pond	Ditch or stream	pond	Ditch or stream
Maize	0.131-0.19	0.00759	0.015 to 0.021	0.00323	*0.0145
Cereal and peas	*0.0964	*0.0033	*0.0072	*0.0014	*0.0058
peas			0.0122 R4 stream		

**Note*: these values that are derived from the SWASH drift calculator exclude run-off and drainage inputs which may become of significance as drift is increasingly mitigated.

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

Following FOCUSgw scenarios guidance[20] the most appropriate substance parameters for use in FOCUSgw scenario modelling based on the available (June 2008) data were: component isomers of the active substance single first order soil DT_{50} 15.1 days, K_{foc} 121786 mL/g, 1/n=1.3; *m*PBAcid single first order soil DT_{50} 4.3 days, formation fraction from isomers of the active substance 1, K_{foc} 152 mL/g, 1/n=0.66; DCVA single first order soil DT_{50} 4.2 days, formation fraction from isomers of the active substance 1, K_{foc} 28 mL/g, 1/n=0.64.

The applied for representative use of Spring / Summer applications (28 days after the emergence date defined for each scenario) to maize was simulated using FOCUSPELMO 3.3.2 using the following input parameters: component isomers of the active substance single first order soil DT_{50} 31.1.1 days, K_{foc} 18326 mL/g, 1/n=0.87; *m*PBAcid single first order soil DT_{50} 5.3 days, formation fraction from isomers of the active substance 1, K_{foc} 118 mL/g, 1/n=0.65; DCVA single first order soil DT_{50} 4.8 days, formation fraction from isomers of the active substance 1, K_{foc} for *trans*-DCVA 18 mL/g, 1/n=0.56. The results of this simulation were that at all 9 FOCUS groundwater scenarios the sum of the component isomers of the active substance, *m*PBAcid and sum of isomers of DCVA were calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations of <0.001µg/L. The experts accepted that these simulations demonstrated a low potential for groundwater contamination from the applied for intended uses of zeta-cypermethrin from isomers of the active substance and the identified soil metabolites *m*PBAcid and *trans*-DCVA. However, as already discussed in section 4.1.1, the groundwater exposure assessment regarding

[19] Note: a 30m no spray zone gives > 95% drift reduction which is the maximum admissible following FOCUS Landscape and mitigation (2007) guidance (Sanco/10422/2005, version 2.0, September 2007).
[20] Version 1.1 (April 2002) Generic guidance for FOCUS groundwater scenarios

metabolites cannot be finalised until the data gap for a satisfactory soil route of degradation study is filled and it is confirmed that there are no additional soil metabolites for which a groundwater exposure assessment would be triggered.

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of zeta-cypermethrin ($2.53x10^{-7}$ Pa at 25°C) means that zeta-cypermethrin would be classified under the national scheme of The Netherlands as very slightly volatile, indicating that losses due to volatilisation would not be expected. Based on the results of a laboratory controlled air flow experiment where a cypermethrin formulation was applied to a soil and dwarf bush bean plants, measurements demonstrated that none of the cypermethrin applied was lost to the air compartment (collected in volatile traps) in 24 hours. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half-life estimated at 6 hours (assuming an atmospheric hydroxyl radical concentration of $1.5x10^{6}$ radicals cm^{-3}) indicating that the small proportion of applied zeta-cypermethrin that will volatilise would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

Zeta-cyptermethrin was discussed in the meeting of experts on ecotoxicology, PRAPeR 48 in May 2008 on the basis of the draft assessment report and the addendum from May 2008 and the updated draft assessment report from May 2008. The representative uses evaluated are spray applications as insecticide in maize, cereals and peas. Zeta-cypermethrin consists of 4 enantiomers. Potential different degradation rates or possible epimerisation of the different enantiomers in the environment was not taken into account in the environmental risk assessment. This adds some uncertainty to the environmental risk assessment and needs to be addressed further.

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

5.1. RISK TO TERRESTRIAL VERTEBRATES

No studies with zeta-cypermethrin and birds were submitted. The endpoints for birds were based on studies with cypermethrin. It was evident from studies with mammals that zeta-cypermethrin is more toxic than cypermethrin. The experts agreed to a correction factor of 2 to extrapolate the toxicity of cypermethrin to zeta-cypermethrin based on the comparison of the toxicity to mammals. It was also noted that the content of the toxic isomers 1R *cis* άS and 1R *trans* άS is increased by 2 times in zeta-cypermethrin. The RMS presented a re-calculation of the TERs based on a 2-fold increased toxicity in the updated DAR from July 2008. The acute and short-term TERs were well above the Annex VI

trigger values. However the long-term TERs were below the trigger of 5 for the use in maize (herbivorous and insectivorous birds). The trigger of 5 was exceeded for herbivorous birds in cereals and peas but the TERs for insectivorous birds were calculated as 4.78. The refinement of the risk assessment based on measured residues in plants was agreed by the experts. The suggested mean residue value of 0.49 mg zeta-cypermethin/kg was questioned in the meeting. In the updated addendum from July 2008 the maximum measured initial concentration of 1.02 mg zeta-cypermethrin/kg was used. The refined long-term TER for herbivorous birds was calculated as 8.96 for the use in maize. The suggested RUD (residue per unit dose) values of 5.1 and 0.5 for foliar- and soil dwelling insects was not accepted by the experts to refine the risk assessment for insectivorous birds since data supporting the assumption that birds would feed only on large insects were not provided. The experts identified a data gap for a refined long-term risk assessment for insectivorous birds for all representative uses evaluated.

The first-tier acute and long-term TERs for herbivorous and insectivorous mammals exceeded the Annex VI trigger values except for small herbivorous mammals for the use in maize where a long-term TER of 2.81 was observed. The refined risk assessment for herbivorous mammals in the updated DAR from July 2008 was based on the highest measured initial residues (see also above refinement for herbivorous birds) resulting in a TER of 7.87.

The risk from secondary poisoning of earthworm- and fish-eating birds and mammals was assessed as low for all representative uses. No risk assessment was conducted for the uptake of contaminated drinking water. However, the risk to birds and mammals is likely to be low given the low concentration of the active substance in the spray solution.

Overall it is concluded that the risk to mammals and the acute and short-term risk to birds is low, but a potential high risk to insectivorous birds cannot be excluded for all representative uses evaluated.

5.2. RISK TO AQUATIC ORGANISMS

Zeta-cypermethrin is very toxic to fish and aquatic invertebrates. The lowest endpoints were observed in tests with technical and formulated zeta-cypermethin and *Gammarus pulex* (EC50 = 0.0013 µg a.s./L) The TERs were far below the trigger of 100 and 10 when compared to PECsw from FOCUS step 3. A data requirement for a mesocosm study with zeta-cypermethrin was set by the RMS. Two mesocosm studies with zeta-cypermethrin were submitted by the applicant and evaluated by the RMS in the addendum to the DAR. However, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review. In view of the expert meeting the applicant announced to have obtained access to a mesocosm study with cypermethrin and suggested extrapolating the results to zeta-cypermethrin. This approach was not

required by the RMS or EFSA. It was not presented in the addendum from May 2008 and also not discussed in the experts` meeting. The approach was included and assessed by the RMS in the updated (not peer-reviewed) addendum from July 2008. From a scientific point of view it would be preferable to base the aquatic risk assessment on mesocosm studies conducted with zeta-cypermethrin instead of extrapolating from the results of a mesocosm study with cypermethrin.

During the peer-review it was noted that a fish early life stage study would be triggered since the BCF is >100 and the LC_{50} is < 1mg a.s./L. The available fish juvenile growth test with zeta-cypermethrin was considered as not valid by the experts because of large deviations of measured concentrations from nominal concentrations. The applicant submitted a fish full life cycle test with cypermethrin. The experts were of the opinion that an early life stage test with rainbow trout and zeta-cypermethrin should have been conducted. However, because of animal welfare considerations it was agreed to use the endpoint from an early life stage study with cypermethrin together with a correction factor of 2 which resulted in a NOEC of 0.015 µg a.s./L.

The risk assessment was based on endpoints from standard laboratory tests and maximum initial PECsw values from FOCUS step 4 calculations including a 20 m no-spray buffer zone. The PECsw values were not agreed by the experts on fate and behaviour (see point 4.2) but may be used as a rough estimate. The acute TERs for fish exceeded the Annex VI trigger of 100 in all scenarios for the use in cereals and in all scenarios except R3 and R4 for the use in peas. No full scenario resulted in a TER of >100 for the use in maize. The TERs for aquatic invertebrates were still more than 2 orders of magnitude below the trigger of 100 in all scenarios. The Annex VI long-term trigger of 10 was not met for fish and aquatic invertebrates in any of the FOCUS scenarios.

Formally a bioconcentration study with zeta-cypermethrin and fish was triggered because of the log P_{ow} of 5-6. The log P_{ow} of cypermethrin of 5.3 – 5.6 is similar and the RMS agreed that it may be appropriate to use the BCF value of cypermethrin also for zeta-cypermethrin. Unnecessary animal testing should be avoided and the experts in the PRAPeR meeting agreed to the suggested BCF of 356 – 443 which breaches the Annex VI trigger of 100 for not ready biodegradable substances. However, the risk of bioaccumulation in aquatic food chains was considered to be low since zeta-cypermethrin is applied only once-twice per season and degrades rapidly in the water/sediment studies (DT_{50} whole system = 1.5 – 2.5 days).

The major metabolites *cis*-DCVA, *trans*-DCVA, and *m*PBAcid were of much lower toxicity to aquatic organisms than zeta-cypermethrin. The observed endpoints were > 1 mg/L and the TERs were well above the Annex VI trigger values with initial PEC_{sw} values from FOCUS step 1 calculations.

Overall it is concluded that a high risk to aquatic organisms is indicated for all representative uses evaluated on the basis of the peer-reviewed data.

5.3. RISK TO BEES

Zeta-cypermethrin is very toxic to bees. The acute oral and contact LD_{50} values for zeta-cypermethrin formulated as "Fury 10 EW" were 0.044 and 0.002 µg a.s./bee. The HQ values were above the trigger of 50 indicating a potential high risk to bees. Higher tier cage, tunnel and field tests were submitted. Repellency was observed during the first 1-4 days after treatment. Mortality of adult bees increased for about 4 days following the treatment. No impact on bee brood development was observed in the studies. However, it was noted that no reserves were accumulated in the bee hives. This observation may be explained by the repellent effect of zeta-cypermethrin. The highest application rate used in the studies was 150 mL/ha. This application rate would not cover the use in maize where 0.0375 kg a.s./ha are applied. The experts considered the risk to bees as low for the use in cereals. Risk mitigation measures such as no application during flowering were proposed for the use in peas. A data gap was identified to address the risk to bees further for the use in maize since the available studies do not cover the application rate in maize.

5.4. RISK TO OTHER ARTHROPOD SPECIES

A high in-field risk to non-target arthropods was indicated from the standard laboratory and extended laboratory tests. The applied doses in the field tests were too low for the representative uses. The RMS concluded on a high risk to non-target arthropods and set a data requirement for field studies at appropriate application rates. The experts agreed that the potential high in-field risk and also the off-field risk (initial effects were observed in the field studies, but recovery/recolonisation should not be taken into account in the off-field risk assessment) were not sufficiently addressed by the available studies. The in-field and off-field risk to non-target arthropods needs to be refined further for all representative uses demonstrating that recovery/recolonisation of the in-field area is possible within one year.

5.5. RISK TO EARTHWORMS

The acute toxicity of formulated zeta-cypermethrin and the soil metabolites *cis*-DCVA, *trans*-DCVA and *m*PBAcid was tested. The acute TERs based on PECsoils of 0.038 mg zeta-cypermethrin/kg soil and 0.019 mg/kg soil for each metabolite were several orders of magnitude above the Annex VI trigger value of 10 indicating a low risk to earthworms from the representative uses evaluated. No long-term studies with earthworms were conducted since the DT_{90} in soil is <100 days and zeta-cypermethrin is applied less than 3 times per year.

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

The RMS identified in the DAR the need for studies with soil-dwelling arthropods because of the high toxicity of zeta-cypermethrin to non-target arthropods, and HQ values >2 for the standard indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri*. The experts agreed that studies with

soil-dwelling mites or collembola are formally not triggered since the DT_{90} in soil is <100 days. However, because of the potential high risk to arthropods it was considered necessary that the risk to soil-dwelling arthropods should be addressed in the new field study with non-target arthropods (see data gap above).

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

No effects of >25 % on soil respiration and nitrification were observed in tests with the formulation "Fury 10 EW" at the highest tested concentration of 2 mg formulation/kg soil equivalent to 0.2 mg a.s./kg soil. The maximum initial PECsoils are about one order of magnitude lower than the tested concentrations.

The RMS set a data requirement for the applicant to submit a risk assessment for the soil metabolites *cis*-DCVA, *trans*-DCVA and *m*PBAcid. The applicant commented that the metabolites would have been formed during the test and thus are covered by the risk assessment for the active substance. This line of argumentation was agreed by the experts.

Overall it is concluded that the risk to soil-dwelling micro-organisms is considered to be low for the representative uses evaluated.

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

No effects were observed on seedling emergence of 1 monocotyledon and 2 dicotyledon plant species up to the highest concentration of 100 mg zeta-cypermethrin/kg soil. However, the growth rate of seedlings was reduced at 10 and 100 zeta-cypermethrin/kg soil resulting in an EC_{50} of 43.2 mg zeta-cypermethrin/kg soil. The TERs were far above the trigger of 5 for seedling emergence and growth rate at an off-field dose of 1.39 µg a.s./kg soil (2.77% of the application rate in maize = 1.04 g a.s./ha assuming a soil depth of 5cm and a soil density of 1.5 kg/dm^3). The risk to non-target plants in the off-field area was assessed as low for all representative uses evaluated.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The study which was submitted by the applicant was considered as not valid by the RMS since it was not conducted according to guidelines and cypermethrin was tested instead of zeta-cypermethrin. A new study with zeta-cypermethrin was submitted by the applicant and evaluated by the RMS in the addendum to the DAR from May 2008. However, in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new study could not be considered in the peer review. Therefore a data gap remains.

6. Residue definitions

Soil

Definition for risk assessment:	component isomers of cypermethrin, DCVA and *m*PBAcid
Definition for monitoring:	sum of component isomers of cypermethrin

Water

Ground water

Definition for exposure assessment:	at least component isomers of cypermethrin, DCVA and *m*PBAcid, though a data gap needs to be filled before this definition can be finalised.
Definition for monitoring:	a data gap needs to be filled before this can be finalised

Surface water

Definition for risk assessment:	
surface water:	component isomers of cypermethrin, DCVA and *m*PBAcid
sediment:	component isomers of cypermethrin, DCVA and *m*PBAcid
Definition for monitoring:	sum of component isomers of cypermethrin

Air

Definition for risk assessment:	component isomers of cypermethrin.
Definition for monitoring:	sum of component isomers of cypermethrin.

Food of plant origin

Definition for risk assessment:	cypermethrin, including other mixtures of constituent isomers (sum of isomers)
Definition for monitoring:	cypermethrin, including other mixtures of constituent isomers (sum of isomers)

Food of animal origin

Definition for risk assessment:	cypermethrin, including other mixtures of constituent isomers (sum of isomers)
Definition for monitoring:	cypermethrin, including other mixtures of constituent isomers (sum of isomers)

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
Component isomers of cypermethrin	Low to medium persistence Single first order DT_{50} 89 days (20°C, -10kPa soil moisture) DT_{50} 6-24 days DT_{90} 37-80 days (field studies)	The risk to earthworms and soil micro-organisms was assessed as low. However data are needed for soil-dwelling arthropods.
DCVA (sum of isomers)	Low persistence Single first order DT_{50} 2.4-9.5 days (20°C, -10kPa soil moisture)	The risk to soil-dwelling organisms was assessed as low.
*m*PBAcid	Low persistence Single first order DT_{50} 2.7-7.0 days (20°C, -10kPa soil moisture)	The risk to soil-dwelling organisms was assessed as low.

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
Component isomers of cypermethrin	immobile K_{foc} 72405-285652 mL/g	No	Yes	Yes	Yes
trans-DCVA	Very high mobility K_{foc} 18-48 mL/g	No	No information available, not needed	No information available, not needed	No Low risk to aquatic organisms.
*m*PBAcid	High to medium mobility K_{foc} 118-215 mL/g	No	No information available, not needed	No information available, not needed	No Low risk to aquatic organisms.

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Component isomers of cypermethrin	Very toxic to fish and aquatic invertebrates. A high risk was indicated in the risk assessment for all representative uses.
DCVA (sum of isomers)	Toxicity several orders of magnitude less than for zeta-cypermethrin. Low risk to aquatic organisms.
*m*PBAcid	Toxicity several orders of magnitude less than for zeta-cypermethrin. Low risk to aquatic organisms.

Air

Compound (name and/or code)	Toxicology
Component isomers of cypermethrin	Harmful by inhalation (risk phrase R20 proposed)

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

- Further information or indications available to ensure that none of mentioned unknown compounds is present at a concentration higher than 1 g/kg (relevant for all representative uses evaluated, data gap identified by PRAPeR 46 meeting of experts (May 2008), date of submission unknown; refer to chapter 1)
- 5-batch analysis for the actual industrial scale production. (relevant for all representative uses evaluated, data gap identified by PRAPeR 46 meeting of experts (May 2008), date of submission unknown; refer to chapter 1)
- A revised technical specification taking into account the recommendations of the PRAPeR 46 meeting (relevant for all representative uses evaluated, data gap identified by PRAPeR 46 meeting of experts (May 2008), date of submission unknown; refer to chapter 1)
- An alternative method as replacement for the non-specific method for the determination of impurities (APG 428A) and data on the specificity of the methods used for the determination of significant impurities (relevant for all representative uses evaluated, data gap identified by PRAPeR 46 meeting of experts (May 2008), data were submitted in August 2007, presented in an addendum to Vol. 4 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 1)
- Shelf-life study of the NPE-free formulation (relevant for all representative uses evaluated, data gap identified by PRAPeR 46 meeting of experts (May 2008), data were submitted in August 2007, presented in an addendum to Vol. 3 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 1)
- To address the stability of dilute emulsions and preparations which are emulsions (relevant for all representative uses evaluated, data gap identified by PRAPeR 46 meeting of experts (May 2008), data were submitted in August 2007, presented in an addendum to Vol. 3 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 1)
- To address the resistance of the packaging material to “Fury 10 EW NP Free” (relevant for all representative uses evaluated, data gap identified by PRAPeR 46 meeting of experts (May 2008), data were submitted in August 2007, presented in an addendum to Vol. 3 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 1)

- To address a cypermethrin/zeta-cypermethrin bridging study confirming that there is any preferential metabolism of certain isomers in plant and that the metabolism studies performed with cypermethrin only are also relevant for zeta-cypermethrin. These data were submitted in August 2007, presented in an addendum to Vol. 3 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 3.1)
- Depending on the outcome of the requested residue trials on maize silage and its impact on the animal burden calculations, additional information on the fate of the cyclopropyl moiety in ruminant metabolism, including available data from public literature should be provided. These data were submitted in August 2007, presented in an addendum to Vol. 3 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 3.2)
- To address validation data for the analytical methods used for the generation of the residue trials performed on maize, cereals and peas. These data were submitted in August 2007, presented in an addendum to Vol. 3 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 3.4)
- To address additional residue trials on maize in northern and southern EU supporting the critical dose rate of application and the critical growth stage in order to confirm the provisional MRL value. A complete residue data set is also requested on maize silage. These data were submitted in August 2007, presented in an addendum to Vol. 3 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 3.1)
- To address additional residue data on barley, pulses in order to confirm the provisional MRL value. These data were submitted in August 2007, presented in an addendum to Vol. 3 in May 2008, however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to chapter 3.1).
- An aerobic soil laboratory route of degradation study dosed with zeta-cypermethrin; it is advised that any new study carried out should utilise chiral analytical methods (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; data gap identified in the DAR and confirmed in the meeting of experts; refer to point 4.1.1)
- An anaerobic soil laboratory degradation study (only relevant for the use evaluated of autumn applications to winter cereals in territories where anaerobic conditions cannot be excluded; submission date proposed by the notifier: unknown; data gap confirmed in the meeting of experts; refer to point 4.1.1)

- A ready biodegradability test (relevant for all representative uses evaluated), study already provided by the notifier and evaluated by the RMS in addendum to B.8 dated May 2008 but in accordance with Commission Regulation (EC) No 1095/2007, the new study could not be considered in the peer review; data gap identified in the DAR and confirmed in the meeting of experts; refer to point 4.2.1)
- FOCUS surface water modelling at step 4 for component isomers of cypermethrin. Simulations to utilise single first order soil DT_{50} 15.1 days, water DT_{50} 1000 days, sediment DT_{50} 6.1 days, K_{foc} 121786 mL/g, 1/n=1.3 and include single as well as multiple applications. Sediment as well as surface water concentrations must be reported. Drift inputs to be mitigated by a maximum of 95%. If run-off is mitigated, the mitigation must not exceed 90% (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; data gap confirmed when EFSA was drafting the conclusion; refer to point 4.2.1)
- Zeta-cypermethrin consists of 4 enantiomers. This needs to be taken into account in the environmental risk assessment. Information on the ecotoxicity and/or on the degradation/ possible epimerisation of the different enantiomers in the environment is needed. (relevant for all representative uses evaluated; no submission date proposed by the applicant; refer to sections 4 and 5).
- A refined long-term risk assessment for insectivorous birds is required (relevant for all representative uses evaluated; data gap identified in the PRAPeR 48 meeting of experts in May 2008; no submission date proposed by the applicant; refer to point 5.1.)
- A refined long-term risk assessment for herbivorous birds is required (relevant for the representative use in maize; data gap identified in the PRAPeR 48 meeting of experts in May 2008; no submission date proposed by the applicant; refer to point 5.1.)
- The aquatic risk assessment needs further refinement (relevant for all representative uses evaluated; data requirement for a mesocosm study with zeta-cypermethrin was identified in the DAR by the RMS; two mesocosm studies with zeta-cypermethrin were submitted by the applicant and evaluated by the RMS in the addendum from May 2008; however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to point 5.2.)
- The risk to bees needs to be addressed further (relevant for the representative use in maize; data requirement identified in the DAR by the RMS and confirmed as a data gap in the PRAPeR 48 meeting of experts in May 2008; no submission date proposed by the applicant; refer to point 5.3.)
- The risk to non-target arthropods needs to be addressed further (e.g. field studies) including the risk to soil-dwelling non-target arthropods (relevant for all representative uses; data

requirement identified in the DAR by the RMS and confirmed as a data gap in the PRAPeR 48 meeting of experts in May 2008; no submission date proposed by the applicant; refer to points 5.4. and 5.6.)

- A study investigating effects of zeta-cypermethrin on biological methods of sewage treatment (relevant for all representative uses; study submitted by the applicant and evaluated by the RMS in the addendum from May 2008; however in accordance with Commission Regulation (EC) No 1095/2007, the new data could not be considered in the peer review; refer to point 5.9.)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide as proposed by the applicant, which comprise: foliar spraying to control European cornborer (*Ostrinia nubilalis*) and pink stalk borer (*Sesamia nonagrioides*) in maize, in all EU countries, at single application, at maximum application rate per treatment of 37.5 g a.s./ha;

- foliar spraying to control leaf, flag and ear aphids in cereals, up to growth stage of BBCH 69, in all EU countries, at a maximum of 2 treatments, at maximum application rate per treatment of 15 g a.s./ha, interval between applications of 2-4 weeks, and
- foliar spraying to control pea aphids, pea moth (*Cydia nigricana*) pea weevil (*Bruchus pisorum*) and *Thrips ssp* in peas, in all EU countries, at a maximum of 2 treatments, at maximum application rate per treatment of 15 g a.s./ha, interval between applications of 2-4 weeks.

The representative formulated product for the evaluation was “Fury 10 EW (NP Free)”, an emulsion, oil in water (EW) containing 100 g/L (96.9 g/kg) zeta-cypermethrin, registered under different trade names in Europe.

The technical specification for the active substance was based on pilot scale production and was only partially accepted by the PRAPeR meeting of experts (May 2008).

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

Adequate methods are available to monitor cypermethrin (sum of isomers) residues in food/feed of plant- and animal origin, environmental matrices and in body fluids and tissues.

As for mammalian toxicology, the dossier submitted contained studies on both zeta-cypermethrin and cypermethrin. Considering the ratio of the most potent isomers between zeta-cypermethrin and cypermethrin and focusing on neurotoxicity (difference using the NOAELs and LOAELs of rat studies), a factor of 2 could be established showing that zeta-cypermethrin is more toxic than cypermethrin. When orally administered, zeta-cypermethrin is toxic (proposed to be classified T, R25 – "toxic if swallowed"). It is harmful for inhalation (Xn, R20). No toxic effects were observed after dermal exposure. It is not irritating to eyes or skin but is a skin sensitizer in a Buehler test (Xi, R43 - "irritant; may cause sensitisation by skin contact"). Neurotoxicity is the target effect of zeta-cypermethrin for short term exposures. The relevant NOAEL of 7.5 mg/kg bw/day is derived from the 2-year feeding study in dogs. The classification as R48/22 ("danger of serious damage to health by prolonged exposure, if swallowed") was proposed based on mortality in several studies. Overall, it was concluded that zeta-cypermethrin is neither genotoxic nor carcinogenic under experimental conditions (carcinogenicity was tested with cypermethrin). The relevant long term toxicity and carcinogenicity NOAEL of 7.5 mg/kg bw/day is from the 2-year rat study. The relevant parental and offspring NOAEL in multigeneration studies is 5.9 mg/kg bw/day, while the reproductive NOAEL is 22 mg/kg bw/day. Zeta-cypermethrin was negative for developmental toxicity when tested in rats. The relevant maternal NOAEL in rat and rabbit are 12.5 and ≥120 mg/kg bw/day, respectively; the relevant developmental NOAEL are 35 mg/kg bw/day in rat and ≥120 mg/kg bw/day in rabbit. Zeta-cypermethrin is a neurotoxic agent (acute and subchronic NOAELs 10 mg/kg bw and 5 mg/kg bw/day, respectively). The ADI is 0.04 mg/kg bw/day, based on the overall cypermethrin NOAEL for dogs of 7.5 mg/kg bw/day and a 100-fold safety factor with an additional factor of 2 for the higher toxicity of zeta-cypermethrin vs. cypermethrin. The ARfD is 0.125 mg/kg bw based on the developmental toxicity study in rats supported by the acute neurotoxicity with zeta-cypermethrin, applying a SF of 100. An AOEL of 0.02 mg/kg bw/day was based on the overall cypermethrin NOAEL for dogs of 7.5 mg/kg bw/day using a 100-fold safety factor with an additional factor of 2 for the higher toxicity of zeta-cypermethrin and correcting for 50% oral absorption. The estimated operator, worker and bystander exposure is below the AOEL even without the use of PPE.

In order to support the uses of zeta-cypermethrin the applicant submitted plant metabolism studies performed with cypermethrin. Several groups of plants were investigated: root crops (sugar beet), cereals (maize), pulses/oilseeds (cotton), fruit crops (apples) and leafy crops (lettuce). The major degradation pathway of cypermethrin starts with the cleavage of the parent molecule to yield *cis/trans* DCVA and the *m*PBAldehyde, this latter metabolite being further oxidised or reduced to the corresponding *m*PBAcid or *m*PBAlcohol followed by conjugations. In most of the plant matrices

investigated, unchanged cypermethrin was the predominant residue accounting for more than *c.a.* 50% of the TRR. The meeting discussed on whether the plant metabolism studies performed with cypermethrin were relevant for zeta-cypermethrin and if a preferential metabolism may be suspected for some isomers with a special impact on toxicology. A bridging study on maize detailing the respective metabolism of both cypermethrin and zeta-cypermethrin was provided by the applicant, but in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new study could not be considered in the peer review. However, and taking into account the no residue situation resulting from the intended uses on cereals, maize and peas, the meeting was of the opinion that the possible isomeric conversion from less to more toxic isomers would not be significant, and concluded that a residue definition can be proposed, based on the metabolism studies performed with cypermethrin. Finally, it was concluded that a global residue definition has to be proposed in order to take into account the various mixtures of cypermethrin isomers available on the market. Thus for plants, the residue for monitoring and risk assessment was defined as "cypermethrin, including other mixtures of constituent isomers (sum of isomers)".

Numerous supervised residue trials performed with zeta-cypermethrin were submitted to propose MRLs. Nevertheless, some of them were rejected since growth stages at application were not in compliance with the critical GAP and/or analytical methods were not sufficiently validated. Finally, MRLs were defined for wheat, triticale and pea without pods and, awaiting the evaluation of additional data provided by the applicant that could not be considered in the peer review in accordance with Commission Regulation (EC) No 1095/2007, provisional MRLs were proposed for maize, barley, oat, pea with pods and pulses. No degradation of residues was observed for zeta-cypermethrin in different plant and animal matrices when stored under frozen conditions for up to 18 months. Some instability was observed at some time points for the metabolites *m*PBAcid and *cis* DCVA in some animal matrices, but globally, the results were considered acceptable. No processing studies were provided since no significant residues were observed in any commodities supporting the representative uses. However, the EFSA noted that the cypermethrin hydrolysis breakdown product *m*PBAldehyde, was found in a tomato processing study, and this compound is suspected of endocrine activity. This concern was considered to be not relevant for the intended uses supported in the DAR but the meeting noted that this point has to be re-considered if additional uses are envisaged.

Lactating cow and laying hen metabolism studies performed with cypermethrin were evaluated. The major route of degradation consisted of the hydrolysis of ester linkage to generate the *cis* and *trans* DCVA moiety and the *m*PBAldehyde, which undergoes further oxidation and/or reduction to the

corresponding acid (*m*PBAcid) or alcohol (*m*PBAlcohol) and their hydroxy products. The metabolism of the cyclopropyl moiety was considered as insufficiently investigated in the ruminant metabolism study, since the additional data from literature presented in the addendum of May 2008 could not be considered in the peer review in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007. This point remains open and has to be re-considered. Nevertheless, and taking into account the complete metabolic pathway in poultry, and the data from the rat metabolism study indicating a similar pathway, the meeting of experts concluded that there was enough evidence to propose the residue for monitoring and risk assessment for animal products as "cypermethrin, including other mixtures of constituent isomers (sum of isomers)". Considering the potential livestock exposure to zeta-cypermethrin residues through consumption of treated feed items (maize, cereals, pea and pulses), feeding studies indicate that no measurable residues may be present above the LOQ in the different animal products and the MRLs for animal commodities were proposed at LOQ values.

Considering the representative uses and the toxicological endpoints set for zeta-cypermethrin, no chronic or acute concerns were observed, the theoretical maximum daily intake (TMDI) being less than 2% of the ADI and the maximum national estimated short term intake (NESTI) less than 1% of ARfD. In addition, the meeting concluded on the need for a global risk assessment taking into account the other sources of exposure resulting from the uses of all other cyprermethrin isomer mixtures available on the market and their respective toxicological reference values.

The information available on the fate and behaviour in the environment is sufficient to carry out an environmental exposure assessment at EU level with the notable exception that a satisfactory aerobic soil route of degradation study dosed with zeta-cypermethrin is not available. These data are necessary to confirm whether or not additional metabolites >5% AR are formed in soil, which would trigger an assessment of leaching to groundwater. Therefore the assessment of groundwater exposure by metabolites cannot be finalised. For the applied for intended uses, the potential for groundwater exposure by component isomers of cypermethrin or the known metabolites *m*PBAcid and *trans*-DCVA above the parametric drinking water limit of 0.1 µg/L is low. In territories where anaerobic soil conditions cannot be excluded and autumn or winter applications are requested, the necessary data pertaining to the fate and behaviour of zeta-cypermethrin under anaerobic soil conditions are not available. The peer review did not determine any information on the behaviour of individual component isomers of cypermethrin in the environment following application of zeta-cypermethrin, due to a combination of the way analytical results were conveyed in the dossier and DAR and the

fact that chiral methods of analysis were not employed in the available studies (with the exception of the investigation of alkaline sterile aqueous hydrolysis conditions). Finally, though not requiring additional experimental information, the available FOCUS surface water simulations for components of the active substance are not satisfactory at steps 3 and 4 and a data gap is identified for new simulations at step 4. Some relatively crude estimates of surface water exposure have been provided by EFSA, or in the case of maize extracted from the available simulations, to enable an aquatic risk characterisation to be made. However, risk managers should be aware that these exposure assessments do not comply with agreed methodologies in EU FOCUS surface water guidance.

The risk to mammals was assessed as low but further refinement of the long-term risk assessment is needed for insectivorous birds for all representative uses. Zeta-cypermethrin is very toxic to fish and aquatic invertebrates. The aquatic risk assessment was based on preliminary FOCUS step 4 PECsw values which included a 20m no-spray buffer zone. The acute TERs for fish exceeded the Annex VI trigger of 100 in all scenarios for the use in cereals and in all scenarios except R3 and R4 for the use in peas. However no full scenario resulted in a TER of >100 for the use in maize and the long-term TERs were significantly below the Annex VI trigger of 10 in all scenarios even with a no-spray buffer zone of 20m. A data gap was identified for further refinement of the aquatic risk assessment. Two mesocosm studies with zeta-cypermethrin were submitted by the applicant, but in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new studies could not be considered in the peer review. The risk to aquatic organisms from the metabolites *cis*-DCVA, *trans*-DCVA and *m*PBAcid was assessed as low. Zeta-cypermethrin is very toxic to bees and a potential high risk was indicated in the first-tier risk assessment. On the basis of higher tier data the risk to bees was considered to be addressed for the use in cereals but not for the use in maize. Risk mitigation measures such as no application during flowering were proposed for the use in peas. A high in-field risk to non-target arthropods was indicated from the standard laboratory and the extended laboratory tests. A data gap was identified to address further the in-field and the off-field risk to non-target arthropods for all representative uses. Although formally not triggered, the experts considered it necessary to address the risk to soil dwelling mites and collembola because of the potential high risk to arthropods. It was suggested that investigation of soil dwelling mites and collembola should be included in a field study with non-target arthropods. The study on effects on respiration of activated sewage sludge was assessed as not valid. A new study was submitted by the applicant, but in view of the restrictions concerning the acceptance of new studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No 1095/2007, the new studies could not be considered in the peer review.

The risk to earthworms, soil non-target micro-organisms and non-target plants was assessed as low.

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

- Risk mitigation is necessary for the use in peas to protect bees. The product should not be applied during flowering/bee flight activity. Appropriate labelling is required at Member State level.

Critical areas of concern

- When considering new applications for uses beyond those supported in this review, particular attention should be given to the possible presence of the hydrolysis breakdown product 3-phenoxybenzaldehyde (*m*PBAldehyde), found in a cypermethrin tomato processing study and suspected of endocrine activity.
- The groundwater exposure assessment for metabolites cannot be finalised without the provision of additional data. It was considered necessary to at least have a guideline laboratory aerobic soil route of degradation study dosed with zeta-cypermethrin available to progress such an assessment.
- The long-term risk to insectivorous birds needs to be refined further for all representative uses.
- A high risk to aquatic organisms was indicated.
- The risk to bees is not sufficiently addressed for the use in maize.
- The risk to non-target arthropods needs to be addressed further for all uses evaluated.

Appendix 1 – list of endpoints

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

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

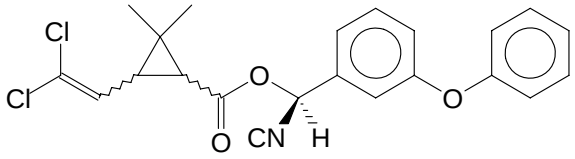
Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Zeta-cypermethrin
Function (*e.g.* fungicide)	Insecticide
Rapporteur Member State	Belgium

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	Mixture of the stereoisomers (*S*)-α-cyano-3-phenoxybenzyl (1*RS*,3*RS*;1*RS*,3*SR*)-3-(2,2-dichlorovinyl)-2,2 dimethylcyclopropanecarboxylate where the ratio of the (*S*);(1*RS*,3*RS*) isomeric pair to the (*S*);(1*RS*,3*SR*) isomeric pair lies in the ratio range 45-55 to 55-45 respectively
Chemical name (CA) ‡	(*S*)-cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate
CIPAC No ‡	733
CAS No ‡	52315-07-8 (undefined stereochemistry, also used for cypermethrin)
EEC No (EINECS or ELINCS) ‡	257-842-9
FAO Specification (including year of publication)‡	No FAO specification available
Minimum purity of the active substance as manufactured (g/kg) ‡	850 g/kg (pilot scale production) *Cis/trans*-ratio should be in range 55/45 – 45/55
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	toluene, max. 2 g/kg tars, max. 12.5 g/kg

Appendix 1 – list of endpoints

Molecular formula ‡	$C_{22}H_{19}Cl_2NO_3$
Molecular mass ‡	416.31 g/mol
Structural formula ‡	

Appendix 1 – list of endpoints

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	- 3°C (85.3%)
Boiling point (state purity) ‡	> 360°C (86.8%)
Temperature of decomposition (state purity)	Not applicable
Appearance (state purity) ‡	Pale yellow, viscous liquid, no significant odour (86.8%)
	Dark reddish brown, very viscous liquid, very faint aromatic odour (83%)
Vapour pressure (state temperature, state purity) ‡	2.53 x 10^{-7} Pa at 25°C (86.8%)
Henry's law constant ‡	2.3 x 10^{-3} $Pa.m^3.mol^{-1}$
Solubility in water (state temperature, state purity and pH) ‡	distilled water (neutral pH), 20°C: 0.0387 mg/L (85.3%)
	No effect of pH (zeta-cypermethrin does not dissociate)
Solubility in organic solvents (state temperature, state purity) ‡	At 20°C (84.43%): *n*-heptane: 40.12 g/L; *p*-xylene, 1,2-dichloroethane, acetone and ethyl acetate: > 1000 g/L; At 25°C (85.3%): methanol, ethyl acetate: readily soluble (>1000 g/L)
Surface tension (state concentration and temperature, state purity) ‡	59.5 mN/m at 25°C (90% saturated solution) (84.43%)
Partition co-efficient (state temperature, pH and purity) ‡	pH 2, 24°C: log P_{OW} = 5 – 6 (85.3%)
	Effect of pH was not investigated, since there is no dissociation in water in the environmentally relevant pH range.
Dissociation constant (state purity) ‡	Not applicable (no dissociation in water occurs) (theoretical justification)

Appendix 1 – list of endpoints

<table>
<tr><td>UV/VIS absorption (max.) incl. ε (state purity, pH) ‡</td><td>85.3% pure, in methanol:
<table>
<tr><th></th><th>λ_{max} (nm)</th><th>ε (L.mol^{-1}.cm^{-1})</th></tr>
<tr><td rowspan="2">acidic</td><td>278</td><td>2472</td></tr>
<tr><td>at λ 290 nm</td><td>765</td></tr>
<tr><td rowspan="2">neutral</td><td>278</td><td>2468</td></tr>
<tr><td>at λ 290 nm</td><td>765</td></tr>
<tr><td>alkaline</td><td colspan="2">formation of hydrolysis product with absorption max. at 308 nm; no significant change upon neutralisation</td></tr>
</table>
86.8% pure, in acetonitrile:
<table>
<tr><th>λ_{max} (nm)</th><th>ε (L.mol^{-1}.cm^{-1})</th></tr>
<tr><td>277</td><td>2170</td></tr>
</table></td></tr>
<tr><td>Flammability (state purity) ‡</td><td>Auto-flammable (auto-ignition temperature = 390°C) (84.7%)
Flash point = 181°C (82.6%)</td></tr>
<tr><td>Explosive properties (state purity) ‡</td><td>Not explosive (statement)</td></tr>
<tr><td>Oxidising properties (state purity)) ‡</td><td>Not oxidising (theoretical justification)</td></tr>
</table>

Appendix 1 – list of endpoints

Summary of representative uses evaluated (zeta-cypermethrin)*

Crop and/or situation (a)	Member State or Country	Product name	F G 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 a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Maize ZEAMX	EU	Fury 10 EW	F	Ostrinia nubilalis (European cornborer)	EW	100 g/l	Spraying	1 to 1.20 m of crop or 50 % male flowering	1	-	0.025-0.009	150 - 400	0.0375	56	[1] [2]
				Sesamia nonagrioides (Pink stalk borer)				Early stages, Apply acc. warnings from officials(1)							

* Uses for which the risk assessment cannot be concluded are marked grey.

Appendix 1 – list of endpoints

Cereals NNNGG (winter/spring wheat, barley, triticale and spring oat)	EU	Fury 10 EW	F	Leaf, flag and ear aphids	EW	100 g/l	Spraying	Apply acc. warnings from officials(1) The latest time of application is BBCH 69 (End of flowering-35 days before harvest).	2	2- 4 weeks	0.01 - 0.0037	150 - 400	0.015	28	[1]
Peas PIBST	EU	Fury 10 EW	F	Pea aphids Pea moth (Cydia nigricana) Pea weevil (Bruchus pisorum) Thrips ssp	EW	100 g/l	Spraying	Apply acc. warnings from officials(1) During early stages of crop developmen t	2	2 - 4 weeks	0.01 - 0.0037	150 - 400	0.015	14	[1]

Appendix 1 – list of endpoints

[1] A high risk and/or data gaps were identified for insectivorous birds, aquatic organisms and non-target arthropods.
[2] The risk to bees needs to be addressed further.

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)
(c) Outdoor or field use (F), glasshouse application (G) or indoor
(d) application (I)
(e) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(f) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(g) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(h) All abbreviations used must be explained
Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between
the plants - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions

(1) : For the pests intended to be controlled, spraying is only recommended when official warnings are given that the pests are likely to reach economically damaging levels. This avoids the use of prophylactic treatments and is a key component of integrated pest management. It is therefore impossible to provide exact growth stages but applications are most likely to be made late spring/summer.

Appendix 1 – list of endpoints

METHODS OF ANALYSIS

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

Technical as (analytical technique)	Zeta-cypermethrin: HPLC-UV
Impurities in technical as (analytical technique)	GPC-Light Scattering Karl Fischer (CIPAC MT 30) HPLC-UV GC-FID
Plant protection product (analytical technique)	Zeta-cypermethrin: HPLC-UV (CIPAC method 332/EC/M/3.2 available for the determination of the total cypermethrin content)

Analytical methods for residues (Annex IIA, point 4.2)

RESIDUE DEFINITIONS FOR MONITORING PURPOSES

Food of plant origin		Cypermethrin, including other mixtures of constituent isomers (sum of isomers)
Food of animal origin		Cypermethrin, including other mixtures of constituent isomers (sum of isomers)
Soil		Sum of component isomers of cypermethrin
Water	Surface	Sum of component isomers of cypermethrin
	Drinking/ground	Sum of component isomers of cypermethrin
Air		Sum of component isomers of cypermethrin

Appendix 1 – list of endpoints

MONITORING/ENFORCEMENT METHODS

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Multi method DFG S19: GC-ECD, conf. by GC-MSD; or GC with column of different polarity; Cypermethrin (sum of isomers): LOQ = 0.01 mg/kg (whole orange, tomato, wheat) GC-MSD; Cypermethrin (sum of isomers): LOQ = 0.02 mg/kg (maize)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Multi method DFG S19: GC-ECD, conf. by GC-MSD; Cypermethrin (sum of isomers): LOQ = 0.01 mg/kg (milk), 0.05 mg/kg (egg, muscle, fat)
Soil (analytical technique and LOQ)	GC-ECD (conf. method: column of different polarity); Cypermethrin (sum of isomers): LOQ = 0.005 mg/kg
Water (analytical technique and LOQ)	GC-ECD (conf. by GC-MS/MS); Cypermethrin (sum of isomers): LOQ = 0.05 µg/L (drinking water and ground water); LOQ = 0.001 µg/L (surface water)
Air (analytical technique and LOQ)	GC -ECD, conf. by GC-MSD; Cypermethrin (sum of isomers): LOQ = 1.7 µg/m³
Body fluids and tissues (analytical technique and LOQ)	GC-ECD, conf. by GC-MSD; Cypermethrin (sum of isomers): LOQ = 0.05 mg/kg (liver, kidney and blood)

Classification and proposed labelling (Annex IIA, point 10)

With regard to physical/chemical data	None

Appendix 1 – list of endpoints

Impact on Human and Animal Health

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

(cypermethrin)

Rate and extent of absorption ‡	50% based on urinary excretion within 24 h Lower absorption at high dose levels
Distribution ‡	Initially widely distributed; highest residues in fat and skin at 8 days
Potential for accumulation‡	Fat ($T_{1/2}$ > 24 h)
Rate and extent of excretion ‡	Rapid and extensive (> 95%) within 1-3 days, mainly via urine (53-74%) and feces (19-35.5%)
Metabolism in animals ‡	Extensively metabolized (>95%) by ester cleavage to 2, 2-dimethyl-3- (2, 2-dichlorovinyl)cyclopropane carboxylic acid and 3-phenoxybenzoyl moiety; further conjugation and oxidation. Most faecal radioactivity was unchanged parent compound
Toxicologically relevant compounds (animals and plants and environment) ‡	Parent compound
Toxicologically relevant compounds (environment) ‡	Parent compound

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡ *(zeta-cypermethrin)*	LD_{50} male= 134 mg/kg bw LD_{50} female= 86 mg/kg bw	**T, R25**
Rat LD_{50} dermal ‡ *(zeta-cypermethrin)*	LD_{50}>2000 mg/kg bw	
Rat LC_{50} inhalation ‡ *(cypermethrin)*	LC_{50}= 1.26 mg/L	**Xn, R20**
Skin irritation ‡ *(zeta-cypermethrin)*	Not irritating	
Eye irritation ‡ *(zeta-cypermethrin)*	Not irritating	
Skin sensitization (test method used and result) ‡ *(zeta-cypermethrin)*	Sensitiser (Buehler test)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Nervous system (block closing gate sodium channels), mortality and severe clinical signs at high dose levels	
Lowest relevant oral NOAEL ‡ *(cypermethrin)*	2-year dog study: 7.5 mg/kg bw/d	**Xn, R48/22**
Lowest relevant dermal NOAEL ‡ *(zeta-cypermethrin)*	< 100 mg/kg bw/d for local effects, > 1000 mg/ kg bw/d for systemic effects	

Appendix 1 – list of endpoints

Lowest relevant inhalation NOAEL ‡ *(cypermethrin)*	10 µg/L (2.7mg/kg bw)	

Genotoxicity (Annex IIA, point 5.4) ‡ *(zeta-cypermethrin)*	No evidence of genotoxicity	

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

Target/critical effect ‡	Nervous system toxicity (rat)	
Lowest relevant NOAEL ‡	7.5 mg/kg bw/d, 2-year, rat	
Carcinogenicity ‡	No carcinogenic potential	

Reproductive toxicity (Annex IIA, point 5.6) *(zeta-cypermethrin)*

Reproduction target / critical effect ‡	Reduced pup body weight during lactation and pup mortality at parental toxic doses	
Relevant parental NOAEL ‡	5.9 mg/kg bw/d	
Relevant reproductive NOAEL ‡	22 mg/kg bw/d	
Relevant offspring NOAEL ‡	5.9 mg/kg bw/d	

Developmental toxicity *(zeta-cypermethrin)*

Developmental target / critical effect ‡	Decreased body weight at maternal toxic doses	
Relevant maternal NOAEL ‡	Rat: 12.5 mg/kg bw/d Rabbit ≥120 mg/kg bw/d	
Relevant developmental NOAEL‡	Rat: 35 mg/kg bw/d Rabbit ≥120 mg/kg bw/d	

Neurotoxicity / Delayed neurotoxicity (Annex IIA, point 5.7) ‡

Acute neurotoxicity‡ *(zeta-cypermethrin)*	NOAEL = 10 mg/kg bw	
Repeated neurotoxicity ‡ *(zeta-cypermethrin)*	NOAEL = 5 mg/kg bw/d	
Delayed neurotoxicity‡	No data-not required	

Other toxicological studies (Annex IIA, point 5.8) ‡

Mechanistic studies‡	- Developmental neurotoxicity study in rats: NOAEL maternal and developmental toxicity = 9 mg/kg bw/d. (maternal and offspring: reduced bw gain) no developmental neurotoxic potential *(zeta-cypermethrin)*

Appendix 1 – list of endpoints

	- Detection/measurement of cypermethrin in maternal plasma and milk as well as in fetuses[21]

Medical data (Annex IIA, point 5.9) ‡

	With the voltage-dependent sodium channel as the target site, pyrethroids induce pronounced repetitive activity characterized grossly by tremor, hypersensitivity, choreoathetosis, and salivation. Cyano-pyrethroids cause transient skin paraesthesia in workers.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.04	Dog, 2 and 1 year study (overall NOAEL)	100×2*
AOEL ‡	0.02	Dog, 2 and 1 year study (overall NOAEL)	100×2*×2**
ARfD ‡	0.125	Rat, developmental study and acute neurotoxicity study	100

**Assessment factor is increased by a factor of 2: in the absence of a dog study with zeta-cypermethrin, a cypermethrin study was used. (zeta-cypermethrin is 2 times more neurotoxic than cypermethrin)*
***Correction for oral absorption (50%)*

Dermal absorption (Annex IIIA, point 7.3) ‡

Fury 10 EW	10% default value

Exposure scenarios (Annex IIIA, point 7.2) ‡

Operator	The estimated exposure for Fury 10 EW according to the -UK POEM model (application rate 37.5 g a.i/ha): Tractor mounted equipment: Field crop with PPEs: 91% of AOEL High crop with PPEs: 104% of AOEL -German Model: Field crop with PPEs: 9.1% High crop with PPEs: 9.4%

[21] R64 to be considered by EChA

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Workers	0.47% of AOEL with PPEs
Bystanders	0.6% of AOEL w/o PPEs (Lloyd and Bell)

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

Zeta cypermethrin	RMS proposal/peer review proposal
	T ; R25 Xn ; R20 Xn ; R48/22 Xi ; R43

Appendix 1 – list of endpoints

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

Plant groups covered	Root and tuber vegetables (sugar beet); cereals (corn); oilseeds (cotton); fruit (apples); leafy vegetables (lettuce) – Cypermethrin metabolism data. Cereals (corn): Zeta-cypermethrin metabolism study
Rotational crops	Wheat, sugar beet, cotton and lettuce – Cypermethrin data.
Metabolism in rotational crops similar to metabolism in primary crops ?	Yes.
Processed commodities	Processing studies not required.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not relevant.
Plant residue definition for monitoring	Cypermethrin, including other mixtures of constituent isomers (sum of isomers)
Plant residue definition for risk assessment	Cypermethrin, including other mixtures of constituent isomers (sum of isomers)
Conversion factor (monitoring to risk assessment)	none

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

Animals covered	Lactating cows, laying hens – Cypermethrin metabolism data.
Time needed to reach a plateau concentration in milk and eggs	**Milk* : The residue levels reached a plateau on the 4th day of dosing **Eggs :yolks* : The plateau level occurred on day 8 of exposure. **Egg whites* : The total residues plateaued on dosing day 7.
Animal residue definition for monitoring	Cypermethrin, including other mixtures of constituent isomers (sum of isomers)
Animal residue definition for risk assessment	Cypermethrin, including other mixtures of constituent isomers (sum of isomers)
Conversion factor (monitoring to risk assessment)	none
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes Log P*o/w* for cypermethrin = 5.3-5.6 at 25 °C. Log P*o/w* for zeta-cypermethrin = 5-6 at pH : 2.

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

Appendix 1 – list of endpoints

The experimental design to conduct the rotational crop study (Woods T.M., 1980) consisted of a soil application at a dose rate of 1 kg a.s./ha and is considered as acceptable. Although non-negligible amounts of radioactivity were recovered in the control plants, it can be assumed that the residue levels in the edible parts of the rotational crops at harvest will be below 0.01 mg/kg. According to the guidance doc. 7524/VI/95 rev.2, no rotational crop study should be triggered (median DT $_{90f}$ Cypermethrin - US studies = 93 days/ DT $_{90f}$ Zeta-cypermethrin – European field studies = 59 days).

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

-Residues of zeta-cypermethrin were stable in dry pea seeds for of 5 months under frozen storage conditions (-25°C). The cereal study showed that the compound was stable for the duration of the storage period (440 days). -The residues of cypermethrin and its metabolites were considered as stable in poultry eggs, muscle and liver for up to 6 months. No data were given for fat. - No significant degradation of cypermethrin and its metabolites occurred in cow muscle and fat stored under frozen conditions for 12 months and in liver and milk for 3 months. For livestock matrices there was some instability seen in eggs for m-PBA at 6 months (64 % recovery). In poultry muscle and liver cis-DCVA also had a low result at 56 % and 58 % but this was not seen in the ruminant tissue.

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

	Ruminant:	Poultry:	Pig:
Intakes by livestock ≥ 0.1 mg/kg diet/day:			
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no-If yes, specify the level) :	Yes Dairy cattle: 0.179 mg/kg diet Beef cattle: 0.193 mg/kg diet	No: 0.040 mg/kg diet	No: 0.04 mg/kg diet)
Potential for accumulation (yes/no) :	Yes	Yes	Yes

Appendix 1 – list of endpoints

Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	A metabolism study was not required.
Available feeding studies	- Exposure rate: 5-15-50 mg/kg diet, dry weight basis. - Overdosing factor : 25	-Exposure rate: 2-6-20 mg/kg diet, dry weight basis. - Overdosing factor : 50	A feeding study in pig was not required considering the similar metabolic pathway in rat and ruminants.
	Residue levels in matrices (mg/kg)		
Muscle	<0.01-0.01	<0.05	-
Liver	<0.01-0.01	<0.05	-
Kidney	<0.01-0.02	<0.05	-
Fat	<0.01-0.02	<0.05	-
Milk	<0.005	-	-
Eggs	-	<0.025	-

Limits of quantification of the analytical method : 0.01 mg/kg for milk , 0.025 mg/kg for eggs and 0.05 mg/kg for tissues.

Appendix 1 – list of endpoints

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

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	**MRL**	**STMR** (b)
In all trials, residues of zeta-cypermethrin were calculated as total cypermethrin (sum of isomers).					
Maize	North Europe	4 trials performed in France and Germany using a dose rate of 0.030-0.038 kg a.s./ha, 1 application at growth stage BBCH 53/59-61 (Middle of heading : half of inflorescence emerged – End of heading : inflorescence beginning of flowering : first anthers visible). - Maize grain : 4x <0.02 mg/kg - Plants without cobs : <0.02, 0.02, 2x 0.03	**- Provisional MRL** proposal on maize grain: 0.02* mg/kg, pending the results of further residue trials performed with the critical dose and critical growth stage and using a completely validated analytical method.	0.02* (provisional)	0.02
	South Europe	No trial was considered as acceptable due to the non validated analytical method. - Maize grain : - Silage :			
Winter wheat	North Europe	7 trials performed at a dose rate of 15 g a.s./ha with 2 applications, the latest at BBCH growth stages ranging from 67 (full flowering) to 83-85 (grain content soft but dry). - Wheat grain: 3x <0.01, (<0.01), 2x 0.01, (0.01), <0.02, 0.02 mg/kg - Wheat straw: 0.12, 2x 0.14, 0.15, 0.18, 0.21, 0.25, (1.0), (1.35) mg/kg	The database was considered as complete. **MRL proposal** on wheat grain: 0.02 mg/kg. The additional residue values in brackets will be taken into account when the validation data package of the analytical	0.02*	0.02

Appendix 1 – list of endpoints

	South Europe	10 trials performed at a dose rate of 15 g a.s./ha with 2 applications, the latest at BBCH growth stages ranging from 69 (end of flowering) to 77 (Late milk). - Wheat grain: 9 x <0.02, 0.01 - Wheat straw: 2x<0.05, 0.08, 0.12, 0.14, 0.26, 0.27, 0.30, 2x 0.38	method is accepted. The residue database for winter/spring wheat can be extrapolated to triticale.		
Winter barley	North Europe	6 trials were performed at a dose rate of 15 g a.s./ha, 2 applications with the latest at the BBCH growth stages ranging between 61 (beginning of flowering) and 73 (early milk). - Barley grain: (<0.01), 0.01, <0.02, .3x 0.02, (0.03), 0.11 The value 0.11 was considered as an outlier. - Barley straw: 0.14, 0.18, 0.19, 0.20, 0.31, (0.32), (0.25), 0.52	**Provisional MRL** proposal on barley grain: 0.05 mg/kg. The values in brackets will be taken into account when the validation data package of the analytical method is accepted. The residue database for winter/spring barley can be extrapolated to spring oat.	0.05 (provisional)	0.02
	South Europe	7 trials were performed at a dose rate of 15 g a.s./ha, 2 applications with the latest at the BBCH growth stages ranging between 61 (beginning of flowering) and 75 (Medium milk). - Barley grain: 4x <0.02, 0.02, 0.03, 0.04 - Barley straw 2x <0.05, 0.08, 0.13, 0.17, 0.33, 0.67			
Triticale	North Europe	No data	MRL for triticale extrapolated from wheat	0.02*	0.02

Appendix 1 – list of endpoints

	South Europe	2 trials performed at a dose rate of 15 g a.s./ha, 2 applic. and BBCH 75-77 (medium/late milk): - Triticale grain: 2x <0.02 - Triticale straw: <0.05, 0.28			
Oat	North Europe	No data	**Provisional MRL** for oat extrapolated from winter barley	0.05 (provisional)	0.02
	South Europe	2 trials performed at a dose rate of 15 g a.s./ha, 2 applic. and BBCH 75-76 (medium milk): - Triticale grain: 2x <0.02 - Triticale straw: 0.18, 0.39			
Peas, green without pods	North Europe	10 trials for peas, green without pods : 10 x <0.01.	The database considered as complete both for Northern and Southern Europe on the basis of the no residue situation and considering the non systemic properties of zeta-cypermethrin.	0.02*	0.01
	South Europe	3 trials for peas, green without pods : 3x <0.02			
Peas with pods (mange tout)	North Europe	6 trials for peas with pods : 2x (<0.01), 3x (0.01), (0.016) mg/kg	**Provisional MRL** for pea with pods: 0.02* mg/kg. The values in brackets will be taken into account when the validation data package of the analytical method is accepted.	0.02* (provisional)	0.02
	South Europe	3 trials : 3x <0.02 mg/kg			
Pulses, dry	North Europe	No trial provided.	A complete residue database should be provided for Northern Europe unless a situation of no residue can be demonstrated for North EU, based on a minimum of 4 trials.	0.02* (provisional)	0.02
	South Europe	6 trials for shelled peas, dry : 6x <0.02 mg/kg			

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

Appendix 1 – list of endpoints

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

ADI	0.04 mg/kg b.w./day
TMDI (European Diet) (% ADI)	-WHO European diet for an adult : 0.6 % ADI -German diet for a 4-6 years old girl : 1.35 % ADI -Most sensitive categories of UK consumers : toddlers (2% of ADI) and 4-6 years old children (2% of ADI).
NEDI (% ADI)	-
Factors included in NEDI	-
ARfD	0.125 mg/kg b.w./day
Acute exposure (% ARfD)	The acute exposure estimates based on UK consumption data and the provisional MRLs do not indicate any of the considered consumer subgroup being at risk (maximum of 0.6 % of ARfD for 4-6 year old child for wheat).

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
No processing studies were required.			

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

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

Maize	0.02* mg/kg (provisional)
Winter/spring Wheat	0.02* mg/kg
Winter/spring Barley	0.05 mg/kg (provisional)
Triticale	0.02* mg/kg
Oat	0.05 mg/kg (provisional)
Peas, green without pods	0.02* mg/kg
Peas green with pods (mange tout)	0.02* mg/kg (provisional)
Pulses (dry)	0.02* mg/kg (provisional)

Appendix 1 – list of endpoints

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

Mineralization after 100 days ‡	(cypermethrin) 35.8 % after 122 d, [^{14}C-cyclopropyl]-label (n= 1) 36.2 % after 122 d, [^{14}C-benzyl]-label (n= 1)
Non-extractable residues after 100 days ‡	19.3 % after 122 d, [^{14}C-cyclopropyl]-label (n= 1) 30.0 % after 122 d, [^{14}C-benzyl]-label (n= 1)
Relevant metabolites - name and/or code, % of applied (range and maximum) ‡	DCVA, max 24.2% at day 62 [^{14}C-cyclopropyl]-label mPBAcid, max 8.4% at day 30 [^{14}C-benzyl]-label (this metabolite is found at level > 10% in several other studies)
Relevant metabolites - name and/or code, % of applied (range and maximum) ‡	(zeta-cypermethrin) Data gap

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

Anaerobic degradation ‡	Data gap
Soil photolysis ‡	(cypermethrin) Mineralisation: max 0.2-3.3% AR after 21 days non-extractable residues: max 31.7% after 28 days Cyperamide formed at similar levels in both irradiated and dark controls (9.2-13.2% at day 35) [^{14}C-benzyl]- and [^{14}C-cyclopropyl]- labels

Appendix 1 – list of endpoints

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

Method of calculation	Laboratory: 1st order (ModelManager 1.1) cypermethrin and DCVA. For mPBAcid biphasic first order Not normalised field studies Timme linear regression best fit Normalised field studies: SFO and FOMC (Modelmaker 4.0)
Laboratory studies (range or median, with n value, with r^2 value) ‡	cypermethrin DT_{50lab} (25°C, aerobic, 75% 1/3 bar MHC): 60 days normalisation to 10kPa or pF2, 20°C (with Q10 of 2.2), 89 days. Though only 1 reliable value is available it was agreed that the available satisfactory field data meant further laboratory soil rate of degradation data was not required.
	mPBAcid: DT_{50lab} (20°C, aerobic): 3-7 d (single first order or slower phase of biphasic single first order, n= 3, r^2 = 0.8107-0.967) cis-DCVA: DT_{50lab} (20°C, aerobic): 2.7-8 d (single first order n= 3, r^2 = 0.923-0.964) Trans-DCVA: DT_{50lab} (20°C, aerobic): 3.1-11 d (single first order n= 3, r^2 = 0.815-0.972) For FOCUS gw modelling mPBAcid, geomean DT_{50lab} of 4.3 d (aerobic, 1st order kinetics, normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). DCVA, geomean DT_{50lab} of 4.2 d (aerobic, 1st order kinetics, normalisation to 10kPa or pF2, 20°C with Q10 of 2.2).
	DT_{50lab} (10°C, aerobic): cypermethrin 196 d (by calculation, with Q10 of 2.2).
	anaerobic study: data gap
	degradation in the saturated zone: not required

Appendix 1 – list of endpoints

Field studies (state location, range or median with
n value) ‡

DT_{50f}: (zeta-cypermethrin) not normalised values.
S France, bare soil, 21 d (n= 1, r^2=0.908) 1st order
Italy, bare soil, 10-11 d (n= 1, r^2= 0.930) 1st order
Germany, bare soil, 6.21 d (n=1, r^2=0.9751) sqr root 1st
Germany, bare soil, 24.24 d (n=1, r^2=0.8675) 1st order
Germany, bare soil, 9.52 d (n=1, r^2=0.9722) 1.5st order
Germany, bare soil, 3.85 d (n=1, r^2=0.9402) sqr root 1st

DT_{90f}: (zeta-cypermethrin) not normalised values.
S France, bare soil, 70-71 d
Italy, bare soil, 34-37 d
Germany, bare soil, 68.50 d
Germany, bare soil, 80.54 d
Germany, bare soil, 49.71 d
Germany, bare soil, 42.47 d

$DT_{50f/90f}$: (zeta-cypermethrin) normalised to FOCUS reference conditions (10kPa or pF2, 20°C with Q10 of 2.2) using time step normalisation

Site	**Kinetic Model**	**Zeta-cypermethrin**			
		χ^2 error	**DT_{50} (days)**	**DT_{90} (days)**	**Modelling DT_{50} (days)** ‡
Borsum	SFO	24.	8.62	28.65	8.62
Christinenthal	FOMC[22]	6.	7.81	50.48	15.20*
Erpolzheim	SFO	10.	12.78	42.44	12.78
Rodenbach	SFO	6.	9.31	30.93	9.31
France (S1)	FOMC[23]	20.	11.04	93.27	28.09*
Italy (S2)	FOMC[24]	16.	8.44	89.16	26.86*

‡ P<0.1 for all SFO models
* DT_{50} calculated by dividing FOMC DT_{90} by 3.32 (FOCUS, 2006)

For FOCUS scenario modelling:
Geomean = 15.08 days (aerobic, 1st order kinetics,

[22] α= 1.41678 ß= 12.3728
[23] α= 1.05707 ß= 11.9102
[24] α= 0.881522 ß=7.0614

Appendix 1 – list of endpoints

	DT_{50f}: (mPBAcid) S France, bare soil, 4.8 d (n= 1, r^2=0.908) 1st order Italy, bare soil, 5.9 d (n= 1, r^2= 0.9.21) 1st order
	DT_{90f}: (mPBAcid) S France, bare soil, 16 d Italy, bare soil, 20 d
	DT_{50f}: (trans-DCVA) S France, bare soil, not detected Italy, bare soil, 2.9 d (n= 1, r^2= 0.930) 1st order
	DT_{90f}: (trans-DCVA) S France, bare soil, not detected Italy, bare soil, 9.5 d
	DT_{50f}: (cis-DCVA) S France, bare soil, not detected Italy, bare soil, not detected
Soil accumulation and plateau concentration ‡	Not required. Field DT90 of zeta-cypermethrin are < 1 year.

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} (mL/g) ‡	K_{foc} cypermethrin 72405-285562 (mean 121786, $^1/_n$= 1.15-1.47, 4 soils) mPBAcid 118-215 (mean 151.67, $^1/_n$= 0.65-0.67, 3 soils trans-DCVA 18-48 (mean 28.33, $^1/_n$= 0.56-0.81, 3 soils
pH dependence (yes / no) (if yes type of dependence) ‡	No .*For FOCUS gw modelling – K_{foc}: cypermethrin mean 121786, $^1/_n$= 1.30 K_{foc}: mPBAcid, mean 151.67, $^1/_n$= 0.66 K_{foc}: trans-DCVA, mean 28.336, $^1/_n$= 0.64

Appendix 1 – list of endpoints

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

Column leaching ‡	(cypermethrin) EPA and SETAC Guidelines Time period (d): 1-2 d Precipitation (mm): 508 mm Leachate: 0.26% total residues/radioactivity in leachate 92.69% total residues/radioactivity retained in top 6 cm (benzyl label) Leachate: 2.06% total residues/radioactivity in leachate 88.14% total residues/radioactivity retained in top 6 cm (cyclopropyl label)
Aged residues leaching ‡	(cypermethrin) EPA and SETAC Guidelines Aged for (d): 30 d Time period (d): 1-2 d Precipitation (mm): 508 mm Leachate: 0.70% total residues/radioactivity in leachate 92.79% total residues/radioactivity retained in top 6 cm (benzyl label) Leachate: 14.53% total residues/radioactivity in leachate 0.3% a.s., 11.7% DCVA 73.15% total residues/radioactivity retained in top 6 cm (cyclopropyl label)
Lysimeter/ field leaching studies ‡	Not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	DT_{50} (zeta-cypermethrin): 24.24 days Kinetics: 1st order representative worst case from not normalised field studies.
Application rate	Crop: maize 25 % plant interception: Post-emergence BBCH 15 – 30 Number of applications: 1 Interval (d): - Application rate(s): 37.5 g as/ha

Appendix 1 – list of endpoints

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.038	-	-	-
Short term	24h	0.036	0.037	-	-
	2d	0.035	0.036		
	4d	0.033	0.035		
Long term	7d	0.031	0.034	-	-
	28d	0.017	0.026		
	50d	0.009	0.020		
	100d	0.002	0.012		

Metabolites

Method of calculation	DT_{50} (DCVA): 11 days Kinetics: 1st order Worst case lab data
Application rate	Crop: maize 25 % plant interception: Post-emergence BBCH 15 – 30 Number of applications: 1 Interval (d): - Application rate(s): 37.5 g as/ha Assuming complete degradation of the a.s. into DCVA, Molecular mass ratio DCVA/a.s. : 209.07/416.31

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.019	-	-	-
Short term	24h	0.017	0.018	-	-
	2d	0.015	0.017		
	4d	0.013	0.016		
Long term	7d	0.009	0.014	-	-
	28d	0.001	0.006		
	50d	0.000	0.004		
	100d	0.000	0.002		

Appendix 1 – list of endpoints

Method of calculation	DT_{50} (mPBAcid): 7 days Kinetics: 1st order Worst case lab data
Application rate	Crop: maize 25 % plant interception: Post-emergence BBCH 15 – 30 Number of applications: 1 Interval (d): - Application rate(s): 37.5 g as/ha Assuming complete degradation of the a.s. into mPBAcid Molecular mass ratio mPBAcid /a.s. : 214.22/416.31

PEC$_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.019	-	-	-
Short term	24h	0.017	0.018	-	-
	2d	0.016	0.018		
	4d	0.013	0.016		
Long term	7d	0.009	0.014	-	-
	28d	0.000	0.007		
	50d	0.000	0.004		
	100d	0.000	0.002		

Appendix 1 – list of endpoints

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature) ‡	(zeta-cypermethrin) pH 4: Hydrolytically stable
	pH 7, 25°C: 25 d
	pH 9: hydrolytically labile
	Metabolites mPBAcid, mPBAlcolhol, cis-DCVA, trans-DCVA are hydrolytically stable at pH 4, 7, 9
Photolytic degradation of active substance and relevant metabolites ‡	(zeta-cypermethrin) At 20°C DT_{50} (direct phototransformation) : 3.05 test system days when equated to central European May sunlight for a 1m light path length 14 days
	MPBAcid pH4, 20°C: DT_{50} = 1.07 d test system days, 77 days pH7, 20°C: DT_{50} = 2.83 d test system days, 120 days pH9, 20°C: DT_{50} = 4.07 d test system days, 170 days second values are equated to central European May sunlight for a 1cm light path length
Readily biodegradable (yes/no) ‡	Data gap, no in the absence of peer reviewed data
Degradation in water/sediment - DT_{50} water ‡ - DT_{90} water ‡ - DT_{50} whole system ‡ - DT_{90} whole system ‡	(zeta-cypermethrin) 0.1 days (dissipation values) 2.1-3..5 days (dissipation values biphasic degr., r^2= 0.992-1.000, n= 4) 1.5-2.5 days 16.0-26.0 days (biphasic degr., r^2= 0.9912-0.9983, n= 4) Selected for FOCUSsw modelling (single first order DT_{50}): water 1000 days (default) sediment 6.12 days (geomean of whole system biphasic DT90 divided by 3.32)
Mineralization	15.91-21.05% AR (at 99 d, n=2, cyclopropyl label) 51.81-57.43% AR (at 99 d, n=2, benzyl label)
Non-extractable residues	15.97-21.55% AR (at 99 d, n=2, cyclopropyl label) 25.97-26.61% AR (at 99 d, n=2, benzyl label)
Distribution in water / sediment systems (active substance) ‡	Maximum of 44.11-46.57 %AR in sediment after 0.25 day. DT_{50} in sediment 4.9-8.2 days (DT_{90} 31.8-53.4 days, biphasic degr.,, r^2= 0.9804-0.9917, n= 4)

Appendix 1 – list of endpoints

Distribution in water / sediment systems (metabolites) ‡	Water: mPBAcid: max of 33.44-37.58% (8 days, n= 2, benzyl label) trans-DCVA: max of 47.23-35.22% (14 days, n= 2, cyclopropyl label) cis-DCVA: max of 20.16-15.94% (62 days, n= 2, cyclopropyl label) Sediment: mPBAcid: max of 4.96-6.25% (8 days, n= 2, benzyl label) trans-DCVA: max of 4.72-8.5% (99-29 days, n= 2, cyclopropyl label) cis-DCVA: max of 2.13-3.11% (62 days, n= 2, cyclopropyl label) DT_{50} cis-DCVA 79.1-63.0 days, (whole system, graphical estimate from max. observed, n= 2) DT_{50} trans-DCVA 117.5-94.9 days, (whole system graphical estimate from max. observed, n= 2) DT_{50} mPBAcid 12.9-145.2 days, (whole system graphical estimate from max. observed, n= 2)

Appendix 1 – list of endpoints

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

Parent Parameters used in FOCUSsw step 1	Molecular weight (g/mol): 416.31 Water solubility (mg/L): 0.0387 Koc (L/kg): 18326 DT_{50} soil (d): 31.1 days (median lab. In accordance with FOCUS SFO) DT50 water/sediment system (d): 1.90 DT50 water (d): 0.10 DT50 sediment (d): 6.00 Crop interception (%): 25% partitioning to top 5 cm layer of sediment
	Vapour pressure: 2.53 10^{-7} Pa Koc: 18326 1/n: 0.873
Application rate	Crop: maize Crop interception: 25% Number of applications: 1 Interval (d): - Application rate(s): 37.5 g as/ha Depth of water body: 30 cm Application window:
Main routes of entry	2.759 % drift from 1 meter 10% runoff/drainage respectively at FOCUSsw Step 1

Appendix 1 – list of endpoints

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0	0.84	-	90.06	-
	24	0.35	0.59	64.26	77.16
	2d	0.24	0.44	44.62	65.50
	4d	0.12	0.31	21.51	48.59
	7d	0.04	0.21	7.20	33.37
	14d	0.00	0.11	0.56	17.98
	21d	0.00	0.07	0.04	12.06
	28d	0.00	0.06	0.00	9.05
	42d	0.00	0.04	0.00	6.03

Parent Parameters used in FOCUSsw step 3 and 4	Molecular weight (g/mol): 416.31 Water solubility (mg/L): 0.0387 Koc (L/kg): 18326 1/n: 0.873 DT_{50} soil (d): 31.1 days (median lab. In accordance with FOCUS SFO (though lab studies were not reliable this value is longer than the geomean normalised field value (15.1 days)) DT50 water (d): 0.10, Note 1000 days should have been used but this would not impact on maximum initial PEC retained as reliable endpoints DT50 sediment (d): 6.00
Application rate	Spring cereals, peas: 2 x 15 g a.s. /ha at 14 day interval, note simulations with 1 x 15 g a.s. /ha should have been simulated to generates the highest PECsw due to spray drift assumptions but were not **so there is a data gap for PEC for the uses on cereals and peas.** Maize: once at 37.5 g a.s. /ha Application window: 1st March to 14th June depending on scenarios
Main routes of entry	Step 3: standard scenarios Step 4: 20 meter buffer implemented

Appendix 1 – list of endpoints

FOCUS step 3 PECsw

Crop	Location	Water body	Global Max in ppb
Cereals and peas	Swash drift calculator nominal concentration	Ditch / stream	0.0964
Cereals and peas		pond	0.0033
Maize	D3	ditch	0.190000
Maize	D4	pond	0.007590
Maize	D4	stream	0.160000
Maize	D5	pond	0.007590
Maize	D5	stream	0.162000
Maize	D6	ditch	0.190000
Maize	R1	pond	0.007590
Maize	R1	stream	0.131000
Maize	R2	stream	0.175000
Maize	R3	stream	0.186000
Maize	R4	stream	0.131000

FOCUS step 4 PECsw

Crop	Location	Water body	Global Max in ppb
Cereals and peas	Swash drift calculator nominal concentration	Ditch / stream	0.0072
Cereals and peas		pond	0.0014
Legume – Pea	R4	stream	0.01220
Maize	D3	ditch	0.01700
Maize	D4	pond	0.00323
Maize	D4	stream	0.01850
Maize	D5	pond	0.00323
Maize	D5	stream	0.01860
Maize	D6	ditch	0.01700
Maize	R1	pond	0.00323
Maize	R1	stream	0.01510
Maize	R2	stream	0.02010
Maize	R3	stream	0.02140
Maize	R4	stream	0.01760

Appendix 1 – list of endpoints

PEC sediment **Data gap**

Metabolite DCVA Parameters used in FOCUSsw step 1	Molecular weight: 209.07 Water solubility (mg/l): - Soil or water metabolite: Koc (L/kg): 18 DT_{50} soil (d): 4.8 days Crop interception (%): 25% Maximum occurrence observed (69.58% molar basis with respect to the parent) in w/s system Maximum occurrence observed (51.40% molar basis with respect to the parent) in soil system
Application rate	Crop: maize Number of applications: 1 Interval (d): - Application rate(s): 37.5 g as/ha Depth of water body: 30 cm Application window:
Main routes of entry	2.759 % drift from 1 metre 10 % runoff/drainage (at FOCUSsw Step 1)

FOCUS STEP 1 Scenario Metabolite DCVA	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	0.25	-	23.25	-
	24h	0.09	0.17	16.74	20.00
	2d	0.06	0.12	11.63	17.01
	4d	0.03	0.08	5.60	12.63
	7d	0.01	0.06	1.88	8.68
	14d	0.00	0.03	0.15	4.68
	21d	0.00	0.02	0.01	3.14
	28d	0.00	0.02	0.00	2.35
	42d	0.00	0.01	0.00	1.57

Appendix 1 – list of endpoints

Metabolite mPBAcid Parameters used in FOCUSsw step 1	Molecular weight: 214.22 Water solubility (mg/l): - Soil or water metabolite: Koc (L/kg): 118 DT_{50} soil (d): 5.3 days Crop interception (%): 25% Maximum occurrence observed (48.3% molar basis with respect to the parent) in w/s system Maximum occurrence observed (59.9% molar basis with respect to the parent) in soil system
Application rate	Crop: maize Number of applications: 1 Interval (d): - Application rate(s): 37.5 g as/ha Depth of water body: 30 cm Application window:
Main routes of entry	2.759 % drift from 1 metre 10 % runoff/drainage (at FOCUSsw Step 1)

FOCUS STEP 1 Scenario Metabolite mPBAcid	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	0.23	-	27.76	-
	24h	0.11	0.17	19.66	23.71
	2d	0.07	0.13	13.65	20.09
	4d	0.04	0.09	6.58	14.89
	7d	0.01	0.06	2.20	10.22
	14d	0.00	0.03	0.17	5.51
	21d	0.00	0.02	0.01	3.69
	28d	0.00	0.02	0.00	2.77
	42d	0.00	0.01	0.00	1.85

Appendix 1 – list of endpoints

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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	Modelling using FOCUS model(s), with appropriate FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS PELMO 3.2.2 Scenarios : Chateaudun , irrigated; Hamburg; Kremsmunster; Okehampton; Piacenza, irrigated; Porto; Sevilla, irrigated; Thiva Crop: maize median parent DT_{50lab} 31.1 d (normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). K_{oc}: parent, 18326 $^{1}/_{n}$= 0.873. arithmetic mean DCVA DT_{50lab} 4.8 d (normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). K_{oc}: DCVA, 18 $^{1}/_{n}$= 0.555. arithmetic mean mPBAcid DT_{50lab} 5.3 d (normalisation to 10kPa or pF2, 20°C with Q10 of 2.2). K_{oc}: mPBAcid, 118 $^{1}/_{n}$= 0.6452.
Application rate	Application rate: 37.5 g/ha, 25% plant interception No. of applications: 1 Time of application (month or season): post-emergence, BBCH 15-30

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

Model /Crop	Scenario	Parent (µg/L)	Metabolite (µg/L)	
			DCVA	mPBAcid
	Chateaudun , irrigated	<0.001	<0.001	<0.001
	Hamburg	<0.001	<0.001	<0.001
	Kremsmunster	<0.001	<0.001	<0.001
	Okehampton	<0.001	<0.001	<0.001
	Piacenza, irrigated	<0.001	<0.001	<0.001
	Porto	<0.001	<0.001	<0.001
	Sevilla, irrigated	<0.001	<0.001	<0.001
	Thiva	<0.001	<0.001	<0.001

Appendix 1 – list of endpoints

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

Direct photolysis in air	Not studied - no data requested
Quantum yield of direct phototransformation	active substance: $\phi = 0.0511$, mPBAcid (pH 7): $\phi = 0.462 \times 10^{-3}$
Photochemical oxidative degradation in air	DT_{50} of 0.499 hours (12-hrs-day) derived by the Atkinson method of calculation
Volatilisation	(cypermethrin) from plant surfaces (BBA guideline): 0 % after 24 hours
	(cypermethrin) from soil (BBA guideline): 0% after 24 hours

PEC (air)

Method of calculation	Not required

$PEC_{(a)}$

Maximum concentration	Not required

Definition of the Residue (Annex IIA, point 7.3)

Residue for which assessment by other disciplines is triggered or for which a groundwater exposure assessment is required.	Data gap needs to be filled before the definition for groundwater can be finalised For risk assessment : Soil: component isomers of cypermethrin, DCVA, mPBAcid Groundwater: component isomers of cypermethrin, DCVA, mPBAcid Surface water: component isomers of cypermethrin, DCVA, mPBAcid Sediment : component isomers of cypermethrin, DCVA, mPBAcid Air: component isomers of cypermethrin

Appendix 1 – list of endpoints

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

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	The monitoring data from France are rather ancient (1987-1989). They show that the contamination of surface water and groundwater by cypermethrin is limited. These data are considered as confirmatory information.
Ground water (indicate location and type of study)	The monitoring data from France are rather ancient (1987-1989). They show that the contamination of surface water and groundwater by cypermethrin is limited. These data are considered as confirmatory information.
Air (indicate location and type of study)	Not available

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	R53

Appendix 1 – list of endpoints

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

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Anas platyrhynchos	cypermethrin	Acute	> 10248 (m) > 12085 (f)	- -
	zeta-cypermethrin	Acute	> 5124 (m) > 6043 (f)	- -
Anas platyrhynchos	cypermethrin	Short-term	> 1201	> 20000
	zeta-cypermethrin	Short-term	> 601	-
Colinus virginianus	cypermethrin	Short-term	> 1600	> 20000
	zeta-cypermethrin	Short-term	> 800	-
Colinus virginianus	cypermethrin	Long-term	4.29	50
	zeta-cypermethrin	Long-term	2.15	-
Anas platyrhynchos	cypermethrin	Long-term	5.58	50
	zeta-cypermethrin	Long-term	2.79	-
Mammals ‡				
rat	zeta-cypermethrin	Acute	86	-
rat	zeta-cypermethrin	Long-term	5.9	-
Additional higher tier studies ‡				
Not required.				

As RMS, we accepted to conduct the risk assessment of zeta-cypermethrin for birds based on studies conducted with cypermethrin.

- The toxicological endpoints and the subsequent risk assessment have shown an acceptable risk for birds. The acute and short-term risk is acceptable with a large margin of safety. The reproductive risk to birds is also acceptable based on a low NOEL value due to low testing dosage in the test and assuming a worst case assumption of ingestion of 100 % contaminated diet.
- The pyrethroid compounds (cypermethrin, alpha-cypermethrin) are known to have an acceptable risk to birds.
- For reasons of animal welfare, it is not recommended to conduct studies on birds with zeta-cypermethrin.

In the meeting of experts PRAPeR 48 in May 2008 it was agreed that the endpoints for cypermethrin should be divided by a factor of 2 to extrapolate to zeta-cypermethrin.

Appendix 1 – list of endpoints

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

Crop and application rate : maize, 1 x 0.0375 kg a.s./ha

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Large herbivorous bird (early crop stage)	Acute	2.34	> 2190	10
	Short-term	1.25	> 481	10
	Long-term	0.66	3.26	5
Insectivorous bird (early/late crop stage)	Acute	2.03	> 2524	10
	Short-term	1.13	> 532	10
	Long-term	1.13	1.91	5
Earthworm-eating bird	Long-term	0.12	18	5
Fish-eating bird	Long-term	0.00027	7963	5
Higher tier refinement (Birds)				
Large herbivorous bird (early crop stage)	Long-term	0.24 (residues)	8.96	5
Notifier to refine the long-term risk to insectivorous birds.				
Tier 1 (Mammals)				
Small herbivorous mammal (early crop stage)	Acute	7.40	11.6	10
	Long-term	2.10	2.81	5
Insectivorous mammal (late crop stage)	Acute	0.33	260	10
	Long-term	0.12	49.0	5
Earthworm-eating mammal	Long-term	0.15	39.3	5
Fish-eating mammal	Long-term	0.00017	34911	5
Higher tier refinement (Mammals)				
Small herbivorous mammal (early crop stage)	Long-term	0.75 (max residue, f_{twa})	7.87	5

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

Appendix 1 – list of endpoints

Crop and application rate : cereals, 1-2 x 0.015 kg a.s./ha

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Large herbivorous bird (early crop stage)	Acute	1.12	> 4575	10
	Short-term	0.70	> 859	10
	Long-term	0.37	5.81	5
Insectivorous bird (early/late crop stage)	Acute	0.81	> 6326	10
	Short-term	0.45	> 1336	10
	Long-term	0.45	4.78	5
Higher tier refinement (Birds)				
Notifier to refine the long-term risk to insectivorous birds.				
Tier 1 (Mammals)				
Small herbivorous mammal (early crop stage)	Acute	3.55	24.2	10
	Long-term	1.18	5.02	5
Insectivorous mammal (late crop stage)	Acute	0.13	650	10
	Long-term	0.048	122	5
Higher tier refinement (Mammals)				
Not required.				

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

Crop and application rate : peas, 1-2 x 0.015 kg a.s./ha

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Large herbivorous bird (early crop stage)	Acute	1.19	> 4306	10
	Short-term	0.64	> 939	10
	Long-term	0.34	6.32	5
Insectivorous bird (early/late crop stage)	Acute	0.81	> 6326	10
	Short-term	0.45	> 1336	10
	Long-term	0.45	4.78	5
Higher tier refinement (Birds)				
Notifier to refine the long-term risk to insectivorous birds.				

Appendix 1 – list of endpoints

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Mammals)				
Medium herbivorous mammal (early/late crop stage)	Acute	0.44	196	10
	Long-term	0.12	47.3	5
Higher tier refinement (Mammals)				
Not required.				

[1] in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
[2] for cereals indicate if it is early or late crop stage
[3] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	zeta-cypermethrin	96 h (flow-through)	Mortality, LC_{50}	**0.00069 mg a.s./L** (mm)
Cyprinodon variegatus	zeta-cypermethrin	96 h (flow-through)	Mortality, LC_{50}	0.00237 mg a.s./L (mm)
Oncorhynchus mykiss	cypermethrin	96 h (flow-through)	Mortality, LC_{50}	0.0009 mg a.s./L (mm)
Cyprinodon variegatus	cypermethrin	96 h (flow-through)	Mortality, LC_{50}	0.00345 mg a.s./L (mm)
Oncorhynchus mykiss	Fury 10 EW	96 h (flow-through)	Mortality, LC_{50}	0.013 mg form/L (**0.0013 mg a.s./L**) (nom)
Pimephales promelas	cypermethrin	34 d (flow-through)	Growth NOEC	0.000030 mg cypermethrin/L (**0.000015 mg zeta-cypermethrin/L**) (mm)
Oncorhynchus mykiss	cis-DCVA	96 h (static)	Mortality, LC_{50}	> **1.0 mg/L (nom)**
Oncorhynchus mykiss	trans-DCVA	96 h (static)	Mortality, LC_{50}	> **1.0 mg/L (nom)**
Oncorhynchus mykiss	3-phenoxy-benzoic acid	96 h (static)	Mortality, LC_{50}	> **1.0 mg/L (nom)**

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Aquatic invertebrate				
Daphnia magna	zeta-cypermethrin	48 h (semi-static)	Mortality, EC_{50}	0.000141 mg a.s./L (mm)
Gammarus pulex	zeta-cypermethrin	96 h (static)	Mortality, EC_{50}	**0.0000013 mg a.s./L** (nom)
Daphnia magna	Fury 100 EW	48 h (semi-static)	Mortality, EC_{50}	0.000827 mg form/L (0.000085 mg a.s./L) (mm)
Gammarus pulex	Fury 100 EW	96 h (static)	Mortality, EC_{50}	0.0000069 mg form/L (**0.00000069 mg a.s./L**) (nom)
Daphnia magna	Fury 10 EW	21 d (semi-static)	Reproduction, NOEC	0.0001 mg form/L (**0.00001 mg a.s./L**) (nom)
Daphnia magna	cis-DCVA	48 h (static)	Mortality, EC_{50}	> 1.0 mg/L (nom)
Daphnia magna	trans-DCVA	48 h (static)	Mortality, EC_{50}	> 1.0 mg/L (nom)
Daphnia magna	3-phenoxy-benzoic acid	48 h (static)	Mortality, EC_{50}	> 1.0 mg/L (nom)
Sediment dwelling organisms				
Chironomus riparius	Fury 10 EW	28 d (static) (spiked water)	NOEC	0.001 mg form/L (**0.0001 mg a.s./L**) (nom)
Algae				
Pseudokirchne-riella subcapitata	zeta-cypermethrin	96 h (static)	EC_{50}	> 1.0 mg a.s./L (nom)
Pseudokirchne-riella subcapitata	Fury 10 EW	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	1.1 mg form/L (**0.11 mg a.s./L**) 1.6 mg form/L (0.16 mg a.s./L) (96 h measured)
Pseudokirchne-riella subcapitata	cis-DCVA	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	> 1.0 mg/L (nom) > 1.0 mg/L (nom)
Pseudokirchne-riella subcapitata	trans-DCVA	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	> 1.0 mg/L (nom) > 1.0 mg/L (nom)
Pseudokirchne-riella subcapitata	3-phenoxy-benzoic acid	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	> 1.0 mg/L (nom) > 1.0 mg/L (nom)

Appendix 1 – list of endpoints

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Higher plant				
Not required.				
Microcosm or mesocosm tests				
Two mesocosm studies with zeta-cypermethrin were submitted by the applicant and evaluated by the RMS in the addendum to the DAR. However in view of the restrictions concerning the acceptance of new (i.e. newly submitted) studies after the submission of the DAR to EFSA, as laid down in Commission Regulation (EC) No. 1095/2007, the new studies could not be considered in the peer review.				

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

Fury 10 EW : equivalent to Fury 100 EW, both formulations containing 100 g/L zeta-cypermethrin

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

FOCUS Step1

FOCUS Step 2

No acceptable aquatic risk assessment based on FOCUS step 1 and step 2 calculations.

Appendix 1 – list of endpoints

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Crop and application rate : maize, 1 x 0.0375 kg a.s./ha

Test substance	Scena-rio	Water body type	Test species	Time-scale	End-point (µg a.s./L)	Buffer-zone	PEC_{SW}, max (µg a.s./L)	TER	Annex VI Trigger value
zeta-cypermethrin	D 3	ditch	*Oncorhynchus mykiss*	96 h	0.69	1 m	0.190000	3.63	100
	D 4	pond				1 m	0.007590	90.9	100
	D 4	stream				1 m	0.160000	4.31	100
	D 5	pond				1 m	0.007590	90.9	100
	D 5	stream				1 m	0.162000	4.26	100
	D 6	ditch				1 m	0.190000	3.63	100
	R 1	pond				1 m	0.007590	90.9	100
	R 1	stream				1 m	0.131000	5.27	100
	R 2	stream				1 m	0.175000	3.94	100
	R 3	stream				1 m	0.186000	3.71	100
	R 4	stream				1 m	0.131000	5.27	100
Fury 10 EW	D 3	ditch	*Oncorhynchus mykiss*	96 h	1.3	1 m	0.190000	6.84	100
	D 4	pond				1 m	0.007590	171	100
	D 4	stream				1 m	0.160000	8.13	100
	D 5	pond				1 m	0.007590	171	100
	D 5	stream				1 m	0.162000	8.02	100
	D 6	ditch				1 m	0.190000	6.84	100
	R 1	pond				1 m	0.007590	171	100
	R 1	stream				1 m	0.131000	9.92	100
	R 2	stream				1 m	0.175000	7.43	100
	R 3	stream				1 m	0.186000	6.99	100
	R 4	stream				1 m	0.131000	9.92	100

Appendix 1 – list of endpoints

zeta-cypermethrin	D 3	ditch	*Pimephales promelas*	34 d	0.015	1 m	0.190000	0.079	10
	D 4	pond				1 m	0.007590	1.98	10
	D 4	stream				1 m	0.160000	0.094	10
	D 5	pond				1 m	0.007590	1.98	10
	D 5	stream				1 m	0.162000	0.093	10
	D 6	ditch				1 m	0.190000	0.079	10
	R 1	pond				1 m	0.007590	1.98	10
	R 1	stream				1 m	0.131000	0.11	10
	R 2	stream				1 m	0.175000	0.086	10
	R 3	stream				1 m	0.186000	0.081	10
	R 4	stream				1 m	0.131000	0.11	10
zeta-cypermethrin	D 3	ditch	*Gammarus pulex*	96 h	0.0013	1 m	0.190000	0.01	100
	D 4	pond				1 m	0.007590	0.17	100
	D 4	stream				1 m	0.160000	0.01	100
	D 5	pond				1 m	0.007590	0.17	100
	D 5	stream				1 m	0.162000	0.01	100
	D 6	ditch				1 m	0.190000	0.01	100
	R 1	pond				1 m	0.007590	0.17	100
	R 1	stream				1 m	0.131000	0.01	100
	R 2	stream				1 m	0.175000	0.01	100
	R 3	stream				1 m	0.186000	0.01	100
	R 4	stream				1 m	0.131000	0.01	100
Fury 10 EW	D 3	ditch	*Gammarus pulex*	96 h	0.00069	1 m	0.190000	0.004	100
	D 4	pond				1 m	0.007590	0.091	100
	D 4	stream				1 m	0.160000	0.004	100
	D 5	pond				1 m	0.007590	0.091	100
	D 5	stream				1 m	0.162000	0.004	100
	D 6	ditch				1 m	0.190000	0.004	100
	R 1	pond				1 m	0.007590	0.091	100
	R 1	stream				1 m	0.131000	0.005	100
	R 2	stream				1 m	0.175000	0.004	100

Appendix 1 – list of endpoints

	R 3	stream				1 m	0.186000	0.004	100
	R 4	stream				1 m	0.131000	0.005	100
Fury 10 EW	D 3	ditch	*Daphnia magna*	21 d	0.01	1 m	0.190000	0.05	10
	D 4	pond				1 m	0.007590	1.32	10
	D 4	stream				1 m	0.160000	0.06	10
	D 5	pond				1 m	0.007590	1.32	10
	D 5	stream				1 m	0.162000	0.06	10
	D 6	ditch				1 m	0.190000	0.05	10
	R 1	pond				1 m	0.007590	1.32	10
	R 1	stream				1 m	0.131000	0.08	10
	R 2	stream				1 m	0.175000	0.06	10
	R 3	stream				1 m	0.186000	0.05	10
	R 4	stream				1 m	0.131000	0.08	10
zeta-cypermethrin	D 3	ditch	*Pseudokirch-neriella subcapitata*	96 h	> 1000	1 m	0.190000	5263	10
	D 4	pond				1 m	0.007590	131752	10
	D 4	stream				1 m	0.160000	6250	10
	D 5	pond				1 m	0.007590	131752	10
	D 5	stream				1 m	0.162000	6173	10
	D 6	ditch				1 m	0.190000	5263	10
	R 1	pond				1 m	0.007590	131752	10
	R 1	stream				1 m	0.131000	7634	10
	R 2	stream				1 m	0.175000	5714	10
	R 3	stream				1 m	0.186000	5376	10
	R 4	stream				1 m	0.131000	7634	10

Appendix 1 – list of endpoints

Fury 10 EW	D 3	ditch	*Pseudokirch-neriella subcapitata*	96 h	110	1 m	0.190000	572	10
	D 4	pond				1 m	0.007590	14493	10
	D 4	stream				1 m	0.160000	688	10
	D 5	pond				1 m	0.007590	14493	10
	D 5	stream				1 m	0.162000	679	10
	D 6	ditch				1 m	0.190000	579	10
	R 1	pond				1 m	0.007590	14493	10
	R 1	stream				1 m	0.131000	840	10
	R 2	stream				1 m	0.175000	629	10
	R 3	stream				1 m	0.186000	591	10
	R 4	stream				1 m	0.131000	840	10
Fury 10 EW	D 3	ditch	*Chironomus riparius*	28 d	0.1	1 m	0.190000	0.53	10
	D 4	pond				1 m	0.007590	13.2	10
	D 4	stream				1 m	0.160000	0.63	10
	D 5	pond				1 m	0.007590	13.2	10
	D 5	stream				1 m	0.162000	0.62	10
	D 6	ditch				1 m	0.190000	0.53	10
	R 1	pond				1 m	0.007590	13.2	10
	R 1	stream				1 m	0.131000	0.76	10
	R 2	stream				1 m	0.175000	0.57	10
	R 3	stream				1 m	0.186000	0.54	10
	R 4	stream				1 m	0.131000	0.76	10

Fury 10 EW : equivalent to Fury 100 EW, both formulations containing 100 g/L zeta-cypermethrin

Appendix 1 – list of endpoints

Crop and application rate : cereals / peas, 1-2 x 0.015 kg a.s./ha

Test substance	Water body type	Test species	Time-scale	End-point (µg a.s./L)	Buffer-zone	PEC_{SW}, max (µg a.s./L)	TER	Annex VI Trigger value
zeta-cypermethrin	Ditch/stream	*Oncorhynchus mykiss*	96 h	0.69	1m	0.0964	7.16	100
	pond				1m	0.0033	209	100
Fury 10 EW	Ditch/stream	*Oncorhynchus mykiss*	96 h	1.3	1m	0.0964	13.5	100
	pond				1m	0.0033	394	100
zeta-cypermethrin	Ditch/stream	*Pimephales promelas*	34 d	0.015	1m	0.0964	0.16	10
	pond				1m	0.0033	4.5	10
zeta-cypermethrin	Ditch/stream	*Gammarus pulex*	96 h	0.0013	1m	0.0964	0.01	100
	pond				1m	0.0033	0.39	100
Fury 10 EW	Ditch/stream	*Gammarus pulex*	96 h	0.00069	1m	0.0964	0.01	100
	pond				1m	0.0033	0.23	100
Fury 10 EW	Ditch/stream	*Daphnia magna*	21 d	0.01	1m	0.0964	0.10	10
	pond				1m	0.0033	3.03	10
zeta-cypermethrin	Ditch/stream	*Pseudokirch-neriella subcapitata*	96 h	> 1000	1m	0.0964	10373	10
	pond				1m	0.0033	303030	10
Fury 10 EW	Ditch/stream	*Pseudokirch-neriella subcapitata*	96 h	110	1m	0.0964	1141	10
	pond				1m	0.0033	33333	10

Appendix 1 – list of endpoints

Fury 10 EW	Ditch /stream	*Chironomus riparius*	28 d	0.1	1m	0.0964	1141	10
	pond				1m	0.0033	33333	10

Fury 10 EW : equivalent to Fury 100 EW, both formulations containing 100 g/L zeta-cypermethrin

Appendix 1 – list of endpoints

FOCUS Step 4

Crop and application rate : maize, 1 x 0.0375 kg a.s./ha

Test substance	Scen a-rio	Water body type	Test species	Time - scale	End-point (µg a.s./L)	Buffer-zone	PEC_{SW}, max (µg a.s./L)	TER	Annex VI Trigge r value
zeta-cypermethrin	D 3	ditch	*Oncorhynchus mykiss*	96 h	0.69	20 m	0.01700	40.6	100
	D 4	pond				20 m	0.00323	214	100
	D 4	stream				20 m	0.01850	37.3	100
	D 5	pond				20 m	0.00323	214	100
	D 5	stream				20 m	0.01860	37.1	100
	D 6	ditch				20 m	0.01700	40.6	100
	R 1	pond				20 m	0.00323	214	100
	R 1	stream				20 m	0.01510	45.7	100
	R 2	stream				20 m	0.02010	34.3	100
	R 3	stream				20 m	0.02140	32.2	100
	R 4	stream				20 m	0.01760	39.2	100
Fury 10 EW	D 3	ditch	*Oncorhynchus mykiss*	96 h	1.3	20 m	0.01700	76.5	100
	D 4	pond				20 m	0.00323	402	100
	D 4	stream				20 m	0.01850	70.3	100
	D 5	pond				20 m	0.00323	402	100
	D 5	stream				20 m	0.01860	69.9	100
	D 6	ditch				20 m	0.01700	76.5	100
	R 1	pond				20 m	0.00323	402	100
	R 1	stream				20 m	0.01510	86.1	100
	R 2	stream				20 m	0.02010	64.7	100
	R 3	stream				20 m	0.02140	60.8	100
	R 4	stream				20 m	0.01760	73.9	100
zeta-cypermethrin	D 3	ditch	*Pimephales promelas*	34 d	0.015	20 m	0.01700	0.88	10
	D 4	pond				20 m	0.00323	4.64	10
	D 4	stream				20 m	0.01850	0.81	10
	D 5	pond				20 m	0.00323	4.64	10

Appendix 1 – list of endpoints

	D 5	stream				20 m	0.01860	0.81	10
	D 6	ditch				20 m	0.01700	0.88	10
	R 1	pond				20 m	0.00323	4.64	10
	R 1	stream				20 m	0.01510	0.99	10
	R 2	stream				20 m	0.02010	0.75	10
	R 3	stream				20 m	0.02140	0.70	10
	R 4	stream				20 m	0.01760	0.85	10
zeta-cypermethrin	D 3	ditch		96 h	0.0013	20 m	0.01700	0.08	100
	D 4	pond				20 m	0.00323	0.40	100
	D 4	stream				20 m	0.01850	0.07	100
	D 5	pond				20 m	0.00323	0.40	100
	D 5	stream				20 m	0.01860	0.07	100
	D 6	ditch				20 m	0.01700	0.08	100
	R 1	pond				20 m	0.00323	0.40	100
	R 1	stream				20 m	0.01510	0.09	100
	R 2	stream				20 m	0.02010	0.06	100
	R 3	stream				20 m	0.02140	0.06	100
	R 4	stream				20 m	0.01760	0.07	100
Fury 10 EW	D 3	ditch		96 h	0.00069	20 m	0.01700	0.04	100
	D 4	pond				20 m	0.00323	0.21	100
	D 4	stream				20 m	0.01850	0.04	100
	D 5	pond				20 m	0.00323	0.21	100
	D 5	stream				20 m	0.01860	0.04	100
	D 6	ditch				20 m	0.01700	0.04	100
	R 1	pond				20 m	0.00323	0.21	100
	R 1	stream				20 m	0.01510	0.05	100
	R 2	stream				20 m	0.02010	0.03	100
	R 3	stream				20 m	0.02140	0.03	100
	R 4	stream				20 m	0.01760	0.04	100

Appendix 1 – list of endpoints

Fury 10 EW	D 3	ditch		21 d	0.01	20 m	0.01700	0.59	10
	D 4	pond				20 m	0.00323	3.10	10
	D 4	stream				20 m	0.01850	0.54	10
	D 5	pond				20 m	0.00323	3.10	10
	D 5	stream				20 m	0.01860	0.54	10
	D 6	ditch				20 m	0.01700	0.59	10
	R 1	pond				20 m	0.00323	3.10	10
	R 1	stream				20 m	0.01510	0.66	10
	R 2	stream				20 m	0.02010	0.50	10
	R 3	stream				20 m	0.02140	0.47	10
	R 4	stream				20 m	0.01760	0.57	10
zeta-cypermethrin	D 3	ditch	*Pseudokirch-neriella subcapitata*	96 h	> 1000	20 m	0.01700	58824	10
	D 4	pond				20 m	0.00323	309598	10
	D 4	stream				20 m	0.01850	54054	10
	D 5	pond				20 m	0.00323	309598	10
	D 5	stream				20 m	0.01860	53763	10
	D 6	ditch				20 m	0.01700	58824	10
	R 1	pond				20 m	0.00323	309598	10
	R 1	stream				20 m	0.01510	66225	10
	R 2	stream				20 m	0.02010	49751	10
	R 3	stream				20 m	0.02140	46729	10
	R 4	stream				20 m	0.01760	56818	10

Appendix 1 – list of endpoints

Fury 10 EW	D 3	ditch	*Pseudokirch-neriella subcapitata*	96 h	110	20 m	0.01700	6471	10
	D 4	pond				20 m	0.00323	34056	10
	D 4	stream				20 m	0.01850	5946	10
	D 5	pond				20 m	0.00323	34056	10
	D 5	stream				20 m	0.01860	5914	10
	D 6	ditch				20 m	0.01700	6471	10
	R 1	pond				20 m	0.00323	34056	10
	R 1	stream				20 m	0.01510	7285	10
	R 2	stream				20 m	0.02010	5473	10
	R 3	stream				20 m	0.02140	5140	10
	R 4	stream				20 m	0.01760	6250	10
Fury 10 EW	D 3	ditch	*Chironomus riparius*	28 d	0.1	20 m	0.01700	5.88	10
	D 4	pond				20 m	0.00323	31.0	10
	D 4	stream				20 m	0.01850	5.41	10
	D 5	pond				20 m	0.00323	31.0	10
	D 5	stream				20 m	0.01860	5.38	10
	D 6	ditch				20 m	0.01700	5.88	10
	R 1	pond				20 m	0.00323	31.0	10
	R 1	stream				20 m	0.01510	6.62	10
	R 2	stream				20 m	0.02010	4.98	10
	R 3	stream				20 m	0.02140	4.67	10
	R 4	stream				20 m	0.01760	5.68	10

Appendix 1 – list of endpoints

Crop and application rate : cereals and peas, 1-2 x 0.015 kg a.s./ha

Test substance	Water body type	Test species	Time-scale	End-point (µg a.s./L)	Buffer-zone	PEC_{SW}, max (µg a.s./L)	TER	Annex VI Trigger value
zeta-cypermethrin	Ditch/stream	*Oncorhynchus mykiss*	96 h	0.69	20m	0.0072	95.8	100
	pond				20m	0.0014	493	100
Fury 10 EW	Ditch/stream	*Oncorhynchus mykiss*	96 h	1.3	20m	0.0072	180	100
	pond				20m	0.0014	928	100
zeta-cypermethrin	Ditch/stream	*Pimephales promelas*	34 d	0.015	20m	0.0072	2.08	10
	pond				20m	0.0014	10.71	10
zeta-cypermethrin	Ditch/stream	*Gammarus pulex*	96 h	0.0013	20m	0.0072	0.18	100
	pond				20m	0.0014	0.93	100
Fury 10 EW	Ditch/stream	*Gammarus pulex*	96 h	0.00069	20m	0.0072	0.09	100
	pond				20m	0.0014	0.49	100
Fury 10 EW	Ditch/stream	*Daphnia magna*	21 d	0.01	20m	0.0072	1.39	10
	pond				20m	0.0014	7.1	10
zeta-cypermethrin	Ditch/stream	*Pseudokirch-neriella subcapitata*	96 h	>1000	20m	0.0072	138889	10
	pond				20m	0.0014	714286	10
Fury 10 EW	Ditch/stream	*Pseudokirch-neriella subcapitata*	96 h	110	20m	0.0072	15278	10
	pond				20m	0.0014	78571	10

Appendix 1 – list of endpoints

Fury 10 EW	Ditch /stream	*Chironomus riparius*	28 d	0.1	20m	0.0072	13.9	10
	pond				20m	0.0014	71.4	10

Fury 10 EW : equivalent to Fury 100 EW, both formulations containing 100 g/L zeta-cypermethrin

Appendix 1 – list of endpoints

Crop and application rate : peas, 1-2 x 0.015 kg a.s./ha

Test substance	Scena-rio	Water body type	Test species	Time-scale	End-point (µg a.s./L)	Buffer-zone	PEC_{SW}, max (µg a.s./L)	TER	Annex VI Trigger value
zeta-cypermethrin	R 4	stream	*Oncorhynchus mykiss*	96 h	0.69	20 m	0.01220	56.6	100
Fury 10 EW	R 4	stream	*Oncorhynchus mykiss*	96 h	1.3	20 m	0.01220	107	100
zeta-cypermethrin	R 4	stream	*Pimephales promelas*	34 d	0.015	20 m	0.01220	1.23	10
zeta-cypermethrin	R 4	stream	*Gammarus pulex*	96 h	0.0013	20 m	0.01220	0.11	100
Fury 10 EW	R 4	stream	*Gammarus pulex*	96 h	0.00069	20 m	0.01220	0.06	100
Fury 10 EW	R 4	stream	*Daphnia magna*	21 d	0.01	20 m	0.01220	0.82	10
zeta-cypermethrin	R 4	stream	*Pseudokirch-neriella subcapitata*	96 h	> 1000	20 m	0.01220	81967	10
Fury 10 EW	R 4	stream	*Pseudokirch-neriella subcapitata*	96 h	110	20 m	0.01220	9016	10
Fury 10 EW	R 4	stream	*Chironomus riparius*	28 d	0.1	20 m	0.01220	8.20	10

Fury 10 EW : equivalent to Fury 100 EW, both formulations containing 100 g/L zeta-cypermethrin

Appendix 1 – list of endpoints

Bioconcentration	
	Zeta-cypermethrin
$logP_{O/W}$	5 – 6
Bioconcentration factor (BCF)[1] ‡	356 ± 107 (benzyl-labeled, whole fish) 443 ± 261 (cyclopropyl-labeled, whole fish)
Annex VI Trigger for the bioconcentration factor	100
Clearance time (days) (CT_{50})	1.2 ± 0.26 days (benzyl-labeled) 1.2 ± 0.5 days (cyclopropyl-labeled)
(CT_{90})	3.9 ± 0.85 days (benzyl-labeled) 4.1 ± 1.7 days (cyclopropyl-labeled)
Level and nature of residues (%) in organisms after the 14 day depuration phase	Benzyl-labeled residues : - in fillet : 19 % - in viscera : 18 % - in whole fish : 23 % Cyclopropyl-labeled : - in fillet : 5 % - in viscera : 15 % - in whole fish : 17 %

Appendix 1 – list of endpoints

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)
Fury 10 EW[1]	0.436 µg form/bee (48 h) (0.044 µg a.s./bee)	0.021 µg form/bee (48 h) (0.002 µg a.s./bee)
Field or semi-field tests		

Conclusions of the cage tests :
The application of Fury at 300 mL/ha in Phacelia in the evening after flight activity of the bees caused a visible repellent effect for 1-2 days, a higher mortality than in the water control for 1-2 days and no impact on the bee brood development.
The application of Fury at 150 mL/ha in Phacelia during foraging activity of the bees caused a visible repellent effect for 1-3 days, a higher mortality than in the water control for 1-3 days and no impact on the bee brood development.

Conclusions of the field tests :
The application of Fury at 150 mL/ha in oilseed rape caused a repellent effect for 1 day, a higher mortality than in the water control for 4 days and no impact on the bee brood.
The application of Fury at 150 mL/ha in Phacelia during flight activity caused a repellent effect for 1 day, a higher mortality than in the water control for 2 days and no impact on the bee brood.
The application of Fury at 300 mL/ha in Phacelia after flight activity caused no repellent effect, a higher mortality than in the water control for 1 day and no impact on the bee brood.
The application of Fury at 15 g a.s./ha in Phacelia during flight activity caused a repellent effect for 1-4 days, a higher mortality than in the water control for 1-8 days and no impact on the bee brood.

Conclusions of the tunnel tests :
The application of Fury at 150 mL/ha on honeydew on wheat during foraging activity caused a repellent effect for 8 days, a higher mortality than in the water control for 2 days and no accumulation of reserves whereas an increase of 7 kg in the water control was observed.
In a second tunnel test, the application of Fury at 150 mL/ha on honeydew on wheat during foraging activity caused a repellent effect for 6 days, a higher mortality than in the water control for 1 day and no accumulation of reserves whereas an increase of 7 kg in the water control was observed.
In a third tunnel test, the application of Fury at 150 mL/ha on honeydew on wheat during foraging activity caused a repellent effect for 4 days, a higher mortality than in the water control for 6 days and no accumulation of reserves whereas an increase of 3.5 kg in the water control and the reference substance tunnel was observed.
The tunnel tests on flower of oilseed rape were not acceptable due to bad weather conditions or irregular mortality evolution.

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Appendix 1 – list of endpoints

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

Crop and application rate : maize, 1 x 0.0375 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
zeta-cypermethrin	oral	852	50
	contact	18750	50

Crop and application rate : cereals and peas, 1-2 x 0.0015 kg a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
zeta-cypermethrin	oral	341	50
	contact	7500	50

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

Species	Life stage	Test substance, substrate and duration	Dose	Endpoint	% effect	Trigger value
Laboratory tests						
Typhlodromus pyri	proto-nymphs	Fury 100 g/L EW, glass plates, 7 d	1.6 g a.s./ha, initial	Corrected mortality	3.9 %	50 %
			8 g a.s./ha, initial	Corrected mortality	21.6 %	50 %
			40 g a.s./ha, initial	Corrected mortality	70.6 %	50 %
			200 g a.s./ha, initial	Corrected mortality	90.2 %	50 %
			1000 g a.s./ha, initial	Corrected mortality	100.0 %	50 %
			LR_{50} = 23.18 mg a.s./ha			

Appendix 1 – list of endpoints

Species	Life stage	Test substance, substrate and duration	Dose	Endpoint	% effect	Trigger value
Extended laboratory tests						
Aphidius rhopalosiphi	adults	Fury 10 EW, barley seedlings, 48 h + 11 d	1.02 mL a.s./ha, initial	Corrected mortality Reproduction	5.13 % + 33.74 %	50 % 50 %
			2.04 mL a.s./ha, initial	Corrected mortality Reproduction	20.51 % - 4.71 %	50 % 50 %
			4.08 mL a.s./ha, initial	Corrected mortality Reproduction	55.92 % + 45.57 %	50 % 50 %
			8.16 mL a.s./ha, initial	Corrected mortality Reproduction	61.54 % + 6.32 %	50 % 50 %
			16.32 mL a.s./ha, initial	Corrected mortality Reproduction	75.71 % - 68.97 %	50 % 50 %
			LR_{50} = 5.48 mL a.s./ha			
Typhlodromus pyri	proto-nymphs	Fury 10 EW, bean plants, 7 d	0.010 g a.s./ha, initial	Corrected mortality Reproduction	3.5 % + 2.0 %	50 % 50 %
			0.029 g a.s./ha, initial	Corrected mortality Reproduction	5.3 % - 10.9 %	50 % 50 %
			0.086 g a.s./ha, initial	Corrected mortality Reproduction	54.4 % -	50 % 50 %
			0.254 g a.s./ha, initial	Corrected mortality Reproduction	92.9 % -	50 % 50 %
			0.750 g a.s./ha, initial	Corrected mortality Reproduction	100.0 % -	50 % 50 %
			LR_{50} = 0.085 g a.s./ha			

Appendix 1 – list of endpoints

Species	Life stage	Test substance, substrate and duration	Dose	Endpoint	% effect	Trigger value
Typhlodromus pyri	proto-nymphs	Fury 10 EW, maize plants, 7 d	1.04 g a.s./ha, initial	Corrected mortality Reproduction	100.0 % -	50 % 50 %
			2.81 g a.s./ha, initial	Corrected mortality Reproduction	100.0 % -	50 % 50 %
			37.5 g a.s./ha, initial	Corrected mortality Reproduction	100.0 % -	50 % 50 %
			1.04 g a.s./ha, 7 DAA	Corrected mortality Reproduction	4.4 % 0.0 %	50 % 50 %
			2.81 g a.s./ha, 7 DAA	Corrected mortality Reproduction	4.4 % + 20.6 %	50 % 50 %
			37.5 g a.s./ha, 14DAA	Corrected mortality Reproduction	48.9 % - 33.7 %	50 % 50 %
			37.5 g a.s./ha, 21 DAA	Corrected mortality Reproduction	1.1 % + 37.0 %	50 % 50 %
Episyrphus balteatus	larvae	Fury 10 EW, barley plants, 6-12 d	15.9 mL a.s./ha, initial	Corrected mortality Reproduction	66 % - 79.4 %	50 % 50 %

Fury 10 EW : equivalent to Fury 100 EW, both formulations containing 100 g/L zeta-cypermethrin

Corrected mortality : positive values : adverse effects
Reproduction : negative values : adverse effects; positive values : no adverse effects
DAA : days after application

Appendix 1 – list of endpoints

Field tests
In a first field test, Fury 10 EW was applied at a single application rate of 75 mL/ha (equivalent to 8.5 mL a.s./ha) in winter sown wheat at BBCH 65. Shortly after treatment, the number of carabid beetles decreased with full recovery for all the carabid taxa within 36 days (*Pterostichus madidus*, *Loricera pilicornis*, *Trechus quadristriatus*). Due to bad weather conditions the number of staphylinid beetles declined. No clear effects of Fury could be demonstrated however one species had not recovered after 1 month (*Tachyporus chrysomelinus*). A transitional increase in the number of spiders with subsequent population reduction after 1 month was observed in the control plots. In the Fury plots a decrease of the population was observed after application and no evolution of the population occurred during the whole study period. There was no indication of any harmful effect on Collembola (Entomobryoidea and Sminthuridae). Cereal aphids, mostly *Sitobion avenae*, are target organisms. In control plots the number of *Sitobion avenae* continued to rise whereas in the Fury treated plots the numbers per ear fell almost to zero. Some recovery took place during the remainder of the study. The emergence of parasitoids from aphid mummies collected in the field was assessed. The number of parasitoids collected in the Fury plot was limited and did not allow to perform very robust statistics. However, the emergence of parasitoids was similar in the Fury and the control plots. Larvae of the noctuid moth *Agrotis segetum* are also target organisms. The larval mortality in the Fury treated plots was significantly higher than in the control plots.
In a second field test, at application of 150 mL/ha (equivalent to 15 mL a.s./ha) in apple orchards, Fury has an effect on target insects (*Panonychus ulmi*), non-target insects (predatory Heteroptera, Coccinellidae (*Stethorus*), Neuroptera), predatory mites (*Neoseiulus californicus*) and Hymenoptera (genus *Encarsia*). This leads to an important increase of the target organism for 1.5 months and afterwards a natural decline in the population is observed. Overall, the product Fury is non-selective to non-target arthropods.

The PRAPeR 48 meeting concluded that the in-field risk to non-target arthropods needs to be further addressed by field studies and off-field risk also needs to be addressed.

Appendix 1 – list of endpoints

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

Test organism	Test substance	Time scale	End point[1]
Earthworms			
Eisenia foetida	Fury 10 EW	Acute	LC_{50} = 750 mg form/kg soil d.w. (75 mg a.s/kg soil d.w.) LC_{50corr} = 37.5 mg a.s./kg soil d.w.
Eisenia foetida	cis-DCVA	Acute	LC_{50} = 103 mg/kg soil d.w. **LC_{50corr} = 51.5 mg/kg soil d.w.**
Eisenia foetida	trans-DCVA	Acute	LC_{50} = 111 mg/kg soil d.w. LC_{50corr} = 55.5 mg/kg soil d.w.
Eisenia foetida	3-phenoxybenzoic acid	Acute	LC_{50} = 148 mg/kg soil d.w. LC_{50corr} = 74 mg/kg soil d.w.
Other soil macro-organisms			
The PRAPeR 48 meeting concluded that studies with Collembola and mites were not formally triggered (DT_{90} < 100 days). However, the meeting agrees that the in-field risk assessment should be covered by a new field study for non-target arthropods.			
Soil micro-organisms			
N-transformation	Fury 10 EW	91 d	+ 19 % effect at day 91 at 0.2 mg form/kg soil d.w. (0.02 mg a.s./kg soil d.w.) in soil 1
			- 5 % effect at day 91 at 0.2 mg form/kg soil d.w. (0.02 mg a.s./kg soil d.w.) in soil 2
			+ 40 % effect at day 91 at 2.0 mg form/kg soil d.w. (0.2 mg a.s./kg soil d.w.) in soil 1
			- 4 % effect at day 91 at 2.0 mg form/kg soil d.w. (0.2 mg a.s./kg soil d.w.) in soil 2
	Fury 10 EW	59 d	+ 2 % effect at day 59 at 0.2 mg form/kg soil d.w. (0.02 mg a.s./kg soil d.w.)
			- 5 % effect at day 59 at 2.0 mg form/kg soil d.w. (0.2 mg a.s./kg soil d.w.)

Appendix 1 – list of endpoints

Test organism	Test substance	Time scale	End point[1]
C-transformation	Fury 10 EW	91 d	+ 34 % effect at day 91 at 0.2 mg form/kg soil d.w. (0.02 mg a.s./kg soil d.w.) in soil 1
			+ 9 % effect at day 91 at 0.2 mg form/kg soil d.w. (0.02 mg a.s./kg soil d.w.) in soil 2
			+ 37 % effect at day 91 at 2.0 mg form/kg soil d.w. (0.2 mg a.s./kg soil d.w.) in soil 1
			+ 4 % effect at day 91 at 2.0 mg form/kg soil d.w. (0.2 mg a.s./kg soil d.w.) in soil 2
	Fury 10 EW	59 d	+ 12 % effect at day 59 at 0.2 mg form/kg soil d.w. (0.02 mg a.s./kg soil d.w.)
			+ 10 % effect at day 59 at 2.0 mg form/kg soil d.w. (0.2 mg a.s./kg soil d.w.)
Field studies[2]			
The PRAPeR 48 meeting concluded that studies with Collembola and mites were not formally triggered (DT_{90} < 100 days). However, the meeting agrees that the in-field risk assessment should be covered by a new field study for non-target arthropods.			

[1] indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})
[2] litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

Fury 10 EW : equivalent to Fury 100 EW, both formulations containing 100 g/L zeta-cypermethrin

Toxicity/exposure ratios for soil organisms

Crop and application rate : maize, 1 x 0.0375 kg a.s./ha

Test organism	Test substance	Time scale	Max plateau PEC_{SOIL}[2] (mg/kg)	TER	Trigger
Earthworms					
Eisenia foetida	zeta-cypermethrin ‡	Acute	0.038	987	10
Eisenia foetida	cis-DCVA	Acute	0.019	2711	10
Eisenia foetida	trans-DCVA	Acute	0.019	2921	10
Eisenia foetida	3-phenoxybenzoic acid	Acute	0.019	3895	10
Other soil macro-organisms					
A study addressing the risk to Collembola reproduction or gamasid mites at the correct dose is required.					

[1] to be completed where first Tier triggers are breached
[2] indicate which PEC soil was used (e.g. plateau PEC)

Appendix 1 – list of endpoints

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

Preliminary screening data

Not required.

Laboratory dose response tests

Most sensitive species	Test substance	EC_{50} (mg/kg soil d.w.)[2] vegetative vigour	ER_{50} (mg/kg soil d.w.)[2] emergence	Exposure[1] (µg/kg soil d.w.)[2]	TER	Trigger
ryegrass	zeta-cypermethrin	> 100	> 100	1.39	> 71942	5
radish	zeta-cypermethrin	-	> 100	1.39	> 71942	5
		43.2	-	1.39	31079	5
red clover	zeta-cypermethrin	> 100	> 100	1.39	> 71942	5

[1] explanation of how exposure has been estimated should be provided (e.g. based on Ganzelmeier drift data)
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation

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

Not required.

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

Test type/organism	Endpoint
Activated sludge	EC_{50} (3 h) > 100 mg a.s./L

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

	RMS/peer review proposal
zeta-cypermethrin	N, R50

	RMS/peer review proposal
Fury 10 EW	N, R50

Appendix 2 – abbreviations used in the list of endpoints

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
BCF	bioconcentration factor
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DFR	dislodgeable foliar residue
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
FOMC	first order multi compartment
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MSD	gas chromatography with mass-selective detection
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GPC	gel-permeation chromatography
GS	growth stage
h	hour(s)

Appendix 2 – abbreviations used in the list of endpoints

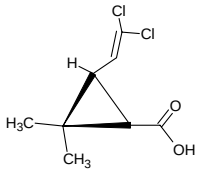
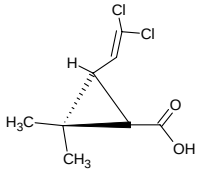
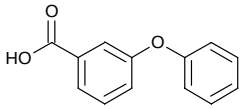
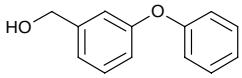
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography
	or high performance liquid chromatography
HQ	hazard quotients
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
MHC	moisture holding capacity
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
MTD	maximum tolerable dose
MW	molecular weight
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NPE	nonyl-phenyl-ethoxylate
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PND	post-natal-day

Appendix 2 – abbreviations used in the list of endpoints

PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UDS	unscheduled DNA synthesis
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

Appendix 3 – used compound code(s)

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
cis-DCVA	(1*R*,3*R*)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid	
trans-DCVA	(1*R*,3*S*)-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid	
*m*PBAcid (3PBA)	3-phenoxybenzoic acid	
*m*PBAlcohol	(3-phenoxyphenyl)methanol	
*m*PBAldehyde	3-phenoxybenzaldehyde