TECHNICAL REPORT

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Outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for gamma-cyhalothrin in light of confirmatory data

European Food Safety Authority (EFSA)

Abstract

The European Food Safety Authority (EFSA) was asked by the European Commission to provide scientific assistance with respect to the risk assessment for an active substance in light of confirmatory data requested following approval in accordance with Article 6(1) of Directive 91/414/EEC and Article 6(f) of Regulation (EC) No 1107/2009. In this context EFSA's scientific views on the specific points raised during the commenting phase conducted with Member States, the applicant and EFSA on the confirmatory data and their use in the risk assessment for gamma-cyhalothrin are presented. The current report summarises the outcome of the consultation process organised by the rapporteur Member State the United Kingdom and presents EFSA's scientific views and conclusions on the individual comments received.

Keywords: gamma-cyhalothrin, peer review, confirmatory data, risk assessment, pesticide, insecticide

Requestor: European Commission

Question number: EFSA-Q-2019-00110

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Summary

Gamma-cyhalothrin has been approved on 1 April 2015 under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 1334/2014. It was a specific provision of the approval that the applicant was required to submit to the European Commission further studies on

(1) analytical methods for the monitoring of residues in body fluids, tissues and environmental matrices;

(2) the toxicity profile of the metabolites CPCA, PBA and PBA(OH);

(3) the long-term risk to wild mammals;

(4) the potential for biomagnification in terrestrial and aquatic food chains

by 31 March 2017.

In accordance with the specific provision, the applicant, Cheminova A/S, submitted an updated dossier in March 2017, which was evaluated by the designated rapporteur Member State (RMS), the United Kingdom, in the form of an addendum to the draft assessment report. In compliance with guidance document SANCO 5634/2009-rev.6.1, the RMS distributed the addendum to Member States, the applicant and EFSA for comments on 31 July 2018. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA on 14 February 2019. EFSA added its scientific views on the specific points raised during the commenting phase in column 4 of the reporting table.

The current report summarises the outcome of the consultation process organised by the RMS, the United Kingdom, and presents EFSA's scientific views and conclusions on the individual comments received.

Gamma-cyhalothrin is the ISO common name for (*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate or (*S*)-α-cyano-3-phenoxybenzyl (1*R*)-*cis*-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropane-carboxylate (IUPAC).

The representative formulated product for the evaluation was 'Corello' (GF-317)', a capsule suspension (CS) formulation containing 60 g/L gamma-cyhalothrin (5.92 % w/w). The representative uses evaluated were foliar spraying applications to control a range of insects on winter and spring wheat and barley.

The analytical methods for the monitoring of residues in body fluids, tissues and environmental matrices submitted as confirmatory data are capable of distinguishing between residues of gamma-cyhalothrin and lambda-cyhalothrin. The confirmatory data requirement has been fulfilled, however the LOQ of 0.003 µg/L for drinking and surface water is above the refined endpoint of 0.002 µg/L that was defined on the basis of the mesocosm study and other additional information submitted under the confirmatory data procedure.

Regarding the plant and animal metabolite cyclopropyl carboxylic acid (CPCA), there is a consensus among Member State experts that the metabolite is unlikely to be genotoxic and the toxicological reference values of the parent are applicable to the metabolite since it is a major metabolite in the rat metabolism. With regards to metabolites 3-phenoxybenzoic acid (PBA) and 3-(4'-hydroxyphenoxy)benzoic acid (PBA(OH)), their genotoxic profile either regarding mutagenicity or clastogenicity potential could not be concluded and a peer review consultation is proposed. The use of a TTC approach for these metabolites common to several pyrethroid active substances would also merit peer review discussion in mammalian toxicology and residues.

The new FOCUSsw modelling submitted by the applicant was considered not appropriate for consideration as part of a regulatory risk assessment as the input parameters used were not in line with the gamma-cyhalothrin agreed endpoints (EFSA, 2014) and historic versions of the FOCUSsw tools rather than the current versions were used. The predicted environmental concentrations (PEC) in surface water and sediment re-evaluated by the RMS were considered valid and used in the risk assessment.

Two foliar residue decline studies on cereals and oilseed rape were submitted and the estimated DT50 of 4.9 days was used by the applicant in the higher tier mammalian risk assessment. However, due to several shortcomings in the study design and in the kinetic evaluation, it was concluded that the default 10 days DT50 should be used in the higher tier assessment. Based on the information provided to fulfil the confirmatory data requirement, the long-term risk to herbivorous and omnivorous mammals from the proposed representative uses of gamma-cyhalothrin was not addressed. The risk from potential for biomagnification in terrestrial and aquatic food chains was concluded as low.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Gamma-cyhalothrin has been approved on 1 April 2015 under Regulation (EC) No 1107/2009[1], in accordance with Commission Implementing Regulation (EU) No 540/2011[2], as amended by Commission Implementing Regulation (EU) No 1334/2014[3].

It was a specific provision of the approval that the applicant was required to submit to the European Commission further studies on

(1) analytical methods for the monitoring of residues in body fluids, tissues and environmental matrices;

(2) the toxicity profile of the metabolites CPCA, PBA and PBA(OH);

(3) the long-term risk to wild mammals;

(4) the potential for biomagnification in terrestrial and aquatic food chains

by 31 March 2017.

In accordance with the specific provision, the applicant, Cheminova A/S, submitted an updated dossier in March 2017, which was evaluated by the designated rapporteur Member State (RMS), the United Kingdom, in the form of an addendum to the draft assessment report (United Kingdom, 2019). In compliance with guidance document SANCO 5634/2009-rev.6.1 (European Commission, 2013), the RMS distributed the addendum to Member States, the applicant and EFSA for comments on 31 July 2018. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA on 14 February 2019. EFSA added its scientific views on the specific points raised during the commenting phase in column 4 of the reporting table.

The current report summarises the outcome of the consultation process organised by the RMS, the United Kingdom, and presents EFSA's scientific views and conclusions on the individual comments received.

1.2. Interpretation of the Terms of Reference

On 22 December 2014 the European Commission requested EFSA to provide scientific assistance with respect to the risk assessment of confirmatory data following approval of an active substance in accordance with Article 6(1) of Directive 91/414/EEC and Article 6(f) of Regulation (EC) No 1107/2009. EFSA's scientific views on the specific points raised during the commenting phase conducted with Member States, the applicant and EFSA on the risk assessment of confirmatory data for gamma-cyhalothrin are presented.

To this end, a technical report containing the finalised reporting table is being prepared by EFSA. The deadline for providing the finalised report is 14 March 2019.

On the basis of the reporting table, the European Commission may decide to further consult EFSA to conduct a full or focused peer review and to provide its conclusions on certain specific points.

[1] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1-50.

[2] Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p.1-186.

[3] Commission Implementing Regulation (EU) No 1334/2014 of 16 December 2014 approving the active substance gamma-cyhalotrin, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011 and allowing Member States to extend provisional authorisations granted for that active substance. OJ L 360, 17.12.2014, p. 1–5

2. Assessment

The comments received on the pesticide risk assessment for the active substance gamma-cyhalothrin in light of confirmatory data and the conclusions drawn by the EFSA are presented in the format of a reporting table.

The comments received are summarised in column 2 of the reporting table. The RMS' considerations of the comments are provided in column 3, while EFSA's scientific views and conclusions are outlined in column 4 of the table.

The finalised reporting table is provided in Appendix A of this report.

Documentation provided to EFSA

1. United Kingdom, 2019. Addendum to the assessment report on gamma-cyhalothrin, confirmatory data, July 2018, updated in January 2019. Available online: www.efsa.europa.eu.

2. United Kingdom, 2019. Reporting table, comments on the pesticide risk assessment for gamma-cyhalothrin in light of confirmatory data, February 2019.

References

EFSA (European Food Safety Authority), 2009. Guidance on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009;7(12):1438, 358 pp. doi:10.2903/j.efsa.2009.1438

EFSA (European Food Safety Authority), 2014. Conclusion on the peer review of the pesticide risk assessment of the active substance gamma-cyhalothrin. EFSA Journal 2014;12(2):3560, 93 pp. doi:10.2903/j.efsa.2014.3560

European Commission, 2013. Guidance document on the procedures for submission and assessment of confirmatory information following approval of an active substance in accordance with Regulation (EC) No 1107/2009. SANCO 5634/2009-rev. 6.1

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2000. FOCUS groundwater scenarios in the EU review of active substances. Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference SANCO/321/2000-rev. 2, 202 pp., as updated by the generic guidance for FOCUS groundwater scenarios, v. 1.1, April 2002.

Abbreviations

1/n	slope of Freundlich isotherm
a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BAF	bio-accumulation factor
BBCH	Biologische Bundesanstalt, Bundessortenamt und CHemische Industrie
DAR	draft assessment report
DT50	period required for 50% dissipation
GAP	good agricultural practice
GEF	global evaluation factor
GW	groundwater
HCD	historical control data
HPLC-MS	high-pressure liquid chromatography–mass spectrometry
ILV	interlaboratory validation
Kdoc	organic carbon linear adsorption coefficient
LoEP	list of end points
LOQ	limit of quantification
MAF	multiple application factor
MF	mutant frequency
MLA	mouse lymphoma mutation assay
MN	micronucleus
MOA	mode of action
MS	Member State
NESTI	national estimated short-term intake
NEU	northern Europe
NOEC	no observed effect concentration
OECD	Organisation for Economic Co-operation and Development
OSR	oilseed rape
QSAR	quantitative structure–activity relationship
RAC	regulatory acceptable concentration
PEC_{GW}	predicted environmental concentration in ground water
PEC_{sw}	predicted environmental concentration in surface water
PD	proportion of different food types
PT	proportion of diet obtained in the treated area
RMS	rapporteur Member State
SFO	single first-order

TER	toxicity exposure ratio
TG	test guideline
TMDI	theoretical maximum daily intake
TWA	time-weighted average
TTC	threshold toxicological concern
SEU	southern Europe

Appendix A – Collation of comments from Member States, applicant and EFSA on the pesticide risk assessment for the active substance gamma-cyhalothrin in light of confirmatory data and the conclusions drawn by EFSA on the specific points raised

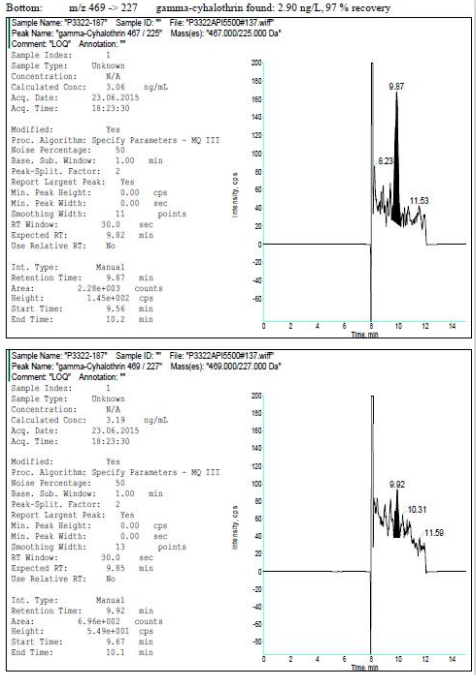
1. Physical/Chemical Properties; Details of Uses and Further Information; Methods of Analysis

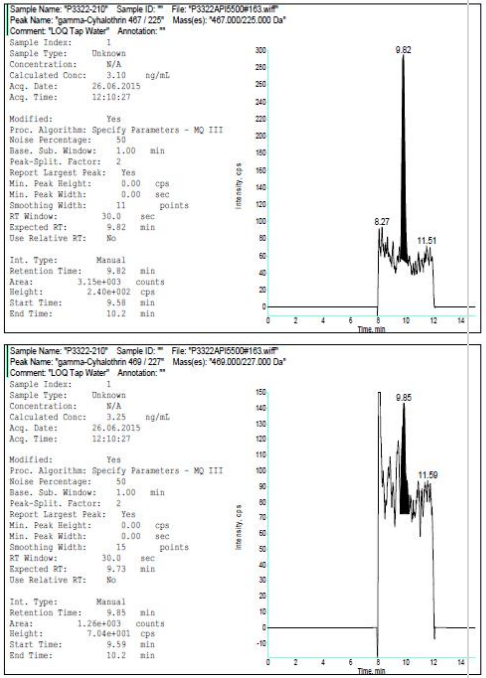
Methods of analysis (B.5)

No.	Column 1 Reference to addendum to assessment report	Column 2 Comments from Member States / applicant / EFSA	Column 3 Evaluation by rapporteur Member State	Column 4 EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data
1(1)	Conf. data addendum, Analytical methods, soil, p.13	EFSA: just a small clarification: is our understanding correct that by the peak at retention time 6.9 min, called lambda-cyhalothrin means the other compound forming lambda? ((*R*)-α-cyano-3-phenoxybenzyl (1*S*,3*S*)-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate)	UK: This is correct. **Addressed**	Addressed.
1(2)	Conf. data addendum, Analytical methods, Determination of the Degradation of Residues of Gamma-Cyhalothrin, p.29	EFSA: It is stated that the objective of the analytical phase was to measure degradation of residue levels of gamma-cyhalothrin, however the column used is not separating the enantiomers, i.e. more precisely gamma-cyhalothrin and its enantiomer. The method is acceptable for the residue definition for monitoring defined as gamma-cyhalothrin and its enantiomer (any ratio of constituent isomers in lambda-cyhalothrin).	UK: The method supporting studies 1660 GCH and 1661 GCH is a risk assessment method and as such there is no need for the method to be able to distinguish between residues of gamma-cyhalothrin and lambda cyhalothrin. Conversion of gamma-cyhalothrin to lambda-cyhalothrin is not considered likely. **Addressed.**	Addressed: The method used is not selective to gamma-cyhalothrin.
1(3)	Conf. data addendum, Analytical methods,	EFSA: Clarification is needed if the comparison of the ratios of the two ions	UK: No data on the ratio of the ions has been presented in the study reports for lambda-cyhalothrin. However it is noted	See comment 1(2)

Methods of analysis (B.5)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
	Determination of the Degradation of Residues of Gamma-Cyhalothrin, p.29	observed (m/z 205 and 241) to those observed in the standards of gamma- and lambda-cyhalothrin would allow to monitor the degradation of gamma-cyhalothrin in the methods in soil, water, sediment, feed and any additional matrices used in support of ecotoxicology studies capable of determining residues of gamma-cyhalothrin in whole cereal plants as they do not separate the two enantiomers.	that the method supporting studies 1660 GCH and 1661 GCH is a risk assessment method and as such there is no need for the method to be able to distinguish between residues of gamma-cyhalothrin and lambda cyhalothrin. Conversion of gamma-cyhalothrin to lambda-cyhalothrin is not considered likely. **Addressed**	
1(4)	Conf. data addendum, Analytical methods, Overall conclusion, p.6	EFSA agrees that the methods for monitoring purposes submitted as confirmatory data for the determination of gamma-cyhalothrin in soil, surface and drinking water, air and body fluids and tissues are capable of distinguishing between residues of gamma-cyhalothrin and lambda-cyhalothrin.	UK: Noted. Thank you. **Addressed**	Addressed.
1(5)	Confirmatory data B5 – analytical method for water (W. Wadim, 2015, report 1629GCH)	FR: The ratio signal/noise seems very low for the confirmatory transitions when chromatograms of fortified water samples at LOQ are analysed (see column further explanations). Consequently, FR is not convinced of the validation data for the second mass transition. Additionally, the LOQ (3ng/l) of this new	UK: It is acknowledged that the signal: noise is low for the confirmatory transition. However, the method is nevertheless satisfactorily validated in accordance with SANCO/825/00 rev. 8.1. In terms of the LOQ, according to SANCO/825/00 rev 8.1 the monitoring method for surface water should have an LOQ that complies with the lowest effect	The refined endpoint based on mesocosm study and additional data/information is 0.002 µg a.s/L Method W. Wadim (2015) submitted as confirmatory data has a LOQ of 0.003 µg a.s/L, slightly above the lowest endpoint.

Methods of analysis (B.5)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		method (Wadim, 2015) does not comply with the lowest CE50 (0.3 ng/L). The previous method described in the DAR (Hamberger, 2010) was capable to quantify lambda cyhalothrin (the two enantiomers including gamma cyhalothrin) up to 0.0003µg/L. Therefore, a new highly specific method with a LOQ of 0.3ng/L should be provided to cover this data gap. Additionally, an ILV should be provided at the renewal of the active substance.	concentration mentioned in Table 4. Of the study endpoints mentioned in table 4, the lowest for gamma-cyhalothrin from the LOEP is 0.0155 µg a.s./L (long-term fish NOEC). Therefore the LOQ does comply with this value. The derivation of the 0.3 ng a.s./L LOQ is not clear. However, this is equivalent to the overall Regulatory Acceptable Concentration (RAC) for surface water. This RAC was derived from a mesocosm study (which is not referred to in table 4) and includes an assessment or uncertainty factor (again not referred to in table 4). Therefore compliance with an LOQ of 0.3 ng a.s./L is not considered necessary. **Addressed.**	

Methods of analysis (B.5)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		PTRL Europe ID P 3322 G Page 37 **Figure 13 LC-MS/MS Chromatograms: Surface Water Fortified at LOQ** Top: m/z 467 -> 225 gamma-cyhalothrin found: 2.78 ng/L, 93 % recovery Bottom: m/z 469 -> 227 gamma-cyhalothrin found: 2.90 ng/L, 97 % recovery 		

Methods of analysis (B.5)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		PTRL Europe ID P 3322 G Page 33 **Figure 9 LC-MS/MS Chromatograms: Tap Water Fortified at LOQ** Top: m/z 467 -> 225 gamma-cyhalothrin found: 2.82 ng/L, 94 % recovery Bottom: m/z 469 -> 227 gamma-cyhalothrin found: 2.95 ng/L, 98 % recovery  		
1(6)	Addendum – Confirmatory Data, B.5, Methods of Analysis, Page 13	FMC: UK: HLPC coupled to MS/MS NOT: Please amend the typographic error to read "HPLC coupled to MS/MS"	UK: Noted. Amended. **Addressed**	Addressed.

Methods of analysis (B.5)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		appears on two occasions.		
1(7)	Addendum – Confirmatory Data, B.5, Methods of Analysis, Page 16	FMC: UK: HLPC coupled to MS/MS NOT: Please amend the typographic error to read "HPLC coupled to MS/MS" appears on one occasion.	UK: Noted. Amended. **Addressed**	Addressed.
1(8)	Addendum – Confirmatory Data, B.5, Methods of Analysis, Page 23	FMC: UK: HLPC coupled to MS/MS NOT: Please amend the typographic error to read "HPLC coupled to MS/MS" appears on one occasion.	UK: Noted. Amended. **Addressed**	Addressed.
1(9)	Addendum – Confirmatory Data, Methods of Analysis, Page 26	FMC: UK: HLPC coupled to MS/MS NOT: Please amend the typographic error to read "HPLC coupled to MS/MS" appears on one occasion.	UK: Noted. Amended. **Addressed**	Addressed.

2. Mammalian toxicology

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
2(1)	Vol. 3, Conf. data addendum, B.6.8.1.1 CPCA	EFSA: Gene mutation tests in bacterial and mammalian cells conducted with CPCA in vitro were all negative. CPCA presented positive results in a chromosome aberration assay in vitro with metabolic activation; positive results were also seen in mouse lymphoma assay (dose-related increase in number of small colonies without metabolic activation). These results were not reproduced in another mouse lymphoma assay and an in vitro micronucleus test. An in vivo micronucleus test was negative although bone marrow exposure was not directly evidenced, clear signs of toxicity were observed. On this basis, we agree with the assessment provided by the RMS with regards to the genotoxicity potential of CPCA that the metabolite is unlikely to be genotoxic or clastogenic in vivo. It is however noted that the relative toxicity of the metabolite in comparison with the parent gamma-cyhalothrin has not been	UK: Thank you. UK: To estimate the relative toxicity of CPCA compared to the parent, additional vertebrate data would be required. The RMS considers that these are not necessary and that the confirmatory data requirements have been fulfilled. A QSAR assessment for CPCA shows no additional hazards	Addressed. In EFSA's view the use of QSAR may support hazard identification in some cases, but is not informative on the hazard characterisation of substances. However, it is agreed that CPCA appears to be a major metabolite in the rat metabolism studies conducted with cyhalothrin (although it would be helpful to see a tabular presentation of the percentage of the administered dose metabolites retrieved in the different compartments in the confirmatory data evaluation addendum). We agree with the RMS that the toxicity profile of the metabolite CPCA is covered by the toxicological reference values established for the parent. The confirmatory data requirement is considered fulfilled for this metabolite. See also 2(19)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		addressed (as identified in the data gap reported in the EFSA conclusion of 2014). Accordingly, this information is needed for the assessment of consumer exposure in the residue section, possibly to be included in the metabolite in the residue definition, and the confirmatory data requirement has not been fulfilled.	beyond those of the parent. CPCA is also a major rat metabolite. A conservative TTC assessment against the Cramer Class III threshold shows no unacceptable risk. If CPCA is included in the RoD based on its absolute and relative prevalence in crops/livestock, the parent reference values could be used for the dietary risk assessment of CPCA. **Addressed**	
2(2)	Vol. 3, Conf. data addendum B.6.8.1.2 3-Phenoxybenzoic acid (PBA) B.6.8.1.3 PBA (OH)	EFSA: It is noted that, for these metabolites, although they were investigated for their genotoxic potential, their relative toxicity in comparison with the active substance, cyhalothrin, has not been addressed (repeated-dose toxicity) as requested in the confirmatory data requirements.	UK: To estimate the relative toxicity of PBA and PBA (OH) compared to the parent, additional vertebrate data would be required. The RMS considers that these are not necessary and that the confirmatory data requirements have been fulfilled. A QSAR assessment for PBA and PBA (OH) shows no additional hazards beyond those of the parent. A conservative TTC assessment against the Cramer Class III threshold shows no unacceptable risk. If PBA and PBA (OH) are included in the RoD based on their absolute and relative prevalence in crops/livestock, the parent reference values could be used for the dietary	See peer review consultations proposed below regarding the genotoxic potential of PBA and PBA(OH). As mentioned above, the QSAR analysis is not informative on the relative toxicity of the metabolites in comparison with the parent. PBA and PBA(OH) would also be considered major metabolites of gamma-cyhalothrin, although in this case it is unclear to which extent these metabolites may be further metabolised – and therefore less represented by the parent toxicity profile. In addition, the genotoxicity profile of the metabolite is not

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
			risk assessment of PBA and PBA (OH). **Addressed**	consensual among MSs experts (see comments below), therefore at this stage it is not possible to propose toxicological reference values for these two metabolites.
2(3)	Vol. 3, Conf. data addendum, overall conclusion on the toxicity profile of the metabolites CPCA, PBA and PBA(OH), p. 6.	EFSA: It should be noted that, in order to use the TTC approach, the sum of all metabolites forming the residues has to be considered in a cumulative way since consumers will be exposed at the same time to the mixture. This approach follows EFSA documents on the use of the TTC including the EFSA GD on Residue Definition and others, not yet taken note by the EC and MSs; therefore it may not be appropriate currently to use the TTC.	UK: A cumulative assessment is required if similar toxicity/MoA for these three metabolites is predicted. There is no suggestion from the QSAR analysis that these metabolites share the same toxicity. Therefore, a cumulative assessment is not required. Although the EFSA RoD guidance (2016) has not been noted, the TTC approach is a well-established scientific approach for the risk assessment of substances with poor datasets and should be used where appropriate, especially if it leads to avoidance of unnecessary animal testing. **Addressed**	Peer review consultation is proposed. It has been agreed in previous comments that CPCA is expected to share the toxicity profile of the parent and as such the consumer assessment should sum up these compounds. However, the same conclusion cannot be reached for the metabolites PBA and PBA (OH) since their genotoxic potential is not clarified among MSs experts.
2(4)	Vol. 3, B.6.8.1, Studies on metabolites/impurities	AT: We agree with the assessment of the RMS regarding the metabolites CPCA, PBA and PBA(OH).	UK: Thank you. **Addressed**	Noted.
2(5)	B.6, Mammalian Toxicology, General	DE: The confirmatory data only partially fulfil the requirements.	UK: We are confused by this comment; genotoxicity tests are	Addressed in the comments below.

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
	Comment	According to the information supplied, all metabolites have an acute oral toxicity above 2000 mg/kg bw, however, it remains unclear whether the metabolites CPCA, PBA and PBA(OH) are genotoxic. For further explanation, please also refer to the technical comments made below.	available or were submitted for all three metabolites and it is concluded, on the basis of these studies, that CPCA, PBA and PBA (OH) are not genotoxic. **Addressed**	
2(6)	B.6.8.1.1.2 CPCA p. 34	DE: Please include a specific reference (i.e. Author, year, etc) for the cited *in vivo* micronucleus test with lambda-cyhalothrin. Moreover, were clinical signs observed in the *in vivo* micronucleus test for CPCA? If so, please state which, and how severe. This provides more concrete, if indirect, evidence that the bone marrow may have been exposed.	UK: Thank you - the reference and information on toxicity has now been added in a footnote. **Addressed**	Addressed.
2(7)	B.6.8.1.1.2 CPCA p. 38	DE: The mouse lymphoma mutation assay (Wallner 2015) was conducted according to OECD TG 476 (1997). The stated purpose of this assay is to detect gene mutations, not assess a substance´s clastogenic potential. As a consequence, the conclusion that "CPCA does not induce [...] clastogenicity in the mouse	UK: It is agreed that the MLA was conducted according to the OECD TG 476 (1997); however, the assay also conforms to the OECD TG 490 (2016) which replaces the aforementioned guideline. According to this test guideline a small colony count of >40% indicates clastogenicity. As there was no increase in mutant frequency it was not necessary to size	Addressed.

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		lymphoma cell line L5178Y" is incorrect.	the colonies (apart from the controls). In this case, however, the applicant had sized the colonies of the highest tested concentration in addition to the controls and that is why clastogenicity (lack thereof) was addressed in this case. **Addressed**	
2(8)	B.6.8.1.1.2 CPCA p. 40	DE: All CPCA gene tox studies should be included here, including the positive Ames test and the subsequent *in vivo* micronucleus test mentioned in the summary. The *in vivo* micronucleus assay does not actually resolve the issue of mutagenicity, rather clastogenicity, which is not the unresolved issue. An *in vivo* transgenic rodent assay according to OECD TG 488 needs to be performed to duly assess the mutagenic potential of CPCA.	UK: This is incorrect. All Ames tests were negative, and mutagenicity was not the issue. The issue was clastogenicity owing to a positive result in an *in vitro* micronucleus assay; this was resolved by the negative *in vivo* micronucleus assay. Therefore, a transgenic rodent assay is not appropriate. **Addressed**	It should be clarified whether there is a positive Ames test for CPCA, EFSA is not aware of such a study.
2(9)	B.6.8.1.2.2 PBA p. 41	DE: In the *in vitro* mouse mutagenicity assay by Trenz (2015) a statistically significant increase in the mutation frequency was reported after a 44 hour exposure in the absence of S9 metabolic activation. The results do not meet neither the current	UK: Paragraph 64 of OECD 490 (2016) outlines the criteria that must be fulfilled in order for a result (MLA) to be considered as clearly negative. i.e. there is no concentrated response, or if there is an increase in MF, it does not exceed the GEF. Therefore, the	Peer review consultation is proposed to discuss the mutagenic potential of PBA. See also 2(14, 20)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		(2016) OECD TG 476 nor OECD 490 (2016) criteria for classification as clearly negative. As a consequence, the result is to be considered equivocal. As a minimum, this needs to be repeated to give a clear result according to the OECD TG 490 (2016).	slight increase in MF observed in the absence of metabolic activation (which did not exceed the GEF) does not preclude the result from being a clear negative. **Addressed**	
2(10)	B.6.8.1.2.2 PBA p. 42	DE: In the PBA human lymphocyte assay by Donath (2015) a dose-dependent increase in micronuclei was reported after a 44 hour exposure in the absence of S9 metabolic activation. The increase was significant at the highest concentration of 8.0 mM. The results do not meet the current (2010) OECD TG 487 criteria for classification as clearly negative. As a consequence, the result is to be considered equivocal. As a minimum, this needs to be repeated to give a clear result according to the OECD TG 487 (2010).	UK: The provision exists in the OECD TG 487 (2010) that in case a substance does not meet all three criteria for a clearly negative result, then the data should be evaluated by expert judgment and/or further investigations. The statistically significant increase observed at the highest concentration was within the range of the historical control data and so was therefore not considered to be biologically relevant. **Addressed**	Peer review consultation is proposed to discuss the clastogenic potential of PBA. See also 2(15, 21)
2(11)	B.6.8.1.3.2 PBA(OH) p. 48	DE: The result of the PBA(OH) *in vitro* mouse lymphoma mutagenicity assay for PBA(OH) by Trenz (2015) is not negative, but equivocal. As a minimum, this needs to be repeated to give a clear result according to	UK: The increases in MF observed did not exceed the GEF and there was no concentration related increase. Therefore, the result is clearly negative (see response to point 2(9) above).	Peer review consultation is proposed to discuss the genotoxicity potential (mutagenicity and clastogenicity) of PBA (OH). See also 2(12, 13, 16, 17, 22, 23)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		the OECD TG 490 (2016).	**Addressed**	
2(12)	B.6.8.1.3.2 PBA(OH) p. 48	DE: In the PBA(OH) human lymphocyte assay by Donath (2015) a dose-dependent increase in micronuclei was reported after a 44 hour exposure in the absence of S9 metabolic activation. The increase was significant at the highest concentration of 8.0 mM. The results do not meet the current (2010) OECD TG 487 criteria for classification as clearly negative. As a consequence, the result is to be considered equivocal. As a minimum, this needs to be repeated to give a clear result according to the OECD TG 487 (2010).	UK: The observed increase in micronuclei was within the range of the historical control data; therefore, the result can be considered negative. **Addressed**	See peer review consultation proposed in 2(11)
2(13)	B.6.8.1.5.3 PBA(OH) p. 54	DE: The positive alert for oncologic primary classification of PBA(OH) using the QSAR toolbox, together with positive alerts for both *in vitro* and *in vivo* mammalian chromosomal damage using a Nexus-Derek 6.0.1 analysis and the fact that both the *in vitro* mammalian micronucleus study by Donath (2015) and the *in vitro* mammalian mutagenicity study by	UK: We disagree. See response to points above. **Addressed**	See peer review consultation proposed in 2(11)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		Trenz (2015) were equivocal strongly indicate that this issue has not been resolved. *In vitro* tests of both mammalian mutagenicity and clastogenicity with clear results are still required.		
2(14)	B.6.8.1.2.3 (PBA) Genotoxicity, p. 43 *In vitro* mammalian cell gene mutation assay	SE: This study on PBA has also been submitted as confirmatory data for lambda-cyhalothrin. Sweden as RMS for lamda-cyhalothrin has recently evaluated the study but not yet submitted the evaluation to COM (deadline for submission: 28/9-2018). However, we will not consider the study result as negative. Instead we think that the experimental data need to be evaluated more closely before a conclusion can be drawn, see below for further explanations. In experiment I with S9 there was a statistically significant increase in the mutation frequency at 1.6, 1.9, 2.3 and 2.5 µg/l and in experiment II with S9 at 2.2 and 2.6 µg/l. No trend test has been conducted. To be able to evaluate the results, an appropriate trend test needs to be conducted to determine if there is a	UK: A trend test is not necessary as the concurrent control value + GEF was not exceeded by any test concentration. As a consequence, the study can be considered to be negative. **Addressed**	See peer review consultation proposed in 2(9)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		concentration-related increase in mutant frequency. A concentration – related increase is a strong indicator of the biological relevance of an effect. In case a concentration-related effect exists (using a trend test) we will judge the result of the study to be positive in accordance to the Guidance Document "Overview of the set of OECD Genetic Toxicology Test Guidelines and updates performed in 2014-2015" (ENV/JM/MONO(2016)33, 13-Jul-2016). In this guidance document, the need for data to be more closely evaluated is recommended as stated in section 4.3.6.2: *"if the response is neither clearly negative not clearly positive the TGs recommend that expert judgment be applied. Test results that do not meet all the criteria may also be judged to be positive or negative without further experimental data, but they need to be evaluated more closely before any final conclusion is reached."* We suggest that the analysis (trend test) should be based on the recommendations in Robinson *et al*:		

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		Statistical evaluation of bacterial/mammalian fluctuation test (In: Kirkland (Ed.) Statistical evaluation of mutagenicity test data, Cambridge Univ. Press, 1989). The RMS could not carry out such a trend test because it is recommended that a laboratory-specific heterogeneity factor (ratio of variances from several experiments to the theoretical binomial variances) is used (section 4.2.2 in Robinson *et al*).		
2(15)	B.6.8.1.2.3 (PBA) Genotoxicity, p. 45 *In vitro* micronucleus assay	SE: This study on PBA has also been submitted as confirmatory data for lambda-cyhalothrin. Sweden as RMS for lamda-cyhalothrin has recently evaluated the study but not yet submitted the evaluation to COM (deadline for submission: 28/9-2018). However, we will not consider the study result as negative. Instead we think that the experimental data need to be evaluated more closely before a conclusion can be drawn, see below for further explanations. There was a statistically significant increase of micronucleus frequency	UK: A trend test is not necessary as the statistically significant increase in micronuclei (1.53% vs 0.93% in controls) noted in experiment I without metabolic activation at the highest concentration of 8.5 mM was still within appropriate laboratory HCD. As a consequence, the study can be considered to be negative. **Addressed**	See peer review consultation proposed in 2(10)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		(1.53%) noted in experiment I without metabolic activation at the highest concentration of 8.5 mM. It could be noted that the number of micronucleated cells was at the upper range of the historical negative control data (0.50-1.55%). No trend test was conducted. To be able to evaluate the results, an appropriate trend test needs to be conducted to determine if there is a concentration-related increase. A concentration –related increase is a strong indicator of the biological relevance of an effect. In case a concentration-related effect exists we will judge the result of the study to be positive in accordance to the Guidance Document "Overview of the set of OECD Genetic Toxicology Test Guidelines and updates performed in 2014-2015" (ENV/JM/MONO(2016)33, 13-Jul-2016). In this guidance document, the need for data to be more closely evaluated is recommended as stated in section 4.3.6.2: *"if the response is neither clearly negative not clearly positive the TGs recommend that expert judgment be applied. Test results that do not*		

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		meet all the criteria may also be judged to be positive or negative without further experimental data, but they need to be evaluated more closely before any final conclusion is reached."		
2(16)	B.6.8.1.3 (PBA(OH)) Genotoxicity, p. 48 *In vitro* mammalian cell gene mutation assay	SE: This study on PBA(OH) has also been submitted as confirmatory data for lambda-cyhalothrin. Sweden as RMS for lamda-cyhalothrin has recently evaluated the study but not yet submitted the evaluation to COM (deadline for submission: 28/9-2018). However, we will not consider the study result as negative. Instead we think that the experimental data need to be evaluated more closely before a conclusion can be drawn, see below for further explanations. There was a statistically significant increase in the mutation frequency in both experiments (with and without metabolic activation). In Experiment II without metabolic activation, the increase in mutation frequencies noted at 0.9 mM (122.8 mutants per 10^6 cells) and 1.0 mM (115.4 mutants per 10^6 cells) were also close to the GEF of	UK: A trend test is not necessary as the concurrent control value + GEF was not exceeded by any test concentration. As a consequence, the study can be considered to be negative. **Addressed**	See peer review consultation proposed in 2(11)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		126 mutants per 10^6 cells. No trend test has been conducted. To be able to evaluate the results, an appropriate trend test needs to be conducted to determine if there is a concentration-related increase in mutant frequency. A concentration – related increase is a strong indicator of the biological relevance of an effect. In case a concentration-related effect exists (using a trend test) we will judge the result of the study to be positive in accordance to the Guidance Document "Overview of the set of OECD Genetic Toxicology Test Guidelines and updates performed in 2014-2015" (ENV/JM/MONO(2016)33, 13-Jul-2016). In this guidance document, the need for data to be more closely evaluated is recommended as stated in section 4.3.6.2 of the document: *"if the response is neither clearly negative nor clearly positive the TGs recommend that expert judgment be applied. Test results that do not meet all the criteria may also be judged to be positive or negative without further experimental data, but they need to be evaluated more closely before any final*		

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		conclusion is reached." We suggest that the analysis (trend test) should be based on the recommendations in Robinson *et al*: Statistical evaluation of bacterial/mammalian fluctuation test (In: Kirkland (Ed.) Statistical evaluation of mutagenicity test data, Cambridge Univ. Press, 1989). The RMS could not carry out such a trend test because it is recommended that a laboratory-specific heterogeneity factor (ratio of variances from several experiments to the theoretical binomial variances) is used (section 4.2.2 in Robinson *et al*).		
2(17)	B.6.8.1.2.3 (PBA(OH)) Genotoxicity, p. 51 *In vitro* micronucleus assay	SE: This study on PBA(OH) has also been submitted as confirmatory data for lambda-cyhalothrin. Sweden as RMS for lamda-cyhalothrin has recently evaluated the study but not yet submitted the evaluation to COM (deadline for submission: 28/9-2018). However, we will not consider the study result as negative. Instead we think that the experimental data need to be evaluated more closely before a conclusion can be drawn, see below for further explanations.	UK: A trend test is not necessary as the statistically significant increase in micronuclei (1.10% vs 0.55% in controls) noted in experiment I without metabolic activation at the highest concentration of 10 mM was still within appropriate laboratory HCD. As a consequence, the study can be considered to be negative. **Addressed**	See peer review consultation proposal in 2(11)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		There was a statistically significant increase of micronucleus frequency (1.10%) noted in experiment I without metabolic activation at the highest concentration of 10 mM. No trend test was conducted. To be able to evaluate the results, an appropriate trend test needs to be conducted to determine if there is a concentration-related increase. A concentration –related increase is a strong indicator of the biological relevance of an effect. In case a concentration-related effect exists we will judge the result of the study to be positive in accordance to the Guidance Document "Overview of the set of OECD Genetic Toxicology Test Guidelines and updates performed in 2014-2015" (ENV/JM/MONO(2016)33, 13-Jul-2016). In this guidance document, the need for data to be more closely evaluated is recommended as stated in section 4.3.6.2: *"if the response is neither clearly negative not clearly positive the TGs recommend that expert judgment be applied. Test results that do not meet all the criteria may also be*		

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		judged to be positive or negative without further experimental data, but they need to be evaluated more closely before any final conclusion is reached."		
2(18)	B.6.8	FR: Since the metabolites under consideration are common to many pyrethroids, a cross-cutting evaluation of all the data available from the different dossiers would be of value to harmonize their assessment for the different active substances	UK: This is a valid point; however, the UK has not been mandated to consider all the available data (owned by different applicants) on these metabolites from the different approved pyrethroids. **Addressed**	Noted.
2(19)	B.6.8.1.1 **CPCA**	FR: It is agreed that genotoxic potential can be excluded. As it is a major metabolite in rat, the reference values of the parent can apply. The use of TTC value is not agreed upon since CPCA is also a metabolite of lambda-cyhalothrin, which represents another source of exposure.	UK: Please see response to point 2(1) above. However, please note that the additional contribution to the CPCA exposure estimate arising from lambda-cyhalothrin (over and above that arising from gamma-cyhalothrin) would apply whether the risk assessment for CPCA is performed using the parent reference values or the TTC Cramer Class III value. **Addressed**	See 2(1)
2(20)	B.6.8.1.2 3- **PBA Mammalian cell gene mutation assay**	FR: Has a trend analysis been performed with an appropriate trend test? If so, could you please report the results of the trend test?	UK: See response to comment 2(14). **Addressed**	See peer review consultation proposed in 2(9)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		It should be noted that with S9 activation, statistically significant increase in mutation frequency was observed in several concentrations in both experiment I and II. While GEF was not exceeded, this test cannot be concluded as clearly negative with S9 activation but rather as equivocal.		
2(21)	B.6.8.1.2 3- **PBA** **In vitro micronucleus assay**	FR: Has a trend analysis been performed with an appropriate trend test? If so, could you please report the results of the trend test? Are the HCD considered relevant? In experiment I 4 hours treatment, the MN frequency in the highest concentration is at the upper limit of HCD and is statistically significant by pairwise analysis. Therefore, under those conditions, this test cannot be concluded as clearly negative.	UK: See response to comment 2(15) above. **Addressed**	See peer review consultation proposed in 2(10)
2(22)	B.6.8.1.3 **PBA (OH)** **Mammalian cell gene mutation assay**	FR: Has a trend analysis been performed with an appropriate trend test? If so, could you please report the results of the trend test? It should be noted that both with and without S9 activation, statistically significant increase in mutation	UK: See response to comment 2(16) above. **Addressed**	See peer review consultation proposed in 2(11)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		frequency was observed in several concentrations in both experiment I and II. While GEF was not exceeded, this test cannot be concluded as clearly negative but rather equivocal.		
2(23)	B.6.8.1.3 **PBA (OH)** ***In vitro*** **micronucleus assay**	FR: Has a trend analysis been performed with an appropriate trend test? If so, could you please report the results of the trend test? Are the HCD considered relevant?	UK: See response to comment 2(17) above. **Addressed**	See peer review consultation proposed in 2(11)
2(24)	B.6.8.1.6 Threshold of toxicological concern (TTC) assessment **CPCA**	FR: It is agreed that genotoxic potential can be excluded. As it is a major metabolite in rat, the reference values of the parent can apply. The use of TTC value is not agreed upon since CPCA is also a metabolite of lambda-cyhalothrin, therefore other source of exposure can occur.	UK: See response to comment 2(19) above. **Addressed**	See 2(1)
2(25)	B.6.8.1.6 Threshold of toxicological concern (TTC) assessment **PBA** and **PBAOH**	FR: The genotoxic profile of PBA and PBAOH is not fully clarified. If it was the case, the reference values of the parent could apply. Since both metabolites PBA and PBAOH are common metabolites of many pyrethroids (e.g. cyhalothrin,	UK: Please see response to point 2(2) above. However, please note that the additional contribution to the PBA and PBA (OH) exposure estimates (over and above that arising from gamma-cyhalothrin) arising from other pyrethroids would apply whether the	Peer review consultation proposed to discuss the appropriateness of the TTC approach for PBA and PBA (OH)

Toxicological data on metabolites				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		cypermethrin, deltamethrin), the TTC approach is not appropriate.	risk assessment for PBA and PBA (OH) is performed using the parent reference values or the TTC Cramer Class III value. **Addressed**	
2(26)	B.6.8.1.3.2 (pg 52, paragraph 2)	FMC: There is a typo. The metabolite should be listed as PBA (OH), not CPCA (OH).	UK: Thank you. It has been amended. **Addressed**	Addressed.

3. Residues

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
3(1)	Vol. 3 B.7, Estimated consumer exposure of Gamma-cyhalothrin metabolites, TTC threshold values	FR: The consumer risk assessment for the metabolites CPCA, PBA and PBA(OH) has been performed using the threshold values for the Cramer class III molecule. However these TTC values are higher than the toxicological reference values of gamma-cyhalothrin (Chronic TTC threshold of 0.0015 mg/kg bw/d vs an ADI of 0.0012 mg/kg bw/d and an acute TTC threshold of 0.005 mg/kg bw vs an ARfD of 0.0025 mg/kg bw). Consequently FR wonders if in this case the TTC approach could applied.	UK: The TTC Cramer Class III thresholds used in the consumer risk assessment of CPCA, PBA and PBA(OH) are very similar to the toxicological reference values of the parent. Given the huge uncertainties involved and considering that the metabolite exposure estimates were significantly below the TTC thresholds, the RMS remains of the view that the approach followed is still highly conservative and appropriate. **Addressed**	Pending the clarification of the existence of a positive Ames test for **CPCA** (see 2(8)) it has been agreed that the toxicity profile of the metabolite CPCA is covered by the toxicological reference values established for the parent (see 2(1)). The TTC concept cannot be applied to the toxicologically characterised metabolite CPCA. The consumer risk assessment should be conducted using the reference values of parent compound. See also 3(4) As regards the presented consumer exposure assessment for **PBA and PBA (OH)** as the basis for application of the TTC, a robust assessment is necessary which currently has not been provided. The assessment approach used by the RMS to support the TTC does not follow any agreed strategy or guidance in the residues area for calculation of exposure for metabolites common to other

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
				pyrethroids. Moreover it is noted that for PBA and PBA(OH), peer review consultations are proposed in the tox section to discuss their genotoxicity profile either regarding mutagenicity or clastogenicity potential and the appropriateness of the TTC for PBA and PBA (OH) (see 2(10), 2(11), 2(25)), i.e. the Cramer Class III thresholds used in the consumer risk assessment are pending confirmation. Hence, ESFA agrees with the views by FR and does not share the RMS view that the approach followed in the consumer risk assessment is highly conservative and appropriate. Peer review consultation is proposed to discuss the appropriateness of the consumer exposure assessment submitted for PBA and PBA (OH), provided the mammalian toxicology experts agree that the TTC might be used. See also 3(2) and 3(3)
3(2)	Vol. 3 B.7, Estimated consumer exposure of	FR: In order to use the TTC approach the exposition to the metabolites of	UK: It is acknowledged that more robust estimations of the levels of	See 3(1)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
	Gamma-cyhalothrin metabolites, Characterisation of the exposition	concern (CPCA, PBA and PBA(OH)) need to be clearly define with robust residue data whereas the levels of corresponding metabolites have only been estimated. Consequently residue trials and suitable livestock study should be required to have a strong estimation of residues of CPCA, PBA and PBA(OH) in plant and ruminant commodities.	CPCA, PBA and PBA(OH) derived from residue trials and feeding studies would be preferable. However, using the estimations derived from the metabolism studies (with livestock feeding data), chronic and acute exposure are significantly below the TTC thresholds (maximum chronic exposure: 10% for FR toddler; maximum acute exposure: 7.5% for milk). On this basis, the UK does not consider there to be a need for additional residue trials and livestock studies to determine the levels of CPCA, PBA and PBA(OH). **Addressed**	
3(3)	Vol. 3 B.7, Estimated consumer exposure of Gamma-cyhalothrin metabolites	FR: As underline in the EFSA conclusions (EFSA Journal 2014;12(2):3560) metabolites PBA and PBA(OH) are common metabolites to many pyrethroid. Consequently, FR wonders if in its case the TTC approach could applied.	UK: The RMS notes that the additional contribution to PBA and PBA(OH) exposure estimates (over and above that arising from gamma-cyhalothrin) arising from other pyrethroids would apply whether the risk assessment for PBA and PBA (OH) is performed using the TTC Cramer Class III values or other chemical-specific reference values.	See 3(1)

MRLs related issues and Consumer Risk Assessment (B.7.10 to B.7.15)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
			Addressed	
3(4)	Vol. 3 B.7, Estimated consumer exposure of Gamma-cyhalothrin metabolites	FR: Metabolite CPCA is a common metabolite to several pyrethroid (lambda-cyhalothrin, tefluthrin…). Consequently, FR wonders if in its case, the TTC approach could applied.	UK: See response to point 3(3) above. **Addressed**	See 3(1) The TTC concept cannot be applied to CPCA since it has been toxicologically characterised, i.e. it has been agreed that the toxicological reference values established for the parent should be applied to CPCA. Hence, the consumer risk assessment should be conducted using the reference values of parent compound and not the TTC.

4. Environmental fate and behaviour

PEC in surface water and in ground water (B.8.6)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
4(1)	Conf. data addendum, B.8 Environmental fate, PECsw and PECsed	EFSA: the reasons provided by the RMS for not accepting the new modelling report submitted by the applicant are agreed. The FOCUSsw modelling conducted by the RMS and reported in the addendum of the confirmatory data are considered appropriate and can be used in the risk assessment.	UK: Noted. Thank you for the confirmation. No action needed. **Addressed**	Addressed.
4(2)	Addendum – confirmatory data, B8	FR: 1/n of 1 (instead of 0.9) should have been used for PECsw calculations, as only Kdoc values are available. This would also be in line with the comment made for PECgw calculations in LoEP and with the recommendation in FOCUS SW guidance document. Influence of 1/n on PECsw cannot be excluded. A geometric mean Koc could have been used for the PECsw calculations according to EFSA DegT50 guidance document (2014).	UK: The endpoints as listed within the LoEP and agreed during the EU review were considered within the surface modelling. As such it is considered that re-calculation of the Kdoc value is not required at this time. In regards to the 1/n value, the following footnote is made in reference to the 1/n value used within groundwater (GW) modelling: *"a 1/n = 1.0 should be used as worst case when only Kd estimated (no impact on the results is expected in this case)"* While comment is made within the GW section no footnote is present	Addressed. It is agreed that 1/n of 1 (instead of 0.9) should have been used for PECsw calculations, as only Kdoc values are available. This has been clarified in the LoEP in Appendix C. However, due to the high Kdoc value the use of 0.9 is not expected to impact the results of the surface water modelling where drift was the dominant entry route for all crops and scenarios.

PEC in surface water and in ground water (B.8.6)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
			within the surface water section. The LoEP has been updated to also report a 1/n value of 1 should be considered within the surface water modelling. As was the case for the groundwater modelling, due to the high Kdoc value the use of 0.9 is not expected to impact the results of the surface water modelling where drift was the dominant entry route for all crops and scenarios (the evaluation has been updated to report this). Therefore new PEC values are not required at this time. **Addressed**	

5. Ecotoxicology

Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
5(1)	Conf. data addendum, B.9.1.1. Long-term risk to mammals	EFSA: the overall evaluation and the argumentations of the RMS are agreed. In particular: - EFSA considers the selection of the reproductive endpoint appropriate because, as explained by RMS, effects on body weight cannot be dismissed at population level. -EFSA considers the proposal from the RMS on the selection of focal species and ecological data justified, on the basis of the data provided.	UK: Noted. Thank you for the confirmation. No action needed. **Addressed**	Addressed
5(2)	Conf. data addendum, B.9.1.1.2 Residue decline data	EFSA: overall the RMS' evaluation of the residue decline studies is acceptable and we support the conclusion that the default 10 day DT50 should be used in the higher tier risk assessment for mammals. Regarding these foliar residue decline studies on cereals and OSR and their kinetic evaluation it is mainly agreed that: - the uncertainties over whether the studies conducted in April-June would cover conditions in early spring or late autumn;	UK: The comment confirms the overall conclusions of the RMS regarding the use of the residue decline dataset. The following responses are in regard to some of the additional specific points raised by EFSA. Since these do not impact the overall DT50 used in the risk assessment the confirmatory data addendum has not been updated. The view of EFSA on the concern over the distance between the study and weather monitoring sites for all trials except trial S15-02677-02 is accepted.	Addressed. Several shortcomings in the study design and in the kinetic evaluation were identified and therefore it was concluded that the default 10 days DT50 should be used in the higher tier mammalian risk assessment.

Birds and mammals (B.9.1 and B.9.3)				
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		- insufficient weather data (i.e. daily temperature and precipitation values from the study sites during sampling) are available; - the early rainfall events that occurred at some sites, and consequently the wash off process, could potentially have caused residue decline to be overestimated at these sites; - extrapolation of the SEU residue decline for the NEU representative use of gamma-cyhalothrin has not been appropriately justified However, it should be noted that: - further details on the residue trials (e.g. plot characteristics, number of samples per site, field sample size and sampling procedures…) should be provided; - it is agreed with the applicant that a distance up to 20 km for the weather station is considered acceptable to represent the conditions at the	Given there was one trial where the distance was >20 km (28 km) and since this point does not impact the overall conclusions regarding the DT50 refinement and risk assessment outcomes, the addendum has not been updated. It should be noted that the fit for trial S15-02676-04 was considered reasonable by the RMS and the DT50 of 4.92 d from this trial was taken into account when deriving the overall DT50 used in the risk assessment. The RMS remains of the view that the SFO fit for trial S15-02677-04 is not acceptable but notes that this difference of opinion does not impact the DT50 value used in the risk assessment. **Addressed**	

Birds and mammals (B.9.1 and B.9.3)				
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		trial site; - without details on the number and the size of the samples for each trial, the argumentation provided by the RMS on the unevenness of the application method and the low initial residues is questionable; - the kinetic evaluation conducted by the RMS in line with the FOCUS kinetics guidance is considered appropriate and acceptable; however, we consider unnecessary investigating further the bi-phasic kinetic models as long as the EFSA GD on Birds and Mammals recommends the SFO kinetic "to ensure a worst case" (refer to p. 88 of the GD for the details); - in two cases (Sites S15-02676-04 and S15-02677-04) the SFO kinetic (rejected by the RMS) could be considered acceptable in our view; overall, the data set available for wheat and barley (NEU and SEU) could be considered sufficient to		

Birds and mammals (B.9.1 and B.9.3)				
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		derive an acceptable substance and use-specific DT50 value based on the experimental evidences. However, taking into consideration the variability of the trials and the fact the only 3 reliable DT50 values are available for NEU and only 3 reliable DT50 values are available for SEU, we would select the worst-case value (= 10.75d), which confirm that the default value of 10 days is justified.		
5(3)	Conf. data addendum, B.9.1.2 Bioaccumulation and biomagnification	EFSA: the overall RMS' evaluation of the biomagnification is agreed.	UK: Noted. Thank you for the confirmation. No action needed. **Addressed**	Addressed
5(4)	Risk assessment for mammals, pp. 174 including interpretation of field study B.9.1.1.3	DE: Regarding evaluation of proposed refinement steps (applicant) and risk assessment by RMS UK we comprehend and agree with (e.g. PD refinement by applicant with study of Hansen (1991) is not matching the definition of refining PD as proposed by EFSA, etc.). It should be noted that using updated FOCUS groundwater values from the year 2014 has not been adapted into EFSA GD Birds & Mammals (2009) yet which means if	UK: Given that the bird and mammal guidance document (2009) indicates that deposition values may be refined using the more detailed values stated in the FOCUS groundwater guidance (2000), the RMS considers it to be also appropriate to utilise updated deposition values from the latest version of the FOCUS groundwater guidance (2014) available at the time of submission when refining the deposition values. **Addressed**	See comment 5(1)

Birds and mammals (B.9.1 and B.9.3)				
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		using the higher values for deposition factor(s) from EFSA (2009) the TER values are even lower and the risk higher.		
5(5)	Addendum, Overall Conclusion, (3) the long-term risk to wild mammals	DE: It remains unclear how the remaining long-term risk for mammals can finally be excluded since "the long-term risks to herbivorous and omnivorous mammals from the proposed representative uses of gamma-cyhalothrin remain unacceptable."	UK: Noted. In comment 5(15) the applicant has stated that for product applications at MS level a single application is likely to be proposed. The RMS has therefore checked the impact of changing the GAP to a single application on the overall outcomes of the reproductive risk assessment for mammals. A single application and therefore a MAF of 1 would be sufficient to result in an acceptable reproductive TER for the common vole at BBCH 40-69 (revised TER = 7.27) but not at BBCH 70-77 (revised TER = 3.64). However, the relevance of common voles for the risk assessment can also be considered further at national level (e.g. this species is not a relevant UK focal species). Additionally the timing of application could be restricted to BBCH < 70 to address the risk to this focal species. For the focal species wood mouse a MAF of 1 would result in acceptable reproductive TERs for all application	Addressed In the context of the peer review of the confirmatory data the overall conclusion is that confirmatory data requirements have not been completely addressed. The long-term risks to herbivorous and omnivorous mammals from the proposed representative uses of gamma-cyhalothrin remain unresolved. It is acknowledged that further refinements and risk assessment based on GAP restriction (e.g. single application as mentioned by the applicant in 5(17)) were not part of this peer review. See 5(17)

Birds and mammals (B.9.1 and B.9.3)				
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			timings (lowest revised TER = 6.66). For the lagomorph focal species brown hare, even with a revised MAF of 1 the TER would remain below the trigger of 5 (revised TER = 3.06). However, it may be possible to further refine this TER at MS level, for example, through consideration of additional data on brown hare diets. It is also noted that consideration of this scenario is only triggered at BBCH 10-29 (early shoots stage) and therefore at BBCH 30-77 this focal species is not considered relevant and does not need to be assessed. Overall, the RMS considers that there is the potential to further refine the reproductive risk assessment for mammals at MS level and that through such refinements and/or restrictions to the GAP, there is the potential to demonstrate acceptable reproductive risks to mammals from use of gamma-cyhalothrin (noting that further efficacy consideration would be needed in light of any restrictions to the GAP). **Open point - Issue to be dealt with at Member State level**	

Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
5(6)	Addendum, Overall Conclusion, (3) the long-term risk to wild mammals	DE: We agree with the conclusions by UK within the part "proposal" as stated: "Overall the UK RMS considers the confirmatory data requirements have not been completely addressed and further data is required to the risk to herbivorous and omnivorous mammals." HOWEVER, we do disagree that this should be solely addressed "on Member State level", since potential refinement options based on biological aspects (PT, PD, species distribution etc.) might be exhausted. We would like to ask RMS UK and EFSA to reconsider this matter and show a possible reasonable path to zonal regulation (approval disapproval).	UK: Noted. Thank you for the confirmation. See also 5(5).	See 5(5)
5(7)	Vol B.9. confirmatory data	FR: FR agrees with RMS's opinions and support the subsequent risk assessment performed by RMS and the overall conclusions.	UK: Noted. Thank you for the confirmation. No action needed. **Addressed**	Addressed
5(8)	Vol. B.9.1.1.1 Reproductive mammalian toxicity endpoint	FR: Could you, please, provide a short summary of the study performed by Ruckman & Brooks (2017)?	UK: Ruckman & Brooks (2017) is a position paper on the mammalian reproductive toxicity endpoint for use in the long-term risk assessment. It is	Addressed

Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
			not a study and does not contain primary data. The lines of evidence/reasoning provided in Ruckman & Brooks (2017) have been discussed by the RMS in the confirmatory data addendum for gamma-cyhalothrin and therefore an additional summary of this paper is not considered necessary. **Addressed**	
5(9)	Vol. B.9.1.2, Table B.9.2.1-5	FR: Could you, please, provide more details about how the BAF soil-earthworms was calculated?	UK: The BAF soil-earthworms was calculated using the standard dry soil method detailed in section 5.6 of the EFSA guidance on bird and mammal risk assessment (2009). This calculation is described in the DAR for gamma-cyhalothrin and hence was not repeated in the confirmatory data addendum. **Addressed**	Addressed
5(10)	Vol. 3, B.9.1.1.2, Residue decline data	FMC: UK: There are uncertainties over whether the studies conducted in April-June would cover conditions in early spring or late autumn. Residue decline may be more rapid at warmer temperatures.	UK: Given the small number of DT50 values considered reliable for NEU and SEU MS by the RMS, a clear comparison of the effect of temperature on the DT50 is not possible.	Addressed. The overall impact of the different agro-climatic conditions in early spring or late autumn has not been properly addressed.

Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		NOT: Table 9.1.1.2-37 showing the DT50 values which the RMS have determined are acceptable show comparable DT50 values between NEU and SEU; given the expected warmer conditions present in SEU compared to NEU, this suggests that temperature would have limited effect.	**Addressed**	
5(11)	Vol. 3, B.9.1.1.2, Residue decline data	FMC: UK: Extrapolation of residue decline data from growth stages BBCH 39-65 to early growth stages (from BBCH 12) is uncertain. NOT: It could be reasoned that at higher growth stages, the canopy would be larger and fully formed, therefore there would be no effect of dilution of growth for these results; at earlier BBCH stages, the decline would be offset by the rapid growth of the plant, making results obtained from the later BBCH stage trials (BBCH 39+) more	UK: In the absence of clear data to demonstrate this point, the RMS considers that uncertainty in the extrapolation of residue decline data from BBCH 39-65 to earlier growth stages remains. However, it is acknowledged that residue decline at BBCH 39-65 could be slower than at earlier growth stages, and hence the data could be conservative (though this has not been clearly demonstrated). **Addressed**	Addressed. The uncertainty in the extrapolation of residue decline data from BBCH 39-65 to earlier growth stages has not been properly addressed.
5(12)	Vol. 3, B.9.1.1.2, Residue decline data	FMC: UK: Due to the low initial residues close to the LOQ along with the apparent unevenness of the application method, the measured residues in the cereal and OSR trials	UK: Noted. The RMS has considered all trials with acceptable fits when concluding on the appropriate DT50 for the refined risk assessment.	Addressed.

Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		are not fully suitable to be used for deriving reliable foliar half-life values for gamma-cyhalothrin. NOT: Whilst some of the trials have results close to the LOQ, several of these trials have yielded acceptable foliar half-lives which could be used to obtain an overall DT50.	**Addressed**	
5(13)	Vol. 3, B.9.1.1.2, Residue decline data	FMC: UK: The RMS kinetic evaluation identified that for some sites either no clear residue decline was evident or an acceptable fit for the residue decline curve could not derived. In total no reliable DT50 could be determined for 11/20 sites. Due to the low number of sites with reliable DT50 values it is not possible to confirm whether it is appropriate to pool data for cereals and OSR or to pool data from Northern and Southern MS as has been done by the Applicant in the geometric mean calculation NOT: The FOCUS (2014) Guidance for Estimating Persistence and Degradation specifically states that the 15% Chi^2 criterion "…should not be considered an absolute cut-off criterion. There will be cases where	UK: Noted. Already addressed within the evaluation. As explained within the assessment, 15% was not used as an absolute cut off. The RMS accepted kinetic fittings where values >15% were presented (e.g. trial S15-02676-07). In regards to the t-test, expert judgement is used to consider whether a failure is sufficient to reject the fit; the results of the t-test are not considered in isolation from the other goodness of fit tests. **Addressed**	Addressed.

Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		the error value to pass the [Chi^2] test is higher, but the fit still represents a reasonable description of the degradation behaviour". The notifier does not consider it appropriate to dismiss trials based on exceedance of this 15% value. The notifier also believes that, given the field nature of these trials, a P value of 0.1 may be more appropriate than a P value of 0.05 when assessing the statistical acceptability of the modelling parameters.		
5(14)	Vol. 3, B.9.1.1.2, Residue decline data	FMC: UK: Extrapolation of the Southern European residue decline data for the Northern European representative uses of gamma-cyhalothrin has not been appropriately justified. Neither has extrapolation of OSR residue decline data to cereal crops NOT: it can be seen from an examination of the DT50s of the trials deemed acceptable by the RMS (Table B.9.1.1.2-37) that (at least for wheat and barley) the faster DT50s are not limited to the SEU trials, and the DT50s between	UK: Given the small number of DT50 values considered reliable by the RMS, a clear comparison of potential differences in the DT50 values between NEU and SEU MS and between crops is not possible. **Addressed**	Addressed.

Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		NEU and		
5(15)	Vol. 3, B.9.1.1.2, Residue decline data	FMC: UK: Rainfall occurred relatively early in the study at some sites, meaning that washoff could potentially have caused residue decline to be overestimated at these sites. However, this is considered a minor issue since at most of these sites the RMS could not determine a reliable DT50 and at the only other site with rainfall within the first 5 days (OSR trial 3), there was no indication of a washoff effect in the residue data. NOT: Agreed that this is a minor issue; rainfastness data was presented that demonstrated product	UK: Noted. No action needed. **Addressed**	Addressed.
5(16)	Vol. 3, B.9.1.1.2, Residue decline data	FMC: UK: Detailed daily weather data is not available from the actual study sites, with the nearest weather station being up to 28 km away. While it is noted that distances between weather recording sites and study locations of up to 20 km are permissible for some fate and behaviour studies, it must be remembered that the purpose of such studies and the timescales	UK: Noted. No action needed **Addressed**	Addressed.

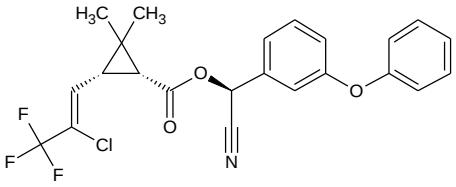
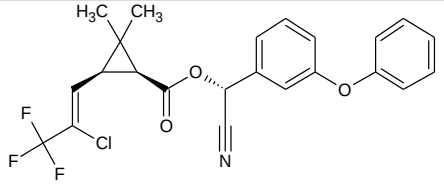
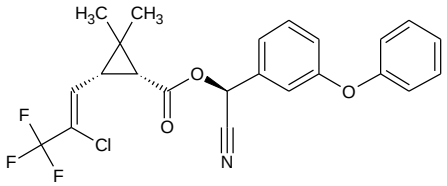
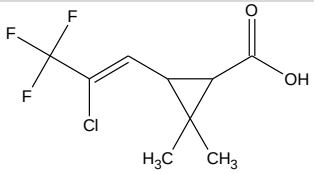
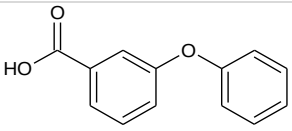
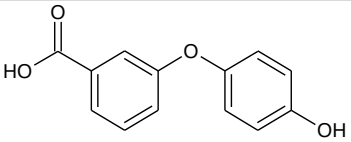
Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		involved are different. However, overall this is considered to be a relatively minor limitation with the study data NOT: Agreed that this is a minor limitation.		
5(17)	Vol. 3, B.9.1.1.6, Overall conclusions regarding the long-term risk to mammals	FMC: UK: In light of the above risk assessment, the long-term risks to herbivorous and omnivorous mammals from the proposed representative uses of gamma-cyhalothrin remain unacceptable. Acceptable risks to the focal species common vole, wood mouse and brown hare have not been sufficiently demonstrated. NOT: It should be noted that the representative use of gamma-cyhalothrin considered during the renewal of approval was for three applications per season. However, moving forward the proposed uses of gamma-cyhalothrin will be for just a single application. Thus, the predicted exposure to birds and mammals will be less than the levels estimated here. The bird and mammal risk assessment can therefore be addressed at individual	UK: Noted. See 5(5).	See 5(5)

Birds and mammals (B.9.1 and B.9.3)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		Member State level using the GAP relevant to that MS and will likely result in a much more favourable risk assessment.		
5(18)	Vol. 3, B.9.1.2, Bioaccumulation and biomagnification	FMC: UK: Overall the RMS concludes that the risks from the proposed uses of gamma-cyhalothrin to birds and mammals via biomagnification in terrestrial food chains are acceptable. NOT: Agreed	UK: Noted. Thank you for the confirmation. No action needed. **Addressed**	Addressed

Aquatic organisms (B. 9.2)				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
5(19)	Vol. 3, B.9.2.1, Bioaccumulation via aquatic food chain	FMC: UK: All the FOCUS Step 3 7, 14 and 21-d TWA PEC_{SW} values are lower than the RAC_{SP} of 0.0242 µg a.s./L for mammals (noting that the risk to birds was shown to be acceptable using maximum values). An acceptable risk via biomagnification in the aquatic food	UK: Noted. Thank you for the confirmation. No action needed. **Addressed**	Addressed

		chain is therefore concluded and no further consideration is needed. NOT: Agreed		

Appendix B – Used compound codes

Code/trivial name[(a)]	IUPAC name/SMILES notation/InChiKey[b)]	Structural formula[c)]
gamma-cyhalothrin	(*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate or (*S*)-α-cyano-3-phenoxybenzyl (1*R*)-*cis*-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropane-carboxylate Cl\C(=C/[C@H]1[C@@H](C(=O)O[C@H](C#N)c2cccc(Oc3ccccc3)c2)C1(C)C)C(F)(F)F ZXQYGBMAQZUVMI-GCMPRSNUSA-N	
lambda-cyhalothrin	(*R*)-α-cyano-3-phenoxybenzyl (1*S*,3*S*)-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate (*S*)-α-cyano-3-phenoxybenzyl (1*R*,3*R*)-3-[(*Z*)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate 1:1 Cl\C(=C/[C@H]1[C@@H](C(=O)O[C@H](C#N)c2cccc(Oc3ccccc3)c2)C1(C)C)C(F)(F)F.FC(F)(F)C(/Cl)=C/[C@@H]1[C@H](C(=O)O[C@@H](C#N)c2cccc(Oc3ccccc3)c2)C1(C)C BFPGVJIMBRLFIR-GUCBCRIZSA-N	 
cyclopropyl carboxylic acid (CPCA)	(1*RS*,3*RS;* 1*RS*,3*SR*)-3-[(1*Z*)-2-chloro-3,3,3-trifluoro-1-propen-1-yl]-2,2-dimethylcyclopropanecarboxylic acid (unstated stereochemistry) Cl\C(=C/C1C(C(=O)O)C1(C)C)C(F)(F)F SPVZAYWHHVLPBN-HYXAFXHYSA-N	
3-phenoxybenzoic acid (PBA)	3-phenoxybenzoic acid O=C(O)c1cc(Oc2ccccc2)ccc1 NXTDJHZGHOFSQG-UHFFFAOYSA-N	
3-(4′-hydroxyphenoxy)benzoic acid (PBA(OH))	3-(4-hydroxyphenoxy)benzoic acid O=C(O)c1cc(Oc2ccc(O)cc2)ccc1 OSGCDVKVZWMYBG-UHFFFAOYSA-N	

(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2017.2.1 ACD/Labs 2017 Release (File version N40E41, Build 96719, 06 Sep 2017)
(c): ACD/ChemSketch 2017.2.1 ACD/Labs 2017 Release (File version C40H41, Build 99535, 14 Feb 2018)

Appendix C – List of endpoints – updated parts

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Soil	gamma-cyhalothrin
Water surface	gamma-cyhalothrin
drinking/ground	gamma-cyhalothrin
Air	gamma-cyhalothrin
Body fluids and tissues	gamma-cyhalothrin

Monitoring/Enforcement methods

Soil (principle of method and LOQ)	chiral reverse phase HLPC-MS/MS LOQ = 0.05 mg/kg
Water (principle of method and LOQ)	chiral reverse phase HLPC-MS/MS LOQ = 0.003 µg/L (drinking and surface water) open: the refined endpoint based on mesocosm study and additional data/information: 0.002 µg/L
Air (principle of method and LOQ)	chiral reverse phase HLPC-MS/MS LOQ = 0.07 µg/m^3
Body fluids and tissues (principle of method and LOQ)	chiral reverse phase HLPC-MS/MS LOQ = 0.02 mg/L in blood and urine LOQ = 0.01 mg/kg in liver and fat

Impact on Human and Animal Health

Other toxicological studies (Annex IIA, point 5.8) ‡

inactive isomer	Low acute oral toxicity of the inactive isomer of lambda-cyhalothrin (LD_{50} >2000 mg/kg bw)
CPCA	Major metabolite in rat metabolism (Z)-3-(2-Chloro-3,3,3-trifluoroprop-1-en-1-yl)-2,2-dimethylcyclopropane-1-carboxylic acid): Rat acute oral LD_{50} > 2000 < 4000 mg/kg bw; 3 Ames tests ± S9: negative 2 *In vitro* mammalian gene mutation assays (MLA): ±S9: negative *In vitro* micronucleus test (MN) ± S9: 1 positive (clastogenic), 1 negative *In vivo* micronucleus test: negative
PBA	Rat acute oral LD_{50} > 2000 mg/kg bw Ames test ± S9: negative *In vitro* MLA ± S9: **open** *In vitro* MN ± S9: **open**
PBA (OH)	Rat acute oral LD_{50} > 2000 mg/kg bw

	Ames test ± S9: negative *In vitro* MLA ± S9: **open** *In vitro* MN ± S9: **open** *In silico* predictions: alerts for chromosome damage *in vitro* (plausible) and *in vivo* (equivocal)
epimer	Rat acute oral LD50 > 300 < 2000 mg/kg bw Ames test ± S9: negative

Residues

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

Plant groups covered	Wheat and grape (Gamma-cyhalothrin) wheat, cotton and soybean (Lambda cyhalothrin)
Rotational crops	Study with lambda cyhalothrin No further data required
Plant residue definition for monitoring	Lambda-cyhalothrin
Plant residue definition for risk assessment	Lambda-cyhalothrin
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	
Animal residue definition for monitoring	Lambda-cyhalothrin
Animal residue definition for risk assessment	Lambda-cyhalothrin
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes (Lambda cyhalothrin)
Fat soluble residue: (yes/no)	Yes

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

.	Based on data generated with lambda cyhalothrin, it is unlikely that there would be significant residues of Gamma-cyhalothrin in rotational or succeeding crops.

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

	Only moderate degradation of gamma-cyhalothrin occurs in broccoli, tomato, cotton seed, wheat grain, field peas, grape wine and corn oil when stored at -20 ^{o}C for a period of up to 385 days.

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: yes	Poultry: no	Pig: Yes*
Muscle	0.01 mg/kg (1.0 mg/kg feeding level)	ND (1.0 mg/kg feeding level)	0.01 mg/kg (1.0 mg/kg feeding level)
Liver	0.01 mg/kg (1.0 mg/kg feeding level)	ND (1.0 mg/kg feeding level)	0.01 mg/kg (1.0 mg/kg feeding level)
Kidney	0.01 mg/kg (1.0 mg/kg feeding level)	ND (1.0 mg/kg feeding level)	0.01 mg/kg (1.0 mg/kg feeding level)
Fat	0.1 mg/kg (1.0 mg/kg feeding level)	<0.01 mg/kg (1.0 mg/kg feeding level)	0.1 mg/kg (1.0 mg/kg feeding level)
Milk	0.01 mg/kg (1.0 mg/kg feeding level)	Not applicable	Not applicable
Eggs	Not applicable	ND (1.0 mg/kg feeding level)	Not applicable

(*) Based on ruminant study conducted with lambda cyhalothrin.

Table 2.4.1: Summary of residue trials data for gamma-cyhalothrin in wheat and barley.

Crop	No of Trials	Grain / Seed Range of residues (mg/kg)	Grain / Seed STMR (mg/kg)	Grain / Seed HR (mg/kg)	MRL (mg/kg)	Straw Range of residues (mg/kg)	Straw STMR (mg/kg)	Straw HR (mg/kg)
Wheat	11	<0.002 - <0.01	<0.01	<0.01	0.01	0.08 – 0.25	0.15	0.25
Barley	8	<0.002 – 0.02	0.01	0.02	0.05	0.09 – 0.31	0.23	0.31

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)
Winter wheat	Northern region	1 x <0.002, 4 x <0.01	5 trials – all acceptable	0.01	<0.01
Spring wheat	Northern region	3 x <0.002, 3 x <0.01	6 trials – all acceptable	0.01	<0.01
Winter barley	Northern region	2 x 0.01, 2 x 0.02	4 trials – all acceptable	0.05	0.01
Spring barley	Northern region	3 x 0.01, 1 x <0.002	4 trials – all acceptable	0.05	0.01

(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

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

ADI	0.0025 mg/kg bw/day
TMDI (European Diet) (% ADI)	29 %
NEDI (% ADI)	43% (Infant)
Factors included in NEDI	
ARfD	0.004 mg/kg bw/day
Acute exposure (% ARfD)	62% (Maximum reached in infants resulting from milk consumption).

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Wheat grain	0#		
Barley grain	0#		

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

Residue levels in the fractions normally processed (grain for wheat and barley) were all significantly below 0.1 mg/kg. The highest residues were < 0.01 mg/kg for wheat grain and 0.02 mg/kg for barley grain. Therefore processing studies examining the nature of the residue are not required.

Fate and Behaviour in the Environment

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

Parent Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: Version 2.1 (2001) Molecular weight 449.9 g/mol: Water solubility 0.0021 mg/L: KOC/KOM: 59677mL/g DT50 soil : 26.8 days (geometric mean) DT50 water/sediment system : 32.4 days DT50 water (d): 32.4 days DT50 sediment (d): 1000 days Crop: Cereals (Winter and Spring)
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software (version numbers are for the model): SWASH 3.1; MACRO 4.4.2; PRZM 1.5.6; TOXSWA 2.6. Vapour pressure: 1.03 x $^{10-7}$ at 20ºC Kdoc: 59677 mL/g 1/n: 0.9[4] DT50 soil 26.8 days DT50 water 32.4 days DT50 sediment 1000 days Q_{10}: 2.58

[4] a 1/n = 1.0 should be used as worst case when only Kd estimated (no impact on the results is expected in this case)

Application rate

Crop: Cereals (winter and spring)
Number of applications: 3
Interval: 10 days
Application rate: 1 x 4.5 g as/ha (single)
3 x 4.5 g as/ha (multiple)
Application window:

Scenario	Winter cereals (autumn application)	Winter cereals (spring application)	Spring cereals
	1st application		
D1	23-Oct (296)	07-Mar (066)	17-Jun (168)
D2	28-Nov (332)	12-Mar (071)	-
D3	10-Dec (344)	29-Feb (01 Mar) (060)	20-Apr (110)
D4	26-Oct (299)	01-Mar (060)	30-May (150)
D5	27-Nov (331)	07-Mar (066)	08-Apr (098)
D6	30-Dec (364)	05-Mar (064)	-
R1	27-Nov (331)	17-Mar (076)	-
R2	-	-	-
R3	15-Dec (349)	01-Mar (060)	-
R4	10-Dec (344)	05-Mar (64)	29-Mar (088)

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

FOCUS modelling studies using FOCUS PEARL 4.4.4 and FOCUS-PELMO (version 3.3.2)	Scenarios :Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva (where applicable)
Inputs and results presented for winter and cereal GAP (3 x 4.5 g a.s./ha, 10day interval	Crop: Winter and spring cereals Q_{10}: 2.58 Gamma-cyhalothrin Normalised geometric mean DT_{50lab} 26.8 days . K_{doc}: 59677 mL/g, $^1/_n$ = 0.9* 3-(4-OHPh) DT_{50}1000 days (default) Formation fraction: 1.0 K_{doc}: 324 mL/g, $^1/_n$ = 0.9* * a 1/n = 1.0 should be used as worst case when only Kd estimated (no impact on the results is expected in this case)
Application rate	Winter and spring cereals Application rate: 4.5 g a.s./ha. No. of applications: 3, 10 day interval 25% crop interception Relative application dates,; Spring cereals: 14 days after emergence Winter cereal (autumn application): 14 days after emergence Winter cereal (spring application): 1st March
Gamma-cyhalothrin PEC_{gw}	For all requested crops at every FOCUS standard scenario defined as growing that crop 80th percentile annual average concentrations of gamma-cyhalothrin a in leachate (recharge) at the 1 m evaluation depth were <0.001µg/l.
3-(4-OHPh) PEC_{gw}	All calculated values are less than 0.75µg/L, however for many scenarios the levels are >0.1 g/l and as such relevance assessment will be required. It must be noted that the modelling conducted for the 3-(4-OHPh) is highly conservative with the use of 1000days; as summarised in previous sections, this value is the only default currently available for use within modelling where reliable degradation rates cannot be ascertained. As such this modelling and potential risk from 3-(4-OHPh) could be revised in light of further data concerning the degradation rate of metabolite.