TECHNICAL REPORT

APPROVED: 17 April 2019

doi:10.2903/sp.efsa.2020.EN-1627

Outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for thifensulfuron-methyl 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 thifensulfuron-methyl 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: thifensulfuron-methyl, peer review, confirmatory data, risk assessment, pesticide, herbicide

Requestor: European Commission

Question number: EFSA-Q-2019-00212

Correspondence: pesticides.peerreview@efsa.europa.eu

Suggested citation: EFSA (European Food Safety Authority), 2020. Technical report on the outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for thifensulfuron-methyl in light of confirmatory data. EFSA supporting publication 2020:EN-1627. 86 pp. doi:10.2903/sp.efsa.2020.EN-N1627

ISSN: 2397-8325

Summary

Thifensulfuron-methyl was first included in Annex I to Directive 91/414/EEC on 20 November 2001 by Commission Directive 2001/99/EC. Its approval was renewed in accordance with Regulation (EC) No 1107/2009 on 1 November 2016, by Commission Implementing Regulation (EU) No 2016/1424, amending Commission Regulation (EU) No 540/2011. EFSA previously finalised a Conclusion on this active substance on 6 July 2015.

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

(1) the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and IN-W8268;

(2) mechanistic data to rule out an endocrine mediated mode of action for mammary gland tumours;

(3) the risk to aquatic organisms from thifensulfuron-methyl and metabolite IN-D8858 and the risk to soil organisms from metabolites IN-JZ789 and 2 acid 3 triuret; and

(4) the relevance of the metabolites IN-A4098, IN-L9223 and IN-JZ789 if thifensulfuron-methyl is classified as reprotoxic category 2 under Regulation (EC) No 1272/2008 of the European Parliament and of the Council and the risk that those metabolites contaminate groundwater.

The applicant shall submit the information requested under point (1) by 31 March 2017, under points (2) and (3) by 30 June 2017 and under point (4) within six months after the notification of the classification decision concerning thifensulfuron-methyl. Data requirement 4 is now obsolete as ECHA did not classify thifensulfuron-methyl as reprotoxic category 2 (RAC Opinion adopted 9 December 2016).

In accordance with the specific provision, the applicant, DuPont and the TSM Task Force, submitted an updated dossier by the respective deadlines, which was evaluated by the designated rapporteur Member State (RMS), the United Kingdom, in the form of revised parts if the renewal assessment report. In compliance with guidance document SANCO 5634/2009-rev.6.1, the RMS distributed the revised renewal assessment report to Member States, the applicant and the EFSA for comments on 21 December 2018. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA on 22 March 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.

Thifensulfuron is the ISO common name for 3-(4-methoxy-6-methyl-1,3,5-triazin-2 ylcarbamoylsulfamoyl)thiophene-2-carboxylic acid (IUPAC). Thifensulfuron-methyl is the modified ISO common name of the variant considered (methyl 3-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoylsulfamoyl)thiophene-2-carboxylate) (IUPAC).

EFSA considered that the available confirmatory data on IN-B5528 and IN-A5546 did not raise concerns for genotoxicity whereas for IN-W8268 peer-review on its genotoxic potential is proposed. Regarding the carcinogenic potential of thifensulfuron-methyl, ECHA RAC did not consider mammary gland tumours in rats as treatment-related. Therefore, it was not necessary to consider any mode of action for tumours. Given that the ECHA RAC did not classify thifensulfuron-methyl as reprotoxic category 2 it was also not necessary to consider further the relevance of the metabolites IN-A4098, IN-L9223 and IN-JZ789. Further peer review on IN-A4098 is not proposed given that the EFSA PPR panel is currently assessing it.

Actual Predicted Environmental Concentration (PEC) in soil and PECsoil accumulation values were provided for thifensulfuron-methyl and its metabolites IN-L9225, IN-JZ789, IN-A4098, IN-L9223, 2-acid-3-triuret, IN-W8268, IN-V7160, IN-L9226 and IN-A5546, for the highest application rates of 37.5 g a.s./ha and 51 g a.s./ha to winter cereals. A worst case crop interception of 0% and a tillage depth of 5 cm for soil accumulation calculations were used as a conservative first tier. The confirmatory information is considered acceptable and the PECsoil values can be used in the risk assessment.

A revised surface water and sediment exposure assessment to address the risk to aquatic organisms from thifensulfuron-methyl was submitted using step 3 and step 4 calculations. The step 4 calculations appropriately followed the FOCUS guidance, with no-spray drift buffer zones (BZ) of up to 20 m being implemented for the drainage scenarios and combined no-spray buffer zones with vegetative filter strips (VFS) of up to 20 m being implemented for the run-off scenarios. PECsw and PECsed at steps 3 and 4 for the parent compound for the D1 scenario using refined application dates were also available. This refinement exposure clearly demonstrated that thifensulfuron-methyl is very sensitive to application timing, particularly with regard to drainflow events, and can highly affect the PECsw value. As drainflow mitigation options are currently limited and are the least developed across the EU, the peer review concluded that further investigation into the effects of application timing and possible restriction of application timing is recommended to be performed for national assessments of Member States for which drainflow events are a concern, particularly those for which the FOCUS D1 scenario is relevant. Further step 4 modelling with mitigation measures to refine the calculation was not provided for the representative uses on cereals with higher rates of 40.8 and 51 g a.s./ha. Additional surface water modelling at steps 1-2 for metabolite IN-D8858 was provided using specific endpoints from the list of endpoints, rather than the previous conservative approach for all metabolites using worst case values. The available FOCUS Step 3-4 PECsw/sed as calculated by the RMS with mitigation measures from combined BZ and VFS up to 20 m are agreed and can be used in the risk assessment.

The available confirmatory data are considered acceptable regarding the risk assessment for aquatic organisms for the metabolite IN-D8858 and the risk to soil organisms from metabolites IN-JZ789 and 2 acid 3 triuret. However, an experts' consultation is proposed to further discuss the available refinements of the risk assessment for aquatic organisms when exposed to thifensulfuron-methyl.

Table of contents

Abstract 1
Summary 3
1. Introduction 6
1.1. Background and Terms of Reference as provided by the requestor 6
1.2. Interpretation of the Terms of Reference 6
2. Assessment 8
Documentation provided to EFSA 8
References 8
Abbreviations 9
Appendix A – Collation of comments from Member States, applicant and EFSA on the pesticide risk assessment for the active substance thifensulfuron-methyl in light of confirmatory data and the conclusions drawn by EFSA on the specific points raised 11
Appendix B – Used compound codes 84
Appendix C – List of endpoints – updated parts 86

1. Introduction

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

Thifensulfuron-methyl was first included in Annex I to Directive 91/414/EEC on 20 November 2001 by Commission Directive 2001/99/EC. Its approval was renewed in accordance with Regulation (EC) No 1107/2009[1] on 1 November 2016, by Commission Implementing Regulation (EU) No 2016/1424[2], amending Commission Regulation (EU) No 540/2011[3]. EFSA previously finalised a Conclusion on this active substance on 6 July 2015 (EFSA, 2015a).

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

(1) the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and IN-W8268;

(2) mechanistic data to rule out an endocrine mediated mode of action for mammary gland tumours;

(3) the risk to aquatic organisms from thifensulfuron-methyl and metabolite IN-D8858 and the risk to soil organisms from metabolites IN-JZ789 and 2 acid 3 triuret; and

(4) the relevance of the metabolites IN-A4098, IN-L9223 and IN-JZ789 if thifensulfuron-methyl is classified as reprotoxic category 2 under Regulation (EC) No 1272/2008 of the European Parliament and of the Council and the risk that those metabolites contaminate groundwater.

The applicant shall submit the information requested under point (1) by 31 March 2017, under points (2) and (3) by 30 June 2017 and under point (4) within six months after the notification of the classification decision concerning thifensulfuron-methyl. Data requirement 4 is now obsolete as ECHA did not classify thifensulfuron-methyl as reprotoxic category 2 (RAC Opinion adopted 9 December 2016).

In accordance with the specific provision, the applicant, DuPont and the TSM Task Force, submitted an updated dossier by the respective deadlines, which was evaluated by the designated rapporteur Member State (RMS), the United Kingdom, in the form of revised parts if the renewal assessment report (United Kingdom, 2018). In compliance with guidance document SANCO 5634/2009-rev.6.1 (European Commission, 2013), the RMS distributed the revised renewal assessment report to Member States, the applicant and the EFSA for comments on 21 December 2018. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA on 22 March 2019 (United Kingdom, 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 thifensulfuron-methyl are presented.

[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] 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.

[3] 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.

To this end, a technical report containing the finalised reporting table is being prepared by EFSA. The deadline for providing the finalised report is 19 April 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.

2. Assessment

The comments received on the pesticide risk assessment for the active substance thifensulfuron-methyl 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, 2018. Revised renewal assessment report on thifensulfuron-methyl, confirmatory data, December 2018, revised March 2019. Available online: www.efsa.europa.eu.

2. United Kingdom, 2019. Reporting table, comments on the pesticide risk assessment for thifensulfuron-methyl in light of confirmatory data, March 2019.

References

EFSA (European Food Safety Authority), 2015a. Conclusion on the peer review of the pesticide risk assessment of the active substance thifensulfuron-methyl. EFSA Journal 2015;13(7):4201, 144 pp. doi:10.2903/j.efsa.2015.4201

EFSA (European Food Safety Authority), 2015b. Technical report on the outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology. EFSA supporting publication 2015:EN-924. 62pp.

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 186 pp. doi:10.2903/j.efsa.2013.3290

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), 2001. FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev. 2, 245 pp., as updated by Generic guidance for FOCUS surface water scenarios, v. 1.4, May 2015.

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 2007. Landscape and mitigation factors in aquatic risk assessment. Volume 1. Extended summary and recommendations. Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment. EC Document Reference SANCO/10422/2005 v. 2.0, 169 pp.

Abbreviations

AGD	aquatic guidance document
a.s.	active substance
BMD	benchmark dose
BMDL	benchmark dose lower confidence limit
BMR	benchmark response
CA	chromosome aberration
DAR	draft assessment report
DG SANCO	European Commission Directorate General Health and Consumers
DT50	period required for 50% dissipation
GAP	good agricultural practice
ED	endocrine disruptor
EU	European Union
GAP	Good Agricultural Practice
GEF	global evaluation factor
HCD	historical control data
HPRT	hypoxanthine phosphoribosyltransferase
ILV	independent laboratory validation
KOC	sorption coefficient
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LoEP	list of endpoints
LOQ	limit of quantification
MF	mutant frequencies
MLA	mouse lymphoma assay
MN	micronucleus
MoA	mode of action
MRL	maximum residue level
MS	Member State
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NESTI	national estimated short-term intake
OECD	Organisation for Economic Co-operation and Development
OSR	oilseed rape
PBI	plant-back interval
PEC	predicted environmental concentration
PEC_{sed}	predicted environmental concentration in sediment

PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
PEC_{twa}	predicted environmental concentration (using time-weighted average approach)
PRIMo	Pesticide Residue Intake Model
RAC	risk assessment committee
RAR	renewal assessment report
RMS	rapporteur Member State
RTG	relative total growth
TER	toxicity exposure ratio
TK	thymidine kinase
TMDI	theoretical maximum daily intake
TWA	time-weighted average
UF	uncertainty factor
QSAR	quantitative structure-activity relationship

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

0. General

General				
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**
0(1)	List of endpoints	DE: An explanation in the header, which colours were used at the different time points of revision would have been very helpful when reviewing the changes made after the evaluation of confirmatory data. At least in the environmental fate section, the colours were not used consistently when adding the new results and some changes between the LoEP of the EFSA conclusion of 2015 and the current LoEP were not marked at all. This makes it very difficult to review the new data.	RMS: A colour key is presented at the start of the LoEP. Regarding the environmental fate section, the changes to the surface water exposure section following the confirmatory data assessment have been incorrectly highlighted turquoise. These were then highlighted in the correct colour pink, however this change has not saved in the final document. This has now been amended. The changes in the soil section were correctly highlighted pink. Any new changes to the LoEP following EFSA/MS commenting have been highlighted teal. **Addressed.**	Addressed: A colour key was presented at the beginning of the LoEP and the changes in the sections were correctly highlighted.
0(2)	Vol 1, page 117	FMC: The Data gap listed under 3.1.4.7, "DuPont – Further investigation of the metabolism of Thifensulfuron-methyl in grass is	RMS UK: Agree with FMC. This point was addressed previously.	Noted.

General				
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**
		required to concludeon the residue definition. The notifier will be required to provide a metabolism study for thifensulfuron.methy in grass." as "No confirmation that study available or ongoing" is not correct. This request was related to Reporting Table, 21 Nov 2014, point 3(34). The Reporting table states: Experts consultation: To consider whether the metabolic pathway of thifensulfuron-methyl in grass is dissimilar to that in cereals, and if therefore an additional metabolism data in pasture / grass are necessary to conclude on the residue definition for risk assessment with respect to grass. Information was indeed provided by applicant and assessed. According to the Peer Review Report report, 03- Expert meeting report, May 2015, on page 4 it is stated "The metabolism of thifensulfuron-methyl in grass is expected to be	This is no longer a data gap. The Vol. 1 has been updated. **Addressed.**	

General				
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**
		qualitatively similar to the one depicted in cereals based on the evidence available. A new metabolism study on grass is therefore not required". Hence this is no longer a data gap.		

1. Physical/Chemical Properties; Data on application and efficacy; Further Information; Methods of Analysis

Methods of analysis

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)	B.5.6 references relied on	EU TSM TF : The owner of 3 studies in the relied-on list is written as Du Pont when it should be Du Pont, Cheminova and ROTAM. These studies were co-sponsored by the 3 companies.	RMS UK: RMS agrees. As stated by EU TSM TF, these 3 studies are: 1) DuPont-44802 2) DuPont -28722 3) Brougher, D.S.; DuPont-46007 The relied-on reference list in the B.5.6 has been updated to change the owner of the three studies from 'Du Pont' to 'Du Pont, Cheminova and ROTAM' **Addressed**	Addressed: The ownership of the 3 studies co-sponsored by the 3 companies in the relied-on list has been updated.
1(2)	**LOEP** - Analytical methods for residues (Annex IIA, point 4.2)	FMC: There is an error in the LOEP page 14, the DuPont soil method LOQ is listed as 0.05 mg/kg when it should be 0.05 µg/kg.	RMS UK: RMS agrees. The LOEP has been updated to correct the LOQ for the DuPont soil method. **Addressed**	Addressed: The LOQ of the DuPont soil method was amended to 0.05 µg/kg in the revised LoEP.
1(3)	Vol 1, page 114	FMC: The Data gap listed under 3.1.4.5, "DuPont - For method M6136.220.01.ST, the nominal concentration of ....set in SANCO	RMS UK: Agree with FMC. This point was addressed previously by a case.	Addressed: The data gap has been deleted from the updated Vol.1

Methods of analysis				
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**
		3030/00 rev 4." as "No confirmation that study available or ongoing" is not correct. This request was related to Reporting Table, 21 Nov 2014, point 1(67). Information was indeed provided by applicant and assessed. According to the Peer Review Report, July 2015, 05- Comments on the additional information assessment, on page 4-5 it is stated "The case provided was acceptable". Hence this is no longer a data gap.	This is no longer a data gap. The Vol. 1 has been updated. **Addressed**	
1(4)	Vol 1, page 115	FMC: The Data gap listed under 3.1.4.5, "DuPont to provide furhter validatiion data to support the method for the determination of Thifensulfuron-methyl in Harmony SG (in terms of assay precision)....." as "No confirmation that study available or ongoing" is not correct. This request was related to Reporting Table, 21 Nov 2014, point 1(69). Information was indeed provided by applicant and assessed. According to the Peer Review Report, July 2015, 05- Comments on the	RMS UK: Agree with FMC. This point was addressed previously. This is no longer a data gap. The Vol. 1 has been updated. **Addressed**	Addressed: The data gap has been deleted from the updated Vol.1

Methods of analysis				
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**
		additional information assessment, on page 5 it is stated "Adressed additional data were provided". Hence this is no longer a data gap.		
1(5)	Vol 1, page 115	FMC: The Data gap listed under 3.1.4.5, "DuPont to provide either a new ILV study to support DuPont-5367, or provide a reasoned case as to why the ILV study for DuPont-5367 (DuPont-8054) was conducted at the same laboratory as the primary study." as "No confirmation that study available or ongoing" is not correct. This request was related to Reporting Table, 21 Nov 2014, point 1(70). The Reporting table states: RMS: The response provided by the Notifier (above) and the summary of communications listed in Appendix 1 of the report DuPont-8054 is considered to address the requirement stated in the SANCO 825/00 rev 8.1 guidance: "The laboratory may be in the applicant's organisation, but should not be in the same	RMS UK: Agree with FMC. This point was addressed previously. This is no longer a data gap. The Vol. 1 has been updated. **Addressed**	Addressed: The response provided by the applicant and the summary of communications listed in Appendix 1 of the report DuPont-8054 is considered to address the requirement stated in the guidance SANCO 825/00 rev 8.1. The data gap has been deleted from the updated Vol.1

Methods of analysis				
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**
		location. In the exceptional case that the lab chosen to conduct the ILV is in the same location, evidence must be provided that different personnel, as well as different instrumentation and stocks of chemicals etc have been used." This will be reflected in a revised RAR. The Notifier's comment regarding method DuPont-13412, Supplement No. 4 is noted. This study can be addressed in the updated RAR if requested. Information was indeed provided (DuPont-13412, Supplement No. 4) by applicant and assessed. According to the Peer Review Report, July 2015, 05- Comments on the additional information assessment, page 5 it is stated "Taking the data set as a whole sufficient data were available to conclude on this point." Hence this is no longer a data gap.		

2. Effects on human and animal health

Long-term toxicity and carcinogenicity				
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)	Mechanistic data for mammary gland tumours	AT: We understand that these data has been already considered by RAC for their decision/weight of evidence that mammary gland tumours observed in rats are not treatment-related. No further comments on this data has been done therefore.	RMS UK: Thank you. Noted. **Addressed**	Addressed
2(2)	Vol 3B6, page 62	FR: As according to ECHA-RAC, mammary gland tumours in rats are not treatment-related (and classification as Carc 2 is not warranted), there is no need to address the point (2) of confirmatory data (*mechanistic data to rule out an endocrine mediated mode of action for mammary gland tumours*). Nevertheless, although already considered by ECHA in the context of harmonised classification and labelling of thifensulfuron-methyl, it would have been of value to provide detailed summaries of the new studies listed on page 62 of Vol	RMS UK: Thank you. Noted. No change is necessary. **Addressed**	Addressed

Long-term toxicity and carcinogenicity				
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**
		3B6.		
2(3)	Confirmatory Info Point 2, Lee, 2015, In silico QSAR evaluation	DE: The significant limitations of the QSAR analyses mentioned in the studies need also be mentioned in the report summaries. Namely: "No scope or applicability domain is offered for this endpoint by the OECD QSAR Toolbox.", "TIMES indicated that all molecules were out of the structural scope of the models" and "over half of the estrogen receptor binding predictions lacked confidence values, indicating that these compounds were outside the applicability domain of the model".	RMS UK: Limitations of the QSAR analyses have been included in an amended document. **Addressed**	Addressed
2(4)	Confirmatory Info Point 2, Hsing, 2015, Dopamine receptor binding assay	DE: Is the dopamine receptor D4.1 mentioned in the report summary the same as the dopamine transporter mentioned in the table on page 11 of the study? Please clarify.	RMS UK: Thank you. Yes it is. **Addressed**	Addressed
2(5)	Confirmatory Info Point 2, IN-A4098 Receptor Binding Studies	DE: Not having the original studies prevents a comprehensive assessment of the 3 studies addressing the oestrogenic potential of IN-A4098. Based on the summaries presented in the report,	RMS UK: Thank you. Noted. No amendment necessary. Also, see response to comment 2(6) below. **Addressed**	Addressed

Long-term toxicity and carcinogenicity				
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 appears to be no reason for concern.		
2(6)	Confirmatory data on "mechanistic data to rule out an endocrine mediated mode of action for mammary gland tumours"	EFSA: this point should be considered addressed given that the ECHA RAC did not consider treatment-related mammary gland tumours, therefore there is no need to consider any mode of action for tumours that are not considered treatment-related. The endocrine disruption potential of thifensulfuron-methyl, as general, should be considered in a more in-depth manner considering all data available. The relevance and reliability of all studies should be clearly assessed (e.g. is the maximun tolerable dose reached in the 2 year rat study?). However, it is noted that the endocrine disruption potential of thifensulfuron-methyl is not subject to confirmatory data but it should be considered during future re-assessment according to the ECHA/EFSA guidance on endocrine disruptors.	RMS UK: Thank you. Noted. **Addressed** Agree that the full ED assessment of thifensulfuron-methyl is outside the scope of this confirmatory data evaluation. Document has been amended to clarify this. **Addressed**	Addressed Full ED assessment of thifensulfuron-methyl is outside the scope of this confirmatory data evaluation.

Reproductive toxicity				
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(7)	Vol 3B6, page 83	FR: As according to ECHA-RAC, classification as Repr 2 is not warranted, there is no need to address the point (4) of confirmatory data (*the relevance of the metabolites IN-A4098, IN-L9223 and IN-JZ789 if thifensulfuron-methyl is classified as reprotoxic category 2 under Regulation (EC) No 1272/2008 of the European Parliament and of the Council and the risk that those metabolites contaminate groundwater*).	RMS UK: Thank you. Noted. This is clarified in Appendix VI (relevance assessment of gw metabolites) of Vol 1. **Addressed**	Addressed
2(8)	Confirmatory data on "the relevance of the metabolites IN-A4098, IN-L9223 and IN-JZ789 if thifensulfuron-methyl is classified as reprotoxic category 2 under Regulation (EC) No 1272/2008 of the European Parliament and of the Council(2) and the risk that those	EFSA: given that ECHA RAC did not classify thifensulfuron-methyl as reprotoxic category 2 there is no need to consider the relevance of the metabolites according to the confirmatory data.	RMS UK: Thank you. Noted. This is clarified in Appendix VI (relevance assessment of gw metabolites) of Vol 1. **Addressed**	Addressed. Given that ECHA RAC did not classify thifensulfuron-methyl as reprotoxic category 2 there is no need to consider the relevance of the metabolites according to the confirmatory data.

Reproductive toxicity				
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**
	metabolites contaminate groundwater".			

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(9)	At Vol. 1, 3.1.5	NL: Following renewal of thifensulfuron-methyl, Commission Implementing Regulation (EU) 2016/1424 requested the applicants to provide confirmatory information. We wonder whether this data requirement should be described at toxicology in paragraph 3.1.5.	RMS UK: Thank you. This is not necessary, in our view. **Addressed**	Addressed
2(10)	At Vol. 1 Studies on metabolites	NL: The conclusion on metabolite IN-W8268 is described as not mutagenic *in vivo* while on other places in the RAR the conclusion is described as non genotoxic. Please check whether it should be mutagenic *in vivo* or genotoxic and	RMS UK: Thank you. The correct wording is "not mutagenic in vivo". Consistency with other parts of the RAR has now been ensured in an amended document.	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**
		make consistent.	**Addressed**	
2(11)	Volume 1, page 106	FMC: RMS states that "Metabolite IN-L9223 and IN-L9225 are considered non-relevant based on the submitted information. Further information on metabolites IN-A4098, IN-W8268, IN-JZ789, and 2-acid-3-triuret is required in order to conclude on the non-relevance of these metabolites. Following the submission of confirmatory information, these metabolites are not relevant." The applicant agrees with this conclusion. However, there are conflicting statements about the relevance of metabolite IN-L9223 on page 41, page 97 , and 179 of volume 1. The applicant requests that the discussion of metabolite IN-L9223 on pages 41, 97, and 179 be updated with the above conclusion.	RMS UK: Thank you. Documents have been updated. **Addressed**	Addressed
2(12)	QSAR	AT: Although many experimental data are available, also QSAR analysis	RMS UK: Thank you. As the genotoxicity QSAR predictions are	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**
		was provided. It would be appreciated to include more information on QSAR analysis in the evaluation, as currently this is summerised very briefly.	only supplementary to the available test data, the addition of further detail does not appear to be necessary. **Addressed**	
2(13)	Vol 3, B.6.8.1, Metabolites - IN-A4098 (triazine amine)	SE: We refrain from commenting on the confirmatory data provided on potential genotoxicity of IN-A4098, since it is already clear that different experts interpret these studies differently, in particular this refers to studies by Clarke (2009), Woods (2011b) and Lloyd (2016a). Instead we refer to the evaluation of confirmatory data on triazine amine carried out in 2018 by Sweden and France (RMSs for Iodosulfuron and Prosulfuron, respectively) and the Technical report from EFSA (doi:10.2903/sp.efsa.2018.EN-1470) which summarise the peer review on that evaluation. The evaluation carried out on confirmatory data provided for Iodosulfuron and Prosulfuron was essentially based on the same data	RMS UK: Thank you. We are aware of this conclusion for IN-A4098 and referral to the PPR panel. However, this evaluation of the genotoxicity of IN-A4098 (which reflects the UK RMS' views) in the context of the confirmatory data for thifensulfuron-methyl was performed by the UK before the SE/FR assessment was finalised and the PPR panel referral issued. This has now been clarified in updated documents. **Addressed**	Addressed Further discussion on **IN-A4098** (triazine amine) is not proposed given that the EFSA PPR panel is currently assessing IN-A4098 (triazine amine). See also 2(14, 15, 16, 17, 18, 20, 21, 22)

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**
		as evaluated for Thifensulfuron-methyl. Given that the assessments resulted in divergent opinions on the genotoxic potential of IN-A4098 the Commission has asked the PPR Panel to provide their opinion by end of July 2019.		
2(14)	Genotoxicity IN-A4098, Clark 2009	AT: RMS has not included the information that the increase in MF in two highest doses was outside the HCD. This information is available in the Triazine amine evaluation performed by SE and FR (June 2018). In this evaluation there are also other details mentioned which could have been included, or reference to this evaluation would be also sufficient. In general, no further comments on the final outcome for IN-A4098 has been done, since this is a subject to an evaluation on the EFSA level.	RMS UK: Thank you. This has now been added. Also see response to comment 2(12) above. **Addressed**	See 2(13).
2(15)	Confirmatory Info Point 1, Genotoxicity of IN-A4098	DE: As previously indicated during the commenting phase of the evaluation by SE/FR (confirmatory data on the common metabolite triazine amine), DE does not agree	RMS UK: Thank you. See response to comment 2(12) above. **Addressed**	See 2(13).

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**
		that the weight of evidence indicates that IN-A4098 (triazine amine) is not genotoxic, rather, DE considers the genotoxic potential of IN-A4098 to be unresolved. For an explanation, see DE´s comments on the evaluation. As IN-A4098 is a common metabolite for many active substances, conclusions only for some actives substances should not be made. Rather, a comprehensive evaluation approach is necessary to address the question whether IN-A04098 has a genotoxic potential or not. Thus, the above mentioned procedure (confirmatory data on the common metabolite triazine amine) need to be finalised as soon as possible.		
2(16)	Confirmatory Info Point 1, Genotoxicity of IN-A4098	DE: A cross reference to the assessment of the RMS Sweden, Co-RMS France regarding the confirmatory data on the common metabolite triazine amine (IN-A4098) should be added.	RMS UK: Thank you. It has been added. **Addressed.**	See 2(13).
2(17)	Genotoxicity IN-A4098, Woods, 2011	AT: RMS has not mentioned in the re-evaluation that the criteria for	RMS UK: As explained in the evaluation, although no	See 2(13).

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**
		selection of highest dose were not fully met while for poor soluble substances tested dose should produce some precipitation. So here potentially higher concentrations could have been tested. Additionally, cytotoxicity at highest dose was not very high (mean RTG 54%)	precipitation was observed, there are indications that it would not have been possible to test higher concentrations as it is most likely the top concentration was not a true solution and was only achieved by some very aggressive measures (heating at 45^{O}C, sonication for 90 min and vortexing for 15 min). **Addressed**	
2(18)	Confirmatory data on "the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and IN-W8268" **IN-A4098**	EFSA: the EFSA PPR panel is currently assessing available genotoxicity data on **IN-A4098** submitted under the confirmatory data on metsulfuron-methyl, prosulfuron and iodosulfuron-methyl.	RMS UK: Thank you. See response to comment 2(12) above. **Addressed**	See 2(13).
2(19)	Confirmatory data on "the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and IN-W8268"	EFSA: Could you give further details on how electro/topological similarity is defined between IN-B5528 and IN-A4098?	RMS UK: Further details have been added. The electrotopological similarity is defined by a comparison of the electrotopological index of the two molecules. The electrotopological index combines the electronic and	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**
	IN-A4098		topological characteristics of a molecule. **Addressed**	
2(20)	28 days rat study IN-A4098	AT. We agree with RMS that LOAEL should be set at 50 ppm (based on effects on bwc and food efficiency in males) and that the $BMDL_{10}$ at 0.7 mg/kg bww/d is sufficiently protective.	RMS UK: Thank you. **Addressed**	See 2(13)
2(21)	RAR 08 vol3 b6 tox updated 2018-12-21 pp107-108 – BMD for 28 day toxicity data for IN-A4098	DK: The use of the BMD approach is still a bit controversiel as is has not been agreed upon among MS. In addtion, the BMD GD propose a BMR of 5% for continous data. No justification for BMR of 10% was given. Therefore, we do not agree in using this approach. For reference value the LOAEL should be used with an extra UF of 3 for extrapolation to a NOAEL. Regardless of the approach, IN-A4098 seems more toxic than the parent.	RMS UK: A BMR of 10% was used as 10% is normally the threshold that defines adversity for changes in body weights and food consumption. The BMD approach (when properly applied) is a scientifically superior method compared to the NOAEL approach. Please also note that the resultant BMDL10 of 0.7 mg/kg bw/d is more conservative than a LOAEL of 3.6 mg/kg bw/d divided by 3 (1.2 mg/kg bw/d). **Addressed**	See 2(13)
2(22)	Vol 3B6, page 114, Summary of studies on	FR: Concerning genotoxicity studies conducted on the triazine amine	RMS UK: See response to comment 2(12) above.	See 2(13)

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**
	IN-A4098	metabolite IN-A4098, the same original dataset has already been peer-reviewed in the context of confirmatory data for iodosulfuron and prosulfuron (except some position papers/revision of original study reports). The outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for iodosulfuron and prosulfuron in light of confirmatory data (EFSA Supporting publication 2018:EN-1470) concluded: "*There was general agreement that triazine amine does not induce gene mutations in bacteria in vitro and chromosome aberration in vitro. However, no firm conclusion could be drawn regarding the gene mutation potential of triazine amine on the basis of the confirmatory information submitted, since some issues were identified with regard to the quality and the interpretation of the results of two in vitro gene mutation studies*". Consequently, the genotoxic potential of triazine	**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**
		amine will be discussed by the PPR Panel.		
2(23)	Vol 3, B.6.8.5, Metabolites – IN-W8268 (thiophene sulphonimide), d) Second MCGM test (by DuPont and EU TSM TF) (Lloyd, 2017d)	SE: Summary of more elaborated comment in column 3: From the wording of the criteria (§ 63 and §64 in OECD 490) it is obvious that the criteria are composed of two independent parts. When applying this interpretation of the criteria the result of this test is neither clearly positive nor clearly negative, since, in either case, only one of the two criteria that should be fulfilled is met, i.e. the increase in MF is concentration related and no single treated group has an increase exceeding the GEF. It is, however, possible to conclude that a result is positive or negative even if all criteria for a clearly positive or clearly negative result are not met. A closer evaluation of the results shows that six of the seven treatment conditions investigated in this study produced a highly statistically significant	RMS UK: Thank you. We disagree. We do not question that there are treatment-related statistically significantly increased trends in 6 of the 7 experiments, but none are biologically significant. Therefore, overall, the study should be considered negative. See also response to comment 2(24) below. **Addressed or EFSA peer-review to be considered**	Peer-review proposed to discuss the genotoxic potential of **IN-W8268** (thiophene sulphonimide). See also 2(24, 25, 26, 27, 28, 29, 30).

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 MF. The probability to obtain a highly statistically concentration related increase in six of seven investigations by chance only is extremely low. Therefore, we are of the opinion that the result of this study should be concluded to be positive.		
2(24)	Vol 3, B.6.8.5, Metabolites – IN-W8268 (thiophene sulphonimide), d) Second MCGM test (by DuPont and EU TSM TF) (Lloyd, 2017d)	SE: In the TK gene mutation test mutants can be scored as slow growing (small colonies) associated with structural changes at the chromosomal level or normal growing (large colonies) associated with point mutations. This type of scoring was not made for test-chemical treated groups. Thereby, no information about the nature of the induced mutations is available. A new TK test with colony sizing should therefore be performed to determine if it is likely that point mutations were induced before deciding about the requirement of a follow-up study *in vivo* on this endpoint.	RMS UK: Colony sizing is required only if the study is positive. As the study was negative (see above), colony sizing was not performed. **Addressed**	See 2(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**
2(25)	Vol 3B6, page 143, Second MCGM test on IN-W8268, Lloyd 2017d Vol3B6, page 154	FR: MLA/TK study (Lloyd 2017d) on IN-W8268: It is considered that the biological relevance of the concentration-related increased mutant frequency (substantiated by positive trend tests) observed in the 3 experiments with and without metabolic activation, cannot be excluded, although below the negative control + GEF. The results of this study are therefore not clearly negative and should be considered equivocal with and without metabolic activation. Overall, 3 *in vitro* gene mutation assays in mammalian cells are available for IN-W8268. Although the MLA/HPRT (Lloyd 2017c) assay is negative, the CHO/HGPRT (San & Clarke, 2002) and MLA/TK (Lloyd 2017) assays are not clearly negative and should be considered equivocal. It is therefore concluded that no firm conclusion can be drawn on the gene mutation potential of the metabolite IN-W8268.	RMS UK: We agree the MLA/TK study (Lloyd 2017d) is not clearly negative; however, this does not mean that it is equivocal. It should be noted that in all (except one) experiments the highest increase was significantly below the biological threshold (GEF). On this basis, therefore, we conclude that the study is negative. This is further supported by the negative result obtained in another modern MCGM study (Lloyd, 2017c). Overall, we disagree that no firm conclusion can be drawn on the gene mutation potential of the metabolite IN-W8268. **Addressed or EFSA peer-review to be considered**	See 2(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**
2(26)	Vol 3, B.6.8.5, Metabolites – IN-W8268 (thiophene sulphonimide), e) Third MCGM test (by DuPont and EU TSM TF) (Lloyd, 2017c)	SE: We agree that the result of this study was negative.	RMS UK: Thank you. **Addressed**	See 2(23).
2(27)	Vol 3, B.6.8.5, Metabolites – IN-W8268 (thiophene sulphonimide), g) Proof of target tissue exposure in mice to support the validity of the DuPont-11124 (2002) study above (by DuPont and EU TSM TF) (DuPont-47638, 2017)	SE: Please include in the RAR the information that DuPont-47638 (2017) used the same strain of mice, and from the same breeder, as DuPont-11124 (2002) (we checked this in the studies).	RMS UK: Thank you. Document amended. **Addressed**	See 2(23).
2(28)	Vol 3, B.6.8.5, Metabolites – IN-W8268 (thiophene sulphonimide), h) QSAR analysis (by DuPont)	SE: Test results are available from studies with IN-W8268 and therefore prediction of an effect by QSAR analyses is not relevant. Actual test data always overrule QSAR predictions.	RMS UK: Thank you. The QSAR analysis is used only as supplementary information. **Addressed**	See 2(23).
2(29)	Vol 3, B.6.8.5, Metabolites – IN-W8268 (thiophene sulphonimide), k)	SE: With regard to clastogenicity, we agree that the study by DuPont-11124 (2002) together with the result of DuPont-47638 (2017)	RMS UK: See responses to comments 2(23) - 2(25) above.	See 2(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**
	Summary of studies on IN-W8268, Genotoxicity	shows that the positive result from *in vitro* (and QSAR alerts) was not confirmed *in vivo*. But regarding the gene mutation tests we do not consider that the two studies submitted (Lloyd 2017c and d) are sufficient to clarify the equivocal result from the first study (San & Clarke, 2002). As commented above, our conclusion is that Lloyd (2017d) showed a positive result. Furthermore, colony sizing was not performed in the study, and a new TK test (with colony sizing) should therefore be performed to determine if it is likely that point mutations were induced before deciding about the requirement of a follow-up study *in vivo* on this endpoint. It would not be ethically justified to request an *in vivo* study to clarify the available results.	**Addressed or EFSA peer-review to be considered**	
2(30)	Confirmatory data on "the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and	EFSA: available genotoxicity data on **IN-W8268** indicated that IN-W8268 is clastogenic *in vitro*. In the negative *in vivo* MN test, no evidence of bone marrow exposure was observed. The	RMS UK: Thank you. Noted.	See 2(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**
	IN-W8268" **IN-W8268**	applicant provided evidence that the metabolite is found in plasma. It might be questioned whether the amount found in plasma is sufficient, but taken into acccount that the dose level chosen in the toxicokinetic study (500 mg/kg) compared to the *in vivo* MN test (limit dose of 2000 mg/kg bw), overall there would be no or very low concern for clastogenicity/aneugenicity *in vivo*. It is acknowleged that according to current criteria for assessing the results of the *in vitro* gene mutation "a test chemical is considered to be clearly negative if, there is no concentration related response or, if there is an increase in MF, it does not exceed the Global Evaluation Factor". According to the result of the test (Lloyd, 2017d; MLA, *tk* locus) there was a concentration related response but not increase in MF. Given that colony size was included in the test, could you	See responses to comments 2(23) - 2(25) above. Colony sizing (except for negative and positive controls) was not conducted as, in accordance with the guideline, this is required only in case of positive results.	

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**
		please analyse the results according to colony size?. Is there any indication that the trend is due to clastogenicity rather than gene mutation?. This assumption would be more in line with the results of other tests indicating clastogenic potential in vitro. It is also noted that the results of new MLA (hprt locus; Lloyd, 2017c)) were negative indicating no potential for gene mutation.	Noted. **Addressed or EFSA peer-review to be considered**	
2(31)	Vol 3, B.6.8.7, Metabolites – IN-A5546 (2-Ester-3-sulfonamide), b) Second Ames test (by DuPont) (Waalkens & Enninga, 1987)	SE: We agree that the result of this study was negative but, as pointed out in the evaluation, Salmonella strain TA102 or E.coli WP2 should also have been tested compared to the current guideline.	RMS UK: Thank you. Noted. **Addressed**	Addressed Available genotoxicity data on **IN-A5546** do not raise concern for genotoxicity. See also 2(32, 33, 34)
2(32)	Vol 3, B.6.8.7, Metabolites – IN-A5546 (2-Ester-3-sulfonamide), c) In vitro chromosome aberration test (by DuPont and EU TSM TF) (Kellum,	SE: We agree that the result of this study was negative.	RMS UK: Thank you. Noted. **Addressed**	See 2(31).

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))			
2(33)	Confirmatory data on "the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and IN-W8268" **IN-A5546**	EFSA: available genotoxicity data on **IN-A5546** do not raise concern for genotoxicity, however aneugenicity might not be appropiately addressed on the basis of available genotoxicity tests. In the *in vitro* CA test there was no indication of poliploidy, however the test is mainly measuring structural chromomosome aberrations. In the negative *in vivo* MN test, no evidence of bone marrow exposure was observed. Some uncertainties remain regarding aneugenicity.	RMS UK: Thank you. As explained in the evaluation, although confirmation of bone marrow exposure was not included in the *in vivo* MN study, it is considered that it is most likely the bone marrow was exposed to the test substance (and hence, aneugenicity investigated *in vivo*) as the top dose used was half of the dose which caused mortality in mice in a preliminary study. **Addressed**	See 2(31).
2(34)	Vol 3, B.6.8.7, Metabolites – IN-A5546 (2-Ester-3-sulfonamide), e) QSAR analysis (by DuPont)	SE: Test results are available from studies with IN-A5546 and therefore prediction of an effect by QSAR analyses is not relevant. Actual test data always overrule QSAR predictions.	RMS UK: Thank you. The QSAR analysis is used only as supplementary information. **Addressed**	See 2(31).
2(35)	Vol 3, B.6.8.8, Metabolites – IN-B5528 (O-demethyl triazine amine), a) Ames test	SE: We agree that the result of this study was negative.	RMS UK: Thank you. Noted. **Addressed**	Addressed Available genotoxicity data on **IN-B5528** do not raise concern for

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**
	(by DuPont and EU TSM TF) (Myhre, 2017)			genotoxicity. See also 2(36, 37, 38, 39, 40).
2(36)	Vol 3, B.6.8.8, Metabolites – IN-B5528 (O-demethyl triazine amine), b) MCGM test (by DuPont and EU TSM TF) (Lloyd, 2017a)	SE: We agree that the result of this study was negative. However, it is unclear why 240 µg/mL was chosen as the highest test concentration since IN-B5528 apparently was soluble in culture medium at 300 µg/mL. A clear increase in MF was noted from 200 to 240 µg/mL. Therefore, results at a higher dose would have been useful.	RMS UK: Thank you. 240 µg/mL was the maximum in-culture practicable concentration which was obtained by adding 16 mL of test substance formulated in RPMI medium at 300 µg/mL to achieve a final total volume of 20 mL culture. This information has been added to a revised document. There was only a slight (not clear), if any, increase in the MF at 240 µg/mL –S9. **Addressed**	See 2(35).
2(37)	Vol 3, B.6.8.8, Metabolites – IN-B5528 (O-demethyl triazine amine), c) *In vitro* micronucleus test (by DuPont and EU TSM TF) (Lloyd, 2017b)	SE: We agree that the result of this study was negative.	RMS UK: Thank you. Noted. **Addressed**	See 2(35).
2(38)	Genotoxicity IN-B5528, Lloyd 2017b	AT: RMS is kindly asked to include the information upon what the highest	RMS UK: Thank you. See response to comment 2(36) above.	See 2(35).

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 was chosen. RTG was not very reduced and no precipation was observed. The highest concentration was defined as "practicabel", however, this is not further explained. As IN-B5528 is structurally very similar to IN-A4098, detailed information on choice dose and solubility is crucial.	**Addressed**	
2(39)	Confirmatory data on "the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and IN-W8268" **IN-B5528**	EFSA: available genotoxicity data on **IN-B5528** do not raise concern for genotoxicity.	RMS UK: Thank you. Noted. **Addressed**	See 2(35).
2(40)	Vol 3, B.6.8.8, Metabolites – IN-A5528 (2-Ester-3-sulfonamide), d) QSAR analysis (by DuPont)	SE: Test results are available from studies with IN-A5528 and therefore prediction of an effect by QSAR analyses is not relevant. Actual test data always overrule QSAR predictions.	RMS UK: Thank you. The QSAR analysis is used only as supplementary information. **Addressed**	See 2(35).
2(41)	LOEPs Studies performed on metabolites or impurities ‡	NL: Please add the conclusions on the genotoxicity etc. of the metabolite IN-B5528 in the LOEPs.	RMS UK: Thank You. Required information has been added to a revised document.	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**
			Addressed	

Other comments, incl comments on volume 4 (impurities, batches)				
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(42)	General	AT: It is very difficult to follow the text shaded blue. We would have appreciated e.g. yellow, as no other colour has been used in this DRAR.	RMS UK: Thank you. Noted. Yellow highlight had been used before to mark changes in the sections of the RAR at AIR 2 renewal. To avoid confusion with any previous references to yellow text in the documents it was decided not to use this colour shading for the confirmatory data assessment. **Addressed**	Addressed
2(43)	General	NL: We agree that there are no relevant metabolites. However, the concentration in groundwater could be >0.75 µg/L for several metabolites. Please make an overview of all metabolites with concentrations in groundwater	RMS UK: Thank you. A relevance assessment of gw metabolites is already included in Appendix VI of Volume 1. **Addressed**	Addressed

Other comments, incl comments on volume 4 (impurities, batches)				
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**
		above 0.75 µg/L and make a risk assessment for the consumers drinking 2 L water while presenting the threshold values used (and explaining the derivation) in the same overview table. We suggest to include this information in Vol. 1.		
2(44)	Genneral comment on mammalian toxicology	EFSA: It is noted that the assessment report included the full assessment of thifensulfuron-methyl. For the purpose of confirmatory data on thifensulfuron-methyl EFSA only commented on those points subject to confirmatory data by the European Commission: • the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and IN-W8268; • mechanistic data to rule out an endocrine mediated mode of action for mammary gland tumours; the relevance of the metabolites IN-A4098, IN-L9223 and IN-JZ789 if thifensulfuron-methyl is classified as reprotoxic category 2 under	RMS UK: Thank you. Noted. **Addressed**	Addressed EFSA only commented on those points subject to confirmatory data by the European Commission: • the absence of genotoxicity of metabolites IN-A4098 and its derivative IN-B5528, IN-A5546 and IN-W8268; • mechanistic data to rule out an endocrine mediated mode of action for mammary gland tumours; • the relevance of the metabolites IN-A4098, IN-L9223 and IN-JZ789 if thifensulfuron-methyl is classified as reprotoxic category 2 under Regulation (EC) No 1272/2008 of the European Parliament and of the Council and the risk that those metabolites contaminate groundwater

Other comments, incl comments on volume 4 (impurities, batches)				
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**
		Regulation (EC) No 1272/2008 of the European Parliament and of the Council(2) and the risk that those metabolites contaminate groundwater		
2(45)	B.6.14 Refrence supporting the confirmatory data evaluation and relied upon	EU TSM TF: The owner of 7 studies in the relied is written as Du Pont when it should be Du Pont, Cheminova and ROTAM. These studies were co-sponsored by the 3 companies.	RMS UK: Thank you. Document amended. **Addressed.**	Addressed

4. Environmental fate and behaviour

Fate and behaviour in water and sediment and effect of water treatment procedures on the nature of residues				
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)	Vol 1, page 118	FMC: The Data gap listed under 3.1.4.8, "DuPont and Task Force to provide further information to confirm the identity of the aqueous photolysis metabolite currently identified as either thiophenyl triazinyl amine (Task Force) or IN-D8856 (DuPont)- see also 3.1.4.9 below" as "No confirmation that study available or ongoing" is not correct. This request was related to Reporting Table, 21 Nov 2014, point 4(86) and 4 (87). Information was indeed provided (DuPont- 41912) by applicant and assessed. According to the Peer Review Report, July 2015, 05-Comments on the additional information assessment, on page 18 it is stated "EFSA: the new information has been considered acceptable." Please also note that the correct code for this metabolite is IN-D8858. Hence this is no longer a data gap.	RMS UK: Agreed, this is no longer a data gap. The table has been updated to reflect this. **Addressed**	Addressed. Vol 1, paragraph 3.1.4.8 has been amended to indicate that the data gap on the identity of the aqueous photolysis metabolite has been fulfilled.

PEC in soil				
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(2)	B.8.3. PECsoil	AT does not support the introduction of 5 cm tillage depth for cereals and recommends to still use 20 cm depth for accumulation calculations.	RMS UK: The RMS considers that the FOCUS DG SANTE "soil persistence models and EU registration" 1997 working group report does not specify which tillage depth should be used for PEC_{soil} accumulation calculations. Therefore, the UK approach to accumulation calculations is to use 5 cm as a conservative first tier, which accounts for "min-till" or no till scenarios. A 20 cm depth is appropriate for specific crops for which commercial cultivation involves annual mixing to a deeper layer (e.g. potatoes, sugar beet), or for substances where there is evidence of leaching to a deeper layer. In this case, cereals can be cultivated using the "min-till" approach, and so 5 cm tillage depth is used. The RMS accepts that most cereal crops across Europe will experience deeper cultivation, however this presents	Addressed. PECsoil calculations based on 5 cm tillage depth for cereals can be considered a conservative first tier assessment.

PEC in soil				
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**
			a conservative first tier. As this approach provides an acceptable soil risk assessment, a refinement with 20 cm tillage depth is not considered necessary. **Addressed**	
4(3)	B.8.3 PECs	NL: has no comments on the PECscalculations but onlywonders why fort he AS normalised maximum value is used an fort he metabolites the non-normalised value is used.	RMS UK: Agreed, the longest normalised soil DT_{50} has been used for the parent compound. According to guidance, the non-normalised value should be used for PEC_{soil} calculations, however in this case the RMS has selected the more conservative value. **Addressed**	Addressed. A clarification note on the deviation for selection of the longest normalised soil DT_{50} used for PECsoil calculations for the parent compound could be added in the LoEP.
4(4)	List of endpoints, PECsoil of metabolites	DE: Could the molecular weights, DT_{50} values and the maximum occurrences of the metabolites used to derive the application rates for PECsoil calculations please also be added to the LoEP? This will make it easier for later authorisations of PPP to know which endpoints are needed for PECsoil calculations.	RMS UK: Agreed. The metabolite parameters used in the PEC_{soil} calculations have been added to the LoEP, highlighted teal. **Addressed**	Addressed. The metabolite parameters (molecular weights, DT_{50} values and the maximum occurrences) used in the PEC_{soil} calculations have been added to the LoEP.
4(5)	B.8.3 p. 431	EU TSM TF : It is written that "*The RMS used a tillage depth of 5 cm for accumulation calculations.*" In our opinion, the standard agreed	RMS UK: Please see response to comment 4(2). **Addressed**	Addressed. PECsoil calculations based on 5 cm

PEC in soil				
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**
		value of 20cm should be used.		tillage depth for cereals can be considered a conservative first tier assessment.
4(6)	B.8.3 p. 434	EU TSM TF : It is written that "*The applicant used a tillage depth of 20 cm for accumulation calculations; however, the RMS considers it is appropriate to use the more conservative value of 5 cm depth for cereals.*" In our opinion, the standard agreed value of 20cm should be used.	RMS UK: Please see response to comment 4(2). **Addressed**	Addressed. PECsoil calculations based on 5 cm tillage depth for cereals can be considered a conservative first tier assessment.
4(7)	Vol. 3, B.8.3 PECsoil, thifensulfuron-methyl and its metabolites LoEP, PECsoil, thifensulfuron and its metabolites	EFSA: the confirmatory information regarding the Predicted Environmental Concentration (PEC) in soil for thifensulfuron-methyl and its soil metabolites is considered valid and the calculated PEC_{soil} and $PEC_{soil\ accumulation}$ values can be appropriately used to address the risk to soil macroorganisms. For reason of transparency, it would be better to include in the LoEP in the PECsoil calculations of the metabolites the molecular weight of each metabolite and to clarify that a	RMS UK: Thank you for your agreement. The metabolite parameters used in the PEC_{soil} calculations have been added to the LoEP, highlighted teal. A sentence has also been added to clarify that 0% crop interception was used, in accordance with the parent PEC_{soil} assessment. There is already a sentence explaining that a 5 cm tillage depth was used for accumulation calculations. Table footnotes have been added for clarity. **Addressed**	Addressed. See response to comments 4(2) and 4(4).

PEC in soil				
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**
		worst case crop interception of 0% and a tillage depth of 5 cm for accumulation calculations were assumed.		

PEC in surface water and ground water				
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(8)	B.8.6 PECsw	AT supports the argumentation provided by RMS UK on the application timing of scenario D1.	RMS UK: Thank you for your comment. **Addressed**	Noted.
4(9)	Vol. 3, B.8, PECsw of parent	DE: At least in Northern Europe, herbicides to winter cereals will normally be applied in autumn. Has it been tested that the application timing from December to March really is a worst case also for the autumn application of thifensulfuron-methyl to winter cereals? In our experience, the chosen application window can have a huge impact on the derived PECsw values (based on the run-off	RMS UK: The requested use 1x 30 g a.s./ha (DuPont/FMC GAP) to winter cereals applied in the autumn was considered in the original renewal assessment and the step 3 and step 4 values are presented in volume 3 B.8 Table B.8.333 and Table B.8.342 respectively. The applicant did not submit additional modelling for this use in light of the revised aquatic RAC for the purpose of	Addressed. PECsw and PECsed at steps 3 and 4 for the parent compound for the D1 scenario using refined application dates were available. This refinement exposure clearly demonstrated that thifensulfuron-methyl is very sensitive to application timing, particularly with regard to drainflow events, and can greatly affect the PECsw value. As

PEC in surface water and ground water				
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**
		events that will or will not occur during the application window).	confirmatory assessment. However, the original values are retained and can illustrate autumn applications to winter cereals. The PECsw values are lower for the D1 scenario autumn applied than the winter applied, but higher for the D2 scenario autumn applied. However, it is not possible to compare properly as the application rates are different. Overall, the D1 and D2 scenarios relevant for Northern Europe, are driven by drainage for all requested cereal application rates and timings, and all PECsw values exceed the RAC. This is the case for previously calculated values and those newly calculated for the confirmatory assessment. The D1 refinement section, initially submitted by DuPont, demonstrates that thifensulfuron-methyl is very sensitive to application timing, particularly with regard to drainflow events. The RMS agrees that the chosen application window can have a	drainflow mitigation options are currently limited and are the least developed across the EU, the peer review concluded that further investigation into the effects of application timing and possible restriction of application timing is recommended to be performed for national assessments of Member States for which drainflow events are a concern, particularly those for which the FOCUS D1 scenario is relevant.

PEC in surface water and ground water				
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**
			large impact on the resulting PECsw. Further investigation into the effects of application timing and possible restriction of application timing is recommended to be performed by MS for national product evaluations. **Addressed**	
4(10)	Vol. 3, B.8 and LoEP, PECsw of parent	DE: Step 3 and Step 4 PECsw values for the maximum application rate of 51 g/ha and for 41 g/ha thifensulfuron-methyl to winter cereals are missing from the LoEP (only tables that have been striked through are available). However, they are listed in Vol. 3, B.8. Could this values please be added to the LoEP?	RMS UK: The higher application rates of 40.8 a.s./ha and 51 g a.s/ha are the requested uses within the Task Force GAP. The Task Force did not provide additional modelling with mitigation measures to refine the PECsw values for these rates. However, the previously calculated values are still relevant to the risk assessment and so have not been striked through in the volume 3. They will be shown in the LoEP. **Addressed**	Addressed. As no additional Step 3 and Step 4 PECsw/PECsed values for thifensulfuron-methyl for the maximum application rate of 51 g a.s./ha and for 41 g a.s./ha to winter cereals were available, the previously calculated values are still relevant to the risk assessment.
4(11)	Vol. 3, B.8 and LoEP, PECsw of IN-D8858	DE: It is not clear, why the molecular weight of the parent was used for PECsw calculations since the molecular weight of IN-D8858 is known. On the other hand as worst	RMS UK: The RMS notes that the molecular weight of IN-D8858 is not listed within the environmental fate or physical/chemical sections of the RAR. The RMS has	Addressed. The available aquatic exposure assessment for metabolite IN-D8858 is

PEC in surface water and ground water				
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**
		case Koc for water 0 is generally assumed (and was used for the other metabolites) and not 10 which was used here for IN-D8858.	calculated a value of 280.3 g/mol using ChemDraw4. The use of the parent molecular weight is considered conservative. The RMS agrees that a Koc of 0 is ultimately the most conservative value, however section 6.2.2 of the EFSA aquatic guidance document states a default Koc 10 should be used for water column calculations. The other metabolites were assessed using worst case parameters as first tier. The separate IN-D8858 assessment is a refinement. **Addressed**	considered valid.
4(12)	List of endpoints, PECsw of thifensulfuron-methyl and IN-D8858	DE: The colour coding between the PECsoil and the PECsw section is inconsistent. In the PECsoil section the current changes were marked in pink. Previous revisions were marked in green, yellow and turquoise. However, in the PECsw section new changes were also marked in turquoise (e.g. tables for Step 3 starting at page 65 and tables for step 4 starting at page 74) or were only striked through	RMS UK: The changes to the surface water exposure section following the confirmatory data assessment have been incorrectly highlighted turquoise. These were then highlighted in the correct colour pink, however this change has not saved in the final document. This has now been amended. Any new changes to the LoEP following EFSA/MS commenting have been highlighted teal.	Addressed.

PEC in surface water and ground water				
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**
		but not marked at all (previous tables for step 3 starting at page 69 and for step 4 starting at page 78). This makes it very difficult to evaluate the current changes. Could all new changes please be marked in pink?	**Addressed**	
4(13)	LoEP, PECsw of IN-D8858	DE: Could the metabolite IN-D8858 please be deleted from the PECsw section for all other metabolites (under metabolite X) since separate PECsw were derived for this metabolite further below?	RMS UK: Agree, this has been amended and highlighted teal with a footnote to explain. **Addressed**	Addressed. LoEP has been amended.
4(14)	LoEP, Step 3 PECsw thifensulfuron-methyl	EFSA: FOCUS Step 3 PECsw for thifensulfuron-methyl after application of 1 x 30 g a.s./ha to winter cereals in the autumn at BBCH 12-39 are used in the ecotox section to derive the TERs. Although these PECs were not considered in the submission of the confirmatory data (Vol. 3, B.8.6.1), they are available in Table B.8.333 and should be reported in the LoEP (where they are currently strikethrough). This is also valid for Step 3 PECsw for: - Application of 1 x 51 h a.s./ha	RMS UK: Agreed, the applicants have not provided additional modelling with mitigation measures for these uses, however they are still presented in the volume 3 and will be shown in the LoEP. **Addressed**	Addressed. LoEP has been amended. See also response to comment 4(10)

PEC in surface water and ground water				
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**
		to winter cereals in the spring at BBCH 13-39 Application of 1 x 40.8 h a.s./ha to spring cereals in the spring at BBCH 13-39		
4(15)	LoEP, Step 4 PECsw thifensulfuron-methyl	EFSA: it is noted that in the ecotox section of the LoEP max PECsw at Step 4 based on **5 m** NSBZ were used in the aquatic risk assessment (e.g. algal risk assessment with 1 application at 37.5 g a.s./ha to winter cereals in the winter at BBCH 12-39). These PECs are not reported in the fate section of the LoEP.	RMS UK: Agreed, these will be shown without strike through in the fate LoEP. **Addressed**	Addressed. LoEP has been amended.
4(16)	Vol. 3, B.8.6.1 PECsw, thifensulfuron-methyl , Step 3-4	EFSA: FOCUS Step 3-4 PECsw/sed calculated by the RMS with mitigation measures up to 20 m are agreed and can be used in the risk assessment.	RMS UK: Thank you for your comment. **Addressed**	Noted.
4(17)	Vol. 3, B.8.6.2 Step 1-2 surface water assessment: IN-D8858	EFSA: in the additional surface water modelling to address the aquatic risk of metabolite IN-D8858, it is indicated that "specific endpoints from the LoEP (EFSA Journal 2015;13(7):4201), rather than worst case values" were used. However, it is not clear the source	RMS UK: The use of the parent water solubility is considered an appropriate surrogate. The RMS notes that the use of either 1000 or 2400 mg/L does not impact step 1-2 PECsw values. The RMS agrees that a Koc of 0 is ultimately the most conservative	An aquatic exposure assessment for metabolite IN-D8858 to support the highest requested GAP application rates of 40.8 and 51 g a.s./ha is not available.

PEC in surface water and ground water				
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**
		of some of the input parameters (Table B.8.6.2-1 and LoEP) deviating from the values used in the first evaluation: - Water solubility: 2240 mg/L (previously 1000 mg/L) - Koc: 10 L/kg (previously 0 L/kg) - DT50 soil: 10 d (previously 1000 d as no experimental data are available) Additionally, PECsw for metabolite IN-D8858 are not available for the highest application rates on cereals of 40.8 and 51 g a.s./ha. It is agreed with the RMS that the latest model version of the FOCUS step 1-2 calculator 3.2 should be used for the confirmatory assessment.	value, however section 6.2.2 of the EFSA aquatic guidance document states a default Koc 10 should be used for water column calculations. The RMS considers this acceptable as a refinement to the general approach used for the other metabolites. The RMS notes that this metabolite is not observed in soil and considers the use of soil DT50 1000 days to be overly conservative. Furthermore, the RMS confirms the PECsw values are not effected by use of soil DT50 10 or 1000 days. Text has been added to the volume 3 B.8. The Task Force did not submit any modelling for IN-D8858 to support their highest requested GAP application rates of 40.8 51 g a.s./ha. **Addressed**	
4(18)	Vol. 3, B.8.6.2 Step 3-4 parent assessment recalculated for the D1 ditch and stream scenarios only based on revised application	EFSA: the RMS conclusion on the revised application dates to calculate Step 3-4 PECsw for the D1 scenario for thifensulfuron-methyl is agreed: - For winter cereals the	RMS UK: Thank you for your comment. **Addressed**	Noted.

PEC in surface water and ground water				
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**
	dates	application date of 1st of May is too late for the earliest growth stage of BBCH 12 For early springtime applications, the results of the exercise conducted by the RMS with different application dates clearly indicated that even small differences in the application window can greatly affect the PECsw value. Therefore, a refinement of Step 3-4 parent assessment based on the choice of application timing is recommended at MS level only for product evaluations within the national assessments.		

Other comments incl. available monitoring data				
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(19)	LoEP, residues requiring further assessment and classification and proposed labelling with	DE: There are differences between the previous LoEP in the EFSA Journal 2015;13(7):4201 and the new LoEP although to our information, these	RMS UK: The IN-F5475 metabolite is included in the general "metabolite X" surface water assessment, with simple first tier	Addressed. LoEP has been amended.

	regard to fate and behaviour data	sections have not been revised. Under residues requiring further assessment in surface water two additional metabolites IN-F5475 and IN-RDF00 are listed in the new LoEP (and for IN-RDF00 no PECsw values are available but for IN-F5475). Under proposed classification R53 is listed in the new LoEP and Candidate for chronic (long term) aquatic hazard is listed in the previous LoEP. These differences should be checked and the correct changes should also be marked in pink.	step 1-2 PECsw values for all metabolites. There was a step 3 refinement performed for IN-RDF00 as part of renewal (page 86 LoEP). Regarding the classification, this has not been re-visited by the RMS during the confirmatory data process. For consistency the wording has been amended in the LoEP to match the previous consideration. **Addressed**	

5. Ecotoxicology

Acquatic organism				
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)	Vol.3, B.9, HLR 321-91 (1991); Flow-through, 21-day toxicity of DPX-M6316-100 (technical) to rainbow trout (Oncorhynchus mykiss)	EFSA: it is acknowledged that the method of analysis has not been satisfactorily validated in accordance with SANCO 3029/99/rev.4. Can the RMS please assess whether the method can be considered fit for purpose despite not validated?	RMS UK: The HLR 321-91 (1991) study was not considered fit for purpose as the method was not satisfactorily validated. To make this clearer the endpoint has been struck through in the risk assessment section and LoEP. It should be noted this doesn't impact the risk assessment as there is another chronic fish study (DuPont -28722, A 2010) with a more sensitive endpoint that was valid for use. **Addressed**	Addressed
5(2)	B.9.2 Effects on aquatic organisms, Arnie, J. et al.(2015a)	AT: The Lemna study by Arnie et al. (2015a) was conducted under semi-static conditions. The endpoints were expressed based on geometric mean measured concentrations. However, according to the Aquatic GD corrigendum the endpoints should be based on arithmetic mean or	RMS UK: Noted. **Addressed**	Addressed

Acquatic organism				
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**
		time-weighted average / time-weighted geomean. But AT agrees with the RMS that under consideration of the analytical measurements (> 100% recovery) the use of measured concentrations is suitable protective.		
5(3)	B.9.2 Effects on aquatic organisms, Arnie, J. et al.(2015b)	AT: The Lemna study (low temperatures) by Arnie et al. (2015b) was conducted under static conditions. The endpoints are based on arithmetic mean measured concentrations. According to the Aquatic GD corrigendum endpoints from static test designs should be based on geometric mean concentrations.	RMS UK: When comparing geometric and arithmetic means there are negligible differences. In some cases, arithmetic means are more protective and others there is no difference at 1 d.p.: 0.18, 0.44, 1.9, 7.41, 30.51, 121.49 compared to 0.19, 0.44, 1.9, 7.4, 31 and 122 µg a.s./L respectively. It should also be noted that the growth rate endpoint was greater than the highest test concentration and not statistically calculated. Given the negligible difference and stable analytical recoveries the RMS does not consider any changes are required for this endpoint. In addition, the EFSA 2013 GD corrigendum has not been published and the points	Addressed

Acquatic organism				
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**
			raised are from meeting minutes. Furthermore OECD 221 states that if the concentrations are maintained within ± 20 % of nominals that nominal or mean measured values can be used (noting only a single sample was outside this range i.e. lowest test concentration at study termination- 158 %). Overall the RMS considers the calculated endpoint valid and no further consideration is required. **Addressed**	
5(4)	B.9.2 Effects on aquatic organisms, Arnie, J. et al.(2016b)	AT: The Lemna study by Arnie et al. (2016b) was conducted under semi-static conditions. The endpoints are based on geometric mean measured concentrations. However, according to the Aquatic GD corrigendum the endpoints should be based on arithmetic mean or time-weighted average / time-weighted geomean.	RMS UK: It should be noted the EFSA 2013 GD corrigendum has not been published and the points raised by AT are from meeting minutes. The RMS has confirmed the geometric mean calculations reported and notes these have been calculated allowing for the time between sampling points which varied between 2-3 days i.e. the geometric mean approach	Addressed

Acquatic organism				
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**
			described in OECD 23 (Annex 2). Overall the RMS considers the calculated endpoint valid, protective and that no further consideration is required. **Addressed**	
5(5)	Vol.3 B.9 DuPont-43963	EFSA: it is noted that the endpoint was only calculated for the period 9-16 days. However, it would be good to also have the endpoint calculated for the exposure period between 0-7 days.	RMS UK: Noted. However, it is not possible based on the study conducted as frond counts were made on days 0, 9, 12, 14 and 16, noting this was a modified study design (extended duration and lower temperature). **Addressed**	Addressed
5(6)	B.9.2 Effects on aquatic organisms, Kirkwood(2015a)	AT: The Myriophyllum study by Kirkwodd (2015a) was conducted under semi-static conditions. The endpoints were expressed based on geometric mean measured concentrations. However, according to the Aquatic GD corrigendum the endpoints should be based on	RMS UK: It should be noted the EFSA 2013 GD corrigendum has not been published and the points raised by AT are from meeting minutes. In addition, the geometric mean concentrations are more protective than arithmetic mean for this study.	Addressed

Acquatic organism				
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**
		arithmetic mean or time-weighted average / time-weighted geomean.	Given the rate of decline (variable but not within ± 20 % of nominals for all test concentrations) in aged samples the RMS considers a geometric mean approach acceptable. This is supported by OECD 221 that states if concentrations are not maintained within ± 20 % of nominals that geometric mean measured values should be used. Overall the RMS agrees with the use of the geometric mean measured concentrations calculated by the study author, noting there was an even spacing between sampling points i.e. 7 days on each occasion. **Addressed**	
5(7)	B.9.2 Effects on aquatic organisms, Kirkwood(2015a)	AT: Analytical measurements: No information is given on the measured concentrations in the sediment. In addition, no information regarding possible effects on the roots of	RMS UK: The study did not measure analytical concentrations in sediment. Additional information has been added to the study regarding root development. Effects on root development were	Addressed

Acquatic organism				
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**
		Myriophyllum is given in the study summary.	observed only for a single plant at 2 µg a.s./L suggesting this was not treatment related. However, the majority of plants had no roots at the highest test concentration of 5.9 µg a.s./L. All calculated endpoints are 2 µg a.s./L or below and are therefore considered protective of potential effects on root development by the RMS. **Addressed**	
5(8)	Study by Kirkwood (2015a)	AT: Only two concentrations have been included, that is rather not considered sufficient to demonstrate linear reciprocity. A graph like presented in EFSA (2015b, recurring issues report) with time x concentration against effects could have been helpful. Generally, we agree that no PECtwa should be used, mainly simply based on the fact that the pre-condition for its used have not been	RMS UK: Noted. **Addressed**	Noted

Acquatic organism				
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**
		sufficiently specified in the current EFSA GD.		
5(9)	Vol. 3, B.9, Kirckwood, A. (2015a)	DE: We agree with the setting of the E_rC_{50} = 2.0 µg a.s./L (dry weight) as well as the NOEC = 0.2 µg a.s./L (wet weight) even if there is no statistical significance. The percentage effect rates should be considered, as from the RMS proposed.	RMS UK: Noted. **Addressed**	Noted
5(10)	Vol. 9 Effects on Aquatic Plants p.134	FMC: 21-d ErC50 (dry weight) Footnote "a" provides explanation for a visual determination of an endpoint that provides no scientific justification. While we agree that this is not the endpoint used in the risk assessment, sound scientific principles should be applied to all endpoints. The endpoint was determined with the most scientifically sound available statistical approach and should be > 5.9 ug/L.	RMS UK: We appreciate the E_rC_{50} was derived as > 5.9 µg a.s./L, noting that this is an extrapolated value and a statistically derived value is not possible given the dose response. The RMS has highlighted uncertainty based on the experimental data and 50 % effects observed at 2.0 µg a.s./L. Whilst this endpoint has not been statistically derived it is considered conservative and protective of potential effects based on the observed data. Therefore, no changes have been made. Furthermore, as highlighted by the applicant this value was not used	Addressed

Acquatic organism				
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**
			in the risk assessment. **Addressed**	
5(11)	Vol. 9 Effects on Aquatic Plants p.135	FMC: The NOEC provided in the study report (0.2 ug/L) is the correct endpoint. The study report states that the NOEC was determined statistically. The proposed NOEC is based on a visual interpretation of the results that is not justifiable in this situation. The response observed in the 0.2 ug/L treatment group was statistically determined to not be different from the control and was thus the scientifically sound and statistically supported NOEC. Footnote "b" provides explanation and should be deleted.	RMS UK: Whilst the statistically derived NOEC was 0.20 µg a.s./L, based on yield wet weight there was 16 % inhibition at this concentration. Therefore, the RMS has proposed a lower NOEC value that based on the experimental data has < 10 % inhibition. It is noted there was a typo underneath table CA 8.2.7/03-4 which has been corrected. **Addressed**	Addressed
5(12)	B.9.2 Effects on aquatic organisms	AT: Thank you for the detailed and well-structured evaluation of the confirmatory data. AT agrees with the risk assessment provided by the RMS.	RMS UK: Thank you. **Addressed**	Noted

Acquatic organism				
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(13)	Reciprocity	AT: It seems that for some studies on aquatic on plants reciprocity was discussed based on phytotoxic effects, but according to the endpoint overview table endpoints were not based on phytotoxic effects. We also question whether phytotoxicity in general is a suitable parameter to discuss Haber`s law.	RMS UK: That is correct that endpoints were not based on phytotoxic effects but growth rate values in-line with EFSA 2013 aquatic guidance. In terms of Haber's law phytotoxicity was used to give an indication of potential effects. As stated in the RAR some growth rate endpoints calculated were not considered protective of phytotoxicity. Overall the RMS considers the approach taken as appropriate, noting it is identical to the previous consideration. **Addressed**	Addressed
5(14)	Vol. 3, B.9, Higher tier RA for aquatic organisms Arnie et al (2015a&b), Kirckwood (2015a) reciprocity	DE: We agree with the RMS, reciprocity has not shown by this studies and delayed effects can not be excluded. In order to demonstrate linear reciprocity, more measurements would be necessary.	RMS UK: Noted. **Addressed**	Noted
5(15)	Delayed effect	AT: We agree with the conclusion: " [...]*While these effects are not considered to be 'delayed' they do*	RMS UK: Noted. We acknowledge the additional uncertainty regarding study duration. Nonetheless there remains uncertainty over the	Noted

Acquatic organism				
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**
		indicate that there remains some uncertainty over the period of exposure that is causing the effects seen, due to a potentially slow mode of action of the active substance." In addition to the relevance of this aspect for the discussion, the question somehow remains open whether the test haven been long enough to detect the maximum effect. However, this would be the case for a number of substances.	period of exposure that is causing the effects observed regardless of whether maximum effects occurred. **Addressed**	
5(16)	Vol. 9, B. Effects on Aquatic Plants p.140	FMC: Variable duration observation times. The RMS states that interpretation of the study is difficult because no observations were made in the 1-day treatment at 1 day post exposure and thus there was essentially a 2-day recovery period. While FMC understands this concern, the study was designed such that time was allowed for the plant to respond to the exposure. Previous experience has shown that	RMS UK: We acknowledge the reference to potential delayed effects of the active. However, the point highlighted by the RMS is that the period of time following exposure varies between the two tests on each measurement day which may have impacted results. This is shown in the table below: **Measurement** | **Days after exposure**	Addressed

Acquatic organism

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
		with exposure to thifensulfuron-methyl (or any other sulfonyl urea herbicide) *Myriophyllum* responds somewhat slowly to the exposure, such that any measurements made at 1-day post exposure are meaningless. There is simply not enough time to see a meaningful change in plant growth after 24 hours of exposure compared to the controls. The MOA of thifensulfuron methyl does not result in acute observations of toxicity, thus the effects of exposure manifest more slowly in aquatic plants. This necessitates a measurement of the 1-day exposure group at 3-days post exposure. It was not intended as a recovery period. Had there been a true recovery, the 1-day exposure group would have had significantly better growth at the 3-day observation than the 3-day exposure group. This was not the case, and FMC believes that the 3-day observation time is appropriate given the test material and the growth characteristics of	<table><tr><th>(day)</th><th>Test 1</th><th>Test 2</th></tr><tr><td>3</td><td>2</td><td>0</td></tr><tr><td>7</td><td>6</td><td>4</td></tr><tr><td>14</td><td>13</td><td>11</td></tr></table> The point made by the RMS is that there is uncertainty when comparing the above measurements given the variable durations after exposure. In addition whilst it is unclear whether recovery occurs during the study it is noted that there is lower inhibition for some parameters at day 14 than day 7 e.g. growth rate shoot length; statistically significant at day 7 but not 14. **Addressed**	

Acquatic organism				
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**
		myriophyllum. The point of the study is that regardless of the product of exposure duration and concentration, the 7-day and 14-day observation of growth reduction as a result of exposure to thifensulfuron methyl is the same, which has demonstrated.		
5(17)	Vol. 3, B.9, Higher tier RA for aquatic organisms Kirckwood (2015b)	DE: We agree with the RMS, this study can be used as supporting information of potential linear reciprocity for *Myriophyllum spicatum*.	RMS UK: Noted. **Addressed**	Noted
5(18)	Vol. 3, B.9, Higher tier RA for aquatic organisms, Geometric mean	DE: The Geometric mean approach for the parameter "dry weight" is not scientifically justified as it is based on unbound values. We would suggest to remove these values. The RMS presented a "weight of evidence justification" demonstrating that the geometric mean approach for all groups (mono- and dicots) is applicable. This is justified by the factor of 2.5 between the most sensitive E_rC_{50} values. Therefore, the overall geomean = 0.53 µg/L should be	RMS UK: We acknowledge the concern raised regarding the inclusion of unbound values for the geometric mean based on "dry weight" but consider the endpoint derived should be conservative and result in < 50 % effects. As only unbound values for this parameter were available they were included to consider potential effects on dry weight and to ensure any endpoint used in the risk assessment was protective. In addition, the geometric mean	Peer Review proposed The use of the geometric mean as tier 2 approach in the risk assessment for aquatic plants is proposed to be discussed in an experts' meeting. Please note that there are divergent views of some Member States regarding the use of this approach as proposed in the RAR by the RMS.

Acquatic organism				
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**
		used for the higher tier risk assessment. The geometric mean = 0.5 µg/L is not in line with the decision of comparability presented in the RAR.	based on dry weight was not used in the risk assessment hence the outcome of the risk assessment is not impacted. The RMS has added a section to the RAR regarding these concerns. In relation to geometric mean used in the risk assessment the RMS considered the endpoint based on monocots appropriate for use. We note the point regarding the factor between the most sensitive endpoints. However, where comparisons are possible between parameters (limited data set) it appears that monocots are more sensitive. The difference between the shoot height endpoints suggests monocots are more sensitive by a factor of 4.8. Therefore, to account for potential differences between mono and dicots the RMS has taken a conservative approach using the lowest geometric mean endpoint. **Addressed**	

Acquatic organism				
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, Higher tier RA for aquatic organisms, Geometric mean	DE: We have a general comment regarding the most sensitive variable and the MoA of the a.s. thifensulfuron-methyl. As the parameter "wet weight" has not been analysed for Lemna and Vallisneria, the calculated geomean might not be protective.	RMS UK: We acknowledge the points raised regarding wet weight being the most sensitive parameter for sulfonylurea herbicides. However, it appears this observation is for sulfonylurea herbicides in general rather than thifensulfuron methyl specifically i.e. this is not adverse data and just indicative. Furthermore, it should be noted that the standard *Lemna* study met the guideline criteria (OECD 221) i.e. frond counts, and one other parameter measured. Where wet weight was measured the proposed geometric mean endpoint is protective, noting this parameter was only measured for dicots (that appear to be less sensitive based on available data). Ideally more parameters would have been measured. However, the RMS considers there are enough studies and parameters to justify a geometric mean approach and the proposed endpoint is	See 5(18)

Acquatic organism				
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**
			protective, noting assessment factors have also been used in the tier 2 risk assessment. Finally, the RMS notes that if a geometric mean is not accepted, the lower tier endpoint (previously accepted) is also not based on wet weight, therefore the same concerns would still apply. **Addressed**	
5(20)	B.9 geomean	NL agrees with differentiating between monocotyledons and dicotyledons. NL is of opinion that the preconditions required to apply the chronic geometric mean are not fullfilled: 1) According to the AGD (EFSA 2013) primary producers belong to chronic toxicity data and therefore only comparable endpoints should be used within the same taxonomic group. Separate geomeans for each variable should be calculated. This is not fulfilled. 2) For using the geomean approach, the endpoints	RMS UK: Noted, please also refer to points raised in response to comment 5(19). **Addressed**	See 5(18)

Acquatic organism				
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**
		should be derived by highly comparable tests (including duration of the tests and how these tests cover the life cycle of the tested species). This is not fulfilled. The RMS argues that duration differs depending on the species. NL agrees. The *Myriophyllum* study was based on a draft guidance with a test duration of 21 days (instead of 14 days) which affects the study. This can be considered worst case. It also concerned a sediment study. NL agrees with the argumentation of UK regarding geometirc mean mesuread concentrations and therefore, the studies can be considered comparable.		
5(21)	Risk assessment for aquatic organisms	EFSA: the assessment of the RMS is agreed. For summarizing, only the geomean approach was considered a suitable effect refinement which was used in combination with Focus Step 4. The confirmatory data address the concern on the metabolite IN-D8858.	RMS UK: Noted. **Addressed**	See 5(18)

Acquatic organism				
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(22)	Vol. 3, B.9, Higher tier RA for aquatic organisms Pec twa approach	DE: We fully agree with the RMS to not apply the PECtwa since its potential applicability was not demonstrated for all species tested (i.e., result not clear for Vallisneria sp., right?).	RMS UK: Based on the decision scheme in EFSA 2013 AG use of $PEC_{sw;twa}$ is not considered to be appropriate by RMS based on the reasons discussed from p547 onwards. The RMS notes the additional argumentation provided by DE further detailing why a $PEC_{sw;twa}$ is not appropriate for thifensulfuron-methyl. **Addressed**	Addressed
5(23)	B.9 PECtwa	NL agrees with the RMS, a7 day PECtwa cannot be used: 1) reciprocity cannot be addressed. 2) latency cannot be addressed. 3) the most sensitive species was not addressed.	RMS UK: Noted. **Addressed**	Noted
5(24)	Vol. 3, B.9, Higher tier RA for aquatic organisms Dormancy	DE: A "dormancy study" has been conducted for *Lemna gibba*, only. It is not clear, if the observed effects on *Lemna sp.* could be transferred to other species, especially the much slower growing and most sensitive species *Vallisneria sp.*. Therefore, the dormancy study	RMS UK: Noted and we agree. **Addressed**	Addressed

Acquatic organism				
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**
		should not be used in the higher tier risk assessment – as stated by the RMS, already.		
5(25)	Vol. 9 B.9.2.2 Representative Formulations p.155	FMC: RMS Comments to Study Typing error – written as 92 hours, should be 96 hours	RMS UK: We agree and RAR has been amended. **Addressed**	Addressed
5(26)	EC10/EC20 for chronic studies on fish and invertebrates	EFSA: according to Regulation 283/2013 EC10/EC20 should be estimated and provided together with the NOEC. When those cannot be calculated, a justification should be provided.	RMS UK: Chronic fish study **HLR 321-91, 1991**: The maximum effects in this study were 10 % and there was no dose response, therefore the RMS considers that it is not possible to derive robust $EC_{10}/_{20}$ values. In addition, based on the fact that the analytical method could not be validated this study has been removed from the LoEP. Chronic fish study **DuPont -28722, 2010**: The NOEC was the highest concentration tested and there were less than 10 % effects compared to control at all treatment rates. Therefore, the RMS considers that it is not	The reply from the RMS is acknowledged. No further data can be accepted at this stage.

Acquatic organism				
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**
			possible to derive robust $EC_{10/20}$ values. Chronic *Daphnia* study **Samel, 2000** metabolite IN-L9223 (TF): It appears $EC_{10/20}$ values can be calculated. Chronic *Daphnia* study **Vinken & Wydra, 2007a** metabolite IN-L9223 (TF): It appears $EC_{10/20}$ values can be calculated. Chronic *Daphnia* study **Hoke, 2001** metabolite IN-V7160 (DuPont): 17 % reduction in reproduction compared to control at highest concentration. All other treatment rates < 10 % effects. Therefore, potentially an EC_{10} value could be calculated. Chronic *Daphnia* study **Vinken & Wydra, 2007b** metabolite IN-V7160/TA-U (TF): 13 % reduction in reproduction compared to control at highest concentration. All other treatment rates < 10 % effects. Therefore, potentially an EC_{10} value could be calculated. Chronic *Daphnia* study **Samel, 1999**	

Acquatic organism				
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**
			metabolite IN-A4098 (DuPont): NOEC is highest test concentration and there are < 10 % reproductive effects compared to control at all treatment rates. Therefore, the RMS considers that it is not possible to derive robust $EC_{10/20}$ values. Chronic *Daphnia* study **Samel, 1999** metabolite IN-A4098 (TF): 15.1 % reduction in reproduction compared to control at highest concentration. All other treatment rates < 10 % effects. Therefore, potentially an EC_{10} value could be calculated. Overall the RMS considers $EC_{10/20}$ values can only be calculated for metabolite *Daphnia* studies; IN-L9223 (**Samel, 2000, Vinken & Wydra, 2007a**). EC_{10} values may be possible for IN-V7160 & IN-V7160/TA-U (**Hoke, 2001 & Vinken & Wydra, 2007b**), IN-A4098 (**Samel, 1999**).	

Acquatic organism				
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**
			Open point (EFSA to consider above and decide whether further data is required)	
5(27)	Vol. 3, B.9.2.5.7.1, Overall conclusion for aquatic plants	DK: the RMS writes: "RMS considers the conclusions reached at step 4 in table B.9.2.5.7.1-31 are valid." Shouldn't it be table B.9.2.5.7.1-32 (typo)?	RMS UK: RAR has been amended. **Addressed**	Addressed
5(28)	Vol. 3, B.9.2.5.7.1, Overall conclusion for aquatic plants	DK: maybe in the "overall conclusion for aquatic plants" the RMS's statement could be clarified by adding that the additional refinements proposed by the applicant (i.e. use of 7days PECsw, twa and dormancy endpoints) are not accepted (hence reference is made to table B.9.2.5.7.1-32)?	RMS UK: Further clarification has been added to the dossier. **Addressed**	Addressed
5(29)	Vol. 9 B.9.2.5 p.547	FMC: RMS latency of effects conclusion. FMC does not agree with the determination that latency of effects or delayed effects are potentially occurring in studies exposing thifensulfuron methyl to aquatic plants.	RMS UK: The RMS has stated that delayed or latency of effects are potentially occurring. It is unclear to the RMS the reason for stating that the test design was responsible for the potential delayed effects but at the same	Addressed

Acquatic organism				
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**
		While the mode of action is considered "slow," this observation is a product of the response of the plant and the inherent variability in growth during the study. Exposure to sulfonyl urea herbicides reduces the plant's ability to synthesize amino acids, thus reducing the ability of the plant to grow. During the standard tests for *Lemna* and *Myriophyllum*, the control organisms are growing unabated in the test, and regardless of exposure duration, the exposed plants experience a reduction in the ability to grow. However, due to the test designs, this cannot be observed immediately (unlike insecticides or other herbicides with an immediate effect). It takes a period of 3-5 days before a significant reduction in growth, compared to the controls, can be observed. This is not a latent effect, but a product of the test design and the intrinsic ability to statistically detect a difference from the growth of the control.	time stating it is suitable for other herbicides that have an immediate effect. This seems to suggest that for thifensulfuron methyl effects are potentially delayed, noting points about "slow" mode of action. Regardless the wider point is whether TWA is appropriate, and the RMS does not consider there is sufficient information to demonstrate that Haber's law applies for thifensulfuron methyl. **Addressed**	
5(30)	Vol. 9 B.9.2.5 p.547	Table B9.2.5.7.1-44 It is the position of FMC that none of	RMS UK: We disagree and consider there is some evidence for potential delayed effects. Most	Addressed

Acquatic organism				
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 provided studies demonstrated evidence of delayed effect. As noted in the previous comment 5(29), the observed effect is a product of growth compared with an unaffected control. Regardless of the duration of the exposure, the effect of the exposure was observable through to the end of the test. This is not latency or delayed effects, rather an effect manifesting through comparison to the control that occurred only during the exposure. Additionally, recovery would not be observed, or recovery would stop if a latent effect was occurring. The recovery data presented for *Lemna* in Kannuck and Samel (1995) indicates that the plants do recover from exposure, and thus a latent effect is not occurring after the termination of the exposure. The plants in Kannuck and Samel (1995) return to the exponential	studies seem to suggest effects occur around 7 to 14 days after exposure. The recovery study (Kannuck and Samel (1995)) was not considered valid for use in the risk assessment due to issues with the analytical method. Nonetheless it should be noted this was a 14-day exposure study followed by 14 days in clean media (recovery part). It was a static test design with single exposure at start of study. The frond number increased by a factor of 9.6 over the first 7 days in control and observations were only made at the end of the recovery period. This would mean effects would have to still occur a total of 28 days after exposure and be sufficient to inhibit the growth of new fronds. It should also be noted that 'recovery' only occurred in the two lowest test concentrations during this study. Essentially the RMS does not	

Acquatic organism				
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**
		growth phase after 7 days, thus eliminating the possibility of a latent effect.	consider this study sufficient to determine that a latent effect is not occurring. **Addressed**	
5(31)	Vol. 9 B.9.2.5 p. 549	Point 8 Based on the comment above (5(30)) this clearly should be a YES and move on to Step 5.	RMS UK: We do not agree, see response to 5(30). **Addressed**	Addressed
5(32)	Vol. 9 B.9.2.5 p. 555	FMC: RMS conclusion on the use of a PECsw 7-day TWA in the aquatic risk assessment. It is the position of FMC that reciprocity has been demonstrated. It is not possible to observe an effect in the reciprocity study at 1 day due to the lack of growth in both the controls and the treatment systems after only one day of exposure. The study design is valid and represents the most logical sampling points for the assessment of reciprocity (see	RMS UK: We do not agree. See response to 5(16, 29, 30). Noting comment number 3 quoted by applicant is number 5(16) in the consolidated reporting table. For the reasons stated in the RAR (p496-497) we consider it appropriate to consider the *Vallisneria* endpoint. **Addressed**	Addressed

Acquatic organism				
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**
		above (No. (3)) for further explanation). FMC continues to assert that the *Vallisneria* study is not valid for the same reasons that the *Ceratophyllum* and Elodea studies are not valid. The continued use of these studies in the presence of valid *Myriophyllum* and *Lemna* studies is not a scientifically sound approach. Latency is clearly not an issue in these studies, and the perception that there is a delayed effect present in any of the aquatic plants studies, is simply the effect not being observed until a later timepoint because of difficulty in statistically identifying a change in growth at earlier time points. It is a product of the study design, not a latent effect. FMC believes that it has satisfied the requirements in the guidance document		

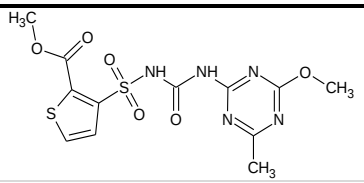
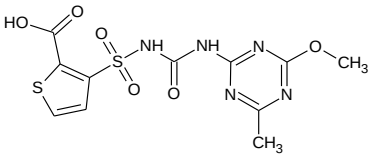
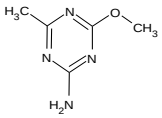
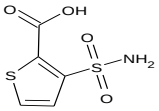
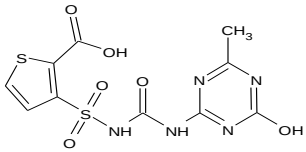
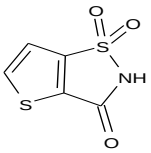
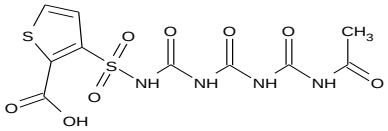
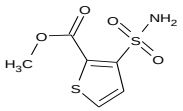
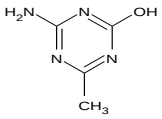
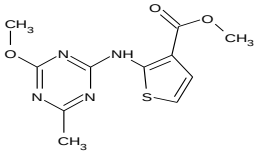
Acquatic organism				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		for the application of the PECSW,TWA and that this refinement should be applied to the risk assessment.		
5(33)	Vol 1, page 119	FMC: The Data gap listed under 3.1.4.9, "DuPont and Task Force: Furher information to confirm the identity of the aqueous photolysis metabolite currently identified as either thiophenyl triezinyl amine (Task Force) or IN-D8856 (DuPont) before any further ecotoxicological information is required" as "No confirmation that study available or ongoing" is not correct. This request was related to Reporting Table, 21 Nov 2014, point 4(86) and 4 (87). Information was indeed provided (DuPont- 41912) by applicant and assessed. According to the Peer Review Report, July 2015, 05-Comments on the additional information assessment, on page 18 it is stated "EFSA: the new information has been considered acceptable". Please also note that the correct code for this	RMS UK: We agree and volume 1 has been updated. **Addressed**	Addressed

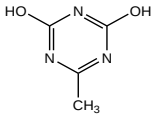
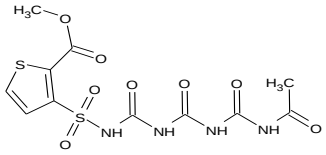
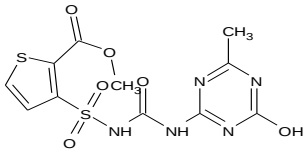
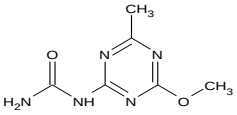
Acquatic organism				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		metabolite is IN-D8858. The risk to aquatic organism for IN-D8858 was part of the confirmatory data submission and have been assessed and the RAR has been updated with this information. Hence this is no longer a data gap.		

Earthworms and other non-target soil macro- and mesofauna				
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(34)	Risk assessment for soil organisms	EFSA: it is considered that the available confirmatory data address the concern highlighted in the EFSA conclusion for the2 soil pertinent metabolites IN-JZ789 and 2 acid 3 triuret.	RMS UK: Noted. **Addressed**	Addressed The available confirmatory data address the concerns highlighted in the EFSA conclusion regarding the 2 soil pertinent metabolites IN-JZ789 and 2 acid 3 triuret

Other comments incl. available monitoring data				
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(35)	Vol. 3, B.9	DE: Would it be possible to include a table of contents in the document and format the headlines? It would be much easier to navigate in the document.	RMS UK: The RAR was presented in an old format (used for AIR 2 renewals) that was acceptable previously. Therefore, it has not been updated. **Addressed**	Addressed
5(36)	General comment	EFSA: it is unclear why the study by HLR 321-91 (1991) is reported twice in the revised RAR. In addition, it is also unclear why the chronic tests on fish are reported in 2 different places. Can the RAR be amended to have a more logical structure?	RMS UK: This is an error, HLR 321-91 (1991) was considered originally and the previous evaluation included in the RAR. However, the study was submitted again during confirmatory data. The RAR has been amended so the original evaluation can be seen followed by the updated version as part of confirmatory data. The structure regarding study summaries has also been changed so it is more logical. **Addressed**	Addressed

Appendix B – Used compound codes

Code/trivial name[a]	Chemical name/SMILES notation/InChiKey[b]	Structural formula[b]
thifensulfuron-methyl	methyl 3-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoylsulfamoyl)thiophene-2-carboxylate O=S(=O)(NC(=O)Nc1nc(C)nc(OC)n1)c1ccsc1C(=O)OC AHTPATJNIAFOLR-UHFFFAOYSA-N	
thifensulfuron	3-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoylsulfamoyl)thiophene-2-carboxylic acid OC(=O)c1sccc1S(=O)(=O)NC(=O)Nc1nc(C)nc(OC)n1 LOQQVLXUKHKNIA-UHFFFAOYSA-N	
IN-A4098	4-methoxy-6-methyl-1,3,5-triazin-2-amine Cc1nc(N)nc(OC)n1 NXFQWRWXEYTOTK-UHFFFAOYSA-N	
IN-L9223	3-sulfamoyl-2-thiophenecarboxylic acid OC(=O)c1sccc1S(=O)(N)=O NRAVSUNXRBRPRE-UHFFFAOYSA-N	
IN-JZ789	3-{[(4-hydroxy-6-methyl-1,3,5-triazin-2-yl)carbamoyl]sulfamoyl}thiophene-2-carboxylic acid OC(=O)c1sccc1S(=O)(=O)NC(=O)Nc1nc(C)nc(O)n1 UMLCJPSDEOEISZ-UHFFFAOYSA-N	
IN-W8268	thieno[2,3-*d*][1,2]thiazol-3(2*H*)-one 1,1-dioxide O=S1(=O)NC(=O)c2sccc21 XVCRMQNYJBQTPD-UHFFFAOYSA-N	
2-acid-3-triuret	3-({[(acetylcarbamoyl)carbamoyl]carbamoyl}sulfamoyl)-2-thiophenecarboxylic acid OC(=O)c1sccc1S(=O)(=O)NC(=O)NC(=O)NC(=O)NC(C)=O XMFZBVHLTGXKFD-UHFFFAOYSA-N	
IN-A5546	methyl 3-sulfamoyl-2-thiophenecarboxylate O=S(N)(=O)c1ccsc1C(=O)OC PMXNPOJHBQDJKS-UHFFFAOYSA-N	
IN-B5528	4-amino-6-methyl-1,3,5-triazin-2-ol Nc1nc(C)nc(O)n1 UUTHDVPZNWJUFV-UHFFFAOYSA-N	
IN-D8858 (IN-D8856)	methyl 2-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]-3-thiophenecarboxylate COC(=O)c1ccsc1Nc1nc(C)nc(OC)n1 ITUORYVYTKYTRM-UHFFFAOYSA-N	

IN-F5475	6-methyl-1,3,5-triazine-2,4-diol Oc1nc(C)nc(O)n1 KZVYWMJOLANZSI-UHFFFAOYSA-N	
IN-RDF00	methyl 3-({[(acetylcarbamoyl)carbamoyl]carbamoyl}sulfamoyl)-2-thiophenecarboxylate O=S(=O)(NC(=O)NC(=O)NC(=O)NC(C)=O)c1ccsc1C(=O)OC OHNOIMQIGGUKIP-UHFFFAOYSA-N	
IN-L9226	methyl 3-{[(4-hydroxy-6-methyl-1,3,5-triazin-2-yl)carbamoyl]sulfamoyl}thiophene-2-carboxylate O=S(=O)(NC(=O)Nc1nc(C)nc(O)n1)c1ccsc1C(=O)OC GKVBQTUDNBQJLK-UHFFFAOYSA-N	
IN-V7160	1-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea Cc1nc(NC(N)=O)nc(OC)n1 NEVDMPLXCGERDI-UHFFFAOYSA-N	

(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2018.2.2 ACD/Labs 2018 Release (File version N50E41, Build 103230, 21 Jul 2018)
(c): ACD/ChemSketch 2018.2.2 ACD/Labs 2018 Release (File version C60H41, Build 106041, 07 Dec 2018)

Appendix C – List of endpoints

The updated List of endpoints is available as part of United Kingdom, 2018, published as background document to this technical reports.