FINAL REGISTRATION REPORT

Part B

Section 9

Ecotoxicology

Detailed summary of the risk assessment

Product code: JME-HER 12 OD

Product name(s): -

Chemical active substance:

iodosulfuron-methyl-sodium, 2 g/L

mesosulfuron methyl, 10 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Pestila Sp. z o.o.

Submission date: December 2023, revision: April 2024

MS Finalisation date: 03/10/2024

Version history

When	What
January 2024	Dossier sent for evaluation
April 2024	Update of dRR on evaluator's request
July 2024	zRMS finalised evaluation
October 2024	Final version prepared by zRMS after Commenting period

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9 Ecotoxicology (KCP 10)

This document has been prepared by copying the risk assessments and summary of studies included in the Atlantis 12 OD renewal Registration Report (zRMS: Poland, MS finalisation: 12/02019). The information and studies used in this document are not protected in accordance with Art. 59 Reg. 1107/2009 and can be used for purpose of JME-HER 12 OD registration.

*The ecotoxicological properties of the **active substance iodosulfuron-methyl-sodium** have been evaluated on EU level according to the Commission Regulation (EU) N° 1107/2009, full details are provided in the EU renewal assessment report and related documents and are summarised in the EFSA conclusion (EFSA Journal 2016;14(4):4453).*

*The ecotoxicological properties of the **active substance mesosulfuron-methyl** have been evaluated on EU level according to the Commission Regulation (EU) N° 1107/2009, full details are provided in the EU renewal assessment report and related documents and are summarised in the EFSA conclusion (EFSA Journal 2016;14(10): 4584).*

Based on the Core assessment of Atlantis 12 OD since the same approach is taken in this dRR following information has been supplemented:
*The ecotoxicological properties of the **safener mefenpyr-diethyl** have been reviewed in a work-sharing project of European competent authorities, in analogy to the procedures foreseen for active substances in Directive 91/414/EEC: France and Austria prepared an assessment report for this substance in the format of a Draft Assessment Report which was "peer-reviewed" (in an unscheduled procedure on voluntary basis) by all Member States in September 2011. The revised assessment report can be found on CIRCA (Archive individual substances – Mefenpyr-diethyl (safener)).*

Following recommendation by the central zone Steering Committee (czSC) as well as by the RMS of mesosulfuron-methyl, France, exposure and risk assessments for the application of mefenpyr-diethyl with the present formulation are not presented in the core assessment.

Review Comments:

This application was submitted by Pestila Sp. z o. o. for approval of the formulation JME-HER 12 OD

an oil dispersion, containing active substances: iodosulfuron-methyl-sodium 2g/L and mesosulfuron-methyl 10 g/L. For use as a herbicide on: cereals (winter wheat, winter triticale and rye).

This is the application for registration according to Article 33 of Regulation 1107/2009 based on data for which a 10-year protection period has expired (acc. Art. 34 of Reg. 1107/2009).

The risk assessment of JME-HER 12 OD reference to Core Assessment for the already registered product

Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

From ecotoxicological point of view JME-HER 12 OD is considered equivalent/comparable to already registered Atlantis 12 OD, therefore the unprotected ecotoxicological studies performed for Atlantis 12 OD can be used for risk assessment purposes of JME-HER 12 OD.

Already evaluated studies during authorisation of Atlantis 12 OD were not re-evaluated. For details please refere to Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).

Since this document is based on the information provided by the Applicant, all review comments, additions, and corrections have been made using commenting boxes or highlighted in grey. Any incorrect data or text not evaluated by the zRMS has been crossed out.

9.1 Critical GAP and overall conclusions

Table 9.1-1: Table of critical GAPs

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Use-No. *	**Member state(s)**	**Crop and/or situation (crop destination / purpose of crop)**	**F, Fn, Fpn G, Gn, Gpn or I ****	**Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)**	**Application**				**Application rate**			**PHI (days)**	**Remarks: e.g. g safener/ synergist per ha**	**Conclusion**						
					Method / Kind	**Timing / Growth stage of crop & season**	**Max. number a) per use b) per crop/ season**	**Min. interval between applications (days)**	**kg or L product/ha a) max. rate per appl. b) max. total rate per crop/season**	**g or kg as/ha a) max. rate per appl. b) max. total rate per crop/season**	**Water L/ha min/max**			**Birds**	**Mammals**	**Aquatic organisms**	**Bees**	**Non-target arthro-**	**Soil organisms**	**Non-target plants**
Zonal uses (field or outdoor uses, certain types of protected crops)																				
1	PL	Winter wheat	F	Please refer to Part A	Spray/ broadcast	BBCH 21 - BBCH 31	a) 1 b) 1	-	a) 1.2 l/ha b) 1.2 l/ha	a) 2.4 - iodosulfuron 12 - mesosulfuron b) same as a)	200-300	-	-							
2	PL	Winter triticale	F	Please refer to Part A	Spray/ broadcast	BBCH 21 - BBCH 31	a) 1 b) 1	-	a) 1.2 l/ha b) 1.2 l/ha	a) 2.4 - iodosulfuron 12 - mesosulfuron b) same as a)	200-300	-	-							
3	PL	Winter wheat	F	Please refer to Part A	Spray/ broadcast	BBCH 21 - BBCH 31	a) 1 b) 1	-	a) 0.45 L/ha b) 0.45 L/ha	a) 0.9 - iodosulfuron 4.5 - mesosulfuron b) same as a)	200-300	-	-							
4	PL	Winter triticale	F	Please refer to Part A	Spray/ broadcast	BBCH 21 - BBCH 31	a) 1 b) 1	-	a) 0.45 L/ha b) 0.45 L/ha	a) 0.9 - iodosulfuron 4.5 - mesosulfuron b) same as a)	200-300	-	-							
5	PL	Rye	F	Please refer to Part A	Spray/ broadcast	BBCH 21 - BBCH 31	a) 1 b) 1	-	a) 0.45 L/ha b) 0.45 L/ha	a) 0.9 - iodosulfuron 4.5 - mesosulfuron b) same as a)	200-300	-	-							

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

Explanation for column 15 – 21 “Conclusion”

A	Acceptable, Safe use
R	Further refinement and/or risk mitigation measures required
C	To be confirmed by cMS
N	No safe use

Remarks table:

(1) Numeration necessary to allow references
(2) Use official codes/nomenclatures of EU
(3) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
(4) F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application
(5) Scientific names and EPPO-Codes of target pests/diseases/ weeds or when relevant the common names of the pest groups (e.g. biting and sucking insects, soil born insects, foliar fungi, weeds) and the developmental stages of the pests and pest groups at the moment of application must be named
(6) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(7) Growth stage at first and last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(8) The maximum number of application possible under practical conditions of use must be provided
(9) Minimum interval (in days) between applications of the same product.
(10) For specific uses other specifications might be possible, e.g.: g/m³ in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products
(11) The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha).
(12) If water volume range depends on application equipments (e.g. ULVA or LVA) it should be mentioned under “application: method/kind”.
(13) PHI - minimum pre-harvest interval
(14) Remarks may include: Extent of use/economic importance/restrictions

Review Comments:

GAP presented in the Table 9.1-1 of this document is revised with consideration of the outcome of the evaluation performed in area of ecotoxicology.

9.1.1 Overall conclusions

9.1.1.1 Effects on birds (KCP 10.1.1), Effects on terrestrial vertebrates other than birds (KCP 10.1.2), Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)

~~**Birds**~~

~~Not relevant. See point 9.2.1.~~

~~**Terrestrial vertebrates (other than birds)**~~

~~Not relevant. See point 9.3.1.~~

The risk assessment for birds and mammals was carried out according to the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438).

The risk assessments for birds and mammals meet the trigger criteria at screening level, for all intended uses of product IMS+MSM+MPR OD 42 (2+10+30). No unacceptable risk resulted also from the assessment of exposure via drinking water, and for secondary poisoning via prey like fish and earthworms. The above assessments do not raise specific concern for other terrestrial vertebrate wildlife such as reptiles and amphibians.

No measures for exposure mitigation need to be taken into account for the protection of birds, mammals, and other terrestrial vertebrate wildlife.

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the TER values exceed the trigger values of 10 for acute and 5 for reproductive/long-term risk. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to birds and mammals. No risk mitigations are required.

9.1.1.2 Effects on aquatic organisms (KCP 10.2)

~~Not relevant. See point 9.5.1.~~

Acceptable risk for all aquatic organisms other than macrophytes could be demonstrated in a screening-level risk assessment (FOCUS Steps 1-2) for the active substances contained in product IMS+MSM+MPR OD 42 (2+10+30), and their metabolites.

Overall conclusion of risk migiatation measures using max PECsw STEP 4 calculations based on active substance - mesosulfuron methyl risk assessment.

Winter cereals, end of winter-spring use, 15 g a.s./ha

The R3 stream scenario is resolved when considering a 20 meter high buffer zone; the R4 scenario is resolved when considering a 10 meter low buffer zone.
As this refinement is Member State-specific, Member States should decide if this is acceptable according to their own national rules on mitigation.
Furthermore, as the D scenarios are driven by drainage there is no mitigation by FOCUS Step 4 and member states should consider the relevance of these scenarios to their national conditions.

ZRMS overall conclusion with consideration the combined risk assessment for both the active substances and metabolite AE F075736, based on max PEC_{sw} values.

use group B

(end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM):

The product can be safely applied with no precautionary measures required for exposure mitigation in all European regions other than those represented by drainage scenarios D1 and D2. In a Central Zone context, however, both of these scenarios are considered not representative.
In case of ~~R3, R4~~, R1 (stream) and D3 (ditch) scenarios the product can be safely when:

~~- For R3 and R4 scenarios 20 meter high vegetative buffer zone will be applied~~
- For R1 (stream) and D3 (ditch) 10 meter low vegetative buffer zone zone will be applied

9.1.1.3 Effects on bees (KCP 10.3.1)

~~Not relevant. See point 9.6.1.~~

The evaluation of the risk for bees has been performed in line with SANCO/10329/2002 rev 2 final.

The risk to bees was demonstrated to be acceptable for all intended uses of product IMS+MSM+MPR OD 42 (2+10+30), based on assessments for the active substances, and the formulated product.

No measures for exposure mitigation need to be taken into account for the protection of bees.

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the HQ values were below the relevant trigger values. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to bees and bumblebees. No risk mitigations are required.

9.1.1.4 Effects on arthropods other than bees (KCP 10.3.2)

~~Not relevant. See point 9.7.1.~~

The evaluation of the risk for non-target arthropods was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002), and in consideration of the recommendations of the guidance document ESCORT 2.

The risk to arthropods other than bees is acceptable for all intended uses of product IMS+MSM+MPR OD 42 (2+10+30), based on the presented assessments for the in-field and the off-field exposure situations.

No measures for exposure mitigation need to be taken into account for the protection of arthropods other than bees.

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the HQ values were below the relevant trigger value of 2. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to arthropods. No

risk mitigations are required.

9.1.1.5 Effects on non-target soil meso- and macrofauna (KCP 10.4), Effects on soil microbial activity (KCP 10.5)

~~**Macro-organisms**~~

~~Not relevant. See point 9.8.1.~~

~~**Micro-organisms**~~

~~Not relevant. See point 9.9.1.~~

No unacceptable risk to the soil meso- and macrofauna and to the soil microbial activity is concluded from the risk assessments presented, for all intended uses of the product IMS+MSM+MPR OD 42 (2+10+30).

No measures for exposure mitigation need to be taken into account for the protection of soil organisms.

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. According to the performed risk assessment it was concluded that the application of JME-HER 12 OD in accordance with GAP does not pose unacceptable risk to soil macro and micro-organisms. No risk mitigations are required.

9.1.1.6 Effects on non-target terrestrial plants (KCP 10.6)

~~Not relevant. See point 9.10.1.~~

Based on the probabilistic risk assessment it is concluded that the use of the product will not produce unacceptable effects on terrestrial non-target plants growing near treated fields, when considering the following mitigation measures:

- a 5 m buffer zone, or alternatively 75% drift reducing spray nozzles for application rate 1.2 L prod/ha (use group F)
- no mitigation measures are needed for application rate 1 x 0.45 L product/ha (use group K).

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the TER values exceeded the relevant trigger value of 5 or 1. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to non-target plants provided above mentioned risk mitigations measures are applied.

9.1.1.7 Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)

Not relevant.

9.1.2 Grouping of intended uses for risk assessment

~~Not relevant. No new risk assessments submitted.~~

The following table documents the grouping of the intended uses to support application of the risk envelope approach (according to SANCO/11244/2011).

Table 9.1-2: Critical use pattern of JME-HER 12 OD / Atlantis 10 OD / IMS+MSM+MPR OD 42 (2+10+30)

Grouping according to use rate				
Group	***Intended uses***	***relevant use parameters for grouping***	***relevant parameter or value for sorting***	***relevant for risk assessment areas***
A	*Generic risk envelope covering all product uses of active substances IMS and MSM in Europe, see explanation below #)*	*Application rates: 10 g IMS/ha 15 g MSM/ha BBCH <20 [no crop interception], year-round use.*	*Maximum application rate per a.s. (covering all products and uses in Europe)*	*Active substance based screening or Tier 1 level risk assessments for Birds / Mammals / Aquatic Organisms / Bees / Soil organisms.*
B	*winter cereals, end of winter-spring use [e.g. use no. 5]*	*Application rate: 1.5 L/ha, BBCH <20 [no crop interception]*	*Worst case use rate and BBCH for end winter-spring use on crop type winter cereals.*	*Active substance based assessments for aquatic macrophytes*
E	*Cereals* Covered uses: 1, 2, 3, 4, 5	*Application rate: 1.5 L/ha*	*Maximum application rate of product.*	*Formulation-based risk assessments for all areas*
F	*Cereals* Covered uses: 1, 2	*Application rate: 1.2 L/ha*	*Maximum application rate of product.*	*Non-target terrestrial plants §)*
K	*Cereals* Covered uses: 3, 4, 5	*Application rate: 0.45 L/ha*	*Maximum application rate of product.*	*Non-target terrestrial plants §)*

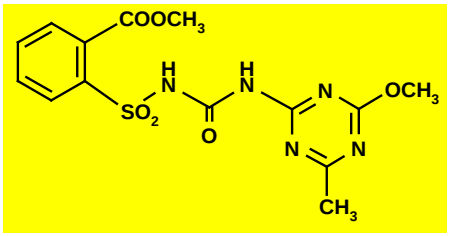
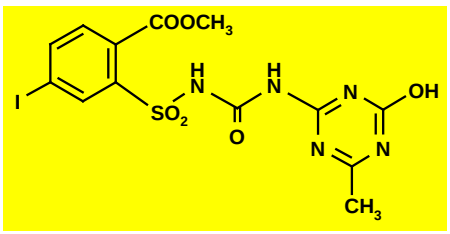
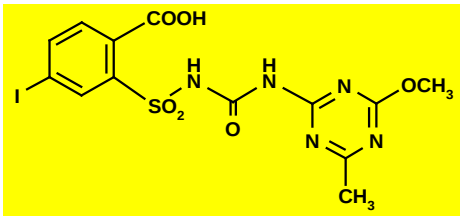
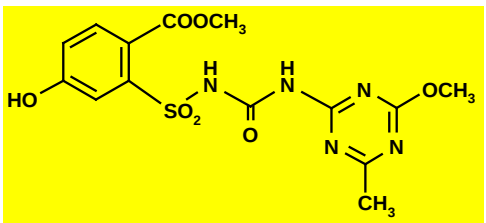
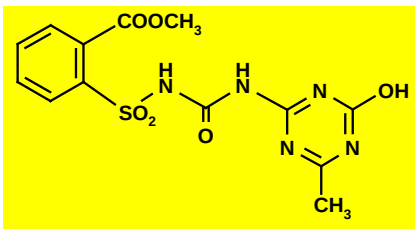
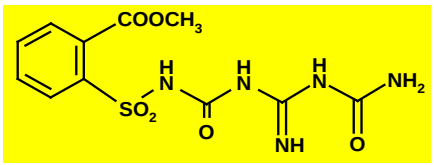
) In cases where the risk assessment is passed with a wide margin of safety already on screening or 1st tier level, exposure and risk characterisations for the active substances iodosulfuron-methyl-sodium and mesosulfuron-methyl are presented as a generic 'risk envelope' approach, which will cover all intended uses of these active substances across products marketed by Bayer in Europe. The European envelope rate considered for iodosulfuron-methyl-sodium is 10 g a.s./ha, for mesosulfuron-methyl is 15 g a.s./ha. Other crop or GAP dependent parameters relevant for the assessments are all set to the worst case (BBCH 00-39, 0 % crop interception, no tillage, application all year round). Even though for a particular product lower use rates or less critical application parameters may apply, this generic risk envelope provides a simple and efficient tool to conservatively cover many areas of the risk assessment.
§) to enable differentiated definition of mitigation setting adapted to the various intended product use rates.

9.1.3 Consideration of metabolites

~~Information concerning metabolites relevant for risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD.~~

A list of metabolites found in environmental compartments is provided below.

Table 9.1-3 Metabolites of iodosulfuron-methyl-sodium

Metabolite	Molar mass	Chemical structure	Maximum observed occurrence in compartments	Exposure assessment required due to
AE F075736	381.4		Soil: 88.5% (aerobic), 67.9% (anaerobic) Water: 57.0% Sediment: 15.9% Water/sediment: 67.8%	PEC_{soil} PECgw $PEC_{sw/sed}$
AE F145741	493.2		Soil: 6.9% (aerobic) Water: 7.0% Sediment: 1.9% Water/sediment: 8.7%	PEC_{soil} PECgw $PEC_{sw/sed}$
AE F145740	493.2		Soil: 8.7% (aerobic) Water: 9.2% Sediment: 3.5% Water/sediment: 12.6%	PEC_{soil} PECgw $PEC_{sw/sed}$
AE 0002166	397.4		Soil: 20.0% (photolysis) Water: 25.1% (photolysis in natural water)	PEC_{soil} PECgw $PEC_{sw/sed}$
AE F161778	367.3		Soil: 14.5% (aerobic) Water/sediment: 2.6%	PEC_{soil} PECgw $PEC_{sw/sed}$
BCS-CW81253	343.3		Soil: 35.1% (aerobic) Water/sediment: 0.0001%	PEC_{soil} PECgw $PEC_{sw/sed}$
AE 0000119	183.2		Soil: 19.9% (aerobic) Water: 17.7% Sediment: 15.0% Water/sediment: 24.9%	PEC_{soil} PECgw $PEC_{sw/sed}$

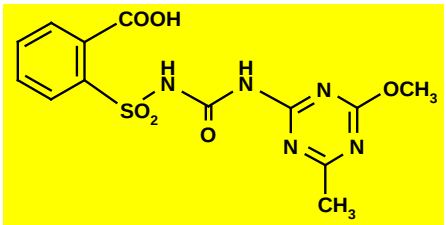
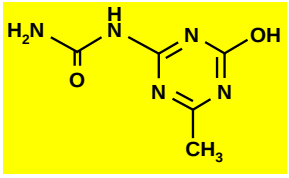
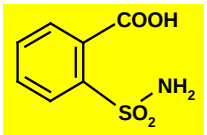
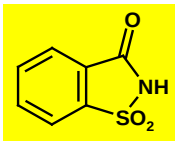
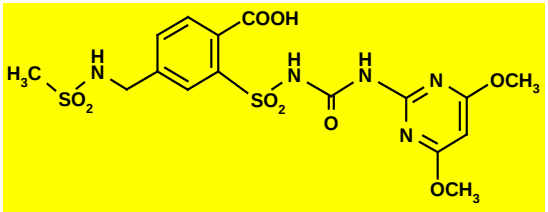
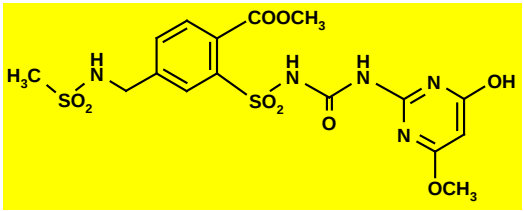
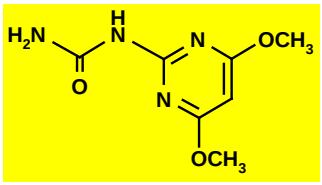
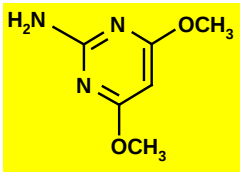
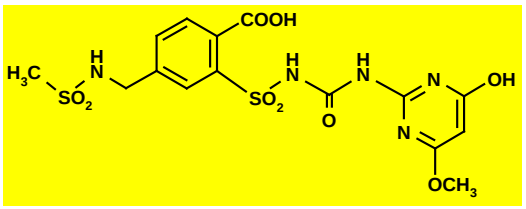
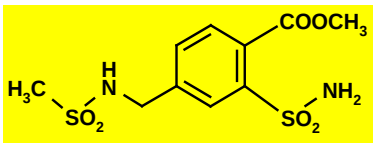
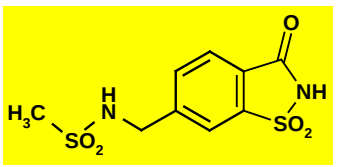
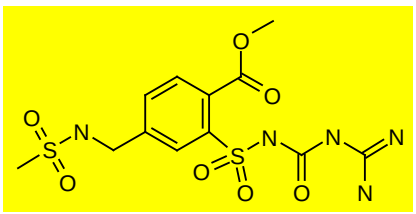
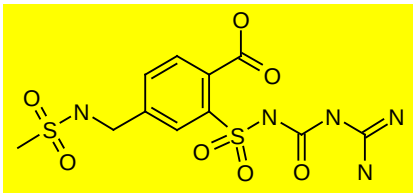
Metabolite	Molar mass	Chemical structure	Maximum observed occurrence in compartments	Exposure assessment required due to
AE F059411	140.2		Soil: 40.9% (aerobic), 23.6% (anaerobic) Water: 19.3% Sediment: 8.3 Water/sediment: 27.5%	PEC_{soil} PEC_{gw} $PEC_{sw/sed}$
AE 0014966	367.3		Water: 11.8% Sediment: 5.9% Water/sediment: 15.5%	$PEC_{sw/sed}$
AE 0034855	169.1		Water: 16.7% Sediment: 10.7% Water/sediment: 24.2%	$PEC_{sw/sed}$
AE 1234964	201.2		Water: 6.8% Sediment: 0.6% Water/sediment: 7.4%	$PEC_{sw/sed}$
AE F159737	183.2		Water: 6.1% Sediment: 1.6% Water/sediment: 7.8%	$PEC_{sw/sed}$
AE F154781	126.1		Water: 8.7% (aerobic mineralisation in surface water)	$PEC_{sw/sed}$

Table 9.1-4 Metabolites of mesosulfuron-methyl

Metabolite	Molar mass	Chemical structure	Maximum observed occurrence in compartments	Exposure assessment required due to
AE F154851 (mesosulfuron, mesosulfuron-acid)	489.5		Soil: 16.2% (aerobic) Water/sediment: 4.9%	PEC_{soil} PEC_{gw} $PEC_{sw/sed}$
AE F160459	489.5		Soil: 8.9% (aerobic), 25.9% (anaerobic) Water/sediment: 21.6%	PEC_{soil} PEC_{gw} $PEC_{sw/sed}$

Metabolite	Molar mass	Chemical structure	Maximum observed occurrence in compartments	Exposure assessment required due to
AE F099095	198.2		Soil: 29.2% (aerobic) Water/sediment: 0.9%	PEC_{soil} PEC_{gw} $PEC_{sw/sed}$
AE F092944	155.2		Soil: 10.1% (aerobic) Water/sediment: 3.2%	PEC_{soil} PEC_{gw} $PEC_{sw/sed}$
AE F160460	475.5		Soil: 8.6% (aerobic) Water/sediment: 8.4%	PEC_{soil} PEC_{gw} $PEC_{sw/sed}$
AE F140584	322.4		Soil: 5.1% (aerobic) Water/sediment: 1.9%	PEC_{soil} PEC_{gw} $PEC_{sw/sed}$
AE F147447	290.3		Soil: 5.8% (aerobic), 6.5% (anaerobic) Water/sediment: 10.9%	PEC_{soil} PEC_{gw} $PEC_{sw/sed}$
BCS-CO60720	407.4		Water/sediment: 13.1%	$PEC_{sw/sed}$
BCS-CV14885	393.4		Water/sediment: 22.0%	$PEC_{sw/sed}$ PEC_{gw}

9.2 Effects on birds (KCP 10.1.1)

9.2.1 Toxicity data

The risk assessment for birds and mammals was carried out according to the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438).

~~Information concerning studies with birds and risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD. No further data are required.~~

Iodosulfuron-methyl-sodium
Avian toxicity studies have been carried out with iodosulfuron-methyl-sodium. Full details of these studies are provided in the EU Renewal Assessment Report and related documents, presented agreed end-points were taken from EFSA Journal 2016;14(4):4453.

Table 9.2-1: Endpoints and effect values relevant for the risk assessment for birds - Iodosufuronmethyl-sodium

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Bobwhite quail Mallard duck Japanese quail	*Iodosulfuron-methyl-sodium*	*Oral Acute*	*LD_{50} = > 2000 mg as/kg bw*	*EFSA Journal 2016;14(4):4453*
Bobwhite quail	*Iodosulfuron-methyl-sodium*	*Dietary reproductive toxicity, 23 weeks*	*NOEL = 78 mg/kg bw/d*	*EFSA Journal 2016;14(4):4453*

Mesosulfuron-methyl
Avian toxicity studies have been carried out with mesosulfuron-methyl. Full details of these studies are provided in the EU Renewal Assessment Report and related documents, presented agreed endpoints were taken from EFSA Journal 2016;14(10):4584.

Table 9.2-2: Endpoints and effect values relevant for the risk assessment for birds - Mesosulfuron-methyl

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Bobwhite quail Mallard duck	*Mesosulfuron-methyl*	*Oral Acute*	*LD_{50} > 2000 mg/kg bw*	*EFSA Journal 2016;14(10):4584*
Bobwhite quail	*Mesosulfuron-methyl*	*Reproductive toxicity, 20 weeks*	*NOEL = 93 mg/kg bw/d*	*EFSA Journal 2016;14(10):4584*

JME-HER 12 OD based on endpoints of the formulation IMS+MSM+MPR OD 42 (2+10+30)
Possible risk to birds exposed to the formulated product JME-HER 12 OD (IMS+MSM+MPR OD 42 (2+10+30) can be predicted on the basis of data for the individual active substances in a combined toxicity assessment. Therefore, no toxicity data of a vertebrate study with the formulation is presented here.
In addition , it should be noted that, the results of the acute product study on mammals (LD_{50} > 5000 mg product/kg bw) do not indicate increased toxicity of the formulation compared to the individual active substances.

9.2.1.1 Justification for new endpoints

~~Not relevant. See point 9.2.1.~~

No deviation from the EU agreed endpoints.

9.2.2 Risk assessment for spray applications

~~Not relevant. See point 9.2.1.~~

The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438).

9.2.2.1 First-tier assessment (screening/generic focal species)

~~Not relevant. See point 9.2.1.~~

Iodosulfuron-methyl-sodium
For the active substance iodosulfuron-methyl-sodium – as the risk assessment is passed on screening level - exposure and risk characterisation is presented as a generic 'risk envelope' approach: The risk assessment is based on worst case application rates which cover all intended European uses across different products in which the mentioned compounds may be included.

Table 9.2-3: Screening assessment of the acute and long-term/reproductive risk for birds of iodosulfuron-methyl-sodium due to the use of JMD-HER 12 OD ~~IMS+MSM+MPR OD 42 (2+10+30)~~ in cereals

Intended use	**Risk envelope approach (use group A):** **Cereals~~, maize, non-cropped area, BBCH 00-39~~**				
Active substance/product	iodosulfuron-methyl-sodium				
Application rate (g/ha)	risk envelope approach: 1 × 10				
Acute toxicity (mg/kg bw)	>2000				
TER criterion	10				
Crop scenario Growth stage	**Indicator/generic focal species**	**SV_{90}**	**MAF_{90}**	**DDD_{90} (mg/kg bw/d)**	**TER_a**
Cereals	Small omnivorous bird	158.8	1.0	1.6	>1250
Reprod. toxicity (mg/kg bw/d)	78				
TER criterion	5				
Crop scenario Growth stage	**Indicator/generic focal species**	**SV_m**	**MAF_m × TWA**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
Cereals	Small omnivorous bird	64.8	1.0 x 0.53	0.3	260

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.
** covers also non-cropped areas*

Mesosulfuron-methyl

For the active substance mesosulfuron-methyl – as the risk assessment is passed on screening level – exposure and risk characterisation is presented as a generic 'risk envelope' approach: The risk assessment is based on worst case application rates which cover all intended European uses across different products in which the mentioned compounds may be included.

Table 9.2-4: Screening assessment of the acute and long-term/reproductive risk for birds of mesosulfuron-methyl due to the use of JMD-HER 12 OD ~~IMS+MSM+MPR-OD 42 (2+10+30)()~~ in cereals

Intended use	**Risk envelope approach (use group A):** **Cereals~~, maize, non-cropped area, BBCH 00-39~~**				
Active substance/product	mesosulfuron-methyl				
Application rate (g/ha)	risk envelope approach: 1 × 15				
Acute toxicity (mg/kg bw)	>2000				
TER criterion	10				
Crop scenario Growth stage	**Indicator/generic focal species**	**SV_{90}**	**MAF_{90}**	**DDD_{90} (mg/kg bw/d)**	**TER_a**
Cereals	Small omnivorous bird	158.8	1.0	2.4	>833
Reprod. toxicity (mg/kg bw/d)	93				
TER criterion	5				
Crop scenario Growth stage	**Indicator/generic focal species**	**SV_m**	**MAF_m × TWA**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
Cereals	Small omnivorous bird	64.8	1.0 x 0.53	0.5	186

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Birds - Assessment of combined toxicity

As requested by the Central Zone when a product contains more than one active substance, an additional assessment on combined toxicity risk has to be presented. It is considered that a quantitative toxicity risk assessment according to concentration addition is not needed if one of the following points applies:
- The risk assessment for all active substances in the product passes with a high margin of safety
- One active substance clearly drives the risk assessment
These conditions are assessed following a step-wise approach. A detailed description of this approach is presented in a separate document (Gladbach, A., Ebeling, M., Weyers, A., 2016). Note that for the calculation only the scenario with the lowest TER values was considered (most critical scenario). This safely covers all other scenarios.

1st step: Margin of safety

Condition: all TER values are > Trigger x n (n = number active substances in the mixture)

2nd step: Risk per fraction

Condition: One a.s. contributes to ≥ 90% of the predicted combined toxicity of the product.
Assessment: The contribution of each individual a.s. to the combined toxicity (risk per fraction, rpf) is estimated based on the following equation:

$$rpf_{a.s.1} = \frac{1}{TER_{a.s.1}} / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} \ldots + \frac{1}{TER_{a.s.i}}\right)$$

The estimation is based on TER values from the same refinement level to assure comparability.

3rd step: TERMIX calculation
Condition: The combined toxicity is acceptable if TERMIX ≥ 10 (acute) or 5 (long-term)
Assessment: The combined toxicity risk (TERMIX) with concentration-addition is estimated based on the following equation:

$$TER_{mix} = 1/(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} \ldots + \frac{1}{TER_{a.s.i}})$$

As the notifier experienced differing preferences by national reviewers for one or the other step, results of all three steps are considered below:

Table 9.2-5: Combined toxicity assessment – birds

Intended use	*Risk envelope approach (use group A)*
Active substance/product	*iodosulfuron-methyl-sodium + mesosulfuron-methyl*
Application rate (g/ha)	*1 x (10 g/ha + 15 g/ha)*

Scenario / Generic focal species	***TER values***		***Trigger a.s.1/a.s.2***	***1st step All TER > trigger×n?***	***2nd step rpfMAX***	***3rd step TERMIX***
	IMS[1)]	***MSM[1)]***				
Acute / small omnivorous bird	*>1250*	*>840*	*10/10*	*Yes*	*not applicable#*	*502.51*
Long-term / small omnivorous bird	*260*	*181*	*5/5*	*Yes*	*not applicable#*	*107.52*

1) Worst-case TER values as listed in point 9.2.2.1
 # The rpf calculation is not meaningful if due to a risk envelope approach for one or more individual substances the ratio of the active substances in the assessed mixture differs from the ratio in the formulation.

In all cases the TER values are ≥ Trigger × n (n = number of active substances in the mixture), indicating no unacceptable risk from the use of the product.

9.2.2.2 Higher-tier risk assessment

Not relevant. ~~See point 9.2.1.~~

9.2.2.3 Drinking water exposure

~~Not relevant. See point 9.2.1.~~

When necessary, the assessment of the risk for birds due to uptake of contaminated drinking water is conducted for a small granivorous bird with a body weight of 15.3 g (Carduelis cannabina) and a drinking water uptake rate of 0.46 L/kg bw/d (cf. Appendix K of EFSA/2009/1438).

Leaf scenario
Since the product is not intended to be applied on leafy vegetables forming heads or crop plants with

comparable water collecting structures at principal growth stage 4 or later, the leaf scenario does not have to be considered.

Puddle scenario
Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances (Koc < 500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥ 500 L/kg).

Iodosulfuron-methyl-sodium
With a $K(f)_{oc}$ of 50.8, iodosulfuron-methyl-sodium belongs to the group of less sorptive substances.

Iodosulfuron-methyl-sodium			
Effective application rate (g/ha) =	*10*		
Acute toxicity (mg/kg bw) =	*>2000*	*Quotient =*	*<0.01*
Reprod. toxicity (mg/kg bw/d) =	*78*	*Quotient =*	*0.13*

Mesosulfuron-methyl
With a $K(f)_{oc}$ of 64 L/kg, mesosulfuron-methyl belongs to the group of less sorptive substances.

Iodosulfuron-methyl-sodium			
Effective application rate (g/ha) =	*15*		
Acute toxicity (mg/kg bw) =	*>2000*	*Quotient =*	*<0.01*
Reprod. toxicity (mg/kg bw/d) =	*93*	*Quotient =*	*0.16*

9.2.2.4 Effects of secondary poisoning

~~Not relevant. See point 9.2.1.~~

Iodosulfuron-methyl-sodium
The log Pow of iodosulfuron-methyl-sodium (-0.70) and does not exceed the trigger value of 3. The logPow of all iodosulfuron-methyl-sodium metabolites are below the trigger value of 3 as stated in the EFSA Journal 2016;14(4):4453. In accordance with the Guidance Document on Risk Assessment for Birds and Mammals, a risk assessment for effects due to secondary poisoning is not required.

Mesosulfuron-methyl
The log Pow of mesosulfuron-methyl (-0.48) does not exceed the trigger value of 3. The log Pow values of the mesosulfuron-methyl metabolites are all below the trigger of 3 as EU agreed in EFSA Journal 2016;14(10):4584. In accordance with the Guidance Document on Risk Assessment for Birds and Mammals, a risk assessment for effects due to secondary poisoning is not required.

9.2.2.5 Biomagnification in terrestrial food chains

Not relevant. ~~See point 9.2.1.~~

9.2.3 Risk assessment for baits, pellets, granules, prills or treated seed

Not relevant. ~~See point 9.2.1.~~

9.2.4 Overall conclusions

~~Not relevant. See point 9.2.1.~~

Iodosulfuron-methyl-sodium
The acute and long-term risks of iodosulfuron-methyl-sodium to birds were assessed from toxicity exposure ratios between toxicity endpoints, estimated from studies on the active substance and maximum residues occurring on food items following applications according to the proposed use pattern. For iodosulfuron-methyl-sodium, the acute and long-term screening step TER values, calculated for the recommended scenario, were above the trigger value of 10 and 5, respectively, according to the proposed use pattern.

Furthermore, due to the k(f)oc and log Pow values, the risk assessment for exposure via drinking water from puddles and risk of secondary poisoning was not considered necessary.

Mesosulfuron-methyl
The acute and long-term risks of mesosulfuron-methyl to birds were assessed from toxicity exposure ratios between toxicity endpoints, estimated from studies on the active substance and maximum residues occurring on food items following applications according to the proposed use pattern. For mesosulfuron methyl, the acute and long-term screening step TER values, calculated for the recommended scenario, were above the trigger value of 10 and 5, respectively, according to the proposed use pattern.

Furthermore, due to the k(f)oc and log Pow values, the risk assessment for exposure via drinking water from puddles and risk of secondary poisoning was not considered necessary.

In overall conclusion, the risk for ~~wild~~ birds is acceptable for the use of JME-HER 12 OD *~~IMS+MSM+MPR OD 42 (2+10+30)~~ according to the intended use pattern.*

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the TER values exceed the trigger values of 10 for acute and 5 for reproductive/long-term risk. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to birds. No risk mitigations are required.

Review comments:

In the risk assessment for birds the Applicant used higher doses of both active substances than are in the GAP. The Applicant followed a generic ‘risk envelope’ approach, where the European envelope rate considered for iodosulfuron-methyl-sodium is 10 g a.s./ha, for mesosulfuron-methyl is 15 g a.s./ha.
Since this is worst case, already accepted in the Core Report for Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)) this approach is accepted for risk assessment purposes for JME-HER 12 OD by zRMS.

The acute and long-term risk assessment for birds was performed in line with recommendations of the EFSA (2009) with assumption of EU agreed endpoints. No formulation study was required.
Overall, acceptable acute and reproductive risk to birds may be concluded for application of JME-HER 12 OD to cereals, according to GAP.

9.3 Effects on terrestrial vertebrates other than birds (KCP 10.1.2)

9.3.1 Toxicity data

~~Information concerning studies with mammals and risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD. No further data are required.~~

Iodosulfuron-methyl-sodium

Mammalian toxicity studies have been carried out with iodosulfuron-methyl-sodium. Full details of these studies are provided in the EU Renewal Assessment Report and related documents, presented agreed end-points were taken from EFSA Journal 2016;14(4):4453.

Table 9.3-1: Endpoints and effect values relevant for the risk assessment for mammals - Iodosulfuron-methyl-sodium

Species	Substance	Exposure System	Results	Reference
Rat	*Iodosulfuron-methyl-sodium*	*Oral Acute*	*LD_{50} = 2678 mg/kg bw*	*EFSA Journal 2016;14(4):4453*
Rat	*Iodosulfuron-methyl-sodium*	*Combined chronic toxicity and oncogenicity study (2 years)*	*NOAEL=♂: 2.96 mg/kg bw/day, ♀: 3.91 mg/kg bw/day*	*EFSA Journal 2016;14(4):4453*

Mesosulfuron-methyl

Mammalian toxicity studies have been carried out with mesosulfuron-methyl. Full details of these studies are provided in the EU Renewal Assessment Report and related documents, presented agreed endpoints were taken from EFSA Journal 2016;14(10):4584.

Table 9.3-2: Endpoints and effect values relevant for the risk assessment for mammals – Mesosulfuron-methyl

Species	Substance	Exposure System	Results	Reference
Rat	*Mesosulfuron-methyl*	*Oral Acute*	*LD_{50} > 5000 mg/kg bw*	*EFSA Journal 2016;14(10):4584*
Rat	*Mesosulfuron-methyl*	*Dietary Reproductive toxicity Two-generation study*	*NOEL = 840 mg/kg bw/d*	*EFSA Journal 2016;14(10):4584*

JME-HER 12 OD based on endpoints of the formulation IMS+MSM+MPR OD 42 (2+10+30)

*Effects on mammals of **JME-HER 12 OD** (IMS+MSM+MPR OD 42 (2+10+30)) were evaluated as part of the EU assessment of the active substance mesosulfuron-methyl (representative formulation). No new studies are submitted with this formulation, reference is made to the agreed endpoints reported in EFSA Journal 2016;14(10):4584, and RAR Volume 3 – B.9 (PPP) – ATLANTIS OD (revised version 2016-06).*

Table 9.3-3: Endpoints and effect values relevant for the risk assessment for mammals - IMS+MSM+MPR OD 42 (2+10+30)

Species	Substance	Exposure System	Results	Reference
Rat	*IMS+MSM+MPR OD 42 (2+10+30)*	*Oral Acute*	*LD_{50} > 5000 mg/kg bw*	*EFSA Journal 2016;14(10):4584*

9.3.1.1 Justification for new endpoints

~~Not relevant. See point 9.3.1.~~

No deviation to EU agreed endpoints.

9.3.2 Risk assessment for spray applications

~~Not relevant. See point 9.3.1.~~

The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438).

9.3.2.1 First-tier assessment (screening/generic focal species)

~~Not relevant. See point 9.3.1.~~

Iodosulfuron-methyl-sodium

For the active substance iodosulfuron-methyl-sodium– as the risk assessment is passed on screening or 1st tier level - exposure and risk characterisation is presented as a generic 'risk envelope' approach: The risk assessment is based on worst case application rates which cover all intended European uses across different products in which the mentioned compounds may be included.

Table 9.3-4: Screening assessment of the acute and long-term/reproductive risk for mammals of Iodosulfuron-methyl-sodium due to the use of JME-HER 12 OD ~~IMS+MSM+MPR OD 42 (2+10+30)~~ in cereals

Intended use		***Risk envelope approach (use group A):*** ***Cereals~~, maize, non-cropped area, BBCH 00-39~~***			
Active substance/product		*iodosulfuron-methyl-sodium*			
Application rate (g/ha)		*risk envelope approach:* *1 × 10*			
Acute toxicity (mg/kg bw)		*2678*			
TER criterion		*10*			
Crop scenario ***Growth stage***	***Indicator/generic focal species***	***SV_{90}***	***MAF_{90}***	***DDD_{90}*** ***(mg/kg bw/d)***	***TER_a***
Cereals	*Small herbivorous mammal*	*118.4*	*1.0*	*1.2*	*2232*
Reprod. toxicity (mg/kg bw/d)		*2.96*			
TER criterion		*5*			
Crop scenario ***Growth stage***	***Indicator/generic focal species***	***SV_m***	***MAF_m × TWA***	***DDD_m*** ***(mg/kg bw/d)***	***TER_{lt}***
Cereals	*Small herbivorous mammal*	*48.3*	*1.0 x 0.53*	*0.3*	*12*

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Mesosulfuron-methyl

For the active substance mesosulfuron-methyl – as the risk assessment is passed on screening or 1st tier

level - exposure and risk characterisation is presented as a generic 'risk envelope' approach: The risk assessment is based on worst case application rates which cover all intended European uses across different products in which the mentioned compounds may be included.

Table 9.3-5: Screening assessment of the acute and long-term/reproductive risk for mammals of Mesosulfuron methyl due to the use of* JME-HER 12 OD ~~*IMS+MSM+MPR OD 42 (2+10+30)*~~ *in cereals

Intended use		***Risk envelope approach (use group A):*** ***Cereals*** ~~***, maize, non-cropped area, BBCH 00-39***~~			
Active substance/product		*iodosulfuron-methyl-sodium*			
Application rate (g/ha)		*risk envelope approach:* *1 × 15*			
Acute toxicity (mg/kg bw)		*>5000*			
TER criterion		*10*			
Crop scenario Growth stage	***Indicator/generic focal species***	***SV_{90}***	***MAF_{90}***	***DDD_{90} (mg/kg bw/d)***	***TER_a***
Cereals	*Small herbivorous mammal*	*118.4*	*1.0*	*1.78*	*>2809*
Reprod. toxicity (mg/kg bw/d)		*840*			
TER criterion		*5*			
Crop scenario Growth stage	***Indicator/generic focal species***	***SV_m***	***MAF_m × TWA***	***DDD_m (mg/kg bw/d)***	***TER_{lt}***
Cereals	*Small herbivorous mammal*	*48.3*	*1.0 x 0.53*	*0.40*	*2100*

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Mammals - Assessment of combined toxicity

As requested by the Central Zone when a product contains more than one active substance, an additional assessment on combined toxicity risk has to be presented. It is considered that a quantitative toxicity risk assessment according to concentration addition is not needed if one of the following points applies:
- The risk assessment for all active substances in the product passes with a high margin of safety
- One active substance clearly drives the risk assessment

These conditions are assessed following a step-wise approach. A detailed description of this approach is presented in a separate document (Gladbach, A., Ebeling, M., Weyers, A., 2016). Note that for the calculation only the scenario with the lowest TER values was considered (most critical scenario).
This safely covers all other scenarios.

1st step: Margin of safety

Condition: all TER values are > Trigger x n (n = number active substances in the mixture)

2nd step: Risk per fraction

Condition: One a.s. contributes to ≥ 90% of the predicted combined toxicity of the product.
Assessment: The contribution of each individual a.s. to the combined toxicity (risk per fraction, rpf) is estimated based on the following equation:

$$rpf_{a.s.1} = \frac{1}{TER_{a.s.1}} / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} \ldots + \frac{1}{TER_{a.s.i}}\right)$$

The estimation is based on TER values from the same refinement level to assure comparability.

3rd step: TER_{MIX} calculation
Condition: The combined toxicity is acceptable if TERMIX ≥ 10 (acute) or 5 (long-term)
Assessment: The combined toxicity risk (TERMIX) with concentration-addition is estimated based on the following equation:

$$TER_{mix} = 1/(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} \ldots + \frac{1}{TER_{a.s.i}})$$

As the notifier experienced differing preferences by national reviewers for one or the other step, results of all three steps are considered below:

Table 9.3-6: Combined toxicity assessment – mammals

Intended use	*Risk envelope approach (use group A)*
Active substance/product	*iodosulfuron-methyl-sodium + mesosulfuron-methyl*
Application rate (g/ha)	*1 x (10 g/ha + 15 g/ha)*

Scenario / Generic focal species	***TER values***		***Trigger a.s.1/a.s.2***	***1st step All TER > trigger×n?***	***2nd step rpfMAX***	***3rd step TERMIX***
	IMS[1)]	***MSM[1)]***				
Acute / small omnivorous bird	*2232*	*>2809*	*10/10*	*yes*	*not applicable#*	*1204.8*
Long-term / small omnivorous bird	*12*	*2100*	*5/5*	*yes*	*not applicable#*	*12.43*

1) Worst-case screening step TER values as listed in point 9.3.2.1
 # The rpf calculation is not meaningful if due to a risk envelope approach for one or more individual substances the ratio of the active substances in the assessed mixture differs from the ratio in the formulation.

In the combined toxicity for acute/ small herbivorous mammal and for long-term/ small herbivorous mammal the TER values are ≥ Trigger × n (n = number of active substances in the mixture), indicating no unacceptable risk from the use of the product.

9.3.2.2 Higher-tier risk assessment

Not relevant. ~~See point 9.3.1.~~

9.3.2.3 Drinking water exposure

~~Not relevant. See point 9.3.1.~~

When necessary, the assessment of the risk for mammals due to uptake of contaminated drinking water is conducted for a small omnivorous mammal with a body weight of 21.7 g (Apodemus sylvaticus) and a drinking water uptake rate of 0.24 L/kg bw/d (cf. Appendix K of EFSA/2009/1438).

Leaf scenario
Since the product is not intended to be applied on leafy vegetables forming heads or crop plants with comparable water collecting structures at principal growth stage 4 or later, the leaf scenario does not have to be considered.

Puddle scenario
Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances (Koc < 500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥ 500 L/kg).

Iodosulfuron-methyl-sodium
With a K(f)$_{oc}$ of 50.8, iodosulfuron-methyl-sodium belongs to the group of less sorptive substances.

Iodosulfuron-methyl-sodium			
Effective application rate (g/ha) =	*10*		
Acute toxicity (mg/kg bw) =	*2678*	*Quotient =*	*0.004*
Reprod. toxicity (mg/kg bw/d) =	*2.96*	*Quotient =*	*3.34*

Mesosulfuron-methyl
With a K(f)$_{oc}$ of 64 L/kg, mesosulfuron-methyl belongs to the group of less sorptive substances.

Iodosulfuron-methyl-sodium			
Effective application rate (g/ha) =	*15*		
Acute toxicity (mg/kg bw) =	*>5000*	*Quotient =*	*<0.01*
Reprod. toxicity (mg/kg bw/d) =	*840*	*Quotient =*	*0.018*

9.3.2.4 Effects of secondary poisoning

~~Not relevant. See point 9.3.1.~~

Iodosulfuron-methyl-sodium
*The log P$_{ow}$ of **iodosulfuron-methyl-sodium** (-0.70) does not exceed the trigger value of 3. The log Pow of all iodosulfuron-methyl-sodium metabolites are below the trigger value of 3 as stated in the EFSA Journal 2016;14(4):4453. In accordance with the Guidance Document on Risk Assessment for Birds and Mammals a risk assessment for effects due to secondary poisoning is not required.*

Mesosulfuron-methyl
The log P$_{ow}$ of mesosulfuron-methyl (-0.48) does not exceed the trigger value of 3.
*The log P$_{ow}$ values of the **mesosulfuron-methyl** metabolites are all below the trigger of 3 as stated in EFSA Journal 2016;14(10):4584. In accordance with the Guidance Document on Risk Assessment for Birds and Mammals, a risk assessment for effects due to secondary poisoning is not required.*

9.3.2.5 Biomagnification in terrestrial food chains

Not relevant. ~~See point 9.3.1.~~

9.3.3 Risk assessment for baits, pellets, granules, prills or treated seed

Not relevant. ~~See point 9.3.1.~~

9.3.4 Overall conclusions

~~Not relevant. See point 9.3.1.~~

Iodosulfuron-methyl-sodium
The acute and long-term risks of iodosulfuron-methyl-sodium to mammals were assessed from toxicity exposure ratios between toxicity endpoints, estimated from studies on the active substance and maximum residues occurring on food items following applications according to the proposed use pattern. For iodosulfuron-methyl-sodium, the acute and long-term screening step TER values, calculated for the recommended scenario, were above the trigger value of 10 and 5, respectively, according to the proposed use pattern.
Furthermore, due to the k(f)oc and log Pow values, the risk assessment for exposure via drinking water from puddles and risk of secondary poisoning was not considered necessary.

Mesosulfuron-methyl
The acute and long-term risks of mesosulfuron-methyl to mammals were assessed from toxicity exposure ratios between toxicity endpoints, estimated from studies on the active substance and maximum residues occurring on food items following applications according to the proposed use pattern. For mesosulfuron-methyl, the acute and long-term screening step TER values, calculated for the recommended scenario, were above the trigger value of 10 and 5, respectively, according to the proposed use pattern.

Furthermore, due to the k(f)$_{oc}$ and log P$_{ow}$ values, the risk assessment for exposure via drinking water from puddles and risk of secondary poisoning was not considered necessary.
In overall conclusion, the risk for ~~wild~~ mammals is acceptable for the use of JME-HER 12 OD *~~IMS+MSM+MPR OD 42 (2+10+30~~) according to the intended use pattern.*

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the TER values exceed the trigger values of 10 for acute and 5 for reproductive/long-term risk. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to mammals. No risk mitigations are required.

Review comments:

In the risk assessment for mammals the Applicant used higher doses of both active substances than are in the GAP. The Applicant followed a generic ‘risk envelope’ approach, where the European envelope rate considered for iodosulfuron-methyl-sodium is 10 g a.s./ha, for mesosulfuron-methyl is 15 g a.s./ha. Since this is worst case, already accepted in the Core Report for Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)) this approach is accepted for risk assessment purposes for JME-HER 12 OD by zRMS.

The acute and long-term risk assessment for mammals was performed in line with recommendations of the EFSA (2009) with assumption of EU agreed endpoints. No formulation study was required.
Overall, acceptable acute and reproductive risk to mammals may be concluded for application of JME-HER 12 OD to cereals, according to GAP.

9.4 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)

Not relevant.

The assessments on birds and terrestrial vertebrates other than birds presented in Sections 9.2 and 9.3 before do not raise particular concern for further terrestrial vertebrate wildlife such as reptiles and amphibians. Moreover, the ALS mode of action of all three active substances in the present formulation is well known to be highly specific for plants. Therefore, no testing on other vertebrate organisms is deemed necessary.

9.5 Effects on aquatic organisms (KCP 10.2)

9.5.1 Toxicity data

~~Information concerning studies with aquatic organisms and risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD. No further data are required.~~

Iodosulfuron-methyl-sodium
Studies on the toxicity to aquatic organisms have been carried out with iodosulfuron-methyl-sodium and its relevant metabolites. Full details of these studies are provided in the EU Renewal Assessment Report, as well as in Appendix 2 of this document (new studies).

The selection of studies and endpoints for the risk assessment for iodosulfuron-methyl-sodium is basically in line with the Results of the EU review process (EFSA Journal 2016;14(4):4453). However, in some cases clarity is missing regarding the endpoints which should be chosen for others than the "representative" formulation, or regarding endpoints which should be used when the new aquatic guidance document (EFSA Journal 2013;11(7):3290) is applied. In these cases, justifications for the selection are provided below.

For the provision of "further information to refine the risk to aquatic plants for iodosulfuron-methylsodium" (data gap acc. point 7 of EFSA conclusion), refined exposure type studies on the most sensitive macrophyte species Lemna gibba have been generated for the active substance and its metabolite AE F075736 after the EU review. The studies are presented as new data below, and were used to establish refined risk assessments following options Tier 2C and Tier 3 of the EFSA Aquatic Guidance Document.

Table 9.5-1: Endpoints and effect values relevant for the risk assessment for aquatic organisms – iodosulfuron-methyl-sodium and relevant metabolites

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Oncorhynchus mykiss	*Iodosulfuron-methyl-sodium*	*96 h, s*	*LC_{50} >100 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Oncorhynchus mykiss	*Iodosulfuron-methyl-sodium*	*28 d, f*	*NOEC = 7.79 mg a.s./L $_{mm}$*	*EFSA Journal 2016;14(4):4453*
Daphnia magna	*Iodosulfuron-methyl-sodium*	*48 h, s*	*EC_{50} >100 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Daphnia magna	*Iodosulfuron-methyl-sodium*	*21 d, ss*	*NOEC = 7.9 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Pseudokirchneriella subcapitata	*Iodosulfuron-methyl-sodium*	*96 h, s*	*E_rC_{50} = 0.152 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*Iodosulfuron-methyl-sodium*	*14 d semi static*	*7 d EC_{50} = 0.00079 mg a.s./L $_{nom}$ 14 d EC= 0.00083 mg a.s./L $_{nom}$ 7 d E_rC_{50}= 0.00134 mg a.s./L $_{nom}$ NOEC =0.0040 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*

Species	Substance	Exposure System	Results	Reference
Lemna gibba (duck weed)	*iodosulfuron-methyl-sodium + mefenpyr-diethyl (formulated as OD)*	*7 d static*	*frond number 7d E_rC_{50}= 0.0084 mg product/L (nom) 0.00074 mg a.s./L (nom)* *frond dry weight 7dE_rC_{50}>0.100 mg product/L (nom) >0.00882mg a.s./L (nom*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*Iodosulfuron-methyl-sodium*	*7 d, ss*	*E_rC_{50} = 0.00108 mg a.s./L $_{nom}$ 6 w ErC_{50}=0.000679 mg a.s./L $_{nom}$ NOEC = 0.0004 mg a.s./L $_{nom}$ Frond area 7 d E_rC_{50} = 0.00112.s./L $_{nom}$ 6 w E_rC_{50}=0.000609 mg a.s./L $_{nom}$ NOEC = 0.0004 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE F075736*	*7 d, ss*	*E_rC_{50} = 0.00057 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453; EFSA Journal 2015;13(1):*
Pseudokirchneriella subcapitata	*AE F145741*	*72 h, s*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE F145741*	*7 d, ss*	*E_rC_{50} = 3.84 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Pseudokirchneriella subcapitata	*AE F145740*	*72 h, s*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE F145740*	*7 d, ss*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Pseudokirchneriella subcapitata	*AE 0002166*	*72 h, s*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE 0002166*	*7 d, ss*	*E_rC_{50} = 0.0230 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Pseudokirchneriella subcapitata	*AE F161778*	*72 h, s*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE F161778*	*7 d, ss*	*E_rC_{50} = 0.0281 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Pseudokirchneriella subcapitata	*BCS-CW81253*	*72 h, s*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Lemna gibba	*BCS-CW81253*	*7 d, ss*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE 0000119*	*7 d, ss*	*E_rC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Daphnia magna	*AE F059411*	*48 h, s*	*LC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Pseudokirchneriella subcapitata	*AE F059411*	*96 h, s*	*E_rC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE F059411*	*7 d, ss*	*E_rC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE 0014966*	*7 d, ss*	*E_rC_{50} = 0.575 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE 0034855*	*7 d, ss*	*E_rC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Oncorhynchus mykiss	*AE 1234964*	*96 h, s*	*LC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Daphnia magna	*AE 1234964*	*48 h, s*	*LC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE 1234964*	*7 d, ss*	*E_rC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Oncorhynchus mykiss	*AE F159737*	*96 h, s*	*LC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Daphnia magna	*AE F159737*	*48 h, s*	*LC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE F159737*	*7 d, ss*	*E_rC_{50} >100 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Pseudokirchneriella subcapitata	*AE F154781*	*72 h, s*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Lemna gibba	*AE F154781*	*7 d, ss*	*E_rC_{50} >10 mg met./L $_{nom}$*	*EFSA Journal 2016;14(4):4453*
Higher-tier studies				
Lemna gibba	*Iodosulfuron-methyl-sodium*	*<u>Design 1:</u> 2 peaks lasting 24h on day 0 and 3. Test duration 7 d* *<u>Design 2:</u> 2 peaks lasting 24h on day 0 and 7. Test duration 14 d*	*E_rC_{50} = 0.00462 mg a.s./L $_{nom}$ (frond area)* *1st week E_rC_{50} = 0.0272 mg a.s./L $_{nom}$ (frond area)* *2nd week E_rC_{50} =0.0159 mg a.s./L $_{nom}$ (frond area)*	*Kuhl, K.; 2016 New study; See justification.*

Species	Substance	Exposure System	Results	Reference
Lemna gibba	*AE F075736*	*Design 1: 2 peaks lasting 24h on day 0 and 3. Test duration 7 d*	*E_rC_{50} = 0.00203 mg a.s./L $_{nom}$ (frond number)*	*Kuhl, K.; 2017 New study; See justification.*
Lemna gibba	*AE F075736*	*Design 2: 2 peaks lasting 24h on day 0 and 7. Test duration 14 d*	*1st week E_rC_{50} = 0.00585 mg a.s./L $_{nom}$ (frond area)* *2nd week E_rC_{50} = 0.00422 mg a.s./L $_{nom}$ (frond area)*	*Kuhl, K., 2017 New study; See justification.*
Higher-tier studies (micro- or mesocosm studies)				
Higher tier Aquatic macrophytes 9 species	*Iodosulfuron-methyl-sodium*	*6 weeks, s*	*NOEAEC = 0.00027 mg a.s./L measured initial NOEAEC = 0.00016 mg a.s./L geomean measured*	*EFSA Journal 2016;14(4):4453*
Endpoints used for metabolites risk assessment in case that no test data are available				
Fish acute Oncorhynchus mykiss	*Metabolites of iodosulfuron-methyl-sodium 1)*	*96 h, s*	*LC_{50} >100 mg a.s./L $_{nom}$*	*from parent compound - see justification for new endpoints*
Fish prolonged Oncorhynchus mykiss	*Metabolites of iodosulfuron-methyl-sodium 2)*	*28 d, f*	*NOEC = 7.79 mg a.s./L $_{mm}$*	*from parent compound - see justification for new endpoints*
Invertebrates acute Daphnia magna	*Metabolites of iodosulfuron-methyl-sodium 3)*	*48 h, s*	*EC_{50} >100 mg a.s./L $_{nom}$*	*from parent compound - see justification for new endpoints*
Invertebr. prolonged Daphnia magna	*Metabolites of iodosulfuron-methyl-sodium 2)*	*21 d, ss*	*NOEC = 7.9 mg a.s./L $_{nom}$*	*from parent compound - see justification for new endpoints*
Algae Pseudokirchneriella subcapitata	*Metabolites of iodosulfuron-methyl-sodium 5)*	*96 h, s*	*E_rC_{50} = 0.152 mg a.s./L $_{nom}$*	*from parent compound - see justification for new endpoints*

s: static; ss: semi-static; f: flow-through; nom: based on nominal concentrations; mm: based on mean measured concentrations; im: based on initial measured concentrations
1) AE F145741, AE F145740, AE 0002166, AE F161778, BCS-CW81253, AE 0000119, AE F059411, AE 0014966, AE 0034855, AE F154781
2) AE F145741, AE F145740, AE 0002166, AE F161778, BCS-CW81253, AE 0000119, AE F059411, AE 0014966, AE 0034855, AE 1234964, AE F159737, AE F154781
3) AE F145741, AE F145740, AE 0002166, AE F161778, BCS-CW81253, AE 0000119, AE 0014966, AE 0034855, AE F154781
5) AE 0000119, AE 0014966, AE 0034855, AE 1234964, AE F159737

Mesosulfuron-methyl

Studies on the toxicity to aquatic organisms have been carried out with mesosulfuron-methyl and its relevant metabolites. Full details of these studies are provided in the EU Renewal Assessment Report and

related documents, as well as in Appendix 2 of this document (new studies). Presented agreed endpoints were taken from EFSA Journal 2016;14(10):4584, if not otherwise stated.

The selection of studies and study-derived endpoints for the Tier 1 risk assessment is in line with the Results of the EU review process, except for one new study submitted on metabolite BCS-CV14885, see justification provided below. In some cases, where surrogate RAC values for metabolites should be used according to the new aquatic guidance document (EFSA Journal 2013;11(7):3290) in the absence of a test, justifications on the derivation of these endpoints are provided.

For the provision of "further information to address the risk identified to aquatic plants for mesosulfuron-methyl" (data gap acc. point 7 of EFSA conclusion), a refined exposure type study on the most sensitive macrophyte species Lemna gibba has been generated for the active substance after the EU review. The study is presented as new data below, and was used to establish refined risk assessments following options Tier 2C and Tier 3 of the EFSA Aquatic Guidance Document.

Table 9.5-2: Endpoints and effect values relevant for the risk assessment for aquatic organisms – mesosulfuron-methyl and relevant metabolites

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Oncorhynchus mykiss Lepomis macrochirus Cyprinodon variegates	*Mesosulfuron-methyl*	*96 h, s*	*LC_{50} > 100 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Oncorhynchus mykiss	*Mesosulfuron-methyl*	*28 d (juvenile growth test), ss*	*NOEC = 32 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Daphnia magna	*Mesosulfuron-methyl*	*48 h, s*	*EC_{50} > 100 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Daphnia magna	*Mesosulfuron-methyl*	*21 d, ss*	*NOEC = 1.8 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Pseudokirchneriella subcapitata	*Mesosulfuron-methyl*	*72 h, s*	*E_rC_{50} = 3.99 mg a.s./L $_{mm}$ 1)*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*Mesosulfuron-methyl*	*Lemna gibba*	*E_rC_{50} = 0.001717 mg a.s./L$_{(twa)}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*Mesosulfuron-methyl*	*7 d, ss*	*E_rC_{50} = 0.00129 mg a.s./L $_{nom}$ 2)*	*EFSA Journal 2016;14(10):4584*
Pseudokirchneriella subcapitata	*AE F154851*	*72 h, s*	*E_rC_{50} = 38 mg/L $_{mm}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*AE F154851*	*7 d, s*	*E_rC_{50} = 0.11 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Pseudokirchneriella subcapitata	*AE F160459*	*72 h, s*	*E_rC_{50} > 100 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*AE F160459*	*7 d, s*	*E_rC_{50} = 2.6 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Oncorhynchus mykiss	*AE F099095*	*96 h, s*	*LC_{50} > 70.7 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584***
Daphnia magna	*AE F099095*	*48 h, s*	*EC_{50} > 100 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584***
Pseudokirchneriella subcapitata	*AE F099095*	*72 h, s*	*E_rC_{50} = 99.1 mg/L*	*EFSA Journal 2016;14(10):4584****

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Lemna gibba	*AE F099095*	*7 d, s*	*E_rC_{50} > 100 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Oncorhynchus mykiss	*AE F092944*	*96 h, s*	*LC_{50} > 97 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584**
Daphnia magna	*AE F092944*	*48 h, s*	*EC_{50} = 223 mg/L_{nom} [3)]*	*EFSA Journal 2016;14(10):4584**
Daphnia magna	*AE F092944*	*21 d, ss*	*NOEC = 24.9 mg/L $_{mm}$*	*EFSA Journal 2016;14(10):4584**
Scenedesmus subspicatus	*AE F092944*	*72 h, s*	*E_rC_{50} > 100 mg/L*	*EFSA Journal 2016;14(10):4584****
Lemna gibba	*AE F092944*	*7 d, ss*	*E_rC_{50} > 100 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*AE F160460*	*7 d, ss*	*E_rC_{50} > 100 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*AE F140584*	*7 d, ss*	*E_rC_{50} > 10 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Pseudokirchneriella subcapitata	*AE F147447*	*72 h, s*	*E_rC_{50} > 100 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*AE F147447*	*7 d, ss*	*E_rC_{50} > 100 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Pseudokirchneriella subcapitata	*BCS-CO60720*	*72 h, s*	*E_rC_{50} > 10 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Pseudokirchneriella subcapitata	*BCS-CO60721*	*72 h, s*	*E_rC_{50} > 10 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*BCS-CO60720*	*7 d, s*	*E_rC_{50} > 11.8 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*BCS-CV14885*	*7 d, s*	*E_rC_{50} = 0.00129 mg/L $_{nom}$* *E_rC_{50} > 100 mg/L $_{nom}$*	*generic surrogate value, EFSA Journal 2016;14(10):4584* *Kuhl, K.; 2017 New study; See justification.*
Higher-tier studies				
Lemna gibba	*Mesosulfuron-methyl*	*mimicking exposure of outdoor study 8 weeks*	***7 -day E_rC_{50} (frond area) = 0.00129 mg a.s./L $_{nom}$ [2)]*** *7 -day E_rC_{50} (frond number) = 0.00161 mg a.s./L $_{nom}$* *7-day NOErC = 0.00039 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(10):4584*

Species	***Substance***	***Exposure System***	***Results***	***Reference***
			8-week E_rC_{50} = 0.00190 mg a.s./L $_{nom}$ 8-week NOErC (frond area/number) = 0. 000388 mg a.s./L $_{nom}$	
Aquatic macrophytes (9 species) Elodea canadensis Potamogeton pectinatus Pontederia cordata Nymphaea odorata Cabomba caroliniana Cerat. demersum Glyceria maxima Mentha aquatica Myriophyll.heterophyllum	*Mesosulfuron-methyl*	*outdoor growth inhibition, static 8 weeks*	*NOAEC (shoot length/dry weight) = 0.00057 mg a.s./L_{mm}*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*Mesosulfuron-methyl*	*<u>Design 1:</u> 2 peaks lasting 24h on day 0 and 3. Test duration 7 d* *<u>Design 2:</u> 2 peaks lasting 24h on day 0 and 7. Test duration 14 d*	*E_rC_{50} = 0.0109 mg a.s./L $_{nom}$ (frond area)* *1st week E_rC_{50} > 0.100 mg a.s./L $_{nom}$ (frond area and frond number)* *2nd week E_rC_{50} > 0.100 mg a.s./L $_{nom}$ (frond area and frond number)*	*Kuhl, K.; 2016 New study; See justification.*
Endpoints used for metabolites risk assessment in case that no test data are available				

s: static; ss: semi-static; f: flow-through; nom: based on nominal concentrations; mm: based on mean measured concentrations; a.s.: active substance.

** Refers to the EFSA conclusion on the peer review of the active substance flupyrsulfuron-methyl, EFSA Journal 2014;12(11):3881*

*** Refers to the EFSA conclusion on the peer review of the active substance orthosulfamuron, EFSA Journal 2014;12(3):3353*

**** Refers to the EFSA conclusion on the peer review of the active substance bensulfuron, EFSA Journal 2009;7(1):RN-178, 102 pp.*

***** Refers to the EFSA conclusion on the peer review of the active substance flazasulfuron, EFSA Journal 2016; 14(8): 4575*

[1)] Results of two studies on Pseudokirchneriella subcapitata are tabulated in the EFSA List of Endpoints, thereof the discrete numeric value of E_rC_{50} = 3.99 mg a.s./L is deemed relevant for risk assessment, cf.clarification in RAR MCA Vol 3 B.9: introduction text of B.9.2.6 (page 44) and RMS comment on study KCA 8.2.6.1 /01 (page 46).

[2)] Results of several studies on aquatic plant are tabulated in the EFSA List of Endpoints, thereof the endpoint value for Lemna gibba 7 d E_rC_{50} (frond area) = 1.29 µg/L is deemed relevant for Tier 1 risk assessment, cf.clarification in RAR MCA Vol 3 B.9: RMS comments on study KCA 8.2.7 /07 (page 74) and study KCA 8.2.7 /10 (page 82).

[3)] Results of two studies on Daphnia magna are tabulated in the EFSA List of Endpoints, thereof the discrete numeric value of EC_{50} = 223 mg/L is deemed relevant for risk assessment, as not in contradiction to the non-discrete value of EC_{50} > 100 mg/L resulting from the peer review of the active substance flupyrsulfuron-methyl, EFSA Journal 2014;12(11):3881.

[4)] AE F154851, AE F160459, AE F160460, AE F140584, BCS-CO60720, AE F147447, BCS-CV14885

[5] *AE F154851, AE F160459, AE F099095, AEF092944, AE F160460, AE F140584, AE F147447, BCS-CV14885, BCS-CO60720*
[6] *AE F154851, AE F160459, AE F099095, AE F160460, AE F140584, AE F147447, BCS-CV14885, BCS-CO60720*
[7] *AE F160460, AE F140584, BCS-CV14885*

IMS+MSM+MPR OD 42 (2+10+30)

Effects on aquatic organisms of IMS+MSM+MPR OD 42 (2+10+30) were evaluated as part of the EU assessment of the active substance mesosulfuron-methyl (representative formulation). No new studies are submitted with this formulation, reference is made to the agreed endpoints reported in EFSA Journal 2016;14(10):4584, and RAR Volume 3 – B.9 (PPP) – ATLANTIS OD (revised version 2016-06).

Table 9.5-3: Endpoints and effect values relevant for the risk assessment for aquatic organisms – IMS+MSM+MPR OD 42 (2+10+30)

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Oncorhynchus mykiss	*IMS+MSM+MPR OD 42 (2+10+30)*	*96 h, s*	*LC_{50} = 8.83 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Daphnia magna	*IMS+MSM+MPR OD 42 (2+10+30)*	*48 h, s*	*EC_{50} = 7.6 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Pseudokirchneriella	*IMS+MSM+MPR OD 42 (2+10+30)*	*72 h, s*	*E_rC_{50} = 6.71 mg/L $_{nom}$*	*EFSA Journal 2016;14(10):4584*
Lemna gibba	*IMS+MSM+MPR OD 42 (2+10+30)*	*7 d, s*	*E_rC_{50} = 0.0884 mg a.s./L $_{nom}$*	*EFSA Journal 2016;14(10):4584*

Review comments

The risk assessment of JME-HER 12 OD reference to risk assesment provided in Core Assessment of the already registered product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

From ecotoxicological point of view JME-HER 12 OD is considered equivalent/comparable to already registered Atlantis 12 OD, therefore the unprotected ecotoxicological studies performed for Atlantis 12 OD can be used for risk assessment purposes of JME-HER 12 OD.

In current assessment the same approach is taken as was provided in the risk assessment of reference product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

9.5.1.1 Justification for new endpoints

~~Not relevant. See point 9.5.1.~~

Growth-rate-related endpoints are proposed to be used in risk assessment for algae and macrophytes according to the EFSA aquatic guidance document (2013) and the EFSA (2015) Technical report on the outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology (EFSA supporting publication 2015:EN-924. 62 pp.).

Iodosulfuron-methyl-sodium

Table 9.5-4: Justification for new endpoints*

Species	***Substance***	***Exposure System***	***Justification***
Lemna gibba	*Iodosulfuron-methyl-sodium*	*Higher tier: refined exposure test* *Design 1:* *2 peaks lasting 24h on day 0 and 3. Test duration 7 d* *Design 2:* *2 peaks lasting 24h on day 0 and 7. Test duration 14 d*	*New peak-exposure studies on Lemna gibba were performed with iodosulfuron-methyl sodium and its metabolite AE F075736 to support the refinement options presented in this dossier. The need for further information to address the risk to aquatic plants was stated in the EFSA conclusion on iodosulfuron-methyl sodium (EFSA Journal 2016;14(4):4453).*
Lemna gibba	*metabolite AE F075736*	*Higher tier: refined exposure test* *Design 1:* *2 peaks lasting 24h on day 0 and 3. Test duration 7 d* *Design 2:* *2 peaks lasting 24h on day 0 and 7. Test duration 14 d*	

In the review process for Annex I Renewal three Lemna-studies have been reviewed, two with iodosulfuron-methyl-sodium active substance and one with the formulation IMS+MPR OD 400 (Hussar OD). The end-points from these studies (as given in the EFSA conclusion report EFSA Journal 2016;14(4):4453) are listed in the table below.

Table 9.5-5: Survey of results obtained from Lemna-growth inhibition tests conducted with iodosulfuron-methyl-sodium active substance and Hussar OD

Species	***Test substance***	***Design***	***Endpoint***	***Concentration***
Lemna gibba (duck weed)	*iodosulfuron-methyl-sodium*	*14 d (semi-static)*	*frond number* *7d EC_{50}* *14d EC_{50}* *7d E_rC_{50}* *NOEC*	 *0.00079 mg a.s./L (nom)* *0.00083 mg a.s./L (nom)* *0.00134 mg a.s./L (nom)* *0.00040 mg a.s./L (nom)*
Lemna gibba (duck weed)	*iodosulfuron-methyl-sodium + metsulfuron-methyl*	*6 weeks (semi-static)*	*frond number* *7d E_rC_{50}* *6w E_rC_{50}* *NOEC* *frond area* *7d E_rC_{50}* *6w E_rC_{50}* *NOEC*	 *0.00108 mg a.s./L (nom)* *0.000679 mg a.s./L (nom)* *0.000400 mg a.s./L (nom)* *0.00112 mg a.s./L (nom)* *0.000609 mg a.s./L (nom)* *0.000400 mg a.s./L (nom)*
Lemna gibba (duck weed)	*iodosulfuron-methyl-sodium +*	*7 d static*	*frond number* *7d E_rC_{50}*	 *0.0084 mg product/L (nom)*

	mefenpyr-diethyl (formulated as OD)		*biomass 7d E_rC_{50}*	*0.00074 mg a.s./L (nom)* *> 0.100 mg product/L (nom)* *> 0.00882 mg a.s./L (nom)*

The first Lemna study with the active ingredient is a 14-day study conducted in 1997 by Christ & Ruff according to EPA Guideline 122-2. In this study, only frond number was determined on days 2, 5, 7, 9, 11 and 14. A second measurement variable like frond dry weight or frond area, which is mandatory according to OECD 221 (2006), had not been determined. Moreover, inhibition percentages were only calculated by using the absolute frond counts in the treatments compared to the control. The originally reported endpoints are biomass endpoints (7d E_bC_{50} and 14d E_bC_{50}), i.e. endpoints are based on final frond numbers after 7 and 14 days, respectively. Nowadays a 7-day E_rC_{50} based on growth rate inhibition is recommended to be used in the risk assessment for aquatic plants according to the EFSA AGD (2013). Therefore, during the review process for Annex I Renewal the RMS calculated the specific growth rate at day 7 and the corresponding E_rC_{50} using non-linear regression and concluded a 7d E_rC_{50} of 1.34 µg a.s./L.

The second study (Bruns 2013) was performed according to the currently valid guideline OECD 221 (2006) including two measurement variables, frond number and frond area. As the study was designed to mimic the exposure of a prolonged outdoor study, the total study duration was longer than what is specified in the guideline. This was done to obtain 6-week effect data for Lemna – a species that was not able to grow outdoors under pond study conditions. Beside the 6-week endpoints, effect data were calculated on a weekly basis. Thus, the first 7 days of this study are in accordance with the current guideline and can be considered as a fully valid study without restrictions. The obtained 7-day endpoints can be used in the risk assessment. The lowest E_rC_{50} of 1.08 µg a.s./L is very close to, but slightly lower than the calculated E_rC_{50} of 1.34 µg/L from the old study.

The third study was done with IMS+MPR OD 400, which was the representative formulation in the Annex I Renewal process of iodosulfuron-methyl-sodium (containing, beside iodosulfuron-methyl-sodium, the safener mefenpyr-diethyl). An E_rC_{50} of 8.4 µg formulation/L was derived from the test results. This refers to 0.74 µg iodosulfuron a.s./L.
In their Conclusion on iodosulfuron (EFSA Journal 2016;14(4)) EFSA has performed the macrophyte risk assessment for the representative formulation Hussar OD with the endpoint from the formulation study only (instead of using an endpoint derived with the tech. a.s. as test substance). It is worth noting that the formulation has a very low content of iodosulfuron-methyl sodium (less than 9%), therefore the extrapolation of the toxicity of the whole mixture to the active substance only is less accurate than a test with the active substance itself. Consequently, for the aquatic macrophyte risk assessment for other mixture formulations containing additional active substances and/or other safeners this endpoint is neither considered appropriate due to the nature of the tested material, nor is it considered necessary for precaution to ensure a sufficient conservatism.

Overall, it is proposed that the new fully valid and according to current state of the science performed 7-day Lemna-study supersedes the old 14-day study which was based on frond counts solely. Consequently the new 7-day E_rC_{50} of 1.08 µg a.s./L is used in the tier 1 risk assessment for aquatic plants.

A multispecies outdoor growth inhibition study (Hoberg, 2011) together with the related 6-week Lemna test originally was conducted in order to obtain dose-response relationships (EC_{50} values) for species other than Lemna and using those endpoints to build a species sensitivity distribution (SSD), finally delivering an HC_5 for the refined aquatic plant risk assessment.
The outdoor and large scale test design had been chosen as previous experiments had revealed that most macrophyte species do not perform well under lab conditions under lab conditions. Algal infestation, artificial illumination and slow growth even in the controls were the main issues.
The outdoor study was not designed as a mesocosm and not to deliver an overall NOEC. Spacing of test concentrations and numbers of replicates were chosen to cover a wide range of concentrations, instead of using narrow spacing and many replicates around the level of the expected NOEC. Therefore, the derivation of an NOEAEC (0.27 µg a.s./L) that has been done by EFSA and its use in the refined aquatic plant

risk assessment with additional assessment factor is considered not appropriate by the notifier.
While EFSA concluded that the study results should not be used for a species sensitivity distribution (SSD) analysis and calculation of statistically valid HC_5, the study nevertheless gives valuable information to compare the sensitivity of the different tested species within the test and relative to Lemna:
The multispecies outdoor pond study had been started with ten species. Glyceria maxima were removed from the study on exposure day 29 due to generally poor health in all treated and control ponds. Thus, the evaluation was done with the remaining nine species. Lemna has been tested as the 10th species in the 6-week laboratory study mentioned above. The studies led to a broad range of EC_{50}-figures from 0.5 µg a.s./L (6 wk E_rC_{50} (leaf dry weight) Salvinia) up to greater than 61 µg a.s./L. With regard to NOECs, Salvinia, Potamogeton and Elodea were most sensitive in the multispecies test design.

Review comments

In the current risk assessment for JME-HER 12 OD the same approach is followed as in Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL). Here for the clarity of report accepted endpoints are listed. For detailed information please, refer to Core Assessment of Atlantis 12 OD.

In the opinion of ZRMS-PL the following endpoints can be considered in the risk assessment for a.s. - iodosulfuron-methyl-sodium

First Tier:
7 d ErC_{50}=0.74 µg a.s./L with AF of 10 (laboratory study) → RAC = 0.074 µg a.s./L)

It is notable that the higher tier endpoints provided in the EFSA conclusion ends up to the slightly lower RAC-values than the first Tier RAC of 0.074 or 0.108 µg a.s./L:
NOEAEC = 0.27 µg a.s./L (measured initial concentration) with AF of 3 → RAC = 0.09 µg a.s./L
NOEAEC = 0.16 µg a.s./L (geomean measured concentration) with AF of 3 → RAC = 0.053 µg a.s./L

However, the geomean approach with the the three valid Lemna laboratory studies in EFSA LoEP by Christ & Ruff (1997), Bruns (2013), and Dorgerloh (2004) from endpoints (7d ErC50) of 1.34, 1.08 and 0.74 µg a.s./L-
geomean 7 d ErC50 = 1.02 µg a.s./L with AF of 10 (laboratory study) → RAC = 0.102 µg a.s./L
If only a.s. studies are included: the geomean 7 d ErC50 of 1.34 and 1.08 would be 1.20 µg a.s./L and the RAC = 0.12 µg/L.
The geomean approach is in line with the recommondations of EFSA Aquatic Guidance Document , 2013 and also included in the last EFSA Guidane document, June 2019.

The sensitivity of Salvinia, Potamogeton and Elodea relative to Lemna is discussed below:

Which is the most sensitive species …

… based on 6-week NOEC?
The 6-week-Lemna test was conducted at iodosulfuron concentrations of 0.1, 0.2, 0.4, 0.8 and 1.6 µg a.s./L. The lowest concentrations of the outdoor growth inhibition study with macrophytes were 0.25, 0.63 and 1.6 µg a.s./L. A survey of NOECs and concentrations tested in both studies is given in Table 9.5-6.
Table 9.5-6 shows that the NOECs for all four species Lemna, Salvinia, Elodea and Potamogeton are very close and give no clear indication which species is the most sensitive to iodosulfuron:

For Potamogeton, a NOEC of 0.25 µg a.s./L was reported, while for Lemna the NOEC over the whole 6-weeks period was 0.4 µg a.s./L. However, due to the nature of the NOEC endpoint, these figures do not show that Potamogeton is more sensitive to iodosulfuron-methyl-sodium than Lemna:
NOECs are defined as highest tested concentration where no effect was observed. They depend on the actually chosen test concentrations, and do not give information whether at slightly higher concentrations

an effect would have occurred. The "highest possible NOEC", meaning the highest concentration at which no effect would occur, would be somewhere between the NOEC and the next higher actually tested concentration.
For Lemna the next higher concentration in the test was 0.8 µg a.s./L. Thus, the "highest possible NOEC" would have been between 0.4 and 0.8 µg/L.
For Potamogeton the next higher test concentration where effects were observed was 0.63 µg a.s./L. Accordingly, with differently chosen test concentrations, in the range of 0.25 and 0.63 µg a.s./L both species could have shown the same sensitivity, or even reverse - Lemna more sensitive than Potamogeton.

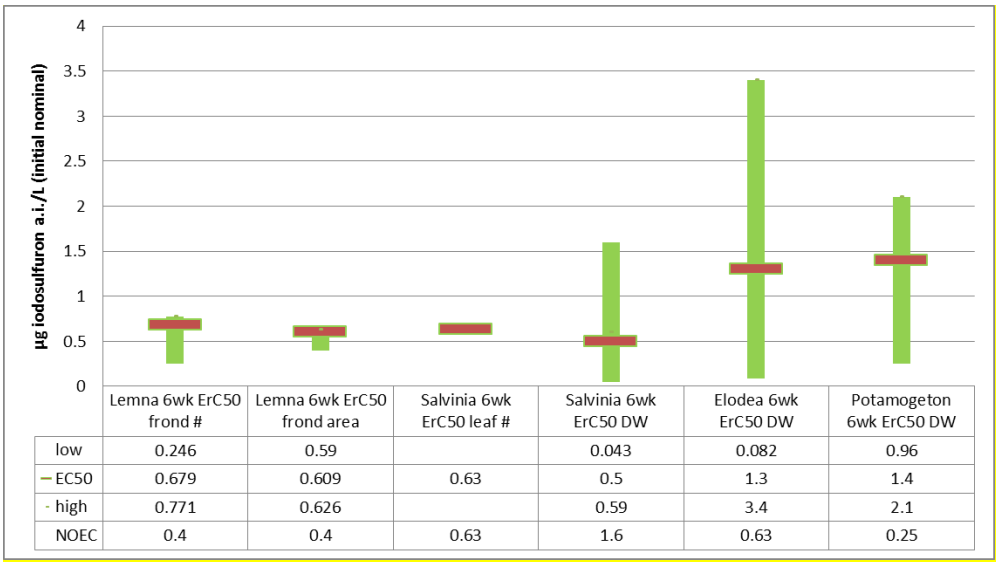
Table 9.5-6: ***Survey of 6-week-NOECs (in µg/L) for Lemna and the three most sensitive macrophyte species. The respective NOEC is printed in bold. Concentrations in brackets have not been included in the respective test.***

Lemna	***Salvinia***	***Elodea***	***Potamogeton***
0.1	*(0.1)*	*(0.1)*	*(0.1)*
0.2	*(0.2)*	*(0.2)*	*(0.2)*
(0.25)	*0.25*	*0.25*	***0.25***
0.4	*(0.4)*	*(0.4)*	*(0.4)*
(0.63)	***0.63***	***0.63***	*0.63*
0.8	*(0.8)*	*(0.8)*	*0.8*
1.6	*1.6*	*1.6*	*1.6*

Green cells (in black-white-presentation: medium grey): concentration included in respective test, but no effect.
Red cells (in black-white-presentation: dark grey): concentration included in respective test, significant effect.
White cells: concentration not included in respective test, concentration below NOEC.
Yellow cells (in black-white-presentation: light grey): concentration not included in respective test, concentration above NOEC.

… based on 6-weeks E_rC_{50}?
The lowest E_rC_{50} derived from the 6-week pond study for the macrophytes is 0.54 µ a.s./L, derived for Salvinia minima. This endpoint is only slightly lower than the 6-week E_rC_{50} value derived for Lemna gibba (0.609 and 0.679 µg a.s./L, for frond area and frond no., respectively). The species with the next higher E_rC_{50} value was Elodea with an E_rC_{50} of 1.3 µg a.s./L. Obviously, Lemna is the second most sensitive species out of ten species tested in the two tests, with an endpoint very near to the most sensitive species Salvinia minima.
Considering that the Salvinia endpoint has an extreme control variability (CV = 79.4%), it seems not justified to put emphasis on the slight difference of 0.1 µg/L between Salvinia and Lemna and to consider one more sensitive than the other. The similarity of Salvinia and Lemna becomes even more obvious, when the 6-week E_rC_{50} values together with their 95% confidence limits are compared:

In Figure 9.5-1 6-week- E_rC_{50} values for the 4 sensitive species are shown, together with their 95% confidence limits. For Lemna confidence limits are in a very narrow range, while for the other species Salvinia, Elodea and Potamogeton wide ranges were found, all showing a complete overlap with the E_rC_{50} confidence limits for Lemna.
This analysis visualizes that Salvinia and Lemna can be regarded equally sensitive to iodosulfuron-methyl-sodium.



	Lemna 6wk ErC50 frond #	Lemna 6wk ErC50 frond area	Salvinia 6wk ErC50 leaf #	Salvinia 6wk ErC50 DW	Elodea 6wk ErC50 DW	Potamogeton 6wk ErC50 DW
low	0.246	0.59		0.043	0.082	0.96
EC50	0.679	0.609	0.63	0.5	1.3	1.4
high	0.771	0.626		0.59	3.4	2.1
NOEC	0.4	0.4	0.63	1.6	0.63	0.25

Figure 9.5-1: ***Lowest 6-week E_rC_{50}-figures for Lemna and the three most sensitive macrophyte species. The range of 95% confidence limits is given as green bars.***

Conclusion

Neither the comparison of 6-week-E_rC_{50}-figures nor the interpretation of NOEC-levels give a clear indication, that one of the species tested in the macrophyte pond study is more sensitive to iodosulfuron-methyl-sodium than Lemna. On the other hand, it is shown that Lemna is clearly at the left hand side of the species sensitivity distribution.

In conclusion, the macrophyte pond study in the risk assessment for the current formulation should be considered as supplemental information, which supports that Lemna is clearly among the most sensitive species to iodosulfuron, and that a risk assessment based on Lemna is fully protective also for other macrophyte species.

Therefore, and as for Lemna by far the most comprehensive and reliable data set is available, it is justified to base the aquatic macrophyte risk assessment for iodosulfuron-methyl-sodium on the Tier 1 endpoint derived with Lemna.

Review comments:
zRMS agree that *Lemna sp.* is the most sensitive species for exposure for the iodosulfuron-methyl.

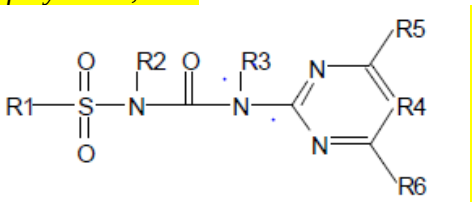
Iodosulfuron-methyl-sodium metabolites, where no test data are available

As the dossier for Renewal of approval for iodosulfuron-methyl-sodium had been submitted shortly before the implementation of the Aquatic Guidance Document (EFSA:3290 (2013), the complete risk assessment in the review process was done according to the "old" guidance SANCO/3268/2001-rev. 4 (final), 17 October 2002. Following this guidance, the risk assessment for metabolites where no test data were available was based on the endpoint of the parent compound, reduced by an additional safety factor of 10.
These "surrogate endpoints" used in the risk assessment were not listed as EU agreed toxicity endpoints for any metabolite in the "EFSA Conclusion on Iodosulfuron-methyl-sodium" (EFSA Journal 2016;14(4)), but just noted in the respective risk assessment tables.
The risk assessment for the present submission has to follow the requirements and approaches of the "new" Aquatic Guidance Document (EFSA:3290 (2013). Therefore, also the approach for metabolites where no

test data are available and no EU agreed toxicity endpoint has been defined, is revised according to this guidance.

The approach for metabolite risk assessment refers to part 10.2.4 decision scheme of the Aquatic Guidance Document (EFSA:3290 (2013)). The decision scheme is followed step by step.

***Step 1:** none of the studies with the active substance is adequate for assessing the potential effect of the metabolites: ⇨ step 3.*
***Step 3:** As mentioned in the Aquatic Guidance Document, toxophores for major classes of PPP have been identified ([1]Sinclair, 2009), for sulfonylureas, it is:*



On this basis, it is considered that metabolites AE F075736, AE F145741, AE F145740, AE 0002166, AE F161778 and AE 0014966 still contain the toxophore (⇨step 4). The other metabolites (BCS CW81253, AE 0000119, AE F059411, AE0034855, AE 1234964, AE F159737 and AE F154781) have lost it (⇨step 6).
***Step 4**: Identify the species or taxonomic group determining the lowest tier 1 $RAC_{sw,ac}$ for the active substance. Is the acute metabolite $L(E)C_{50}$ > 10 times the a.s. $L(E)C_{50}$ (on a molar basis)?*
The active substance is not acutely toxic on fish and daphnia. Consequently it is proposed to use the macrophyte endpoint to compare the level of effects of the parent and the metabolites even though it is not considered as an acute endpoint.
This approach shows that only AE F075736 EC_{50} is NOT greater than 10 times the a.s. EC_{50} (on a molar basis).
*AE F075736 ⇨ **step 5**, i.e. risk assessment is performed with available data on macrophytes (Lemna) as the most sensitive organism. All other metabolites ⇨ **step 6**, i.e. risk assessment will address all taxonomic groups with parent endpoints when no study was performed with the metabolite.*

Iodosulfuron metabolite AE F075736: Refined risk assessment for aquatic macrophytes

Metabolite AE F075736 of iodosulfuron-methyl-sodium is identical to the active substance metsulfuron-methyl. The approval of this active substance in accordance with Regulation (EC) No 1107/2009 has been renewed in Reg. (EU) 2016/139 of 2 Feb 2016.
According to EFSA Journal 2016;14(4):4453 (EFSA conclusion of iodosulfuron) 2 studies are available describing the toxicity of AE F075736 to aquatic macrophytes (Lemna gibba). The study with the lower endpoints (E_rC_{50} = 0.57 µg/L; E_bC_{50} = 0.365 µg/L) EFSA has used in the risk assessment.

No study with these endpoints is owned or submitted by or even just known to Bayer, while the figures are identical to those listed as critical endpoints in the metsulfuron-methyl EFSA conclusion (EFSA Journal 2015;13(1):3936). Therefore, it is concluded that EFSA considers the study delivering the critical endpoints agreed for metsulfuron-methyl also as relevant for AE F075736.

Based on this study, a refined risk assessment has been agreed and described by EFSA in the Conclusions of the evaluation (Chapter 5) of EFSA Journal 2015;13(1):3936 (metsulfuron-methyl):

[1] CJ Sinclair PhD Thesis University of York Predicting the environmental fate and ecotoxicological and toxicological effects of pesticide transformation products https://www.researchgate.net/publication/235934684_Predicting_the_environmental_fate_and_ecotoxicological_and_toxicological_effects_of_pesticide_transformation_products - BCS documentation no. M-551653-01-1 - see Appendix 2, A.2.2.

"The experts agreed on the use of the 7-day TWA PECsw as a risk assessment refinement.

Furthermore, considering that a set of additional studies was available on aquatic macrophytes and all the Results showed Lemna to be the most sensitive macrophyte among the tested species, the experts also agreed to apply a lower assessment factor for the risk assessment. Overall, the experts agreed to use the endpoint for Lemna gibba and to use the 7-day TWA in combination with an assessment factor of 5."

To conclude, we propose to use the E_rC_{50} of 0.57 µg a.s./L for the risk assessment of metabolite AE F075736. This endpoint is from the study listed in EFSA Journal 2016;14(4):4453 (EFSA conclusion of iodosulfuron) and EFSA Journal 2015;13(1):3936 (EFSA conclusion of metsulfuron-methyl) as the appropriate study to be used. Furthermore, being a growth rate endpoint, using the E_rC_{50} for macrophytes is in line with the recommendations of the new aquatic guidance document (EFSA:3290 (2013)). If a refined risk assessment using the 7-day TWA PEC_{sw} is to be done, we follow the approach recommended in the EFSA Conclusion on metsulfuron of using the lower endpoint E_bC_{50} of 0.365 µg a.s./L from the same study, in combination with an assessment factor of 5.

Review comments

In current dossier zRMS follow approach taken in Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).

For Lemna sp., in case of using the endpoint ErC_{50} of 0.57 µg/L with AF of 10 should be used.
For metsulfuron-methyl during Pesticides Peer Review Meeting 115 the experts agreed to use AF 5 only in combination with the Lemna E_bC_{50} endpoint of 0.365 µg/L.

Mesosulfuron-methyl

Table 9.5-7: Justification for new endpoints*

Species	***Substance***	***Exposure System***	***Justification***
Lemna gibba	*BCS-CV14885*	*7 d, s*	*Metabolite BCS-CV14885 was agreed devoid of biological activity on aquatic plant based on extensive structure-activity-relationship considerations (cf. RAR MCP Vol.3 B.9 (PPP), pages 18-23). Nevertheless, a simplistic risk assessment PECsw FOCUS Step 2 vs. surrogate parent endpoint was adopted by EFSA to conclude "A low risk to aquatic organisms was identified for all pertinent surface water metabolites of mesosulfuron-methyl for all the representative uses."* *Using this approach, the aquatic risk assessment is not passed for newer FOCUSsw model versions (v3.1 and higher), as model update led to change in PECsw of BCS-CV14885 now exceeding of the surrogate RAC value.* *A Lemna 7d growth inhibition test on BCS-CV14885 was therefore performed to generate a measured endpoint in replace of the surrogate value, which is essential to pass the EFSA proposed numeric risk assessment.*
Lemna gibba	*Mesosulfuron-methyl*	*Higher tier: refined exposure test* *Design 1:* *2 peaks lasting 24h*	*New peak-exposure studies on Lemna gibba were performed with mesosulfuron to support the refinement options presented in this dossier. The need for further information to address the risk to aquatic plants was stated in the EFSA conclusion on mesosulfuron (EFSA Journal 2016;14(10):4584).**

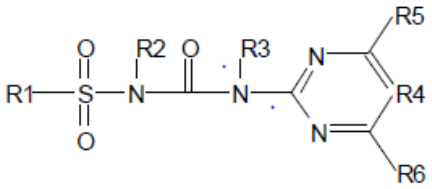
Species	***Substance***	***Exposure System***	***Justification***
		on day 0 and 3. *Test duration 7 d* *Design 2:* *2 peaks lasting 24h on day 0 and 7.* *Test duration 14 d*	

Mesosulfuron-methyl metabolites, where no test data are available

As the dossier for Renewal of approval for mesosulfuron-methyl had been submitted shortly before the implementation of the Aquatic Guidance Document (EFSA:3290 (2013), the complete risk assessment in the review process was done according to the "old" guidance SANCO/3268/2001-rev. 4 (final), 17 October 2002. Following this guidance, the risk assessment for metabolites where no test data were available was based on the endpoint of the parent compound, reduced by an additional safety factor of 10.
These "surrogate endpoints" used in the risk assessment were not listed as EU agreed toxicity endpoints for any metabolite in the "EFSA Conclusion on Mesosulfuron-methyl" (EFSA Journal 2016;14(10)), but just noted in the respective risk assessment tables.
The risk assessment for the present submission has to follow the requirements and approaches of the "new" Aquatic Guidance Document (EFSA:3290 (2013). Therefore, also the approach for metabolites where no test data are available and no EU agreed toxicity endpoint has been defined, is revised according to this guidance.

The approach for metabolite risk assessment refers to part 10.2.4 decision scheme of the Aquatic Guidance Document (EFSA:3290 (2013)). The decision scheme is followed step by step.

Step 1: *none of the studies with the active substance is adequate for assessing the potential effect of the metabolites: ⇨ step 3.*
Step 3: *As mentioned in the Aquatic Guidance Document, toxophores for major classes of PPP have been identified ([2]Sinclair, 2009), for sulfonylureas, it is:*



On this basis, it is considered that metabolites AE F154851, AE F160459 and AE F160460 still contain the toxophore. The other metabolites (AE F099095, AE F092944, AE F140584, AE F147447, BCS-CV14885 and BCS-CO60720) have lost it.
However, this basic assessment can be refined with information on the herbicidal activity and on the toxicity on the most sensitive aquatic organisms (macrophytes). The herbicidal activity tests performed with AE F154851, AE F160459, AE F160460, AE F099095, AE F092944, AE F140584 and AE F147447 (cf. RAR MCA Vol 3 B.9: RMS comment on page 180) and BCS-CV14885 (KCA 8.6.1 /02 and KCA 8.6.1 /03) showed that these metabolites have no activity or an activity 10 to 100 times lower than the active substance.
Moreover, AE F154851, the metabolite displaying the lowest E_rC_{50} on macrophytes (0.11 mg/L) is 65 times less toxic to Lemna than the active substance.
Therefore, it can be concluded that all metabolites have lost the toxophore ⇨ step 6, i.e. risk assessment

[2] CJ Sinclair PhD Thesis University of York, Predicting the environmental fate and ecotoxicological and toxicological effects of pesticide transformation products https://www.researchgate.net/publication/235934684_Predicting_the_environmental_fate_and_ecotoxicological_and_toxicological_effects_of_pesticide_transformation_products - BCS documentation no. M-551653-01-1 - see Appendix A 2.2.

will address all taxonomic groups with parent endpoints when no study was performed with the metabolite.

Review comments
zRMS agrees with the Applicant decision scheme for metabolites according to Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters EFSA Journal 2013;11(7):3290, point: 10.2.4.

9.5.2 Risk assessment

~~Not relevant. See point 9.5.1.~~

Methodology of stepwise risk assessment

The evaluation of the risk for aquatic and sediment-dwelling organisms was performed in accordance with the recommendations of the "Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters in the context of Regulation (EC) No 1107/2009", as provided by the Commission Services (SANTE-2015-00080, 15 January 2015). (Cited as EFSA Aquatic Guidance Document or "AGD" in the following pages.)

Following the Technical Guidelines on the format of the dRR (SANCO/6895/2009 rev 2.2) the risk envelope concept exploits the idea that the risk assessment for several use groups can be simplified by focusing on the group with worst-case characteristics as a representative for all other use groups.
This concept is also followed in the present submission – worst case critical uses are assessed to cover also less critical uses with similar characteristics. Refinements are performed to the level at which the assessment for the critical use is passed, while intermediate steps only relevant for less critical uses are not presented. However, in cases where a reviewer does not agree to refinement steps presented by the notifier, this might lead situations where unnecessarily severe risk mitigation measures are applied to less critical uses. In this case, adaptation of the risk assessment for less critical uses may be necessary.

Via stepwise procedure as follows, a comprehensive risk assessment was established for product IMS+MSM+MPR OD 42 (2+10+30), the different active substances contained therein, and their corresponding relevant metabolites. Each assessment of individual components is followed by a combined toxicity assessment, considering the two active substances and the active metabolite AE F075736:

- *As a first step of the assessment, a **spray-drift assessment for the formulated product** is presented, based on the measured formulation endpoints for each organism group.*
- *As an **MDR calculation** indicates concentration additive toxicity behaviour of the formulation, any further risk assessment considerations and refinements are made on the level of the individual active components.*
- *At a **screening level**, a "generic risk envelope approach" is presented for FOCUS steps 1 and 2. For the inactive metabolites, all risk assessments for aquatic organisms are passed at this stage without any refinement and even if worst case PECsw values are considered. Therefore, to simplify the assessment, only the maximum registered application rate and overall worst case exposure situation (application all year round, no crop interception) relevant for the compound in any product supported by Bayer AG in Europe is adressed.*
- *An AGD **Tier 1** risk assessment is performed based on the accurate GAP and FOCUS Step 3, where risk assessment is not passed at the before screening level. For the present product and uses, this applies only for the group of aquatic macrophytes, on which all further risk assessments will concentrate.*

Tier 1 assessment could resolve the majority of critical use scenarios of the present product; however this conclusion requires a regulatory acceptance of TWA-based approaches in the risk assessment. As current lack of agreed final guidance may lead into formal rejection of such approach by some regulators, despite of notifier's provision of sound scientific justification for applicability demonstration, alternative higher tier level risk assessments are provided in addition:

- *Refinement based on AGD option **Tier 2C via experimental testing** of representative time-variable exposure patterns, and comparison of the FOCUSsw predicted exposure patterns vs. the tested representative patterns.*

- *Refinement based on AGD option **Tier 2C via TKTD effect modelling (in-silico virtual laboratory testing)** of the time-variable exposure patterns predicted in $FOCUS_{sw}$ calculations according to EFSA Scientific Opinion (2018)[3] on Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms.*

- *Refinement based on AGD option **Tier 3 via population effect modelling for macrophytes growing in exposed FOCUS surface water bodies.***

All TKTD modelling approaches presented here are based on the Lemna model by Schmitt et al. (2013) [cf. Appendix A3.4(a) of this dRR], which has been evaluated by EFSA's working panel. In their Scientific Opinion, in the section on Evaluation of the application in risk assessment of this model, the experts concluded as follows:

"The model seems to work well for the sulfonyl-urea compound and the validation data as presented in Schmitt et al., 2013, but the model should be validated on herbicides with other modes of action. Summarising, the Lemna model appears suitable for use in risk assessment to evaluate effects of time-variable exposure on Lemna growth."

All aspects identified by EFSA to require further attention have been picked up in the respective modelling reports to the present submission.

For those risk assessment options relying on the timecourse output of the $FOCUS_{sw}$ exposure model, additional simulations for an extended period (20 years instead of 1 year) of scenario weather are provided as a confirmatory information, taking into account specific recent reviewer's concerns over year-on-year variability.

The refined risk assessments by purpose follow a strategy of redundancy in procedures, aiming to clearly demonstrate safe use via the presentation of several alternative options leading to consistent conclusions. In recent product evaluations, the notifier experienced differing procedural preferences for refinements and acceptance criteria applied by national reviewers. As final clarification on the EFSA Aquatic Guidance Document is not yet available at the time of dossier authoring, a choice of options following state of the art science and addressing known concerns will therefore be presented.

A tabular overview of the tiered approach and the outcome of each risk assessment are presented at the end of this chapter, together with the overall conclusions (9.5.3).

[3] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2018. Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA Journal 2018;16(8):5377, 188 pp. https://doi.org/10.2903/j.efsa.2018.5377

Mechanistic background of population effect modelling: Adverse outcome pathway (AOP) for sulfonylurea herbicides

Extensive research over the last decades by industry and academia has led to a deep molecular level understanding of the biological effects of the active substances used in the present formulation, with both mesosulfuron-methyl and iodosulfuron-methyl-sodium being members of the sulfonylurea chemical class of herbicides.
Based on this detailed biochemical information and aiming to provide fundamental mechanistic insight into the aquatic macrophyte risk due to the present product, a pathway scheme [Figure 2] has been established that illustrates key events which interconnect the aquatic exposure with the assessment relevant effects on population level. Such approach is based on elements of the «Adverse Outcome Pathways (AOP) » concept[4,5] and the scheme template of the AOP Wiki website[6], being amended for preceding exposure aspects:

(1) After a sulfonylurea substance enters surface water, as a first key event of relevance for possible effects, uptake will occur from the dissolved state into the macrophyte organism. Due to high polarity and water solubility, transport can be assumed as a diffusion controlled equilibrium process. The rate constant for exchange between external and internal substance can be calculated from laboratory study data via TK modelling approaches.

(2) Once inside the organism, a specific Molecular Initiating Event [MIE] has been identified responsible for the component's biological activity: sulfonylurea-type herbicides form a highly selective, non-covalent bonding to the anabolic enzyme acetolactate synthase (ALS, EC 2.2.1.6)[7]. This enzyme catalyses a reaction step from pyruvate / 2-ketobutyrate to 2-acetolactate / 2-acetobutyrate, which are key intermediates within the synthesis pathways of the branched-chain amino acids valine, leucine, and isoleucine. Recently, high resolution crystal structures of exemplary enzyme-sulfonylurea complexes could be studied in detail[8]: As the binding site is located inside a molecular channel required for substrate transport to the enzyme active center, the presence of a sulfonylurea component results in a temporal non-competitive interruption of the enzyme operation.

(3) On cellular level, ALS blockage by the sulfonylurea component leads into an imbalance of enzyme substrates vs. downstream products. From the observation that plant growth inhibition of sulfonylurea herbicides can entirely be reversed by supplementation with branched-chain amino acids[9], it is concluded that the key event of relevance for adverse effects is to be seen in the development of intracellular deficiency of these particular downstream products. As amino acids are essential building blocks for anabolic protein synthesis, their shortage will slow down de-novo biosynthesis. On a macroscopic level, cell proliferation will hereby be impaired to a degree dependent on the severity and duration of the ALS enzyme blockage.

[4] Ankley et al. (2010): ADVERSE OUTCOME PATHWAYS: A CONCEPTUAL FRAMEWORK TO SUPPORT ECOTOXICOLOGY RESEARCH AND RISK ASSESSMENT. Environmental Toxicology and Chemistry, Vol. 29, No. 3, pp. 730–741, 2010.

[5] OECD ENV/JM/MONO(2016)12: USERS' HANDBOOK SUPPLEMENT TO THE GUIDANCE DOCUMENT FOR DEVELOPING AND ASSESSING AOPs. Series on Testing & Assessment No. 233, Series on Adverse Outcome Pathways No. 1. Version 14 February 2018.
[available online free of charge at: https://one.oecd.org/document/ENV/JM/MONO(2016)12/en/pdf)

[6] Society for the Advancement of Adverse Outcome Pathways (SAAOP): Collaborative Adverse Outcome Pathway Wiki (AOP-Wiki) [accessible online free of charge at: https://aopwiki.org/]

[7] Acetolactate synthase (ALS, EC 2.2.1.6) is also known as acetohydroxy acid synthase (AHAS – former code EC 4.1.3.18c)

[8] McCourt et al. (2005): Elucidating the Specificity of Binding of Sulfonylurea Herbicides to Acetohydroxyacid Synthase. *Biochemistry* **2005,** *44,* 2330-2338

[9] e.g. Ray (1984): Site of Action of Chlorsulfuron. Plant Physiol. (1984) 75, 827-831

(4) Severity and duration of the ALS enzyme blockage will be a function of the concentration and timecourse of substance presence in the water body. Macrophyte internal substance concentration - and in consequence its enzyme-bound state equilibrium - will follow the external water phase concentration in both directions, as given by the exchange rate constant.

[Sulfonylurea substance detoxification via plant metabolism processes may represent an additional route of dissipation, which was identified of relevance in particular for herbicide tolerant crops varieties. In the present context of aquatic macrophyte risk assessment, however, such route can be conservatively ignored since risk assessment will focus on the most sensitive organism, likely not capable of a rapid substance detoxification.]

(5) On individual organism level, slowdown of de-novo protein synthesis shows expression as a slow-down of plant biomass generation, i.e. a reduction of growth and propagation rate compared to an unexposed organism. In consequence of the above mode of action, effects on organism level will only become manifest during phases of active growth with a prevailing high demand for anabolic building blocks[10].

(6) Adverse Outcome [AO] of relevance for risk assessment in case of macrophytes are negative effects on population level[11], i.e. a decrease in population growth rate leading into reduction of population biomass of an exposed vs. an unexposed population. Effect expression can be expected to dynamically follow the actual aquatic exposure. A short time delay will occur given by the rate of uptake/excretion into and out of the organism, and by the time until a deficiency in - or a reconstitution of - the cellular amino acid balance is developed.

Such population growth effects can be directly assayed for defined exposure situations in the laboratory.The most sensitive macrophyte species for sulfonylurea herbicides is Lemna and standard tests with this organism are performed with populations that increase by vegetative reproduction. Since in the test system Lemna is maintained at conditions fostering optimum (exponential) growth, such test design will provoke maximized effects for the present mode of action (worst-case approach).

For more complex exposure patterns and / or for an additional consideration of modulating environmental factors leading to non-optimal growth conditions, population effect modelling systems are a valuable tool.

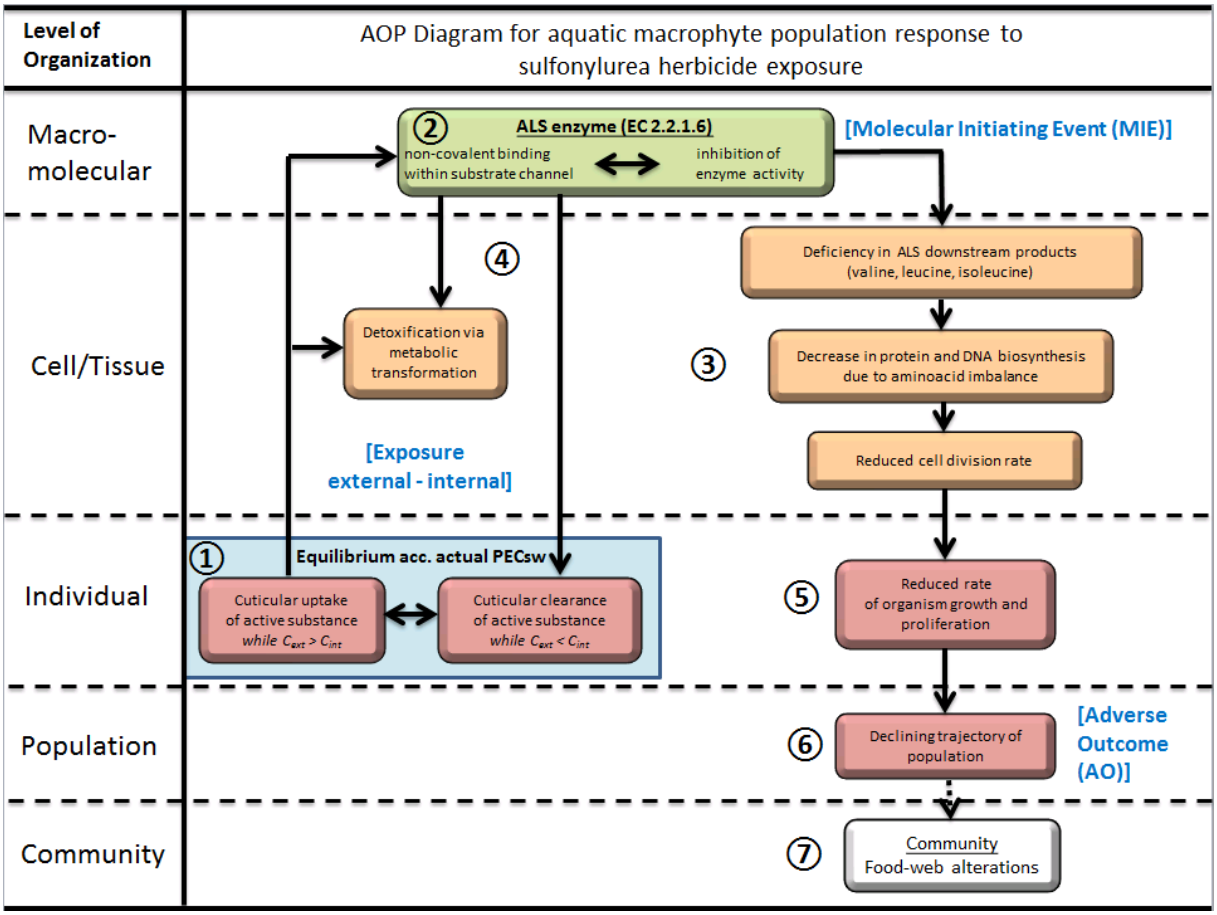
(7) Effects on community level could occur indirectly via food-web alterations, as a consequence of severe and long-lasting depression of macrophyte population growth. Due to the above mode of action, development of such effect would require a significant exposure over long time.

In summary, both the Molecular Initiating Event and the subsequent Adverse Outcome Pathway lead to the same conclusion regarding assessment relevant effects: Sulfonylurea class compounds do not produce an irreversible (lethal) threshold event. They just lead to temporary decrease of macrophyte growth and proliferation rate. The degree and duration of population level response will be a dynamic function of the exposure concentration over time.
Any evaluation based on laboratory study data will provide a most conservative risk assessment, since in these studies the test organisms are maintained under optimum growth conditions fostering most pronounced substance effect for this mode of action. Population effect modelling provides a valuable tool for investigation of population response on differing exposure situations. By considering variation of growth

[10] This is a substance class property well-known also from agricultural practice, i.e. effective weed control requires the product to be used in a phase of active growth of the weeds to be controlled.
[11] See also EFSA Aquatic Guidance Document, Chapter 5.4 - Table 12: The aquatic key drivers and their ecological entity to be protected as proposed in EFSA PPR Panel (2010a) and the current standard aquatic test species related to these key drivers (Commission Regulation (EU) 283/2013)

relevant environmental factors, it also enables to study population responses under non-optimal growing conditions (e.g. lower temperatures).

Figure 2: ALS inhibition [Molecular Initiating Event - MIE] after exposure to sulfonylurea class herbicides leading to growth depression of aquatic macrophyte populations [Adverse Outcome - AO]



Review comments

In current dossier for JME-HER 12 OD the same approach is taken as in Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).

1. The Applicant proposed to use in the risk assessment a PEC 7d-twa. However The risk assessment based on PECsw twa at STEP 3 was not considered acceptable by zRMS -PL.
Therefore, the risk assessment based on max PECsw STEP 1-4 values and with 7 d ErC_{50} of 1.29 µg/L, is considered acceptable.
2. A pulsed dose study with *Lemna gibba* submitted with EPAT analysis was not suitable for Risk assessment purposes. Therefore, 2C higher Tier approaches , was also not evaluated in the current dossier.
3. Applicant presented the Tier 3- TK-TD modelling in order to resolve the failing scenarios There were several uncertainties highlighted with the pulsed dose study and EPAT analysis thus in current risk assessment this approach would not be considered.

9.5.2.1 Spray drift exposure assessment for the formulated product - IMS+MSM+MPR OD 42 (2+10+30)

As a first step of the assessment, a simple "spray-drift only"- assessment is presented for the formulated product, based on the measured endpoints for each organism group, and exposure being calculated based on Rautmann drift values:

Table 9.5-8: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for IMS+MSM+MPR OD 42 (2+10+30) for each organism group based on Screening level (drift only) calculations for the use in cereals – 1.5 L prod./ha (Use group E)

Group		***Fish acute***	***Inverteb. acute***	***Algae***	***Aquatic macrophyte***
Test species		*Oncorhynchus mykiss*	*Daphnia magna*	*Pseudokirchneriella subcapitata*	*Lemna gibba*
Endpoint		LC_{50}	EC_{50}	E_rC_{50}	E_rC_{50}
(µg/L)		*8830*	*7600*	*6710*	*88.4*
AF		*100*	*100*	*10*	*10*
RAC (µg/L)		*88.3*	*76*	*671*	*8.84*
Drift only	***PEC $_{gl\text{-}max}$ (µg/L)***				
no buffer					
0 % drift reduction	*13.85*	*0.16*	*0.18*	*0.02*	***1.57***
50% drift reduction	*6.925*				*0.78*
5 meters buffer					
0 % drift reduction	*2.85*				*0.32*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold***

Conclusion: *In a screening level risk assessment for 1.5 L product/ha (use group E), measures for drift exposure mitigation equivalent to a 5 m buffer zone or a use of 50% drift reducing spray equipment would be required to pass the risk assessment for aquatic macrophytes.*
This simplistic screening conclusion is however subject to higher tiered assessments on the basis of the individual active substances, which allow for more detailed and sophisticated risk analysis and the consideration of further possible entry routes, presented in the subsequent sections here below.
For less critical uses the screening level risk assessment would be passed without drift exposure mitigation. In case higher tier assessments on the basis of individual active substances are not considered to overrule the conclusion of this screening assessment, formulation risk assessment should be expanded for the lower use

rates, to avoid unnecessarily severe mitigation measures for these less critical uses.

9.5.2.2 MDR calculation for the formulated product - IMS+MSM+MPR OD 42 (2+10+30)

To-check plausibility of the hypothesis that concentration-additive toxicity of the individual components applies for the present active substances and formulation, measured toxicity of the formulation on the most sensitive organism (driver of the risk assessment) is compared to the expected toxicity for this organism when predicted via concentration-addition (Finney calculation). This is performed using the MDR approach as defined in the EFSA Aquatic Guidance document (page 33):

Table 9.5-9: Calculation of the acute mixed toxicity of IMS+MSM+MPR OD 42 (2+10+30) to Lemna according to Finney additivity assumption

	Iodosulfuron-methyl-sodium	***Mesosulfuron-methyl***	***Formulation***	
Content within the product [%] as tested	*0.21*	*1.06*	*-*	*-*
Effects on aquatic plants				
ErC_{50} [µg/L]	~~*1.08*~~ *0.74*	*1.29*	*Expected*	*0.0011*
			Measured	*0.0884*
			MDR (Model deviation ratio)	*1.082*

The MDR is 1.082 clearly falling into the threshold corridor between 0.2 and 5 defined in the Aquatic Guidance document as criterion for the conclusion of concentration additive toxicity behaviour of a formulation.

In consequence, any further risk assessment considerations and refinements can safely be made on the level of the individual active components. Where required, toxicity of a mixture (e.g. the formulation, or a combination of substances simultaneously present in a surface water body) can be described as the arithmetic sum of individual toxicity contributions ($RQ_{mix} = \sum RQ_i$).

This approach will be applied in all subsequent assessments.

Review comments
zRMS agree with the MDR calculation presented above.

9.5.2.3 Screening Level: Risk envelope assessment based on FOCUS Steps 1-2, all active substances and metabolites

In this step, the risk is assessed substance by substance including all metabolites which may potentially enter surface water, for all groups of organisms. The assessment considers all possible entry routes to surface water (drift, run-off, drainage), with exposure calculated on screening level (FOCUS Step 1-2) for the generic risk envelope use pattern (use group A) covering all possible uses.

Iodosulfuron-methyl-sodium and metabolites

Table 9.5-10: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium for each organism group based on FOCUS Steps 1, 2 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		**Aquatic plants**				
Test species		**Lemna gibba**				
Endpoint		**E_rC_{50}**	**NOEAEC (Higher tier)**	**NOEAEC (Higher tier)**	**Geomean E_rC50**	**Geomean E_rC50**
(µg/L)		**0.74***	**0.27****	**0.16****	**1.02*****	**1.20*****
AF		**10**	**3**	**3**	**10**	**10**
RAC (µg/L)		**0.074**	**0.09**	**0.053**	**0.10**	**0.12**
FOCUS Scenario	**PEC $_{gl-max}$ (µg/L)**					
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)						
	3.2832	**44.37**	**36.48**	**61.94**	**32.83**	**27.36**
Step 2 (risk envelope approach: 10 g/ha, year-round use, no crop interception)						
N-Europe	*0.6491*	**8.77**	**7.21**	**12.24**	**6.49**	**5.40**
S-Europe	*0.5348*	**7.22**				

** the endpoint used in EU review report (2016). Study was done with IMS+MPR OD400, which was the representative formulation in the Annex I Renewal process of iodosulfuron-methyl-sodium*
*** A modified outdoor exposure study, this RAC is used in the final risk assessment (EFSA Conclusion 2016)*
**** Geomean approach*

For aquatic plants PEC/RAC values are >1 at STEP 1-2 calculations and considering all toxicity endpoints, indicating an unacceptable risk for Lemna sp. Further refinement with consideration the PEC_{sw} values at STEP 3 calculations is needed.

Review comments
zRMS agrees with the provided endpoints and calculations. PEC/RAC values are >1 at STEP 1-2 for aquatic plants, indicating an unacceptable risk for *Lemna* sp. Further refinement with consideration the PECsw values at STEP 3 calculations is needed.

Table 9.5-11: ***Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F075736 for macrophytes based on FOCUS Steps 1, 2 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).***

Note: according to EFSA aquatic guidance document, the risk assessment for metabolites with the toxophore of the parent substance has to be performed on the most sensitive organisms only (i.e. Lemna in this specific case)

Group		***Aquatic plants***
Test species		***Lemna gibba***
Endpoint		E_rC_{50}
(µg/L)		*0.57*
AF		*10*
RAC (µg/L)		*0.057*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***	
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)		
	3.7303	***65.44***
Step 2 (risk envelope approach: 10 g/ha, year-round use, no crop interception)		
N-Europe	*1.2631*	***22.15***
S-Europe	*1.0192*	***17.88***

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold**

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-11: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F145741 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*>10000*	*3840*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*>1000*	*384*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.4920	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.001*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-12: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F145740 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*>10000*	*>10000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*>1000*	*>1000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.6570	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-13: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE 0002166 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*>10000*	*20.3*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*>1000*	*2.03*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	1.1460	*< 0.001*	*0.001*	*< 0.001*	*0.001*	*< 0.001*	*0.564*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-14: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F161778 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*>10000*	*28.1*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*>1000*	*2.81*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.3821	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.136*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-15: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite BCS-CW81253 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		**Fish acute**	**Fish prolonged**	**Inverteb. acute**	**Inverteb. prolonged**	**Algae**	**Aquatic macrophyte**
Test species		**Oncorhynchus mykiss**	**Oncorhynchus mykiss**	**Daphnia magna**	**Daphnia magna**	**Pseudokirchneriella subcapitata**	**Lemna gibba**
Endpoint		LC_{50}	NOEC	EC_{50}	NOEC	E_rC_{50}	E_rC_{50}
(µg/L)		>100000	7790	>100000	7900	>10000	>10000
AF		100	10	100	10	10	10
RAC (µg/L)		>1000	779	>1000	790	>1000	>1000
FOCUS Scenario	**PEC $_{gl\text{-}max}$ (µg/L)**						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.7188	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-16: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE 0000119 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*ErC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*152*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*15.2*	*>10000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.4549	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.030*	*<0.001*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-17: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F059411 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*>100000*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*>10000*	*>10000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.5756	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-18: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE 0014966 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*ErC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*152*	*575*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*15.2*	*57.5*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.3684	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.024*	*0.006*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-19: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE 0034855 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*ErC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*152*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*15.2*	*>10000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.2648	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.017*	*<0.001*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-20: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE 1234964 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*ErC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*152*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*15.2*	*>10000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.0964	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.006*	*<0.001*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-21: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F159737 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata a***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*ErC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*152*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*15.2*	*>10000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.0925	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*0.006*	*<0.001*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-22: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F154781 for each organism group based on FOCUS Step 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*7790*	*>100000*	*7900*	*>10000*	*>10000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*779*	*>1000*	*790*	*>1000*	*>1000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 10 g/ha, year-round use, no crop interception)							
	0.0710	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-23: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl for each organism group based on FOCUS Steps 1, 2 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		**Fish acute**	**Fish prolonged**	**Inverteb. acute**	**Inverteb. prolonged**	**Algae**	**Aquatic plants**
Test species		**Oncorhynchus mykiss**	**Oncorhynchus mykiss**	**Daphnia magna**	**Daphnia magna**	**Pseudokirchneriella subcapitata**	**Lemna gibba**
Endpoint		LC_{50}	NOEC	EC_{50}	NOEC	E_rC_{50}	E_rC_{50}
(µg/L)		>100000	32000	>100000	1800	3990	1.29
AF		100	10	100	10	10	10
RAC (µg/L)		>1000	3200	>1000	180	399	0.129
FOCUS Scenario	**PEC $_{gl\text{-}max}$ (µg/L)**	-	-	-	-	-	-
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	4.7448	0.005	0.001	0.005	0.026	0.012	**36.78**
Step 2 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
N-Europe	2.3009	-	-	-	-	-	**17.84**
S-Europe	1.8652	-	-	-	-	-	**14.46**

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in ***bold***

Review comments

zRMS agrees with the provided endpoints and calculations.

PEC/RAC values are >1 at STEP 1-2 for aquatic plants, indicating an unacceptable risk for Lemna sp. Further refinement with consideration the PECsw values at STEP 3 calculations is needed.

Table 9.5-24: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite AE F154851 for each organism group based on FOCUS Steps 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic plants***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*32000*	*>100000*	*1800*	*38000*	*110*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*3200*	*>1000*	*180*	*3800*	*11*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	0.9504	*<0.01*	*0.001*	*<0.01*	*0.026*	*<0.001*	*0.86*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold***

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-25: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite AE F160459 for each organism group based on FOCUS Steps 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic plants***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*32000*	*>100000*	*1800*	*>100000*	*2600*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*3200*	*>1000*	*180*	*>10000*	*260*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	1.4744	*<0.015*	*0.001*	*<0.015*	*0.026*	*<0.0015*	*0.006*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold***

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-26: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite AE F099095 for each organism group based on FOCUS Steps 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic plants***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>70700*	*32000*	*>100000*	*1800*	*99100*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>707*	*3200*	*>1000*	*180*	*9910*	*>10000*
FOCUS Scenario	***$PEC_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	0.4104	*<0.001*	*0.001*	*<0.001*	*0.026*	*<0.001*	*<0.001*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold***

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-27: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite AE F092944 for each organism group based on FOCUS Steps 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic plants***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Scenedesmus subspicatus***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>97000*	*32000*	*>100000*	*24900*	*>100000*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>970*	*3200*	*>1000*	*2490*	*>10000*	*>10000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	0.1486	*<0.001*	*0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold***

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-28: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite AE F160460 for each organism group based on FOCUS Steps 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic plants***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*32000*	*>100000*	*1800*	*3990*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*3200*	*>1000*	*180*	*399*	*>10000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	0.8008	*<0.01*	*0.001*	*<0.01*	*0.026*	*0.012*	*<0.001*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold***

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-29: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite AE F140584 for each organism group based on FOCUS Steps 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic plants***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*32000*	*>100000*	*1800*	*3990*	*>10000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*3200*	*>1000*	*180*	*399*	*>1000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	0.2898	*<0.003*	*0.001*	*<0.003*	*0.026*	*0.012*	*<0.001*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold***

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-30: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite AE F147447 for each organism group based on FOCUS Steps 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic plants***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*32000*	*>100000*	*1800*	*>100000*	*>100000*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*>1000*	*3200*	*>1000*	*180*	*>10000*	*>10000*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	0.4868	*<0.001*	*0.001*	*<0.001*	*0.026*	*<0.001*	*<0.001*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold***

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-31: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite BCS-CV14885 for each organism group based on FOCUS Steps 1,2 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		**Fish acute**	**Fish prolonged**	**Inverteb. acute**	**Inverteb. prolonged**	**Algae**	**Aquatic plants**	
Test species		**Oncorhynchus mykiss**	**Oncorhynchus mykiss**	**Daphnia magna**	**Daphnia magna**	**Pseudokirchneri-ella subcapitata**	**Lemna gibba**	
Endpoint		LC_{50}	NOEC	EC_{50}	NOEC	E_rC_{50}	E_rC_{50}	E_rC_{50}
(µg/L)		>100000	32000	>100000	1800	>100000	1.29 [LoE surrogate endpoint]	>100000 [new measured end-point]
AF		100	10	100	10	10	10	10
RAC (µg/L)		>1000	3200	>1000	180	>10000	0.129	>10000
FOCUS Scenario	**PEC $_{gl\text{-}max}$ (µg/L)**							
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)								
	1.0542	<0.001	0.001	<0.001	0.026	<0.001	**8.172**	<0.001
Step 2								
N-Europe	0.5125						**3.97**	
S-Europe	0.4145						**3.21**	

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in ***bold***

Review comments
zRMS agrees with the provided endpoints and calculations.

Table 9.5-32: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl metabolite BCS-CO60720 for each organism group based on FOCUS Steps 1 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A).

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic plants***
Test species		***Oncorhynchus mykiss***	***Oncorhynchus mykiss***	***Daphnia magna***	***Daphnia magna***	***Pseudokirchneriella subcapitata***	***Lemna gibba***
Endpoint		*LC_{50}*	*NOEC*	*EC_{50}*	*NOEC*	*E_rC_{50}*	*E_rC_{50}*
(µg/L)		*>100000*	*32000*	*>100000*	*1800*	*> 10000*	*> 11800*
AF		*100*	*10*	*100*	*10*	*10*	*10*
RAC (µg/L)		*> 1000*	*3200*	*> 1000*	*180*	*> 1000*	*> 1180*
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***						
Step 1 (risk envelope approach: 15 g/ha, year-round use, no crop interception)							
	0.5446	*<0.005*	*0.001*	*<0.005*	*0.026*	*<0.001*	*<0.001*

*AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in **bold**.*

Review comments
zRMS agrees with the provided endpoints and calculations.

Combined risk assessment - Screening Level

According to current requirements when a product contains more than one active substance, an additional assessment on combined toxicity risk has to be presented. It is considered that a quantitative assessment according to concentration addition is however not needed if one of the following points applies:

- *The risk assessment for all active substances in the product passes with a high margin of safety.*
- *One active substance clearly drives the risk assessment.*

These conditions are assessed following a step-wise approach. A detailed description of this approach is presented in a separate document (Gladbach, A., Ebeling, M., Weyers, A., 2016, M-571377-02-1). The assessment is based on RQ values (risk quotient RQ = PEC/RAC). Note that RQ values which actually pass the risk assessment are used and if different mitigation measures result in an acceptable risk, the highest RQ value per individual substance is used.

1st step: Margin of safety
Condition: all RQ values are < 1/n (n = number active substances in the mixture).

2nd step: Risk per fraction
Condition: One active substance contributes to ≥ 90% of the predicted combined toxicity of the product.
Assessment: The contribution of each individual active substance to the combined toxicity (risk per fraction, rpf) is estimated based on the following equation:

The $rpf_{a.s.1} = RQ_{a..s.1} / (RQ_{a.s.1} + RQ_{a.s.2} ... + RQ_{a..s.i})$ *estimation is based on RQ values from the same FOCUS Step to assure comparability.*

3rd step: RQ_{MIX} calculation
Condition: The combined risk is acceptable when $RQ_{MIX} \leq 1$.
Assessment: The combined toxicity risk (RQ_{MIX}) with concentration-addition for aquatic organisms is estimated according to the following formula:

$$RQ_{mix} = \sum_{i=1}^{n} \frac{PEC_i}{RAC_i}$$

Table 9.5-33: Combined toxicity risk assessment for aquatic organisms – Screening Tier, FOCUS Step 1-2 for generic risk envelope (use group A)

Group		Fish, acute	Fish, prolonged	Invertebrates, acute	Invertebrates, prolonged	Algae	Aquatic macrophytes
RQ values[1)]	MSM	0.005	0.001	0.005	0.026	0.012	17.84[2)]
	IMS	< 0.003	0.004	< 0.003	0.004	0.216	6.01[2)]
	AE F075736	-	-	-	-	-	22.15[2)]
Trigger		1	1	1	1	1	1
1/n		0.50	0.50	0.50	0.50	0.50	0.33
1st step: All RQ < 1/n		yes	yes	yes	yes	yes	Not profitable at screening level, as risk envelope assessment remained unresolved for individual substances MSM, IMS, and AE F075736. **Combined assessment for macrophytes is therefore presented at Tier 1, Tier 2, and Tier 3 for the accurate GAP below.**
2nd step: RPF_{max}		Not needed	Not needed	Not needed	Not needed	Not needed	
3rd step: RQ_{mix}		Not needed	Not needed	Not needed	Not needed	Not needed	

MSM = mesosulfuron-methyl, IMS = iodosulfuron-methyl-sodium
1) Based on FOCUS step 1 calculations
2) Based on FOCUS Step 2 calculations

Combined toxicity risk is resolved for all aquatic organism groups other than macrophytes via a simple FOCUS Step 1-2 based screening level asessment for the generic risk envelope use pattern (use group A), covering all uses.

Overall conclusion from Screening Level risk assessment:

Assuming a highly conservative generic exposure situation (FOCUS Step 1-2 exposure simulations for risk envelope use pattern covering all uses, use group A), risk assessment including combination toxicity could be resolved for all groups of aquatic organisms other than macrophytes. Acceptable risk was also demonstrated for all biologically inactive metabolites (i.e. other than AE F075736), for all groups of organisms.

Subsequent assessment steps will therefore concentrate on the biologically active components of relevance for this formulation, i.e. iodosulfuron-methyl-sodium,

metabolite AE F075736, and mesosulfuron-methyl.

9.5.2.4 9.5.2.4 Tier 1: Accurate GAP assessment based on FOCUS Step 3, all active substances and metabolite AE F075736

In the following section the risk assessment will focus on macrophytes, as only for this group the risk was left unresolved after the FOCUS Step 1-2 based screening level assessments presented before. Tier 1 level risk assessment will start from FOCUS step 3 exposure calculations for the three critical GAP situations of use groups B-D covering all intended product uses of IMS+MSM+MPR OD 42 (2+10+30) in countries requiring FOCUSsw calculations.

The Tier 1 risk assessment will follow the recommendations of the EFSA Aquatic guidance document for chronic risk assessment, as found visualised in "Decision scheme B" on guidance page 15, and further outlined in the subsequent text of pages 15-16. In the chronic risk assessment, the RAC_{sw} is, in the first instance, compared with the $PEC_{sw;max}$, and under certain conditions with a $PEC_{sw;twa}$ (the predicted time-weighted average (TWA) concentration in surface water). A decision scheme on when to use the $PEC_{sw;max}$ or the $PEC_{sw;twa}$ in the chronic RA is presented in the guidance and will be applied below to the components to be addressed.

Iodosulfuron-methyl-sodium

TWA applicability check and justification: *The AGD proposes the use of a time weighted average (TWA) concentration in the risk assessment of aquatic organisms in order to address a possible discrepancy between the duration of an exposure event and the exposure period in the corresponding effect study. Specific prerequisites have to be fulfilled before the use of a TWA approach can be justified. In* ***Appendix A 3.1****, it is discussed for the active ingredient Iodosulfuron-methyl-sodium and the test organism Lemna gibba whether the $PEC_{sw,twa}$ can be compared to the $RAC_{sw,ch}$ in the risk assessment using the TWA approach by (i) showing reciprocity for this species compound combination, (ii) using a decision scheme presented in the EFSA AGD and (iii) direct proof of conservatism of the TWA approach itself. All lines of evidence are supported by biological data derived from static exposure or peak exposure studies and/or by simulations (in silico experiments) using a mechanistic Lemna model. As a crucial first step, it is shown that linear reciprocity can be ascertained for the combination of Lemna and Iodosulfuron-methyl-sodium forming the basis of the TWA approach. Furthermore, the EFSA AGD decision scheme clearly allows for the use of TWA in the case presented here, putting a special focus on the evaluation of onset of effects and potential delayed effects. An additional alternative 'direct proof of conservatism' test presented by the notifier compares effect levels from short-term and long-term studies, and also confirms that the TWA approach in the case of Lemna and Iodosulfuron-methyl sodium can be regarded as conservative and therefore protective.*

Table 9.5-34: Overview on methodologies used to demonstrate the applicability of the TWA approach: (for detailed assessment see Appendix A 3.1 (a): Isemer-Kellner, R.; Heine, S.; 2017; M-607957-01-1)

Criteria addressed / methodology		*Analysis of biological data*	*In silico experiment*
Reciprocity		*X*	*-*
Decision scheme	*Generic parts*	*X*	*-*

	Early onset of effects	*X*	*X*
	Delayed effects	*X*	*X*
Direct proof of conservatism		*Graphical data comparison between constant exposure and pulse exposure studies.*	

As an overall conclusion, it is considered justified to base the Tier 1 risk assessment for Lemna gibba and Iodosulfuron-methyl-sodium on 7d time-weighted average concentrations ($PEC_{sw,\ 7d\text{-}twa}$).

Risk Assessment: *In the following, therefore both, a risk assessment based on $PEC_{sw,max}$ and a risk assessment based on $PEC_{sw,\ 7d\text{-}twa}$ will be shown side-by-side, as they are considered to represent alternative Tier 1 approaches applicable for iodosulfuron-methyl-sodium.*

Table 9.5-35: ***Aquatic organisms: acceptability of risk (PEC/RAC<1) for iodosulfuron-methyl-sodium for aquatic macrophytes based on FOCUS Step 3 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals.***

Group		***Aquatic plants***				
Test species		***Lemna gibba***				
Endpoint		***E_rC_{50}***	***NOEAEC (Higher tier)***	***NOEAEC (Higher tier)***	***Geomean E_rC50***	***Geomean E_rC50***
(µg/L)		***0.74****	***0.27****	***0.16****	***1.02*****	***1.20****
AF		***10***	***3***	***3***	***10***	***10***
RAC (µg/L)		***0.074***	***0.09***	***0.053***	***0.10***	***0.12***
FOCUS Scenario	***$PEC_{gl\text{-}max}$ (µg/L)***					
use group B ***(end of winter to spring use on winter cereals / rate = 3 g/ha)***						
D1/ditch	*0.0197*	*0.266*	*0.219*	*0.372*	*0.197*	*0.164*
D1/stream	*0.0165*	*0.223*	*0.183*	*0.311*	*0.165*	*0.138*
D2/ditch	*0.1540*	***2.081***	***1.711***	***2.906***	***1.540***	***1.283***
D2/stream	*0.0962*	***1.300***	***1.069***	***1.815***	*0.962*	*0.802*
D3/ditch	*0.0191*	*0.258*	*0.212*	*0.360*	*0.191*	*0.159*
D4/pond	*0.0007*	*0.009*	*0.008*	*0.013*	*0.007*	*0.006*
D4/stream	*0.0144*	*0.195*	*0.160*	*0.272*	*0.144*	*0.120*

Group		***Aquatic plants***				
Test species		***Lemna gibba***				
D5/pond	*0.0007*	*0.009*	*0.008*	*0.013*	*0.007*	*0.006*
D5/stream	*0.0149*	*0.201*	*0.166*	*0.281*	*0.149*	*0.124*
D6/ditch	*0.0190*	*0.257*	*0.211*	*0.358*	*0.190*	*0.158*
R1/pond	*0.0007*	*0.009*	*0.008*	*0.013*	*0.007*	*0.006*
R1/stream	*0.0139*	*0.188*	*0.154*	*0.262*	*0.139*	*0.116*
R3/stream	*0.0428*	*0.578*	*0.476*	*0.808*	*0.428*	*0.357*
R4/stream	*0.0292*	*0.395*	*0.324*	*0.551*	*0.292*	*0.243*
use group B ***(end of winter to spring use on winter cereals / rate = 3 g/ha)*** ***– Refinement: exposure simulation based on field soil kinetics data***						
D1/ditch	*0.0198*	*0.268*	*0.220*	*0.374*	*0.198*	*0.165*
D1/stream	*0.0165*	*0.223*	*0.183*	*0.311*	*0.165*	*0.138*
D2/ditch	*0.1788*	***2.416***	***1.987***	***3.374***	***1.788***	***1.490***
D2/stream	*0.1119*	***1.512***	***1.243***	***2.111***	*1.119*	*0.933*
D3/ditch	*0.0191*	*0.258*	*0.212*	*0.360*	*0.191*	*0.159*
D4/pond	*0.0007*	*0.009*	*0.008*	*0.013*	*0.007*	*0.006*
D4/stream	*0.0144*	*0.195*	*0.160*	*0.272*	*0.144*	*0.120*
D5/pond	*0.0007*	*0.009*	*0.008*	*0.013*	*0.007*	*0.006*
D5/stream	*0.0149*	*0.201*	*0.166*	*0.281*	*0.149*	*0.124*
D6/ditch	*0.0190*	*0.257*	*0.211*	*0.358*	*0.190*	*0.158*
R1/pond	*0.0007*	*0.009*	*0.008*	*0.013*	*0.007*	*0.006*
R1/stream	*0.0149*	*0.201*	*0.166*	*0.281*	*0.149*	*0.124*
R3/stream	*0.0453*	*0.612*	*0.503*	*0.855*	*0.453*	*0.378*
R4/stream	*0.0314*	*0.424*	*0.349*	*0.592*	*0.314*	*0.262*

** the endpoint used in EU review report (2016). Study was done with IMS+MPR OD400, which was the representative formulation in the Annex I Renewal process of iodosulfuron-methyl-sodium*
*** A modified outdoor exposure study, this RAC is used in the final risk assessment*

*** *Geomean approach*

For three lowest toxicity endpoints : E_rC_{50} of 0.74 µg/L, NOEAC of 0.16 µg/L and NOAEC of 0.27 µg/L, the acceptable risk cannot be demonstrated for Central Zone relevant scenarios, only in case of R3 stream scenario for winter cereals (use B, autumn use in winter cereals).
The Applicant calculated FOCUS Step 4 values for the failing scenarios; FOCUS Step 4 values were calculated for all scenarios for completeness, however for D1 and D2 scenarios it is not possible to mitigate using FOCUS Step 4 as the main input is from drainage.
As such, the ZRMS has only considered the R3 scenario in the calculations.

Therefore, ZRMS provided the risk assessment for R3 scenario (winter cereals, autum use, 2 g a.s.ha) with consideration of PEC_{sw} STEP 4 values for Lemna sp following the risk assessment provided in Core Assessment for Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

Metabolite AE F075736 of Iodosulfuron-methyl-sodium

This metabolite is also known as metsulfuron-methyl, another active substance having undergone EU review for Annex I inclusion. EFSA concluded[12] that the PEC_{twa} can be used for risk assessment, in combination with the E_bC_{50} endpoint and a safety factor of 5. As this procedure has been previously EU agreed, no further applicability check according to AGD decision scheme is presented here.

Risk Assessment: *In the following, therefore both, a risk assessment based on $PEC_{sw,max}$ and a risk assessment based on $PEC_{sw,\ 7d\text{-}twa}$ with associated RAC according EFSA will be shown side-by-side, as they are considered to represent alternative Tier 1 approaches applicable for metabolite AE F075736.*

Table 9.5-36: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F075736 for aquatic plants based on FOCUS Step 3 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals.

Group		***Aquatic plants***		***Aquatic plants[1)]***
Test species		***Lemna gibba***		***Lemna gibba***
Endpoint (µg/L)		E_rC_{50} 0.57		E_bC_{50} 0.365
AF		10		5
RAC (µg/L)		0.057		0.073
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***		***7-d PEC_{twa} (µg/L)***	

[12] EFSA (European Food Safety Authority), 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance metsulfuron-methyl. EFSA Journal 2015;13(1):3936, 106 pp. doi:10.2903/j.efsa.2015.3936

Group		***Aquatic plants***		***Aquatic plants[1)]***
use group B – FOCUS Step 3 ***(end of winter to spring use on winter cereals / rate = 3 g a.s./ha)***				
D1/ditch	*0.0348*	*0.611*	*0.0342*	*0.468*
D1/stream	*0.0282*	*0.495*	*0.0201*	*0.275*
D2/ditch	*0.1583*	***2.777***	*0.1122*	***1.537***
D2/stream	*0.1302*	***2.284***	*0.0697*	*0.955*
D3/ditch	*0.0053*	*0.093*	*0.0053*	*0.073*
D4/pond	*0.0123*	*0.216*	*0.0123*	*0.168*
D4/stream	*0.0065*	*0.114*	*0.0062*	*0.085*
D5/pond	*0.0024*	*0.042*	*0.0024*	*0.033*
D5/stream	*0.0013*	*0.023*	*0.0011*	*0.015*
D6/ditch	*0.0010*	*0.018*	*0.0010*	*0.014*
R1/pond	*0.0003*	*0.005*	*0.0003*	*0.004*
R1/stream	*0.0071*	*0.125*	*0.0004*	*0.005*
R3/stream	*0.0133*	*0.233*	*0.0009*	*0.012*
R4/stream	*0.0111*	*0.195*	*0.0013*	*0.018*
use group B – FOCUS Step 3 ***(end of winter to spring use on winter cereals / rate = 3 g/ha)*** ***– Refinement: exposure simulation based on field soil kinetics data***				
D1/ditch	*0.0156*	*0.274*	*0.0154*	*0.211*
D1/stream	*0.0134*	*0.235*	*0.0091*	*0.125*
D2/ditch	*0.0880*	***1.544***	*0.0618*	*0.847*
D2/stream	*0.0867*	***1.521***	*0.0442*	*0.605*
D3/ditch	*0.0002*	*0.004*	*0.0002*	*0.003*
D4/pond	*0.0006*	*0.011*	*0.0006*	*0.008*

Group		***Aquatic plants***		***Aquatic plants[1)]***
D4/stream	*0.0003*	*0.005*	*0.0003*	*0.004*
D5/pond	*0.0002*	*0.004*	*0.0002*	*0.003*
D5/stream	*0.0002*	*0.004*	*<0.0001*	*<0.001*
D6/ditch	*0.0003*	*0.005*	*0.0003*	*0.004*
R1/pond	*0.0002*	*0.004*	*0.0002*	*0.003*
R1/stream	*0.0040*	*0.070*	*0.0002*	*0.003*
R3/stream	*0.0090*	*0.158*	*0.0006*	*0.008*
R4/stream	*0.0062*	*0.109*	*0.0007*	*0.010*

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in ***bold***
[1)] according to EFSA conclusion; (EFSA Journal 2015;13(1):3936)

When the risk assessment is based on $PEC_{sw,\ max,}$ one FOCUS scenario is left unresolved (i.e. D2 ditch/stream) for the intended end of winter application in winter cereals, or two scenarios (i.e. D1 ditch/stream and D2 ditch/stream) for the intended autumn use. Scenario D2 can be resolved for the end of winter application in winter cereals, when applying assessment parameters and procedures as are EU agreed for metsulfuron-methyl, i.e. based on 7d-TWA PEC_{sw} with a dedicated RAC value, and a refined exposure assessment based on field soil kinetics data.
As demonstrated in the exposure simulations (see Efate section), exposure in the D1 and D2 scenarios is driven by the entry route drainage. Drainage entry cannot be mitigated by the options considered in FOCUS Landscape & Mitigation. Therefore, no additional assessment based on FOCUS Step 4 is deemed necessary here, as it would not exert effect on the D1 and D2 exceedances[13].
Overall, therefore for metabolite AE F075736 of iodosulfuron-methyl-sodium the risks are acceptable at Tier 1 level for all intended uses of the product in all European geoclimatic regions other than those represented by soil/climate scenario situations D1 and D2. Both of these scenarios are considered not representative in a Central Zone context.
A more in depth refined assessment of the potential risk for macrophytes posed by these scenario situations will be made in Section 9.5.2.7 of this document, as part of the Tier 3 level assessment.

Review comments:
We agree with the presented assessment and approach taken for metabolite AE F075736 of iodosulfuron-methyl-sodium.

For metabolite AE F075736 of iodosulfuron-methyl-sodium the risk is acceptable at Tier 1 level with PECsw STEP 3values for all intended uses of the product in Central Zone countries other than those represented by soil/climate scenario situations D1 and D2.Both of these scenarios are considered not representative in a Central Zone countries.
A more in depth refined assessment of the potential risk for macrophytes posed by these scenario situations will be made in Section 9.5.2.7 of this document, as part of the Tier

[13] For formal completeness, RQ calculations to FOCUS Step 4 PEC_{sw} values can be found in Appendix A 3.6 of the present document.

3 level assessment. This assessment was not evaluated by zRMS.

Mesosulfuron-methyl

TWA applicability check and justification: *The EFSA Aquatic Guidance Document (EFSA, 2013) proposes the use of a time weighted average (TWA) concentration in the risk assessment of aquatic organisms in order to address a possible discrepancy between the duration of an exposure event and the exposure period in the corresponding effect study. Specific prerequisites have to be fulfilled before the use of a TWA approach can be justified. In the full document presented in* ***Appendix A 3.1****, it is discussed for the active ingredient Mesosulfuron-methyl and the test organism Lemna gibba whether the* $PEC_{sw,twa}$ *can be compared to the* $RAC_{sw,ch}$ *in the risk assessment using the TWA approach by (i) showing reciprocity for this species compound combination, (ii) using a decision scheme presented in the EFSA AGD and (iii) direct proof of conservatism of the TWA approach itself. All lines of evidence are supported by biological data derived from static exposure or peak exposure studies and/or by simulations (in silico experiments) using a mechanistic Lemna model. As a crucial first step, it is shown that linear reciprocity can be ascertained for the combination of Lemna and Mesosulfuron-methyl forming the basis of the TWA approach. Furthermore, the EFSA AGD decision scheme clearly allows for the use of TWA in the case presented here, putting a special focus on the evaluation of onset of effects and potential delayed effects. An additional alternative direct test presented by the notifier also confirms that the TWA approach in the case of Lemna and Mesosulfuron-methyl can be regarded as conservative and therefore protective.*

Table 9.5-37: Overview on methodologies used to demonstrate the applicability of the TWA approach (for detailed assessment see Appendix A 3.1 (b): Sowig, P.; Herno, V.; Heine, S.; 2017; M-602786-01-1)

Criteria addressed / methodology		*Analysis of biological data*	*In silico experiment*
Reciprocity		*X*	*-*
Decision scheme	*Generic parts*	*X*	*-*
	Early onset of effects	*X*	*X*
	Delayed effects	*X*	*X*
Direct proof of conservatism		*Graphical data comparison between constant exposure and pulse exposure studies.*	

As an overall conclusion, it is considered justified to base the Tier 1 risk assessment for Lemna gibba and mesosulfuron-methyl on 7d time-weighted average concentrations ($PEC_{sw,\ 7d\text{-}twa}$*).*

Risk Assessment: *In consequence of the above, in the following therefore both, a risk assessment based on* $PEC_{sw,max}$ *and a risk assessment based on* $PEC_{sw,\ 7d\text{-}twa}$ *will be shown side-by-side, as they are considered to represent alternative Tier 1 approaches applicable for mesosulfuron-methyl.*

Table 9.5-38: ***Aquatic organisms: acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl for aquatic macrophytes based on FOCUS Step 3 calculations for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals.***

Group		***Aquatic plants***		~~***Aquatic plants***~~
Test species		***Lemna gibba***		~~***Lemna gibba***~~
Endpoint		E_rC_{50}		~~E_rC_{50}~~
(µg/L)		*1.29*		~~*1.29*~~
AF		*10*		~~*10*~~
RAC (µg/L)		*0.129*		~~*0.129*~~
FOCUS Scenario	***PEC $_{gl\text{-}max}$ (µg/L)***		***7-d PEC$_{twa}$ (µg/L)***	
use group B – FOCUS Step 3 (end of winter to spring use on winter cereals / rate = 15 g/ha)				
D1/ditch	*0.2187*	***1.695***	*0.1926*	~~***1.493***~~
D1/stream	*0.1410*	***1.093***	*0.1264*	~~*0.980*~~
D2/ditch	*1.6040*	***12.434***	*0.9150*	~~***7.093***~~
D2/stream	*1.0230*	***7.930***	*0.5414*	~~***4.197***~~
D3/ditch	*0.0982*	*0.761*	*0.0156*	~~*0.121*~~
D4/pond	*0.0412*	*0.319*	*0.0410*	~~*0.318*~~
D4/stream	*0.0770*	*0.597*	*0.0306*	~~*0.237*~~
D5/pond	*0.0198*	*0.153*	*0.0194*	~~*0.150*~~
D5/stream	*0.0827*	*0.641*	*0.0097*	~~*0.075*~~
D6/ditch	*0.1009*	*0.782*	*0.0133*	~~*0.103*~~
R1/pond	*0.0063*	*0.049*	*0.0059*	~~*0.046*~~
R1/stream	*0.1008*	*0.781*	*0.0099*	~~*0.077*~~
R3/stream	*0.3099*	***2.402***	*0.0217*	~~*0.168*~~
R4/stream	*0.2646*	***2.051***	*0.0321*	~~*0.249*~~

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in ***bold***

When the risk assessment is based on $PEC_{sw,\ max,}$ RQ values in excess of 1 are observed for several FOCUS scenarios: D1, D2, D4, D5, D6, R3, R4, depending on the use group considered. Alternatively applying an assessment based on 7d-TWA PEC_{sw}, scenarios D5, D6, R3, R4 can be resolved, whilst D-scenarios D1, D2, and D4 remain unresolved.

As demonstrated in the exposure simulations (see Efate section), specifically those finally unresolved scenarios (D1 ditch, D2 ditch/stream for the end of winter use, D1 ditch/stream, D2 ditch/stream, D4 pond stream/stream for the autumn use, and D1 ditch for spring use) are driven by the entry route drainage. Drainage entry cannot be mitigated by the options considered in FOCUS Landscape & Mitigation. Therefore, no additional assessment based on FOCUS Step 4 is deemed necessary here[14], as it would not exert effect on the D1, D2, D4 exceedances.

Overall, therefore for mesosulfuron-methyl the risks are acceptable at Tier 1 level for all intended uses of the product in European regions other than those represented by soil/climate scenario situations D1, D2, and D4. Thereof, scenarios D1 and D2 are considered not representative in a Central Zone context.

A more in depth refined assessment of the potential risk for macrophytes posed by these scenario situations will be made later in Section 9.5.2.1 of this document, as part of the Tier 3 level assessment.

Table 9.5-39: ***Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: winter cereals, 1 × 15 g mesosulfuron-methyl /ha, end of winter use***

Winter cereals, end of winter-spring use, 15 g a.s./ha	***Scenario***	***PECsw STEP 4 - mesosulfuron-methyl***						***PECsw / RAC*** *RAC = 0.129 µg/L*					
		PEC gl-max						***PEC gl-max***					
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*R3 Stream*	*0.3099*	*0.3099*	*0.3099*	*0.3099*	*0.1370*	*0.0710*	***2.402***	***2.402***	***2.402***	***2.402***	***1.062***	*0.550*
50 %		*0.3099*	*0.3099*	*0.3099*	*0.3099*	*0.1370*	*0.0710*	***2.402***	***2.402***	***2.402***	***2.402***	***1.062***	*0.550*

[14] For formal completeness, RQ calculations to FOCUS Step 4 PEC_{sw} values can be found in Appendix A 3.6 of the present document.

Winter cereals, end of winter-spring use, 15 g a.s./ha	***Scenario***	***PECsw STEP 4 - mesosulfuron-methyl***						***PECsw / RAC*** *RAC = 0.129 µg/L*					
		PEC gl-max						***PEC gl-max***					
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*
75 %		*0.3099*	*0.3099*	*0.3099*	*0.3099*	*0.1370*	*0.0710*	***2.402***	***2.402***	***2.402***	***2.402***	***1.062***	*0.550*
90 %		*0.3099*	*0.3099*	*0.3099*	*0.3099*	*0.1370*	*0.0710*	***2.402***	***2.402***	***2.402***	***2.402***	***1.062***	*0.550*
None	*R4 Stream*	*0.2646*	*0.2646*	*0.2646*	*0.2646*	*0.1203*	*0.0631*	***2.051***	***2.051***	***2.051***	***2.051***	*0.933*	*0.489*
50 %		*0.2646*	*0.2646*	*0.2646*	*0.2646*	*0.1203*	*0.0631*	***2.051***	***2.051***	***2.051***	***2.051***	*0.933*	*0.489*
75 %		*0.2646*	*0.2646*	*0.2646*	*0.2646*	*0.1203*	*0.0631*	***2.051***	***2.051***	***2.051***	***2.051***	*0.933*	*0.489*
90 %		*0.2646*	*0.2646*	*0.2646*	*0.2646*	*0.1203*	*0.0631*	***2.051***	***2.051***	***2.051***	***2.051***	*0.933*	*0.489*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Therfore, the risk for a.s. is acceptable for R3 scenario when 20 meter vegetative buffer zone will be implemented.
Therfore, the risk for a.s. is acceptable for R4 scenario when 10 meter vegetative buffer zone will be implemented.

Review comments:

The Applicant presented risk assessment for Winter cereals, end of winter-spring use, 15 g a.s./ha following the approach presented in Core Assessment for the Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

The R3 stream scenario is resolved when considering a 20 metre high buffer zone; the R4 scenario is resolved when considering a 10 metre low buffer zone.

Combined risk assessment - Tier 1 level

A combined toxicity risk assessment of biologically active components is presented here below, considering Iodosulfuron-methyl-sodium, metabolite AE F075736, and Mesosulfuron-methyl via the methodology of concentration addition, i.e. calculation of RQmix based the above individual substance assessment results.

As before in the assessments on individual substance level both, a risk assessment based on $PEC_{sw,max}$ and a risk assessment based on $PEC_{sw,\ 7d\text{-}twa}$ will be shown side-by-side, as these are considered justified alternative Tier 1 approaches with applicability for the present product demonstrated in details to fulfil respective AGD criteria.

Table 9.5-40: Combined toxicity assessment – aquatic macrophytes, Tier 1

	RQ values based on EU endpoints			***RQ_{MIX}***
Aquatic macrophytes	***IMS***	***AE F075736***	***MSM***	
use group B – FOCUS Step 3 (end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM)				
D1/ditch	*2.429*	*0.468*	*1.695*	***4.592***
D1/stream	*1.591*	*0.275*	*1.093*	***2.959***
D2/ditch	*16.052*	*1.537*	*12.434*	***30.023***
D2/stream	*10.185*	*0.955*	*7.930*	***19.07***
D3/ditch	*1.092*	*0.073*	*0.761*	***1.926***
D4/pond	*0.496*	*0.168*	*0.319*	*0.983*
D4/stream	*0.877*	*0.085*	*0.597*	***1.559***
D5/pond	*0.195*	*0.033*	*0.153*	*0.381*
D5/stream	*0.857*	*0.015*	*0.641*	***1.513***
D6/ditch	*1.053*	*0.014*	*0.782*	***1.849***
R1/pond	*0.062*	*0.004*	*0.049*	*0.115*
R1/stream	*0.974*	*0.005*	*0.781*	***1.76***
R3/stream	*2.992*	*0.012*	*2.402*	***5.406***
R4/stream	*2.464*	*0.018*	*2.051*	***4.533***

use group B – FOCUS Step 3

(end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM)
Refinement: exposure simulations for IMS and AE F075736 based on field soil kinetics data

D1/ditch	*0.268*	*0.211*	*1.695*	***2.174***
D1/stream	*0.223*	*0.125*	*1.093*	***1.441***
D2/ditch	***2.416***	*0.847*	*12.434*	***15.697***
D2/stream	***1.512***	*0.605*	*7.93*	***10.047***
D3/ditch	*0.258*	*0.003*	*0.761*	***1.022***
D4/pond	*0.009*	*0.008*	*0.319*	*0.336*
D4/stream	*0.195*	*0.004*	*0.597*	*0.796*
D5/pond	*0.009*	*0.003*	*0.153*	*0,165*
D5/stream	*0.201*	*<0.001*	*0.641*	*0.843*
D6/ditch	*0.257*	*0.004*	*0.782*	***1.043***
R1/pond	*0.009*	*0.003*	*0.049*	*0.061*
R1/stream	*0.201*	*0.003*	*0.781*	*0.985*
R3/stream	*0.612*	*0.008*	*2.402*	***3.022***
R4/stream	*0.424*	*0.010*	*2.051*	***2.485***

MSM = mesosulfuron-methyl, IMS = iodosulfuron-methyl-sodium

In case that reviewers for formal reason would not accept the proposed use of TWA approach for iodosulfuron-methyl-sodium and mesosulfuron-methyl, additionally runoff scenarios R3 stream and R4 stream would be left unresolved for use groups B and D at Tier 1[15]. These scenarios will therefore proactively be further addressed in the following, applying Aquatic Guidance Document Tier 2C methodology. These higher tier assessments may in reverse conclusion be seen a further confirmative evidence for correctness of the Tier 1 TWA approach assumptions.

Table 9.5-41: Combined toxicity assessment – aquatic macrophytes for R 3 and R4 senarios.

	RQ values based on EU endpoints			***RQ$_{MIX}$***
Aquatic macrophytes	***IMS***	***AE F075736***	***MSM***	
use group B (end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM)				
R3/stream	*0.255****	*0.012**	*0.550***	*0.817*
R4/stream	*0.179****	*0.018**	*0.489***	*0.686*

MSM = mesosulfuron-methyl, IMS = iodosulfuron-methyl-sodium
**STEP 3*

[15] Note for scenario D3 ditch, use group B, an RQmix <1 could be demonstrated not requiring TWA acceptance for IMS and MSM already via a field study-parameterised PECsw-simulation for IMS and AE F075736. For dossier simplification, therefore no follow-up at Tier 2C will be presented for this scenario situation.

*** 20 meter vegetative buffer strip*
**** 10 meter vegetative buffer strip*

For simplicity and comparability, all subsequent confirmatory higher tier effect assessments are consistently based on standard level exposure predictions (founded on laboratory soil degradation data, non-refined).

The combined toxicity for R4 scenario for application in autumn rate of 2 g /ha IMS + 10 g /ha MSM is considered acceptable when 20 high vegetative buffer zone will be applied.

The ZRMS provided the assessment of the combined chronic risk from the active substances and metabolite- AE F075736, taking into account in the calculations of RQ the following RAC values:RAC=0.074 ***µg/L*** *for IMS, RAC-0.057* ***µg/L*** *for AE F075736 and RAC - 0.129* ***µg/L*** *for MSM and max PEC_{sw} values calculated with FOCUS STEP 3-4.*

Table 9.5-42 ***:Combined toxicity assessment – aquatic macrophytes***

	RQ values based on EU endpoints			***RQ_{MIX}***
Aquatic macrophytes	***IMS***	***AE F075736***	***MSM***	
use group B – FOCUS Step 3 (end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM)				
D1/ditch	*0.266*	*0.611*	*1.695*	***2.572***
D1/stream	*0.223*	*0.495*	*1.093*	***1.811***
D2/ditch	*2.081*	*2.777*	*12.434*	***17.292***
D2/stream	*1.3*	*2.284*	*7.930*	***11.514***
D3/ditch	*0.258*	*0.093*	*0.761*	***1.112***
D4/pond	*0.009*	*0.216*	*0.319*	*0.544*
D4/stream	*0.195*	*0.114*	*0.597*	*0.906*
D5/pond	*0.009*	*0.042*	*0.153*	*0.204*
D5/stream	*0.201*	*0.023*	*0.641*	*0.865*
D6/ditch	*0.257*	*0.018*	*0.782*	***1.057***
R1/pond	*0.009*	*0.005*	*0.049*	*0.063*
R1/stream	*0.188*	*0.125*	*0.781*	***1.094***
R3/stream	*0.578*	*0.233*	*2.402*	***3.213***
R4/stream	*0.395*	*0.195*	*2.051*	***2.641***
use group B – FOCUS Step 3 (end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM) Refinement: exposure simulations for IMS and AE F075736 based on field soil kinetics data				

D1/ditch	*0.268*	*0.274*	*1.695*	***2.237***
D1/stream	*0.223*	*0.235*	*1.093*	***1.551***
D2/ditch	***2.416***	*1.544*	*12.434*	***16.394***
D2/stream	***1.512***	*1.521*	*7.93*	***10.963***
D3/ditch	*0.258*	*0.004*	*0.761*	***1.023***
D4/pond	*0.009*	*0.011*	*0.319*	*0.339*
D4/stream	*0.195*	*0.005*	*0.597*	*0.797*
D5/pond	*0.009*	*0.004*	*0.153*	*0.166*
D5/stream	*0.201*	*0.004*	*0.641*	*0.846*
D6/ditch	*0.257*	*0.005*	*0.782*	***1.044***
R1/pond	*0.009*	*0.004*	*0.049*	*0.062*
R1/stream	*0.201*	*0.07*	*0.781*	***1.052***
R3/stream	*0.612*	*0.158*	*2.402*	***3.172***
R4/stream	*0.424*	*0.109*	*2.051*	***2.584***

MSM = mesosulfuron-methyl, IMS = iodosulfuron-methyl-sodium
[§]For metabolite AE F075736 (= metsulfuron-methyl), ZRMS used E_rC_{50} value with AF=10 agreed at EU level.

Table 9.5-43: Combined toxicity assessment – aquatic macrophytes with consideration STEP 3-4 PECsw values

	RQ values based on EU endpoints			***RQ_{MIX}***
Aquatic macrophytes	***IMS***	***AE F075736***	***MSM***	
use group B (end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM)				
R3/stream	*0.255***	*0.104***	*0.550***	*0.909*
R4/stream	*0.179***	*0.088***	*0.489***	*0.756*
R1 stream	*0.077***	*0.125* *0.007 [1]*	*0.322***	*0.524*
D3 ditch	*0.035***	*0.093* *0.004 [1]*	*0.1325***	*0.2605*

MSM = mesosulfuron-methyl, IMS = iodosulfuron-methyl-sodium
STEP 3
*** 20 meter vegetative buffer strip*
**** 10 meter vegetative buffer strip*
[1] value with refined DT_{50}

Review comments:
The Applicant presented risk assessment for Winter cereals, end of winter-spring use, 15 g a.s./ha following the approach presented in Core Assessment for the Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

The combined toxicity for R1 (stream) and D3 scenarios for application of end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM is considered acceptable when low 10 meter vegetative buffer zone will be applied.

use group B

(end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM):

The product can be safely applied with no precautionary measures required for exposure mitigation in all European regions other than those represented by drainage scenarios D1 and D2. R 1 (stream) and D3 scenarios the product can be safely applied when:
- For R1 (stream) and D3 (ditch) 10 meter low vegetative buffer zone should be applied

9.5.2.5 Tier 2C: Higher-tier assessment based on refined exposure testing combined with exposure pattern analysis

Review comments:
zRMS agree the final conclusions presented in core assessment for the product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)). Therefore, zRMS does not consider further this study in the refinement for aquatic macrophytes.

It should be noted that the evaluation of the endpoints from the study Kuhl, K.; 2016; EBMMN160; M-577164-01-1 , for the active substance - mesosulfuron-methyl based on peak exposure were already evaluated in the dRR for the other formulations containing a.s.-mesosulfuron-methyl, for which UK was zRMS. All evaluation is available on platform Circa, Monolith, Ecotoxicology B9, ZRMS-UK, 2019.

This higher tier assessment addresses particularly those FOCUS scenarios that are characterized by pronounced time-variability of the exposure, and short-lasting exposure events such as drift or run-off entry. The procedure was recommended by the experts of the ELINK workshop[16] that took place in 2007, and is foreseen in the Aquatic Guidance Document as option Tier 2C, proposed by the PPR Panel of EFSA "to explore a higher tier RAC derivation on the basis of the refined exposure laboratory-AF approach if predicted (modelled) exposure profiles for edge-of-field surface waters differ considerably from exposure regimes in standard toxicity studies and if the PECsw;twa cannot be used in the chronic RA."

With regard to the present product, these characteristics apply in particular for the R3 stream and R4 stream scenarios (runoff-driven) failing Tier 1 assessment based on $PEC_{sw,max}$ for the active substance mesosulfuron-methyl, but being resolved with a large margin of safety when Tier 1 assessment is based on $PEC_{sw,twa}$.

Consequently, higher tier refinement options for R3 and R4 stream scenarios are evaluated at Tier 2C level in this section, confirmative to - or alternative for - the Tier 1 TWA solutions presented before. There will be no further attempt at this stage to refine the risk assessment of drainage-dominated scenarios, as for this entry route exposure variability over time is typically less pronounced and follows more complex patterns; these scenarios will be further addressed later at Tier 3 level (cf. Section 9.5.2.7).

The Tier 2C refined exposure approach is based on the concentration-time profiles of those FOCUS step 3 PEC_{sw} simulations used for assessment at Tier 1 before, and the results of refined exposure type laboratory tests studying the effects of a pulsed exposure on the most sensitive organism, Lemna gibba.

For the assessment, an exposure pattern is characterized by four properties which are

- *the PEC_{max},*
- *the number of peak events above the Tier 1 RAC,*
- *the duration of these peak events, and*
- *the interval between these peak events.*

A peak event is identified as such when a concentration in the exposure profile exceeds the relevant Tier 1 RAC value which in the case of mesosulfuron-methyl is 0.129 µg a.s./L (EU agreed endpoint of 1.29 µg/L, divided by standard assessment factor 10).

The exposure profiles for the entire FOCUS year of simulation are plotted graphically from the model

[16] Brock TCM, Alix A, Brown CD, Capri E, Gottesbüren BFF, Heimbach F, Lythgo CM, Schulz R and Streloke M (Eds), 2010a. Linking aquatic exposure and effects: risk assessment of pesticides. SETAC Press & CRC Press, Taylor & Francis Group, Boca Raton, FL, USA, 398 pp.

output files, and are amended with a numeric characterisation for event identification according to the above descriptors, extracted by the EPAT Exposure Profile Analysis Tool[17].

These characterised exposure patterns are then assessed versus the findings from refined exposure type tests, which studied the effects of two sequential pulse exposure events of mesosulfuron-methyl, for two test designs with different spacing intervals (new study: Kuhl, 2016; M-577164-01-1; detailed study summary see Appendix A 2.2.1.4; summary of study results see ***Błąd! Nie można odnaleźć źródła odwołania.****). As suggested in the EFSA Aquatic Guidance Document, Section 2.1.5, this test is performed with the tier 1 standard species that drives the aquatic risk (i.e. Lemna), and simulates a realistic worst-case exposure relative to that predicted for the edge-of-field. The RACs derived from the refined exposure toxicity tests should always be expressed in terms of peak exposure concentration in these tests, for comparison with the* $PEC_{sw,max.}$ *According to the EFSA Aquatic Guidance Document Table 7, for chronic risk assessment of plant, the* EC_{50} *is the relevant endpoint of the refined exposure toxicity test, and the RAC is calculated as* $EC_{50}/10$.

The results of this study are suitable to address three different peak exposure situations as predicted by FOCUS:

1. *A single peak exceeding the Tier 1 RAC: can be addressed with design 2, first week (study duration of 7 days with 24 h-exposure peak on d0) which delivered a peak-ErC50 of > 100 µg/L, resulting in a peak-RAC of > 10 µg/L.*
2. *Two peak events with short interval (approx. 3 days): can be addressed with design 1 (study duration of 7 days with 24 h-exposure peaks on d0 and d3) which delivered a peak-ErC50 of 10.9 µg /L, resulting in a peak-RAC of 1.09 µg/L. The stronger effects observed in this design compared to a single peak indicate that, for mesosulfuron-methyl, two peaks with short interval cannot be considered as being toxicologically independent.*
3. *Two peak events with longer interval (≥ 7 days): can be addressed with design 2 (study duration of 14 days with 24 h-exposure peaks on d0 and d7) which delivered a peak-ErC50 of > 100 µg/L, resulting in a peak-RAC of > 10 µg/L. With this design, it was demonstrated that toxicological independence of peaks is given if the interval between peaks is sufficiently long. To verify this statistically, the similarity of effect patterns following each of the 2 peaks was compared by running t-tests on paired samples (*$\alpha = 0.05$*). For all concentrations and all biological parameters (i.e. frond number and frond area), no statistically significant difference was observed between the growth rates of the 1st and the 2nd week.*

Table 9.5-44: Derivation of peak-RACs from the Lemna 2-peak study with mesosulfuron-methyl

Test species	***Test system***	***Test duration***	***Endpoint [µg as/L]***		***Peak-RAC [µg as/L]***	***Reference***
Lemna gibba (duck weed)	*growth inhibition, 2-peak exposure*	*7 d peaks on d0 & d3 [Design 1]*	E_rC_{50} *(days 0-7)*	*10.9 µg/L*	***1.09 µg/L***	*Kuhl, 2016, M-577164-01-1 (see Appendix A 2.2.1.4)*
		14 d peaks on d0 & d7 [Design 2]	E_rC_{50} *(days 0-7)*	*> 100.0 µg/L*	*> 10.0 µg/L*	
			E_rC_{50} *(days 7-14)*	*> 100.0 µg/L*	*> 10.0 µg/L*	

[17] Bastiansen, F., Nickisch, D., Wang, M. (2016): EPAT v. 1.1 – Exposure Pattern Analysis Tool. European Crop Protection Association (ECPA), Brussels. Program Manual: RIFCON GmbH Report No. R1520392. Program download: https://www.rifcon.de/files/downloads/EPAT_1.1.1_setup.exe.

It is worth noting that similar peak exposure studies are available as well for iodosulfuron-methyl-sodium and its metabolite AE F075736. The results are presented in Table 9.5-1 but are not repeated here, as no detailed discussion on these components is triggered in the context of the current product's Tier 2 C risk assessment; all applicable FOCUS scenarios were resolved at Tier 1 level already, and the combined risk assessment at Tier 2C is clearly dominated by mesosulfuron-methyl (see below). The studies are nevertheless part of the present submission and summaries can be found in Appendix 2.2.1.4, since they are used in context of the Tier 1 (TWA justification for iodosulfuron-methyl-sodium) and Tier 3 (population model calibration/validation) assessments.

Iodosulfuron-methyl-sodium

No Tier 2C refined assessment is presented for iodosulfuron-methyl-sodium use with the present product, as all FOCUS scenarios with an exposure situation addressable by this methodology (particularly runoff or drift entry to stream or ditch type water bodies) were found resolved already in the $PEC_{sw,max}$-based Tier 1 level assessment.

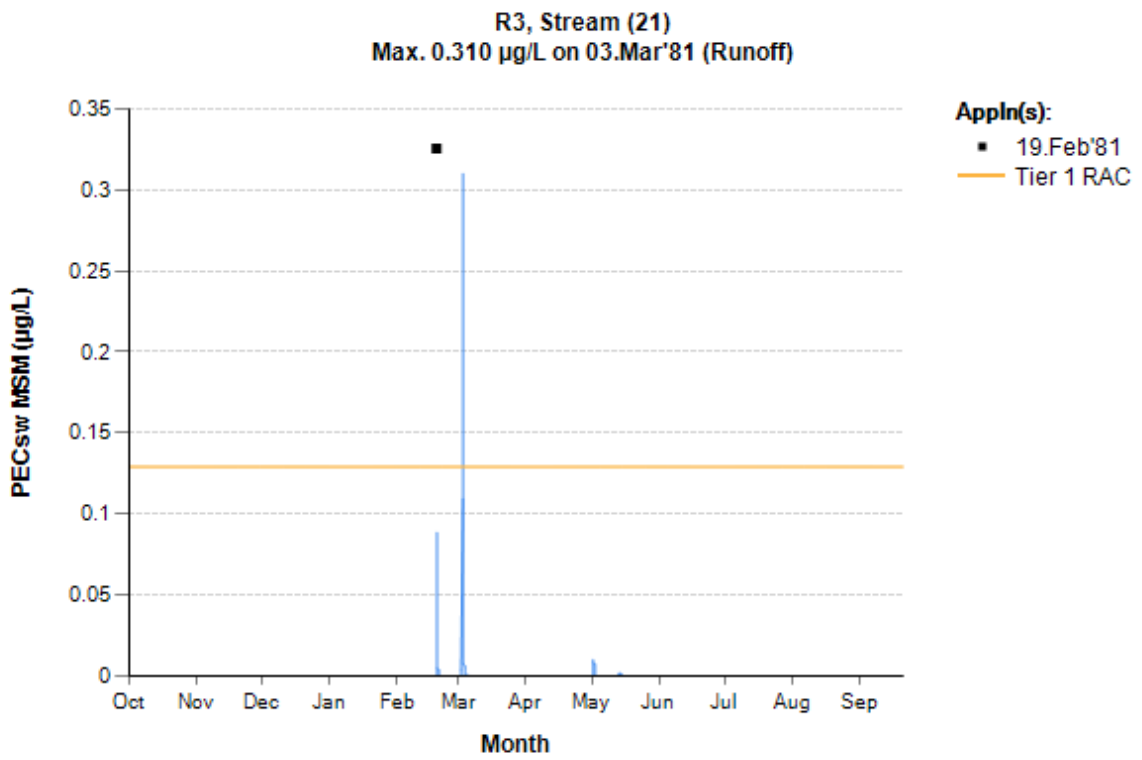
Metabolite AE F075736 of Iodosulfuron-methyl-sodium

No Tier 2C assessment is presented for metabolite AE F075736 of iodosulfuron-methyl-sodium for the present product, as all FOCUS scenarios with an exposure situation addressable by this methodology were found resolved already in the $PEC_{sw,max}$-based Tier 1 level assessment.

Mesosulfuron-methyl

Tier 2C refined assessment as described above is presented for R3 stream and R4 stream FOCUS scenarios for use groups B and D, alternative to or confirmatory for the TWA approach previously used to resolve these scenarios at Tier 1 level.
Graphs of the exposure profiles are taken from the FOCUSsw Step 3 calculations (see Part B - Section 8.9). Further and more detailed PECsw time course plots can be found provided in the respective modelling reports referenced in Part B - Section 8, Appendix 3.3.2.

use group B – FOCUS Scenario R3 stream:
*(end of winter to spring use on winter cereals / **rate = 15 g/ha MSM**)*



Tier 1-RAC = 0.129 µ/L

EPAT analysis:

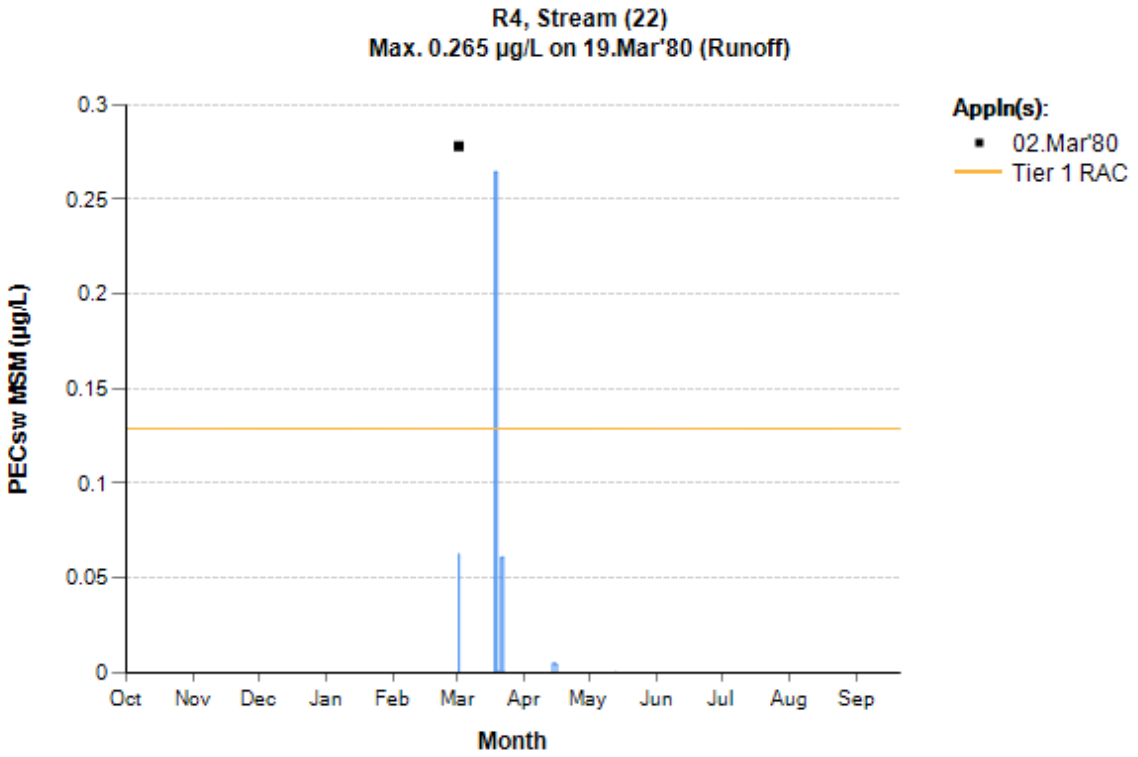
Compound	***PECmax [µg/L]***	***events above Tier 1 RAC***	***event duration above Tier 1 RAC [d]***	***interval betw. events above Tier 1 RAC [d]***	***Relevant peak-RAC from Lemna 2-peak study***		***RQ = PECmax / peakRAC***
					Study duration	***Peak-RAC [µg a.s./L]***	
Mesosulfuron-methyl	*0.3099*	*1 peak*	*0.5*	*not applicable*	*14 d peaks on d0 & d7*	*> 10.0 µg/L*	*< 0.03*

[event recognition threshold: 0.129 µg/L = Tier 1 RAC of mesosulfuron-methyl]

The PEC pattern of the FOCUS year consists of 1 prominent peak that reaches a maximum concentration of 0.3099 µg a.s./L which is well below the peak-RAC of > 10.0 µg a.s./L applicable for single or independent peaks. With the duration of 0.5 days the peak is shorter than the exposure of 1 day tested in the underlying refined exposure experiment.

Consequently, the risk to aquatic macrophytes arising from this peak is considered to be low, with a resulting RQ of < 0.03.

use group B – FOCUS Scenario R4 stream:
*(end of winter to spring use on winter cereals / **rate = 15 g/ha MSM**)*



Tier 1-RAC = 0.129 µ/L

EPAT analysis:

Compound	***PECmax [µg/L]***	***events above Tier 1 RAC***	***event duration above Tier 1 RAC [d]***	***interval betw. events above Tier 1 RAC [d]***	***Relevant peak-RAC from Lemna 2-peak study***		***RQ =*** *PECmax / peakRAC*
					Study duration	***Peak-RAC [µg a.s./L]***	
Mesosulfuron-methyl	*0.2646*	*1 peak*	*0.75*	*not applicable*	*14 d peaks on d0 & d7*	*> 10.0 µg/L*	*< 0.03*

[event recognition threshold: 0.129 µg/L = Tier 1 RAC of mesosulfuron-methyl]

The PEC pattern of the FOCUS year consists of 1 prominent peak that that reaches a maximum concentration of 0.2646 µg a.s./L which is well below the peak-RAC of > 10.0 µg a.s./L applicable for single or independent peaks. With the duration of 0.75 days the peak is shorter than the exposure of 1 day tested in the underlying refined exposure experiment.

Consequently, the risk to aquatic macrophytes arising from this peak is considered to be low, with a resulting RQ of < 0.03.

The analysis of concentration over time patterns for both use groups B revealed that the exposure situation experienced by macrophytes in the water bodies represented by scenarios R3 and R4 stream is characterised by a single peak-shaped and short-term exposure event. For both uses and scenarios, this predicted exposure situation could be addressed by the results of a refined exposure laboratory test. Accordingly, the peak PECsw can be compared to matching peak-RAC values, clearly showing that the risk for macrophytes is acceptable.

Combined risk assessment - Tier 2C level

To present a combined toxicity risk assessment according to the concept of Tier 2C, it is necessary to review the concentration profiles of all considered components in time relation to each other, in order to investigate if the cumulated substance exposure would still follow a time-course falling into the boundaries of the available refined exposure test designs. To enable such analysis, graphical plots have been generated from the modelling data showing exposure time-course per the individual substance for iodosulfuron-methyl-sodium, metabolite AE F075736, and mesosulfuron-methyl in parallel, as well as their arithmetic curve addition yielding an exposure profile for the 'sum of sulfonylurea substances'.

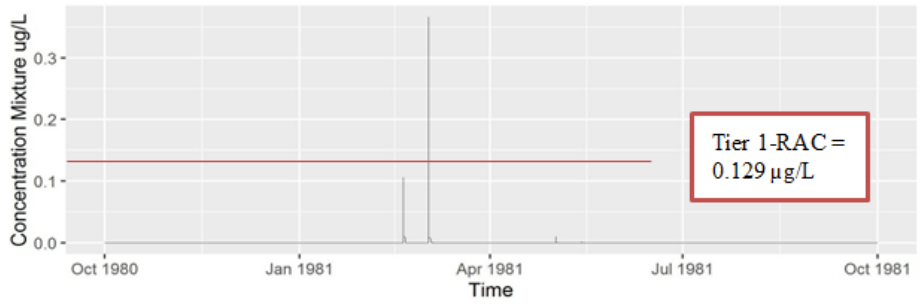
The procedure clearly illustrates that for the concerned substances and water bodies of relevance for assessment here, the exposure events occur simultaneously for all biologically active components, with the sum line still following a time evolution pattern that can be addressed via the dosing regimes tested in the higher tier pulsed exposure studies. No qualitatively new and / or more complex exposure patterns resulted from the curve addition.

Moreover, the graphs clearly reveal that the exposure is by far dominated by the active substance mesosulfuron-methyl, with only little contribution of iodosulfuron-methyl-sodium and very small amounts of its metabolite AE F075736. Therefore, even though experimental information would allow for a detailed assessment considering all three components, to avoid unnecessary complexity a simplified procedure is proposed, using:

- *the Tier 1-RAC value of mesosulfuron-methyl (0.129 µg/L) as 'event' threshold for the evaluation via the EPAT tool*
- *the peak-RAC values of mesosulfuron-methyl for final assessment of the 'sum of sulfonylurea substances' exposure profiles.*

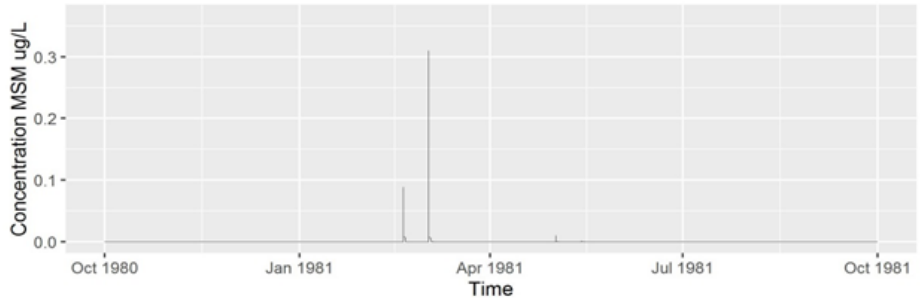
Combined risk assessment at Tier 2C level as described above is presented for those FOCUS scenarios where combined toxicity assessment at Tier 1 level required the acceptance of TWA approaches to pass, and which are dominated by drift or run-off entry route: R3 stream, R4 stream.

use group B – FOCUS Scenario R3 stream:
*(end of winter to spring use on winter cereals / **rate = 3 g/ha IMS + 15 g/ha MSM)***

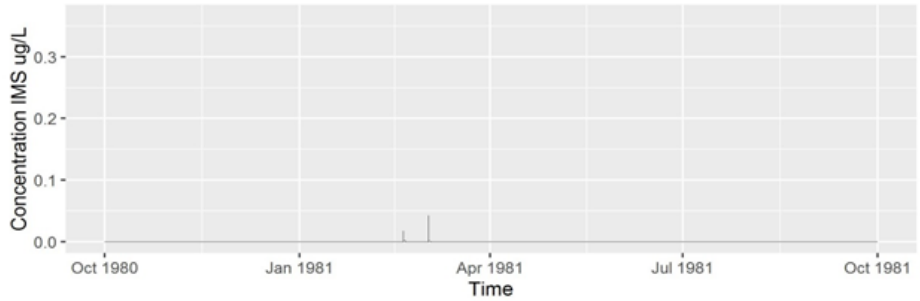


Curve addition

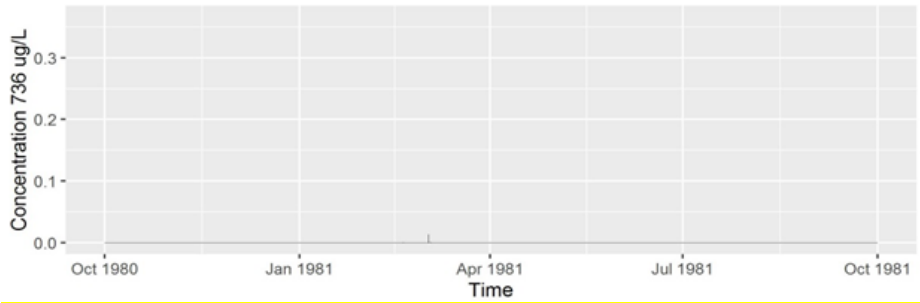
"sum of sulfonyl-urea compounds"



Mesosulfuron-methyl



Iodosulfuron-methyl-sodium



Metabolite AE F075736

EPAT analysis for "sum of sulfonylurea compounds"
for use group B – FOCUS Scenario R3 stream
(end of winter to spring use on winter cereals / ***rate = 3 g/ha IMS + 15 g/ha MSM):***

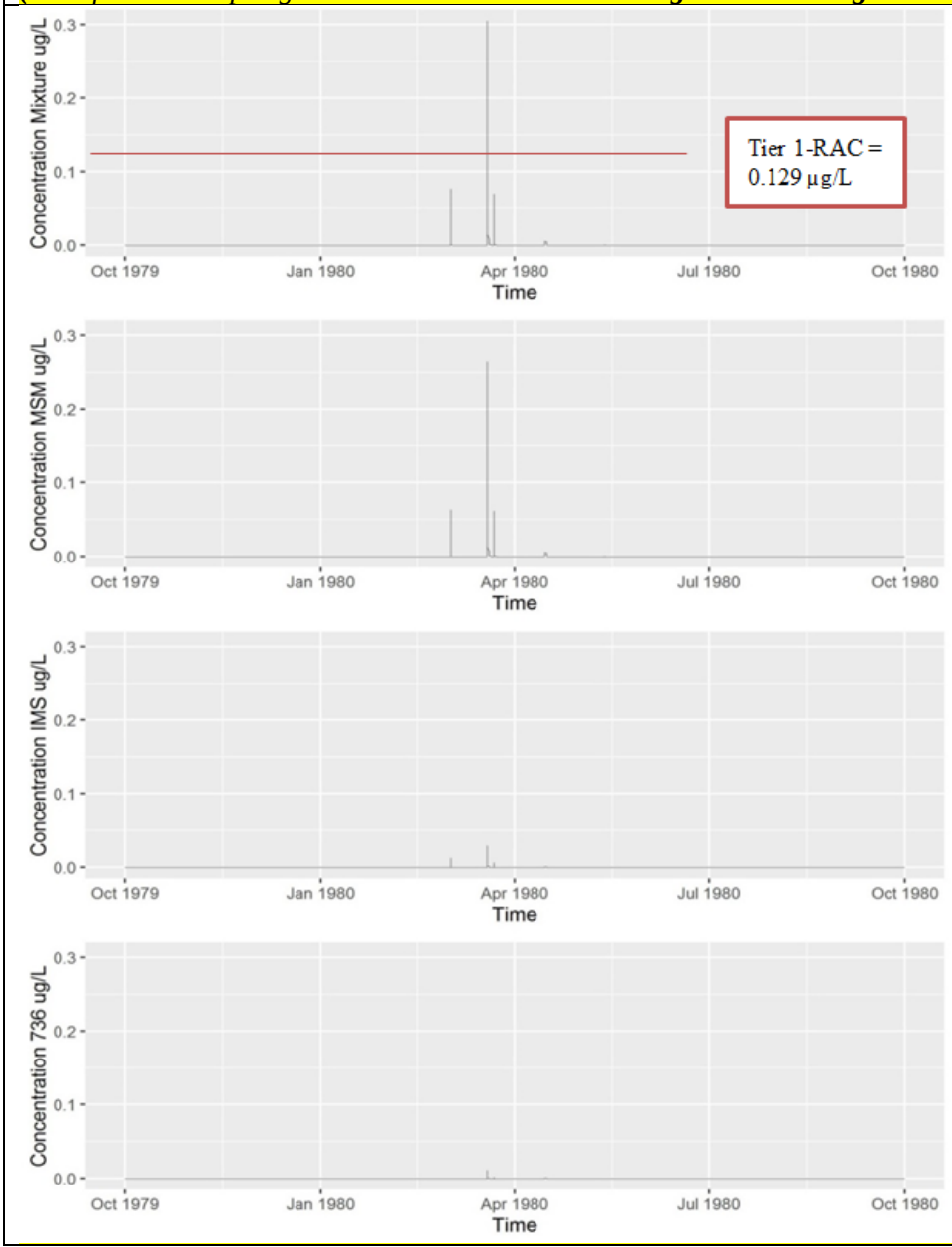
Compound	***PECmax [µg/L]***	***events above Tier 1 RAC***	***event duration above Tier 1 RAC [d]***	***interval betw. events above Tier 1 RAC [d]***	***Relevant peak-RAC from Lemna 2-peak study***		***RQ =*** *PECmax/ peakRAC*
					Study duration	***Peak-RAC [µg a.s./L]***	
sum of sulfonylurea compounds	*0.366*	*1 peak*	*0.6*	*not applicable*	*14 d peaks on d0 & d7*	*> 10.0 µg/L*	*< 0.04*
Mesosulfuron-methyl	*0.3099*	*1 peak*	*0.5*	*not applicable*			
Iodosulfuron-methyl-sodium	*0.0428*	-	-	-			
AE F075736	*0.0133*	-	-	-			

[event recognition threshold: 0.129 µg/L = Tier 1 RAC of mesosulfuron-methyl]

The PEC pattern for "sum of sulfonylurea substances" of the FOCUS year consists of 1 prominent peak that has a concentration of 0.366 µg a.s./L. This is well below the peak-RAC of > 10.0 µg a.s./L for independent peaks of substance mesosulfuron-methyl, the component clearly dominating this exposure. With the duration of 0.6 days the peak is shorter than the exposure of 1 day in the peak study.

Consequently, the risk to aquatic macrophytes arising from this peak is considered to be low.
The resulting RQ is < 0.04.

use group B – FOCUS Scenario R4 stream:
*(end of winter to spring use on winter cereals / **rate = 3 g/ha IMS + 15 g/ha MSM)***



Curve addition

"sum of sulfonyl-urea compounds"

Mesosulfuron-methyl

Iodosulfuron-methyl-sodium

Metabolite AE F075736

EPAT analysis for "sum of sulfonylurea compounds"
for use group B – FOCUS Scenario R4stream
(end of winter to spring use on winter cereals / ***rate = 3 g/ha IMS + 15 g/ha MSM):***

Compound	***PECmax [µg/L]***	***events above Tier 1 RAC***	***event duration above Tier 1 RAC [d]***	***interval betw. events above Tier 1 RAC [d]***	***Relevant peak-RAC from Lemna 2-peak study***		***RQ =*** *PECmax / peakRAC*
					Study duration	***Peak-RAC [µg a.s./L]***	
sum of sulfonylurea compounds	*0.3056*	*1 peak*	*0.8*	*not applicable*	*14 d peaks on d0 & d7*	*> 10.0 µg/L*	*< 0.03*
Mesosulfuron-methyl	*0.2646*	*1 peak*	*0.75*	*not applicable*			
Iodosulfuron-methyl-sodium	*0.0292*	-	-	-			
AE F075736	*0.0111*	-	-	-			

[event recognition threshold: 0.129 µg/L = Tier 1 RAC of mesosulfuron-methyl]

The PEC pattern for "sum of sulfonylurea substances" of the FOCUS year consists of 1 prominent peak that has a concentration of 0.305 µg a.s./L. This is well below the peak-RAC of > 10.0 µg a.s./L for independent peaks of substance mesosulfuron-methyl, the component clearly dominating this exposure. With the duration of 0.8 days the peak is shorter than the exposure of 1 day in the peak study.

Consequently, the risk to aquatic macrophytes arising from this peak is considered to be low. The resulting RQ is < 0.03.

9.5.2.6 Tier 2C: Higher-tier assessment based on refined exposure testing combined with exposure pattern analysis - considering multi-year exposure simulations

Review comments:
This approach was not evaluated in the current risk assessment.

In previous submissions the notifier had experienced eventual reviewer's concerns over the representativeness of current FOCUS calculations for exposure time-course interpretation based risk assessments. The approach has been challenged due to the model's limitation in weather data (single weather year). Multi-year FOCUS calculations are a possible way to overcome this concern. However, no guidance is available yet on the way to perform these calculations. Nevertheless, a methodology has been established by the notifier following FOCUS principles, to enable the simulation of product uses over a period of 20 years in the FOCUSsw scenarios. From these 20 years simulations a surrogate exposure pattern is derived, describing the 90th percentile worst case exposure pattern for a respective FOCUS scenario.

For reason of dossier simplicity, since for the present product clearly only one active component is driving the risk, application of the approach was confined to mesosulfuron-methyl only.

As this matter and novel approaches are expected to be of interest only for specific national reviewers, no detailed explanation is provided here in the dRR main part and the methodology is fully described in the Appendix (A3.3), but it is worth noting that the conclusions drawn from the refined exposure based on FOCUS step 3 one year calculations were confirmed by the 20 years calculations:

Table 9.5-45: Tier 2C risk assessment for aquatic macrophytes for mesosulfuron-methyl, based on refined exposure testing and 90th percentile worst case exposure patterns derived from multi-year (20 years) exposure simulations

FOCUS multiyear Scenario	80th perc. PECmax [µg/L]	80th perc. events above Tier 1 RAC	80th perc. event duration above Tier 1 RAC [d]	20th per. interval betw. events above Tier 1 RAC [d]	Relevant peak-RAC from Lemna 2-peak study		RQ = PECmax/ peakRAC
					Study duration	Peak-RAC [µg a.s./L]	
Use group B (end of winter to spring use on winter cereals / **rate = 15 g/ha MSM**)							
R3 stream	0.4524	2 peaks	0.8	7.3	14 d peaks on d0 & d7	> 10.0 µg/L	< 0.045
R4 stream	0.4918	2 peaks	0.6	4.4	7 d peaks on d0 & d3	1.09 µg/L	0.45

The above assessments based on multiyear simulations confirmed the conclusion of acceptable risk for macrophytes previously made for the standard FOCUS year.

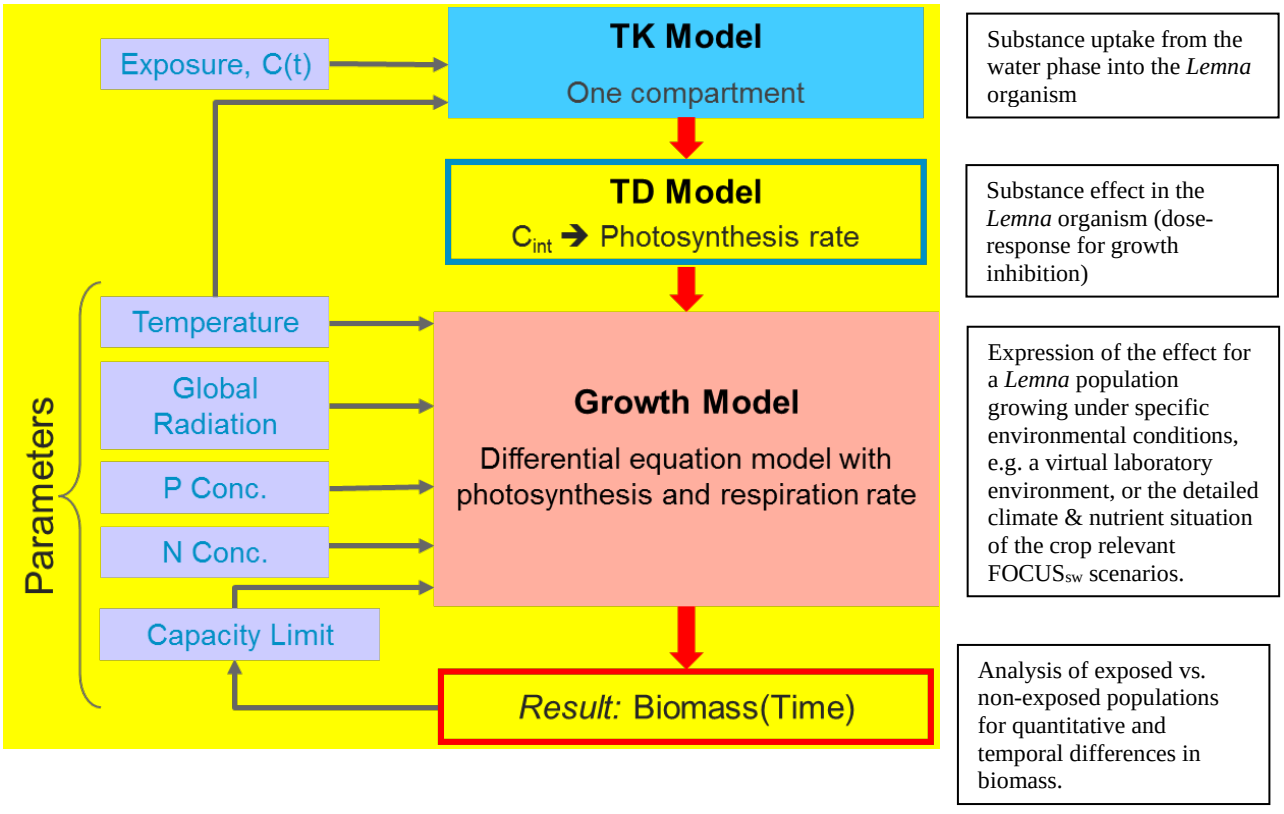
9.5.2.7 9.5.2.7 Tier 2C and Tier 3: Ecological modelling approaches, and their use in higher-tier risk assessments for the present product

Testing of exposure patterns, Tier 2C as described before, is an option to generate and consider information on the effects of time-variable aquatic exposure situations. As experimental testing will in practice be limited in regard to the number of different exposure patterns that can be studied, the combination with ecological modelling is a promising tool. Once established based on a set of measured experimental information, a modelling approach allows for a transfer to and mechanistic understanding of realistic exposure scenarios, which would not be possible to that level of detail via laboratory tests.

According to the EFSA Aquatic Guidance Document (EFSA, 2013), "to better address risks of time-variable exposures the tier 2 assessment may be complemented with toxicokinetic/toxicodynamic (TK/TD) models." This assessment which aims to combine experimental data and modelling is part of the Tier 2 assessment level (Tier 2C). It may further on lead to prediction of responses at population-level which are defined as Tier 3 level.

The here presented approach used a previously published TK/TD population model of Lemna (Schmitt et al. 2013) to link FOCUS$_{sw}$ exposure patterns to predicted effects on populations. The model comprises of a toxicokinetic, a toxicodynamic, and a growth sub-model, together enabling simulations for a comparative analysis of the growth of exposed vs. non-exposed populations for quantitative and temporal differences in biomass. Hereby, the model can also consider the influence of environmental conditions such as e.g. temperature, radiation and nutrients.

A schematic of the model principle is shown in the Figure here below, for a detailed description reference is made to ***Appendix A 3.4*** *of the present document.*



The model by Schmitt et al. (2013) has been evaluated by EFSA's working panel. In their recent Scientific Opinion[18], in the section on Evaluation of the application in risk assessment of this model, the experts concluded as follows:

"The model seems to work well for the sulfonyl-urea compound and the validation data as presented in Schmitt et al., 2013, but the model should be validated on herbicides with other modes of action. Summarising, the Lemna model appears suitable for use in risk assessment to evaluate effects of time-variable exposure on Lemna growth."

[18] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2018. Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA Journal 2018;16(8):5377, 188 pp. https://doi.org/10.2903/j.efsa.2018.5377

All aspects identified by EFSA to require further attention have been picked up in the respective modelling reports to the present submission.

Before the model was used to address the risk assessment relevant questions, substance specific parameters were calibrated for each compound using experimental information from standard studies. The calibrated substance models were then validated by a check of the model's predictive power: Effects independently predicted for certain time-variable exposure patterns were compared with measured results of experimental studies for those exposure patterns. Details on the specific parameters including their calibration and validation are reported in Heine 2017a (M-602805-01-1) for iodosulfuron-methyl-sodium and its metabolite AE F075736 [metsulfuron-methyl], and in Heine 2017b (M-600766-01-1) for mesosulfuron-methyl. Summaries of these reports including the validation graphs and model efficiency information are presented in Appendix A 3.4 of the present dRR, clearly demonstrating the model fitness for a prediction of effects from complex exposure situations.

The successfully calibrated and validated Lemna models were then applied in two ways in order to address the present product risk assessment, referring to AGD levels Tier 2C and Tier 3:

Concept of model application for risk assessment Tier 2C

In-silico time-variable exposure testing of Lemna: *'Virtual laboratory tests' on Lemna were performed to address FOCUSsw exposure patterns of particular interest, applying the model as a confirmation to the assessments made before at Tier 2C (Section 9.5.2.5). Starting from the condensed exposure pattern representations previously derived via EPAT tool analysis of the FOCUSsw output (number, duration, maximum concentration, and interval of events exceeding the Tier 1 RAC), the biological effect of such patterns was simulated for a Lemna population assumed to grow under constant environmental conditions representing an 'in-silico laboratory'. To investigate the dose-response relationship, the simulation was repeated multiple times with arbitrarily scaled concentration dimension of the exposure pattern, while keeping constant all other parameters. Based on the so generated data set, an $EC_{50pattern}$ could be derived in analogy to the procedures of a standard laboratory experiment. This $EC_{50pattern}$ is a descriptor which specifically reflects macrophyte sensitivity for the exposure time course experienced in the regarded FOCUSsw scenario of interest, and can be compared to the PECsw,max predicted for this scenario.*

Concept of model application for risk assessment Tier 3

Population effect modelling for outdoor FOCUSsw water bodies: *Dynamics of a Lemna population growing outdoors in an edge-of-field surface water body were simulated for each of the crop relevant $FOCUS_{sw}$ exposure scenarios, for the critical GAP situations of the present product. To realistically simulate the biological impact of the predicted exposure patterns, the model environmental scenarios were constructed to reflect the properties of each associated FOCUS surface water body[19]. Additionally, to generate information on the margin of safety, Lemna population dynamics were simulated as well for exaggerated exposure situations, generated via a multiplication of the concentration dimension of the exposure patterns with exemplary scaling factors of either 10 or 100. Scaling the exposure supports the assessment and is intended to demonstrate that the model is able to predict considerable inhibitions of population dynamics. Following the standard concept of concentration addition, the population modelling approach can consider and combine the effect contributions of all biologically active components relevant to a product, i.e. can directly provide a combined risk assessment for the detailed and potentially complex exposure situation of macrophytes in surface water bodies.*

Results of model application for risk assessment:

(a) Tier 2C: In-silico time-variable exposure testing of

[19] In order to account for the uncertainty resp. natural variation in some model relevant parameters, e.g. waterbody nutrient concentrations, a stochastic simulation was performed varying those parameters in a Monte-Carlo approach. Therefore, actually 100 model runs were made per scenario, yielding output ranges.

Lemna

For the present product, as discussed before in Section 9.5.2.5, in particular scenarios R3 stream and R4 stream were of interest for confirmatory or complementary activity at Tier 2C, specifically for the active substance mesosulfuron-methyl for which the assessments at Tier 1 were failed when based on $PEC_{sw,max}$, but were resolved with a large margin of safety when Tier 1 assessment is based on $PEC_{sw,twa}$.

*An overview summary of the results is provided below; more detailed information including dose-effect curves can be found in **Appendix A 3.4**.*

To reduce dossier complexity, in view of the very clear outcome of these simulations no further attempts were made at this stage for a generation of combined toxicity information. The low concentration contributions of iodosulfuron-methyl-sodium and metabolite AE F075736 would obviously not be expected to impact on the overall regulatory conclusion of the assessment.

*For **use group B** (winter cereals – end of winter to spring application), the exposure patterns predicted for mesosulfuron-methyl in FOCUS scenarios R3 stream and R4 stream were both characterised by a single dominant exposure event only, with a duration of 0.5 or 0.75 days, respectively (cf. Section 9.5.2.5) . In a virtual laboratory test on such exposure pattern, to achieve an inhibition of the relative growth rate by 50% ($EC_{50pattern}$), the concentrations had to be increased to 4166 and 1838 µg/L for the two scenarios, respectively. In agreement with an assessment factor of 10 the $RAC_{pattern}$ were therefore both > 100 µg/L for the specific exposure situation predicted for mesosulfuron-methyl in scenarios R3 stream and R4 stream.*

For risk assessment, the $RAC_{pattern}$ can be compared to the $PEC_{sw,max}$ concentrations of 0.3099 µg/L and 0.2646 µg/L for these scenarios, respectively, indicating again very large margins of safety and confirming the conclusions drawn before at Tier 1 (considering TWA) and Tier 2C (experimental).

Table 9.5-46:** **Assessing exposure patterns for mesosulfuron-methyl derived from FOCUSsw calculation to determine the corresponding exposure pattern that causes 50% effect by increasing the event concentration and keeping all other pattern characteristics;
- Use group B (winter cereals – end of winter to spring application / rate = 15 g/ha MSM)

Scenario	Pattern characteristics				Event conc. causing 50% effect [µg/L]	$RAC_{pattern}$ [µg/L]	RQ = PECmax / $RAC_{pattern}$)
	Event concentration [µg/L] (PECmax)	Number of events	Event duration [d]	Interval between events [d]			
R3 stream	0.3099	1	0.5	-	4166	416.6	0.0007
R4 stream	0.2646	1	0.75	-	1838	183.8	0.0014

(b) Tier 3: Population effect modelling for FOCUSsw water bodies

Dynamics of Lemna populations growing in edge-of-field FOCUS surface water bodies were simulated for all crop relevant $FOCUS_{sw}$ scenarios, for two critical GAP situations of the present product[20]: use group

B (winter cereals – end of winter-spring application). These simulations considered the effect contributions by all three biologically active components of relevance to the product, i.e. represent a combined toxicity assessment for iodosulfuron-methyl-sodium, its metabolite AE F075736 [metsulfuron-methyl], and mesosulfuron-methyl.

An overview of the results is provided in condensed tabular form here below; for detailed information including a higher resolved presentation of effect classes and ranges, reference is made to ***Appendix A 3.4****.*

Table 9.5-47: ***Effect magnitude and duration caused by FOCUSsw exposure patterns from use group B. Columns highlighted in grey are results for the original FOCUS predicted exposure patterns, other columns represent simulations for exaggerated exposure.***

Level ►	***Step3***		
Scaling factor ►	***1***	***10***	***100***
Scenario ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*		
D1 (Ditch)	*Neg.*	***>70%<80% (109d)***	***>90% (259d)***
D1 (Stream)	*Neg.*	***>20%<30% (57d)***	***>80%<90% (136d)***
D2 (Ditch)	***>20%<30% (62d)***	***>90% (286d)***	***>90% (352d)***
D2 (Stream)	***>10%<20% (16d)***	***>80%<90% (129d)***	***>90% (352d)***
D3 (Ditch)	*Neg.*	*Neg.*	***>90% (357d)***
D4 (Pond)	*Neg.*	*Neg.*	***>90% (283d)***
D4 (Stream)	*Neg.*	*Neg.*	***>70%<80% (130d)***
D5 (Pond)	*Neg.*	*Neg.*	***>80%<90% (175d)***
D5 (Stream)	*Neg.*	*Neg.*	***>50%<60% (121d)***
D6 (Ditch)	*Neg.*	*Neg.*	***>20%<30% (63d)***
R1 (Pond)	*Neg.*	*Neg.*	*Neg.*
R1 (Stream)	*Neg.*	*Neg.*	*Neg.*
R3 (Stream)	*Neg.*	*Neg.*	*Neg.*
R4 (Stream)	*Neg.*	*Neg.*	*Neg.*

Neg. = negligible (i.e. ≤ 10% effects);
d = days with predicted effects >10%.

The population simulations showed that no adverse effects for Lemna are predicted for the ***FOCUSsw run-off (R) scenarios*** *for both assessed critical uses of the present product. In all cases, even a 100-fold exaggeration of the exposure patterns resulted in negligible predicted effects (cf. Table above, R1-R4). The*

ecological threshold option can therefore be applied to clearly conclude acceptable risk for macrophytes for R1, R3, and R4 for both assessed critical uses.

For a graphical illustration, exposure concentration profile, effects curve and population biomass development over the simulated year is shown exemplarily for scenario R3 stream for use group B (end of winter-spring use in winter cereals) here below:

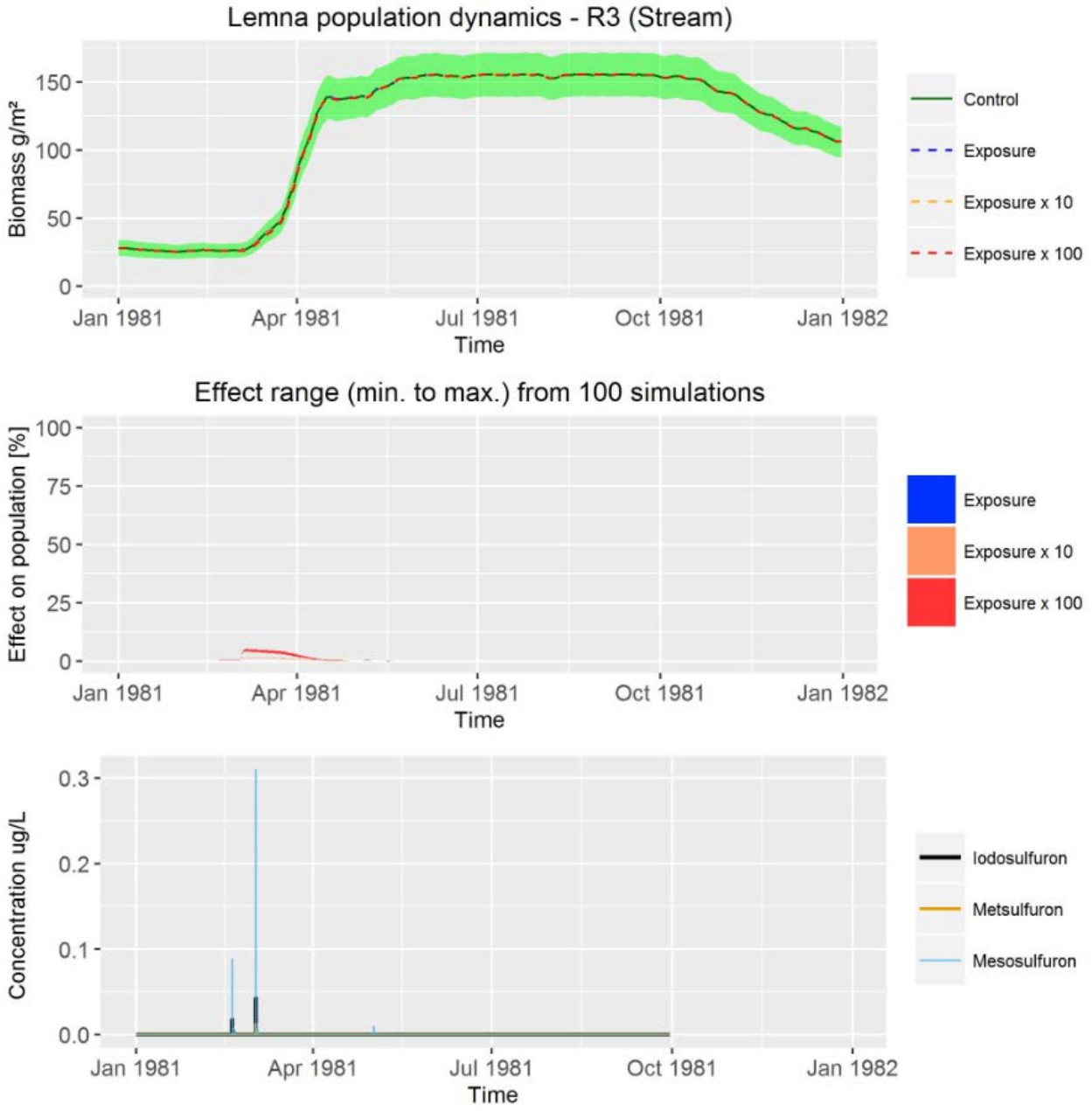


Figure 3: Inhibition of Lemna population dynamics caused by product IMS+MSM+MPR OD 42, exposure pattern R3 stream, for use group B.

bottom: ***Exposure patterns of the two active ingredients, and relevant metabolite AE F075736 (metsulfuron-methyl) on which simulations of population dynamics were based.***

middle: ***Predicted impact on the Lemna population with the areas representing minimum and maximum effects caused.***

top: ***Population dynamics exposed vs. non-exposed, with the green area representing the range of undisturbed population dynamics.***

*For the **FOCUSsw drainage (D) scenarios**, acceptable risk was predicted by the model for most of the scenarios and critical use situation, but a non-negligible level of effects on Lemna population was predicted for the original use pattern for two of the ten drainage scenarios, D2 ditch and D2 stream, for applications in winter cereals by end of winter-spring (use group B). The growth inhibition caused in these scenario water bodies was small with maximum effects < 30% and <20%, respectively. Also, the growth inhibition was reversible, with a predicted exceedance of effects threshold for limited periods of 62 and 16 days out of the simulated 366 days (1 year), respectively.*

The ecological threshold option can therefore be applied to conclude acceptable risk for macrophytes for D1, D3, D4, D5, and D6 scenarios for both assessed critical uses. However, with regard to scenario D2 a risk management decision will be required: The risk may either be regulated based on the 'ecological recovery option' which is described in the EFSA Aquatic guidance document. Or it can be managed via use restriction on drained area represented by D2 scenario, e.g. via the following label phrase which is established in France: „To protect aquatic organisms, do not use on drained soils when topsoil clay content is 45% or more.”.

When exposure patterns of drainage scenarios were exaggerated by factor 10 or 100 to demonstrate sensitivity of the model, clear and in part long lasting effects on population dynamics were predicted for several to all of the D scenarios, for both assessed application timings. Effects were predicted to still be reversible in case of the 10x scaled exposure, however for a 100x exaggerated exposure a population collapse would be predicted for some of the scenarios. These tests clearly demonstrate that the model is capable of describing population sensitivity including an expression of pronounced effects.

For a graphical illustration, exposure concentration profile, effects curve and population biomass development over the simulated year is shown exemplarily for scenario D2 stream for use group B (end of winter-spring use in winter cereals):

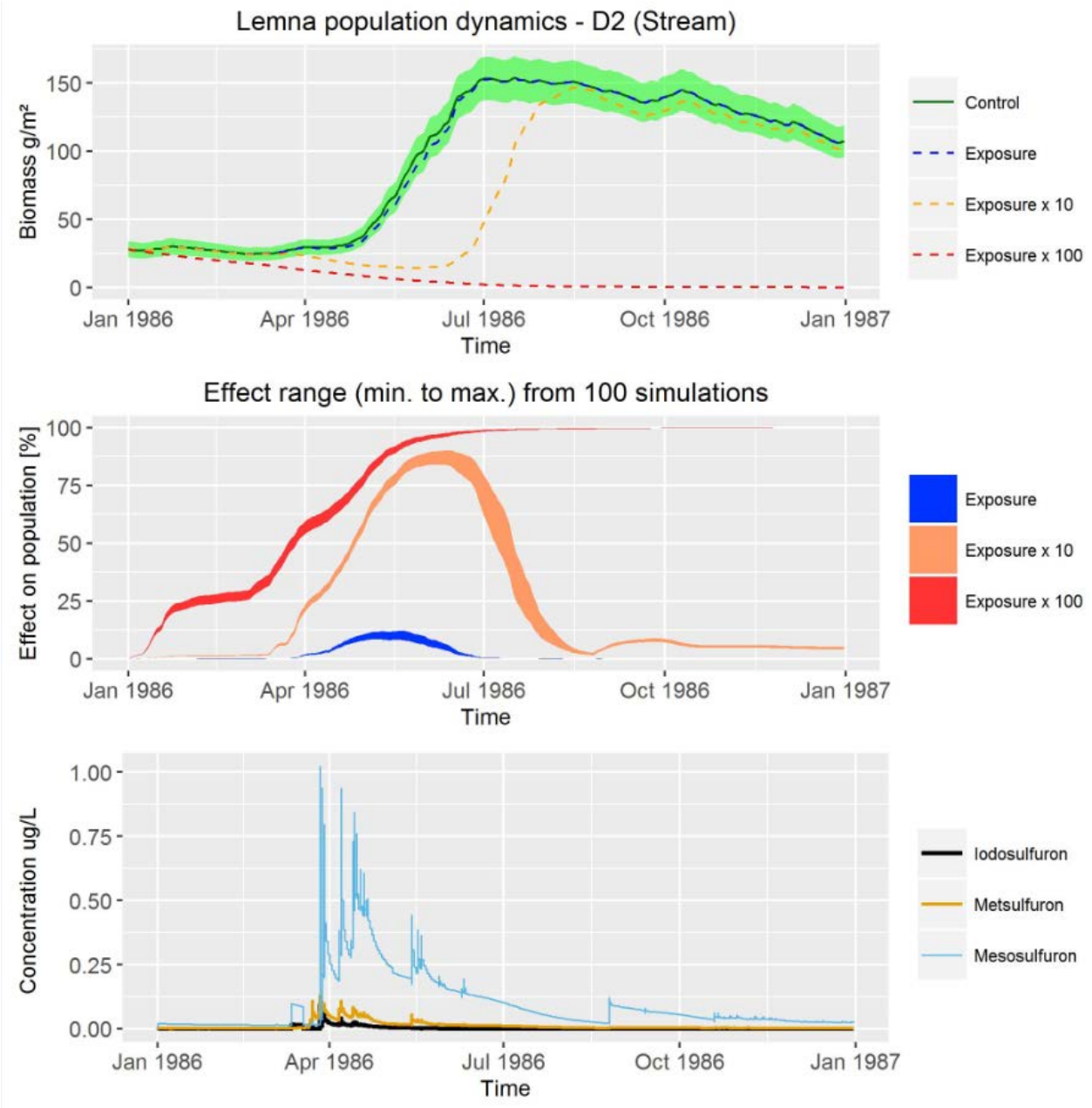


***Figure 4:** Inhibition of Lemna population dynamics caused by product IMS+MSM+MPR OD 42, exposure pattern D2 stream, for use group B.*

***bottom:** Exposure patterns of the two active ingredients, and relevant metabolite AE F075736 (metsulfuron-methyl) on which simulations of population dynamics were based.*

***middle:** Predicted impact on the Lemna population with the areas representing minimum and maximum effects caused.*

***top:** Population dynamics exposed vs. non-exposed, with the green area representing the range of undisturbed population dynamics.*

(c) Overall conclusion from effect modelling based Tier 2C and 3 risk assessment:

Effect modelling approaches were established to generate a more in-depth understanding of the potential risk for macrophytes, and aiming to provide alternative risk assessment routes for countries that might reject the initially proposed Tier 1 -TWA approaches.

*For **all FOCUS runoff ("R") type scenarios** and critical use patterns assessed, effect modelling clearly demonstrated negligible effects. The conclusion of acceptable risk from Tier 1-TWA and Tier 2C was confirmed and a wide additional margin of safety could be shown. For these scenario situations, no specific measures for exposure mitigation are therefore required to protect aquatic organisms for all intended uses of the present product.*

*For **FOCUS drainage ("D") type scenarios**, effect modelling demonstrated negligible predicted effect for all scenarios and uses assessed with the exception of D2 stream and ditch.*
For scenario D2 (stream and ditch) slight effects were predicted in case of the worst case use pattern of use group B. Although these effects were small and temporary for the maximum intended use rate, and still reversible even in an explorative simulation for 10x exaggerated exposure, a regulatory risk assessment based on 'ecological threshold option' of the AGD would not be passed for this particular scenario and use. Therefore, for a regulatory conclusion on those intended uses of the present product that are represented by use group B and European geoclimatic regions covered by FOCUSsw scenario D2, a risk management decision will be required to either regulate based on AGD 'ecological recovery option', or manage the risk via use restriction on drained area represented by D2 scenario (e.g. via the following label phrase which is established in France: „To protect aquatic organisms, do not use on drained soils when topsoil clay content is 45% or more.”). In a Central Zone context, however, scenarios D1 and D2 are considered to not have any area extent.

Therefore, no specific use restrictions or mitigation measures are required to ensure acceptable risk for aquatic organisms for the intended uses assessed for the present product in the Central Zone.

Review comments:

The approaches -2C higher Tier and Tier 3 were not evaluated in the current risk assessment.

9.5.2.8 Tier 2C and Tier 3: Ecological modelling approaches, and their use in higher-tier risk assessments for the present product – considering multiyear exposure simulations

As previously explained under point 9.5.2.6, the representativeness of current FOCUS calculations has been challenged and multi-year FOCUS calculations are a possible way to overcome this concern but are not laid down in agreed guidance documents yet. Nevertheless, for reviewers with deeper interest in this matter, the notifier has applied the novel 20 year-simulation methodology for the FOCUS scenarios as well to generate a more representative exposure data base for the Lemna population modelling.

As this matter and novel approaches are expected to be of interest only for specific national reviewers, no detailed explanation is provided in this dRR main part but it is worth noting that the conclusions drawn from the Lemna population modelling based on FOCUS step 3 one year calculations were overall confirmed by the 20 years calculations.

(a) Tier 2C: In-silico time-variable exposure testing of Lemna – considering multiyear

exposure simulations

In-silico time variable exposure testing for determination of $RAC_{pattern}$ for the 20-year realistic worst case exposure patterns of mesosulfuron-methyl fully confirmed the conclusion previously based on the standard FOCUS year. A wide margin of safety applies for R3 stream and R4 stream, as is indicated by RQ values in the range 0.001 to 0.086.

(b) Tier 3: Population effect modelling for FOCUSsw water bodies – considering multiyear exposure simulations

Population effect modelling over 20 years for a combined assessment of all active components of the product fully confirmed the conclusion of acceptable risk with a large margin of safety drawn for FOCUS runoff ("R") scenarios, as previously drawn for the standard FOCUS year. Even 10-fold exaggerated exposure patterns would lead to negligible risks for R scenarios.

For FOCUS drainage ("D") type scenarios, non-negligible risks were identified only in some years for D1 stream and ditch in addition to those already seen for D2 scenarios with the simulations based on FOCUS standard year.

(c) Overall conclusion from effect modelling based Tier 2C and Tier 3 risk assessment - considering multiyear exposure simulations

Overall, Lemna effect modelling for a 20-year extended period of exposure prediction confirmed the regulatory conclusions drawn in the assessment previously based on the standard FOCUS year period. No further risk mitigation measure than already proposed would be necessary to mitigate these risks, as scenarios D1 and D2 have no regional relevance in the Central Zone.

9.5.3 Overall conclusions

~~Not relevant. See point 9.5.1.~~

Acceptable risk for all aquatic organisms other than macrophytes could be demonstrated in a screening-level risk assessment (FOCUS Steps 1-2) for the active substances contained in product IMS+MSM+MPR OD 42 (2+10+30), and their metabolites.

Review comment:
The evaluation of the risk for aquatic organisms was performed in accordance with Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters in the context of Regulation (EC) No 1107/2009(EFSA Journal 2013;11(7):3290).
The risk assessment scheme base on the risk assessment provided for reference product Atlantis.
The same endpoints and approach is taken for JME-HER 12 OD as was presented in the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).

The Applicant proposed to use in the risk assessment a PEC 7d-twa. However The risk assessment based on PECsw twa at STEP 3 was not considered acceptable by zRMS -PL.
Therefore, the risk assessment based on max PECsw STEP 3 values and with 7 d ErC_{50} of 1.29 µg/L, is considered acceptable.

A pulsed dose study with Lemna gibba submitted with EPAT analysis was submitted for mesosulfuron methyl (R3 and R4 scenarios) , iodosulfuron-methyl and its metabolite (R3 and R4 scenarios) as well as the Tier 2C via TKTD effect modelling (*in-silico* virtual laboratory testing), the TK/TD modelling in order to resolve the failing scenarios were considered by the Applicant.
There were several uncertainties highlighted with the pulsed dose study and EPAT analysis in case of mesosulfuron methyl.

It should be noted that two additional peak exposure studies for Lemna sp. were provided by the Applicant. The first for the a.s-iodosulfuron –methyl (Kuhl K.; 2016; EBIMN158; M-574865-01-1) and the other one for its metabolite -metsulfuron methyl (Kuhl, K.; 2017; EBIM0007; M-600962-02-1) and (Kuhl, K.; 2017; EBIM0007; M-600962-02-1), respectively.
These studies were not included in the current risk assessment.

zRMS overall conclusion with consideration the combined risk assessment for both the active substances and metabolite JME-HER 12 OD, based on max PECsw values.

use group B

(end of winter to spring use on winter cereals / rate = 3 g/ha IMS + 15 g/ha MSM):

The product can be safely applied with no precautionary measures required for exposure mitigation in all European regions other than those represented by drainage scenarios D1 and D2. In a Central Zone context, however, both of these scenarios are considered not representative.
In case of R1 (stream) and D3 (ditch) scenarios the product can be safely when:
- For R1 (stream) and D3 (ditch) 10 meter low vegetative buffer zone will be applied

9.6 Effects on bees (KCP 10.3.1)

9.6.1 Toxicity data

The evaluation of the risk for bees was performed in accordance with the recommendations of the

"Guidance Document on Terrestrial Ecotoxicology". as provided by the Commission Services (SANCO/10329/2002 rev.2 (final). October 17. 2002).
To achieve a concise risk assessment. the risk envelope approach is applied.
~~Information concerning studies with bees and risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD. No further data are required.~~

Iodosulfuron-methyl-sodium
Studies on the toxicity to bees have been carried out with iodosulfuron-methyl-sodium. Full details of these studies are provided in the corresponding document of the EU draft assessment report where the study references can be found; presented agreed endpoints were taken from EFSA Journal 2016;14(4):4453.

Table 9.6-1: Endpoints and effect values relevant for the risk assessment for bees - iodosulfuron-methyl-sodium

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Laboratory tests				
Apis mellifera	*Iodosulfuron-methyl-sodium, techn.*	*Acute, oral*	*LD_{50} > 70 µg a.s./bee*	*EFSA Journal 2016;14(4):4453*
Apis mellifera	*Iodosulfuron-methyl-sodium, techn.*	*Acute, contact*	*LD_{50} > 131 µg a.s./bee*	*EFSA Journal 2016;14(4):4453*
Apis mellifera	*Iodosulfuron-methyl-sodium, techn.*	*Acute, oral*	*LD_{50} > 107.6 µg a.s./bee*	*EFSA Journal 2016;14(4):4453*
Apis mellifera	*Iodosulfuron-methyl-sodium, techn.*	*Acute, contact*	*LD_{50} > 100 µg a.s./bee*	*EFSA Journal 2016;14(4):4453*
Apis mellifera	*Iodosulfuron-methyl-sodium, techn.*	*10-day chronic, oral*	*LDD_{50} > 4.4 µg a.s./bee/d NOEDD ≥ 4.4 µg a.s./bee/d*	*EFSA Journal 2016;14(4):4453*
Higher-tier studies (tunnel test, field studies)				
Apis mellifera	*Iodosulfuron-methyl-sodium (formulated as Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 400 (100+300))*	*Semi-field honey bee brood study (acc. to OECD No. 75; forced exposure conditions) in Phacelia; application during full-bloom and bees actively foraging; 4 d exposure 18 days observation*	*No adverse effects on mortality, flight intensity, behaviour, brood development (brood termination rate, brood index, compensation index) as well as on colony vitality at maximum application rate 10 g iodosulfuron-methyl-sodium/ha*	*EFSA Journal 2016;14(4):4453*

Mesosulfuron-methyl
Studies on the toxicity to bees have been carried out with mesosulfuron-methyl. Full details of these studies are provided in the EU Renewal Assessment Report and related documents; presented agreed endpoints were taken from EFSA Journal 2016;14(10):4584.

Table 9.6-2: Endpoints and effect values relevant for the risk assessment for bees - mesosulfuron-methyl

Species	Substance	Exposure System	Results	Reference
Apis mellifera	*Mesosulfuron-methyl*	*Acute, oral*	*LD_{50} > 105.6 µg a.s./bee*	*EFSA Journal 2016;14(10):4584*
Apis mellifera	*Mesosulfuron-methyl*	*Acute contact*	*LD_{50} > 100 µg a.s./bee*	*EFSA Journal 2016;14(10):4584*
Apis mellifera	*Mesosulfuron-methyl*	*10-day chronic, oral*	*LC_{50} > 120 mg a.s./kg food, equivalent to LDD_{50} > 4.85 µg a.s./bee/d **	*EFSA Journal 2016;14(10):4584*
Higher-tier studies (tunnel test, field studies)				
Apis mellifera	*Mesosulfuron-methyl (formulated as Mesosulfuron-methyl WG)*	*Semi-field honey bee brood study (acc. to OECD No. 75; forced exposure conditions) in Phacelia; application during full-bloom and bees actively foraging*	*No adverse effects on mortality of adult bees and brood, flight intensity, behaviour, brood development (brood termination rate, brood index, compensation index) and colony vitality at 15 g mesosulfuron-methyl/ha*	*EFSA Journal 2016;14(10):4584*

IMS+MSM+MPR OD 42 (2+10+30)

Effects on bees of IMS+MSM+MPR OD 42 (2+10+30) were evaluated as part of the EU assessment of the active substance mesosulfuron-methyl (representative formulation). No new studies are submitted with this formulation, reference is made to the agreed endpoints reported in EFSA Journal 2016;14(10):4584, and RAR Volume 3 – B.9 (PPP) – ATLANTIS OD (revised version 2016-06).

Table 9.6-3: Endpoints and effect values relevant for the risk assessment for bees - IMS+MSM+MPR OD 42 (2+10+30)

Species	Substance	Exposure System	Results	Reference
Apis mellifera	*IMS+MSM+MPR OD 42 (2+10+30)*	*Acute, oral 48 h*	*LD_{50} = 234 µg prod./bee*	*EFSA Journal 2016;14(10):4584*
Apis mellifera	*IMS+MSM+MPR OD 42 (2+10+30)*	*Acute, contact 48h*	*LD_{50} = 498 µg prod./bee*	

Additional endpoints and effect values generated after Peer Review for Renewal of Approval

Table 9.6-4: Endpoints and effect values relevant for the risk assessment for bees - IMS+MSM+MPR OD 42 (2+10+30)

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Laboratory test				
Apis mellifera	***Iodosulfuron**-methyl-sodium, techn.*	*22-day repeated feeding larva exposure test*	*NOEC ≥ 101 mg a.s./kg diet* *NOED ≥ 16 µg a.s./larva*	*Kleebaum, 2017 (Tier 2 summary in Appendix A 2.3.1, study report available upon request)**

**the study is not evaluated in this report*

Table 9.6-5: Endpoints and effect values relevant for the risk assessment for bees - IMS+MSM+MPR OD 42 (2+10+30)

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Laboratory test				
Apis mellifera	***Mesosulfuron**-methyl, techn.*	*22-day repeated feeding larva exposure test*	*NOEC ≥ 81.2 mg a.s./kg diet* *NOED ≥ 12.8 µg a.s./larva*	*Kleebaum, 2017 (Tier 2 summary in Appendix A 2.3.1, study report available upon request)*

**the study is not evaluated in this report*

Review comments

The risk assessment of JME-HER 12 OD reference to Core Assessment of the already registered product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

From ecotoxicological point of view JME-HER 12 OD is considered equivalent/comparable to already registered Atlantis 12 OD, therefore the unprotected ecotoxicological studies performed for Atlantis 12 OD can be used for risk assessment purposes of JME-HER 12 OD.

In current assessment the same approach is taken as was provided in the risk assessment of reference product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

9.6.1.1 Justification for new endpoints

~~Not relevant. See point 9.6.1.~~

In order to complete the data set and the knowledge on effects on developmental stages of honey bees further studies have been performed with the active substances. Since this data has not been part of the renewal process of the individual active substances, an overview is presented in the table above and the detailed reports can be made available upon request.

9.6.2 Risk assessment

~~Not relevant. See point 9.6.1.~~

The evaluation of the risk for bees was performed in accordance with the recommendations of the "Guidance Document on Terrestrial Ecotoxicology", as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002).

9.6.2.1 Hazard quotients for bees

~~Not relevant. See point 9.6.1.~~

Iodosulfuron-methyl-sodium

Table 9.6-6: First-tier assessment of the risk of iodosulfuron-methyl-sodium for bees due to the use of JME-HER 12 OD in cereals

Intended use	***Risk envelope approach (use group A):*** ***Cereals*** ~~***(BBCH 12-39), [maize (BBCH 12-18), non-cropped area]***~~		
Active substance ***Application rate (g/ha)***	*iodosulfuron-methyl-sodium* *Risk envelope approach:* *1 × 10*		
Test design	***LD_{50} (lab.) (µg/bee)***	***Single application rate (g/ha)***	***Q_{HO}, Q_{HC} criterion: $Q_H \leq 50$***
Oral toxicity	*> 107.6*	*10*	*< 0.1*
Contact toxicity	*> 100*		*< 0.1*

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

Mesosulfuron-methyl

Table 9.6-7: First-tier assessment of the risk of mesosulfuron-methyl for bees due to the use of JME-HER 12 OD in cereals

Intended use ***Active substance*** ***Application rate (g/ha)***	***Risk envelope approach (use group A):*** ***Cereals (winter and spring)*** ~~***, BBCH 10-39***~~ *Mesosulfuron-methyl* *Risk envelope approach:* *1 × 15*		
Test design	***LD_{50} (lab.) (µg/bee)***	***Single application rate (g/ha)***	***Q_{HO}, Q_{HC} criterion: $Q_H \leq 50$***
Oral toxicity	*> 105.6*	*15*	*< 0.14*
Contact toxicity	*> 100*		*< 0.15*

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

JME-HER 12 OD based on the endpoints of IMS+MSM+MPR OD 42 (2+10+30)

Table 9.6-8: First-tier assessment of the risk of JME-HER 12 OD ~~IMS+MSM+MPR OD 42 (2+10+30)~~ in cereals

Product	*JME-HER 12 OD based on the endpoints for the formulation IMS+MSM+MPR OD 42 (2+10+30)*		
Application rate (g/ha)	*1 × 1.5 L/ha (use group E)*		
Test design	***LD_{50} (lab.) (µg/bee)***	***Single application rate (g/ha)***	***Q_{HO}, Q_{HC} criterion: $Q_H \leq 50$***
Oral toxicity	*234*	*1500**	*6.4*
Contact toxicity	*498*		*3.0*

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.
** specified density for product IMS + MSM + MPR OD 42: 1.0 g/mL*

Review comments

The risk assessment for both active substances (group A) was performed for higher dose than is in the GAP. The Applicant followed a generic 'risk envelope' approach, where the European envelope rate considered for iodosulfuron-methyl-sodium is 10 g a.s./ha, for mesosulfuron-methyl is 15 g a.s./ha.
For the formulation maximum application rate from group E 1.5 L/formulation/ha was used, which covers the maximum dose of JME-HER 12 OD according to critical GAP.

Since these are worst case, already accepted in the Core Report for Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)) this approach is accepted for risk assessment purposes for JME-HER 12 OD by zRMS.
Since HQ values are < 50, acute risk for adult bees is acceptable.

According to the data requirements No. 284/2013 chronic toxicity to bees, effects on honey bee development and other honey bee life stages and sub-lethal effects should be addressed, whereby it is specifically pointed out that "Pending the validation and adoption of new studies and of a new risk assessment scheme, existing protocols shall be used to address the acute and chronic risk to bees, including those on colony survival and development, and the identification and measurement of relevant sub-lethal effects in the risk assessment".
While laboratory level test method development has progressed, only very recently agreed test methods became available. For example only in July 2016 the OECD TG 239 to assess larval toxicity after repeated feeding and in October 2017 the OECD GL 245 to investigate chronic toxicity in adult honeybees were published. However, such laboratory testing of plant protection products is not yet performed on a routine basis. The test methods that were available at the time of the active substance renewal process, which are still considered suitable to address the above described data requirements, include the study design by Oomen et al. (1992) and the OECD TG 75. Therefore, the study information and data that had been generated based on all available methods for the respective active substance is presented below.

For Iodosulfuron-methyl-sodium a study was performed to determine the effects on honey bee adults in a 10-day chronic feeding test in the laboratory. Adult honey bees were exposed to 50% (w/v) aqueous sucrose feeding solutions containing 3% acetone by continuous ad libitum feeding. Mortality and sublethal effects were assessed daily throughout the 10 day exposure period. Furthermore, the daily consumption, the mean uptake of test item and the accumulated mean uptake of test item were measured so that a daily dose per bee could be determined. The study was performed as a limit test and the feeding of 111.6 mg iodosulfuron-methyl-sodium/kg diet resulted in a LDD50 > 4.4 µg a.s./bee/d and a NOEDD ≥ 4.4 µg a.s./bee/d (values corrected for purity of techn. material) based on 2% mortality being observed at the tested dose. The result of the study indicates that there are no delayed or cumulative toxicity effects when exposure takes place chronically compared with acute testing, i.e. daily dosing with 4.4 µg a.s./bee of iodosulfuron-methyl-

sodium over 10 days (total dose = 44 µg a.s./bee) did not give higher mortality than a single acute oral exposure at 107.6 µg a.s./bee.

In order to investigate whether iodosulfuron-methyl sodium would pose a risk to immature honey bee life stages, a repeated feeding test on honeybee larvae under laboratory conditions has been conducted after finalization of the Annex I Renewal process. The new study data did not result in adverse findings.

In the laboratory test iodosulfuron-methyl sodium was mixed into larval diet at concentrations of 101, 51, 25, 13 and 6 mg a.s./kg diet, together with a parallel running untreated control and a toxic reference item known to cause effects. The volume of the diet fed was increased over the four feeding events to account for higher demands at increasing age of the organisms. The cumulative dose levels of the test item over the entire feeding period amounted to 16, 8, 4, 2 and 1 µg a.s./larva. In this test larval and pupal mortality as well as emergence success were assessed and consequently a 22-day NOED (emergence) of ≥ 16.0 µg iodosulfuron-methyl sodium/larva has been determined, which indicates that this test item does not pose a risk to honeybee development under these laboratory severe exposure conditions.

In addition to the chronic laboratory data on honeybee adults and larvae a higher tier test conducted with Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 400 (100+300 g/L) is available, which had already been assessed during the substance renewal process. In this study the formulation was directly sprayed onto the highly bee-attractive flowering crop Phacelia tanacetifolia during bee activity. After 4 days of exposure inside tunnels followed by an 18-day observation period outside tunnels, the NOEC was set to 10 g iodosulfuron-methyl-sodium/ha for mortality (adult and pupae), brood development and behaviour. Since mefenpyr-diethyl was applied at 30 g a.s./ha as part of the tested formulation, the findings from this study is equally relevant for the safener. Therefore this study provides information on chronic adult and brood exposure and indicates that a low risk is posed to bees by iodosulfuron-methyl-sodium and mefenpyr-diethyl.

For Mesosulfuron-methyl a study was performed to determine the effects of the test substance on honey bee adults in a 10-day chronic feeding test in the laboratory. Adult honey bees were exposed to 50 % (w/v) aqueous sucrose application solution, containing nominally 120 mg a.s./kg of the test item mesosulfuron-methyl (tech.) by continuous and ad libitum feeding. Mortality, sub-lethal effects and behavioural observations were assessed every day throughout the 10 days exposure period. Furthermore, the daily food uptake was determined. The study was performed as a limit test and the feeding of 120 mg mesosulfuron-methyl/kg diet resulted in a LC50 > 120 mg a.s./kg and a NOEC 120 mg a.s./kg based on 0.0% mortality being observed at the tested dose. After 10 days of continuous exposure, by considering the actual food consumption of the honey bees, the accumulated nominal intake of the test item mesosulfuronmethyl (tech.) at the treatment level of 120 mg a.s./kg was 48.5 µg a.s./bee, the corresponding average daily dose was therefore 4.85 µg a.s./bee/day. The result of the study indicates that there are no delayed or cumulative toxicity effects when exposure takes place chronically compared with acute testing, i.e. daily dosing with 4.85 µg a.s./bee of mesosulfuron-methyl over 10 days (total dose = 48.5 µg a.s./bee) did not give higher mortality than a single acute oral exposure at 105.6 µg a.s./bee.

In order to investigate whether mesosulfuron-methyl would pose a risk to immature honey bee life stages, a repeated feeding test on honeybee larvae under laboratory conditions has been conducted after finalization of the Annex I Renewal process. The new study data did not result in adverse findings. Since this data has not yet been evaluated at EU level, it is described in more detail below. The related study report is not included in this submission, but can be made available to the zRMS upon request.

In the laboratory test mesosulfuron-methyl was mixed into larval diet at concentrations of 81.2, 40.6, 20.3, 10.1 and 5.1 mg a.s./kg diet, together with a parallel running untreated control and a toxic reference item known to cause effects. The volume of the diet fed was increased over the four feeding events to account for higher demands at increasing age of the organisms. The cumulative dose levels of the test item over the entire feeding period amounted to 12.8, 6.4, 3.2, 1.6 and 0.8 µg a.s./larva. In this test larval and pupal mortality as well as emergence success were assessed and consequently a 22-day NOED (emergence) of ≥ 12.8 µg mesosulfuron-methyl/larva has been determined, which indicates that this test item does not pose

a risk to honeybee development under these laboratory severe exposure conditions.

In addition to the chronic laboratory data higher tier tests conducted with Mesosulfuron-methyl WG 75 are available. In the honey bee brood study under semi-field conditions Mesosulfuron-methyl WG 75 containing spray solution was directly applied onto the highly bee-attractive flowering crop Phacelia tanacetifolia during bee activity. For the application of 15 g mesosulfuron-methyl/ha and a 4 day exposure period inside tunnels followed by a 23-day observation period outside tunnels, no adverse effects were found regarding mortality (adult and pupae), foraging activity, behaviour, nectar- and pollen storage and queen survival and brood development. No effects were observed on colony development, colony strength and bee brood. Therefore this study provides information on chronic adult and brood exposure and indicates that a low risk is posed to bees by mesosulfuron-methyl.

When considering that the risk assessment can already be passed based on data originating from tier 1 laboratory studies, there is no need for higher tier test data. Furthermore, considering the available data on chronic effects on different bee life stages generated with the straight active substances, further chronic tests with the present mixture product would not be expected to provide any additional relevant information. Exposure (even acute exposure) is unlikely for honeybees when considering the use of a herbicide at BBCH 12-39 (until stem elongation) in cereals, that are seen as a non-bee attractive crop since they neither provide nectar nor pollen (wind pollination) as forage reward for bees.

Exposure of honeybees to flowering weeds is also considered as low. A recent publication (Maynard et al., 201521) showed that the availability of flowering weeds in cereal fields at relevant application times for herbicides is minimal. It was demonstrated here that less than 2% of all weeds recorded in arable crop trials are at a flowering growth stage. For wheat an even lower value of 0.86% was found based on 1024 trials that included 9113 weed recordings.

Generally the presence of flowering plants in/on non-cropped areas is also considered to be low. When conservatively assuming a theoretical exposure situation during which some bee-attractive plants would be present at the flowering stage and when treatment is performed, then the findings from the semi-field study presented above (application scenario onto full flowering and bee-attractive Phacelia) provide sufficient evidence that neither adults nor bee brood would be at risk after application of iodosulfuron-methylsodium at application rates up to 10 g a.s./ha nor after application of mesosulfuron-methyl at application rates up to 15 g a.s./ha.

Therefore, a safe use to bees can be demonstrated based on the low toxicity of iodosulfuron-methylsodium and mesosulfuron-methyl, the outcome of the tier 1 risk assessment (HQ calculation), the additional information on chronic adult toxicity and brood development, as well as based on the use pattern for the product and the exposure situation in a non-bee-attractive crop.

Risk assessment – EFSA Guidance 2013 (EFSA Journal 2013;11(7):3295)

The evaluation of the risk for bees was performed in accordance with the recommendations of the EFSA Guidance Document on the risk assessment of plant protection products on bees (Apis mellifera, Bombus spp. and solitary bees). This guidance document has not yet been noted and is not applicable for this assessment. The following risk assessment is presented simply to further demonstrate acceptable risk. To achieve a concise risk assessment, the risk envelope approach is applied. Here, the risk assessment on bees for the use of Atlantis OD on cereals at 1.5 L product/ha /ha (corresponding to 10 g IDM and 15 g MSM) covers all intended uses . Please note that only risk assessments for the active substances are presented for chronic risk assessment for adult bees. Calculations were performed with the calculator file "BeeTool v.3".

Table 9.6-9: Input parameters used for the risk assessment for iodosulfuron-methyl (honeybees)

Application rate	*0.01 kg a.s./ha*
Toxicity endpoints in µg/bee for contact assessments	

Acute contact – LD_{50}	*>100*
Toxicity endpoints	
Toxicicty endpoints in µg/bee for oral assessments	
Acute oral – LD50	*107.6*
Acute chronic – LDD50	*>4.4*

Table 9.6-10: Input parameters used for the risk assessment for mesosulfuron methyl (honey-bees)

Application rate	*0.015 kg a.s./ha*
Toxicity endpoints in µg/bee for contact assessments	
Acute contact – LD_{50}	*>100*
Toxicity endpoints	
Toxicicty endpoints in µg/bee for oral assessments	
Acute oral – LD50	*105.6*
Acute chronic – LDD50	*>4.85*

Results of risk assessments on several exposures are presented hereafter.

Table 9.6-11: HQ and ETR values on contact and oral routes of exposure for iodosulfuron-methyl

Contact route exposure				
Species	***"calculation factor" (linked with dust)***	***HQ***	***Trigger***	***Risk indicator***
Honeybees	*1*	*0.1*	*42*	*OK*
Oral route exposure (pollen and nectar)				
Honeybees – acute	*7.6*	*0.00*	*0.2*	*OK*
Honeybees – chronic	*7.6*	*0.017*	*0.03*	*OK*

Table 9.6-12: HQ and ETR values on contact and oral routes of exposure for mesosulfuro methyl

Contact route exposure				
Species	***"calculation factor" (linked with dust)***	***HQ***	***Trigger***	***Risk indicator***
Honeybees	*1*	*0.2*	*42*	*OK*
Oral route exposure (pollen and nectar)				
Honeybees – acute	*7.6*	*0.00*	*0.2*	*OK*
Honeybees – chronic	*7.6*	*0.024*	*0.03*	*OK*

Review comments

The evaluation of the risk for bees was performed in accordance with the recommendations of the "Guidance Document on Terrestrial Ecotoxicology", as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002). The risk assessment performed for active substances and the formulated product GLOB2007bF is agreed by the zRMS.

According to Commission regulation (EU) No 284/2013, point 10.3.1. (Effects on bees): Applicant should provide chronic test on bees and evaluation of effects on honey bee development with either formulated product or active substance. The chronic studies were not performed, therefore, for Poland, the deficiencies need to be fill till new guidance would come in to force. Nevertheless, such studies were deemed not necessary to finalize the risk assessment.

9.6.2.2 Higher-tier risk assessment for bees (tunnel test, field studies)

Not relevant. ~~See point 9.6.1.~~

9.6.3 Effects on bumble bees

~~Not relevant. See point 9.6.1.~~

There are no testing requirements for any bee other than the honey bee within the current implemented Regulation (EC) No. 1107/2009. The following studies on bumble bees are presented as additional information.

At present there is not yet a final test guideline available in Europe to assess the acute toxicity to bumble bees. However, sufficient experience within the European bee testing community has been gained to provide some experimental evidence on the acute toxicity to bumble bees and finalisation of an official OECD test guideline is expected within the year 2017. For the determination of the contact toxicity to bumble bees, methods in line with the current ring test have been employed.

Iodosulfuron-methyl-sodium
A study on the toxicity to bumble bees has been carried out with iodosulfuron-methyl-sodium. Full details are provided in the EU Renewal Assessment Report and related documents. The findings indicate that bumble bees are not more sensitive to iodosulfuron-methyl-sodium compared to honey bees.

Table 9.6-13: Endpoints and effect values for bumble bees

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Bombus terrestris	*Iodosulfuron-methyl-sodium, technical*	*Contact*	*LD_{50} > 100 µg a.s./bee*	*EFSA Scientific Report, 2016;14(4):4453*

Mesosulfuron-methyl
A study on the toxicity to bumble bees has been carried out with mesosulfuron-methyl. Full details are provided in the EU Renewal Assessment Report and related documents. The findings indicate that bumble bees are not more sensitive to mesosulfuron-methyl compared to honey bees.

Table 9.6-14: Endpoints and effect values for bumble bees

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Bombus terrestris	*Mesosulfuron-methyl (formulated as Mesosulfuron-methyl WG 75)*	*Contact*	*LD_{50} > 100 µg a.s./bee*	*EFSA Scientific Report, 2016;14(10):4584*

9.6.4 Effects on solitary bees

Not relevant. ~~See point 9.6.1.~~

9.6.5 Overall conclusions

~~Not relevant. See point 9.6.1.~~

The acute risk of the active substances and of the formulated product IMS+MSM+MPR OD 42 (2+10+30) to honeybees was assessed by calculation of hazard quotients between the maximum single application rate, and the respective toxicity endpoints determined as LD50 values following oral and contact exposure. All hazard quotients calculated are lower than 50, indicating that the acute oral and contact risk to bees is acceptable following the use according to the proposed use pattern.

A safe use to bees can be demonstrated based on the low toxicity of the active substances, the outcome of the tier 1 risk assessment (HQ calculation), the additional information from laboratory, semi-field and field testing, as well as based on the use pattern and the exposure situation.

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the HQ values were below the relevant trigger values. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to bees and bumble-bees. No risk mitigations are required.

9.7 Effects on arthropods other than bees (KCP 10.3.2)

9.7.1 Toxicity data

~~Information concerning studies with arthropods and risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD. No further data are required.~~

Effects on non-target arthropods of IMS+MSM+MPR OD 42 (2+10+30) were evaluated as part of the EU assessment of the active substance mesosulfuron-methyl (representative formulation). No new studies are submitted with this formulation, reference is made to the agreed endpoints reported in EFSA Journal 2016;14(10):4584, and RAR Volume 3 – B.9 (PPP) – ATLANTIS OD (revised version 2016-06).

Table 9.7-1: Endpoints and effect values relevant for the risk assessment for non-target arthro-pods - reference formulation Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30))

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Typhlodromus pyri (protonymphs)	*IMS+MSM+MPR OD 42 (2+10+30)*	*Laboratory test glass plates (2D)*	*LR_{50} > 1500 mL/ha*	*EFSA Scientific Report, 2016;14(10):4584*
Aphidius rhopalosiphi (adults)	*IMS+MSM+MPR OD 42 (2+10+30)*	*Laboratory test glass plates (2D)*	*LR_{50} = 877.3 mL/ha*	*EFSA Scientific Report, 2016;14(10):4584*
Aphidius rhopalosiphi (adults)	*IMS+MSM+MPR OD 42 (2+10+30)*	*Extended laboratory test barley plants (3D)*	*LR_{50} > 1500 mL/ha*	*EFSA Scientific Report, 2016;14(10):4584*
Chrysoperla carnea (larvae)	*IMS+MSM+MPR OD 42 (2+10+30)*	*Extended laboratory test maize leaves (2D)*	*LR_{50} > 1500 mL/ha*	*EFSA Scientific Report, 2016;14(10):4584*

Review comments

The risk assessment of JME-HER 12 OD reference to Core Assessment of the already registered product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

From ecotoxicological point of view JME-HER 12 OD is considered equivalent/comparable to already registered Atlantis 12 OD, therefore the unprotected ecotoxicological studies performed for Atlantis 12 OD can be used for risk assessment purposes of JME-HER 12 OD.

In current assessment the same approach is taken as was provided in the risk assessment of reference product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

9.7.1.1 Justification for new endpoints

Not relevant. ~~See point 9.7.1.~~

9.7.2 Risk assessment

~~Not relevant. See point 9.7.1.~~

The evaluation of the risk for non-target arthropods was performed in accordance with the recommendations of the "Guidance Document on Terrestrial Ecotoxicology", as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002), and in consideration of the recommendations of the guidance document ESCORT 2.

9.7.2.1 Risk assessment for in-field exposure

~~Not relevant. See point 9.7.1.~~

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group E also covers the risk for non-target arthropods from all other intended use groups (see 9.1.2).
The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD.

Table 9.7-2: First ~~- and higher -~~tier assessment of the in-field risk for non-target arthropods due to the use of JME-HER 12 OD ~~IMS+MSM+MPR OD 42 (2+10+30)~~ in cereals

Intended use	*Cereals, 1.5 L prod./ha*		
Active substance/product	*JME-HER 12 OD (IMS+MSM+MPR OD 42 (2+10+30))*		
Application rate (g/ha)	*1 × 1.5*		
MAF	*1*		
Test species Tier I	***LR_{50} (lab.) (g/ha)***	***$PER_{in\text{-}field}$ (g/ha)***	***$HQ_{in\text{-}field}$ criterion: HQ ≤ 2***
Typhlodromus pyri	*> 1500*	*1500*	*< 1.0*
Aphidius rhopalosiphi	*877.3*		*1.7*

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment.
Criteria values shown in bold breach the relevant trigger.

9.7.2.2 Risk assessment for off-field exposure

~~Not relevant. See point 9.7.1.~~

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group E also covers the risk for non-target arthropods from all other intended use groups (see 9.1.2).
The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD.

Table 9.7-3: First ~~and higher~~ tier assessment of the off-field risk for non-target arthropods due to the use of JME-HER 12 OD (IMS+MSM+MPR OD 42 (2+10+30)) in cereals

Intended use	*Cereals, 1.5 L prod./ha (use group E)*				
Active substance/product	*JME-HER 12 OD (IMS+MSM+MPR OD 42 (2+10+30))*				
Application rate (L/ha)	*1 × 1.5*				
MAF	*1*				
VDF	*5 (2D) / 1 (3D)*				
Test species Tier I	***LR_{50} (lab.) (g/ha)***	***Drift rate***	***$PER_{off\text{-}field}$ (g/ha)***	***CF***	***$HQ_{off\text{-}field}$ criterion: HQ ≤ 2***
Aphidius rhopalosiphi	*> 1500*	*2.77%*	*83.1*	*10*	*< 0.0277*
Typhlodromus pyri	*877.3*				*0.948*

MAF: Multiple application factor; vdf: Vegetation distribution factor; (corr.) PER: (corrected) Predicted environmental rate; CF: Correction factor; HQ: Hazard quotient. Criteria values shown in bold breach the relevant trigger.

9.7.2.3 Additional higher-tier risk assessment

Not relevant. ~~See point 9.7.1.~~

9.7.2.4 Risk mitigation measures

Not relevant. ~~See point 9.7.1.~~

9.7.3 Overall conclusions

~~Not relevant. See point 9.7.1.~~

It can be concluded that no unacceptable risk to non-target arthropods in the in-field and the off-field is to be expected from the use of JME-HER 12 OD ~~IMS+MSM+MPR OD 42 (2+10+30)~~ according to the intended use pattern.

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the HQ values were below the relevant trigger value of 2. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to arthropods. No risk mitigations are required.

Review comments:

The evaluation of the risk assessment for non-target arthropods was performed in accordance with the recommendations of the guidance document ESCORT 2.

The risk assessment was performed for higher dose than is in the GAP. For the formulation maximum

application rate (group E) 1.5 L/formulation/ha was used, which covers the maximum dose of JME-HER 12 OD according to critical GAP.
Since these are worst case, already accepted in the Core Report for Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)) this approach is accepted for risk assessment purposes for JME-HER 12 OD by zRMS.
The HQ for recommended species: *Typhlodromus pyri* and *Aphidius rhopalosiphi* is below the ESCORT 2 trigger value of 2, indicating acceptable in-field and off-field risk to non-target arthropods already at tier I. On this basis acceptable risk for in-field and off-field habitats is concluded with no need of mitigation measures.

9.8 Effects on non-target soil meso- and macrofauna (KCP 10.4)

9.8.1 Toxicity data

~~Information concerning studies with soil organisms and risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD. No further data are required.~~

Iodosulfuron-methyl-sodium
Studies on the toxicity to earthworms and other non-target soil organisms (meso- and macrofauna) have been carried out with iodosulfuron-methyl-sodium and its relevant metabolites. Full details of these studies are provided in the EU Renewal Assessment Report and related documents; presented agreed endpoints were taken from EFSA Journal 2016;14(4):4453.

Table 9.8-1: Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) -iodosulfuron-methyl-sodium

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Eisenia fetida	*Iodosulfuron-methyl-sodium*	*Mixed into substrate 56 d, chronic 10 % peat content*	*EC_{10} = 7 mg a.s./kg dw*	*EFSA Journal 2016;14(4):4453*
Folsomia candida	*Iodosulfuron-methyl-sodium*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 316 mg a.s./kg dw*	*EFSA Journal 2016;14(4):4453*
Hypoaspis aculeifer	*Iodosulfuron-methyl-sodium*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 1000 a.s./kg dw*	*EFSA Journal 2016;14(4):4453*
Eisenia fetida	*AE F075736*	*Mixed into substrate 56 d, chronic 10 % peat content*	*EC_{10} (estimated) = 0.7 mg/kg dw*	*EFSA Journal 2016;14(4):4453*
Folsomia candida	*AE F075736*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 9.86 mg /kg dw*	*EFSA Journal 2016;14(4):4453*
Hypoaspis aculeifer	*AE F075736*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 9.86 mg /kg dw*	*EFSA Journal 2016;14(4):4453*
Eisenia fetida	*AE F145741*	*Mixed into substrate*	*NOEC = 94.4 mg*	*EFSA Journal*

Species	Substance	Exposure System	Results	Reference
		56 d, chronic 10 % peat content	/kg dw	2016;14(4):4453
Hypoaspis aculeifer	AE F145741	Mixed into substrate 14 d, chronic 5 % peat content	NOEC = 100 mg /kg dw	EFSA Journal 2016;14(4):4453
Eisenia fetida	AE F145740	Mixed into substrate 56 d, chronic 10 % peat content	NOEC = 97.5 mg /kg dw	EFSA Journal 2016;14(4):4453
Hypoaspis aculeifer	AE F145740	Mixed into substrate 14 d, chronic 5 % peat content	NOEC = 97.5 mg /kg dw	EFSA Journal 2016;14(4):4453
Eisenia fetida	AE 0002166	Mixed into substrate 56 d, chronic 10 % peat content	NOEC = 95.0 mg /kg dw	EFSA Journal 2016;14(4):4453
Hypoaspis aculeifer	AE 0002166	Mixed into substrate 14 d, chronic 5 % peat content	NOEC = 95.2 mg /kg dw	EFSA Journal 2016;14(4):4453
Eisenia fetida	BCS-CW81253	Mixed into substrate 56 d, chronic 10 % peat content	NOEC = 99.0 mg /kg dw	EFSA Journal 2016;14(4):4453
Folsomia candida	BCS-CW81253	Mixed into substrate 28 d, chronic 5 % peat content	NOEC = 99.0 mg /kg dw	EFSA Journal 2016;14(4):4453
Hypoaspis aculeifer	BCS-CW81253	Mixed into substrate 14 d, chronic 5 % peat content	NOEC = 99.0 mg /kg dw	EFSA Journal 2016;14(4):4453
Eisenia fetida	AE 0000119	Mixed into substrate 56 d, chronic 10 % peat content	NOEC = 97.8 mg /kg dw	EFSA Journal 2016;14(4):4453
Folsomia candida	AE 0000119	Mixed into substrate 28 d, chronic 5 % peat content	NOEC = 97.8 mg /kg dw	EFSA Journal 2016;14(4):4453
Hypoaspis aculeifer	AE 0000119	Mixed into substrate 14 d, chronic 5 % peat content	NOEC = 97.8 mg /kg dw	EFSA Journal 2016;14(4):4453
Eisenia fetida	AE F059411	Mixed into substrate 56 d, chronic 10 % peat content	NOEC = 30 mg /kg dw	EFSA Journal 2016;14(4):4453
Folsomia candida	AE F059411	Mixed into substrate 28 d, chronic 5 % peat content	NOEC = 99.7 mg /kg dw	EFSA Journal 2016;14(4):4453
Hypoaspis aculeifer	AE F059411	Mixed into substrate 14 d, chronic 5 % peat content	NOEC = 98.7 mg /kg dw	EFSA Journal 2016;14(4):4453

Mesosulfuron-methyl

Studies on the toxicity to earthworms and other non-target soil organisms (meso- and macrofauna) have

been carried out with mesosulfuron-methyl and its relevant metabolites. Full details of these studies are provided in the EU Renewal Assessment Report and related documents; presented agreed endpoints were taken from EFSA Journal 2016;14(10):4584.

Table 9.8-2: Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) - mesosulfuron-methyl

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Eisenia fetida	*Mesosulfuron-methyl*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 125 mg a.s./kg dws*	*EFSA Journal 2016;14(10):4584*
Folsomia candida	*Mesosulfuron-methyl*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 1000 mg a.s./kg dws*	*EFSA Journal 2016;14(10):4584*
Hypoaspis aculeifer	*Mesosulfuron-methyl*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 1000 mg a.s./kg dws*	*EFSA Journal 2016;14(10):4584*
Folsomia candida	*AE F154851*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 100 mg/kg dws*	*EFSA Journal 2016;14(10):4584*
Eisenia fetida	*AE F160459*	*Mixed into substrate 56 d, chronic 5 % peat content*	*NOEC = 90 mg/kg dws*	*EFSA Journal 2016;14(10):4584*
Folsomia candida	*AE F160459*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 100 mg/kg dws*	*EFSA Journal 2016;14(10):4584*
Eisenia fetida	*AE F099095*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 100 mg p.m./kg dws*	*EFSA Journal 2016;14(10):4584*
Eisenia fetida	*AE F092944*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 10 mg/kg dws*	*EFSA Journal 2016;14(10):4584*
Folsomia candida	*AE F092944*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 100 mg/kg dws*[1)]	*EFSA Journal 2016;14(10):4584*[1)]
Hypoaspis aculeifer	*AE F092944*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 100 mg/kg dws*	*EFSA Journal 2016;14(10):4584*
Eisenia fetida	*AE F160460*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 100 mg/kg dws*	*EFSA Journal 2016;14(10):4584*
Eisenia fetida	*AE F140584*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 117 mg/kg dws*	*EFSA Journal 2016;14(10):4584*
Eisenia fetida	*AE F147447*	*Mixed into substrate 56 d, chronic 5 % peat content*	*NOEC = 90 mg/kg dws*	*EFSA Journal 2016;14(10):4584*
Folsomia candida	*AE F147447*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 100 mg/kg dws*	*EFSA Journal 2016;14(10):4584*

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Endpoints used for metabolites risk assessment in case that no EU agreed test data are available				
Eisenia fetida	*AE F154851*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 12.5 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Hypoaspis aculeifer	*AE F154851*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Hypoaspis aculeifer	*AE F160459*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Folsomia candida	*AE F099095*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Hypoaspis aculeifer	*AE F099095*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Folsomia candida	*AE F160460*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Hypoaspis aculeifer	*AE F160460*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Folsomia candida	*AE F140584*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Hypoaspis aculeifer	*AE F140584*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*
Hypoaspis aculeifer	*AE F147447*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 100 mg a.s./kg dws[2)]*	*from parent compound - see EFSA Journal 2016;14(10):4584*

IMS+MSM+MPR OD 42 (2+10+30)

Effects on earthworms and other non-target soil organisms of IMS+MSM+MPR OD 42 (2+10+30) were evaluated as part of the EU assessment of the active substance mesosulfuron-methyl (representative formulation). No new studies are submitted with this formulation, reference is made to the agreed endpoints reported in EFSA Journal 2016;14(10):4584, and RAR Volume 3 – B.9 (PPP) – ATLANTIS OD (revised version 2016-06).

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD.

Table 9.8-3: ***Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna)* - reference formulation Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30))**

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Eisenia fetida	*IMS+MSM+MPR OD 42 (2+10+30)*	*Mixed into substrate 56 d chronic 10 % peat content*	*EC10 = 60 mg/kg soil*	*EFSA Journal 2016;14(10):4584*
Folsomia candida	*IMS+MSM+MPR OD 42 (2+10+30)*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 17 mg/kg soil*	*EFSA Journal 2016;14(10):4584*
Hypoaspis aculeifer	*IMS+MSM+MPR OD 42 (2+10+30)*	*Mixed into substrate 14 d, chronic 5 % peat content*	*EC10 = 297 mg/kg soil*	*EFSA Journal 2016;14(10):4584*

Review comments

The risk assessment of JME-HER 12 OD reference to Core Assessment of the already registered product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

From ecotoxicological point of view JME-HER 12 OD is considered equivalent/comparable to already registered Atlantis 12 OD, therefore the unprotected ecotoxicological studies performed for Atlantis 12 OD can be used for risk assessment purposes of JME-HER 12 OD.

In current assessment the same approach is taken as was provided in the risk assessment of reference product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

9.8.1.1 Justification for new endpoints

~~Not relevant. See point 9.8.1.~~

No deviation from the EU agreed endpoints.

9.8.2 Risk assessment

~~Not relevant. See point 9.8.1.~~

The evaluation of the risk for earthworms and other non-target soil organisms (meso- and macrofauna) was performed in accordance with the recommendations of the "Guidance Document on Terrestrial Ecotoxicology", as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

9.8.2.1 First-tier risk assessment

~~Not relevant. See point 9.8.1.~~

The relevant PEC_{soil} for risk assessments covering the proposed use pattern are taken from Section 8 (Environmental Fate), Chapter 8.7.2. According to the assessment of environmental-fate data, multi-annual accumulation in soil is considered where relevant.

Iodosulfuron-methyl-sodium

For the active substance iodosulfuron-methyl-sodium (and metabolites) risk assessments are passed without any refinement, even if worst case PEC_{soil} values are considered. Therefore, to further simplify the assessment, PEC_{soil} for these compounds is calculated in an additional "risk envelope approach", addressing the maximum registered application rate and overall worst case exposure situation (no tillage, no crop interception) which is relevant for the compound in any product supported by Bayer AG in Europe. The resulting PEC_{soil} calculations may overestimate the actual exposure due to use of the present product, and thus further increase the conservatism of the Tier 1 risk assessments.

Table 9.8-4: First-tier assessment of the chronic risk of iodosulfuron-methyl-sodium for earthworms due to the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A)

Intended use	*Risk envelope approach:* *Cereals~~, maize, non-cropped area, 10 g a.s./ha, BBCH 00-39~~*		
Chronic effects on earthworms			
Product/active substance	***NOEC / EC_{10} (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***TER_{lt} (criterion TER ≥ 5)***
Iodosulfuron-methyl-sodium	*7*	*0.013*	*538*
AE F075736	*0.7*	*0.009*	*78*
AE F145741	*94.4*	*<0.001*	*94400*
AE F145740	*97.5*	*0.001*	*97500*
AE 0002166	*95.0*	*0.001*	*95000*
BCS-CW81253	*99.0*	*0.003*	*33000*
AE 0000119	*97.8*	*0.001*	*97800*
AE F059411	*30*	*0.002*	*15000*

Table 9.8-5: First-tier assessment of the chronic risk of iodosulfuron-methyl-sodium for other non-target soil organisms (meso- and macrofauna) due to the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A)

Intended use	*Risk envelope approach:* *Cereals~~, maize, non-cropped area, 10 g a.s./ha, BBCH 00-39~~*		
Chronic effects on other soil macro- and mesofauna			
Product/active substance	***NOEC (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***TER_{lt} (criterion TER ≥ 5)***
Iodosulfuron-methyl-sodium (F. candida)	*316*	*0.013*	*24308*
AE F075736 (F. candida)	*9.86*	*0.009*	*1096*
BCS-CW81253 (F. candida)	*99.0*	*0.003*	*33000*
AE 0000119 (F. candida)	*97.8*	*0.001*	*97800*
AE F059411 (F. candida)	*99.7*	*0.002*	*49850*

Iodosulfuron-methyl-sodium (H. aculeifer)	*1000*	*0.013*	*76923*
AE F075736 (H. aculeifer)	*9.86*	*0.009*	*1096*
AE F145741 (H. aculeifer)	*100*	*<0.001*	*100000*
AE F145740 (H. aculeifer)	*97.5*	*0.001*	*97500*
AE 0002166 (H. aculeifer)	*95.2*	*0.001*	*95200*
BCS-CW81253 (H. aculeifer)	*99.0*	*0.003*	*33000*
AE 0000119 (H. aculeifer)	*97.8*	*0.001*	*97800*
AE F059411 (H. aculeifer)	*98.7*	*0.002*	*49350*

Mesosulfuron-methyl

For the active substance mesosulfuron-methyl (and metabolites) risk assessments are passed without any refinement, even if worst case PEC_{soil} values are considered. Therefore, to further simplify the assessment, PEC_{soil} for these compounds is calculated in an additional "risk envelope approach", addressing the maximum registered application rate and overall worst case exposure situation (no tillage, no crop interception) which is relevant for the compound in any product supported by Bayer AG in Europe.
The resulting PEC_{soil} calculations may overestimate the actual exposure due to use of the present product, and thus further increase the conservatism of the Tier 1 risk assessments.

Table 9.8-6: First-tier assessments of the acute and chronic risk of mesosulfuron-methyl for earthworms due to the use of* JME-HER 12 OD *~~IMS+MSM+MPR OD 42 (2+10+30)~~ in cereals (use group A)

Intended use	*Risk envelope approach:* *Cereals (winter and spring), 15 g a.s./ha, no crop interception*		
Chronic effects on earthworms			
Product/active substance	***NOEC (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***TER_{lt} (criterion TER ≥ 5)***
Mesosulfuron-methyl	*125*	*0.022*	*5682*
AE F154851	*12.5**	*0.004*	*3125*
AE F160459	*90*	*0.002*	*45000*
AE F099095	*100*	*0.003*	*33333*
AE F092944	*10*	*<0.001*	*>10000*
AE F160460	*100*	*0.002*	*50000*
AE F140584	*117*	*<0.001*	*>117000*
AE F147447	*90*	*<0.001*	*>90000*

TER values shown in bold fall below the relevant trigger.
**assuming it is 10 times more toxic than the parent*

Table 9.8-7: ***First-tier assessments of the acute and chronic risk of mesosulfuron-methyl for other non-target soil organisms (meso- and macrofauna) due to the use of* JME-HER 12 OD *~~IMS+MSM+MPR OD 42 (2+10+30)~~ in cereals (use group A)***

Intended use	*Risk envelope approach:* *Cereals (winter and spring), 15 g a.s./ha, no crop interception*		
Chronic effects on other soil macro- and mesofauna			
Product/active substance	***NOEC*** ***(mg/kg dw)***	***PEC_{soil}*** ***(mg/kg dw)***	***TER_{lt}*** ***(criterion TER ≥ 5)***
Mesosulfuron-methyl *(F. candida)*	*1000*	*0.022*	*45455*
AE F154851 *(F. candida)*	*100*	*0.004*	*25000*
AE F160459 *(F. candida)*	*100*	*0.002*	*50000*
AE F099095 *(F. candida)*	*100**	*0.003*	*3333*
AE F092944 *(F. candida)*	*100*	*< 0.001*	*>100000*
AE F160460 *(F. candida)*	*100**	*0.002*	*50000*
AE F140584 *(F. candida)*	*100**	*<0.001*	*>100000*
AE F147447 *(F. candida)*	*100*	*< 0.001*	*>100000*
Mesosulfuron-methyl *(H. aculeifer)*	*1000*	*0.022*	*45455*
AE F154851 *(H. aculeifer)*	*100**	*0.004*	*25000*
AE F160459 *(H. aculeifer)*	*100**	*0.002*	*50000*
AE F099095 *(H. aculeifer)*	*100**	*0.003*	*33333*
AE F092944 *(H. aculeifer)*	*100*	*< 0.001*	*>100000*
AE F160460 *(H. aculeifer)*	*100**	*0.002*	*50000*
AE F140584 *(H. aculeifer)*	*100**	*<0.001*	*>100000*
AE F147447 *(H. aculeifer)*	*100**	*<0.001*	*>100000*

TER values shown in bold fall below the relevant trigger.
**assuming it is 10 times more toxic than the parent*

JME-HER 12 OD based on the endpoints for the formulation **IMS+MSM+MPR OD 42 (2+10+30)**

Table 9.8-8: ***First-tier assessment of the acute and chronic risk of JME-HER 12 OD ~~IMS+MSM+MPR OD 42 (2+10+30)~~ for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use in cereals (use group E)***

Intended use	***Cereals (winter), 1.5 L/ha, no crop interception***		
Acute effects on earthworms			
Not required according to Regulation (EC) 1107/2009			
Chronic effects on earthworms			
Product/active substance	***NOEC (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***TER_{lt} (criterion TER ≥ 5)***
IMS+MSM+MPR OD 42 (2+10+30)	*60*	*2*	*30*
Chronic effects on other soil macro- and mesofauna			
Product/active substance	***NOEC (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***TER_{lt} (criterion TER ≥ 5)***
IMS+MSM+MPR OD 42 (2+10+30) (F. candida)	*17*	*2*	*8.5*
IMS+MSM+MPR OD 42 (2+10+30) (H. aculeifer)	*297*	*2*	*148.5*

TER values shown in bold fall below the relevant trigger.

9.8.2.2 Higher-tier risk assessment

Not relevant. ~~See point 9.8.1.~~

zRMS comments:
A higher tier assessment is not required based on the low risk indicated in the chronic assessment on earthworms, collembolan, and soil mite.

9.8.3 Overall conclusions

~~Not relevant. See point 9.8.1.~~

The acute and/or long-term risk of the active substances and their relevant metabolites and of the formulated product was assessed, based on maximum PECsoil. All TER values for earthworms and other soil macro-organisms are greater than the relevant triggers indicating acceptable for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals.

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the TER values exceeded the relevant trigger value of 5. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to earthworms and other soil organisms. No risk mitigations are required.

Review comments:

The risk assessment for earthworms and other soil macro-organisms exposed to active substances, its metabolites and the formulation JME-HER 12 OD was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology” (SANCO/10329/2002) was accepted by the zRMS.

The risk assessment for both active substances (group A) was performed for higher dose than is in the GAP. The Applicant followed a generic 'risk envelope' approach, where the European envelope rate considered for iodosulfuron-methyl-sodium is 10 g a.s./ha, for mesosulfuron-methyl is 15 g a.s./ha.
For the formulation maximum application rate from group E 1.5 L/formulation/ha was used, which covers the maximum dose of JME-HER 12 OD according to critical GAP.

The relevant PEC_{soil} for risk assessments is taken from Section 8 (Environmental Fate), for details please, refer to Section 8.

TER_{lt} values calculated for all considered compounds and JME-HER 12 OD were above the respective trigger indicating acceptable long-term risk to earthworms and other soil macro-organisms. No further evaluation is deemed necessary.

9.9 Effects on soil microbial activity (KCP 10.5)

9.9.1 Toxicity data

~~Information concerning studies with microorganisms and risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD. No further data are required.~~

Iodosulfuron-methyl-sodium
Studies on effects soil microorganisms have been carried out with iodosulfuron-methyl-sodium and its relevant metabolites. Full details of these studies are provided in the EU Renewal Assessment Report and related documents; presented agreed endpoints were taken from EFSA Journal 2016;14(4):4453, if not otherwise stated.

Table 9.9-1: Endpoints and effect values relevant for the risk assessment for soil microorganisms – iodosulfuron-methyl-sodium

Endpoint	***Substance***	***Exposure System***	***Results***	***Reference***
N-mineralisation	*iodosulfuron-methyl-sodium*	*28 d, aerobic soil type*	*No unacceptable effects on N-transformations at 0.067 mg/kg soil dw*	*EFSA Journal 2016;14(4):4453*
N-mineralisation	*AE F075736 (as formulated product 20DP submitted for active substance metsulfuron-methyl)*	*28 d, aerobic soil type*	*No unacceptable effects on N-transformations at 0.04 mg/kg soil dw*	*EFSA Journal 2016;14(4):4453 endpoint taken from: Sanco 7593/VI/97-final from 14AUG2000*
N-mineralisation	*AE F145741*	*28 d, aerobic soil type*	*No unacceptable effects on N-transformations at 0.063 mg/kg soil dw*	*EFSA Journal 2016;14(4):4453*
N-mineralisation	*AE F145740*	*28 d, aerobic soil type*	*No unacceptable effects on N-transformations at 0.063 mg/kg soil dw*	*EFSA Journal 2016;14(4):4453*

Endpoint	Substance	Exposure System	Results	Reference
N-mineralisation	AE 0002166	28 d, aerobic soil type	No unacceptable effects on N-transformations at 0,053 mg/kg soil dw	EFSA Journal 2016;14(4):4453
N-mineralisation	AE F161778	28 d, aerobic soil type	No unacceptable effects on N-transformations at 0.049 mg/kg soil dw	EFSA Journal 2016;14(4):4453
N-mineralisation	BCS-CW81253	28 d, aerobic soil type	No unacceptable effects on N-transformations at 0.043 mg/kg soil dw	EFSA Journal 2016;14(4):4453
N-mineralisation	AE 0000119	28 d, aerobic soil type	No unacceptable effects on N-transformations at 0.4 mg/kg soil dw	EFSA Journal 2016;14(4):4453
N-mineralisation	AE F059411	42 d, aerobic soil type	No unacceptable effects on N-transformations at 0.204 mg/kg soil dw	EFSA Journal 2016;14(4):4453

soil dw = soil dry weight

Mesosulfuron-methyl

Studies on effects on soil microorganisms have been carried out with mesosulfuron-methyl and its relevant metabolites. Full details of these studies are provided in the EU Renewal Assessment Report and related documents, presented agreed endpoints were taken from EFSA Journal 2016;14(10):4584.

Table 9.9-2: Endpoints and effect values relevant for the risk assessment for soil microorganisms – mesosulfuron-methyl

Endpoint	Substance	Exposure System	Results	Reference
N-mineralisation	Mesosulfuron-methyl	28 d, aerobic silty sand and loamy silt	No unacceptable effects on N-transformations at 0.1 mg/kg d.w. soil	EFSA Journal 2016;14(10):4584
N-mineralisation	AE F154851	28 d, aerobic sandy loam	No unacceptable effects on N-transformations at 0.1 mg/kg d.w. soil	EFSA Journal 2016;14(10):4584
N-mineralisation	AE F160459	42 d, aerobic sandy loam	No unacceptable effects on N-transformations at 0.1 mg/kg d.w. soil	EFSA Journal 2016;14(10):4584
N-mineralisation	AE F099095	28 d, aerobic sandy loam	No unacceptable effects on N-transformations at 0.1 mg/kg d.w. soil	EFSA Journal 2016;14(10):4584

Endpoint	Substance	Exposure System	Results	Reference
N-mineralisation	*AE F092944*	*28 d, aerobic loamy sand*	*No unacceptable effects on N-transformations at 0.137 mg/kg d.w. soil**	*EFSA Journal 2016;14(10):4584*
N-mineralisation	*AE F147447*	*28 d, aerobic loamy sand*	*No unacceptable effects on N-transformations at 0.057 mg/kg d.w. soil*	*EFSA Journal 2016;14(10):4584*

d.w. soil = dry weight soil
**) Results of two studies on N-mineralisation are tabulated in the EFSA List of Endpoints, thereof the value of "< 25 % effect at day 28 at 0.137 mg/kg d.w.soil" is deemed relevant for risk assessment, since not in contradiction to the value of "<25% effect at day 28 at 0.06 mg/kg d.w.soil" resulting from the peer review of the active substance flazasulfuron (EFSA Journal 2016;14(8):4575).*

JME-HER 12 OD based on the endpoints for the reference formulation IMS+MSM+MPR OD 42 (2+10+30)

Effects on soil microorganisms of IMS+MSM+MPR OD 42 (2+10+30) were evaluated as part of the EU assessment of the active substance mesosulfuron-methyl (representative formulation). No new studies are submitted with this formulation, reference is made to the agreed endpoints reported in EFSA Journal 2016;14(10):4584, and RAR Volume 3 – B.9 (PPP) – ATLANTIS OD (revised version 2016-06).

Table 9.9-3: Endpoints and effect values relevant for the risk assessment for soil microorganisms with the reference formulation Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30))

Endpoint	Substance	Exposure System	Results	Reference
N-mineralisation	*IMS+MSM+MPR OD 42 (2+10+30)*	*42 d, aerobic silty sand*	*No adverse effect at 7.5 L prod./ha = 10 µL prod. /kg soil dw*	*EFSA Journal 2016;14(10):4584*

Review comments

The risk assessment of JME-HER 12 OD reference to Core Assessment of the already registered product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

From ecotoxicological point of view JME-HER 12 OD is considered equivalent/comparable to already registered Atlantis 12 OD, therefore the unprotected ecotoxicological studies performed for Atlantis 12 OD can be used for risk assessment purposes of JME-HER 12 OD.

In current assessment the same approach is taken as was provided in the risk assessment of reference product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

9.9.1.1 Justification for new endpoints

~~Not relevant. See point 9.9.1.~~

No deviation from the EU agreed endpoints.

9.9.2 Risk assessment

~~Not relevant. See point 9.9.1.~~

The evaluation of the risk for soil microorganisms was performed in accordance with the recommendations of the "Guidance Document on Terrestrial Ecotoxicology", as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

The relevant PEC_{soil} for risk assessments covering the proposed use pattern are taken from Section 8 (Environmental Fate), Chapter 8.7.2 and were already used in the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) (see 9.8).

Iodosulfuron-methyl-sodium
For the active substance iodosulfuron–methyl-sodium (and metabolites) risk assessments are passed without any refinement, even if worst case PEC_{soil} values are considered. Therefore, to further simplify the assessment, PEC_{soil} for these compounds is calculated in an additional "risk envelope approach", addressing the maximum registered application rate and overall worst case exposure situation (no tillage, no crop interception) which is relevant for the compound in any product supported by Bayer AG in Europe.
The resulting PEC_{soil} calculations may overestimate the actual exposure due to use of the present product, and thus further increase the conservatism of the Tier 1 risk assessments.

Table 9.9-4: Assessment of the risk of iodosulfuron-methyl-sodium for effects on soil microorganisms due to the use of* JME-HER 12 OD *(IMS+MSM+MPR OD 42 (2+10+30)) in cereals (use group A)

Intended use	*Risk envelope approach:* *Cereals~~, maize, non-cropped area, 10 g a.s./ha, BBCH 00-39~~*		
N-mineralisation			
Product/active substance	***Max. conc. with effects ≤ 25 % (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***Risk acceptable?***
Iodosulfuron-methyl-sodium	*0.067 (at 28 d)*	*0.013*	*yes*
AE F075736	*0.04 (at 28 d)*	*0.009*	*yes*
AE F145741	*0.063 (at 28 d)*	*<0.001*	*yes*
AE F145740	*0.063 (at 28 d)*	*0.001*	*yes*
AE 0002166	*0.053 (at 28 d)*	*0.001*	*yes*
AE F161778	*0.049 (at 28 d)*	*0.001*	*yes*
BCS-CW81253	*0.043 (at 28 d)*	*0.003*	*yes*
AE 0000119	*0.4 (at 28 d)*	*0.001*	*yes*
AE F059411	*0.204 (at 42 d)*	*0.002*	*yes*

dw = dry weight

Mesosulfuron-methyl
For the active substance mesosulfuron-methyl (and metabolites) risk assessments are passed without any refinement, even if worst case PEC_{soil} values are considered. Therefore, to further simplify the assessment, PEC_{soil} for these compounds is calculated in an additional "risk envelope approach", addressing the maximum registered application rate and overall worst case exposure situation (no tillage, no crop inter-ception) which is relevant for the compound in any product supported by Bayer AG in Europe.
The resulting PEC_{soil} calculations may overestimate the actual exposure due to use of the present product, and thus further increase the conservatism of the Tier 1 risk assessments.

Table 9.9-5: Assessment of the risk of mesosulfuron methyl for effects on soil micro-organisms due to the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals (use group A)

Intended use	*Risk envelope approach:* *Cereals (winter and spring), 15 g a.s./ha, BBCH 10-39*		
N-mineralisation			
Product/active substance	***Max. conc. with effects ≤ 25 % (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***Risk acceptable?***
Mesosulfuron-methyl	*0.1 (at 28 d)*	*0.022*	*yes*
AE F154851	*0.1 (at 28 d)*	*0.004*	*yes*
AE F160459	*0.1 (at 42 d)*	*0.002*	*yes*
AE F099095	*0.1 (at 28 d)*	*0.003*	*yes*
AE F092944	*0.137 (at 28 d)*	*<0.001*	*yes*
AE F147447	*0.057 (at 28 d)*	*<0.001*	*yes*

dw = dry weight

JME-HER 12 OD based on the endpoints for the reference formulation IMS+MSM+MPR OD 42 (2+10+30)

Table 9.9-6: Assessment of the risk for effects of IMS+MSM+MPR OD 42 (2+10+30) on soil micro-organisms due to the use in cereals (use group E)

Intended use	***Cereals (winter), 1.5 L/ha, no crop interception***		
N-mineralisation			
Product/active substance	***Max. conc. with effects ≤ 25 % (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***Risk acceptable?***
IMS+MSM+MPR OD 42 (2+10+30)	*10* (at 42 d)*	*2*	*yes*

** specified density for product IMS + MSM + MPR OD 42: 1.0 g/mL*

9.9.3 Overall conclusions

~~Not relevant. See point 9.9.1.~~

The risk of the active substances, their relevant metabolites, and of the formulated product was assessed based on maximum PECsoil, and indicated acceptable for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals.

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. According to the performed risk assessment it was concluded that the application of JME-HER 12 OD in accordance with GAP does not pose unacceptable risk to soil micro-organisms. No risk mitigations are required.

Review comments:

The evaluation of the risk for soil microorganisms was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002) and was accepted by the zRMS.

The relevant PEC_{soil} for risk assessments covering the proposed use pattern are taken from Section 8 (Environmental Fate), for details please, refer to Section 8.

The risk assessment was performed for higher dose than is in the GAP. For the formulation maximum application rate (group E) 1.5 L/formulation/ha was used, which covers the maximum dose of JME-HER 12 OD according to critical GAP.
Since these are worst case, already accepted in the Core Report for Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)) this approach is accepted for risk assessment purposes for JME-HER 12 OD by zRMS.

JME-HER 12 OD by zRMS did not have any long-term adverse effects on the process of nitrogen transformation in aerobic surface soils indicating an acceptable risk to soil microorganism for all proposed uses of the formulation JME-HER 12 OD.

9.10 Effects on non-target terrestrial plants (KCP 10.6)

9.10.1 Toxicity data

~~Information concerning studies with non-target terrestrial plants and risk assessment is included in RR for the reference product Atlantis 12 OD. Please refer to Renewal RR prepared for Atlantis 12 OD. No further data are required.~~

Effects on non-target terrestrial plants of IMS+MSM+MPR OD 42 (2+10+30) were evaluated as part of the EU assessment of the active substance mesosulfuron-methyl (representative formulation). No new studies are submitted with this formulation, reference is made to the agreed endpoints reported in EFSA Journal 2016;14(10):4584, and RAR Volume 3 – B.9 (PPP) – ATLANTIS OD (revised version 2016-06).

Table 9.10-1: Endpoints and effect values relevant for the risk assessment for non-target terrestrial plants with the reference formulation Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30))

Species	***Substance***	***Exposure System***	***Results***	***Reference***
Beta vulgaris. $_d$ [1)] *Brassica napus.* $_d$ [2)] *Cucumis sativus* $_d$ [3)] *Glycine max* $_d$ [4)] *Helianthus annuus* $_d$ [5)] *Raphanus sativus* $_d$ [6)] *Lycopersicon esculentum* $_d$ [7)] *Allium cepa* $_m$ [8)] *Avena sativa* $_m$ [9)] *Zea mays* $_m$ [10)]	*IMS+MSM+MPR OD 42 (2+10+30)*	*21 d Seedling emergence, Tier 2*	[1)] *ER_{50} shoot dry weight = 155 mL product/ha* [2)] *ER_{50} shoot dry weight = 229 mL product/ha* [3)] *ER_{50} shoot dry weight = 327 mL product/ha* [4)] *ER_{50} shoot dry weight > 375 mL product/ha* [5)] *ER_{50} shoot dry weight = 98 mL product/ha* [6)] *ER_{50} shoot dry weight = 136 mL product/ha* [7)] *ER_{50} shoot dry weight = 326 mL product/ha* [8)] ***ER_{50} emergence = 64 mL product/ha*** [9)] *ER_{50} shoot dry weight = 760 mL product/ha* [10)] *ER_{50} shoot dry weight = 631 mL*	*RAR Volume 3 – B.9 (PPP) – ATLANTIS OD [all values]* *EFSA Journal 2016;14(10):4584 [critical values]*

Species	Substance	Exposure System	Results	Reference
			product/ha	
			HR$_5$ shoot dry weight = 54.9 mL product/ha (*calculated with ETX 2.0, unbound figures with values that are shown to be > have been omitted from the calculation)**	
Beta vulgaris. $_d$ [1)] *Brassica napus. $_d$ [2)]* *Cucumis sativus $_d$ [3)]* *Glycine max $_d$ [4)]* *Helianthus annuus $_d$ [5)]* *Raphanus sativus $_d$ [6)]* *Lycopersicon esculentum $_d$ [7)]* *Allium cepa $_m$ [8)]* *Avena sativa $_m$ [9)]* *Zea mays $_m$ [10)]*	*IMS+MSM+MPR OD 42 (2+10+30)*	*21 d Vegetative vigour, Tier 2*	*[1)] ER$_{50}$ shoot dry weight = 144 mL product/ha* *[2)] ER$_{50}$ shoot dry weight = 56 mL product/ha* *[3)] ER$_{50}$ shoot dry weight > 0.188 mL product/ha* *[4)] ER$_{50}$ shoot dry weight = 136 mL product/ha* ***[5)] ER$_{50}$ shoot dry weight = 27 mL product/ha*** *[6)] ER$_{50}$ shoot dry weight = 38 mL product/ha* *[7)] ER$_{50}$ shoot dry weight = 36 mL product/ha* *[8)] ER$_{50}$ shoot dry weight > 188 mL product/ha* *[9)] ER$_{50}$ shoot dry weight = 287 mL product/ha* *[10)] ER$_{50}$ shoot dry weight = 385 mL product/ha*	*RAR Volume 3 – B.9 (PPP) – ATLANTIS OD [all values]* *EFSA Journal 2016;14(10):4584 [critical values]*
			***HR$_5$ shoot dry weight = 16 mL product/ha** (calculated with ETX 2.0, unbound figures with values that are shown to be > have been omitted from the calculation)*	

m: monocotyledonous; d: dicotyledonous
** SSD calculation was done with ER$_{50}$ values based on shoot dry weight except for onion (Allium cepa) where the ER$_{50}$ based on emergence was used. These endpoints represent the lowest endpoint for each tested species. An SSD calculation only based on shoot dry weight values resulted in a higher HR$_5$ of 72 ml product/ha and is therefore regarded less conservative.*

Review comments

The risk assessment of JME-HER 12 OD reference to Core Assessment of the already registered product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

From ecotoxicological point of view JME-HER 12 OD is considered equivalent/comparable to already registered Atlantis 12 OD, therefore the unprotected ecotoxicological studies performed for Atlantis 12 OD can be used for risk assessment purposes of JME-HER 12 OD.

In current assessment the same approach is taken as was provided in the risk assessment of reference product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)).

In order to be able to apply the species sensitivity distribution (SSD) approach for calculation of an HR$_5$, it is required to show that log-normal distribution fits the data adequately. The data sets of both - the seedling emergence study and the vegetative vigour study - meet the criteria of normality (see figure below):

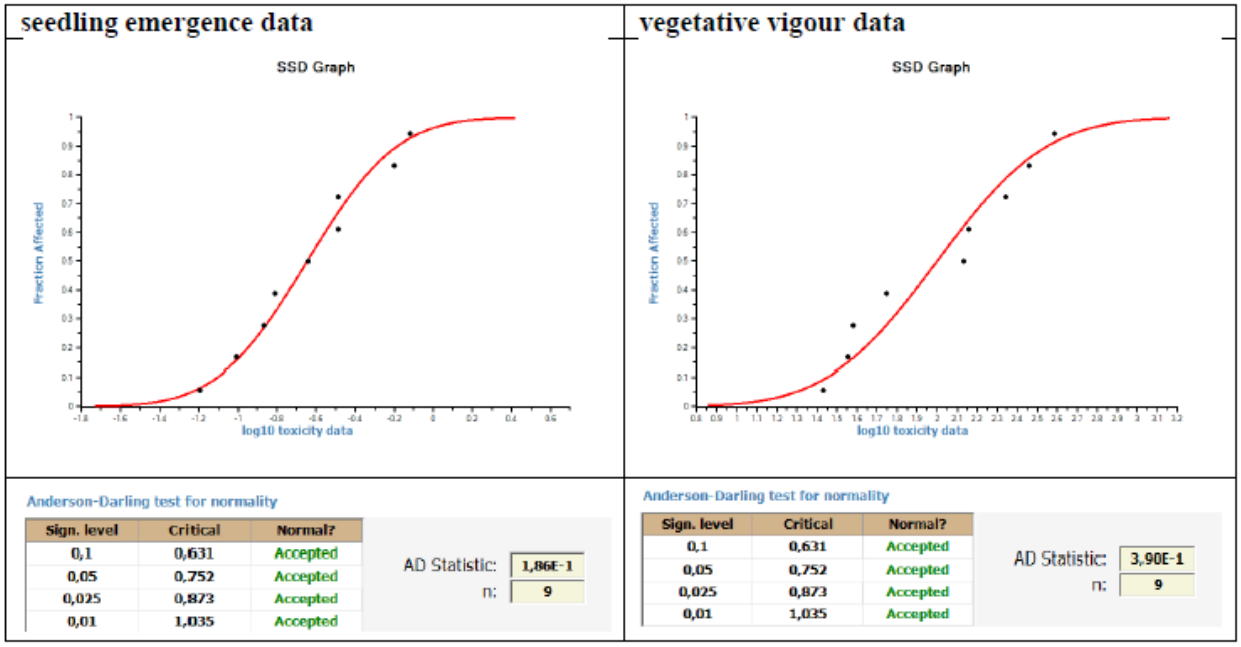


Figure 9.10-1: SSD graphs and results from Anderson-Darling tests for normality of ER_{50}-figures from the seedling emergence test (left) and vegetative vigour test (right).

9.10.1.1 Justification for new endpoints

Not relevant. ~~See point 9.10.1.~~

9.10.2 Risk assessment

9.10.2.1 Tier-1 risk assessment (based screening data)

Not relevant. ~~See point 9.10.1.~~

9.10.2.2 Tier-2 risk assessment (based on dose-response data)

~~Not relevant. See point 9.10.1.~~

The risk assessment is based on the "Guidance Document on Terrestrial Ecotoxicology", (SANCO/10329/2002 rev.2 final, 2002). It is restricted to off-field situations, as non-target plants are non-crop plants located outside the treated area.

*The quantitative risk assessment presented here follows a step-wise approach: First step is a **deterministic risk assessment** based on the lowest endpoints of the Tier-2 greenhouse studies. Second step is a **probabilistic risk assessment** based on the HR_5 which is derived from the species sensitivity distribution (SSD) analysis of the various species tested in the Tier-2 greenhouse studies.*

a) Deterministic risk assessment

According to the Terrestrial Guidance Document, the risk to non-target plants is evaluated by comparing the lowest ER_{50} with the calculated Predicted Environmental Rates (PERoff-field) from spray-drift expo-

sure. A trigger of 5 is considered appropriate if at least six plant species have been tested.

Table 9.10-2: Deterministic assessment of the risk for non-target plants due to the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals

Intended use	***Cereals, 1 x 1.5 l/ha (use group E)***			
Active substance/product	*IMS+MSM+MPR OD 42 (2+10+30)*			
Application rate (mL/ha)	*1 × 1500*			
MAF	*1.0 (single application)*			
Test species	***ER_{50} (mL/ha)***	***Drift rate (%)***	***$PER_{off\text{-}field}$ (mL/ha)***	***TER criterion: TER ≥ 5****
Allium cepa - seedling emergence	*64*	*2.77*	*41.55*	***1.54***
Helianthus annuus - vegetative vigour	*27*	*2.77*	*41.55*	***0.65***
Intended use	***cereals, 1 x 0.45 L prod./ha (use group K)***			
Active substance/product	*IMS+MSM+MPR OD 42*			
Application rate (mL/ha)	*1 × 450*			
MAF	*1.0 (single application)*			
Test species	***ER_{50} (mL/ha)***	***Drift rate (%)***	***$PER_{off\text{-}field}$ (mL/ha)***	***TER criterion: TER ≥ 5****
Allium cepa - seedling emergence	*64*	*2.77*	*12.47*	*5.13*
Helianthus annuus - vegetative vigour	*27*	*2.77*	*12.47*	***2.16***

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.
** TER ≥ 5 for deterministic risk assessment based on ER_{50}*

Conclusion: *The trigger is not met for both, seedling emergence and vegetative vigour, for the highest application rate intended for the product, and it is also failed for vegetative vigour for the lowest rate. As as next step, a probabilistic assessment is therefore provided below.*

Review comments:

Deterministic Risk assessment presented by the applicant is considered acceptable. The risk was performed for the higher dose 1.5 L product/ha than maximum dose in critical GAP (1.2 L product/ha) and for lower dose of 0.45 L prod./ha.
Since the trigger of 5 is not met for seedling emergence and vegetative vigour for higher dose, and for vegetative vigour for lower dose, further refinement with consideration of buffer zones were considered.

b) Probabilistic risk assessment

According to the Guidance Document on Terrestrial Ecotoxicology, the probabilistic method makes use of the species sensitivity distribution (SSD) in order to calculate an HR_5. The HR_5 is the concentration below which less than 5% of the species will be harmed above the ER_{50} level and can be calculated from the data sets of ER_{50} growth inhibition levels. If the HR_5 is below the highest predicted exposure level, the risk for terrestrial plants is deemed to be acceptable. The EU guidance document for terrestrial ecotoxicology states: "If the ED50 for less than 5 % of the species is below the highest predicted exposure level, the risk

for terrestrial plants is assumed to be acceptable. Thus, the HC5 itself (TER =1) can be regarded to be protective."
A probabilistic approach is considered more suitable than the deterministic one to achieve the environmental protection goal, since sensitivity data of several species are taken into account. However, it is applicable only if data of at least 6 species are available, and requires that log-normal or another defined type of distribution of the data has been shown to fit the data adequately. The HR_5 in the present risk assessment was calculated using the ETX2.1 program.

For the present product, applicability criteria for the probabilistic approach are met as has been shown previously in Section 9.10.1 including SSD graph analysis, and this conclusion has been EU agreed in EFSA Journal 2016;14(10):4584, and RAR Volume 3 – B.9 (PPP) – ATLANTIS OD (revised version 2016-06).

Table 9.10-3: Probabilistic assessment of the risk for non-target plants due to the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals

Intended use	***Cereals, 1 x 1.5 l/ha (use group E)***			
Active substance/product	*IMS+MSM+MPR OD 42 (2+10+30)*			
Application rate (mL/ha)	*1 × 1500*			
MAF	*1.0 (single application)*			
Test species	***HR_5 (mL/ha)***	***Drift rate (%)***	***$PER_{off\text{-}field}$ (mL/ha)***	***TER criterion: TER ≥ 1****
HR_5 – seedling emergence	*54.9*	*2.77*	*41.55*	*1.32*
HR_5 – vegetative vigour	*16*	*2.77*	*41.55*	***0.39***
Intended use	***cereals, 1 x 0.45 L prod./ha (use group K)***			
Active substance/product	*IMS+MSM+MPR OD 42*			
Application rate (mL/ha)	*1 × 450*			
MAF	*1.0 (single application)*			
Test species	***HR_5 (mL/ha)***	***Drift rate (%)***	***$PER_{off\text{-}field}$ (mL/ha)***	***TER criterion: TER ≥ 1****
HR_5 – seedling emergence	*54.9*	*2.77*	*12.47*	*4.40*
HR_5 – vegetative vigour	*16*	*2.77*	*12.47*	*1.28*

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.
** TER ≥ 1 for probabilistic risk assessment based on HR_5*

Conclusion: *For the highest intended rate, the trigger is met for seedling emergence, however is not reached for vegetative vigour. Accordingly, further analysis is required and will be presented, considering possible options for exposure mitigation, focused on vegetative vigour. The lowest rate is passed for both, seedlings emergence and vegetative vigour and does not require any further analysis.*

Review comments:

The applicant presented probabilistic risk assessment as a refinement. The probabilistic risk assessment was already evaluated and accepted in the core assessment for product Atlantis 12 OD (IMS+MSM+MPR OD 42 (2+10+30)). No further re-evaluation was needed.

The probabilistic risk was performed for the higher dose 1.5 L product/ha than maximum dose in critical GAP (1.2 L product/ha) and for lower dose of 0.45 L prod./ha.

Based on the probabilistic risk assessment for the highest application dose of 1.5 L product/ha the trigger is met for seedling emergence, however is not reached for vegetative vigour. Therefore, the risk mitigation measures were needed.
For the lower dose 0.45 L prod./ha based on the probabilistic risk assessment no further refinement is needed.

9.10.2.3 Higher-tier risk assessment

Not relevant. ~~See point 9.10.1.~~

9.10.2.4 Risk mitigation measures

~~Not relevant. See point 9.10.1.~~

In order to reduce the off-field exposure, risk mitigation measures can be implemented. These correspond to unsprayed in-field buffer strips of a given width and/or the usage of drift reducing nozzles. The results of the lowest HR_5 (vegetative vigour) and ER_{50} value (vegetative vigour) as well as typical mitigation measures (no-spray buffer zones of 5, 10, 15, 20, 30 m ; drift-reducing nozzles with reduction by 50 %, 75 %, or 90 %) are summarised in the following tables.

Table 9.10-4: Probabilistic ~~Deterministic~~ risk assessment for non-target terrestrial plants considering risk mitigation (in-field no-spray buffer zones, and drift-reducing nozzles) for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals: Use group F

Intended use		*Cereals, 1 x 1.2 L prod./ha (use group F)*			
Product		*IMS+MSM+MPR OD 42*			
Application rate (ml/ha)		*1 × 1200*			
MAF		*1*			
Buffer strip (m)	***Drift rate (%)***	***$PER_{off\text{-}field}$ (g/ha)***	***$PER_{off\text{-}field}$ 50 % drift red. (g/ha)***	***$PER_{off\text{-}field}$ 75 % drift red. (g/ha)***	***$PER_{off\text{-}field}$ 90 % drift red. (g/ha)***
1/3	*2.77*	*33.24*	*16.62*	*8.31*	*3.32*
5	*0.57*	*6.84*	*3.42*	*1.71*	*0.68*
10	*0.29*	*3.48*	*1.74*	*0.87*	*0.35*
Toxicity value		***TER***			
HR_{50} = 16 ml/ha		***criterion: TER ≥ 1***			
1/3		***0.48***	***0.96***	*1.93*	*4.81*
5		*2.34*	*4.68*	*9.36~~*~~*	*23.39~~*~~*
10		*4.60*	*9.20**	*18.39~~*~~*	*45.98~~*~~*

MAF: Multiple application factor; PER: Predicted environmental rates; TER: toxicity to exposure ratio. Criteria values shown in bold breach the relevant trigger of 1.

Table 9.10-5: Deterministic risk assessment for non-target terrestrial plants considering risk mitigation (in-field no-spray buffer zones, and drift-reducing nozzles) for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals: Use group F

Intended use		*Cereals, 1 x 1.2 L prod./ha (use group F)*			
Product		*IMS+MSM+MPR OD 42*			
Application rate (ml/ha)		*1 × 1200*			
MAF		*1*			
Buffer strip (m)	***Drift rate (%)***	***$PER_{off-field}$ (g/ha)***	***$PER_{off-field}$ 50 % drift red. (g/ha)***	***$PER_{off-field}$ 75 % drift red. (g/ha)***	***$PER_{off-field}$ 90 % drift red. (g/ha)***
1/3	*2.77*	*33.24*	*16.62*	*8.31*	*3.32*
5	*0.57*	*6.84*	*3.42*	*1.71*	*0.68*
10	*0.29*	*3.48*	*1.74*	*0.87*	*0.35*
15	*0.20*	*2.40*	*1.20*	*0.60*	*0.24*
20	*0.15*	*1.80*	*0.90*	*0.45*	*0.18*
30	*0.10*	*1.20*	*0.60*	*0.30*	*0.12*
Toxicity value		***TER***			
ER_{50} = 27 ml/ha		***criterion: TER ≥ 5***			
1/3		***0.81***	***1.62***	***3.25***	*8.12*
5		***3.95***	*7.89*	*15.79*	*39.47*
10		*7.76*	*15.52*	*31.03*	*77.59*
15		*11.25*	*22.50*	*45.00*	*112.50*
20		*15.00*	*30.00*	*60.00*	*150.00*
30		*22.50*	*45.00*	*90.00*	*225.00*

MAF: Multiple application factor; PER: Predicted environmental rates; TER: toxicity to exposure ratio. Criteria values shown in bold breach the relevant trigger

9.10.3 Overall conclusions

~~Not relevant. See point 9.10.1.~~

Based on the probabilistic risk assessment it is concluded that the use of the product will not produce unacceptable effects on terrestrial non-target plants growing near treated fields, when considering the following mitigation measures:
- a 5 m buffer zone, or alternatively 75% drift reducing spray nozzles for application rate 1.2 L prod/ha (use group F)
- no mitigation measures are needed for application rate 1 x 0.45 L product/ha (use group K).

The risk assessment performed for IMS+MSM+MPR OD 42 (2+10+30) covers all uses of JME-HER 12 OD. No further calculations are needed. All the TER values exceeded the relevant trigger value of 5 or 1. JME-HER 12 OD used in accordance with proposed GAP, does not pose unacceptable risk to non-target plants provided above mentioned risk mitigations measures are applied.

Review comments:

The risk assessment presented by the Applicant is consider acceptable. In opinion of zRMS trigger value of 1 should be used in the probabilistic risk assessment with a HR_5 value.

Based on the **deterministic** risk assessment it is concluded that the use of the product will not produce unacceptable effects on terrestrial non-target plants growing near treated fields, when considering the following mitigation measures:

For application rate 1.2 L prod/ha (use group F)
-1 m buffer zone with 90% drift reducing spray nozzles or
- 5 m buffer zone with 50% drift reducing spray nozzles or
- 10 m buffer zone

For application rate 1 x 0.45 L product/ha
- 1 m buffer zone with 75% drift reducing spray nozzles or
- 5 m buffer zone

Based on the **probabilistic** risk assessment with trigger value of 1 it is concluded that the use of the product will not produce unacceptable effects on terrestrial non-target plants growing near treated fields, when considering the following mitigation measures:

For application rate 1.2 L prod/ha (use group F)
- 1 m buffer zone with 75% drift reducing spray nozzles or
- 5 m buffer zone

For application rate 1 x 0.45 L product/ha
- no mitigation measures are required

9.11 Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)

Not relevant.

9.12 Monitoring data (KCP 10.8)

Not relevant.

9.13 Classification and Labelling

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the classification and labelling with regard to ecotoxicological data is proposed is included in table below.

JME-HER 12 OD has the same recipe as the reference product Atlantis 12 OD and the classification of JME-HER 12 OD was proposed on the basis of the reference product classification as well as calculation method. The proposed classification of the product JME-HER 12 OD is:

Table 9.13-1: Justified proposals for classification and labelling for JME-HER 12 OD according to Regulation (EC) No 1272/2008

Hazard class(es), categories:	Aquatic Acute 1, H400

	Aquatic Chronic 1, H410
Hazard pictograms or Code(s) for hazard pictogram(s):	 GHS09
Signal word:	Warning
Hazard statement(s):	H410 - Very toxic to aquatic life with long lasting effects.
Precautionary statement(s):	P391 - Collect spillage. P501- Dispose of contents/container in accordance with local regulation
Additional labelling phrases:	EUH401 - To avoid risks to human health and the environment, comply with the instructions for use.

Review comments:

Generally, zRMS agree with the Classification and Labelling proposed by the Applicant. In accordance with indication of Regulation 1272/2008, when formulation is classified as H410, hazard statement regarding acute classification (i.e. H400) may be omitted.
Precautionary statement: P501, should be used for PPP. This information is directly amended above..

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Verte-brate study Y/N	Owner
-	-	-	-	-	-

List of unprotected data referred to by the applicant and relied on, but already evaluated

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Verte-brate study Y/N	Owner
KCP 10.2 / 01	Sinclair, C. J.	2009	Predicting the environmental fate and ecotoxicological and toxicological effects of pesticide transformation products Publisher: unknown Journal: unknown Year: 2009 Report No.: M-551653-01-1 GLP/GEP: n.a. published	No	published
KCP 10.2.1 / 01	Kuhl, K.	2017	Amendment no. 1 to final report - Lemna gibba G3 - Growth inhibition test with BCS-CV14885 under static conditions - Limit test Report No.: EBMM0006, Edition Number: M-602447-02-1 Bayer AG, Crop Science Division, Monheim, Germany **... amended: 2017-11-14** GLP/GEP: Yes unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Verte-brate study Y/N	Owner
KCP 10.2.1 / 02	Kuhl, K.	2016	Lemna gibba G3 - Growth inhibition test with mesosulfuron-methyl tech. (BCS-AK65185) under peak exposure conditions Report No.: EBMMN160, Edition Number: M-577164-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 10.2.1 / 03	Kuhl K.	2016	Lemna gibba G3 - Growth inhibition test with iodosulfuron-methyl-sodium TC (BCS-BB66887) under peak exposure conditions Report No.: EBIMN158, Edition Number: M-574865-01-1 Bayer CropScience AG, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 10.2.1 / 04	Kuhl, K.	2017	Amendment no. 1: Lemna gibba G3 - Growth inhibition test with metsulfuron-methyl (AE F075736) under peak exposure conditions (peaks on day 0 and 3) Report No.: EBIM0007, Edition Number: M-600962-02-1 Bayer AG, Crop Science Division, Monheim, Germany **... amended: 2017-10-27** GLP/GEP: Yes unpublished	No	Bayer
KCP 10.2.1 / 05	Kuhl, K.	2017	Lemna gibba G3 - Growth inhibition test with metsulfuron-methyl (AE F075736) under peak exposure conditions (peaks on day 0 and 7) Report No.: EBIM0008, Edition Number: M-600651-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: Yes unpublished	No	Bayer
KCP 10.2.3 / 01	Isemer-Kellner, R.; Heine, S.	2017	Justification for the use of time-weighted average concentrations in the chronic risk assessment for iodosulfuron-methyl-sodium and aquatic plants Report No.: M-607957-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: n.a. unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Verte-brate study Y/N	Owner
KCP 10.2.3 / 02	Sowig, P.; Herno, V.; Heine, S.	2017	Justification for the use of time-weighted average concentrations in the chronic risk assessment for mesosulfuron-methyl and aquatic plants Report No.: M-602786-01-1 Bayer AG, Germany GLP/GEP: n.a. unpublished	No	Bayer
KCP 10.2.3 / 03	Schmitt, W.; Bruns, E.; Doll-inger, M.; Sowig, P.	2013	Mechanistic TK/TD-model simulating the effect of growth inhibitors on Lemna populations Publisher: Elsevier B.V. Location: Amsterdam Journal: Ecological Modelling Volume: 255 Pages: 1-10 Year: 2013 Report No.: M-455483-01-1 GLP/GEP: n.a. published	No	published
KCP 10.2.3 / 04	Heine, S.	2017	Lemna TK/TD modelling - Compound-specific parameterization and validation for iodosulfuron-methyl-sodium and its metabolite metsulfuron-methyl Report No.: EnSa-17-0639, Edition Number: M-602805-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 10.2.3 / 05	Heine, S.	2017	Lemna TK/TD modelling - Compound-specific parameterization and validation for mesosulfuron-methyl Report No.: EnSa-17-0407, Edition Number: M-600766-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: No unpublished	No	Bayer

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Verte-brate study Y/N	Owner
KCP 10.2.3 / 06	Heine, S.	2018	Lemna TK/TD modelling - Assessing the impact of Atlantis OD applications on Lemna in Europe (FOCUSsw) Report No.: EnSa-18-0974, Edition Number: M-637990-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 10.2.3 / 07	Heine, S.	2018	Lemna TK/TD modelling - Assessing the impact of Atlantis OD applications on Lemna in Europe (FOCUSsw multiyear) Report No.: EnSa-18-0973, Edition Number: M-637995-01-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: No unpublished	No	Bayer
KCP 10.3.1 / 01	Maynard, S. K.; Albuquerque, R.; Weber, C.; von Merey, G.; Geiger, M. F.; Becker, R.; Keppler, J.; Maschke, J.; Brougham, K.; Couson, M.	2015	1.8 Weeds in the treated field - a realistic scenario for pollinator risk assessment ? Publisher: Julius-Kuehn Archiv Location: Ghent, Belgium Journal: 12th International Symposium of the ICP-PR Bee Protection Group Volume: 450 Pages: 56-62 Year: 2015 Report No.: M-542146-01-1 GLP/GEP: n.a. published	No	published
KCP 10.7 / 01	Gladbach, A.; Ebeling, M.; Weyers, A.	2017	Technical stand-alone combined toxicity assessment for the Central zone Report No.: M-571377-02-1 Bayer AG, Crop Science Division, Monheim, Germany GLP/GEP: n.a. unpublished	No	Bayer

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review
Please note that all data mentioned as part of DAR, RAR, or EFSA journals are considered as relied on.

Iodosulfuron-methyl-sodium

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.1.1.1 /01	xxxxxxxxx	1996	Acute oral toxicity in the male and female Japanese quail (Coturnix coturnix japonica) Hoe 115008 substance, technical Code: Hoe 115008 00 ZC89 0001 xxxxxxxxxxxxxxxxxxxxxxx Report No.: A57013, Report includes Trial Nos.: 95.0517 Edition Number: M-140780-01-1 EPA MRID No.: 45109026 Date: 1996-05-23 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.1.1.1 /02	xxxxxxxxxxxxx	1998	Bobwhite quail acute oral toxicity test AE F115008 substance, technical Code: AE F115008 00 1C89 0001 xxxxxxxxxxxxxxxxxxxxxxx Report No.: C000842, Report includes Trial Nos.: 98.0360 Edition Number: M-181334-01-1 EPA MRID No.: 45109027 Date: 1998-08-03 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.1.1.1 /03	xxxxxxxxxx	1997	Acute oral toxicity in the male and female mallard duck (Anas platyrhynchos) Hoe 115008 substance, technical Code: Hoe 115008 00 ZC89 0001 xxxxxxxxxxxxxxxxxxxxxxx Report No.: A58728, Report includes Trial Nos.: 96.0599 Edition Number: M-142450-01-1 Date: 1997-02-13 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.1.1.3 /01	xxxxxxxxxxxxx	1998	Bobwhite quail 6-week dietary reproduction study - Limit-Test Hoe 115008 substance technical Code: Hoe 115008 00 ZC89 0001 xxxxxxxxxxxxxxxxx Report No.: C000807, Report includes Trial Nos.: 98.0011 Edition Number: M-181277-01-1 EPA MRID No.: 45109033 Date: 1998-11-17 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.1.1.3 /02	xxxxxxxxx	2004	Effect of technical Iodosulfuron methyl sodium on northern bobwhite reproduction xxxxxxxxxxxxxxxxxxxxxxxx Report No.: EBIMX013, Report includes Trial Nos.: IM741701 Edition Number: M-242537-01-1 EPA MRID No.: 46431803 Date: 2004-12-21 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.1.1.3 /03	xxxxxxxxxxx	1999	Mallard duck dietary reproduction toxicity study AE F115008 substance technical Code: AE F115008 00 1C89 0001 xxxxxxxxxxxxxxxxxx Report No.: C005102, Edition Number: M-191367-01-1 EPA MRID No.: 45109034 Date: 1999-08-17 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.2.1 /01	xxxxxxxxx	1998	Acute toxicity to rainbow trout (Oncorhynchus mykiss) AE F115008 substance, technical Code: AE F115008 00 1C89 0001 xxxxxxxxxxxxxxxxxx Report No.: A59423,	Y	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Edition Number: M-143096-01-1 EPA MRID No.: 45109035 Date: 1998-02-03 GLP/GEP: yes, unpublished		
KCA 8.2.1 /02	xxxxxxxxxxx	1998	Acute toxicity to bluegill sunfish (Lepomis macrochirus) AE F115008 substance, technical Code: AE F115008 00 1C89 0001 xxxxxxxxxxxxxxxxx Report No.: A59422, Edition Number: M-143095-01-1 EPA MRID No.: 45109101 Date: 1998-02-03 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.2.1 /03	xxxxxxxxxxx	2000	96 hour acute toxicity to the sheepshead minnow, Cyprinodon variegatus, in a static renewal system: AE F115008 technical 89.6% w/w: AE F115008 00 1C89 0001 xxxxxxxxxxxxxxxxxxxxxxxxx Report No.: B002715, Report includes Trial Nos.: BY99W509 BY99W509A Edition Number: M-238449-02-1 Date: 2000-01-14 ...Amended: 2000-02-28 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.2.1 /04	xxxxxxxxxxx	2006	Acute toxicity of MKH 6561-sulfonamide acid to rainbow trout (Oncorhynchus mykiss) in a 96-hour static test - limit test - xxxxxxxxxxxxxxx Report No.: 30183230, Edition Number: M-278097-01-1 Date: 2006-09-25 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.2.1 /05	xxxxxxxxx	2006	Acute toxicity of MKH 6561-saccharine to rainbow trout (Oncorhynchus mykiss) in a 96-hour static test - limit test - xxxxxxxxxxxxxxxxxx Report No.: 30193230, Edition Number: M-278099-01-1 Date: 2006-09-25 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.2.2.1 /01	xxxxxxxxx	1998	Effects on juvenile growth of rainbow trout (Oncorhynchus mykiss) in a 28 days flow-through study AE F115008 substance, technical Code: AE F115008 00 1C89 0001 xxxxxxxxxxxxxxxxx Report No.: A59424, Edition Number: M-143097-01-1 EPA MRID No.: 45109102 Date: 1998-04-29 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.2.2.1 /02	xxxxxxxxxxxx	2004	Early life stage toxicity of AE F115008 Iodosulfuron-methyl-sodium technical to the fathead min-now (Pimephales promelas) under flow-through conditions xxxxxxxxxxxxxx Report No.: 201022, Edition Number: M-240261-01-1 EPA MRID No.: 46431804 Date: 2004-10-14 GLP/GEP: no, unpublished	Y	Bayer Crop-Science
KCA 8.2.4.1 /01	Heusel, R.	1998	Acute toxicity to Daphnia magna (waterflea) AE F115008 substance, technical Code: AE F115008 00 1C89 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A59425, Edition Number: M-143098-01-1 EPA MRID No.: 45109103 Date: 1998-03-26	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			GLP/GEP: yes, unpublished		
KCA 8.2.4.1 /02	Heusel, R.; Weller, O.; Gosch, H.	1998	Acute toxicity to Daphnia magna (waterflea) AE F059411 substance, technical Metabolite of AE F115008 Code: AE F059411 00 1C99 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Report No.: C000840, Edition Number: M-181330-01-1 Date: 1998-10-07 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.4.1 /03	Grade, R.; Wy-dra, V.	2006	Acute toxicity of MKH 6561-sulfonamide acid to Daphnia magna in a 48-hour immobilization test IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 30182220, Edition Number: M-278971-01-1 Date: 2006-10-16 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.4.1 /04	Grade, R.; Wy-dra, V.	2006	Acute toxicity of MKH 6561-saccharine to Daphnia magna in a 48-hour immobilization test IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 30192220, Edition Number: M-278973-01-1 Date: 2006-10-16 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.4.2 /01	Stachura, B. J.; Ruff, D. F.	2000	96 hour acute toxicity to the Mysid shrimp, Mysidopsis bahia, in a static renewal system: AE F115008 technical 89.6 percent w/w: AE F115008 00 1C89 0001 Aventis CropScience USA LP, Ecotoxicology, Pikeville, NC, USA Bayer CropScience, Report No.: B002713, Edition Number: M-238447-02-1 Date: 2000-01-14 ...Amended: 2000-02-28	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			GLP/GEP: yes, unpublished		
KCA 8.2.5.1 /01	Heusel, R.; Gosch, H.	1998	Effects on growth and reproduction of Daphnia magna AE F115008 substance, technical Code: AE F115008 00 1C89 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A59426, Edition Number: M-143099-01-1 EPA MRID No.: 45109104 Date: 1998-08-12 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /01	Heusel, R.	1998	Algal growth inhibition (Pseudokirchneriella subcapitata) AE F115008 substance, technical Code: AE F115008 00 1C89 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A59421, Edition Number: M-143094-01-1 EPA MRID No.: 45109105 Date: 1998-01-28 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1	Hermes, H.; Wy-dra, V.	2015	Iodosulfuron-methyl-sodium, technical: Toxicity to Navicula pelliculosa in an Algal Growth Inhibition Test. Bayer CropScience, Report No.: EBIMN165, Edition Number: M-532054-01-1 Date: 2015-xx-xx GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /04	Kuhl, K.	2013	Pseudokirchneriella subcapitata - Growth inhibition test with BCS-AU71532 - limit test Bayer CropScience, Report No.: E 201 4592-3, Edition Number: M-470687-01-1	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Date: 2013-11-07 GLP/GEP: yes, unpublished		
KCA 8.2.6.1 /05	Hoffmann, K.	2013	Pseudokirchneriella subcapitata growth inhibition test with BCS-AU71533 - limit test Bayer CropScience, Report No.: EBIMN062, Edition Number: M-465388-01-1 Date: 2013-09-10 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /06	Bruns, E.	2013	Pseudokirchneriella subcapitata - Growth inhibition test with BCS-AW35544 - limit test Bayer CropScience, Report No.: E 201 4589-9, Edition Number: M-470669-01-1 Date: 2013-11-04 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /07	Hoffmann, K.	2013	Pseudokirchneriella subcapitata - Growth inhibition test with BCS-AU85549 - limit test Bayer CropScience, Report No.: EBIML036, Edition Number: M-468872-01-1 Date: 2013-09-27 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /08	Hoffmann, K.	2013	Pseudokirchneriella subcapitata - Growth inhibition test with BCS-CW81253 - Limit test Bayer CropScience, Report No.: EBIMN061, Edition Number: M-465389-01-1 Date: 2013-09-10 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /02	Heusel, R.; Weller, O.; Gosch, H.	1998	Algal growth inhibition (Pseudokirchneriella subcapitata) AE F059411 substance, technical Metabo-lite of AE F115008 Code: AE F059411 00 1C99 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Report No.: C000867,	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Edition Number: M-181379-01-1 EPA MRID No.: 45109110 Date: 1998-10-09 GLP/GEP: yes, unpublished		
KCA 8.2.6.1 /14	Bruns, E.	2013	Pseudokirchneriella subcapitata - Growth inhibition test with AE F154781 - limit test Bayer CropScience, Report No.: EBIMN105, Edition Number: M-476160-01-1 Date: 2013-11-08 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /01	Christ, M. T.; Ruff, D. F.	1997	Toxicity to duckweed (Lemna gibba), in a static system AE F115008 technical 87.4% w/w Code: AE F115008 00 1C89 0001 AgrEvo USA Company, Ecotoxicology, Pikeville, NC, USA Bayer CropScience, Report No.: A57770, Report includes Trial Nos.: 501BY Edition Number: M-141441-02-1 EPA MRID No.: 45109111 Date: 1997-10-15 ...Amended: 1998-01-19 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /05	Sowig, P.	2014	Iodosulfuron-methyl-sodium rationale for the replacement of the old 14-day Lemna growth inhibition study (Christ & Ruff 1997; M-141441-02) with the 7-day endpoints from the Lemna study (Bruns 2013; M-469584-01-1) Bayer CropScience, Report No.: M-479697-01-1, Edition Number: M-479697-01-1 Date: 2014-03-11 GLP/GEP: n.a., unpublished	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 8.2.7 /07	Bruns, E.	2013	Lemna gibba G3 - Prolonged growth inhibition test with iodosulfuron-methyl-sodium (AE F115008) with stepwise decreasing concentrations and metsulfuron-methyl (AE F075736) with stepwise increasing concentrations over a 6 week test duration - Amendment 1 to report - Bayer CropScience, Report No.: E 412 3763 - 6, Edition Number: M-469584-02-1 Date: 2013-11-05 ...Amended: 2015-03-04 GLP/GEP: no, unpublished	N	Bayer CropScience
KCA 8.2.7 /08	xxxxxxxxxx	2012	Toxicity of Iodosulfuron-methyl-sodium technical to the aquatic macrophyte, Myriophyllum spicatum xxxxxxxxxxxx Report No.: EBIML032, Edition Number: M-431705-01-1 Date: 2012-05-21 GLP/GEP: yes, unpublished	Y	Bayer CropScience
KCA 8.2.7 /06	Hoberg, J.R.	2011	Outdoor growth inhibition and recovery of aquatic plants exposed to iodosulfuron-methyl-sodium WG50 Smithers Viscient, Wareham, MA, USA Bayer CropScience, Report No.: 13798.6259, Edition Number: M-407716-01-1 Date: 2011-05-10 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.7 /03	Sowig, P.; Weller, O.	1998	Duckweed (Lemna gibba G3) growth inhibition test AE F075736 (metsulfuron-methyl) metabolite of AE F115008 substance, technical Code: AE F075736 00 1C92 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Report No.: C001314, Edition Number: M-182336-01-1 EPA MRID No.: 45109112 Date: 1998-11-16	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			GLP/GEP: yes, unpublished		
KCA 8.2.7 /09	Sowig, P.; Gosch, H.	2001	Duckweed (Lemna gibba G3) growth inhibition test with recovery phase Metsulfuron-methyl substance, pure (metabolite of AE F115008) Code: AE F075736 00 1B98 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C015669, Edition Number: M-200947-01-1 Date: 2001-09-28 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.7 /10	Bruns, E.	2013	Lemna gibba G3 - Growth inhibition test with AE F145741 (metabolite of iodosulfuron-methyl-sodium) under static conditions Bayer CropScience, Report No.: EBIML041, Edition Number: M-462128-01-1 Date: 2013-08-02 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.7 /11	Hoffmann, K.	2013	Lemna gibba G3 - Growth inhibition test with BCS-AU71533 (metabolite of iodosulfuron-methyl-sodium) under static conditions Bayer CropScience, Report No.: EBIMN063, Edition Number: M-462121-02-1 Date: 2013-07-31 ...Amended: 2013-09-09 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.7 /12	Sowig, P.	2002	Duckweed (Lemna gibba G3) growth inhibition test AE 0002166 (metabolite of AE F115008) substance, technical Code: AE 0002166 00 1C92 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C018083, Edition Number: M-205481-01-1	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Date: 2002-05-08 GLP/GEP: yes, unpublished		
KCA 8.2.7 /13	Sowig, P.	2001	Duckweed (Lemna gibba G3) growth inhibition test AE F161778 (metabolite of AE F115008) substance, technical 93.7 percent Code: AE F151778 00 1C94 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C008628, Edition Number: M-197639-01-1 Date: 2001-12-11 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /14	Hoffmann, K.	2013	Lemna gibba G3 - Growth inhibition test with BCS-CW81253 (metabolite of iodosulfuron-methyl-sodium) under static conditions Bayer CropScience, Report No.: EBIMN060, Edition Number: M-462125-01-1 Date: 2013-07-30 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /15	Sowig, P.	2002	Duckweed (Lemna gibba G3) growth inhibition test AE 0000119 (metabolite of AE F115008) substance, pure Code: AE 0000119 00 1B98 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C020878, Edition Number: M-210320-01-1 Date: 2002-05-14 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /02	Sowig, P.; Weller, O.	1998	Duckweed (Lemna gibba G3) growth inhibition test AE F059411 metabolite of AE F115008 substance, technical Code: AE F059411 00 1C99 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Report No.: C000745, Edition Number: M-181177-01-1	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			EPA MRID No.: 45109113 Date: 1998-10-02 GLP/GEP: yes, unpublished		
KCA 8.2.7 /16	Sowig, P.	2002	Duckweed (Lemna gibba G3) growth inhibition test AE F059411 substance, pure (metabolite of AE F115008) Code: AE F059411 00 1B99 0002 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C017092, Edition Number: M-203638-01-1 Date: 2002-06-14 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /17	Sowig, P.	2002	Duckweed (Lemna gibba G3) growth inhibition test AE 0014966 (metabolite of iodosulfuron AE F115008) substance, technical Code: AE 0014966 00 1B98 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C003832, Edition Number: M-186853-01-1 Date: 2002-03-06 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /18	Sowig, P.	2002	Duckweed (Lemna gibba G3) growth inhibition test AE 0034855 (metabolite of AE F115008) substance, pure Code: AE 0034855 00 1B99 0001 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C020876, Edition Number: M-210318-01-1 Date: 2002-06-14 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /19	Grade, R.	2006	Toxicity of MKH 6561-Sulfonamide Acid to the aquatic plant Lemna gibba in a growth inhibition test IBACON GmbH, Rossdorf, Germany	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			BCS, Report No.: 30184240, Edition Number: M-281240-01-1 Date: 2006-10-26 GLP/GEP: yes, unpublished		
KCA 8.2.7 /20	Grade, R.	2006	Toxicity of MKH 6561-Saccharine to the aquatic plant Lemna gibba in a growth inhibition test IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 30194240, Edition Number: M-281250-01-1 Date: 2006-11-01 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /21	Hoffmann, K.	2013	Lemna gibba G3 - Growth inhibition test with AE F154781 (metabolite of iodosulfuron-methyl-so-dium) under static conditions Bayer CropScience, Report No.: E 412 4513 - 0, Edition Number: M-470494-01-1 Date: 2013-10-25 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7/22	Rosenkrantz, R.T.; Cedergreen, N.; Baun, A.; Kusk, K.O.	2013	Influence of pH, light cycle, and temperature on ecotoxicity of four sulfonylurea herbicides towards Lemna gibba. Journal:Ecotoxicology, Volume:22, Issue:1, Pages:33-41, Year:2013, Report No.: M-469998-01-1, Edition Number: M-469998-01-1 GLP/GEP: no, published	N	Literature data

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 8.2.8 /01	Boeri, R. L.; Magazu, J. P.; Ward, T. J.	1999	Flow-through mollusc shell deposition test: AE F115008 Wilbury Laboratories, Inc., Marblehead, MA, USA Bayer CropScience, Report No.: B002674, Edition Number: M-238409-01-2 Date: 1999-12-03 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.3.1.1.1 /01	Waltersdorfer, A.	1996	Oral toxicity (LD50) to honey bees (Apis mellifera L.) Code: Hoe 115008 00 ZC89 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A58108, Edition Number: M-141821-01-1 EPA MRID No.: 45109114 Date: 1996-11-28 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.3.1.1.2 /01	Waltersdorfer, A.	1996	Contact toxicity (LD50) to honey bees (Apis mellifera L.) Code: Hoe 115008 00 ZC89 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A57512, Edition Number: M-141225-01-1 EPA MRID No.: 45109115 Date: 1996-09-24 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.3.1.1 /01	Schmitzer, S.	2004	Effects of iodosulfuron-methyl-sodium tech. (acute contact and oral) on honey bees (Apis mellifera L.) in the laboratory IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 73071035, Edition Number: M-436273-01-1 Date: 2004-08-10 GLP/GEP: yes, unpublished	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.3.1.1 /02	Kling, A.	2014	Iodosulfuron-methyl sodium (tech.): Acute contact toxicity to the bumble bee, Bombus terrestris L. under laboratory conditions eurofins-GAB GmbH, Niefern-Oeschelbronn, Germany Bayer CropScience, Report No.: S13-01780, Edition Number: M-477331-01-1 Date: 2014-02-10 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.3.1.2 /01	Kling, A.	2014	Iodosulfuron-methyl sodium (tech.) - Assessment of chronic effects to the honeybee, Apis mellifera L., in a 10 days continuous laboratory feeding limit test Eurofins Agroscience Services EcoChem GmbH, Niefern-Oeschelbronn, Germany Bayer CropScience, Report No.: S13-00142, Edition Number: M-479396-01-1 Date: 2014-03-07 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.3.1.3 /01	Jeker, L.	2013	Iodosulfuron-methyl-sodium WG 10 - A honeybee brood feeding study to evaluate potential effects on brood development and mortality of the honeybee, Apis mellifera L. (Hymenoptera: Apidae) Innovative Environmental Services (IES) Ltd, Witterswil, Switzerland Bayer CropScience, Report No.: 20110173, Edition Number: M-465335-01-1 Date: 2013-07-15 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.3.1.3 /02	Schmitzer, S.	2014	Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L): Effects on honey bee brood (Apis mellifera L.) under semi-field conditions - Tunnel test - IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 79081033, Edition Number: M-477913-01-1 Date: 2014-02-24	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			GLP/GEP: yes, unpublished		
KCA 8.4.1 /02	Scheffczyk, A.; Moser, T.	2010	Iodosulfuron-methyl-sodium: Reproduction toxicity to the earthworm Eisenia fetida in an artificial soil test ECT Oekotoxikologie GmbH, Floersheim, Germany Bayer CropScience, Report No.: 10P29RR, Edition Number: M-397577-01-1 Date: 2010-12-13 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.1 /01	Sowig, P.	1998	Effects on growth and reproduction of earthworms (Eisenia fetida) AE F075736 (metsulfuron-methyl) metabolite of AE F115008 substance technical Code: AE F075736 00 1C92 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Report No.: C001315, Edition Number: M-182339-01-1 EPA MRID No.: 45109124 Date: 1998-11-11 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.1 /03	Witte, B.	2013	Iodosulfuron-methyl-sodium- AE F145741: Effects on reproduction and growth of earthworms Eisenia fetida in artificial soil IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 82101022, Edition Number: M-457891-01-1 Date: 2013-06-12 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.1 /04	Witte, B.	2013	Iodosulfuron-methyl-sodium- AE F145740: Effects on reproduction and growth of earthworms Eisenia fetida in artificial soil IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 82091022,	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			Edition Number: M-457334-01-1 Date: 2013-06-07 GLP/GEP: yes, unpublished		
KCA 8.4.1 /05	Witte, B.	2013	Iodosulfuron-methyl-sodium- AE 0002166: Effects on reproduction and growth of earthworms Eisenia fetida in artificial soil IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 82111022, Edition Number: M-457338-01-1 Date: 2013-06-12 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.4.1 /06	Friedrich, S.	2013	Iodosulfuron-methyl-sodium-des-iodo-carbamoyl-guanidine (BCS-CW81253): Sublethal toxicity to the earthworm Eisenia fetida in artificial soil BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 091 S, Edition Number: M-462824-01-1 Date: 2013-08-14 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.4.1 /07	Leicher, T.	2011	BCS-AA10579-urea (AE 0000119): Effects on survival, growth and reproduction on the earthworm Eisenia fetida tested in artifical soil with 10% peat- limit test Bayer CropScience, Report No.: LRT-RG-R-104/11, Edition Number: M-404685-01-1 Date: 2011-03-29 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.4.1 /08	Leicher, T.	2011	Aminotriazine (AE F059411): Effects on survival, growth and reproduction on the earthworm Eisenia fetida tested in artificial soil with 5 % peat Bayer CropScience, Report No.: LRT-RG-R-100/11,	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Edition Number: M-410930-01-1 Date: 2011-06-30 GLP/GEP: yes, unpublished		
KCA 8.4.2.1 /01	Kratz, M. A.	2012	Iodosulfuron-methyl-sodium a.s. (BCS-BB66887): Influence on mortality and reproduction on the soil mite species Hypoaspis aculeifer tested in artificial soil Bayer CropScience, Report No.: kra-HR-70/12, Edition Number: M-438590-01-1 Date: 2012-09-04 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /02	Frommholz, U.	2012	Iodosulfuron-methyl-sodium a.s. (BCS-BB66887): Influence on the reproduction of the collembolan species Folsomia candida tested in artificial soil Bayer CropScience, Report No.: FRM-Coll-140/12, Edition Number: M-438498-01-1 Date: 2012-09-14 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /03	Kratz, M. A.	2013	AE F075736 (BCS-AC12303): Influence on mortality and reproduction of the soil mite species Hypoaspis aculeifer tested in artificial soil Bayer CropScience, Report No.: kra-HR-93/13, Edition Number: M-465338-01-1 Date: 2013-08-22 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /04	Frommholz, U.	2013	AE F075736 (BCS-AC12303): Influence on the reproduction of the collembolan species Folsomia candida tested in artificial soil Bayer CropScience, Report No.: FRM-Coll-163/13, Edition Number: M-464404-01-1 Date: 2013-08-29	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			GLP/GEP: yes, unpublished		
KCA 8.4.2.1 /05	Kratz, M. A.	2013	Iodosulfuron-methyl-sodium-AE F145741 (BCS-AU71532): Influence on mortality and reproduction of the soil mite species Hypoaspis aculeifer tested in artificial soil Bayer CropScience, Report No.: kra-HR-85/13, Edition Number: M-462732-01-1 Date: 2013-08-14 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.4.2.1 /06	Kratz, M. A.	2013	Iodosulfuron-methyl-sodium-AE F145740 (BCS-AU71533): Influence on mortality and reproduction of the soil mite species Hypoaspis aculeifer tested in artificial soil Bayer CropScience, Report No.: kra-HR-84/13, Edition Number: M-459885-01-1 Date: 2013-07-05 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.4.2.1 /07	Larnaudie Lopez, M. I.	2013	AE 0002166 (BCS-AW35544): Influence on mortality and reproduction of the soil mite species Hypoaspis aculeifer tested in artificial soil Bayer CropScience, Report No.: LAR-HR-94/13, Edition Number: M-470489-01-1 Date: 2013-10-25 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.4.2.1 /08	Schulz, L.	2013	Iodosulfuron-methyl-sodium-des-iodo-carbamoyl-guanidine (BCS-CW81253): Effects on the reproduction of the predatory mite Hypoaspis aculeifer BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: M-453497-01-1, Edition Number: M-453497-01-1 Date: 2013-04-29 GLP/GEP: no, unpublished	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 8.4.2.1 /09	Friedrich, S.	2013	Iodosulfuron-methyl-sodium-des-iodo-carbamoyl-guanidine (BCS-CW81253): Effects on the reproduction of the collembolan Folsomia candida BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 089 S, Edition Number: M-462821-01-1 Date: 2013-08-02 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.4.2.1 /10	Klug, T.	2010	IN-A4098: Effect on reproduction of the predatory mite Hypoaspis (Geolaelaps) aculeifer Canestrini (Acari: Laelapidae) in artificial soil eurofins-GAB GmbH, Niefern-Oeschelbronn, Germany TF- BCS-DuPont-Syngenta, Report No.: S10-00288, Report includes Trial Nos.: S10-00288-L1_NLHa Edition Number: M-452258-01-1 Date: 2010-06-24 GLP/GEP: yes, unpublished	N	TF- BCS-DuPont-Syngenta
KCA 8.4.2.1 /11	Frommholz, U.	2011	BCS-AA10579-aminotriazine (BCS-AA40997, AE F059411): Influence on the reproduction of the collembolan species Folsomia candida tested in artificial soil Bayer CropScience, Report No.: FRM-Coll-110/11, Edition Number: M-400027-01-1 Date: 2011-01-20 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.4.2.1 /12	Kratz, M.-A.	2010	BCS-AA10579-urea (BCS-AB56501): Influence on mortality and reproduction on the soil mite species Hypoaspis aculeifer tested in artificial soil with 5 % peat Bayer CropScience, Report No.: KRA-HR-33/10, Edition Number: M-386844-01-1 Date: 2010-07-26	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			GLP/GEP: yes, unpublished		
KCA 8.4.2.1 /13	Frommholz, U.	2010	BCS-AA10579-urea (BCS-AB56501): Influence on the reproduction of the collembolan species Folsomia candida tested in artificial soil. Bayer CropScience, Report No.: FRM-COLL-93/10, Edition Number: M-384229-01-1 Date: 2010-06-29 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.5 /01	Heusel, R.	1996	Effects on soil microbial activity (nitrogen turn-over) AE F115008 substance, technical Code: AE F115008 00 1C89 0001 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: A58058, Edition Number: M-141782-01-1 EPA MRID No.: 45109125 Date: 1996-12-02 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.5 /02	Schulz, L.	2013	Iodosulfuron-methyl-sodium-AE F145741 (BCS-AU71532): Effects on the activity of soil microflora (nitrogen transformation test) BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 024 N, Edition Number: M-457273-01-1 Date: 2013-06-11 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.5 /03	Schulz, L.	2013	Iodosulfuron-methyl-sodium-AE F145740 (BCS-AU71533): Effects on the activity of soil microflora (nitrogen transformation test) BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 025 N,	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Edition Number: M-457344-01-1 Date: 2013-06-18 GLP/GEP: yes, unpublished		
KCA 8.5 /04	Schulz, L.	2013	Iodosulfuron-methyl-sodium-AE 0002166 (BCS-AW35544): Effects on the activity of soil micro-flora (Nitrogen transformation test) BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 026 N, Edition Number: M-464391-01-1 Date: 2013-09-11 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.5 /05	Schulz, L.	2013	Iodosulfuron-methyl-sodium-AE F161778 (BCS-AU85549): Effects on the activity of soil micro-flora (nitrogen transformation test) BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 027 N, Edition Number: M-464817-01-1 Date: 2013-09-11 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.5 /06	Schulz, L.	2013	Iodosulfuron-methyl-sodium-des-iodo-carbamoyl-guanidine (BCS-CW81253): Effects on the activ-ity of soil microflora (nitrogen transformation test) BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 028 N, Edition Number: M-459899-01-1 Date: 2013-06-26 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.5 /07	Schulz, L.	2010	BCS-AA10579-urea (BCS-AB56501): Effects on the activity of soil microflora (nitrogen transfor-mation test) BioChem agrar GmbH, Gerichshain, Germany	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			Bayer CropScience, Report No.: 10 10 48 048 N, Edition Number: M-395864-01-1 Date: 2010-11-24 GLP/GEP: yes, unpublished		
KCA 8.5 /08	Reis, K. H.	2003	IN-A4098: Assessment of the effects on soil microflora IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: Dupont-12117, Edition Number: M-448838-01-1 Date: 2003-07-02 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.6.1 /01	Bieringer, H.	1998	Efficacy of the herbicide iodosulfuron-methyl-sodium (AE F115008) on higher plant species as applied under greenhouse conditions Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C001486, Edition Number: M-182753-01-1 EPA MRID No.: 45109133 Date: 1998-11-18 GLP/GEP: no, unpublished ...also filed: KCA 3.3 /01	N	Bayer CropScience
KCA 6.6.2 /04	Thuerwaechter, F	1998	Selectivity thresholds for AE F115008 in various crops- ED10 values in soil Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C001481, Edition Number: M-182740-01-1 Date: 1998-10-15 GLP/GEP: no, unpublished	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.6.2 /01	Kleiner, R.	1999	Acute phytotoxicity to non-target terrestrial plants following the OECD Guideline 208 (proposal 1998) and US EPA OPPTS 850.4250 vegetative vigor, Tier II (public draft 1996) Code: AE F115008 02 WG20 B002 BioChem agrar GmbH, Cunnersdorf, Germany Bayer CropScience, Report No.: C006692, Edition Number: M-194440-01-1 Date: 1999-12-16 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.6.2	Teixeira, D.	2000	Determination of Effects on Vegetative Vigor of Ten Plant Species. Bayer CropScience, Report No.: B002811, Edition Number: M-238538-01-1 Date: 2000-xx-xx GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.8 /02	Reinhardt, J.	1996	Respiration inhibition to activated sludge of AE F115008 substance, technical Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A58107, Edition Number: M-141820-01-1 EPA MRID No.: 45109136 Date: 1996-12-10 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.8 /03	Reinhardt, J.	1996	Inhibitory effect of water constituents on bacteria (Pseudomonas cell multiplication inhibition test) Hoe 115008 substance, technical Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A57292, Edition Number: M-141031-01-1 EPA MRID No.: 45109137 Date: 1996-08-15	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			GLP/GEP: yes, unpublished		

Mesosulfuron-methyl

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.2.1 /03	xxxxxx	2001	96 Hour acute toxicity to the sheepshead minnow, Cyprinodon variegatus, in a static system AE F130060 technical 95.7 percent w/w xxxxxxxxxxxxxxxxxx Report No.: B003157, Edition Number: M-238810-01-1 EPA MRID No.: 45386301 Date: 2001-02-16 GLP/GEP: yes, unpublished	Y	Bayer Crop-Science
KCA 8.2.1 /04	xxxxxxxxxxxxxx	1993	Hoe 092944 - substance, technical (Hoe 092944 00 ZD99 0001) Effect to Oncorhynchus mykiss (Rain-bow trout) in a Static-Acute Toxicity Test (method OECD) xxxxxxxxxxxxx Report No.: A50396, Edition Number: M-131422-01-1 Date: 1993-04-13	Y	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			GLP/GEP: yes, unpublished		
KCA 8.2.2.1 /01	xxxxxxxxxx	2003	Mesosulfuron - The Toxicity to Fathead Minnow (Pimephales promelas) During an Early Life-Stage Exposure xxxxxxxxxxxxxx Report No.: B004569, Edition Number: M-241475-01-1 Date: 2003-10-20 GLP/GEP: yes, unpublished	Y	Bayer CropScience
KCA 8.2.4.1 /02	Heusel, R.	1993	Hoe 092944 - substance, technical (Hoe 092944 00 ZD99 0001) Effect to Daphnia magna (waterflea) in a Static -Acute Toxicity Test (method OECD) Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A50353, Edition Number: M-131382-01-1 Date: 1993-04-13 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.4.2 /01	Abedi, J.; Stachura, B.; Young, B.	2001	96 Hour Acute Toxicity to the Mysid Shrimp, Mysidopsis bahia, in a Static System AE F130060 Technical 95.7% w/w Aventis CropScience USA LP, RTP, NC, USA Bayer CropScience, Report No.: B003158, Edition Number: M-238811-01-1 EPA MRID No.: 45386303 Date: 2001-02-16 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.6.1 /04	Dorgerloh, M.	2005	Pseudokirchneriella subcapitata - growth inhibition test with AE F154851 00 1B96 0001 Bayer CropScience, Report No.: EBMMX093, Edition Number: M-255087-01-1 Date: 2005-07-26	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			GLP/GEP: yes, unpublished		
KCA 8.2.6.1 /05	Dorgerloh, M.	2005	Pseudokirchneriella subcapitata - growth inhibition test with AE F099095 00 1B99 0001 Bayer CropScience, Report No.: EBMMX092, Edition Number: M-254084-01-1 Date: 2005-07-08 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /06	Heusel, R.	1993	Hoe 092944 - substance, technical (Hoe 092944 00 ZD99 0001) Effect to Scenedesmus subspicatus (Green alga) in a Growth Inhibition Test (method OECD) Hoechst AG, Frankfurt am Main, Germany Bayer CropScience, Report No.: A50395, Edition Number: M-131421-01-1 Date: 1993-04-13 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /07	Bruns, E.	2011	Pseudokirchneriella subcapitata growth inhibition test with BCS-CO60720 - limit test Bayer CropScience, Report No.: EBMML012, Edition Number: M-414950-01-1 Date: 2011-10-07 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /08	Bruns, E.	2011	Pseudokirchneriella subcapitata growth inhibition test with BCS-CO60721 - limit test Bayer CropScience, Report No.: EBMML013, Edition Number: M-415112-01-1 Date: 2011-10-06 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.1 /09	Kuhl, K.	2015	Pseudokirchneriella subcapitata growth inhibition test with mesosulfuron-methyl (tech.) Bayer CropScience, Report No.: EBMMN130,	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Edition Number: M-516540-01 Date: 2015-04-15 GLP/GEP: yes, unpublished		
KCA 8.2.6.2 /02	Abedi, J.; Christ, M.; Young, B.	2001	Effect to Anabaena flos-aquae (Blue-Green Alga) in a Growth Inhibition Test, AE F130060 Technical, 95.7% w/w Aventis CropScience USA LP, RTP, NC, USA Bayer CropScience, Report No.: B003222, Edition Number: M-238869-01-1 EPA MRID No.: 45386315 Date: 2001-03-23 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.6.2 /03	Young, B. M.; Abedi, J.	2001	Effect to Skeletonema costatum (Marine Diatom) in a Growth Inhibition Test AE F130060 Technical 95.7% w/w Aventis CropScience USA LP, RTP, NC, USA Bayer CropScience, Report No.: B003156, Edition Number: M-238809-01-1 EPA MRID No.: 45386314 Date: 2001-02-16 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /07	Sowig, P.; Gosch, H.	2002	Duckweed (Lemna gibba G3) - Growth inhibition test with recovery phase AE F130060 substance, pure Code: AE F130060 00 1B98 0002 Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C018852, Edition Number: M-206814-01-1 Date: 2002-02-19 GLP/GEP: yes, unpublished	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.2.7 /08	Hoberg, J.	2009	Outdoor growth inhibition of aquatic plants exposed to Mesosulfuron-methyl Springborn Smithers Laboratories, Wareham, MA, USA Bayer CropScience, Report No.: 13798.6220, Edition Number: M-329474-01-1 Date: 2009-02-17 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /09	Bruns, E.	2013	Lemna gibba G3 - Prolonged growth inhibition test with mesosulfuron-methyl (AE F130060) with step-wise decreasing concentrations over an 8 week test duration Bayer CropScience, Report No.: EBMML017, Edition Number: M-445139-01-1 Date: 2013-01-09 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /11	Dorgerloh, M.	2005	Lemna gibba G3, growth inhibition test with AE F154851 under static conditions, (code: AE F154851 00 1B96 0001) Bayer CropScience, Report No.: EBMMX090, Edition Number: M-255283-01-1 Date: 2005-07-28 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /12	Dorgerloh, M.	2005	Lemna gibba G3 - growth inhibition test with AE F099095 under static conditions (Code: AE F099095 00 1B99 0001) Bayer CropScience, Report No.: EBMMX091, Edition Number: M-254496-01-1 Date: 2005-07-14 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.2.7 /13	Sowig, P.; Weller, O.	2000	Duckweed (Lemna gibba G3) growth inhibition test AE F092944 (metabolite of ethoxysulfuron and ami-dosulfuron) substance technical Code: AE F092944 00 1C99 0001	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Aventis CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: C003865, Edition Number: M-186916-01-1 Date: 2000-11-03 GLP/GEP: yes, unpublished		
KCA 8.2.7 /14	Bruns, E.	2013	Lemna gibba G3 - Growth inhibition test with BCS-AU66443 (AE F 140584) under semi static conditions Bayer CropScience, Report No.: EBMMN119, Edition Number: M-486658-01-1 Date: 2013-10-29 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.7 /15	Bruns, E.	2013	Lemna gibba G3 - Growth inhibition test with BCS-CO60720 under static conditions Bayer CropScience, Report No.: EBMML010, Edition Number: M-449110-01-1 Date: 2013-02-20 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.7 /16	Bruns, E.	2013	Lemna gibba G3 - Growth inhibition test with BCS-CO60721 under static conditions Bayer CropScience, Report No.: EBMML011, Edition Number: M-445154-01-1 Date: 2013-01-23 GLP/GEP: yes, unpublished	N	Bayer CropScience
KCA 8.2.8 /01	Dionne, E.	2000	AE F130060 00 1C96 0004 - Acute Toxicity to Eastern Oysters (Crassostrea virginica) Under Flow-Through Conditions Springborn Laboratories, Inc. (SLS), USA Bayer CropScience, Report No.: B003104,	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Edition Number: M-238739-02-1 EPA MRID No.: 45386302 Date: 2000-11-30 ...Amended: 2000-12-07 GLP/GEP: yes, unpublished		
KCA 8.3.1.1 /01	Schmitzer, S.	2012	Effects of mesosulfuron-methyl tech. (Acute contact and oral) on honey bees (Apis mellifera L.) in the laboratory IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 72941035, Edition Number: M-433998-01-1 Date: 2012-06-22 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.3.1.1 /02	Vergé, E.	2014	Mesosulfuron-methyl WG 75 W: Acute contact toxicity to the bumble bee, Bombus terrestris L. under laboratory conditions Eurofins Agroscience Services,Niefern-Oeschelbronn, Germany Bayer CropScience, Report No.: S13-01778, Edition Number: M-485279-01-1 Date: 2014-02-04 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.3.1.2 /01	Kling, A.	2014	Mesosulfuron-methyl (tech.) - Assessment of chronic effects to the honeybee, Apis mellifera L., in a 10 days continuous laboratory feeding limit test eurofins-GAB GmbH, Niefern-Oeschelbronn, Germany Bayer CropScience, Report No.: S13-00143, Edition Number: M-485655-01-1 Date: 2014-05-02 GLP/GEP: yes, unpublished	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.3.1.3 /01	Jeker, L.	2013	Mesosulfuron-methyl WG 75 - A honeybee brood feeding study to evaluate potential effects on brood development and mortality of the honeybee, Apis mellifera L. (Hymenoptera: Apidae) Innovative Environmental Services (IES) Ltd, Witterswil, Switzerland Bayer CropScience, Report No.: 20110174, Edition Number: M-465325-01-1 Date: 2013-07-15 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.3.1.3 /03	Taenzler, V.	2015	Mesosulfuron-methyl WG 75 W: Effects on honey bee brood (Apis mellifera L.) under semi-field conditions - Tunnel test IBACON GmbH, Rossdorf, Germany Bayer CropScience, Report No.: 87431033, Edition Number: M-510267-01-1 Date: 2015-02-09 GLP/GEP: yes, unpublished ...also filed: Ecotox /02	N	Bayer Crop-Science
KCA 8.4.1 /02	Scheffczyk, A.; Moster, T.	2010	Mesosulfuron-methyl - Reproduction toxicity to the earthworm Eisenia fetida in an artificial soil test ECT Oekotoxikologie GmbH, Floersheim, Germany Bayer CropScience, Report No.: 10P30RR, Edition Number: M-392544-01-1 Date: 2010-10-15 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.1 /03	Moser, T.; Scheff-czyk, A.	2012	AE F154851: Reproduction toxicity to the earthworm Eisenia fetida in an artificial soil test ECT Oekotoxikologie GmbH, Floersheim, Germany Bayer CropScience, Report No.: 11P33RR, Edition Number: M-425013-01-1 Date: 2012-02-16 GLP/GEP: yes, unpublished	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCA 8.4.1 /04	Moser, T.; Scheff-czyk, A.	2012	AE F160459: Reproduction toxicity to the earthworm Eisenia fetida in an artificial soil test ECT Oekotoxikologie GmbH, Floersheim, Germany Bayer CropScience, Report No.: 11P32RR, Edition Number: M-429097-01-1 Date: 2012-04-04 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.1 /05	Kratz, M. A.	2013	AE F099095 (BCS-AB40283): Effects on survival, growth and reproduction of the earthworm Eisenia fetida tested in artificial soil Bayer CropScience, Report No.: kra/Rg-R-158/13, Edition Number: M-473217-01-1 Date: 2013-12-19 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.1 /06	Kratz, M. A.	2013	AE F092944 (BCS-AA25052): Effects on survival, growth and reproduction of the earthworm Eisenia fetida tested in artificial soil Bayer CropScience, Report No.: kra/Rg-R-147/13, Edition Number: M-461051-01-1 Date: 2013-07-31 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.1 /07	Kratz, M. A.	2013	Mesosulfuron-methyl-AE F160460: Effects on survival, growth and reproduction of the earthworm Eisenia fetida tested in artificial soil Bayer CropScience, Report No.: kra/Rg-R-156/13, Edition Number: M-468911-01-1 Date: 2013-10-18 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.1 /08	Kratz, M. A.	2013	Mesosulfuron-methyl-AE F140584 (BCS-AU66443): Effects on survival, growth and reproduction of the earthworm Eisenia fetida tested in artificial soil	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Bayer CropScience, Report No.: kra/Rg-R-155/13, Edition Number: M-468921-01-1 Date: 2013-10-21 GLP/GEP: yes, unpublished		
KCA 8.4.1 /09	Moser, T.; Scheff-czyk, A.	2012	AE F147447: Reproduction toxicity to the earthworm Eisenia fetida in an artificial soil test ECT Oekotoxikologie GmbH, Floersheim, Germany Bayer CropScience, Report No.: 11P34RR, Edition Number: M-428651-01-1 Date: 2012-04-04 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /01	Kratz, M.A.	2012	Mesosulfuron-methyl (AE F130060): Influence on mortality and reproduction on the soil mite species Hypoaspis aculeifer tested in artificial soil Bayer CropScience, Report No.: KRA-HR-67/12, Edition Number: M-429376-01-1 Date: 2012-04-02 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /02	Frommholz, U.	2012	Mesosulfuron-methyl (AE F130060) a.s.: Influence on the reproduction of the collembolan species Folsomia candida tested in artificial soil Bayer CropScience, Report No.: FRM-COLL-138/12, Edition Number: M-426538-01-1 Date: 2012-03-06 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /03	Friedrich, S.	2013	Mesosulfuron-methyl-AE F154851 (BCS-AU80405): Effects on the reproduction of the collembolan Folsomia candida BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience,	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Report No.: 13 10 48 104 S, Edition Number: M-462785-01-1 Date: 2013-08-14 GLP/GEP: yes, unpublished		
KCA 8.4.2.1 /04	Friedrich, S.	2013	Mesosulfuron-methyl-AE F160459 (BCS-AU84907): Effects on the reproduction of the collembolan Folsomia candida BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 103 S, Edition Number: M-462786-01-1 Date: 2013-08-14 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /05	Schulz, L.	2013	AE F092944 (BCS-AA25052): Effects on the reproduction of the predatory mite Hypoaspis aculeifer BioChem agrar, Labor fuer biologische und chemische Analytik GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 044 S, Edition Number: M-454043-01-1 Date: 2013-05-02 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /06	Friedrich, S.	2013	AE F092944 (BCS-AA25052): Effects on the reproduction of the collembolan Folsomia candida BioChem agrar, Labor fuer biologische und chemische Analytik GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 045 S, Edition Number: M-451142-01-1 Date: 2013-03-28 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.4.2.1 /07	Friedrich, S.	2013	Mesosulfuron-methyl-AE F147447 (BCS-AU73625): Effects on the reproduction of the collembolan Folsomia candida BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience,	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Report No.: 13 10 48 105 S, Edition Number: M-462782-01-1 Date: 2013-08-14 GLP/GEP: yes, unpublished		
KCA 8.5 /09	Schulz, L.	2013	AE F092944 (BCS-AA25052): Effects on the activity of soil microflora (Nitrogen transformation test) BioChem agrar GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 018 N, Edition Number: M-453511-01-1 Date: 2013-05-02 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.5 /10	Schulz, L.	2013	Mesosulfuron-methyl-AE F147447 (BCS-AU73625): Effects on the activity of soil microflora (nitrogen transformation test) BioChem agrar, Labor fuer biologische und chemische Analytik GmbH, Gerichshain, Germany Bayer CropScience, Report No.: 13 10 48 076 N, Edition Number: M-460668-01-1 Date: 2013-07-05 GLP/GEP: yes, unpublished	N	Bayer Crop-Science
KCA 8.6.1 /02	Noeding, S.	2013	Evaluation of the pre-emergence biological activity of mesosulfuron and its metabolite BCS-CV 14885 Bayer CropScience GmbH, Frankfurt am Main, Germany Bayer CropScience, Report No.: FFS135005, Edition Number: M-460393-01-1 Date: 2013-03-06 GLP/GEP: no, unpublished	N	Bayer Crop-Science
KCA 8.6.1 /03	Noeding, S.	2013	Evaluation of the post-emergence biological activity of mesosulfuron and its metabolite BCS-CV 14885 Bayer CropScience, Report No.: FFS135004, Edition Number: M-460647-01-1	N	Bayer Crop-Science

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
			Date: 2013-03-06 GLP/GEP: no, unpublished		

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner

List of data relied on not submitted by the applicant but necessary for evaluation

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner

Appendix 2 Detailed evaluation of the new studies

Review comments
Already evaluated studies during authorisation of Atlantis 12 OD were not re-evaluated. For details please refer to Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).

A 2.1 KCP 10.1 Effects on birds and other terrestrial vertebrates

A 2.1.1 KCP 10.1.1 Effects on birds

A 2.1.1.1 KCP 10.1.1.1 Acute oral toxicity

A 2.1.1.2 KCP 10.1.1.2 Higher tier data on birds

A 2.1.2 KCP 10.1.2 Effects on terrestrial vertebrates other than birds

A 2.1.2.1 KCP 10.1.2.1 Acute oral toxicity to mammals

A 2.1.2.2 KCP 10.1.2.2 Higher tier data on mammals

A 2.1.3 KCP 10.1.3 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)

A 2.2 KCP 10.2 Effects on aquatic organisms

Reference:	***KCP 10.2/01***
Title:	*Predicting the environmental fate and ecotoxicological and toxicological effects of pesticide transformation products*
Report:	*Sinclair, C. J.; 2009; M-551653-01-1*
Authority registration No:	
Guideline(s):	*none*
Deviations:	*none*
GLP/GEP:	*no*
Acceptability:	Study already evaluated and accepted in the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).
Duplication (if vertebrate study):	

The overall aim of this work was to investigate and develop pragmatic approaches for assessing the fate and effects of pesticides transformation products in the absence of experimentally determined data. Specific objectives were:

1. To identify relationships that exist between parent pesticides and their transformation products in terms of the physico-chemical properties, ecotoxicology and toxicology;
2. To identify and evaluate methods by which the most important physico-chemical properties and effects of transformation products can be estimated;
3. To develop approaches for assessing the ecotoxicity, toxicity and pesticidal activity (e.g. fungicidal activity) of transformation products to non-target organisms;
4. To develop methodologies for identifying and ranking those transformation products that could pose the greatest risk to the public through exposure via drinking water.
The summary below will not address all these objectives but only those related to the identification of toxophores in pesticide active substances.

Materials and Methods:

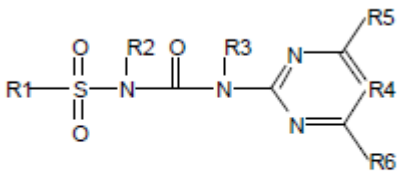
Information on the identity, physico-chemical properties, ecotoxicity, and fate and behaviour of both pesticides and their transformation products was gathered from multiple sources (open literature, databases, UK authority reports). Data quality was checked in the original citation according to the following rules: 1) when a large number of data points were available on a particular substance from a number of sources and where the values for one or more of the data points exhibited a large difference compared to the majority of the data points; and 2) when three or fewer data points were reported for a particular substance. If appropriate, the data were revised in light of the Results of the quality assessment.
The ecotoxicity data for transformation products and their parent compound were compared to determine whether the transformation products had similar ecotoxicity or were more or less toxic.
Toxophores for each of the major classes of pesticides were identified by looking for sub-structural similarities within a pesticide class. The structure of each transformation product for which ecotoxicity data were available was then examined to determine whether or not it contained a pesticide toxophore.

Results and Discussion:

Using the search strategy, information was obtained on the transformation pathways of 60 active substances and based on these pathways; the structures of 485 transformation products were identified. The active substances examined covered a range of pesticide classes and included 27 herbicides, 20 insecticides, 12 fungicides and one compound used as an herbicide, fungicide and insecticide. All the major classes of pesticides were represented by at least one active substance.
The final database only comprised property and ecotoxicity values for 89 transformation products arising from 37 parent compounds. Twenty-three parent compounds with identified transformation pathways had either no corresponding data or only unsuitable data for their respective transformation products.
Fifty-four toxophores associated with a wide range of pesticide classes were identified. It was not possible to identify a toxophore for all the active compounds considered in the study. Some pesticide classes contained too few members for reasonable toxophore identification, whilst some compounds had an undefined mode of action and/or were not a member of a defined pesticide class.

Conclusions:

For the substances iodosulfuron-methyl-sodium and mesosulfuron-methyl, the toxophore is:



sulfonylurea

A 2.2.1 KCP 10.2.1 Acute toxicity to fish, aquatic invertebrates, or effects on aquatic algae and macrophytes

A 2.2.1.1 Fish

A 2.2.1.2 Aquatic invertebrates

A 2.2.1.3 Effects on aquatic algae

A 2.2.1.4 Effects on aquatic macrophytes

Reference:	***KCP 10.2.1/01***
Title:	*Amendment no. 1 to final report - Lemna gibba G3 - Growth inhibition test with BCS-CV14885 under static conditions - Limit test*
Report:	*Kuhl, K.; 2017; EBMM0006; M-602447-02-1*
Authority registration No:	
Guideline(s):	*OECD Guideline 221 (March 23, 2006), US EPA OCSPP 85*
Deviations:	*yes, see report*
GLP/GEP:	*yes*
Acceptability:	Study already evaluated and accepted in the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL). Agreed endpoint: 7d ErC_{50}>100 mg p.m./L
Duplication (if vertebrate study):	

Materials and methods:

Test material	*BCS-CV14885* *Batch No.: BCS-CV14885-01-01* *Specification: not available* *96.3 % w/w*
Guideline(s) adaptation	*Not specified*
Test species	*Duckweed (Lemna gibba) strain G3*
Acclimation	*inoculum pre-culture, preparation 7 – 10 days before the start of the main test* *cultivation under the same conditions as in main test*
Culturing conditions	*20X AAP medium* *6500 – 7000 lux* *temperature of 23 - 26° C*
Test solutions	*Nominal concentrations: 100 mg p.m./L. Limit test.* *Control: test medium* *Evidence of undissolved material: not observed*
Replication	*No. of vessels per concentration (replicates): 6* *No. of vessels per control (replicates): 6*
Organisms per replicate	*No. of fronds per vessel: 12* *No. of fronds per plant: 3-4*
Exposure	*Static* *Total study duration: 7 days*
Test conditions	*Incubation chamber used: not specified* *Temperature: 24.0 °C to 24.5 °C* *Photoperiod: permanent light*

	Light quality: bank light containing fluorescent lamps *Light intensity: 6.61 to 6.96 klux* *pH: 7.4 – 7.7 at day 0; 8.8--8.9 at day 7* *Growth medium: 20X AAP*
Parameters Measured / Observations	*Determination of frond number and total frond area on days 0, 3, 5, 7 by computerized image analysis (LemnaTec Scanalyzer)* *Visual observations of sublethal effects on days 3, 5, 7*
Sampling for chemical analysis	*Day 0 (fresh): Quantitative amounts of BCS-CV14885 were measured in the freshly prepared test level and the control* *Day 7 (aged): Quantitative amounts of BCS-CV14885 were measured in pooled replicates of the test level and the control* *The water samples were analyzed with HPLC-MS/MS*
Data analysis	*The ErC50, LOErC and NOErC (using the ANOVA procedure (p = 0.05, one sided) and properly selected multiple t-tests) was directly determined from the raw data* *All statistical evaluations were done with ToxRatProfessional Version 3.2.1*

Results and Discussion:

Validity criteria:

Validity criterion	***Recommended***	***Obtained***
Doubling time of frond number in the control group	*< 2.5 days (60 hours)*	*2.2 days*
*Control CV for growth rate at test termination**	*< 20%*	*6.6 / 6.1 %*
*Control CV for yield at test termination**	*< 20 %*	*17.3 / 16.6 %*

** Validity element of OCSPP 850.4400; values are presented for frond number / total frond area*

All biological validity criteria for this study were met, requested by the mentioned guidelines.

Analytical findings:

Since the analytical results ranged between 80 and 120 % of nominal, all reported results are related to nominal concentrations.

The detailed results of the analytical measurements of BCS-CV 14885 are shown in the following table:

Nominal concentration [mg p.m./L]	***Day 0 measured concentration [mg p.m./L]***	***Day 0 % nominal***	***Day 7 measured concentration [mg p.m./L]***	***Day 7 % nominal***
control	*<10.0*	*--*	*<10.0*	*--*
100	*99.8*	*99.8*	*98.6*	*98.6*

Concurrent validation:

For the determination of BCS-CV14885 in test water from aquatic tests the analytical method 01542 (Kuhl, K.; 2017; M-602447-02-1) was used. Please refer to part B5 for the respective summary of this method (01542).
In the present study the method was validated concurrently with the sample analyses of the study by evaluation of the standard injections.
The linearity of the MS-detector was checked for BCS-CV14885 in the range from 0.10 µg/L to 10.0 µg/L and was shown to be linear (y = 474040x + 2659.3). The correlation coefficient was 0.9999 (1/x weighted). 5 concentrations were measured in duplicate. If necessary, samples were diluted to achieve final concentrations falling within the calibrated range of detector response.
Because of the direct measurement of the samples recovery rates cannot be calculated. The evaluation of measurements based on HPLC-MS/MS for precision was done by comparison of the peak areas of the samples with the peak areas of the external standard solutions. For this purpose the BCS-CV14885

standard injections were evaluated. Standard solutions of BCS-CV14885 in deonized water/acetonitrile (8/2, v/v) were used. The relative standard deviation of BCS-CV14885 peak areas and retention times are shown in the table below.

Validation of Method 01542 for BCS-CV14885 by HPLC-MS/MS

BCS-CV14885 Standard concentration		***BCS-CV14885***			
		Peak area		***Retention time***	
[µg/L]	***n***	***Mean value [area counts]***	***Rel. std. dev. [%]***	***Mean value [min]***	***Rel. std. dev. [%]***
0.100	*6*	*49180*	*2.2*	*2.91*	*0.2*
0.500	*4*	*241396*	*1.4*	*2.91*	*< 0.1*
1.00	*4*	*486169*	*1.5*	*2.91*	*0.2*
5.00	*4*	*2386005*	*0.8*	*2.91*	*0.2*
10.0	*4*	*4719990*	*1.7*	*2.91*	*0.2*

Conclusion
*The applicability of the HPLC-MS/MS method 01542 for the analysis of BCS-CV14885 in test water samples was tested. The data presented demonstrate that the method allows the determination of BCS-CV14885 with satisfactory precision data given as the relative standard deviation of 4 and 6 replicates, with 0.8% and 2.2%. In addition the specificity of the method was demonstrated as no test item was found in control samples. The method is suitable for the determination of BCS-CV14885 in test water and can be regarded as fit for purpose with regard to the study Kuhl, K.; 2017; M-602447-02-1*dart://dart/edition?ed_no=M-600651-01-1.

Biological findings:

The following table summarizes the effects on growth rate observed after 7 days:

nominal test concentration [mg p.m./L]	***frond number (day 7) mean values from 4 replicates***	***total frond area of plants (day 7) mean values from 4 replicates [mm²]***	***% inhibition***	
			mean growth rate for frond number	***mean growth rate for total frond area of plants***
control	*108*	*916*	*--*	*--*
100	*123*	*1052*	*-6.2*	*-6.6*

Negative inhibition values indicate an increase in growth relative to the control

No sublethal effects on Lemna gibba were observed. No remarkable observations of the test item in the test medium were recorded. Over the whole test period, the media were clear and colourless.

Endpoints were based on nominal concentrations.

Endpoint (0-7 days)	***Effect on mean growth rate of frond number [mg p.m./L]***	***Effect on mean growth rate of total frond area of plants [mg p.m./L]***
E_rC_{50}:	***>100***	***>100***
LOE_rC: lowest concentration with an effect	*>100*	*>100*
NOE_rC: highest concentration without adverse effects	*≥ 100*	*≥ 100*

Conclusions:

BCS-CV14885 caused no adverse effects on the growth of Lemna gibba G3 up to the limit test item concentration of 100 mg pure metabolite/L.

Reference:	***KCP 10.2.1/02***
Title:	*Lemna gibba G3 - Growth inhibition test with mesosulfuron-methyl tech. (BCS-AK65185) under peak exposure conditions*
Report:	*Kuhl, K.; 2016; EBMMN160; M-577164-01-1*
Authority registration No:	
Guideline(s):	*EU Directive 91/414/EEC* *Regulation (EC) Number 1107/2009* *US EPA OCSPP 850.4400*
Deviations:	*yes, see report*
GLP/GEP:	*yes*
Acceptability:	Study already evaluated in the Core Assessment of Atlantis 12 OD, section 9, , 2020, (zRMS:PL) where following conclusions were made: *ZRMS-PL agrees with the evaluation of the effects in this study made by ZRMS-UK.* *ZRMS-PL did not consider it in the current risk assessment as the study is only useful for the Lemna sp. risk assessment and does not cover the other aquatic macrophytes.* *In addition, we are also in the opinion that following the 24 exposure periods, plants were moved to fresh media; which should be noted as an uncertainty and be considered further when comparing the study exposure profile to that modelled for the product risk assessment.*
Duplication (if vertebrate study):	

Material and methods:

Test material	*Mesosulfuron-methyl tech. (MSM), (BCS-AK65185)* *Batch Code AE F130060-01-02* *Origin batch number EFME000144* *Specification: 102000013204* *97.4 % w/w*
Guideline(s) adaptation	*Guidelines were adapted to peak exposure conditions and a prolonged study duration (Design 2)*
Test species	*Duckweed (Lemna gibba)* *strain G3*
Acclimation	*inoculum pre-culture, preparation 7 – 10 days before the start of the main test* *cultivation under the same conditions as in main test*
Culturing conditions	*20X AAP medium* *6500 – 7000 lux* *temperature of 23 - 26° C*
Test solutions	*Nominal concentrations: 1.23, 3.70, 11.1, 33.3 and 100.0 µg a.s./L* *Control: water* *Visual observations of test medium on days 0, 1, 3, 4, 7, 8 gave no evidence of undissolved material*
Replication	*No. of vessels per concentration (replicates): 3* *No. of vessels per control (replicates): 3*
Organisms per replicate	*No. of fronds per vessel: 12* *No. of fronds per plant: 3-4* *To avoid nutrient depletion and space limitations, only 12 fronds of each replicate were transferred into the exposure media at start of the 2ndpeak of design 2 at day 7.*
Exposure	*Peak exposure following 2 different designs* *Total study duration: Design 1: 7 days (two 24 hours lasting peaks, day 0 and 3)*

	Design 2: 14 days (two 24 hours lasting peaks on day 0 and 7)
Test conditions	*Incubation chamber used: Multitron, Infors GmbH* *Temperature: 23.0°C to 24.7 °C* *Photoperiod: permanent light* *Light quality: bank light containing fluorescent lamps* *Light intensity: 6.56 to 7.00 klux* *pH: 7.5 – 8.2 (freshly prepared media), 7.6 – 9.0 (aged media)* *Growth medium: 20X AAP*
Parameters Measured / Observations	*Determination of frond number and total frond area on days 0, 2, 4, 7 (design 1 and 2) and on days 9, 11 and 14 (design 2) by computerized image analysis* *Visual observations of sublethal effects on days 2, 4, 7 (design 1 and 2) and on days 9, 11 and 14 (design 2)*
Sampling for chemical analysis	*Day 0 (design 1+2), 3(design 1) and 7 (design 2) -: fresh media samples were taken from the prepared volume of each test treatment level* *Day 1 (design 1+2), 4 (design 1) and 8 (design 2): after removing the plant material from the test vessels, all replicates of a treatment level were combined and an aged media sample was taken of the combined replicates.* *The water samples were analysed with HPLC-MS/MS.*
Data analysis	*EC_x calculations were performed by probit analysis using linear max. likelihood regression. Effect thresholds (e.g. NOECs) were determined by Williams Multiple Sequential t-test Procedure. Furthermore a trend analysis by contrasts was conducted to justify the procedure.* *All statistical evaluations were done with ToxRatProfessional Version 3.2.1.*

Results and Discussion:

Validity criteria	***Required***		***Obtained***	
Doubling time	*< 2.5 days*		*1.9 - 1.9 – 2.0 days (design 1, design 2 week 1 and week 2, respectively)*	
Control CV for growth rate at test termination	*Design 1/ week 1*	*Design 2/ week 2*	*Design 1/ week 1*	*Design 2/ week 2*
	< 20 %		*2.6 / 1.6 % (frond number / frond area)*	*5.3 / 3.6 % (frond number / frond area)*
Control CV for yield at test termination	*Design 1/ week 1*	*Design 2/ week 2*	*Design 1/ week 1*	*Design 2/ week 2*
	< 20 %		*7.1 / 4.4 % (frond number / frond area)*	*14.6 / 15.0 % (frond number / frond area)*

Analytical results:
In the controls no test substance was detected. Since correct dosing was proven and since the test item was stable over the exposure periods, the study results are presented based on nominal peak concentrations.

The summarised results of the analytical measurements of mesosulfuron-methyl tech. (BCS- AK65185) are shown in the following table:

Table 10.2.1/08-01: Analytical results

	Day 0 (fresh)		*Day 1 (aged)*		*Day 3 (fresh)*		*Day 4 (aged)*		*Day 7 (fresh)*		*Day 8 (aged)*	
Nominal concentration (µg a.s./L)	*Measured concentration (µg a.s./L)*	*% compared to nominal*	*Measured concentration (µg a.s./L)*	*% compared to nominal*	*Measured concentration (µg a.s./L)*	*% compared to nominal*	*Measured concentration (µg a.s./L)*	*% compared to nominal*	*Measured concentration (µg a.s./L)*	*% compared to nominal*	*Measured concentration (µg a.s./L)*	*% compared to nominal*
1.23	*1.2*	*97.56*	*1.19*	*96.75*	*1.16*	*94.31*	*1.15*	*93.50*	*1.23*	*100.00*	*1.21*	*98.37*
3.7	*3.58*	*96.76*	*3.56*	*96.22*	*3.41*	*92.16*	*3.45*	*93.24*	*3.55*	*95.95*	*3.64*	*98.38*
11.1	*11*	*99.10*	*10.7*	*96.40*	*10.3*	*92.79*	*10.1*	*90.99*	*10.5*	*94.59*	*10.8*	*97.30*
33.3	*32.6*	*97.90*	*31.9*	*95.80*	*31.1*	*93.39*	*30.9*	*92.79*	*32.1*	*96.40*	*31.7*	*95.20*

100	99.7	99.70	95.7	95.70	93.3	93.30	92.2	92.20	95.8	95.80	94.8	94.80

	~~Design 1~~ ~~[% of nominal]~~	~~Design 2~~ ~~[% of nominal]~~
~~Day 0 (freshly prepared)~~	~~96.8 – 99.7~~	
~~Day 1 (aged)~~	~~95.7 – 96.7~~	
~~Day 3 (freshly prepared)~~	~~92.2 – 94.3~~	~~–~~
~~Day 4 (aged)~~	~~91.0 – 93.5~~	~~–~~
~~Day 7 (freshly prepared)~~	~~–~~	~~95.2 – 100~~
~~Day 8 (aged)~~	~~–~~	~~94.8 – 98.4~~

~~Design 1: two 24 hour peaks on day 0 and 3~~
~~Design 2: two 24 hour peaks on day 0 and 7~~

Concurrent validation:
The method 01387 (Krebber, R.; Braune, M.; 2013; M-466732-01-1) was validated concurrently with the test solution analyses. For this purpose the mesosulfuron-methyl standard injections were evaluated. The results are presented in the table below.

Validation of Method 01387 for Mesosulfuron-methyl, HPLC-MS/MS

Mesosulfuron-methyl standard concentration (µg/L)	n	Mesosulfuron-methyl			
		Peak area		Retention time	
		Mean value (area counts)	RSD (%)	Mean value (min)	RSD (%)
0.100	5	11440	2.2	2.17	0.2
0.500	6	58449	2.1	2.17	0.2
1.00	6	117443	1.7	2.18	0.2
5.00	6	602881	3.4	2.18	0.3
10.0	6	1188254	1.8	2.17	< 0.1

The precision data given as the relative standard deviation (%) for five different concentrations with five or six replicates each. The relative standard deviations were very low and varied between 1.7 % and 3.4 %. In addition the specificity of the method was demonstrated as no test item was found in control samples. Therefore, the analytical method 01387 can be regarded as fit for purpose with regard to the actual study.

Biological results:

The following table summarizes the growth effects observed in design 1 after 7 days:

Experiment 1

The mean frond number and mean frond area for each measurement period is presented below in table 10.2.1/08-02. Exposure occurred at day 0 and day 3 for a duration of 24 hours in each case before being moved to untreated media for the remaining time of the study.

Table 10.2.1/08-02: Mean frond number and frond area for each measurement period for experiment 1.

nominal concentration [µg a.s./L]	Mean frond number				Mean frond area (mm^2)			
	Day 0	Day 2	Day 4	Day 7	Day 0	Day 2	Day 4	Day 7
control	12	27.0	56.0	159.7	112.7	220.3	473.7	1375.7
1.23	12	22.7	45.7	138.0	112.0	192.0	404.3	1121
3.70	12	19.0	33.0	80.7	113.7	164.3	285.3	642.3
11.1	12	16.0	26.7	46.3	116.7	150.3	206.7	360.0
33.3	12	14.3	17.0	32.3	117.7	146.3	170.7	239.3
100	12	13.3	15.7	22.7	113.3	133.3	150.3	182.7

Effects on growth inhibition for the period 0 -7 days and 0 – 2 days are presented in tables 10.2.1/08-03 and 10.2.1/08-4 respectively.

Table 10.2.1/08-03: Growth effects observed in design 1 after 0 - 7 days

Nominal test concentration [µg a.s./L]	Frond number (day 7) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 7) mean values from 3 replicates [mm^2]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	159.7	0.370	1375.7	0.358	--	--
1.23	138.0	0.349	1121.0	0.329●	5.7	8.1●
3.70	80.7	0.271●	642.3	0.247●	26.7●	30.9●
11.1	46.3	0.192●	360.0	0.161●	48.0●	55.0●
33.3	32.3	0.142●	239.3	0.101●	61.7●	71.6●
100	22.7	0.090●	182.7	0.068●	75.7●	81.0●

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
Design 1: two 24 hour peaks on day 0 and 3

Table 10.2.1/08-04: Growth effects observed in design 1 after 0 - 2 days

Nominal test concentration [µg a.s./L]	Frond number (day 2) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 2) mean values from 3 replicates [mm^2]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	27.0	0.405	220.3	0.335	--	--
1.23	22.7	0.319	192.0	0.269	22.26	20.74
3.70	19.0	0.230	164.3	0.184	43.96	45.86
11.1	16.0	0.144	150.3	0.127	64.92	62.79
33.3	14.3	0.088	146.3	0.109	78.62	68.01
100	13.3	0.051	133.3	0.081	87.46	76.09

Growth inhibition at day 0 – 2 and day 0 – 7 for frond number and frond area has been presented above. Although there was a further exposure event at day 3, as the frond number and frond area were measured only on days 0, 2, 4, 6 and 7, the zRMS did not consider it appropriate to present data for any other sampling period as there were no day 3 data for the beginning of the second exposure period for comparison to the subsequent time periods.

Experiment 2 – Week 1

The mean frond number and mean frond area for each measurement period is presented below in table 10.2.1/08-05. Exposure occurred at day 0 for duration of 24 hours.

Table 10.2.1/08-05: Mean frond number and frond area for each measurement period for experiment 2, week 1.

nominal concentration [µg a.s./L]	Mean frond number				Mean frond area (mm²)			
	Day 0	Day 2	Day 4	Day 7	Day 0	Day 2	Day 4	Day 7
control	12	28.7	56.7	153.7	120.3	236.0	487	1308.7
1.23	12	24.3	48.7	141.7	117.0	210.7	442.7	1160.7
3.70	12	18.7	37.7	116.3	115.0	171.3	324.3	920.3
11.1	12	16.0	31.0	94.3	116.3	149.7	244.7	727.3
33.3	12	15.7	28.0	91.3	120.0	150.3	213.0	654.0
100	12	15.0	20.3	71.3	109.0	131.3	167.3	521.7

Effects on growth inhibition for the period 0 - 7 days, 0 – 2 and 0 – 4 days are presented in tables 10.2.1/08-06, 10.2.1/08-07 and 10.2.1/08-08 respectively.

The following table summarizes the growth effects observed in design 2 after 7 days (week 1):

Table 10.2.1/08-06: Growth effects observed in design 2 after 0 - 7 days (week 1)

Nominal test concentration [µg a.s./L]	Frond number (day 7) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 7) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	153.7	0.364	1308.7	0.341	--	--
1.23	141.7	0.352	1160.7	0.328	3.3	3.9
3.70	116.3	0.322●	920.3	0.295●	11.5●	13.4●
11.1	94.3	0.293●	727.3	0.260●	19.5●	23.7●
33.3	91.3	0.288●	654.0	0.241●	20.9●	29.3●
100	71.3	0.254●	521.7	0.224●	30.1●	34.4●

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
-% inhibition: increase in growth relative to the control
Design 2: two 24 hour peaks on day 0 and 7

Table 10.2.1/08-07: Growth effects observed in design 2 after 0 - 2 days (week 1)

Nominal test concentration [µg a.s./L]	***Frond number (day 2) mean values from 3 replicates***	***Mean growth rate for frond number***	***Total frond area of plants (day 2) mean values from 3 replicates [mm²]***	***Mean growth rate for total frond area of plants***	***% Inhibition***	
					Mean growth rate for frond number	***Mean growth rate for total frond area of plants***
control	*28.7*	*0.436*	*236.0*	*0.337*	*--*	*--*
1.23	*24.3*	*0.353*	*210.7*	*0.294*	*19.09*	*13.49*
3.70	*18.7*	*0.222*	*171.3*	*0.199*	*49.13*	*41.40*
11.1	*16.0*	*0.144*	*149.7*	*0.126*	*67.01*	*62.87*
33.3	*15.7*	*0.134*	*150.3*	*0.113*	*69.18*	*66.89*
100	*15.0*	*0.112*	*131.3*	*0.093*	*74.41*	*72.63*

Table 10.2.1/08-08: Growth effects observed in design 2 after 0 - 4 days (week 1)

Nominal test concentration [µg a.s./L]	***Frond number (day 4) mean values from 3 replicates***	***Mean growth rate for frond number***	***Total frond area of plants (day 4) mean values from 3 replicates [mm²]***	***Mean growth rate for total frond area of plants***	***% Inhibition***	
					Mean growth rate for frond number	***Mean growth rate for total frond area of plants***
control	*56.7*	*0.388*	*487.0*	*0.350*	*--*	*--*
1.23	*48.7*	*0.350*	*442.7*	*0.333*	*19.68*	*4.95*
3.70	*37.7*	*0.286*	*324.3*	*0.259*	*34.36*	*25.95*
11.1	*31.0*	*0.237*	*244.7*	*0.186*	*45.58*	*46.87*
33.3	*28.0*	*0.212*	*213.0*	*0.143*	*51.42*	*59.01*
100	*20.3*	*0.131*	*167.3*	*0.107*	*69.86*	*69.40*

The zRMS has presented the growth inhibition for frond area and frond number for time periods 0 – 2 days and 0 – 4 days above to determine if growth inhibition was greater following the initial exposure at 0 days.

Experiment 2 – Week 2

The mean frond number and mean frond area for each measurement period is presented below in table 10.2.1/08-09. Exposure occurred at day 7 for duration of 24 hours before plants were moved to untreated media for the remaining time of the study.

Table 10.2.1/08-09: Mean frond number and frond area for each measurement period for experiment 2, week 2.

nominal concentration [µg a.s./L]	***Mean frond number***				***Mean frond area (mm²)***			
	Day 7	***Day 9***	***Day 11***	***Day 14***	***Day 7***	***Day 9***	***Day 11***	***Day 14***
control	*12*	*26.3*	*54.3*	*145.0*	*108.3*	*224.3*	*488.7*	*1262.7*
1.23	*12*	*26.3*	*46.7*	*146.7*	*112.0*	*200.3*	*420.3*	*1231.7*
3.70	*12*	*20.3*	*39.7*	*132.7*	*109.3*	*165.3*	*338.3*	*1056*
11.1	*12*	*16.0*	*34.0*	*108.0*	*102.7*	*140.0*	*235.0*	*802.0*
33.3	*12*	*13.3*	*19.7*	*78.7*	*84.7*	*110.3*	*145.0*	*510.0*
100	*12*	*14.3*	*17.7*	*66.3*	*90.0*	*110.3*	*134.3*	*439.7*

Effects on growth inhibition for the period 7 - 14 days, 7 – 9 and 7 – 11 days are presented in tables 10.2.1/08-10, 10.2.1/0811 and 10.2.1/08-12 respectively.

The following table summarizes the growth effects observed in design 2 after 14 days (week 2):

Table 10.2.1/08-10: Growth effects observed in design 2 after 7 - 14 days (week 2)

Nominal test concentration [µg a.s./L]	Frond number (day 7) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 7) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	145.0	0.355	1262.7	0.350	--	--
1.23	146.7	0.357	1231.7	0.342	-0.7	2.2
3.70	132.7	0.343	1056.0	0.324●	3.4	7.5●
11.1	108.0	0.314●	802.7	0.294●	11.6●	16.1●
33.3	78.7	0.268●	510.0	0.257●	24.4●	26.6●
100	66.3	0.243●	439.7	0.227●	31.5●	35.1●

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
Design 2: two 24 hour peaks on day 0 and 7

No sublethal effects were observed in any test concentration during the test period.

Table 10.2.1/08-11: Growth effects observed in design 2 after 7 - 9 days (week 1)

Nominal test concentration [µg a.s./L]	Frond number (day 9) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 9) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	26.3	1.246	224.3	1.228	--	--
1.23	26.3	1.252	200.3	1.199	-0.14	2.53
3.70	20.3	1.202	165.3	1.134	3.87	7.80
11.1	16.0	1.099	140.0	1.028	12.11	16.45
33.3	13.3	0.940	110.3	0.898	24.77	27.02
100	14.3	0.855	110.3	0.793	31.63	35.52

Table 10.2.1/08-12: Growth effects observed in design 2 after 7 -11 days (week 1)

Nominal test concentration [µg a.s./L]	Frond number (day 11) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 11) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	54.3	0.377	488.7	0.377	--	--
1.23	46.7	0.340	420.3	0.331	10.60	13.00
3.70	39.7	0.299	338.3	0.282	21.29	25.67
11.1	34.0	0.260	235	0.207	31.48	45.54
33.3	19.7	0.124	145.0	0.134	67.39	64.63
100	17.7	0.097	134.3	0.100	74.43	73.67

The zRMS has presented the growth inhibition for frond area and frond number for time periods 7 - 9 days 7 - 11 days above to determine if growth inhibition was greater following the subsequent exposure at 7 days.

No sublethal effects were observed in any test concentration during the test period.

Conclusions:

Table 10.2.1/08-10: Derived toxicity endpoints for L. gibba following pulsed exposure for 7 or 14 days.

	Effect on mean growth rate of frond number	Effect on mean growth rate of total frond area of plants

	[µg a.s./L]	[µg a.s./L]
Endpoint (0-7 days) **Design 1**:		
E_rC_{50} (95% C.I.):	**16.6 (15.2 – 18.1)**	**10.9 (10.5 – 11.3)**
E_rC_{20} (95% C.I.):	2.53 (2.17 – 2.91)	2.00 (1.87 – 2.12)
E_rC_{10} (95% C.I.):	< 1.23	< 1.23
LOE_rC: lowest concentration with an effect	3.70	≤ 1.23
NOE_rC: highest concentration without adverse effects	1.23	< 1.23
Endpoint (0-7 days) **Design 2**:		
E_rC_{50} (95% C.I.):	**> 100**	**> 100**
E_rC_{20} (95% C.I.):	22.5 (14.8 – 33.1)	11.7 (9.20 – 14.3)
E_rC_{10} (95% C.I.):	3.09 (1.14 – 5.62)	1.82 (1.13 – 2.63)
LOE_rC: lowest concentration with an effect	3.70	3.70
NOE_rC: highest concentration without adverse effects	1.23	1.23
Endpoint (7-14 days) **Design 2:**		
E_rC_{50} (95% C.I.):	**> 100**	**> 100**
E_rC_{20} (95% C.I.):	30.9 (26.4 – 35.6)	20.3 (17.3 – 23.5)
E_rC_{10} (95% C.I.):	8.91 (6.67 – 11.2)	4.98 (3.69 – 6.35)
LOE_rC: lowest concentration with an effect	11.1	3.70
NOE_rC: highest concentration without adverse effects	3.70	1.23

Endpoints were based on nominal concentrations.
Calculations for frond numbers and for total frond area of plants based on mean growth rates.
Design 1: two 24 hour peaks on day 0 and 3
Design 2: two 24 hour peaks on day 0 and 7

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Reference:	***KCP 10.2.1/03***
Title:	*Lemna gibba G3 - Growth inhibition test with **iodosulfuron-methyl-sodium** TC (BCS-BB66887) under peak exposure conditions.*
Report:	*Kuhl K.; 2016; EBIMN158; M-574865-01-1*
Authority registration No:	
Guideline(s):	*EU Directive 91/414/EEC* *Regulation (EC) Number 1107/2009* *US EPA OCSPP 850.4400*
Deviations:	*yes, see report*
GLP/GEP:	*yes*
Acceptability:	Study already evaluated in the Core Assessment of Atlantis 12 OD, sec-tion 9, 2020, (zRMS:PL) where following conclusions were made: *zRMS did not consider the PECtwa approach and population model in the current risk assessment.*
Duplication (if vertebrate study):	

Material and methods:

Test material	*Iodosulfuron-methyl-sodium TC (IMS), (BCS-BB66887)* *Batch No. AE F115008-01-03* *Specification: 102000000739* *92.4 % w/w*
Guideline(s) adaptation	*Guidelines were adapted to peak exposure conditions and a prolonged study duration (Design 2)*
Test species	*Duckweed (Lemna gibba)* *strain G3*
Acclimation	*inoculum pre-culture, preparation 7 – 10 days before the start of the main test* *cultivation under the same conditions as in main test*
Culturing con-ditions	*20X AAP medium* *6500 – 7000 lux* *temperature of 23 - 26° C*
Test solutions	*Nominal concentrations: 1.91, 6.10, 19.5, 62.5 and 200.0 µg a.s./L* *Control: water* *Evidence of undissolved material: visual observations of test medium on days 0, 1, 3, 4, 7, 8; no visual effects of the test substance were found*
Replication	*No. of vessels per concentration (replicates): 3* *No. of vessels per control (replicates): 3*
Organisms per replicate	*No. of fronds per vessel: 12* *No. of fronds per plant: 3-4* *For Design 2, only 12 fronds of each replicate (from week 1) were transferred into the exposure media before the second peak was set on day 7.*
Exposure	*Peak exposure following two different designs* *Total study duration: Design 1: 7 days (two 24 hours lasting peaks, day 0 and 3)* *Design 2: 14 days (two 24 hours lasting peaks on day 0 and 7)*
Test conditions	*Incubation chamber used: Multitron, Infors GmbH* *Temperature: 23.1 °C to 24.4 °C* *Photoperiod: permanent light* *Light quality: bank light containing fluorescent lamps* *Light intensity: 6.51 to 6.73 klux*

	pH: 7.5- 7.8 (freshly prepared media), 8.3 – 9.0 (aged media) *Growth medium: 20X AAP*
Parameters Measured / Observations	*Determination of frond number and total frond area on days 0, 2, 4, 7 (design 1 and 2) and on days 9, 11 and 14 (design 2) by computerized image analysis (LemnaTec Scanalyzer)* *Visual observations of sublethal effects on days 2, 4, 7 (design 1 and 2) and on days 9, 11 and 14 (design 2)*
Sampling for chemical analysis	*Day 0 (design 1+2), 3 (design 1) and 7 (design 2): fresh media samples were taken from the prepared volume of each test treatment level* *Day 1 (design 1+2), 4 (design 1) and 8 (design 2): after removing the plant material from the test vessels, all replicates of a treatment level were combined and an aged media sample was taken of the combined replicates.* *The water samples were analyzed with HPLC-MS/MS.*
Data analysis	*EC_x calculations were performed by probit analysis using linear max. likelihood regression.* *Effect thresholds (e.g. NOECs) were determined by Williams Multiple Sequential t-test Procedure following a trend analysis by contrasts.* *All statistical evaluations were done with ToxRatProfessional Version 3.2.1.*

Results:

Validity criteria	***Required***		***Obtained***	
Doubling time	*< 2.5 days*		*1.8 – 2.1 days*	
*Control CV for growth rate at test termination**	*Design 1/ week 1*	*Design 2/ week 2*	*Design 1 / week 1*	*Design 2/ week 2*
	< 20 %		*8.7 – 18.8 %*	*8.7 – 12.1 %*
*Control CV for yield at test termination**	*Design 1/ week 1*	*Design 2/ week 2*	*Design 2/ week 1*	*Design 1 / week 1*
	< 20 %		*8.4 – 13.3 %*	*1.8 – 10.7 %*

** Validity element of OCSPP 850.4400; values are presented for frond number / total frond area*

Analytical results:

In the controls no test substance was detected. Since correct dosing was proven and since the test item was stable over the exposure periods, the study results are presented based on nominal peak concentrations.
The summarised results of the analytical measurements of iodosulfuron-methyl-sodium are shown in the following table:

	Design 1 [% of nominal]	***Design 2 [% of nominal]***
Day 0 (freshly prepared)	*97 – 110*	
Day 1 (aged)	*96 – 108*	
Day 3 (freshly prepared)	*95 – 100*	*--*
Day 4 (aged)	*94 – 100*	*--*
Day 7 (freshly prepared)	*--*	*97 – 113*
Day 8 (aged)	*--*	*97 – 111*

Design 1: two 24 hour peaks on day 0 and 3
Design 2: two 24 hour peaks on day 0 and 7

*The detailed results of the analytical measurements of iodosulfuron-methyl-sodium (**Design 1 and 2, first***

peak) *are shown in the following table:*

Nominal concentration [µg a.s./L]	***Day 0 measured concentration [µg a.s./L]***	***Day 0 % nominal***	***Day 1 measured concentration [µg a.s./L]***	***Day 1 % nominal***
control	*< 0.104*	*--*	*< 0.104*	*--*
1.91	*1.86*	*97*	*1.83*	*96*
6.10	*6.12*	*100*	*5.93*	*97*
19.5	*19.2*	*99*	*18.9*	*97*
62.5	*69.0*	*110*	*67.8*	*108*
200	*194*	*97*	*192*	*96*

Design 1: two 24 hour peaks on day 0 and 3
Design 2: two 24 hour peaks on day 0 and 7

*The detailed results of the analytical measurements of iodosulfuron-methyl-sodium (**Design 1, second peak**) are shown in the following table:*

Nominal concentration [µg a.s./L]	***Day 3 measured concentration [µg a.s./L]***	***Day 3 % nominal***	***Day 4 measured concentration [µg a.s./L]***	***Day 4 % nominal***
control	*< 0.104*	*--*	*< 0.104*	*--*
1.91	*1.88*	*98*	*1.90*	*99*
6.10	*6.12*	*100*	*6.09*	*100*
19.5	*19.2*	*98*	*18.8*	*96*
62.5	*60.9*	*98*	*61.1*	*98*
200	*189*	*95*	*188*	*94*

Design 1: two 24 hour peaks on day 0 and 3

*The detailed results of the analytical measurements of iodosulfuron-methyl-sodium (**Design 2, second peak**) are shown in the following table:*

Nominal concentration [µg a.s./L]	***Day 7 measured concentration [µg a.s./L]***	***Day 7 % nominal***	***Day 8 measured concentration [µg a.s./L]***	***Day 8 % nominal***
control	*< 0.104*	*--*	*< 0.104*	*--*
1.91	*2.17*	*113*	*2.11*	*111*
6.10	*6.30*	*103*	*6.27*	*103*
19.5	*19.5*	*100*	*19.4*	*99*
62.5	*62.5*	*100*	*61.9*	*99*
200	*194*	*97*	*194*	*97*

Design 2: two 24 hour peaks on day 0 and 7

Concurrent validation:

For the determination of iodosulfuron-methyl in test water the analytical method 01387 (Krebber, R.; Braune, M.; 2013; M-466732-01-1) was used. The analytical method is already EU-agreed and therefore not presented in part B5.

In the present study the method was validated concurrently with the sample analyses of the study by evaluation of the standard injections.The linearity of the MS-detector was checked for iodosulfuron-methyl in the range from 0.100 µg/L to 10 µg/L and was shown to be linear (y = 86842x – 286.48). The correlation

coefficient was 0.9993 (1/x weighted). 5 concentrations were measured in duplicate. If necessary, samples were diluted to achieve final concentrations falling within the calibrated range of detector response.
Because of the direct measurement of the samples recovery rates cannot be calculated. The evaluation of measurements based on HPLC-MS/MS for precision was done by comparison of the peak areas of the samples with the peak areas of the external standard solutions. For this purpose the iodosulfuron-methyl standard injections were evaluated. Standard solutions of iodosulfuron-methyl in acetonitrile were used. The relative standard deviation of iodosulfuron-methyl peak areas and retention times are shown in the table below.

Validation of Method 01387 for Iodosulfuron-methyl by HPLC-MS/MS

Iodosulfuron-methyl Standard concentration		***Iodosulfuron-methyl***			
		Peak area		***Retention time***	
[µg/L]	***n***	***Mean value [area counts]***	***Rel. std. dev. [%]***	***Mean value [min]***	***Rel. std. dev. [%]***
0.10	*6*	*8571*	*1.1*	*2.06*	*0.3*
0.50	*6*	*42194*	*1.7*	*2.06*	*0.2*
1.00	*6*	*85776*	*0.5*	*2.06*	*< 0.1*
5.00	*6*	*440390*	*0.8*	*2.06*	*< 0.1*
10.0	*6*	*863166*	*1.8*	*2.06*	*0.2*

Conclusion
The applicability of the HPLC-MS/MS method 01387 for the analysis of iodosulfuron-methyl in test water samples was tested. The data presented demonstrate that the method allows the determination of iodosulfuron-methyl with satisfactory precision data given as the relative standard deviation of 6 replicates with 0.5% and 1.8%. In addition the specificity of the method was demonstrated as no test item was found in control samples. The method is suitable for the determination of iodosulfuron-methyl in test water and can be regarded as fit for purpose with regard to the study Kuhl K.; 2016; M-574865-01-1.
Biological results:

Experiment 1
The following table summarizes the growth effects observed in design 1, after 7 days:

The effects on growth rate observed in design 1 after 0 - 7 days.

Nominal test concentration [µg a.s./L]	Frond number (day 7) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 7) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	167	0.376	1429	0.365	--	--
1.91	91.7	0.290●	827	0.290●	22.9●	20.6●
6.10	32.7	0.143●	243	0.113●	62.0●	69.2●
19.5	24.3	0.100●	180	0.074●	73.5●	79.8●
62.5	19.7	0.070●	164	0.060●	81.3●	83.5●
200	16.3	0.044●	151	0.038●	88.3●	89.5●

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
Design 1: two 24 hour peaks on day 0 and 3

The effects on growth rate observed in design 1, after 0 - 2 days.

Nominal test concentration [µg a.s./L]	Frond number (day 2) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 2) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
Control	27.3	0.406	234	0.372	-	-
1.91	21.0	0.277	176	0.245	31.7	34.3
6.10	19.3	0.238	156	0.171	41.3	54.1
19.5	16.0	0.136	136	0.120	66.6	67.6
62.5	15.3	0.121	131	0.099	70.2	73.4
200	14.7	0.100	136	0.082	75.3	77.9

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
Design 1: two 24 hour peaks on day 0 and 3

Growth inhibition at day 0 – 2 and day 0 – 7 for frond number and frond area has been presented above. Although there was a further exposure event at day 3, as the frond number and frond area were measured only on days 0, 2, 4, and 7, the ZRMS-PL did not present data for any other sampling period as there were ***no day 3 data*** *for the beginning of the second exposure period for comparison to the subsequent time periods.*

Experiment 2

FIRST WEEK

The following table summarizes the growth effects observed in design 2, after 7 days (week 1, 0-7 days).

Mean frond number and frond area for each measurement period for experiment 2, week 1 (0-7days)

Nominal concentration [µg a.s./L]	Mean frond number				Mean frond area (mm^2)			
	Day 0	Day 2	Day 4	Day 7	Day 0	Day 2	Day 4	Day 7
Control	12	25.3	50.3	123.3	100.7	224.0	436.0	1078.0
1.91	12	21.3	43.7	125.7	113.7	206.7	401.3	1106.3
6.10	12	17.3	21.0	62.7	102.7	140.0	187.3	519.3
19.5	12	17.7	22.0	45.7	108.7	136.3	162.7	359.0
62.5	12	17.3	19.3	38.3	111.3	136.3	154.0	280.0
200	12	15.3	15.3	25.7	112.3	132.7	143.7	194.0

Effects on growth inhibition for the period 0 - 7 days, 0 – 2 and 0 – 4 days are presented in tables respectively.

The effects on growth rate observed in design 2, after 7 days (week 1)

Nominal test concentration [µg a.s./L]	Frond number (day 7) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 7) mean values from 3 replicates [mm^2]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	123	0.333	1078	0.339	--	--
1.91	126	0.335	1106	0.325	-0.7	4.1
6.10	62.7	0.236●	519	0.231●	29.2●	31.7●
19.5	45.7	0.191●	359	0.171●	42.7●	49.6●
62.5	38.3	0.166●	280	0.132●	50.2●	61.0●
200	24.7	0.099●	194	0.077●	70.3●	77.2●

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
-% inhibition: increase in growth relative to the control
Design 2: two 24 hour peaks on day 0 and 7

The effects on growth rate in design 2, after 0 - 2 days (week 1)

Nominal test concentration [µg a.s./L]	Frond number (day 2) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 2) mean values from 3 replicates [mm^2]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
Control	25.3	0.370	224.0	0.401	-	-
1.91	21.3	0.284	206.7	0.299	23.3	25.6
6.10	17.3	0.181	140.0	0.155	51.0	61.4
19.5	17.7	0.192	136.3	0.113	48.1	71.8
62.5	17.3	0.181	136.3	0.101	51.1	74.8
200	15.3	0.122	132.7	0.083	67.0	79.4

The effects on growth rate in design 2, after 0 - 4 days (week 1)

Nominal test concentration [µg a.s./L]	Frond number (day 4) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 4) mean values from 3 replicates [mm^2]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
Control	50.3	0.358	436.0	0.367	-	-
1.91	43.7	0.322	401.3	0.315	10.0	14.1
6.10	21.0	0.139	187.3	0.150	61.1	59.2
19.5	22.0	0.151	162.7	0.100	57.8	72.6
62.5	19.3	0.118	154.0	0.081	67.1	77.9
200	15.3	0.060	143.7	0.061	83.1	83.2

The zRMS has presented the growth inhibition for frond area and frond number for time periods 0 – 2 days and 0 – 4 days above to determine if growth inhibition was greater following the initial exposure at 0 days.

SECOND WEEK

The following table summarizes the effects on growth rate observed in design 2 after 14 days (week 2)

Growth effects observed in design 2 after 0 - 7 days (week 2)

Nominal test concentration [µg a.s./L]	Frond number (day 7) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 7) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	137	0.347	1270	0.346	-	-
1.91	121	0.330	1051	0.312●	4.9	9.9●
6.10	69.3	0.250●	546	0.237●	27.9●	31.6●
19.5	48.0	0.198●	324	0.159●	43.0●	54.0●
62.5	28.3	0.123●	170	0.077●	64.7●	77.7●
200	15.3	0.032●	110	0.027●	90.9●	92.1●

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
Design 2: two 24 hour peaks on day 0 and 7

Growth effects observed in design 2, after 0 - 2 days (week 2)

Nominal test concentration [µg a.s./L]	Frond number (day2) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 2) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	25.0	0.365	240.3	0.381	-	-
1.91	24.0	0.346	208.7	0.285	5.1	25.2
6.10	17.3	0.183	147.3	0.174	49.8	54.3
19.5	21.0	0.279	147.7	0.165	23.5	56.8
62.5	19.0	0.229	124.0	0.112	37.2	70.6
200	14.0	0.071	104.0	0.065	80.4	83.1

Growth effects observed in design 2, after 0 - 4 days (week 2)

Nominal test concentration [µg a.s./L]	Frond number (day4) mean values from 3 replicates	Mean growth rate for frond number	Total frond area of plants (day 4) mean values from 3 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	50.7	0.359	450.7	0.348	-	-
1.91	42.3	0.315	367.3	0.284	12.3	18.4
6.10	22.3	0.155	184.3	0.143	56.8	58.9
19.5	26.0	0.192	166.3	0.112	46.6	67.8
62.5	21.7	0.147	135.0	0.077	59.0	77.8
200	15.7	0.062	108.7	0.044	82.7	87.4

Within 7 days of exposure in design 1 sublethal effects in terms of small fronds were observed in each test concentration up to and including 6.10 µg a.s./L: Additionally, overgrowing fronds were observed in 62.5 and 200 µg a.s./L and arched fronds in 200 µg a.s. /L. In design 2, within the first week, smaller fronds were observed in the concentrations from 19.5 to 200 µg a.s./L. In the second week smaller fronds were recorded in the test concentrations of 6.10 to 200 µg a.s./L.
Additionally, necrotic fronds were recorded in the highest test concentration.

Conclusion:

	Effect on mean growth rate of frond number [µg a.s./L]	*Effect on mean growth rate of total frond area of plants [µg a.s./L]*
Endpoint (0-7 days) ***Design 1****:*		
E_rC_{50} (95% C.I.):	***5.53 (5.20 – 5.87)***	***4.62 (4.51 – 4.74)***
E_rC_{20} (95% C.I.):	*< 1.91*	*< 1.91*
E_rC_{10} (95% C.I.):	*< 1.91*	*< 1.91*
LOE_rC: lowest concentration with an effect	*≤ 1.91*	*≤ 1.91*
NOE_rC: highest concentration without adverse effects	*< 1.91*	*< 1.91*
Endpoint (0-7 days) ***Design 2****:*		
E_rC_{50} (95% C.I.):	***46.1 (39.7 – 54.0)***	***27.2 (25.7 – 28.7)***
E_rC_{20} (95% C.I.):	*4.93 (3.77 – 6.12)*	*3.60 (3.27 – 3.95)*
E_rC_{10} (95% C.I.):	*< 1.91*	*< 1.91*
LOE_rC: lowest concentration with an effect	*6.10*	*6.10*
NOE_rC: highest concentration without adverse effects	*1.91*	*1.91*
Endpoint (7-14 days) ***Design 2***		
E_rC_{50} (95% C.I.):	***25.2 (23.0 – 27.6)***	***15.9 (15.2 – 16.6)***
E_rC_{20} (95% C.I.):	*5.19 (4.44 – 5.96)*	*3.53 (3.28 – 3.78)*
E_rC_{10} (95% C.I.):	*2.27 (1.84 – 2.74)*	*< 1.91*
LOE_rC: lowest concentration with an effect	*6.10*	*≤ 1.91*
NOE_rC: highest concentration without adverse effects	*1.91*	*< 1.91*

Endpoints were calculated based on nominal concentrations.
Design 1: two 24 hour peaks on day 0 and 3
Design 2: two 24 hour peaks on day 0 and 7

Reference:	***KCP 10.2.1/04***
Title:	*Amendment no. 1: Lemna gibba G3 - Growth inhibition test with metsulfuron-methyl (AE F075736) under peak exposure conditions (peaks on day 0 and 3)*
Report:	*Kuhl, K.; 2017; EBIM0007; M-600962-02-1*
Authority registration No:	
Guideline(s):	*EU Directive 91/414/EEC; Regulation (EC) Number 1107/2009; US EPA OCSPP 850.4400*
Deviations:	*During the preparation of the test item concentrations, the pH in the test medium had risen from initial 7.5 (as recommended in the guideline) prior to exposure start to a pH of 8.0 (day 0) and 7.7 (day 1). This slight pH deviation had no negative effect on Lemna growth as shown in a doubling time clearly below the validity criterion of 2.5 days doubling time. The nutrient medium for day 0 was prepared 3 days before use instead of 1 to 2 days as defined in the OECD guideline. Since this recommendation was made to allow the pH to stabilise, this deviation had no impact on the outcome of the study. Additionally, all validity criteria were met.*
GLP/GEP:	*yes*
Acceptability:	Study already evaluated in the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL) where following conclusions were made: *zRMS did not consider the PECtwa approach and population model in the current risk assessment.*
Duplication (if vertebrate study):	

Materials and methods:

Test material	*Metsulfuron-methyl (AE F075736), (BCS-AC12303)* *Batch No. 33074-238* *Specification: Not available* *98.6 % w/w*
Guideline(s) adaptation	*Guidelines were adapted to peak exposure conditions*
Test species	*Duckweed (Lemna gibba)* *strain G3*
Acclimation	*inoculum pre-culture, preparation 7 – 10 days before the start of the main test* *cultivation under the same conditions as in main test*
Culturing conditions	*20X AAP medium* *6500 – 7000 lux* *temperature of 23 - 26° C*
Test solutions	*Nominal concentrations: 0.205, 0.512, 1.28, 3.20, 8.00 and 20.0 µg p.m./L* *Control: growth medium without test substance* *Evidence of undissolved material: visual observations of test medium on days 0, 1(aged), 3 (fresh), 4 (aged): no visual effects of the test substance were found*
Replication	*No. of vessels per concentration (replicates): 4* *No. of vessels per control (replicates): 4*
Organisms per replicate	*No. of fronds per vessel: 12* *No. of fronds per plant: 3-4*
Exposure	*Peak exposure design with 2 peaks* *Total study duration: 7 days (two 24 hours lasting peaks, day 0 and 3)*
Test conditions	*Incubation chamber used: Multitron, Infors GmbH* *Temperature: 23.9 °C to 24.5 °C* *Photoperiod: permanent light* *Light quality: bank light containing fluorescent lamps* *Light intensity: 6.53 to 6.73 klux* *pH: 7.5- 8.0 (freshly prepared media), 8.3 – 9.1 (aged media)* *Growth medium: 20X AAP*
Parameters Measured / Observations	*Determination of frond number and total frond area on days 0, 2, 4, 7 by computerized image analysis (LemnaTec Scanalyzer).* *Visual observations of sublethal effects on days 2, 4, 7 .*
Sampling for	*Day 0 and 3 (fresh): samples of freshly prepared test media were taken from all test*

chemical analysis	*levels and the control. Additionally samples were taken from the freshly prepared stock solution.* *Day 1 and 4 (aged): samples were taken from pooled replicates of each test level and the control* *The water samples were analyzed with HPLC-MS/MS.*
Data analysis	*ECx calculations were performed by probit analysis using linear max. likelihood regression.* *Effect thresholds (e.g. NOECs) were determined by Williams Multiple Sequential t-test Procedure following a trend analysis by contrasts.* *All statistical evaluations were done with ToxRatProfessional Version 3.2.1.*

Results:

Validity criteria	***Required***	***Obtained***
Doubling time	*< 2.5 days*	*1.9 days*
*Control CV for growth rate at test termination**	*< 20 %*	*2.9 / 3.0 %*
*Control CV for yield at test termination**	*< 20 %*	*7.8 / 7.7 %*

** Validity element of OCSPP 850.4400; values are presented for frond number / total frond area*

Analytical results:

In the controls no test substance was detected. Since correct dosing was proven and since the test item was stable over the exposure periods, the study results are presented based on nominal peak concentrations.

The summarised results of the analytical measurements of metsulfuron-methyl (AE F075736) are shown in the following table:

	[% of nominal]
Day 0 (freshly prepared)	*91.0 – 93.8*
Day 1 (aged)	*89.5 – 91.4*
Day 3 (freshly prepared)	*87.5 – 91.1*
Day 4 (aged)	*87.5 – 91.1*

*The detailed results of the analytical measurements of metsulfuron-methyl (AE F075736) (**first peak**) are shown in the following table:*

Nominal concentration [µg p.m./L]	***Day 0 measured concentration [µg p.m./L]***	***Day 0 % nominal***	***Day 1 measured concentration [µg p.m./L]***	***Day 1 % nominal***
control	*<0.015*	*--*	*<0.015*	*--*
0.205	*0.191*	*92.9*	*0.184*	*89.5*
0.512	*0.480*	*93.7*	*0.464*	*90.6*
1.28	*1.19*	*93.0*	*1.17*	*91.0*
3.20	*3.00*	*93.8*	*2.93*	*91.4*
8.00	*7.37*	*92.1*	*7.18*	*89.8*
20.0	*18.2*	*91.0*	*17.9*	*89.5*

LOQ (limit of quantification) = 0.100 µg p.m./L
Design : two 24 hour peaks on day 0 and 3

*The detailed results of the analytical measurements of metsulfuron-methyl (AE F075736) (**second peak**) are shown in the following table:*

Nominal concentration [µg p.m./L]	Day 3 measured concentration [µg p.m./L]	Day 3 % nominal	Day 4 measured concentration [µg p.m./L]	Day 4 % nominal
control	<0.015	--	<0.015	--
0.205	0.185	90.2	0.184	89.8
0.512	0.467	91.1	0.467	91.1
1.28	1.16	90.6	1.15	89.8
3.20	2.89	90.3	2.87	89.5
8.00	7.23	90.3	7.10	88.7
20.0	17.5	87.5	17.5	87.5

LOQ (limit of quantification) = 0.100 µg p.m./L
Design : two 24 hour peaks on day 0 and 3

Concurrent validation:

For the determination of metsulfuron-methyl in test water the analytical method 01387 (Krebber, R.; Braune, M.; 2013; M-466732-01-1) was used. The analytical method is already EU-agreed and therefore not presented in part B5.
In the present study the method was validated concurrently with the sample analyses of the study by evaluation of the standard injections.
The linearity of the MS-detector was checked for metsulfuron-methyl in the range from 0.015 µg/L to 4.0 µg/L and was shown to be linear (y = 552840x – 158.43). The correlation coefficient was 0.999 (1/x weighted). 6 concentrations were measured in duplicate. If necessary, samples were diluted to achieve final concentrations falling within the calibrated range of detector response.
Because of the direct measurement of the samples recovery rates cannot be calculated. The evaluation of measurements based on HPLC-MS/MS for precision was done by comparison of the peak areas of the samples with the peak areas of the external standard solutions. For this purpose the metsulfuron-methyl standard injections were evaluated. Standard solutions of metsulfuron-methyl in acetonitrile were used. The relative standard deviation of metsulfuron-methyl peak areas and retention times are shown in the table below.

Validation of Method 01387 for Metsulfuron-methyl by HPLC-MS/MS

Metsulfuron-methyl Standard concentration		Metsulfuron-methyl			
		Peak area		Retention time	
[µg/L]	n	Mean value [area counts]	Rel. std. dev. [%]	Mean value [min]	Rel. std. dev. [%]
0.0150	4	8567	2.1	1.62	0.4
0.0503	6	27576	1.7	1.62	0.4
0.1006	6	54359	1.4	1.62	0.3
1.006	6	546542	2.2	1.62	0.5
4.022	6	2233719	2.6	1.62	0.3

Conclusion

The applicability of the HPLC-MS/MS method 01387 for the analysis of metsulfuron-methyl in test water samples was tested. The data presented demonstrate that the method allows the determination of metsulfuron-methyl with satisfactory precision data given as the relative standard deviation of 4 and 6 replicates,

with 1.4% and 2.6%. In addition the specificity of the method was demonstrated as no test item was found in control samples. The method is suitable for the determination of metsulfuron-methyl in test water and can be regarded as fit for purpose with regard to the study Kuhl, K.; 2017; M-600962-02-1.

Biological results:

The following table summarizes the effects on growth rate observed after 7 days:

Growth effects observed in the study after 7 days.

Nominal test concentration [µg a.s./L]	Frond number (day 7) mean values from 4 replicates	Mean growth rate for frond number	Total frond area of plants (day 7) mean values from 4 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	154	0.364	1324	0.366	--	--
0.205	166	0.375	1445	0.377	-2.8	-2.8
0.512	155	0.360	1365	0.356	1.2	2.9
1.28	52.5	0.211●	504	0.226●	42.2●	38.4●
3.20	25.5	0.107●	226	0.101●	70.6●	72.3●
8.00	20.0	0.072●	174	0.079●	80.1●	78.5●
20.0	18.8	0.064●	163	0.061●	82.6●	83.2●

● Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control
Negative inhibition values indicate an increase in growth relative to the control

Growth effects observed in the study after 0-2 days.

Nominal test concentration [µg a.s./L]	Frond number (day2) mean values from 4 replicates	Mean growth rate for frond number	Total frond area of plants (day 2) mean values from 4 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	24.0	0.346	228.3	0.403	-	-
0.205	26.8	0.399	238.8	0.420	-15.2	-4.3
0.512	24.0	0.345	234.5	0.378	0.5	6.3
1.28	20.8	0.273	179.5	0.274	21.2	32.1
3.20	16.5	0.153	158.3	0.178	55.7	55.8
8.00	16.5	0.159	137.5	0.158	54.1	60.8
20.0	14.3	0.069	126.3	0.082	80.1	79.7

● Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control
Negative inhibition values indicate an increase in growth relative to the control

*Growth inhibition at day 0 – 2 and day 0 – 7 for frond number and frond area has been presented above. Although there was a further exposure event at day 3, as the frond number and frond area were measured only on days 0, 2, 4, and 7, the ZRMS_PL did not present data for any other sampling period as there were **no day 3 data** for the beginning of the second exposure period for comparison to the subsequent time periods*
The shape of fronds and colonies after the test period of 7 days was not different to those in the control group up to and including the nominal test concentration of 0.512 µg p.m./L. At the nominal test concentrations of 1.28 µg p.m./L to 20.0 µg p.m./L smaller fronds were recorded. Additionally, chlorotic fronds were observed at the highest concentration of 20.0 µg p.m./L.

No remarkable observations of the test item in the test medium were recorded, all media were clear and colourless.

Conclusion:

	Effect on mean growth rate of frond number [µg p.m./L]	Effect on mean growth rate of total frond area of plants [µg p.m./L]

Endpoint (0-7 days)		
E_rC_{50} (95% C.I.):	***2.03 (1.89 – 2.19)***	***2.11 (1.99 – 2.23)***
E_rC_{20} (95% C.I.):	*0.661 (0.587 – 0.735)*	*0.702 (0.640 – 0.764)*
E_rC_{10} (95% C.I.):	*0.368 (0.313 – 0.423)*	*0.395 (0.349 – 0.443)*
LOE_rC: lowest concentration with an effect	*1.28*	*1.28*
NOE_rC: highest concentration without adverse effects	*0.512*	*0.512*

Endpoints were based on nominal concentrations.
The E_rC_{50}, LOE_rC and NOE_rC determination is based on statistical data analysis.

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Reference:	***KCP 10.2.1/05***
Title:	*Lemna gibba G3 - Growth inhibition test with metsulfuron-methyl (AE F075736) under peak exposure conditions (peaks on day 0 and 7)*
Report:	*Kuhl, K.; 2017; EBIM0008; M-600651-01-1*
Authority registration No:	
Guideline(s):	*EU Directive 91/414/EEC; Regulation (EC) Number 1107/2009; OECD Test Guideline 221; US EPA OCSPP 850.4400*
Deviations:	*none*
GLP/GEP:	*yes*
Acceptability:	Study already evaluated in the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL) where following conclusions were made: *zRMS did not consider the PECtwa approach and population model in the current risk assessment.* ~~*Yes*~~
Duplication (if vertebrate study):	

Materials and methods:

Test material	*Metsulfuron-methyl (AE F075736), (BCS-AC12303)* *Batch No. 33074-238* *Specification: Not available* *98.6 % w/w*
Guideline(s) adaptation	*Guidelines were adapted to peak exposure conditions and a prolonged study duration*
Test species	*Duckweed (Lemna gibba)* *strain G3*
Acclimation	*inoculum pre-culture, preparation 7 – 10 days before the start of the main test* *cultivation under the same conditions as in main test*
Culturing conditions	*20X AAP medium* *6500 – 10000 lux* *temperature of 23 - 26° C*
Test solutions	*Nominal concentrations: 0.205, 0.512, 1.28, 3.20, 8.00 and 20.0 µg p.m./L* *Control: growth medium without test substance* *Evidence of undissolved material: visual observations of test medium on days 0, 1, 7, 8: No remarkable observations of the test item in the test medium were recorded, all media were clear and colourless*
Replication	*No. of vessels per concentration (replicates): 4* *No. of vessels per control (replicates): 4*
Organisms per replicate	*No. of fronds per vessel: 12* *No. of fronds per plant: 3-4*
Exposure	*Peak exposure design with 2 peaks*

	Total study duration: 14 days (two 24 hours lasting peaks, day 0 and 7)
Test conditions	*Incubator used: Multitron, Infors GmbH* *Temperature: 23.8 °C to 24.5 °C* *Photoperiod: permanent light* *Light quality: bank light containing fluorescent lamps* *Light intensity: 6.65 to 7.00 klux* *pH: 7.5-7.9 (freshly prepared media), 8.5-9.1 (aged media)* *Growth medium: 20X AAP*
Parameters Measured / Observations	*Determination of frond number and total frond area on days 0, 2, 5, 7, (before and after thinning each replicate to 12 fronds), 9, 12, 14 by computerized image analysis (LemnaTec Scanalyzer).* *Visual observations of sublethal effects on days 2, 5, 7, 9,12, 14 .*
Sampling for chemical analysis	*Day 0 and 7 (fresh): samples of freshly prepared test media were taken from all test levels and the control. Additionally samples were taken from the freshly prepared stock solution.* *Day 1 and 8 (aged): samples were taken from pooled replicates of each test level and the control* *The water samples were analyzed with HPLC-MS/MS.*
Data analysis	*ECx calculations were performed by probit analysis using linear max. likelihood regression.* *Effect thresholds (e.g. NOECs) were determined by Williams Multiple Sequential t-test Procedure following a trend analysis by contrasts.* *All statistical evaluations were done with ToxRatProfessional Version 3.2.1.*

Results:

Validity criteria	***Required***	***Obtained***
Doubling time	*< 2.5 days*	*1.9 days*
*Control CV for growth rate at test termination**	*< 20 %*	*5.0 / 2.7 %*
*Control CV for yield at test termination**	*< 20 %*	*14.5 / 13.0 %*

** Validity element of OCSPP 850.4400; values are presented for frond number / total frond area*

Analytical results:

In the controls no test substance was detected. Since correct dosing was proven and since the test item was stable over the exposure periods, the study results are presented based on nominal peak concentrations.

The summarised results of the analytical measurements of metsulfuron-methyl (AE F075736) are shown in the following table:

	[% of nominal]
Day 0 (freshly prepared)	*97.2 – 99.6*
Day 1 (aged)	*96.8 – 99.6*
Day 7 (freshly prepared)	*94.5 – 97.6*
Day 8 (aged)	*93.8 – 96.9*

*The detailed results of the analytical measurements of metsulfuron-methyl (AE F075736) (**first peak**) are shown in the following table:*

Nominal concentration [µg p.m./L]	***Day 0 measured concentration [µg p.m./L]***	***Day 0 % nominal***	***Day 1 measured concentration [µg p.m./L]***	***Day 1 % nominal***

control	*<0.020*	*--*	*<0.020*	*--*
0.205	*0.204*	*99.6*	*0.204*	*99.4*
0.512	*0.508*	*99.2*	*0.510*	*99.6*
1.28	*1.26*	*98.2*	*1.27*	*99.5*
3.20	*3.16*	*98.9*	*3.14*	*98.0*
8.00	*7.78*	*97.2*	*7.74*	*96.8*
20.0	*19.8*	*99.0*	*19.5*	*97.3*

LOQ (limit of quantification) = 0.020 µg p.m./L
Design: two 24 hour peaks on day 0 and 7

*The detailed results of the analytical measurements of metsulfuron-methyl (AE F075736) (**second peak**) are shown in the following table:*

Nominal concentration [µg p.m./L]	***Day 7 measured concentration [µg p.m./L]***	***Day 7 % nominal***	***Day 8 measured concentration [µg p.m./L]***	***Day 8 % nominal***
control	*<0.020*	*--*	*<0.020*	*--*
0.205	*0.199*	*97.0*	*0.198*	*96.5*
0.512	*0.500*	*97.6*	*0.496*	*96.9*
1.28	*1.22*	*95.3*	*1.21*	*94.6*
3.20	*3.02*	*94.5*	*3.00*	*93.8*
8.00	*7.61*	*95.1*	*7.61*	*95.1*
20.0	*19.0*	*95.1*	*18.9*	*94.5*

LOQ (limit of quantification) = 0.020 µg p.m./L
Design: two 24 hour peaks on day 0 and 7

Concurrent validation:

For the determination of metsulfuron-methyl (AE F075736) in test water the analytical method 01387 (Krebber, R.; Braune, M.; 2013; M-466732-01-1) was used. The analytical method is already EU-agreed and therefore not presented in part B5.
In the present study the method was validated concurrently with the sample analyses of the study by evaluation of the standard injections.
The linearity of the MS-detector was checked for metsulfuron-methyl (AE F075736) in the range from 0.020 µg/L to 2.0 µg/L and was shown to be linear (y = 552840x + 1547.9). The correlation coefficient was 0.999 (1/x weighted). 5 concentrations were measured in duplicate. If necessary, samples were diluted to achieve final concentrations falling within the calibrated range of detector response.
Because of the direct measurement of the samples recovery rates cannot be calculated. The evaluation of measurements based on HPLC-MS/MS for precision was done by comparison of the peak areas of the samples with the peak areas of the external standard solutions. For this purpose the metsulfuron-methyl (AE F075736) standard injections were evaluated. Standard solutions of metsulfuron-methyl in acetonitrile were used. The relative standard deviation of metsulfuron-methyl (AE F075736) peak areas and retention times are shown in the table below.

Validation of Method 01387 for Metsulfuron-methyl (AE F075736) by HPLC-MS/MS

Metsulfuron-methyl (AE F075736) Standard concentration		***Metsulfuron-methyl (AE F075736)***			
		Peak area		***Retention time***	
[µg/L]	***n***	***Mean value [area counts]***	***Rel. std. dev. [%]***	***Mean value [min]***	***Rel. std. dev. [%]***
0.0200	*6*	*12428*	*3.5*	*1.82*	*0.3*
0.100	*4*	*56583*	*1.6*	*1.82*	*0.3*
0.501	*6*	*279501*	*2.4*	*1.82*	*0.2*
1.00	*4*	*578185*	*2.5*	*1.82*	*0.3*
2.00	*6*	*1090062*	*2.3*	*1.82*	*0.2*

Conclusion

The applicability of the HPLC-MS/MS method 01387 for the analysis of metsulfuron-methyl (AE F075736) in test water samples was tested. The data presented demonstrate that the method allows the determination of metsulfuron-methyl with satisfactory precision data given as the relative standard deviation of 4 and 6 replicates, with 1.6% and 3.5%. In addition the specificity of the method was demonstrated as no test item was found in control samples. The method is suitable for the determination of metsulfuron-methyl (AE F075736) in test water and can be regarded as fit for purpose with regard to the study Kuhl, K.; 2017; M-600651-01-1.

Biological results:

WEEK 1

The following table summarizes the effects on growth rate observed after 7 days (week 1, peak on day 0)

Nominal test concentration [µg a.s./L]	***Frond number (day 7) mean values from 4 replicates***	***Mean growth rate for frond number***	***Total frond area of plants (day 7) mean values from 4 replicates [mm²]***	***Mean growth rate for total frond area of plants***	***% Inhibition***	
					Mean growth rate for frond number	***Mean growth rate for total frond area of plants***
control	*148*	*0.359*	*1301*	*0.348*	*--*	*--*
0.205	*137*	*0.348*	*1230*	*0.343*	*3.0*	*1.2*
0.512	*147*	*0.357*	*1290*	*0.349*	*0.3*	*-0.5*
1.28	*90.5*	*0.288●*	*752*	*0.273●*	*19.6●*	*21.4●*
3.20	*59.5*	*0.228●*	*473*	*0.204●*	*36.4●*	*41.4●*
8.00	*37.0*	*0.161●*	*291*	*0.139●*	*55.1●*	*59.9●*
20.0	*32.5*	*0.142●*	*233*	*0.107●*	*60.3●*	*69.3●*

● Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control
Negative inhibition values indicate an increase in growth relative to the control

The following table summarizes the effects on growth rate observed after 0-2 days week 1, peak on day 0)

The effects on growth rate observed after 0-2 days week 1, peak on day 0

Nominal test concentration [µg a.s./L]	***Frond number (day2) mean values***	***Mean growth rate for frond***	***Total frond area of plants (day 2) mean***	***Mean growth rate for total***	***% Inhibition***	
					Mean growth rate	***Mean growth rate***

	from 4 replicates	number	values from 4 replicates [mm²]	frond area of plants	for frond number	for total frond area of plants
control	25.0	0.364	222.5	0.335	-	-
0.205	25.3	0.370	212.0	0.324	-1.6	3.4
0.512	24.3	0.351	213.0	0.323	3.5	3.6
1.28	19.5	0.241	172.8	0.222	33.9	33.8
3.20	18.5	0.211	156.8	0.161	41.9	51.8
8.00	15.3	0.120	141.5	0.128	67.1	61.7
20.0	15.8	0.133	136.0	0.103	63.5	69.1

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
Negative inhibition values indicate an increase in growth relative to the control

The following table summarizes the effects on growth rate observed after 0-5 days (week 1, peak on day 0).

The effects on growth rate observed after 0-5 days (*week 1, peak on day 0)*

Nominal test concentration [µg a.s./L]	Frond number (day 5) mean values from 4 replicates	Mean growth rate for frond number	Total frond area of plants (day5) mean values from 4 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	72.8	0.360	647.3	0.347	-	-
0.205	75.5	0.368	614.5	0.342	-2.3	1.5
0.512	73.3	0.362	642.8	0.350	-0.6	-0.7
1.28	42.5	0.252	363.0	0.237	29.9	31.8
3.20	28.8	0.175	219.5	0.132	51.4	62.1
8.00	20.3	0.104	168.3	0.086	70.9	75.3
20.0	18.3	0.083	155.3	0.068	76.9	80.5

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
Negative inhibition values indicate an increase in growth relative to the control

WEEK 2

The following table summarizes the effects on growth rate observed after 14 days (week 2, peak on day 7)
The effects on growth rate observed after 0-7 days (week 2, peak on day 7)

Nominal test concentration [µg a.s./L]	Frond number (day 14) mean values from 4 replicates	Mean growth rate for frond number	Total frond area of plants (day 14) mean values from 4 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	162	0.370	1426	0.358	-	-
0.205	151	0.361	1323	0.352	2.5	1.6
0.512	169	0.378	1464	0.365	-1.9	-2.1
1.28	124	0.333●	978	0.313●	10.1●	12.5●
3.20	60.5	0.231●	415	0.218●	37.7●	39.1●
8.00	29.5	0.128●	175	0.080●	65.5●	77.5●
20.0	18.3	0.059●	123	0.054●	84.0●	84.8●

● *Results which were significantly different (based on Williams Multiple sequential t-test Procedure) from the control*
Negative inhibition values indicate an increase in growth relative to the control

The following *table summarizes the effects on growth rate observed after 0-2 days (week 2, peak on day 7).*

The effects on growth rate observed after 0-2 days (week 2, peak on day 7)

Nominal test	Frond	Mean	Total frond	Mean	% Inhibition

concentration [µg a.s./L]	number (day- 2) mean values from 4 repli-cates	growth rate for frond number	area of plants (day 2) mean values from 4 replicates [mm²]	growth rate for total frond area of plants	Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	28.5	0.431	247.3	0.376	-	-
0.205	28.3	0.427	238.0	0.375	0.9	0.2
0.512	27.5	0.414	232.3	0.359	3.9	4.6
1.28	23.0	0.325	188.5	0.273	24.7	27.6
3.20	17.0	0.170	140.5	0.222	60.6	41.0
8.00	16.3	0.150	131.3	0.142	65.1	62.3
20.0	14.8	0.097	107.0	0.123	77.6	67.4

The following table summarizes the effects on growth rate observed after 2-5 days (week 2, peak on day 7)

The effects on growth rate observed after 0-5 days (week 2, peak on day 7)

Nominal test concentration [µg a.s./L]	Frond num-ber (day5) mean values from 4 repli-cates	Mean growth rate for frond number	Total frond area of plants (day5) mean values from 4 replicates [mm²]	Mean growth rate for total frond area of plants	% Inhibition	
					Mean growth rate for frond number	Mean growth rate for total frond area of plants
control	89.3	0.401	790.8	0.383	-	-
0.205	83.3	0.387	728.0	0.373	3.5	2.5
0.512	90.3	0.403	772.8	0.384	-0.7	-0.2
1.28	62.3	0.329	489.3	0.300	17.9	21.7
3.20	29.0	0.176	196.5	0.156	56.0	59.4
8.00	22.0	0.120	148.8	0.082	70.0	78.7
20.0	15.0	0.045	113.3	0.060	88.90	84.3

After 7 days of test duration (week 1) sublethal effects in terms of smaller fronds were observed in the test concentrations from 3.20 µg p.m./L to 20.0 µg p.m./L. Additionally, chlorotic fronds were observed at 20.0 µg p.m./L. After a 14 day test duration (week 2), smaller fronds were observed in the concentrations from 1.28 to 20.0 µg p.m./L.

No remarkable observations of the test item in the test medium were recorded, all media were clear and colourless.

Conclusion:

	Effect on mean growth rate of frond number [µg p.m./L]	Effect on mean growth rate of to-tal frond area of plants [µg p.m./L]
Endpoint (0-7 days)		
E_rC_{50} (95% C.I.):	**8.11 (7.64 – 8.62)**	**5.85 (5.54 – 6.17)**
E_rC_{20} (95% C.I.):	1.41 (1.29 – 1.53)	1.26 (1.16 – 1.36)
E_rC_{10} (95% C.I.):	0.564 (0.495 – 0.635)	0.565 (0.500 – 0.631)
LOE_rC: lowest concentration with an effect	1.28	1.28
NOE_rC: highest concentration without adverse effects	0.512	0.512
Endpoint (7-14 days)		
E_rC_{50} (95% C.I.):	**5.09 (4.85 – 5.34)**	**4.22 (4.07 – 4.37)**

E_rC_{20} (95% C.I.):	*1.82 (1.69 – 1.96)*	*1.70 (1.61 – 1.80)*
E_rC_{10} (95% C.I.):	*1.07 (0.96 – 1.18)*	*1.06 (0.983 – 1.14)*
LOE_rC: lowest concentration with an effect	*1.28*	*1.28*
NOE_rC: highest concentration without adverse effects	*0.512*	*0.512*

Endpoints were based on nominal concentrations.
The ErC50, LOErC and NOErC determination is based on statistical data analysis.
Design: two 24 hour peaks on day 0 and 7

A 2.2.2 KCP 10.2.2 Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms

A.2.2.3 KCP 10.2.3 Further testing on aquatic organisms

A.2.3 KCP 10.3 Effects on arthropods

A 2.3.1 KCP 10.3.1 Effects on bees

Reference:	***KCP 10.3.1/01***
Title:	*1.8 Weeds in the treated field - a realistic scenario for pollinator risk assessment ?*
Report:	*Maynard, S. K.; Albuquerque, R.; Weber, C.; von Merey, G.; Geiger, M. F.; Becker, R.; Keppler, J.; Maschke, J.; Brougham, K.; Couson, M.; 2015; M-542146-01-1*
Authority registration No:	
Guideline(s):	--
Deviations:	--
GLP/GEP:	*no*
Acceptability:	Study already evaluated and accepted in the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).
Duplication (if vertebrate study):	

Objective:

This project aims to answer the question posed by the EFSA bee guidance document regarding the relevance of the weeds in the treated field scenario: "Is a significant fraction of the surface area of treated fields covered by attractive weeds for >10% of the area of use?"

Materials and Methods:

A cross-industry group (Syngenta, Bayer, BASF, Dow AgroSciences and Monsanto) collected herbicide efficacy trials data from the control plots of 9 different crop groups (wheat, oilseed rape, sugar beet, sunflower, potatoes, maize, peas, beans and permanent crops (orchards and vines)). The data collected includes crop type, crop growth stage, application date, trial location, tillage information, weed species, growth stage, and ground coverage.

A three stage assessment process was used for analysing the data, to attempt to quantify the coverage of relevant attractive weeds in the in-field area of use:

1. The quantity of weeds recorded within the field at a flowering growth stage was defined as those observed with a growth stage of BBCH ≥ 60.

2. These weeds highlighted as being present and potentially attractive were then assessed for attractiveness to bees. No known definitive list is available for non-crop species and attractiveness to bees, so the species were categorised based on monocotyledonous as a surrogate for non-attractive plants, and dicotyledonous as a surrogate for attractive plants.

3. Finally the data on ground coverage can be combined with that of the above and used to establish the percentage coverage of attractive weeds throughout the area of use.

Results and Discussion:

Percentage of weeds recorded at a flowering growth stage

Database size for each crop and the % of weed recordings which were above a flowering growth stage

Crop	***Total number of trials examined***	***Total number of weed recordings in all trials***	***% weeds recorded at BBCH ≥ 60***
Wheat	*1024*	*9113*	*0.86%*
Maize	*7669*	*38421*	*1.94%*
Oliseed Rape	*1022*	*3587*	*1.28%*
Sunflower	*388*	*1435*	*1.11%*
Potatoes	*182*	*1159*	*1.04%*
Sugar Beet	*156*	*5006*	*0.12%*
Peas	*650*	*5780*	*0.48%*
Beans	*203*	*1807*	*1.49%*
Permanent Crops	*233*	*552*	*37.0%*

For the arable crops studied, weeds at a flowering growth stage account for less than 2% of the weeds present in these trials. In permanent crops, likely due to the difference in agricultural practices, around 37% of the weeds present are at or above a flowering growth stage.

Percentage of weeds assessed to be attractive

Data for permanent crops (orchards and vineyards) showing the number of mono- and dicotyledonous species and the respective percentages in terms of species diversity and abundance in the investigated trials.

Permanent crops (Vineyards/Orchards)	***Total weed species at BBCH ≥ 60***	***Monocotyledonous***	***Dicotyledonous***
Number of species	*77*	*15*	*62*
Number of recordings	*204*	*47*	*157*
Percentage of recordings (n = 552)	*37%*	*8.5%*	*28.5%*

Only 28.5% of weeds in permanent crops are attractive to bees. The classification of attractiveness of weeds in arable crops has not yet been conducted as the percentage of weeds has been shown to be low enough to be of little concern even if all weeds are attractive.

Percentage ground coverage of weeds

Data for permanent crops (orchards and vineyards) showing the number of mono- and dicotyledonous species present at flowering growth stage and above 10% ground coverage and the respective percentages in terms of species diversity and abundance in the investigated trials.

Permanent crops (Vineyards/Orchards)	***Total weed species at BBCH ≥ 60 and ≥ 10% ground cover***	***Monocotyledonous***	***Dicotyledonous***
Number of species	*12*	*5*	*7*
Number of recordings	*35*	*14*	*21*
Percentage of recordings (n = 177)	*20.5%*	*8.2%*	*12.3%*

For permanent crops the authors can demonstrate that, considering weeds at a flowering growth stage and present at ≥ 10% ground cover, only 12.3% are also potentially attractive to bees.

Conclusions:

For the arable crops assessed in this study, the data analysis presented has demonstrated conclusively that the "weeds in the treated field scenario" is not applicable. For the arable crops: wheat, maize, oilseed rape, sunflower, potatoes, sugar beet, beans and peas, less than 2% of all weeds recorded were found to be at a flowering growth stage (BBCH ≥ 60), despite the data being recorded in control trial plots with no weed control measures. When further investigations into the ground coverage of such weeds are carried out, it is clear that the weeds in arable fields do not present a 90th%ile exposure scenario for bees.
For permanent crops a maximum percentage of 12.3% of the recorded weeds were potentially attractive (dicotyledonous) flowering weeds (BBCH ≥ 60) and present at greater than 10% ground coverage. This indicates potential concern for the flowering weeds in the treated field for this crop; although again it is noteworthy that the data examined here represent a very worst-case scenario. Due to current risk assessment schemes, extensive field and semi-field testing and precautionary risk mitigation measures available to risk managers, it is considered that the risk to bees is appropriately controlled using current practices for permanent crops.

A 2.3.1.1 KCP 10.3.1.1 Acute toxicity to bees

KCP 10.3.1.1.1 Acute oral toxicity to bees

KCP 10.3.1.1.2 Acute contact toxicity to bees

A 2.3.1.2 KCP 10.3.1.2. Chronic toxicity to bees

A 2.3.1.3 KCP 10.3.1.3 Effects on honey bee development and other honey bee life stages

In order to complete the data set and the knowledge on effects on developmental stages of honey bees further studies have been performed with the active substances. This study has not yet been evaluated at EU level, however for transparency a detailed Tier 2 summary is provided below. The related study report but can be made available to the zRMS upon request.

Reference:	***- Study report will be made available to the zRMS upon request -***
Title:	*Repeated Exposure of Iodosulfuron-methyl sodium to Honey Bee (Apis mellifera) Larvae under Laboratory Conditions (in vitro)*
Report:	*Kleebaum, K.; 2017; unpublished report No: 16 10 48 141 B; M-578603-01-1*
Authority registration No	
Guideline(s):	*OECD Guidance Document 239 on Honey bee (Apis mellifera) Larval Toxicity Test, Repeated Exposure (2016)*
Deviations:	*None*
GLP:	*yes*
Acceptability:	Study was not evaluated in the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL). The study for the a.s. was also not evaluated by zRMS in the current evaluation.
Duplication (if vertebrate study):	

Objective:

The purpose of this study was to determine the chronic toxicity ($ED_{10/20/50}$, $EC_{10/20/50}$, NOED/NOEC and LOED/LOEC for adult emergence up to day 22) of the test item applied to the honey bee, Apis mellifera L.,

larvae in an in vitro test after repeated oral application. The test item was administered to the larvae at a constant concentration in the diet according to their growth at a range of five increasing doses. Cumulative mortalities of honey bee larvae treated with the test item were assessed daily from day 4 to day 8. Cumulative mortalities during the pupation phase were assessed on day 15 and on day 22. All mortalities were compared to the control. The adult emergence rate was assessed on day 22.

Material and methods:

Test item: Iodosulfuron-methyl sodium; Batch No.: ELIR003050, Sample description: TOX09144-02, Specification No.: 102000000739, Analysed purity a.s.: 92.4 % w/w, Certificate No.: AZ 20346.
Test species: Honey bee (Apis mellifera L., subspecies Buckfast), synchronized first instar (L1, one day old) larvae originating from healthy (free of clinical symptoms of any disease) and queen-right bee colonies. The larvae were taken from hives that had not received treatments with chemical substances for at least one month. The test was conducted at Biochem agrar GmbH, Kupferstrasse 6, 04827 Machern OT Gerichshain, Germany.
Test design: Dose response test with a duration of 22 days from grafting on day 1 to the final assessment on day 22. From day 3 until day 6 of the test, five different concentrations of iodosulfuron-methyl sodium diluted in the larval food (aqueous yeast/sugar solution mixed with royal jelly 1:1 (w/w)) were fed to larvae of the test item groups and one single concentration of the reference item dimethoate was fed to the larvae of the reference item group with diet B or C. After the applications, no additional feeding of the larvae took place.
The analysed purity was considered for the calculation of the test item and reference item concentrations; the daily feeding volume increased from 20 µL to 50 µL diet per larva over the application period. The cumulative feeding volume from day 3 until day 6 of 140 µL diet per larva and the density of the diet (1.13 g/cm^3) were considered for the calculation of the cumulative doses per larva. A control group was included in the test and exposed for the same period of time under identical exposure conditions to the water treated artificial diet. Each treatment group consisted of 36 larvae from three different colonies (each colony representing a replicate). Assessments of larval mortality were done 24, 48, 72, 96 and 120 hours after start of the treatment (respectively day 4 to day 8). Additionally, other observations as small body size or large quantities of remaining food after 96 and 120 hours (on D7 and D8) were noted. Pupal mortality was assessed at day 15 and emergence of adults was evaluated at day 22.
In an analytical phase of the study, the concentration of the active substance in each final diet was determined.
The presence of unconsumed food and/or substantially undersized larvae was recorded on day 7 and 8. Other observations and any other adverse effects were qualitatively recorded to aid in the interpretation of mortality in comparison to the control group.
Test concentrations: One untreated control group; 5 test item groups with 101, 51, 25, 13 and 6 mg a.s./kg diet, equivalent to cumulative doses of 16, 8, 4, 2 and 1 µg a.s./larva per developmental period; One dimethoate reference item group with 46 mg dimethoate/kg diet, equivalent to a cumulative dose of 7.3 µg dimethoate/larva per developmental period.

Dates of work: *August 22 to September 12, 2016*

Results:

Analytical results:
The analytical dose verification of the larval diet of the test item groups from day 3 until day 6 resulted in concentrations that are equivalent to mean recoveries between 100 and 118 % of the nominal test concentration.
Since the mean measured concentrations of the test item in the larval diet were within ± 20 % of nominal for each test item group the presented endpoints are based on nominal concentrations.

Biological results:
On day 8, larval mortality was 2.8 % in the control group and 88.9 % in the reference item group. The larval mortality was 5.6, 8.3, 5.6, 2.8 and 0.0 % in the test item groups of 16, 8, 4, 2 and 1 µg a.s./larva or

101, 51, 25, 13 and 6 mg a.s./kg diet, respectively.
On day 22, the adult emergence rate in the control group was 77.8 %. The adult emergence rates were 77.8, 86.1, 80.6, 80.6 and 86.1 % in the test item groups of 16, 8, 4, 2 and 1 µg a.s./larva or 101, 51, 25, 13 and 6 mg a.s./kg diet, respectively.
Compared to the control group the adult emergence rate on day 22 was not statistically significantly different in any test item group (Multiple Chi²-test with Bonferroni-Holm adjustment, one-sided greater, α = 0.05).
During the assessments of mortality and emergence no other test item related observations such as deviating sizes, appearances and malformations of the test organisms were made.
On day 8, none of the larvae treated with any of the test items showed any signs of abnormal behaviour, such as remaining food or discolouration.
Results for larval mortality until day 8, mean mortality and adult emergence on day 22 and the corresponding endpoints are presented in the following tables.

Mortality and other observations of larvae in the repeated exposure toxicity test

Treat-ment group	Dose	Concen-tration	On day 8			On day 22		
			Larval mortal-ity		Mean OO	Overall mortality		Emergence rate
			[%]		[%]	[%]		[%]
	[µg a.s./ larva]	[mg a.s./ kg food]	abs.	corr.		abs.	corr.	abs.
Control	-	-	2.8	0.0	0.0	22.2	0.0	77.8
Test Item (Iodosulfuron-methyl so-dium)	16	101	5.6	2.9	0.0	22.2	0.0	77.8
	8	51	8.3	5.7	0.0	13.9	-10.7*	86.1
	4	25	5.6	2.9	0.0	19.4	-3.6*	80.6
	2	13	2.8	0.0	0.0	19.4	-3.6*	80.6
	1	6	0.0	-5.9*	0.0	13.9	-10.7	86.1
Reference Item (Dimethoate)	7.3	46	88.9	88.6	83.3	97.2	96.4	2.8

Results are averages based on 3 replicates, containing 12 larvae each; corr.: corrected mortality (according to SCHNEIDER-ORELLI 1947): test and reference item was corrected by AC; abs.: absolute mortality as counted from the results; calculation are performed with non-rounded values;
OO: Other observations (e.g. remaining food);
** Negative values indicate higher mortality in the control group than in the treatment group.*

Calculated endpoints of the repeated exposure larvae toxicity test

Treatment	***Endpoint: Successful adult emergence***	***Up to day 22***
Test item doses	*ED_{50} [µg a.s./larva] [2]*	***> 16***
	ED_{20} [µg a.s./larva] [2]	***> 16***
	ED_{10} [µg a.s./larva] [2]	***> 16***
	LOED [µg a.s./larva] [1]	***> 16***
	NOED [µg a.s./larva] [1]	***≥ 16***
Test item concentrations	*EC_{50} [mg a.s./kg food] [2]*	***> 101***
	EC_{20} [mg a.s./kg food] [2]	***> 101***
	EC_{10} [mg a.s./kg food] [2]	***> 101***
	LOEC [mg a.s./kg food] [1]	***> 101***
	NOEC [mg a.s./kg food] [1]	***≥ 101***
[1] Chi² 2x2 Table Test with Bonferroni Correction; α=0.05; one sided greater *[2] Estimated*		

Validity criteria:
All validity criteria were met in this study.

Validity criteria according to OECD GD 239	***Obtained in this study***
Cumulative larval mortality from day 3 to 8 in control: ≤ 15%	*2.8%*
Mean adult emergence rate on day 22 in control: ≥ 70%	*77.8%*
For reference item dimethoate larval mortality at day 8: ≥ 50%	*88.9%*

Conclusion

In a repeated exposure larval toxicity study with iodosulfuron-methyl sodium and a duration of 22 days, the NOED was ≥ 16 µg a.s./larva and the respective LOED was > 16 µg a.s./larva. The $ED_{50/20/10}$ (successful adult emergence up to D22) were estimated to be > 16 µg a.s./larva, respectively.

The NOEC was ≥ 101 mg a.s./kg food and the respective LOEC was > 101 mg a.s./kg food. The $EC_{50/20/10}$ (successful adult emergence up to D22) were estimated to be > 101 mg a.s./kg food, respectively.

The analysed concentrations of the active ingredient in the diets ranged between 100% and 118% of the nominal test concentrations.

In order to complete the data set and the knowledge on effects on developmental stages of honey bees further studies have been performed with the active substances. This study has not yet been evaluated at EU level, however for transparency a detailed Tier 2 summary is provided below. The related study report but can be made available to the zRMS upon request.

Reference:	***- Study report will be made available to the zRMS upon request -***
Title:	*Repeated Exposure of Mesosulfuron-methyl to Honey Bee (Apis mellifera) Larvae under Laboratory Conditions (in vitro)*
Report:	*Kleebaum, K.; 2017; unpublished report No: 16 10 48 142 B; M-578612-01-1*
Authority registration No	
Guideline(s):	*OECD Guidance Document 239 on Honey bee (Apis mellifera) Larval Toxicity Test, Repeated Exposure (2016)*
Deviations:	*None*

GLP:	*yes*
Acceptability:	
Duplication (if vertebrate study):	

Objective:

The purpose of this study was to determine the chronic toxicity ($ED_{10/20/50}$, $EC_{10/20/50}$, NOED/NOEC and LOED/LOEC for adult emergence up to day 22) of the test item applied to the honey bee, Apis mellifera L., larvae in an in vitro test after repeated oral application. The test item was administered to the larvae at a constant concentration in the diet according to their growth at a range of five increasing doses. Cumulative mortalities of honey bee larvae treated with the test item were assessed daily from day 4 to day 8. Cumulative mortalities during the pupation phase were assessed on day 15 and on day 22. All mortalities were compared to the control. The adult emergence rate was assessed on day 22.

Material and methods:

Test item: Mesosulfuron-methyl; Batch No.: EFME000144, Sample description: TOX09287-02, Specification No.: 102000013204, active ingredient (analysed purity a.s.): 97.4 % w/w, Certificate No.: AZ 19853.
Test species: Honey bee (Apis mellifera L., subspecies Buckfast), synchronized first instar (L1, one day old) larvae originating from healthy (free of clinical symptoms of any disease) and queen-right bee colonies. The larvae were taken from hives that had not received treatments with chemical substances for at least one month. The test was conducted at Biochem agrar GmbH (Germany).
Test design: Dose response test with a duration of 22 days from grafting on day 1 to the final assessment on day 22. From day 3 until day 6 of the test, five different concentrations of Mesosulfuron-methyl diluted in the larval food (aqueous yeast/sugar solution mixed with royal jelly 1:1 (w/w)) were fed to larvae of the test item groups and one single concentration of the reference item dimethoate was fed to the larvae of the reference item group with diet B or C. Larvae of the control treatments received untreated diet B or C. After the applications, no additional feeding of the larvae took place.
The analysed purity was considered for the calculation of the test item and reference item concentrations; the daily feeding volume increased from 20 µL to 50 µL diet per larva over the application period. The cumulative feeding volume from day 3 until day 6 of 140 µL diet per larva and the density of the diet (1.13 g/cm^3) were considered for the calculation of the cumulative doses per larva. A control group was included in the test and exposed for the same period of time under identical exposure conditions to the water treated artificial diet. Each treatment group consisted of 36 larvae from three different colonies. Assessments of larval mortality were done 24, 48, 72, 96 and 120 hours after start of the treatment (respectively day 4 to day 8). Additionally, other observations as small body size or large quantities of remaining food after 96 and 120 hours (on D7 and D8) were noted. Pupal mortality was assessed at day 15 and emergence of adults was evaluated at day 22.
In an analytical phase of the study, the concentration of the active substance in each final diet was determined.
The presence of unconsumed food and/or substantially undersized larvae was recorded on day 7 and 8. Other observations and any other adverse effects were qualitatively recorded to aid in the interpretation of mortality in comparison to the control group.
Test concentrations: One untreated control group; 5 test item groups with 81.2, 40.6, 20.3, 10.1 and 5.1 mg a.s./kg diet, equivalent to cumulative doses of 12.8, 6.4, 3.2, 1.6 and 0.8 µg a.s./larva per developmental period; One dimethoate reference item group with 46 mg dimethoate/kg diet, equivalent to a cumulative dose of 7.3 µg dimethoate/larva per developmental period.

Dates of work: *August 22 to September 12, 2016*

Results:

Analytical results:
The analytical dose verification of the larval diet of the test item groups from day 3 until day 6 resulted in concentrations that are equivalent to mean recoveries between 80 and 100 % of the nominal test concentration.

Biological results:
After 120 hours of repeated oral exposure (on day 8) a larval mortality of 2.8 % were observed in the control. The control group showed an overall mortality of 22.2 % at day 22. In the test item group larval mortalities at day 8 ranged between 2.8 and 22.2 %. Overall mortalities at day 22 ranged between 22.2 and 36.1 %. Mortality in the reference was above 50 % across all replicates on day 8, being 88.9 %.
In the final assessment at day 22, adult emergence rates of 77.8 % were determined for the honey bees in the control group. In the test item group the adult honey bees emerged at rates ranging between 63.9 and 77.8 % following an application of 12.8, 6.4, 3.2, 1.6 and 0.8 µg a.s./larva, respectively, during the larval stages. None of the larvae treated with Mesosulfuron-methyl showed a statistically significantly increased mortality if compared to the control.
The statistical evaluation of the adult emergence rate was done using all absolute mortality data of the final assessment on day 22, in order to correct the adult emergence rate with the control mortality.
On day 8, none of the larvae treated with any of the test items showed any signs of abnormal behaviour, such as remaining food or discolouration, except for the lowest test concentration (1 replicate with remaining food).
Results for larval mortality until day 8, mean mortality and adult emergence on day 22 and the corresponding endpoints are presented in the following tables.

Mortality and other observations of larvae in the repeated exposure toxicity test

Treat-ment group	Dose	Concen-tration	On day 8			On day 22		
			Larval mortal-ity		Mean OO	Overall mortality		Emergence rate
			[%]		[%]	[%]		[%]
	[µg a.s./ larva]	[mg a.s./ kg food]	abs.	corr.		abs.	corr.	abs.
Control	-	-	2.8	0.0	0.0	22.2	0.0	77.8
Test Item (Mesosulfuron-methyl)	12.8	81.2	19.4	17.1	0.0	27.8	7.1	72.2
	6.4	40.6	22.2	20.0	0.0	36.1	17.9	63.9
	3.2	20.3	2.8	-2.9*	0.0	25.0	3.6	75.0
	1.6	10.1	11.1	8.6	0.0	25.0	3.6	75.0
	0.8	5.1	13.9	11.4	3.3	22.2	0.0	77.8
Reference Item (Dimethoate)	7.3	46	88.9	88.6	83.3	97.2	96.4	2.8

Results are averages based on 3 replicates, containing 12 larvae each; corr.: corrected mortality (according to SCHNEIDER-ORELLI 1947): test and reference item was corrected by control; abs.: absolute mortality as counted from the results; calculation are performed with non-rounded values;
OO: Other observations (e.g. remaining food);
** Negative values indicate higher mortality in the control group than in the treatment group.*

Calculated endpoints of the repeated exposure larvae toxicity test

Treatment	***Endpoint: Successful adult emergence***	***Up to day 22***
Test item doses	*ED_{50} [µg a.s./larva]* [2]	***> 12.8***
	ED_{20} [µg a.s./larva] [2]	***> 12.8***
	ED_{10} [µg a.s./larva] [2]	***> 12.8***
	LOED [µg a.s./larva] [1]	***> 12.8***
	NOED [µg a.s./larva] [1]	***≥ 12.8***
Test item concentrations	*EC_{50} [mg a.s./kg food]* [2]	***> 81.2***
	EC_{20} [mg a.s./kg food] [2]	***> 81.2***
	EC_{10} [mg a.s./kg food] [2]	***> 81.2***
	LOEC [mg a.s./kg food] [1]	***> 81.2***
	NOEC [mg a.s./kg food] [1]	***≥ 81.2***

[1] *Chi² 2x2 Table Test with Bonferroni Correction; α=0.05; one sided greater*
[2] *Estimated*

Validity criteria:
All validity criteria were met in this study.

Validity criteria according to OECD GD 239	***Obtained in this study***
Cumulative larval mortality up to day 8 in control: ≤ 15%	*2.8%*
Mean adult emergence rate on day 22 in control: ≥ 70%	*77.8%*
For reference item dimethoate larval mortality at day 8: ≥ 50%	*88.9%*

Conclusion

In a repeated exposure larval toxicity study with Mesosulfuron-methyl, the NOED was ≥ 12.8 µg a.s./larva and the respective LOED was > 12.8 µg a.s./larva. The $ED_{50/20/10}$ (successful adult emergence up to D22) were estimated to be > 12.8 µg a.s./larva, respectively.

The NOEC was ≥ 81.2 mg a.s./kg food and the respective LOEC was > 81.2 mg a.s./kg food. The $EC_{50/20/10}$ (successful adult emergence up to D22) were estimated to be > 81.2 mg a.s./kg food, respectively.

The analysed concentrations of the active ingredient in the diets ranged between 80% and 100% of the nominal test concentrations.

A 2.3.1.4 KCP 10.3.1.4 Sub-lethal effects

A 2.3.1.5 KCP 10.3.1.5 Cage and tunnel tests

A 2.3.1.6 KCP 10.3.1.6 Field tests with honeybees

A 2.3.2 KCP 10.3.2. Effects on non-target arthropods other than bees

A 2.3.2.1 KCP 10.3.2.1. Standard laboratory testing for non-target arthropods

A 2.3.2.2 KCP 10.3.2.2. Extended laboratory testing, aged residue studies with non-target arthropods

A 2.3.2.3 KCP 10.3.2.3. Semi-field studies with non-target arthropods

A 2.3.2.4 KCP 10.3.2.4. Field studies with non-target arthropods

A 2.3.2.5 KCP 10.3.2.5. Other routes of exposure for non-target arthropods

A 2.4 KCP 10.4 Effects on non-target soil meso- and macrofauna

A.2.4.1 KCP 10.4.1 Earthworms

A 2.4.1.1 KCP 10.4.1.1 Earthworms - sub-lethal effects

A 2.4.1.2 KCP 10.4.1.2 Earthworms - field studies

A 2.4.2 KCP 10.4.2 Effects on non-target soil meso- and macrofauna (other than earthworms)

A 2.4.2.1 KCP 10.4.2.1 Species level testing

A 2.4.2.2 KCP 10.4.2.2 Higher tier testing

A 2.5 KCP 10.5 Effects on soil nitrogen transformation

A 2.6 KCP 10.6 Effects on terrestrial non-target higher plants

A 2.6.1 KCP 10.6.1 Summary of screening data

A 2.6.2 KCP 10.6.2 Testing on non-target plants

A 2.6.3 KCP 10.6.3 Extended laboratory studies on non-target plants

A 2.6.4 KCP 10.6.4. Semi-field and field tests on non-target plants

A 2.7 KCP 10.7 Effects on other terrestrial organisms (flora and fauna)

Reference:	***KCP 10.7/01***
Title:	*Technical stand-alone combined toxicity assessment for the Central zone*
Report:	*Gladbach, A.; Ebeling, M.; Weyers, A.; 2017; M-571377-02-1*
Authority registration No:	
Guideline(s):	*none*
Deviations:	*--*
GLP/GEP:	*no*
Acceptability:	Study already evaluated and accepted in the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).
Duplication (if vertebrate study):	

This document summarises the tiered approach to assess the risk due to the combined toxicity of active substances. The approach is based on the conservative assumption of concentration-additive combination toxicity. Where necessary, a more detailed and realistic evaluation (e.g, information on mode of action) may be conducted as a further refinement of the tiered approach presented in this document.

1. *The first step proceeds as a screening to check whether the margin of safety based on the single substance assessments is large enough.*
   The margin of safety is large enough if:
   TER assessments: The TER for each single a.s. exceed the regulatory trigger multiplied by the number of a.s. (trigger × n).
   RQ assessments: The RQ ('risk quotient' = PEC/RAC) for each single a.s. is lower than the regulatory trigger divided by the number of a.s. (1/n).
2. *The second step, in case the first step is not satisfied, investigates whether the combined risk is significantly dominated (>90%) by one substance.*
3. *As the third step, in case the first two steps would not be satisfied, TER_{mix} or RQ_{mix} calculations are performed. These TER_{mix} and RQ_{mix} calculations may include refinement when necessary.*

A 2.8 KCP 10.8 Monitoring data

Additional information provided by the applicant

Detailed information to Section 9.5.2.4:

Analysis of applicability of the TWA approach for Tier 1 risk assessment

(a) TWA justification for Iodosulfuron-methyl-sodium

Reference:	***KCP 10.2.3/01***
Title:	*Justification for the use of time-weighted average concentrations in the chronic risk assessment for iodosulfuron-methyl-sodium and aquatic plants*
Report:	*Isemer-Kellner, R.; Heine, S.; 2017; M-607957-01-1*
Authority registration No:	
Guideline(s):	*none*
Deviations:	*--*
GLP/GEP:	*no*
Acceptability:	For analysis of applicability of the TWA approach for active substance iodosulfuron methyl, please refer to the Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL).
Duplication (if vertebrate study):	

For the references cited in this summary and for the appendix of the document, please go back to the original report (see Appendix 1 – List of data submitted by the applicant).

Summary

The EFSA Aquatic Guidance Document (EFSA, 2013[21]) proposes the use of a time weighted average (TWA) concentration in the risk assessment of aquatic organisms in order to address a possible discrepancy between the duration of an exposure event and the exposure period in the corresponding effect study. Specific prerequisites have to be fulfilled before the use of a TWA approach can be justified. In the present document, it is discussed for the active ingredient Iodosulfuron-methyl-sodium and the test organism Lemna gibba whether the $PEC_{sw,twa}$ can be compared to the $RAC_{sw,ch}$ in the risk assessment using the TWA approach by (i) showing reciprocity for this species compound combination, (ii) using a decision scheme presented in the EFSA AGD and (iii) direct proof of conservatism of the TWA approach itself. All lines of evidence are supported by biological data derived of static exposure or peak exposure studies and/or by simulations (in silico experiments) using a mechanistic Lemna model. As a crucial first step, it is shown that linear reciprocity can be ascertained for the combination of Lemna and Iodosulfuron-methyl-sodium forming the basis of the TWA approach. Furthermore, the EFSA AGD decision scheme clearly allows for the use of TWA in the case presented here, putting a special focus on the evaluation of onset of effects and potential delayed effects. An additional alternative direct test presented by the notifier also confirms that the TWA approach in the case of Lemna and Iodosulfuron-methyl sodium can be regarded as conservative and therefore protective.

Table A 1: Overview on methodologies used in the present document:

Criteria addressed / methodology		***Analysis of biological data***	***In silico experiment***
Reciprocity		*X*	*-*
Decision scheme	*Generic parts*	*X*	*-*
	Early onset of effects	*X*	*X*
	Delayed effects	*X*	*X*
Direct proof of conservatism		*Graphical data comparison between constant exposure and pulse exposure*	

[21] In the following abbreviated as ‘EFSA AGD’

	studies.

As an overall conclusion, it is considered justified to base the risk assessment for Lemna gibba and Iodosulfuron-methyl-sodium on 7d time-weighted average concentrations ($PEC_{sw,\ 7d\text{-}twa}$).

Introduction

In standard studies with macrophytes aiming to derive a Regulatory Acceptable Concentration for surface water bodies ($RAC_{sw,ch}$) the plants are constantly exposed to a test compound over several days. For Lemna, the duration of this exposure period is normally seven days (OECD TG 221, 2016). According to the EFSA AGD, as initial step in Tier 1 risk assessment, the $RAC_{sw,ch}$ derived from this long-term exposure is compared to the maximum concentration of complex exposure scenarios ($PEC_{sw,max}$). Depending on the actual product use situation, exposure scenario and the characteristics of the compound under assessment, the exposure event which defines the $PEC_{sw,max}$ can however be significantly shorter (e.g. < 1 day) than the exposure period in the effect study. This may lead into an overly conservative Tier 1 assessment in some cases.

A possible technique to address this discrepancy is a risk assessment based on time weighted average (TWA) concentration. It should be noted that the TWA approach is still Tier 1 and does not belong to higher tier (Tier 2) refinement options like the geomean approach (Tier 2A), the SSD approach (Tier 2B) or the refined exposure approach (Tier 2C).

According to the EFSA AGD, the TWA approach may be applied if certain criteria are fulfilled. These criteria are included in a decision scheme presented in the EFSA AGD. The scheme has to be successfully passed before it is justified to compare $PEC_{sw,twa}$ to $RAC_{sw,ch}$ in the risk assessment.

This document presents a detailed analysis of the applicability of the time-weighted average approach in the risk assessment for Iodosulfuron-methyl-sodium and aquatic plants. The analysis comprises of two fundamentally different methodologies:

1. Analysis according to the EFSA AGD, addressing all criteria requested for TWA
2. Direct proof of conservatism of TWA by considering results from refined exposure experiments

The direct method 2 was recently developed by the applicant, and will be described in more detail below.

General principle and prerequisites for applying the time-weighted average concept

The use of a TWA concentration approach in the aquatic risk assessment of plant protection products is based on the observation that effects on aquatic organisms may be similar when exposed for a short time to a higher concentration or for a longer time to a lower concentration, a phenomenon referred to as reciprocity (Giesy and Graney, 1989). Reciprocity relates to Haber's law, which assumes that toxicity depends on the product of concentration and time. Linear reciprocity is the basis of the TWA approach, where exposure concentration is integrated over time (= area under the curve, AUC) and then divided by a default of 7 days (or – if differing – the duration of the toxicity test). An example visualizing this assumption is given in Figure A 1. When this approach is applied, different exposure patterns with the same AUC are assumed to have the same effects.

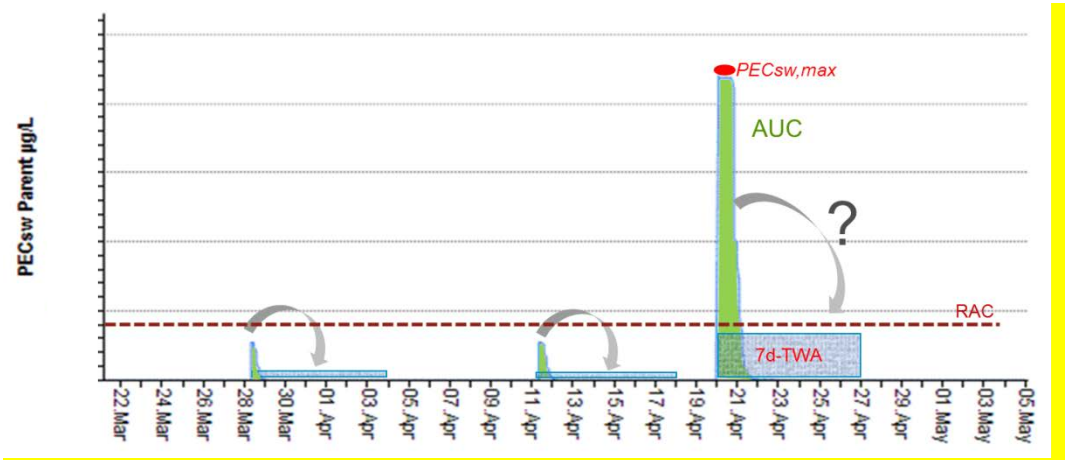


Figure A 1: Theoretical example of FOCUS exposure pattern with two peaks below the Regulatory Acceptable Concentration (RAC) and one prominent peak exceeding this RAC. The blue boxes represent calculated 7d-twa values for the individual peaks, none of them exceeding the RAC.

Due to its importance for the application of the TWA approach, the demonstration of linear reciprocity for a certain compound/species combination is the crucial first step. The analysis of linear reciprocity is usually based on standard study data (e.g. Lemna 7d constant exposure study).
Further aspects to be addressed in context of the TWA approach according to the EFSA AGD are the time to onset of effects and (non-)latency of effects. With macrophytes, the time to onset of effects is investigated to reveal how rapidly a compound affects the plants. This is done to exclude that short exposure to high concentrations as it may occur under realistic outdoor conditions (e.g. runoff events) produces effects that are 'overlooked' when comparing the Tier 1 $RAC_{sw,ch}$ to averaged (and by this lowered) $PEC_{sw,twa}$. Analysis of time to onset of effects can be based on standard study data (e.g. Lemna 7d constant exposure study).
Investigating (non-)latency of effects is done to prove that delayed effects in the post-exposure phase caused by damage during exposure are not to be expected. A possible way to address this point is considering available recovery studies.
Criteria and an evaluation scheme dedicated to this purpose have been set up in the EFSA AGD, chapters 4.5.1 'When and how (not) to use the $PEC_{sw;twa}$ in chronic risk assessments' and 4.5.2 'Decision scheme to use the $PEC_{sw;max}$ or $PEC_{sw;twa}$ in the risk assessment'. Under points 5 and 6 below a detailed step-by-step assessment will be presented, providing analysis and supportive explanation on each evaluation point.

Alternative approach for proving conservatism of TWA:

When using TWA in the aquatic risk assessment, predicted concentrations are averaged over time ($PEC_{sw;twa}$) and these averaged concentrations are compared to an effect endpoint from a constant exposure study. Recently, a number of procedural questions around the demonstration of applicability of the TWA concept with regard to a specific substance have been raised which is reflected in complex and in part controverse discussions on how to practically handle certain elements of the EFSA AGD decision scheme for TWA. As final clarification on these matters is not yet available at the authoring time of the present document, the notifier wishes to provide in addition to the AGD science-based approach a further confirming element, i.e. a novel and practicable screening test for TWA applicability based on simple phaenomenologic considerations. The procedure is laying focus exclusively on the question whether or not a risk assessment based on averaged concentrations is conservative and protective, irrespective of scientific or mechanistic backgrounds. For the intended purpose of risk assessment, ultimately, it has to be ensured that also exceptional exposure events (e.g. runoff peaks, drift peaks) are covered when using $PEC_{sw;twa}$ values.
To demonstrate the conservatism of TWA for specific species-compound-exposure combinations, the notifier recently developed a new approach that was also presented at the SETAC Europe Conference in Brussels 2017 (Preuss et al. 2017). The idea behind this new approach is to provide direct proof, instead of an implicit justification, that the assumption shown in Figure A 1 is conservative. The approach basically

requires two datasets for the same compound and species: 1. A constant exposure study (e.g. Lemna 7-days standard laboratory test); 2. A refined exposure study (Lemna 1-day pulsed exposure + 6 days in clean medium).
The general procedure of this new approach includes the following steps:

1. *Calculate twa-values for the different test levels of the refined exposure study; the time window of the TWA can be set to different values, e.g. the default 7 days as recommended by ELINK (Brock et al. 2010) and adopted in the EFSA AGD*
2. *Insert the obtained twa-values in the dose-response curve of the standard constant exposure study to derive inhibition percentages; this calculates the effects which would be predicted by the twa concentration.*
3. *Compare these predicted inhibition percentages with inhibition percentages as observed in the refined exposure study*
4. *If the predicted inhibition is > the observed inhibition, then TWA is conservative and can be applied (see example below)*

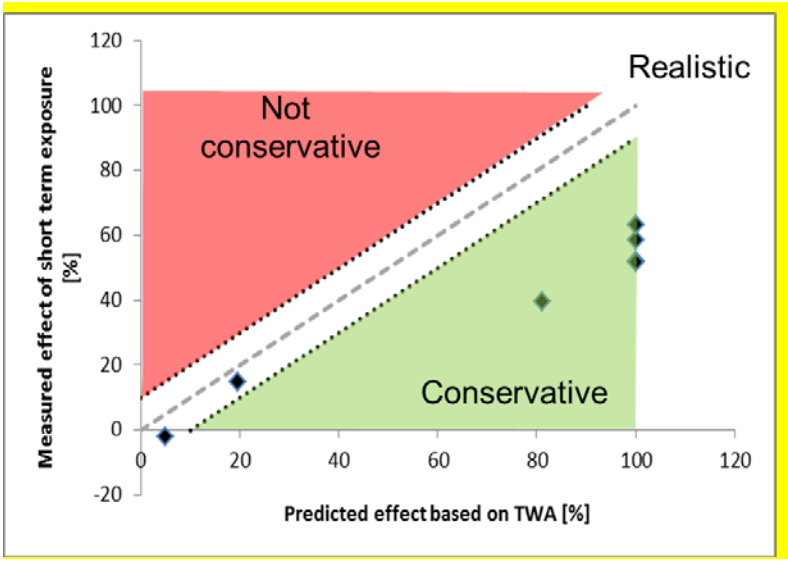


Figure A 2: ***Predicted effects based on TWA vs. measured effects of a short term exposure event.*** *The predicted effects from the concentration response relationship of the standard test using the twa concentration of the refined exposure study are plotted against the measured effect at the respective concentration in the refined exposure test. If Haber's law would apply for this species-compound combination, all data points would be on the dashed 1:1 line ± 10% (white area). In general, data points below the 1:1 line (green area) indicate that TWA over-predicts the effects (TWA is conservative) whereas data points above the 1:1 line (red area) indicate that TWA under-predicts the effects of short term exposure events. In the latter case, TWA would not be protective and should thus not be applied.*

As for reciprocity this approach can theoretically not work in the lower non-linear part of the concentration-response relationship (inhibitions <17.6%, cf. explanations in following chapter). However, since macrophyte risk assessment is based on the EC_{50} (EFSA AGD, p. 17) and the TWA is thus applied to 50% effect, this lower effect range is not relevant for the actual risk assessment question.
A further advantage of this new approach is that the time window for TWA can be modified to either achieve a higher level of conservatism (e.g. 5 instead of standard 7 days for Lemna), or to justify longer time windows, as recommended in the EFSA AGD (p. 49). An example for the increase of conservatism is given in the figure below.

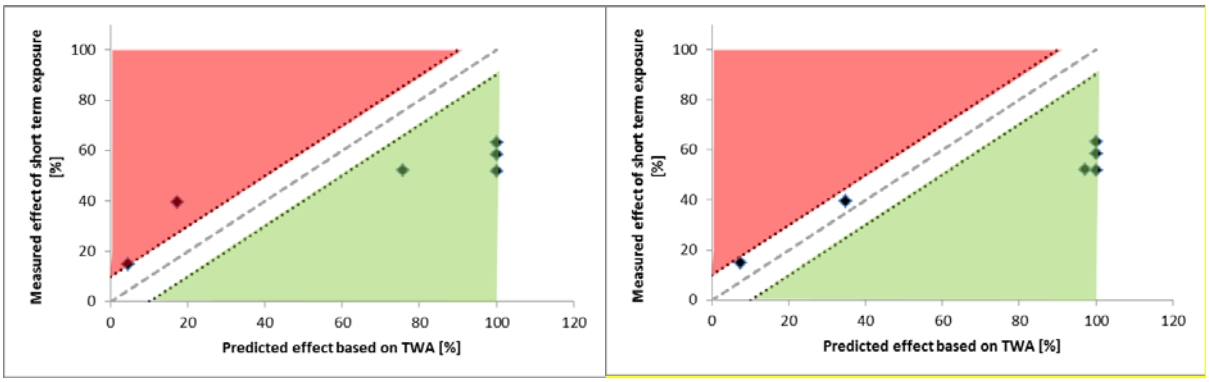


Figure A 3: ***Theoretical example of the impact of the time window on conservatism of the TWA approach.*** *Left: For time window of 7 days TWA is not conservative (data points in red area, some predicted effects < observed effects); Right: For shortened time window of 5 days TWA is conservative (all data points in white or green area, predicted effects always > observed effects). Hence, TWA could be used with 5-day time window.*

For Iodosulfuron-methyl-sodium and aquatic plants the direct proof of conservatism of TWA is provided below.

Analysis of reciprocity:

A prerequisite for applying the EFSA AGD decision scheme is the demonstration of reciprocity for a certain species/compound combination. Reciprocity relates to Haber's law which states that the toxicity depends on the product of concentration and exposure duration. As an example, the same effect is expected to occur if the exposure duration is halved while the concentration is doubled (EFSA AGD, point 4.5). A straightforward way to demonstrate reciprocity is to prove the linear relationship between the effect and the product of exposure duration and test concentration (EFSA, 2015, point 3.3.2). In this context, it is important that the underlying study includes several measurement time points to avoid 'inevitable linearity': if all measurements originate from the same time interval, the generated line just mirrors the dose response curve but does not provide information about reciprocity.
Moreover, linear reciprocity can only be demonstrated for the linear part of a dose-response relationship. As shown by Sebaugh & McGray (2003), the range of this linear part is independent of EC_{50} and slope. For a logistic model, the authors derived an effect range of 17.6% to 82.4% for which linearity is given. Even though the dose-response curve for Iodosulfuron-methyl-sodium was calculated with probit, a similar range can be assumed as the models differ mainly towards their curve tails.
Accordingly, an effect range of 15-85% for the investigation of linear reciprocity was used.
In the case of Iodosulfuron-methyl-sodium the check for linear reciprocity was based on the first 7 days of the Lemna study of Bruns, 2013 (M-469584-02-1) which also delivers the endpoint to be used in the Tier 1 risk assessment for aquatic plants (E_rC_{50} = 1.08 µg a.s./L). This endpoint was presented by EFSA in their conclusion on Iodosulfuron-methyl-sodium (EFSA Journal 2016;14(4)). As stated by EFSA, reciprocity has to be demonstrated for the endpoint that is used for the risk assessment (corrigendum of the Aquatic Guidance Document (EFSA, 2016)). Accordingly, this study was used for the demonstration of linear reciprocity.
Linear reciprocity was investigated for frond number, the most sensitive parameter in the test.
Inhibitions of yield for frond number were considered for the intervals 0-2, 0-4 and 0-7 days. It should be noted that a reciprocity analysis based on growth rate is not meaningful; for an example, see Appendix of the full report.
The relationship between %-inhibitions and time x concentration is shown in the Figure A 4 below. An R^2 of 0.7175 was obtained, indicating a linear correlation.

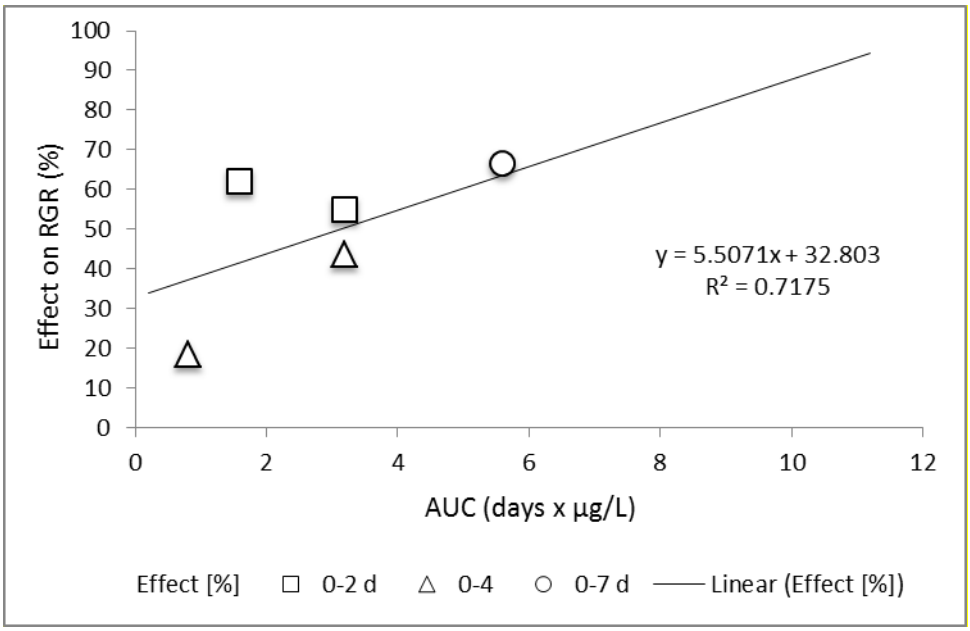


Figure A 4: ***Relationship between %-inhibitions of yield (frond number) and time x concentration for Iodosulfuron-methyl-sodium.*** *An effect range of 15% to 85% was chosen to show linearity (10 data points excluded which were mainly < 10% effect values).*

To conclude, reciprocity can be assumed and Haber's law can be applied to this compound species combination, indicating that a longer exposure of aquatic plants to a lower concentration of Iodosulfuron-methyl-sodium leads to similar effects as a shorter exposure to a higher concentration. The decision scheme as provided in the EFSA AGD (point 4.5.2) thus can be applied.
It should be noted that the RAC (Regulatory Acceptable Concentration) mentioned in the decision scheme is based on the Tier 1 endpoint (here: E_rC_{50} = 1.08 µg a.s./L) which is divided by the standard assessment factor of 10 for aquatic plants, leading to a Tier 1 RAC of 0.108 µg a.s./L.

The EFSA decision scheme for $PEC_{sw;twa}$ in chronic risk assessment:

In the following paragraphs the individual steps of the EFSA decision scheme for $PEC_{sw;twa}$ in chronic risk assessment as provided in the EFSA AGD (2013, pp. 49) are addressed:

1. Chronic Assessment. Is $PEC_{sw;max}$ (of highest available tier) > $RAC_{sw;ch}$ (of highest available tier)?

Yes: Go to 2

No: Low chronic risk

Answer for Iodosulfuron-methyl-sodium & Lemna: *Yes; the risk assessment for Iodosulfuron-methyl-sodium is characterised by short-term exposure events which may result in $PEC_{sw;max}$ to exceed $RAC_{sw;ch}$ in scenarios relevant to the zonal or country evaluation of the product. For a detailed numeric assessment on the specific product GAP, reference is made to the corresponding product dRR.*
The present document exclusively aims at investigating on the question whether the TWA approach can in principle be used for Iodosulfuron-methyl-sodium and Lemna, from the general science perspective.
Moreover, it should be noted that – according to the Aquatic Guidance Document (EFSA, 2013; cf. Decision scheme B of Section 2.1.2) – the use of TWA concentrations in combination with Tier-1 endpoints is by definition no 'refinement' but still Tier-1 within the tiered approach. Accordingly, in the base case the

"highest available tier" refers to Tier-1 data without any further refinements, but the approach may also be applied to any following higher tier level, as a secondary step.

→ Go to 2

2. *Is the $RAC_{sw;ch}$ derived from a test with algae, or from a long-term (≥ 7 days) test with another water organism and the following conditions apply: (i) loss of the a.s. from water is more than 20% of nominal at the end of the exposure period and (ii) the toxicity estimate (e.g. EC_{10} or NOEC) is expressed in terms of nominal/initially measured concentration of the a.s.?*

   Yes: $PEC_{sw;twa}$ not appropriate (low risk not demonstrated)

   No: Go to 3

Answer for Iodosulfuron-methyl-sodium & Lemna: *No. The $RAC_{sw;ch}$ is derived from a 7-day test with Lemna gibba (1st week data of a 6-week test; Bruns, 2013, M-469584-02-1). Measured concentrations at the start and the end of the exposure period ranged between 71-97 % and 73–108 % of nominal, respectively. Thus, there was no indication for a major compound decline and it was justified to express the endpoints in terms of nominal concentrations of Iodosulfuron-methyl-sodium.*

→ Go to 3

3. *Is the $RAC_{sw;ch}$ based on treatment-related responses of the relevant test species early in the chronic test (e.g. during the initial 96-hours observed mortality/immobility in tests with animals, or 50% reduction in growth rate in tests with macrophytes, in the treatment level above the one from which the $RAC_{sw;ch}$ is derived) or is the acute to chronic ratio (acute $L(E)C_{50}$/chronic NOEC or acute $L(E)C_{50}$/chronic EC_{10}) based on immobility or mortality < 10?*

   Yes: $PEC_{sw;twa}$ not appropriate (low risk not demonstrated)

   No: Go to 4

Answer for Iodosulfuron-methyl-sodium & Lemna*: No. In the study of Bruns (2013, M-469584-02-1), maximum effects on frond number of 30.31% were observed on day 2 in the treatment level above the one from which the $RAC_{sw;ch}$ has been derived. The treatment level above the one from which the $RAC_{sw;ch}$ has been derived here is 1.60 µg/L (nominal).*
It has to be made clear that question 3 which deals with the onset of effects should be answered based on biomass rather than on growth rate data. Under constant exposure conditions which are intended for Lemna standard (Tier 1) studies, effects on growth rate are expected to be stable over time. As a consequence, if question 3 is on the concentration above the one delivering the 7d-E_rC_{50}, it is almost inevitable to find a 50% growth rate reduction also for the early phase of the study (i.e. day 0-2 or 0-3).
With regard to the question on acute to chronic ratio, it should be mentioned that this point does not apply to macrophytes for which no acute studies are performed.

To further explore time to onset of effects, simulations (in silico experiments) were performed using a mechanistic Lemna model parameterized for Iodosulfuron-methyl-sodium (Heine 2017a, M-602805-01-1). The development of this mechanistic model has been published in an international peer reviewed journal (Schmitt et al. 2013, M-455483-01-1). The entire results of the model based analysis, including a detailed description of the modelling tasks, are presented in a separate report (Heine 2017b, M-603654-01-1). The calibration and validation of the model can be found in the Appendix of full document.
The Lemna model uses an EC_{50} that is based on internal concentration of Iodosulfuron-methyl-sodium.

This value is used as a reference to define the treatment level above the one from which the $RAC_{sw;ch}$ has been derived. Therefore, for modelling the onset of effects a treatment of 1.8 µg a.s./L was selected. This slightly differs from the treatment that is used to evaluate the onset of effects on an experimental basis (1.60 µg/L, see above).

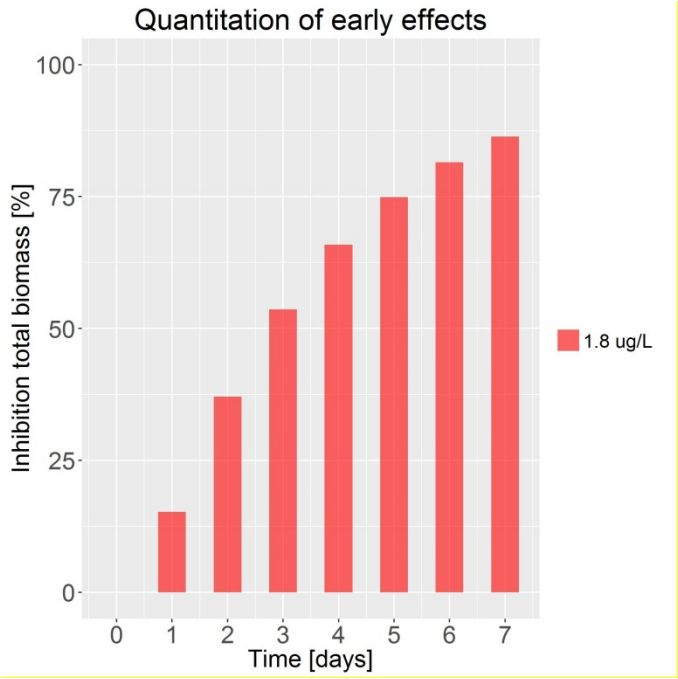


Figure A 5: Simulated effect on biomass during exposure to Iodosulfuron-methyl-sodium using the mechanistic Lemna effect model.

As shown in Figure A 5, predicted effects on biomass at a concentration of 1.8 µg a.s./L during the initial 2 days of the modelling experiment are clearly less than 50% and thus confirm the conclusions from the biological study above.

→ Go to 4

4. Is it demonstrated by the notifier that, for the organisms and the PPP under evaluation and/or PPP with a similar toxic mode of action (read-across information), the following phenomena are not likely: (i) latency of effects due to short-term exposure; (ii) the co-occurrence of exposure and specific sensitive life stages that last a short time only?

Yes: Go to 5

No: $PEC_{sw;twa}$ not appropriate (low risk not demonstrated)

***Answer for Iodosulfuron-methyl-sodium & Lemna**: Yes. In a Lemna peak exposure study performed with Iodosulfuron-methyl-sodium (1+6-day pulsed exposure test; first week of design 2: Kuhl, 2016 (M-574865-01-1)) normal growth was observed already 2 - 7 days after a 24h pulse of up to 62.5 µg a.s./L. This is reflected in the parallel growth lines from day 2 to day 7 in Figure 8 of the study report. Also, no visual signs of phytotoxicity were observed in this study which demonstrates that the compound temporarily inhibited growth but did not produce any irreversible damage, even at unrealistically high short-term exposure concentrations.*
Delayed effects are generally not known for sulfonylurea herbicides and aquatic plants. Moreover, according to the outcome of a consultation for the corrigendum of the Aquatic Guidance Document (EFSA, 2016),

the criterion only needs to be addressed in the specific case of rooted macrophytes and thus not for Lemna. To further explore potential latency of effects, simulations (in silico experiments) were performed with the Lemna model parameterized and validated for Iodosulfuron-methyl-sodium (as explained above). As shown in Figure A 6, the in silico experiments did not give any indication for delayed effects on Lemna growth one day after simulated exposure.

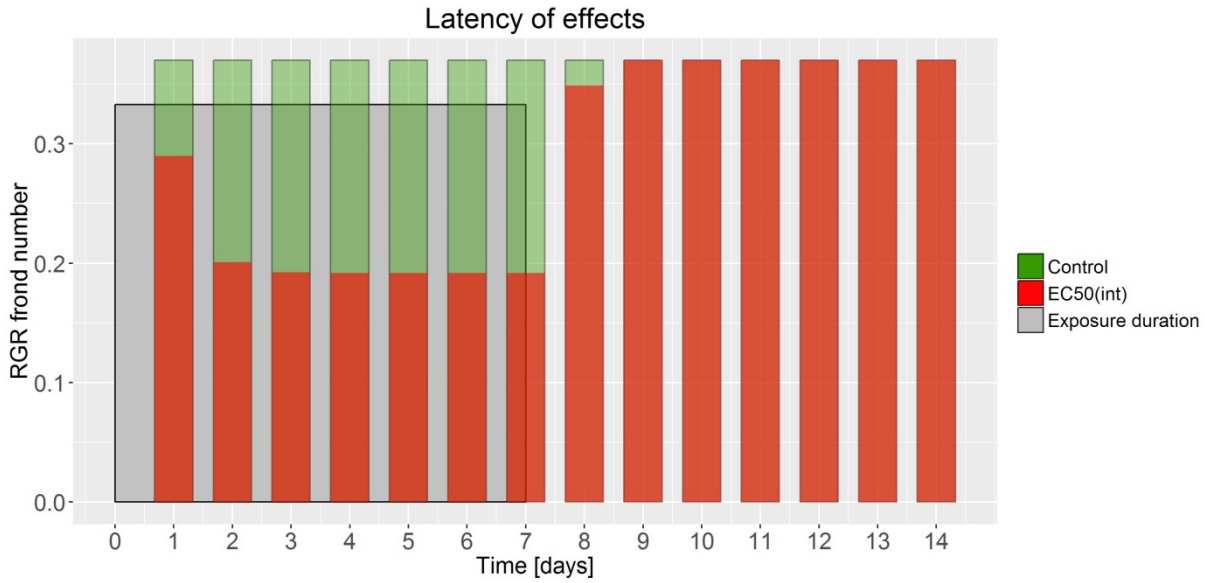


Figure A 6: Simulated effect on growth rate during and after exposure to Iodosulfuron-methyl-sodium using the mechanistic Lemna effect model.

With regard to the second part (ii) of question 4, the EFSA AGD (p. 48) gives examples for specific sensitive life stages: 'e.g. malformations during metamorphosis, effects caused by endocrine disruption'. This point is not related to macrophytes for which coincidence of exposure and a specific sensitive life stage is not an issue, but rather refers to other aquatic organisms, e.g. fish. Lemna propagates by vegetative multiplication. Due to the exponential growth, a Lemna study covers several life cycles of that species and derived endpoints integrate any potential differences in sensitivity (e.g. young vs. older fronds).

→ Go to 5

5. Is $PEC_{sw;7d\text{-}twa}$ (of highest available tier) > $RAC_{sw;ch}$ (of highest available tier)?

Yes: Go to 6

No: Low risk demonstrated

***Answer for Iodosulfuron-methyl-sodium & Lemna**: No. Please refer to the corresponding product dRR document for a detailed risk assessment based on $PEC_{sw;7d\text{-}twa}$ and Lemna.*

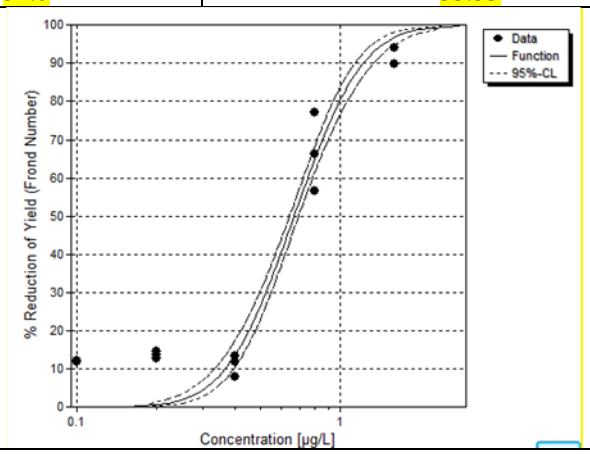
Direct proof of conservatism of TWA for Iodosulfuron-methyl-sodium:

The following two studies were considered in the evaluation of conservatism of TWA for Iodosulfuron-methyl-sodium:

- *6 weeks semi-static study, first 7 days are considered as standard test: Bruns, 2013 (M-469584-02-1)*
- *1+6-day pulsed exposure test (first week of design 2): Kuhl, 2016 (M-574865-01-1)*

In Table A 2, data of the 7d standard test is given, including observed inhibitions of 7d frond number yield and effects as predicted by probit. The table also includes the dose-response curve for the variable 7d frond number yield derived from Toxrat and basic parameters like EC_{50} and slope.

Table A 2: Observed and probit calculated inhibitions of frond number yield for the constant exposure study of Bruns (2003, M-469584-02-1)

7d-exposure concentration [µg/L]	*Inhibition of yield [%]*	
	observed	*calculated according to probit function**
Control	-	-
0.10	*12.0*	*0.37*
0.20	*13.7*	*1.36*
0.40	*10.9*	*10.22*
0.80	*66.7*	*72.92*
1.60	*92.0*	*99.99*
**Parameters for predictions: Model: probit EC_{50} = 0.6684 µg/L Slope= 4.89744*		

In Table A 3, data of the pulsed exposure study is summarized including 7d twa-values calculated for each test level, inhibitions of frond number yield observed in the study and effects predicted based on the dose-response curve from the constant exposure study.

Table A 3: Observed inhibitions of frond number yield in the pulsed exposure study of Kuhl (2016; M-574865-01-1) vs. results of a prediction based on 7d-twa concentrations and probit function from the 7d constant exposure study of Bruns (2003, M-469584-02-1).

Tested 1-day peak concentration [µg/L]	*Calculated equivalent 7d-twa concentration* [µg/L]*	*Inhibition of yield [%]*	
		as experimentally observed in the peak-exposure study	*as predicted for an equivalent 7d-twa concentration based on probit function of the 7 day constant exposure study data*
Control	-	-	-
1.91	*0.27*	*-2.1*	*1.45*
6.10	*0.87*	*54.5*	*77.46*
19.5	*2.79*	*69.8*	*99.99*
62.5	*8.93*	*76.3*	*99.99*
200	*28.57*	*88.6*	*99.99*

** as evaluation can be based on nominal values for the present study, 7 day TWA = 1 day peak concentration / 7.*

Figure A 7 displays the comparison of measured effects of pulsed exposure vs. effects predicted for these pulses based on 7d-twa values. As can be seen the effects directly observed in the pulsed exposure experiment are all smaller than those predicted from the constant exposure study (data points right to the dashed line). Accordingly, the use of TWA is conservative and protective for effects of Iodosulfuron-methyl-sodium on Lemna.

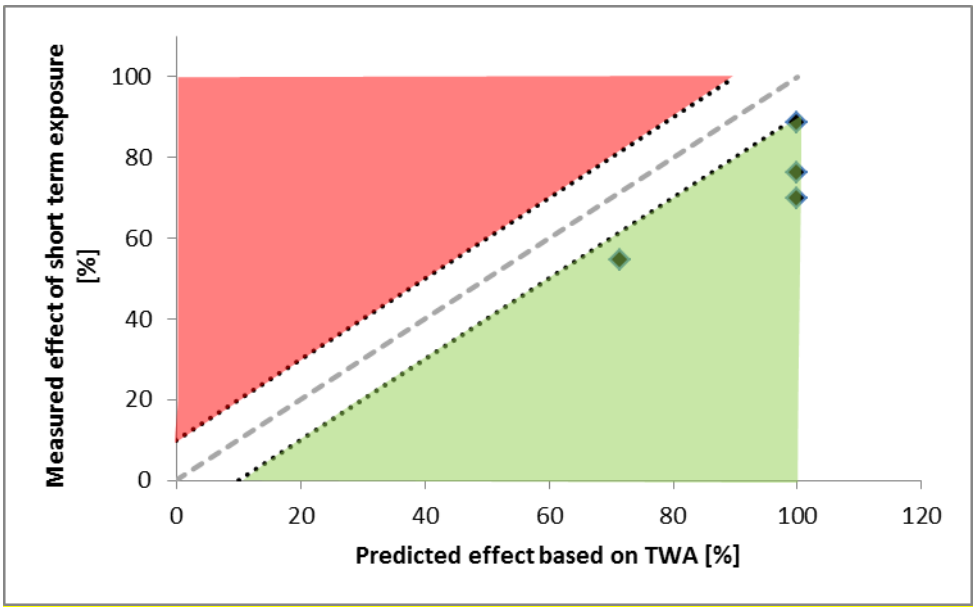


Figure A 7: Comparison of predicted and observed inhibitions for Iodosulfuron-methyl-sodium based on 7d-twa values

Conclusions:

The applicability of $PEC_{sw,twa}$ in the chronic risk assessment for Lemna gibba and Iodosulfuron-methyl-sodium was investigated by using two different approaches: the analysis according to the EFSA AGD and the direct proof of conservatism of TWA. As an overall conclusion, it is considered justified to base the risk assessment for Lemna gibba and Iodosulfuron-methyl-sodium on 7d time-weighted average concentrations ($PEC_{sw,\ 7d\text{-}twa}$).

(b) TWA justification for Mesosulfuron-methyl

Reference:	***KCP 10.2.3/02***
Title:	*Justification for the use of time-weighted average concentrations in the chronic risk assessment for mesosulfuron-methyl and aquatic plants*
Report:	*Sowig, P.; Herno, V.; Heine, S.; 2017; M-602786-01-1*
Authority registration No:	
Guideline(s):	*none*
Deviations:	*--*
GLP/GEP:	*no*
Acceptability:	For analysis of applicability of the TWA approach for active substance mesosulfuron -methyl please refer to Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL). Following conclusion were made: *zRMS did not consider the results of peak exposure studies for active substance.*
Duplication (if vertebrate study):	

For the references cited in this summary and for the appendix of the document, please go back to the original report (see Appendix 1 – List of data submitted by the applicant).

Summary:

The EFSA AGD proposes the use of a time weighted average (TWA) concentration in the risk assessment of aquatic organisms in order to address a possible discrepancy between the duration of an exposure event and the exposure period in the corresponding effect study. Specific prerequisites have to be fulfilled before the use of a TWA approach can be justified. In the present document, it is discussed for the active ingredient Mesosulfuron-methyl and the test organism Lemna gibba whether the $PEC_{sw,twa}$ can be compared to the $RAC_{sw,ch}$ in the risk assessment using the TWA approach by (i) showing reciprocity for this species compound combination, (ii) using a decision scheme presented in the EFSA AGD and (iii) direct proof of conservatism of the TWA approach itself. All lines of evidence are supported by biological data derived from static exposure or peak exposure studies and/or by simulations (in silico experiments) using a mechanistic Lemna model. As a crucial first step, it is shown that linear reciprocity can be ascertained for the combination of Lemna and Mesosulfuron-methyl forming the basis of the TWA approach. Furthermore, the EFSA AGD decision scheme clearly allows for the use of TWA in the case presented here, putting a special focus on the evaluation of onset of effects and potential delayed effects. An additional alternative direct test presented by the notifier also confirms that the TWA approach in the case of Lemna and Mesosulfuron-methyl can be regarded as conservative and therefore protective.

Table A 4: Overview on methodologies used in present document:

Criteria addressed / methodology		***Analysis of biological data***	***In silico experiment***
Reciprocity		*X*	*-*
Decision scheme	*Generic parts*	*X*	*-*
	Early onset of effects	*X*	*X*
	Delayed effects	*X*	*X*
Direct proof of conservatism		*Graphical data comparison between constant exposure and pulse exposure studies.-*	

As an overall conclusion, it is considered justified to base the risk assessment for Lemna gibba and Mesosulfuron-methyl on 7d time-weighted average concentrations ($PEC_{sw,\ 7d\text{-}twa}$).

Introduction:

In standard studies with macrophytes aiming to derive a Regulatory Acceptable Concentration for surface

water bodies ($RAC_{sw,ch}$) the plants are constantly exposed to a test compound over several days. For Lemna, the duration of this exposure period is normally seven days (OECD TG 221, 2016). According to the EFSA AGD, as initial step in Tier 1 risk assessment, the $RAC_{sw,ch}$ derived from this long-term exposure is compared to the maximum concentration of complex exposure scenarios ($PEC_{sw,max}$). Depending on the actual product use situation, exposure scenario and the characteristics of the compound under assessment, the exposure event which defines the $PEC_{sw,max}$ can however be significantly shorter (e.g. < 1 day) than the exposure period in the effect study (7 days). This may lead into an overly conservative Tier 1 assessment in some cases.
A possible technique to address this discrepancy is a risk assessment based on time weighted average (TWA) concentration. It should be noted that the TWA approach is still Tier 1 and does not belong to higher tier (Tier 2) refinement options like the geomean approach (Tier 2A), the SSD approach (Tier 2B) or the refined exposure approach (Tier 2C).

According to the EFSA AGD, the TWA approach may be applied if certain criteria are fulfilled. These criteria are included in a decision scheme presented in the EFSA AGD. The scheme has to be successfully passed before it is justified to compare $PEC_{sw,twa}$ to $RAC_{sw,ch}$ in the risk assessment.
This document presents a detailed analysis of the applicability of the time-weighted average approach in the risk assessment for Mesosulfuron-methyl and aquatic plants. The analysis comprises of two fundamentally different methodologies:

1. Analysis according to the EFSA AGD, addressing all criteria requested for TWA
2. Direct proof of conservatism of TWA by considering results from refined exposure experiments

The direct method 2 was recently developed by the applicant, and will be described in more detail below.

General principle and prerequisites for applying the time-weighted average concept

The use of a TWA concentration approach in the aquatic risk assessment of plant protection products is based on the observation that effects on aquatic organisms may be similar when exposed for a short time to a higher concentration or for a longer time to a lower concentration, a phenomenon referred to as reciprocity (Giesy and Graney, 1989). Reciprocity relates to Haber's law, which assumes that toxicity depends on the product of concentration and time. Linear reciprocity is the basis of the TWA approach, where exposure concentration is integrated over time (= area under the curve, AUC) and then divided by the duration of the toxicity test (or a default of 7 days). An example visualizing this assumption is given in Figure A 8.When this approach is applied, different exposure patterns with the same AUC are assumed to have the same effects.

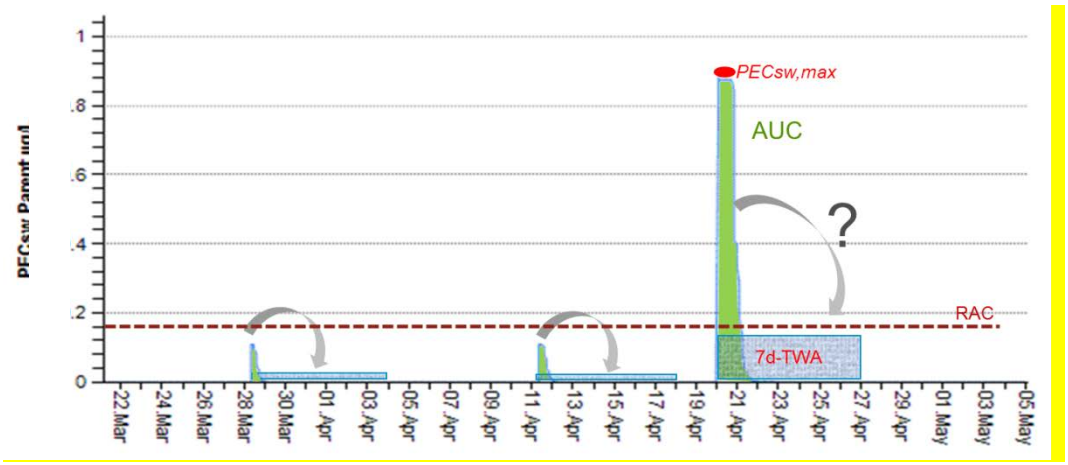


Figure A 8: ***Example of FOCUS exposure pattern with two peaks below the Regulatory Acceptable Concentration (RAC) and one prominent peak exceeding this RAC****. The blue boxes represent calculated 7d-twa values for the individual peaks, none of them exceeding the RAC. The y-axis does not show numbers because this graph shall simply illustrate the statements written above.*

Due to its importance for the application of the TWA approach, the demonstration of linear reciprocity for a certain compound/species combination is the crucial first step. The analysis of linear reciprocity is usually based on standard study data (e.g. Lemna 7d constant exposure study).

Further aspects to be addressed in context of the TWA approach according to the EFSA AGD are the time to onset of effects and (non-)latency of effects. With macrophytes, the time to onset of effects is investigated to reveal how rapidly a compound affects the plants. This is done to exclude that short exposure to high concentrations as it may occur under realistic outdoor conditions (e.g. runoff events) produces effects that are 'overlooked' when comparing the Tier 1 $RAC_{sw,ch}$ to averaged (and by this lowered) $PEC_{sw,twa}$. Analysis of time to onset of effects can be based on standard study data (e.g. Lemna 7d constant exposure study); however, TK/TD modelling approaches may be used in addition.

Investigating (non-)latency of effects is done to prove that delayed effects in the post-exposure phase caused by damage during exposure are not to be expected. A possible way to address this point is considering available recovery studies or to perform TK/TD modelling.

Criteria and an evaluation scheme dedicated to this purpose have been set up in the EFSA AGD, chapters 4.5.1 'When and how (not) to use the $PEC_{sw;twa}$ in chronic risk assessments' and 4.5.2 'Decision scheme to use the $PEC_{sw;max}$ or $PEC_{sw;twa}$ in the risk assessment'. Under points 4 and 5 below a detailed step-by-step assessment will be presented, providing analysis and supportive explanation on each evaluation point.

Alternative approach for proving conservatism of TWA

When using TWA in the aquatic risk assessment, predicted concentrations are averaged over time ($PEC_{sw,twa}$) and these averaged concentrations are compared to an effect endpoint from a constant exposure study. Recently, a number of procedural questions around the demonstration of applicability of TWA concept for a considered substance have been raised by different stakeholders in the regulatory science community, which is reflected in complex and in part controversial discussions on how to practically handle certain elements of the EFSA AGD decision scheme for TWA. As final clarification on these matters is not yet available at the authoring time of the present document, the notifier wishes to provide in addition to the AGD science-based approach a further confirming element, i.e. a novel and practicable screening test for TWA applicability based on simple phaenomenologic considerations. The procedure is laying focus exclusively on the qualitative but target decisive question whether or not a risk assessment based on averaged concentrations is conservative and protective, irrespective of scientific or mechanistic backgrounds. For the intended purpose of risk assessment, ultimately, it has to be ensured that also exceptional exposure events (e.g. runoff peaks, drift peaks) are covered when using $PEC_{sw,twa}$ values.

To demonstrate the conservatism of TWA for specific species-compound-exposure combinations, the notifier recently developed a new approach that was also presented at the SETAC Europe Conference in Brussels 2017 (Preuss et al. 2017, M-602600-01-1). The idea behind this new approach is to provide direct proof, instead of an implicit justification, that the assumption shown in Fig. 1 is conservative. The approach basically requires two datasets for the same compound and species: 1. A constant exposure study (e.g. Lemna 7-days standard laboratory test); 2. A refined exposure study (Lemna 1-day pulsed exposure + 6 days in clean medium; half of the replicate received a second peak at day 7; Kuhl (2016); M-577164-01-1).

The general procedure of this new approach includes the following steps:

1. *Calculate twa-values for the different test levels of the refined exposure study; the time window of the TWA can be set to different values, e.g. the default 7 days as recommended by ELINK (Brock et al. 2010) and adopted in the EFSA AGD*
2. *Insert the obtained TWA-values in the dose-response curve of the standard constant exposure study to derive inhibition percentages; this calculates the effects which would be predicted by the TWA concentration.*
3. *Compare these predicted inhibition percentages with inhibition percentages as observed in the refined exposure study*
4. *If the predicted inhibition is greater than the observed inhibition, then TWA is conservative and can be applied (see example below in Figure A 9)*

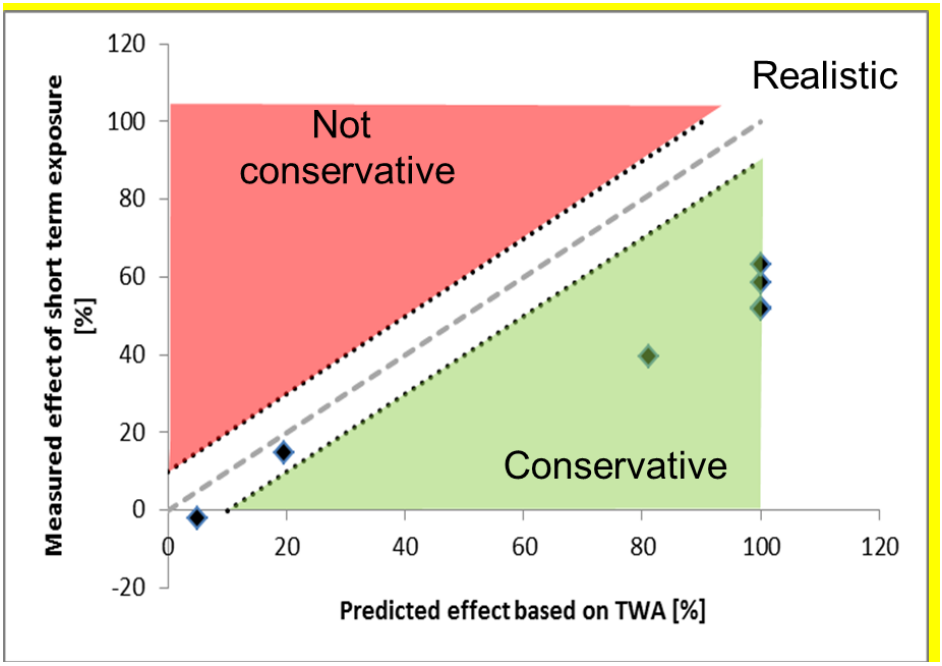


Figure A 9: ***Predicted effects based on TWA vs. measured effects of a short term exposure event.*** *The predicted effects from the concentration response relationship of the standard test, using the TWA concentration of the refined exposure study, are plotted against the measured effect at the respective concentration in the refined exposure test. If Haber's law would apply for this species-compound combination, all data points would be on the dashed 1:1 line ± 10% (white area). In general, data points below the 1:1 line (green area) indicate that TWA over-predicts the effects (TWA is conservative) whereas data points above the 1:1 line (red area) indicate that TWA under-predicts the effects of short term exposure events. In the latter case, TWA would not be protective and should thus not be applied.*

As for reciprocity, this approach can theoretically not work in the lower non-linear part of the concentration-response relationship (inhibitions <17.6%, cf. explanations in following chapter). However, since macrophyte risk assessment is based on the EC_{50} (EFSA AGD, p. 17) and the TWA is thus applied to 50% effect, this lower effect range is not relevant for the actual risk assessment question.

A further advantage of this new approach is that the time window for TWA can be modified to either achieve a higher level of conservatism (e.g. 5 instead of standard 7 days for Lemna), or to justify longer time windows, as recommended in the EFSA AGD (p. 49). An example for the increase of conservatism is given in the Figure A 10 below.

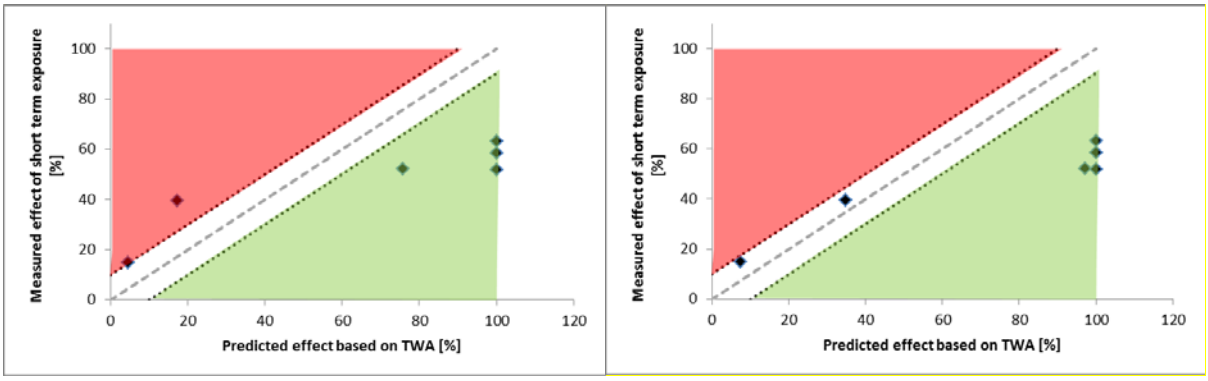


Figure A 10: ***Theoretical example of the impact of the time window on conservatism of the TWA approach*** *Left: For time window of 7 days TWA is not conservative (data points in red area, some predicted effects < observed effects); Right: For shortened time window of 5 days TWA is conservative (all data points in white or green area, predicted effects always > observed effects). Hence, TWA could be used with 5-day time window.*

For Mesosulfuron-methyl and aquatic plants the direct proof of conservatism of TWA is provided under point 6 in this document.

Table A 5: ***Survey of Lemna-studies and their use in the rationale of this statement***

Reference	***Design***	***Endpoint***	***Use***
Bruns, 2013 *M-445139-01-1*	*1st week of the 8 weeks experiment. Continuous exposure*	*Yield of frond area*	*Reciprocity analysis, EFSA decision scheme, Direct proof of conservatism, Model validation*
Kuhl, 2016 *M-577164-01-1*	*Design 1: two 24h-peaks at day 0 and day 3 with endpoints calculated at day 7*	*Yield of frond area*	*Model calibration (Design 1), Model validation (Design 2), EFSA decision scheme, Direct proof of conservatism*
	Design 2: two peaks: the first peak at day 0 and a second peak at day 7 with endpoints calculated at day 14.		
Sowig & Weller, 2000 *M-195390-01-1*	*Standard 7-day Lemna-study according to old OECD draft June 1998*	*Frond number*	*Model calibration*
Sowig, 2001 *M-201731-01-1*	*7-day Lemna study followed by a 4-day recovery period*	*Frond number*	*Model validation, EFSA decision scheme*
Sowig & Gosch, 2002 *M-206814-01-1*	*7-day Lemna study followed by a 7-day recovery period*	*Frond number*	*Model validation, EFSA decision scheme*

Analysis of reciprocity

Analysis based on biological study data

A prerequisite for applying the EFSA AGD decision scheme is the demonstration of reciprocity for a certain species/compound combination. Reciprocity relates to Haber's law which states that the toxicity depends on the product of concentration and exposure duration. As an example, the same effect is expected to occur if the exposure duration is halved while the concentration is doubled (EFSA AGD, point 4.5). A straightforward way to demonstrate reciprocity is to prove the linear relationship between the effect and the product of exposure duration and test concentration (EFSA, 2015, point 3.3.2). In this context, it is important that the underlying study includes several measurement time points to avoid 'inevitable linearity': if all measurements originate from the same time interval, the generated line just mirrors the dose response curve but does not provide information about reciprocity.
Moreover, linear reciprocity can only be demonstrated for the linear part of a dose-response relationship. As shown by Sebaugh & McGray (2003), the range of this linear part is independent of EC_{50} and slope. For a logistic model, the authors derived an effect range of 17.6% to 82.4% for which linearity is given. Even though the dose-response curve for Mesosulfuron-methyl was calculated with probit, a similar range can be assumed as the models differ mainly towards their curve tails.

Accordingly, an effect range of 15-85% for the investigation of linear reciprocity was used.

In the case of Mesosulfuron-methyl the check for linear reciprocity was based on the 1st week data of Lemna study (Bruns 2013; M-445139-01-1) which also delivers the EU agreed endpoint to be used in the Tier 1 risk assessment for aquatic plants ($E_rC_{50\ frond\ area}$ = 1.29 µg a.s./L; $E_rC_{50\ frond\ number}$ = 1.61 µg a.s./L) [EFSA Journal 2016;14(10): 4584] As stated by EFSA, reciprocity has to be demonstrated for the endpoint that is used for the risk assessment (corrigendum of the Aquatic Guidance Document (EFSA, 2016)). Accordingly, this study was used for the demonstration of linear reciprocity.

Linear reciprocity was investigated for yield frond area, the most sensitive parameter in the test. Inhibitions of yield for frond area in the effect range of 15 to 85 % were considered for the intervals 0-3, 0-5 and 0-7 days. It should be noted that a reciprocity analysis based on growth rate is not meaningful; for an example, see Appendix of the full report.

The relationship between %inhibitions and time x concentration is shown in Figure A 11. An R^2 of 0.9352 was obtained, indicating a clear linear correlation and therefore reciprocity is confirmed.

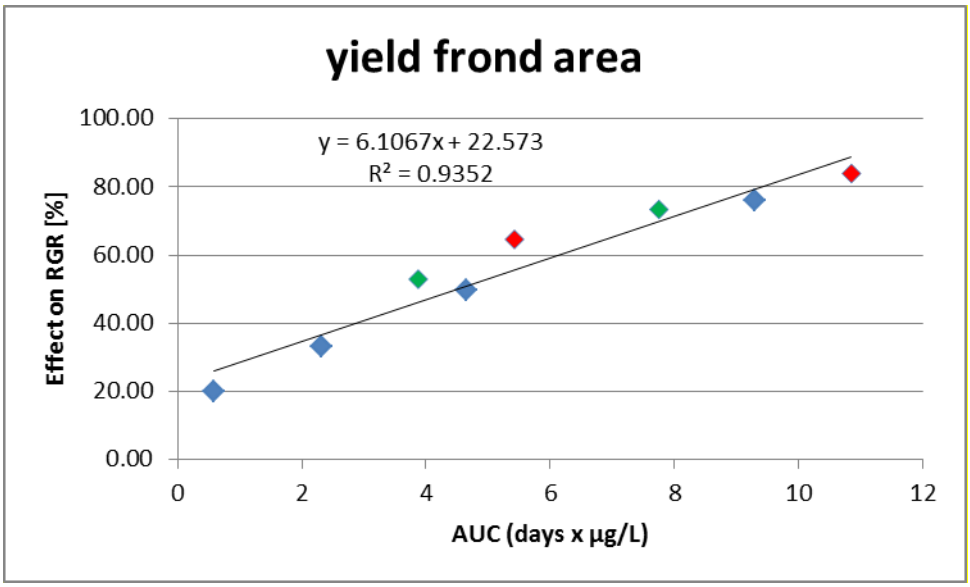


Figure A 11: ***Relationship between %-inhibitions of yield (frond area) and time x concentration for Mesosulfuron-methyl.*** *An effect range of 15% to 85% was chosen to show linearity (4 data points excluded which were < 10% or >90% effect values) - Blue, green and red dots refer to data from day 0 - 3, day 0 - 5 and day 0 - 7, respectively.*

To conclude, reciprocity can be assumed and Haber's law can be applied to this compound species combination, indicating that a longer exposure of aquatic plants to a lower concentration of Mesosulfuron-methyl leads to similar effects as a shorter exposure to a higher concentration. The decision scheme as provided in the EFSA AGD (point 4.5.2) thus can be applied.

It should be noted that the RAC (Regulatory Acceptable Concentration) mentioned in the decision scheme is based on the Tier 1 endpoint (here: E_rC_{50} = 1.29 µg a.s./L) which is divided by the standard assessment factor of 10 for aquatic plants, leading to a Tier 1 RAC of 0.129 µg a.s./L.

The EFSA decision scheme for PECsw,twa in chronic risk assessment

In the following paragraphs the individual steps of the EFSA decision scheme for $PEC_{sw,twa}$ in chronic risk assessment as provided in the EFSA AGD (2013, pp. 49) are addressed:

1. Chronic Assessment. Is $PEC_{sw,max}$ (of highest available tier) > $RAC_{sw,ch}$ (of highest available tier)?

Yes: Go to 2

No: Low chronic risk

Answer for Mesosulfuron-methyl & Lemna: *Yes; the risk assessment for Mesosulfuron-methyl is characterised by short-term exposure events which may result in $PEC_{sw,max}$ to exceed $RAC_{sw,ch}$ in scenarios relevant to the zonal or country evaluation of the product. For a detailed numeric assessment on the specific product GAP, reference is made to the corresponding product dRR.*

The present document exclusively aims at investigating whether the TWA approach can in principle be used for Mesosulfuron-methyl and Lemna, from the general science perspective.

Moreover, it should be noted that – according to the Aquatic Guidance Document (EFSA, 2013; cf. Decision scheme B of Section 2.1.2) - the use of TWA concentrations in combination with Tier-1 endpoints is by definition no 'refinement' but still Tier-1 within the tiered approach. Accordingly, in the base case the "highest available tier" refers to Tier-1 data without any further refinements, but the approach may also be applied to any following higher tier level, as a secondary step.

→ Go to 2

2. Is the $RAC_{sw,ch}$ derived from a test with algae, or from a long-term (≥ 7 days) test with another water organism and the following conditions apply: (i) loss of the a.s. from water is more than 20% of nominal at the end of the exposure period and (ii) the toxicity estimate (e.g. EC_{10} or NOEC) is expressed in terms of nominal/initially measured concentration of the a.s.?

Yes: $PEC_{sw,twa}$ not appropriate (low risk not demonstrated)

No: Go to 3

Answer for Mesosulfuron-methyl & Lemna: *No. The $RAC_{sw,ch}$ is derived from a 7 days constant exposure period with Lemna gibba based on nominal concentrations (KCA 8.2.7/09, Bruns; 2013; M-445139-01-1, 1st week data). There was no indication for a major compound decline. For unknown reasons the recoveries at day 7 were even higher than at day 0 at all treatment levels (see table 4.1 of the report).*

→ Go to 3

3. Is the $RAC_{sw,ch}$ based on treatment-related responses of the relevant test species early in the chronic test (e.g. during the initial 96-hours observed mortality/immobility in tests with animals, or 50% reduction in growth rate in tests with macrophytes, in the treatment level above the one from which the $RAC_{sw,ch}$ is derived) or is the acute to chronic ratio (acute $L(E)C_{50}$/chronic NOEC or acute $L(E)C_{50}$/chronic EC_{10}) based on immobility or mortality < 10?

Yes: $PEC_{sw,twa}$ not appropriate (low risk not demonstrated)

No: Go to 4

Answer for Mesosulfuron-methyl & Lemna**: No. From the study of Bruns (2013); M-445139-01-1, the RAC of 0.129 µg/L has been derived from the $E_rC_{50\ frond\ area}$ = 1.29 µg a.s./L. Maximum effects on growth rate of frond area of 74.92% were observed between day 5 and day 7 at the nominal treatment level of 1.55 µg/L which is above the one from which the $RAC_{sw,ch}$ has been derived. In contrast, the effect on growth rate of frond area was only 36.75% at 1.55 µg/L between day 0 and 3. **The results clearly indicate that no early onset of effects has occurred.

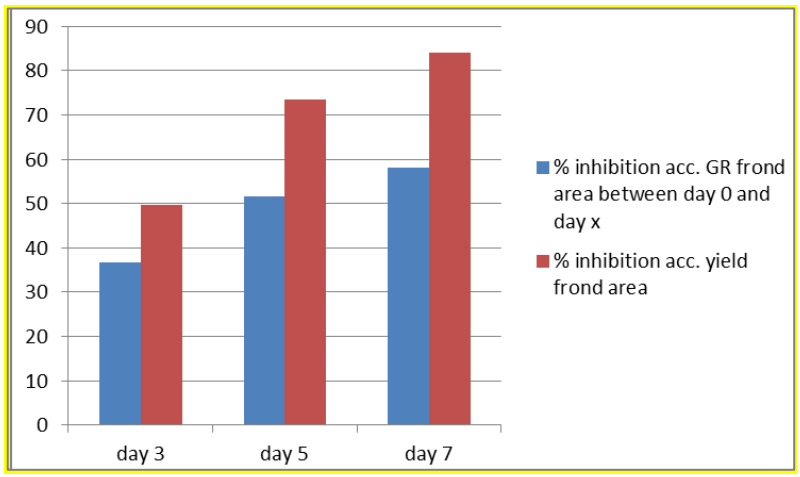


Figure A 12: Percent effects of nominal 1.55 µg mesosulfuron-methyl/L on frond area growth rate and yield

In Figure A 12 both, growth rate and yield data are presented. However, it has to be made clear that question 3 which deals with the onset of effects should be answered based on biomass rather than on growth rate data. Under constant exposure conditions which are intended for Lemna standard (Tier 1) studies, effects on growth rate are expected to be stable over time. As a consequence, if question 3 is on the concentration above the one delivering the 7d-E_rC_{50}, it is almost inevitable to find a 50% growth rate reduction also for the early phase of the study (i.e. day 0-2 or 0-3).
With regard to the question on acute to chronic ratio, it should be mentioned that this point does not apply to macrophytes for which no acute studies are performed.

Analysis based on simulations
To further explore time to onset of effects, simulations (in silico experiments) were performed using a mechanistic Lemna model parameterized for Mesosulfuron-methyl (Heine 2017a, M-600766-01-1). The development of this mechanistic model has been published in an international peer reviewed journal (Schmitt et al. 2013, M-455483-01-1). The entire results of the model based analysis, including a detailed description of the modelling tasks, are presented in a separate report (Heine 2017b, M-600786-01-1). The model was calibrated and validated with Lemna studies.

Model based analysis
The Lemna model uses an EC_{50} that is based on internal concentration of Mesosulfuron-methyl. This value is used as a reference to define the treatment level above the one from which the $RAC_{sw,ch}$ has been derived. Therefore, for modelling the onset of effects a treatment of 1.8 µg a.s./L was selected. This differs from the treatment that is used to evaluate the onset of effects on an experimental basis.

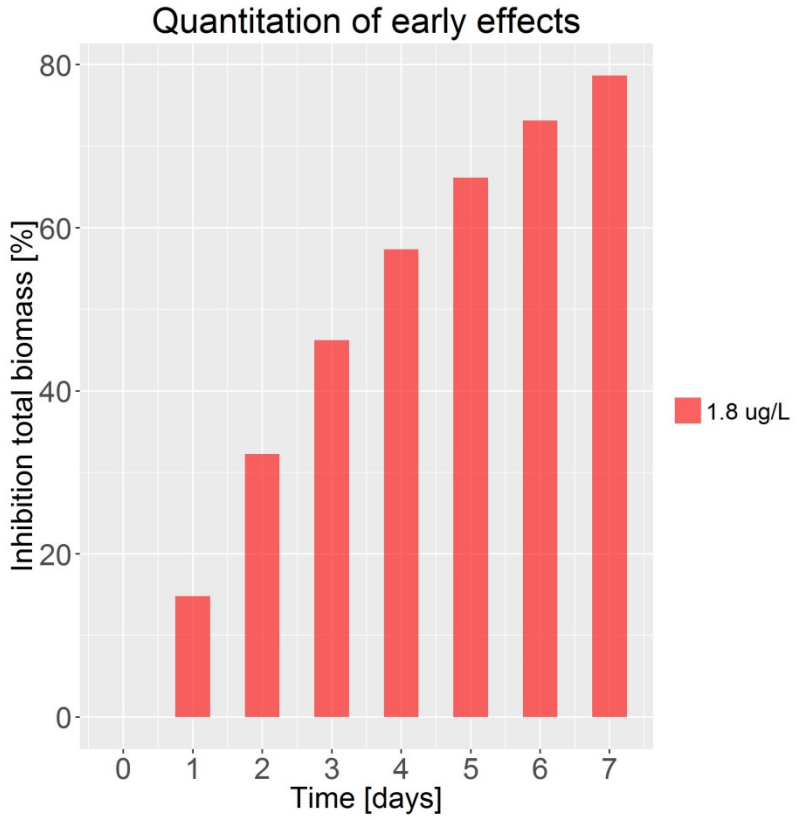


Figure A 13: Simulated effect on biomass during exposure to Mesosulfuron-methyl using the mechanistic Lemna effect model.

As shown in Figure A 13, predicted effects on biomass at the concentration of 1.8 µg a.s./L during the initial 2-3 days of the modelling experiment are clearly less than 50% and thus confirm the conclusions from the biological study above.

→ Go to 4

4. Is it demonstrated by the notifier that, for the organisms and the PPP under evaluation and/or PPP with a similar toxic mode of action (read-across information), the following phenomena are not likely: (i) latency of effects due to short-term exposure; (ii) the co-occurrence of exposure and specific sensitive life stages that last a short time only?

Yes: Go to 5

No: $PEC_{sw,twa}$ not appropriate (low risk not demonstrated)

Answer for Mesosulfuron-methyl & Lemna:
Yes. In a Lemna peak exposure study performed with Mesosulfuron-methyl (Kuhl (2016); M-577164-01-1) normal growth was observed already two days after a 24h pulse of up to 100 µg a.s./L. This is reflected in the parallel growth lines from day 4 to day 7 in Figures 1 to 3 and 7 to 9 of the study report. Also, no visual signs of phytotoxicity were observed in this study which demonstrates that the compound temporarily inhibited growth but did not produce any irreversible damage, even at unrealistically high short-term exposure concentrations.

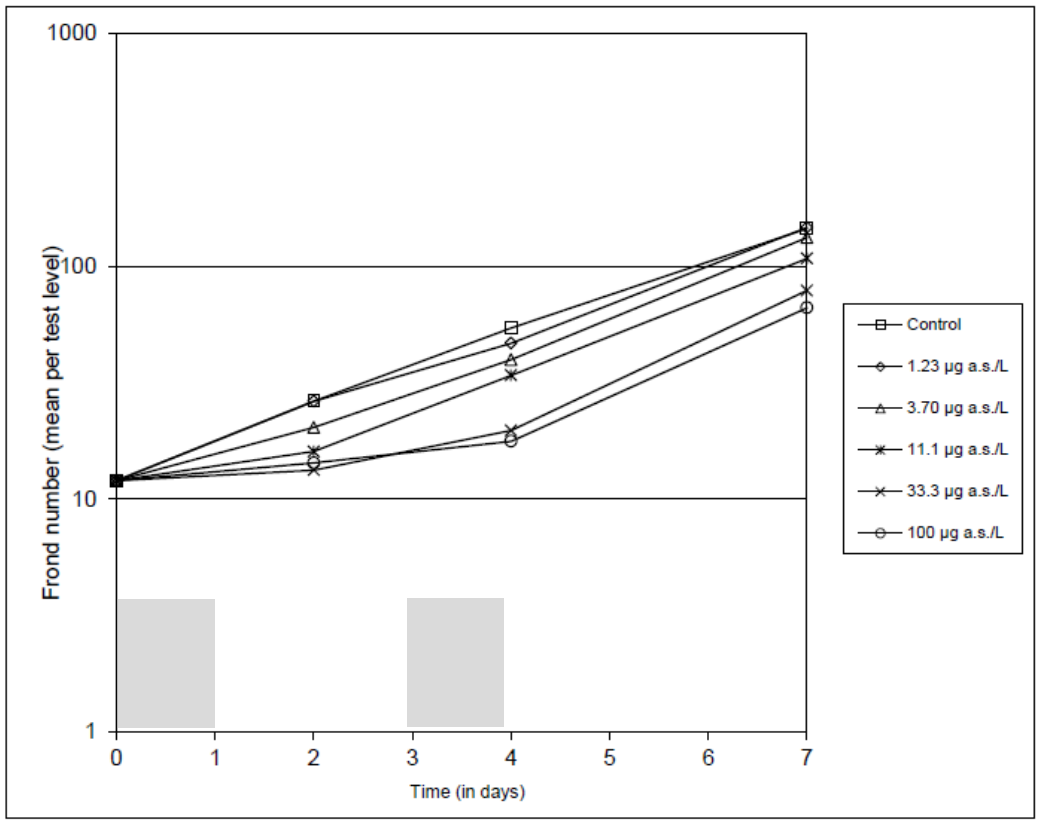


Figure 1: Design 1: Frond numbers over time
Design 1: two 24 hour peaks on day 0 and 3

Figure A 14: Example of one figure from Kuhl (2016; M-577164-01-1) showing the parallel growth lines between day 4 and 7, in grey: exposure pattern.

In addition, in a Lemna recovery study with Mesosulfuron-methyl (KCA 8.2.7/07; Sowig & Gosch (2002); M-206814-01-1) Lemna was exposed to concentrations up to nominal 10 µg a.s./L / mean measured 9.41 µg a.s./L for seven days. During the subsequent seven day recovery phase in clean medium, effects on frond number, frond area and phytotoxicity decreased over time with no indication for any delayed effects as a result of initial high exposure.

Delayed effects are generally not known for sulfonyl urea herbicides and aquatic plants. Moreover, according to the outcome of a consultation for the corrigendum of the Aquatic Guidance Document (EFSA, 2016), the criterion only needs to be addressed in the specific case of rooted macrophytes and thus not for Lemna.

To further explore potential latency of effects, simulations (in silico experiments) were performed with the Lemna model parameterized and validated for Mesosulfuron-methyl (as explained above). As shown in Figure A 15 the in silico experiments did not give any indication for delayed effects on Lemna growth one day after simulated exposure.

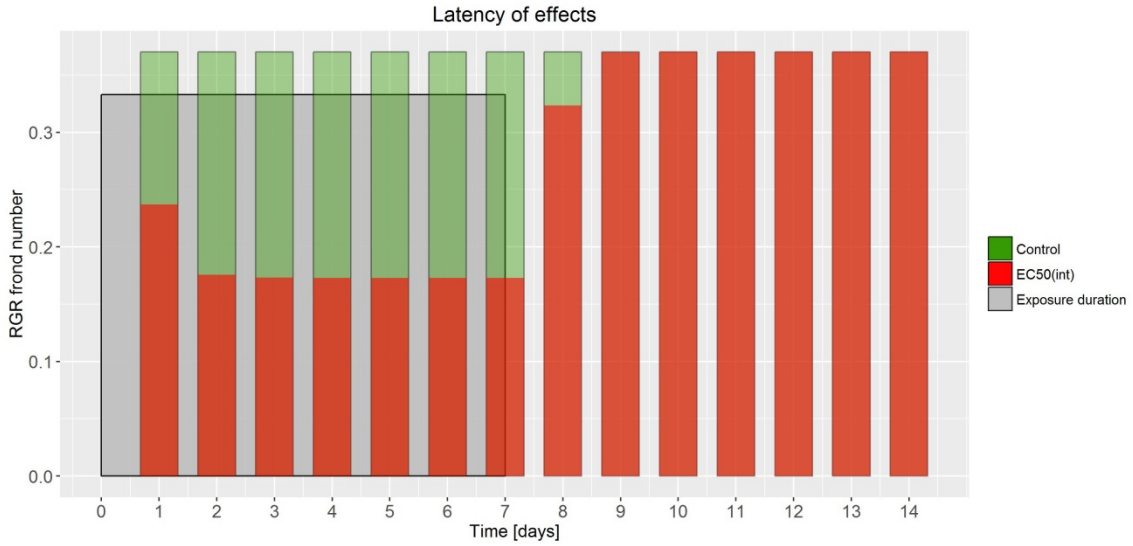


Figure A 15: Simulated effect on growth rate during and after exposure to Mesosulfuron-methyl using the mechanistic Lemna effect model.

With regard to the second part (ii) of question 4, the EFSA AGD (p. 48) gives examples for what is meant by specific sensitive life stages: 'e.g. malformations during metamorphosis, effects caused by endocrine disruption'.
This point is not related to macrophytes for which coincidence of exposure and a specific sensitive life stage is not an issue, but rather refers to other aquatic organisms e.g. fish. Lemna propagates by vegetative multiplication. Due to the exponential growth, a Lemna study covers several life cycles of that species and derived endpoints integrate any potential differences in sensitivity (e.g. young vs. older fronds).

→ Go to 5

5. *Is $PEC_{sw,7d\text{-}twa}$ (of highest available tier) > $RAC_{sw,ch}$ (of highest available tier)?*

Yes: Go to 6

No: Low risk demonstrated

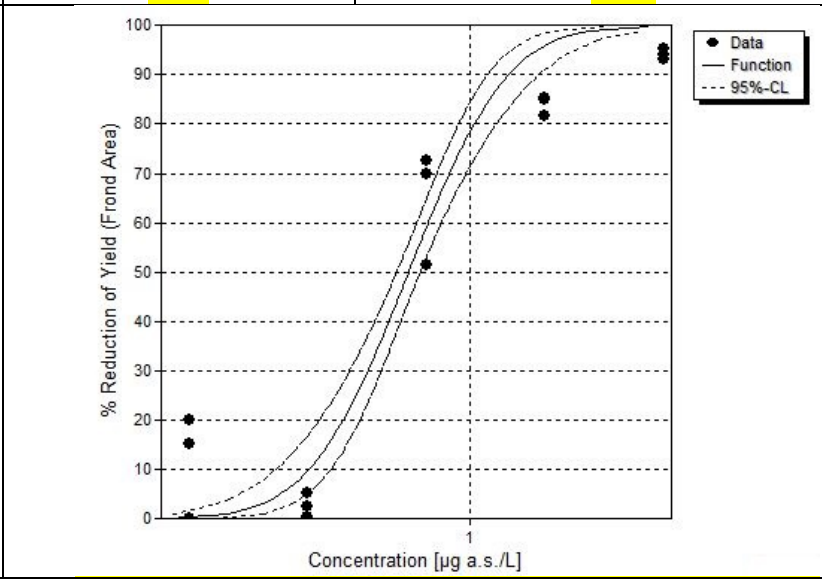
***Answer for Mesosulfuron-methyl & Lemna**: No. Please refer to the corresponding product dRR document) for a detailed risk assessment based on $PEC_{sw,7d\text{-}twa}$ and Lemna.*

Direct proof of conservatism of TWA for Mesosulfuron-methyl
The following two studies were considered in the evaluation of conservatism of TWA for Mesosulfuron-methyl:

- *7-day constant exposure test : first week of study Bruns (2013); M-445139-01-1 [EU evaluated: KCA 8.2.7/09]*
- *1+6-day pulsed exposure test (first week of design 2): Kuhl (2016); M-577164-01-1*

In Table A 6, data of the 7d constant exposure test is given, including observed inhibitions of 7d frond area yield and effects as predicted by probit. The table also includes the dose-response curve for the variable 7d frond number yield derived from Toxrat and basic parameters like EC_{50} and slope.

Table A 6: Observed and probit calculated inhibitions of frond area yield for the constant exposure study of Bruns (2013); M-445139-01-1

7d-exposure concentration [µg/L]	*Inhibition of yield [%]*	
	observed	*calculated according to the probit function**
Control	-	-
0.194	*6.07*	*<0.01*
0.388	*2.57*	*9.0*
0.775	*64.61*	*59.8*
1.55	*83.95*	*96.5*
3.10	*94.18*	*>99.9*
**Parameters for predictions: Model: probit E_yC_{50} = 0.697 µg/L Slope= 5.295*		

In Table A 7, data of the pulsed exposure study is summarized including 7d-TWA-values calculated for each test level (7d-TWA = conc. 1/7), inhibitions of frond area yield observed in this study, and compared versus effects predicted for the same TWA integral exposure based on the concentration-response curve from the constant exposure study.*

Table A 7: 7d-twa concentrations, observed inhibitions of frond area yield in the pulsed exposure study of Kuhl (2016); M-577164-01-1; one peak exposure.

Tested 1-day peak concentration [µg/L]	*Calculated equivalent 7d-TWA concentration* [µg/L]*	*Inhibition of yield [%]*	
		as experimentally observed in the peak-exposure study	*as predicted for an equivalent 7d-TWA concentration based on probit function of the 7 day constant exposure study data*
Control	-	-	-
1.23	*0.176*	*12.2*	*<0.1*
3.70	*0.529*	*32.2*	*26.2*
11.1	*1.586*	*48.6*	*97.1*
33.3	*4.757*	*55.1*	*100.0*
100	*14.286*	*65.3*	*100.0*

** as evaluation can be based on nominal values for the present study, 7 day -TWA = 1 day peak concentration / 7.*

Figure A 16 displays the comparison of measured effects of pulsed exposure vs. effects predicted for these pulses based on 7d-TWA values (see explanations under point 4.1). The TWA approach was able to predict the effects of pulsed exposure either realistically or even conservatively overestimated effects (data points

in white to green diagram area). Only a single data pair (12.2%/<0.1%) is found located borderline in the red diagram area, however this data point is based on a very small measured effect of only 12.2%, i.e. out of the linear dose-response range of 15 - 85%. It should also be noted that Lemna is being regulated at the 50% effect level, for which TWA-based predictions are clearly accurate to conservative. Moreover, even the 7-day TWA value of 0.176 µg/L corresponding to the lowest pulse treatment level of 1.23 µg/L notably exceeds the RAC of 0.129 µg/L, but led to only very little (12.2%) measured effect.

Therefore, it could be demonstrated with this new method based on two independent experiments that the TWA approach with a 7d time window is conservative and can be used within the regulatory aquatic risk assessment for effect of mesosulfuron on Lemna.

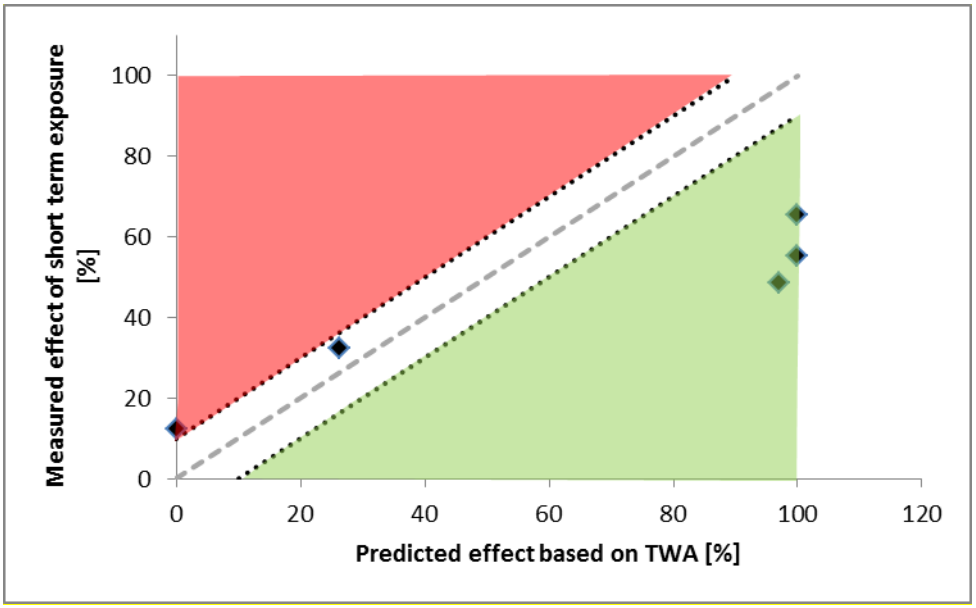


Figure A 16: Comparison of predicted and observed inhibitions for Mesosulfuron-methyl based on 7d-TWA values

Conclusions:

The applicability of $PEC_{sw,twa}$ in the chronic risk assessment for Lemna gibba and Mesosulfuron-methyl was investigated by using two different approaches: the analysis according to the EFSA AGD decision scheme, and the direct proof of conservatism of TWA.
The analysis of biological data from several experiments, on the one hand, and effect modelling on the other hand, both show that all criteria set in the EFSA AGD are fulfilled. Moreover, it was demonstrated phenomenologically that this approach is conservative for this specific substance.

As an overall conclusion, it is considered justified to base risk assessment for Lemna gibba and Mesosulfuron-methyl on 7d time-weighted average concentrations ($PEC_{sw,\ 7d\text{-}twa}$).

Detailed information to Section 9.5.2.5:

Tier 2C: Higher-tier assessment based on refined exposure testing combined with exposure pattern analysis

Additional information on extraction and characterisation of exposure patterns from the FOCUSsw simulations:

In the FOCUS Step 3 simulations, the FOCUS model TOXSWA (TOXic substances in Surface WAters) calculates the pesticide distribution and concentrations in the water body that results for the various scenarios from the different routes of entry, in dependency of the substance parameters. The model version TOXSWA 4.4.3 provides detailed output files (.out) which list surface water concentrations for the whole evaluation period of one year, in an hourly resolution. This data can be used for a refined exposure assessment and analysis of time-variable exposure patterns. In order to obtain a meaningful description of these extensive data an evaluation tool (EPAT, Exposure Pattern Analysis Tool) was developed by Bastiansen et al. (2016), on behalf of the European Crop Protection Association (ECPA). EPAT uses the TOXSWA *.out files as its input together with a user-defined threshold concentration (here: RAC of substance) and scans the concentration time series in the *.out file for the exceedances of that given threshold value.*

*According to the program manual EPAT analyses and presents statistics on "events", which are defined as periods during which pesticide concentrations exceed the defined threshold. For each event EPAT calculates its maximum concentration, duration, number of peaks (local maxima) and interval from the last event to the current event, as well as time weighted average concentration (TWAC) and area under the curve (AUC) for individual events and for moving window analysis. EPAT produces three output files per analysis, one containing a detailed description of exposure events (*_events.txt), one containing a summary of exposure events (*_event summary.txt) and one containing results of the moving window analysis (*_moving window summary.txt). The here presented exposure discussion is based on the results presented in the *_event summary.txt files on the number of events, their duration and interval between events if relevant. Other parameters were not used for the analysis.*

The TOXSWA output files (.out) to the simulation runs of the present assessments are submitted electronically as supplemental modelling information. The EPAT Tool and its Manual are available for download free of charge at the developer's website (RIFCON GmbH): Program download: https://www.rifcon.de/files/downloads/EPAT_1.1.1_setup.exe, Manual: Report No. R1520392.*

Detailed information to Section 9.5.2.6:

Tier 2C: Higher-tier assessment based on refined exposure testing combined with exposure pattern analysis - considering multi-year exposure simulations

In response to concerns over the representativeness of the FOCUS model's inherent single weather year in the context of refined exposure assessment, additional FOCUS exposure simulations have been conducted for an extended period of 20 years (multi-year calculations). For information on the methodology applied, reference is made to the PEC_{sw} FOCUS Multiyear methodology and application reports (Bolekhan A., 2017; M-602115-01-1, and Bolekhan et al., 2017; M-603045- 01-1), and their corresponding summaries in the E-fate section to this dRR.

As it is not possible to easily judge which of the resulting twenty annual exposure patterns per scenario water body should be considered the relevant one for macrophyte risk assessment, the characterizing properties (i.e. PEC_{max}, number of peak events, duration of peaks events, and interval between events) of each simulated year have been assessed separately: For each FOCUS scenario ten cumulative distribution figures were generated (explained example see

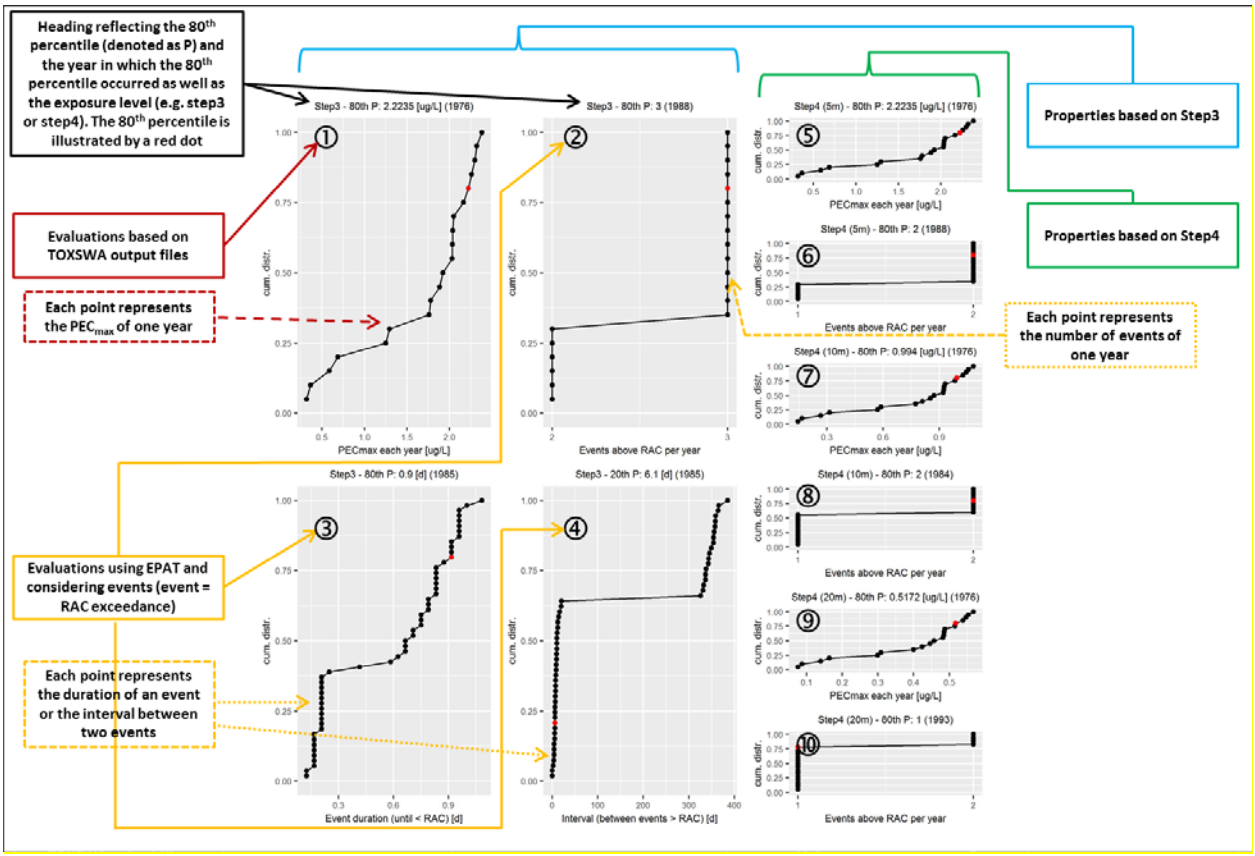
Figure A 17 below), illustrating the statistic of properties of the multiyear simulated exposure patterns. These were then used to synthesize a single surrogate exposure pattern for ecotoxicological risk assessment that describes a realistic worst-case annual exposure situation, by combining the 80th percentile PEC$_{sw,max}$, the 80th percentile number of events and the 80th percentile duration of events with the 20th percentile interval between peak events of the individual exposure pattern properties. Such approach will consolidate the 20-year-data into a single representative 90th percentile worst case exposure pattern usable for conservative risk assessment. This is in accordance with the current concepts of EFSA for groundwater (EFSA, 2013) and soil risk assessment (EFSA, 2016). Since however there exists no EU agreed analysis of percentiles for multi-year FOCUS PECsw calculations so far, a detailed rationale for the above percentile selections, and including vulnerability analysis, is provided in the original modelling report (sections 4.3.1 and 4.3.2).

For risk assessment, the so generated conservative surrogate exposure pattern is then compared to the experimental results of a refined exposure study (2 peaks test, with 2 different time intervals, see A 2.2.3), in analogy to the Tier 2C risk assessment presented before for the standard FOCUS year.

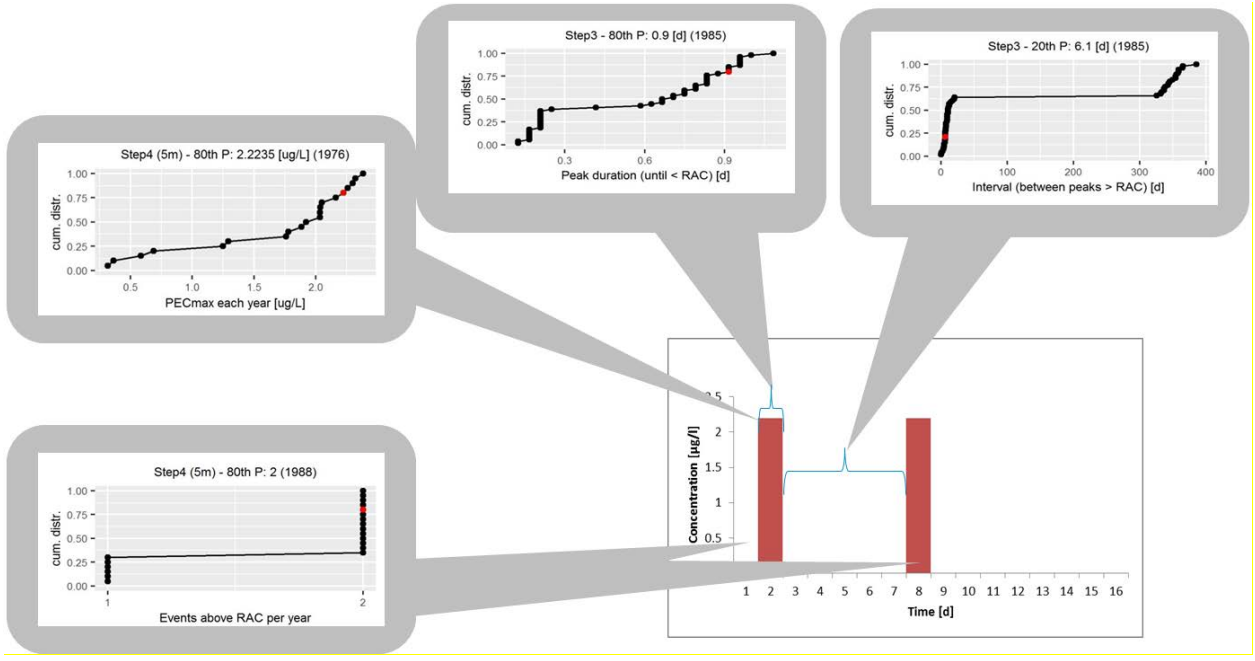
Where necessary to pass a risk assessment, PEC$_{max}$ and the number of peak events (i.e. concentrations above the RAC) can also be analysed at Step 4 (with 5 m, 10 m and 20 m buffer): In the illustrated example (

Figure A 17), at FOCUS Step 3 three events were identified. However, in the ecological tests used for risk assessment only exposure situations up to two events were experimentally addressed. Risk mitigation (Step 4, 5 m drift buffer) could therefore be applied to reduce the number of peak events (i.e. concentrations above the RAC) from three to two, so that the exposure situation could be compared to the ecological tests. To reduce complexity, only FOCUS step 3 level results were used to quantify the duration of and the interval between events, which is a conservative simplification.

Figure A 17: Example figure describing the exposure pattern of a multi-year FOCUS scenario



Synthesis of a 20-year characteristic and conservative exposure pattern:
(example case for Step 4 – 5 m):



FOCUS multiyear Scenario	***80th perc. PECmax [µg/L]***	***80th perc. events above Tier 1 RAC***	***80th perc. event duration above Tier 1 RAC [d]***	***20th per. interval betw. events above Tier 1 RAC [d]***
Example from ***Błąd! Nie można odnaleźć źródła odwołania.*** *– Step 3*	*2.2235*	*3 peaks*	*0.9*	*6.1*
Example from ***Błąd! Nie można odnaleźć źródła odwołania.*** *– Step 4 (5 m)*	*2.2235*	*2 peaks*	*0.9*	*6.1*
Remarks:	*taken from Step 4#*	*taken from Step 4*	*Step 3 value as conservative simplification*	*Step 3 value as conservative simplification*
	80th perc. PECmax assumed for both peaks, as conservative simplification			

 # In this example, PECmax is driven by run-off entry, and therefore not mitigated by 5 m drift buffer. However, one peak at Step 3 is a drift-peak, which is mitigated at Step 4. This reduces the number of events from 3 to 2 peaks.

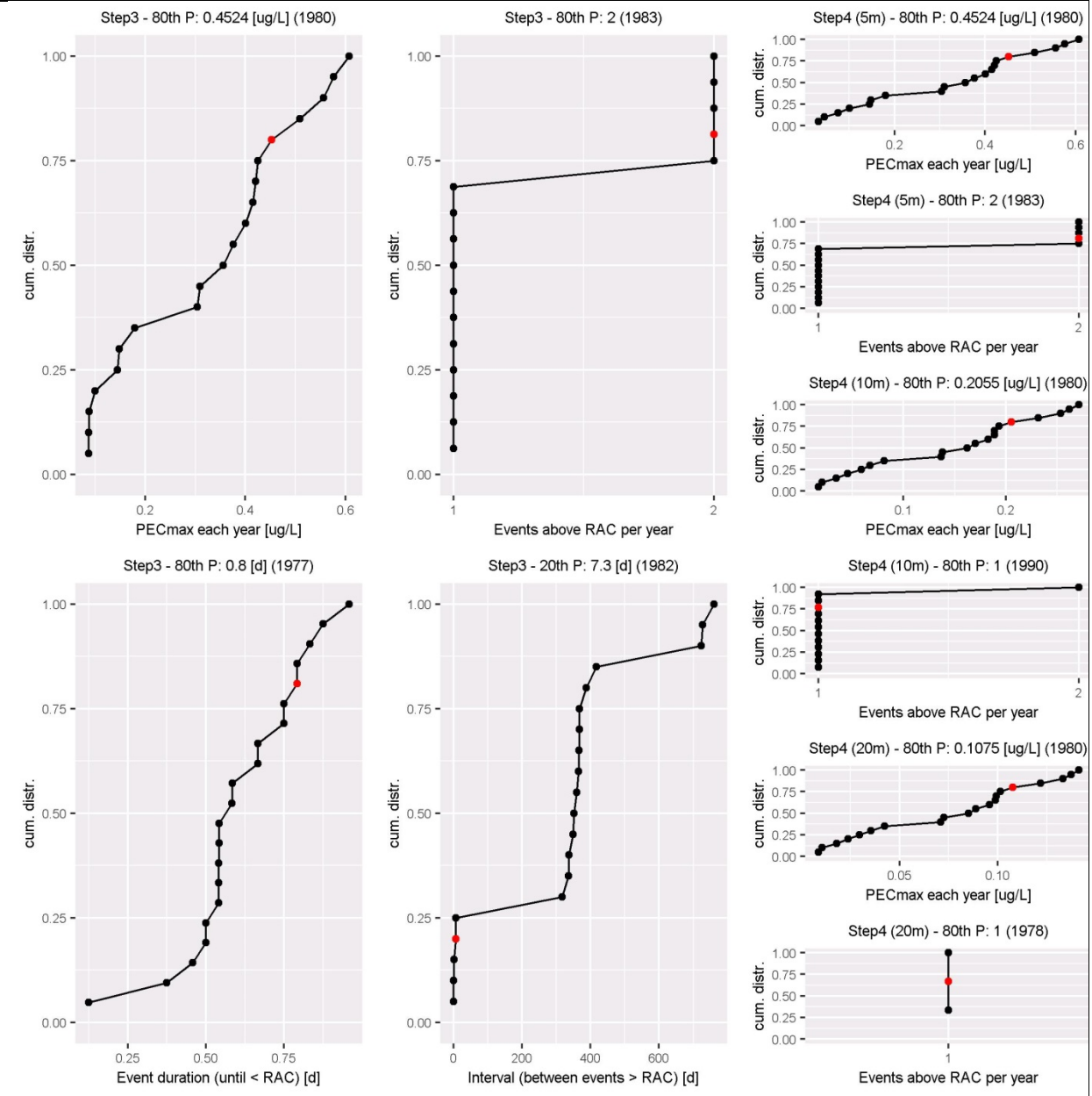
For mesosulfuron-methyl, for peaks with an interval of approx. 3 days, Design 1 of study M-577164-01-1 (study duration of 7 days with peaks on d0 and d3) will be used with a peak-E_rC_{50} of 10.9 µg a.s./L delivering a peak-RAC of 1.09 µg a.s./L. Design 2 (study duration of 14 days with peaks on d0 and d7) demonstrates toxicological independence of peaks at the defined interval. The independence of peaks is ascertained through the similar effect patterns following each of the 2 peaks and statistical analysis with the t-test on paired samples (α = 0.05) which shows that, for all concentrations and all biological parameters (i.e. frond number and frond area), no statistically significant difference is observed between the growth rates of the 1st and 2nd weeks. Accordingly, for peaks that are toxicologically independent (interval of 7 days or more) Design 2 is applicable that resulted in a peak-E_rC_{50} > 100 µg a.s./L which corresponds to a peak-RAC of > 10.0 µg a.s./L. For an overview see the table below.

Table A 8: Derivation of peak-RACs from the Lemna 2-peak study with mesosulfuron-methyl

Test species	***Test system***	***Test duration***	***Endpoint [µg as/L]***		***Peak-RAC [µg as/L]***	***Reference***
Lemna gibba (duck weed)	*growth inhibition, 2-peak exposure*	*Design 1:* *7 d , peaks on d0 & d3*	*E_rC_{50} (days 0-7)*	*10.9 µg/L*	*1.09 µg/L*	*Kuhl, 2016 EBMMN160 M-577164-01-1*
		Design 2: *14 d , peaks on d0 & d7*	*E_rC_{50} (days 0-7)*	*> 100.0 µg/L*	*> 10.0 µg/L*	
			E_rC_{50} (days 7-14)	*> 100.0 µg/L*	*> 10.0 µg/L*	

Risk assessment:

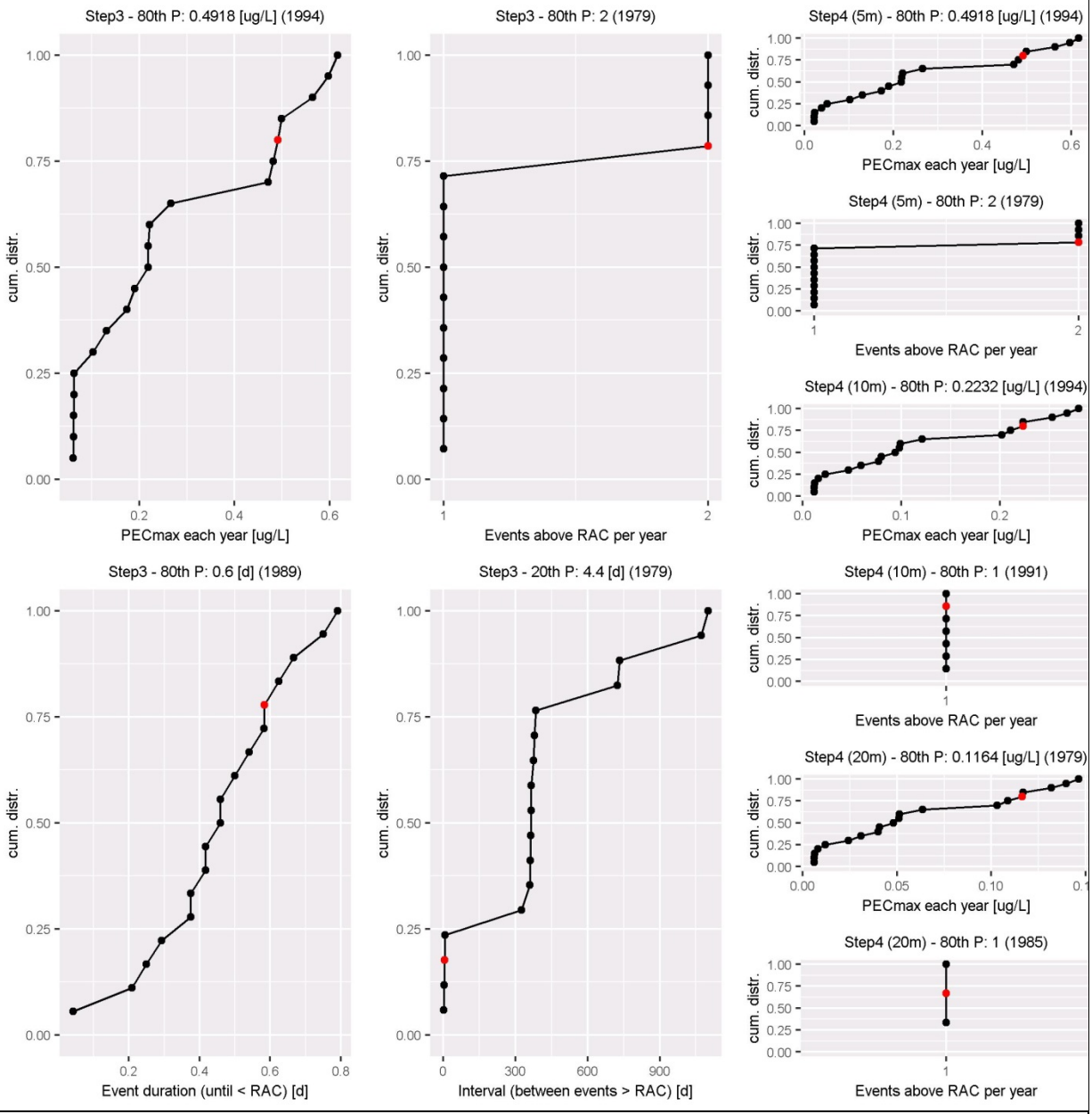
use group B – FOCUS multiyear Scenario R3 stream:
(end of winter to spring use on winter cereals / rate = 15 g/ha MSM)



The 80th percentiles of the peak height, duration and number of peaks at step 3 and 20th percentile of interval show that 2 peaks are expected at a maximum of 0.4524 µg/L for a duration of 0.8 days, 7.3 days apart. The peak exposure Lemna study showed that 24h-peaks having a 7-d interval are independent on an effect point of view.
Thus, these results have to be compared to the peak-RAC of > 10 µg/L for independent peaks. The PEC is lower than the RAC so it can be concluded that the risk is considered acceptable in these conservative conditions of a 20 years FOCUS simulation.

Consequently, the risk to aquatic macrophytes arising from these peaks is considered to be low, with a resulting RQ of < 0.045.

use group B – FOCUS multiyear Scenario R4 stream:
(end of winter to spring use on winter cereals / rate = 15 g/ha MSM)



The 80th percentiles of the peak height, duration and number of peaks at step 3 and 20th percentile of interval show that 2 peaks are expected at a maximum of 0.4918 µg/L for a duration of 0.6 days, 4.4 days apart.
Thus, these results have to be compared to the peak-RAC of 1.09 µg/L for dependent peaks (i.e. 2 peaks of 1 d with a 3-d interval). The PEC is lower than the RAC so it can be concluded that the risk is considered acceptable in these conservative conditions of a 20 years FOCUS simulation.

Consequently, the risk to aquatic macrophytes arising from these peaks is considered to be low, with a resulting RQ of 0.45.

Overall conclusion:
The above assessments based on multiyear simulations confirmed the conclusion of acceptable risk for macrophytes previously made for the standard FOCUS year.

Detailed information to Section 9.5.2.7:

Ecological modelling approaches, and their use in higher-tier risk assessment for the present product

(c) Lemna TK/TD population model - General description

The classical tier 1 macrophyte risk assessment tends to overestimate the impact of time variable and in particular short-term exposure patterns, since only the PECmax and the EC_{50} from toxicological tests with constant concentration over long periods are used for the risk characterization. To increase the realism of risk characterization, different approaches are available (Figure A 18) in the Aquatic Guidance Document. One of the recommendations by EFSA is the use of TK/TD models. For Lemna, as the Tier-1 data is already determined on population level, it is reasonable that all higher Tiers are also addressing the population level.

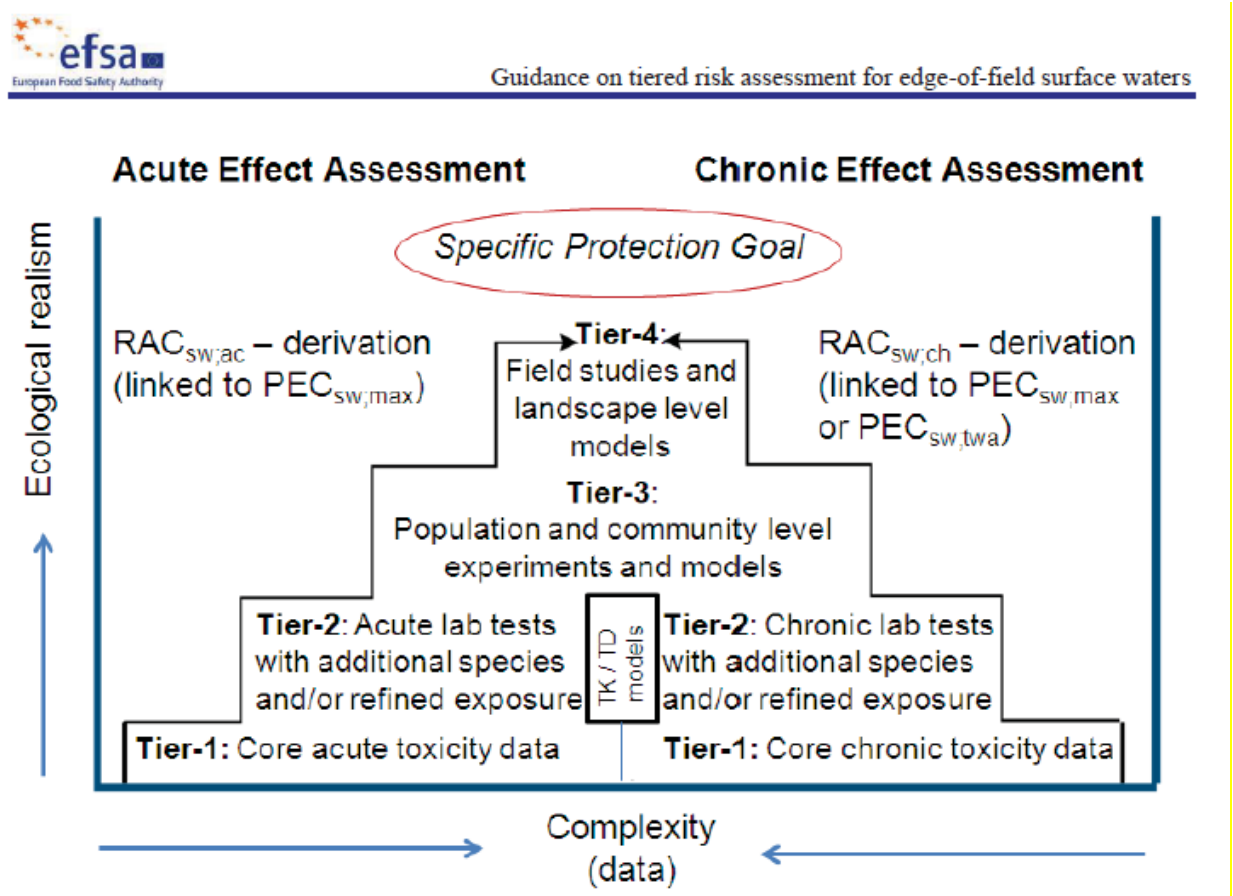


Figure A 18: Schematic presentation of the tiered effect assessment approach for plant protection products taken from EFSA aquatic guidance document (EFSA, 2013)

The here presented approach is based on a TK/TD population model of Lemna published by Schmitt et al (2013), which addresses the issue of time variable exposure by enabling a realistic link of exposure to effects at the population level. As the population level is considered, this approach is in accordance with the specific protection goal for macrophytes.

This specific model has been evaluated and considered suitable by EFSA for aquatic risk assessment in

particular of sulfonlyurea herbicdes, in their Scientific Opinion[22] (2018) on state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models, the experts concluded as follows in the section on Evaluation of the application in risk assessment:

> *"The model seems to work well for the sulfonyl-urea compound and the validation data as presented in Schmitt et al., 2013, but the model should be validated on herbicides with other modes of action. Summarising, the Lemna model appears suitable for use in risk assessment to evaluate effects of time-variable exposure on Lemna growth."*

All aspects identified by EFSA to require further attention have been picked up in the respective modelling reports to the present submission.

Reference:	***KCP 10.2.3/03***
Title:	*Mechanistic TK/TD-model simulating the effect of growth inhibitors on Lemna populations*
Report:	*Schmitt, W.; Bruns, E.; Dollinger, M.; Sowig, P.; 2013; M-455483-01-1*
Authority registration No:	
Guideline(s):	*not applicable*
Deviations:	*not applicable*
GLP/GEP:	*no*
Acceptability:	The same approach which is mentioned in Core Assessment of Atlantis 12 OD, section 9, 2020, (zRMS:PL) is used for the current risk assessment. *The below studies (10.2.3/03, 10.2.3/04, 10.2.3/05, 10.2.3/06, 10.2.3/07) have not been evaluated in this core document.* *The presented approach uses a previously published TK/TD population model of Lemna (Schmitt et al. 2013) to link the effects from FOCUSsw exposure patterns to the specific protection goals. However, the agreed outcome at the 4th Central Zone Harmonisation meeting (Sept 2018, Dessau, DE)- states the follow-ing in the meeting minutes "In principle, MS would tend to follow the recommendations of the Sc Op on TKTD, i.e. DEBtox and primary producers models: considered as not yet fit for purpose"; as such this approach has not been fully evaluated in this core document.*
Duplication (if vertebrate study):	

The primary objective of the model is the extrapolation of effects determined using standardised exposure patterns in laboratory studies to realistic - i.e. temporally varying - exposures as they occur in small water bodies at the edge of fields treated with plant protection products. A key component of the model is thus a toxicokinetic sub-model translating external concentrations into internal concentrations. The model should additionally allow the prediction of effects on Lemna populations under realistic, temporally varying environmental conditions, i.e., temperature and light, based on observations derived under standard laboratory conditions. For use of the model in risk assessments, pure extrapolation of exposure patterns and additional consideration of realistic environmental conditions are considered as two separate steps. The primary endpoint that is derived from the simulation results is the reduction of biomass compared to an unaffected control. As a secondary endpoint, the duration of such effects can also be determined.

The concept of the Lemna TK/TD-population model is visualised in Figure A 19: Three main components, a toxicokinetic (TK), a toxicodynamic (TD) and a growth model can be identified.

[22] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2018. Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA Journal 2018;16(8):5377, 188 pp. https://doi.org/10.2903/j.efsa.2018.5377

Generally, the model is a combination of a one compartment TK model and a differential equation model describing the dynamic development of biomass based on photosynthesis rate and respiration rate. The TK model translates the substance concentration in the water body (external exposure) into a Lemna internal concentration of this substance. Based on the internal concentration the parameter photosynthesis rate is reduced via the TD model, thus reflecting the growth inhibiting effect of the toxicant for the subsequent growth model. Apart from the influence of the toxicant, photosynthesis rate and respiration rate may also be modulated by other external factors such as temperature, radiation, nutrition and biomass density. This allows for an extrapolation of the biomass growth behaviour to realistic environmental conditions. In the present context of providing a regulatory risk assessment based on FOCUSsw procedures (see following sections), the growth model can e.g. be parameterised for the constant conditions of a virtual laboratory, or for the variable environmental and climatic conditions of the FOCUS water bodies associated with the crop relevant FOCUSsw scenarios.

For a detailed description of all model relevant variables and their derivation, reference is made to the original publication; indepth specific information on these matters is also found provided in the model application report cited later under point (c) in the present section.

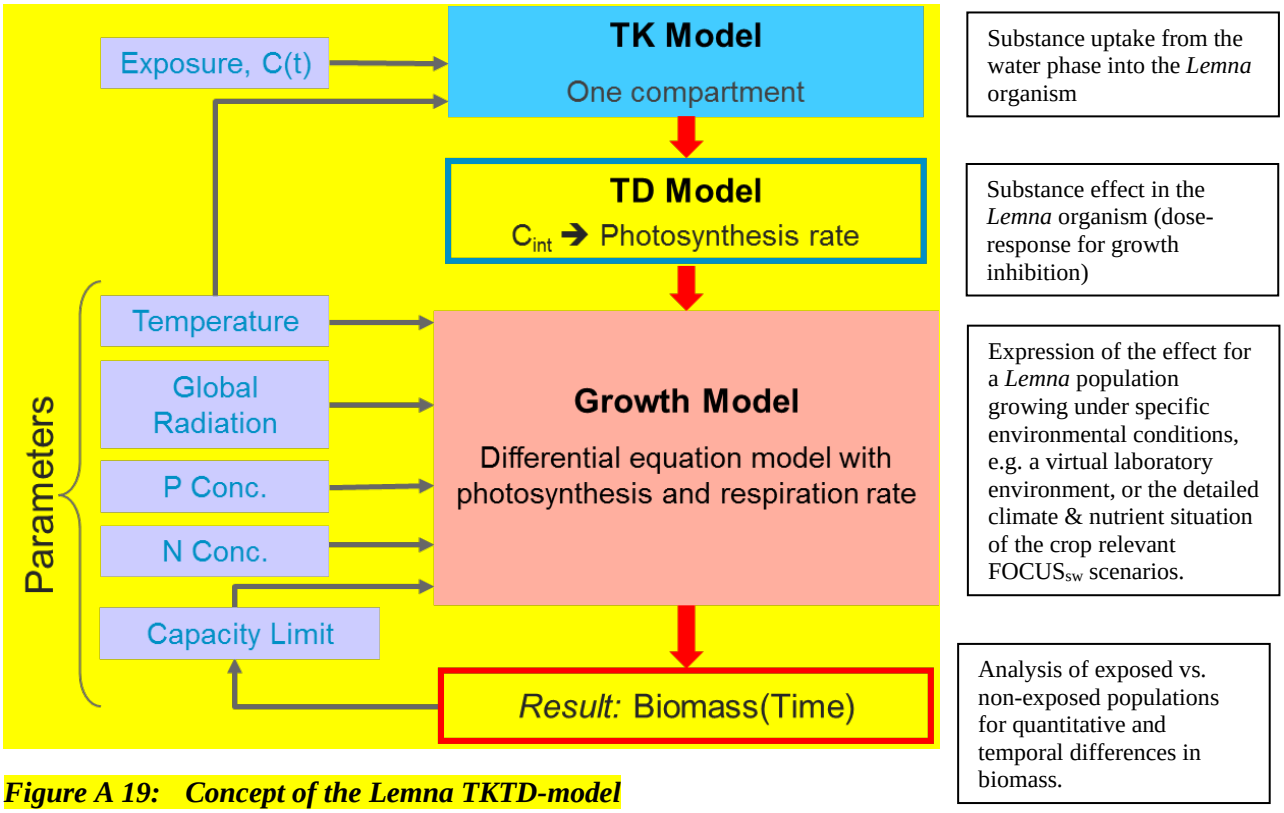


Figure A 19: Concept of the Lemna TKTD-model

(d) Model calibration and validation

The practical use of the model includes 3 major steps:

- *Model Calibration - to adjust the model to compound specific TK/TD parameters.*
- *Model Validation - to check and demonstrate the prediction power and accuracy of the calibrated model.*
- *Model Application - i.e. use of the model for the intended risk assessment purpose.*

The calibration and validation of the model is reported in details in Heine, 2017a. (M-602805-01-1) for iodosulfuron-methyl-sodium and its metabolite metsulfuron-methyl, and in Heine, 2017b; M-600766-01-1 for mesosulfuron-methyl. Summaries of these activities are provided here below:

Reference:	***KCP 10.2.3/04***
Title:	*Lemna TK/TD modelling - Compound-specific parameterization and validation for iodosulfuron-methyl-sodium and its metabolite metsulfuron-methyl*
Report:	*Heine, S.; 2017; EnSa-17-0639; M-602805-01-1*
Authority registration No:	
Guideline(s):	*not applicable*
Deviations:	*none*
GLP/GEP:	*no*
Acceptability:	Have not been evaluated in this core document.
Duplication (if vertebrate study):	

Materials and Methods:

This report describes the compound specific preparation of the generic toxicokinetic and toxicodynamic (TK/TD) Lemna model to be used for iodosulfuron-methyl-sodium and its metabolite metsulfuron-methyl.

In a first step, toxicokinetic and toxicodynamic parameters of the model are calibrated on selected datasets in terms of adjusting them so that the model can describe the measured effects over time in all concentrations of the dataset. Toxicokinetic and toxicodynamic parameters are the uptake rate (P_up) and the internal concentration-response relationship that is based on an $EC(int)_{50}$ and a value defining the slope of the curve (b).

In a second step, the fully parameterized model is validated by testing the predictive power of the model with an independent (different from the datasets used for model calibration) dataset having a different exposure situation. If the calibration and validation are successful it is proven that the model can be used to extrapolate to untested exposure situations for iodosulfuron-methyl-sodium and its metabolite AE F075736 [metsulfuron-methyl] with their specific mechanism of action in Lemna.

Results and Discussion:

Model calibration:
Model calibration is the process of adjusting model parameters until optimal fit to the dataset is obtained.

The plant growths parts of the model were calibrated using the rates of exponential growth measured for the untreated control groups of all studies.

*The TK and TD parts of the model for **iodosulfuron-methyl-sodium** were calibrated with the Lemna standard study Christ & Ruff, 1997 (M-141441-02-1; EU reviewed, see DAR) with constant exposure and with the Lemna peak exposure study (design 1) study of Kuhl (2016, M-574865-01-1; new study, see Appendix A 2.2.3 of this dRR). In this peak exposure study with a total duration of seven days, the effect of two peaks of 24h each on the growth of Lemna had been tested. The calibration results are shown in Figure A 20 and Figure A 21.*

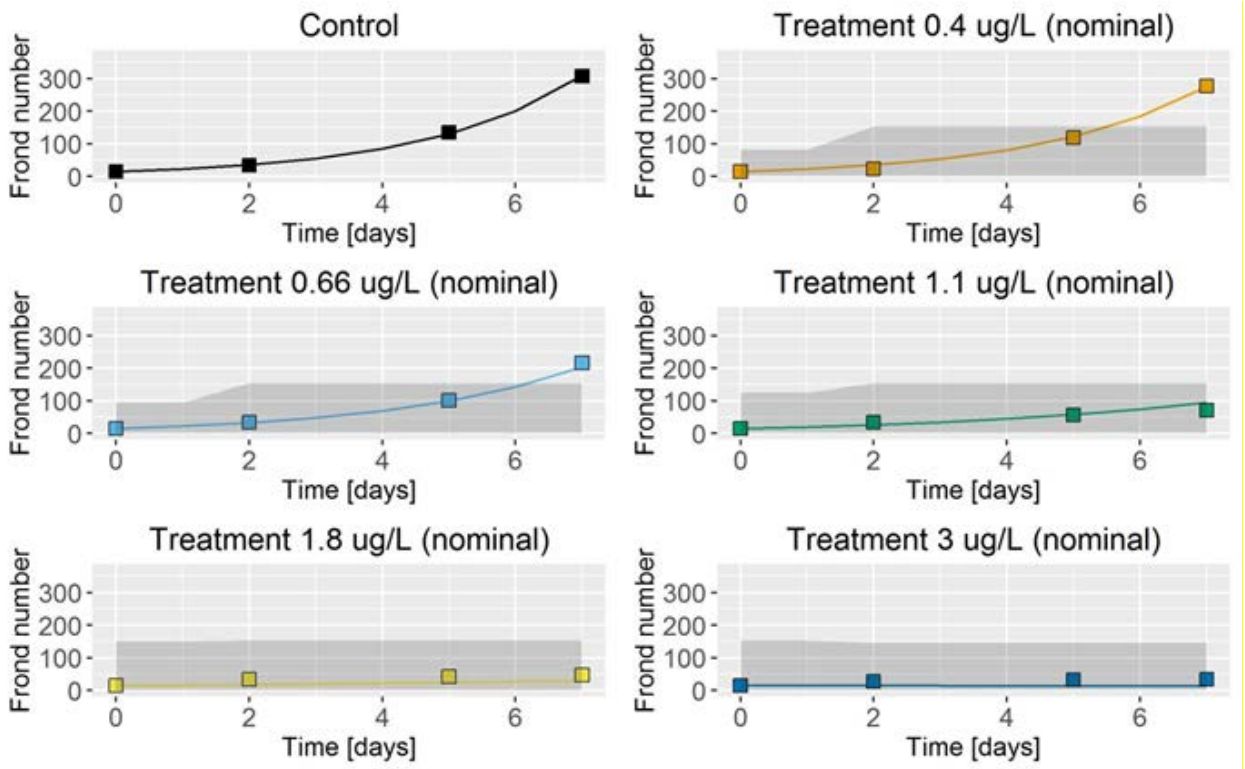


Figure A 20: ***Results of the toxicodynamic calibration for iodosulfuron-methyl-sodium with lines representing model output and symbols representing experimental data (the grey shaded area illustrates the concentration of iodosulfuron-methyl-sodium in water) 7 days constant exposure situation, based on data from study Christ & Ruff, 1997, M-141441-02-1.***

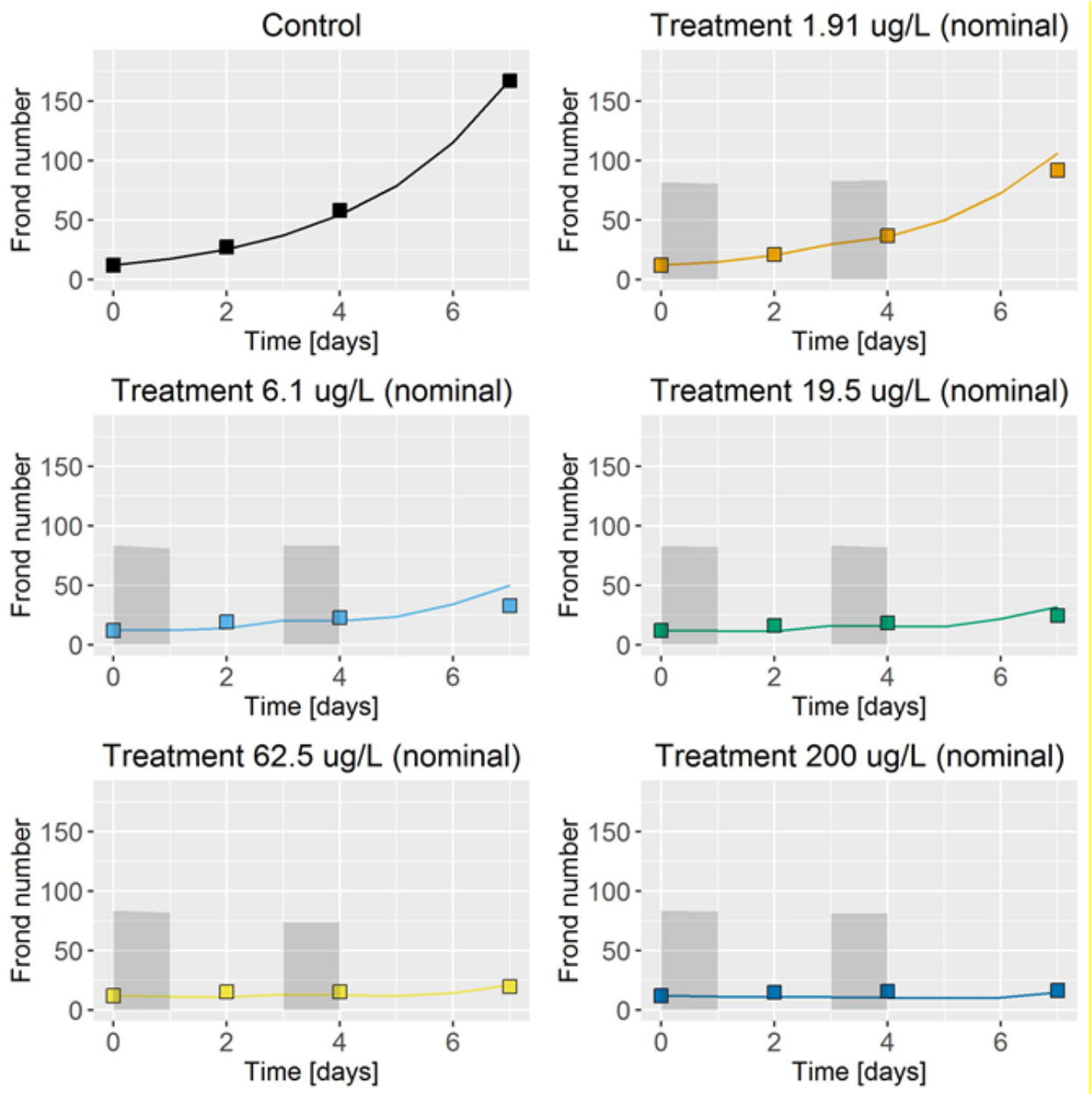


Figure A 21: ***Results of the model calibration for iodosulfuron-methyl-sodium with symbols representing experimental data and lines showing model results (grey areas illustrate the exposure situation): pulsed exposure with two 24 hours peak events at days 0 and 3 of a 7 days observation period, based on data from study Kuhl, 2016, M-574865-01-1; test series of 'design 1' study part***

The TK and TD parts of the model for ***metabolite AE F075736*** *(metsulfuron-methyl) of iodosulfuron-methyl-sodium were calibrated with the Lemna study of Kuhl (2016, M-600962-02-1, new study, see Appendix A 2.2.3 of this dRR). In this peak exposure study with a total duration of seven days, the effect of two peaks of 24h each on the growth of Lemna had been tested.*
The calibration results are shown in Figure A 22.

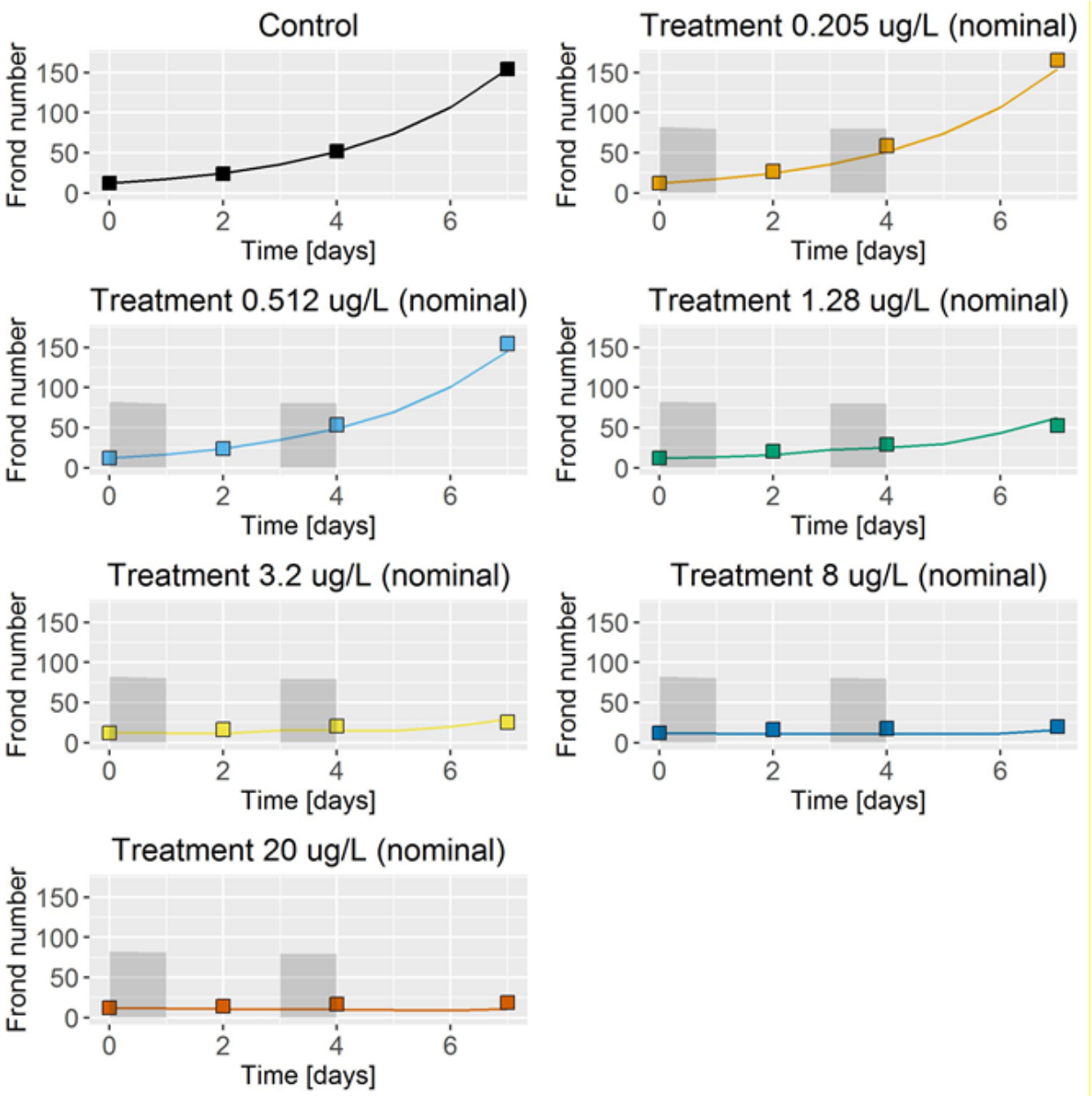


Figure A 22: ***Results of the model calibration for metabolite AE F075736 with symbols representing experimental data and lines showing model results (grey areas illustrate the exposure situation): pulsed exposure with two 24 hours peak events at days 0 and 3 of a 7 days observation period, based on data from study Kuhl, 2016, M-600962-02-1.***

Due to the number of available Lemna studies, the following robust model calibration could be generated:

Table A 9: Compound specific parameterization for iodosulfuron-methyl-sodium

Parameter	***Description***	***Value***	***Unit***	***Remark***
$EC_{50(int)}$	*Effective internal concentration at which 50% response is observed*	*1.3 [1.2 – 1.4]*	*µg/L*	*Calibrated*
b	*Value defining the slope of the dose-response function*	*3.5 [2.9 – 4.1]*	*-*	*Calibrated*

E_{max}	Maximum effect	1	-	Set to 1 to enables effect of up to100%
P_up	Cuticular permeability	0.032 [0.027 – 0.036]	cm/d	Calibrated
Kbm	Plant/water partition coefficient	0.72	-	Estimated

Table A 10: Compound specific parameterization for metabolite AE F075736 of iodosulfuron-methyl-sodium

Parameter	Description	Value	Unit	Remark
$EC_{50(int)}$	Effective internal concentration at which 50% response is observed	0.43 [0.38 – 0.47]	µg/L	Calibrated
b	Value defining the slope of the dose-response function	5.0 [4.8 – 5.2]	-	Calibrated
E_{max}	Maximum effect	1	-	Set to 1 to enables effect of up to100%
P_up	Cuticular permeability	0.017 [0.013 – 0.021]	cm/d	Calibrated
Kbm	Plant/water partition coefficient	0.71	-	Estimated

Model validation:

Exposure situations that were considered for the validation were short-term peaks (Figure A 23 for iodosulfuron-methyl sodium and Figure A 24 for metabolite AE F075736), as well as nearly constant exposure for seven days with a subsequent recovery phase of seven days (Figure A 25 for metabolite AE F075736). Overall, the model parameterization for both iodosulfuron-methyl-sodium and its metabolite AE F075736 can be deemed acceptable considering the excellent visual fit of the validation as shown in the figures below. Besides the visual assessment, the model efficiency (EF) was calculated according FOCUS kinetics (2006) report procedures. EF ranges from minus infinity to +1 with larger values indicating better agreement. EF compares the sum of squared differences between calculated and observed data. For EF > 0, the value gives an indication of the fraction of the dataset that can be explained by the model.

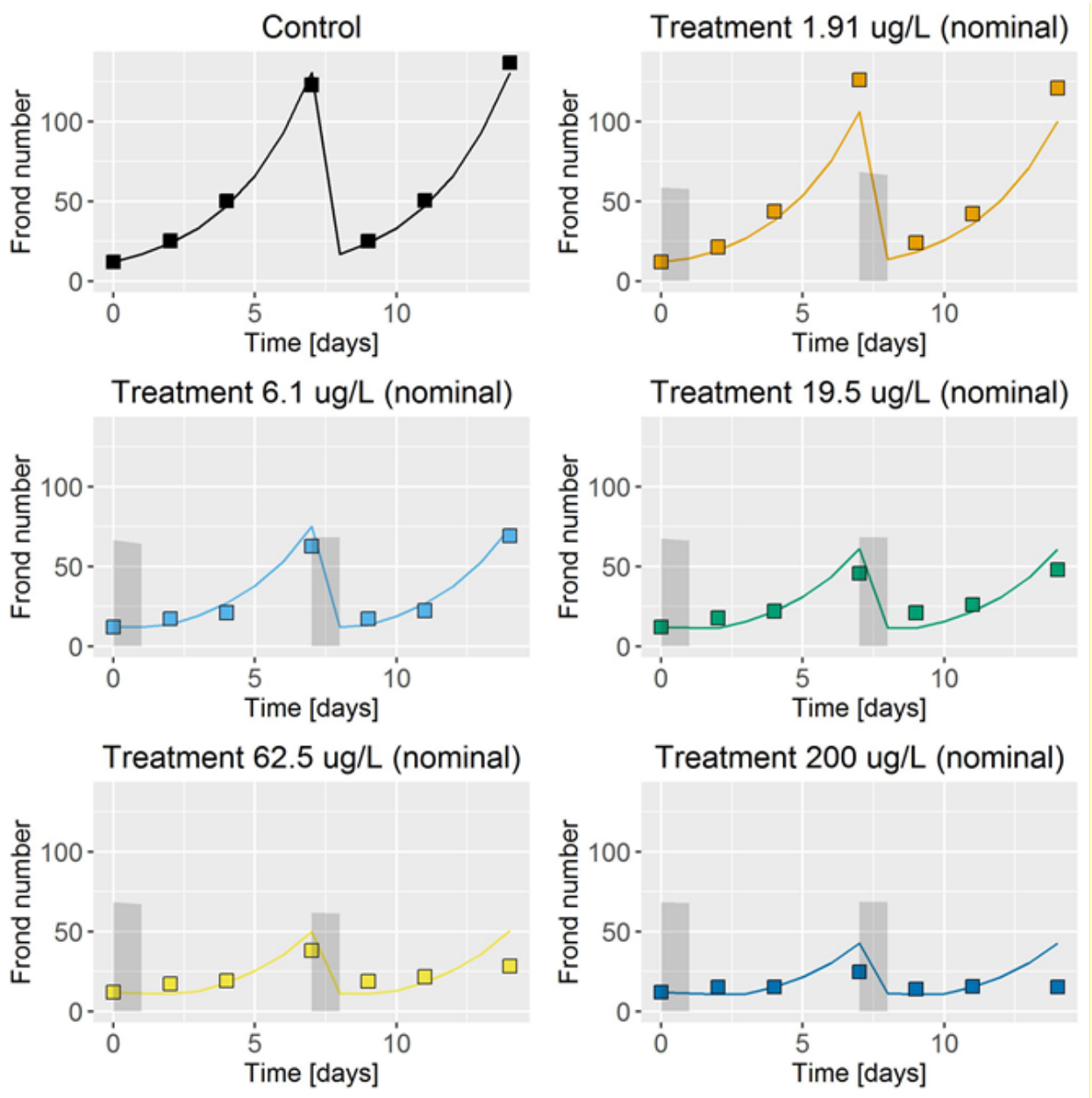


Figure A 23: ***Validation of the calibrated Lemna model for iodosulfuron-methyl-sodium with symbols representing experimental data and lines showing predictions of the model (grey areas illustrate the exposure situation): pulsed exposure with two 24 hours peak events at days 0 and 7 of a 14 days observation period, based on data from study Kuhl, 2016, M-574865-01-1; test series of 'design 2' study part***

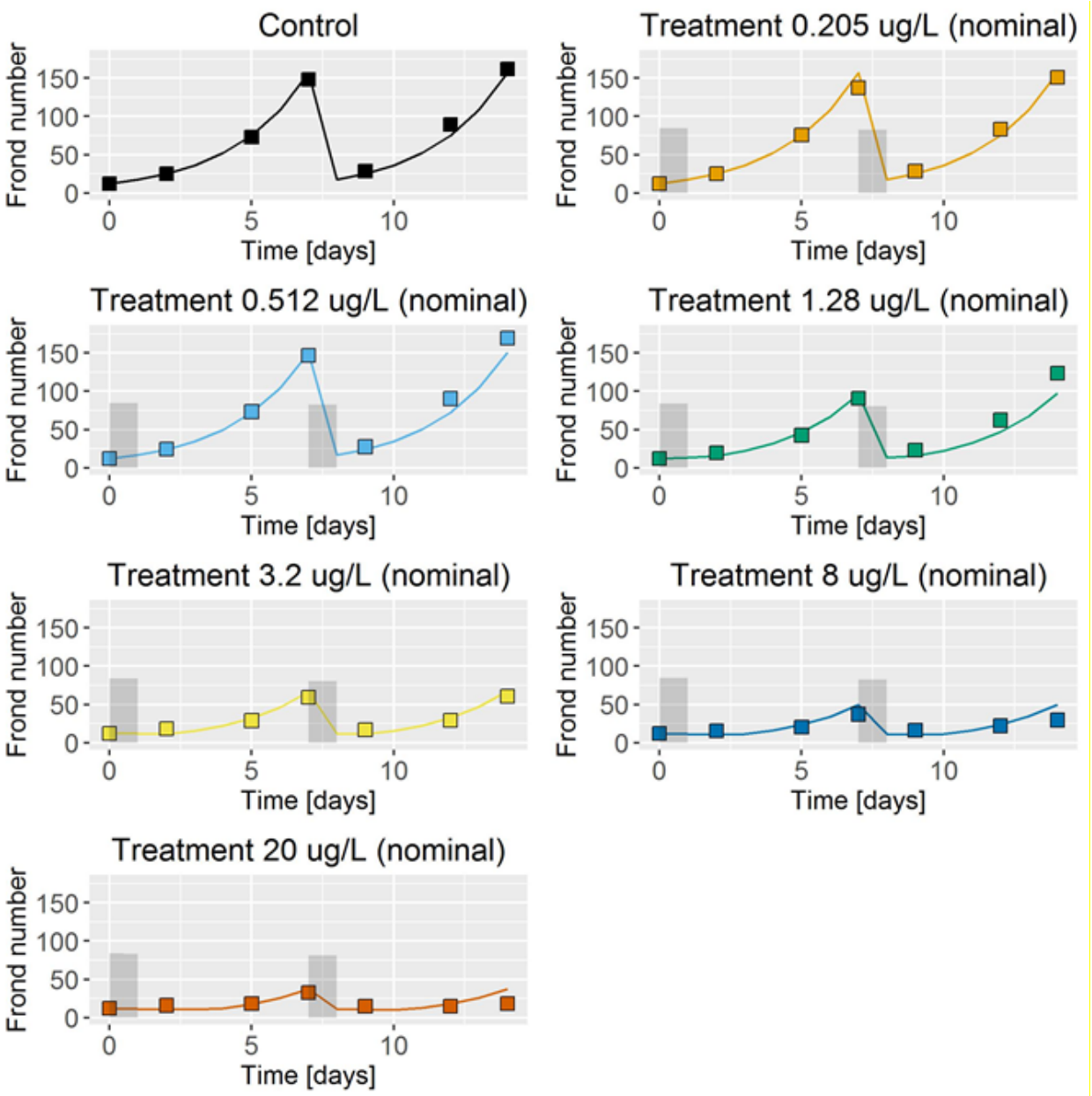


Figure A 24: ***Validation of the calibrated Lemna model for metabolite AE F075736 with symbols representing experimental data and lines showing predictions of the model (grey areas illustrate the exposure situation): pulsed exposure with two 24 hours peak events at days 0 and 7 of a 14 days observation period, based on data from study Kuhl, 2016, M-600651-01-1; test series of 'design 2' study part***

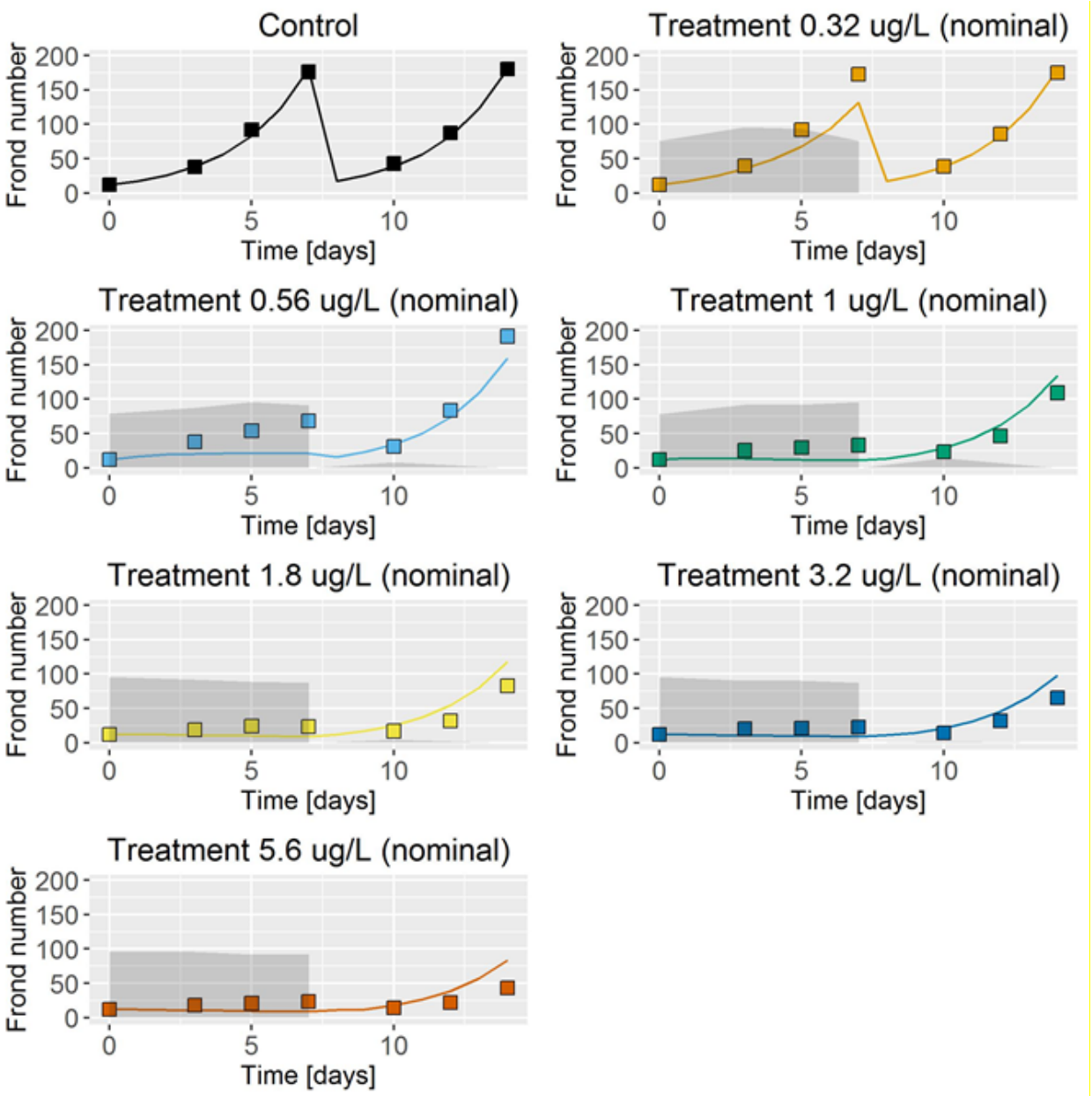


Figure A 25: ***Validation of the calibrated Lemna model for metabolite AE F075736 with symbols representing experimental data and lines showing predictions of the model (grey areas illustrate the exposure situation): 7 days constant exposure + 7 days recovery period situation, based on data from study KCA 8.2.7 /07; Sowig, P.; Gosch, H.; 2001; M-200947-01-1***

Table A 11: Numeric description of validation of the compound specific parameterization with EF being the model efficiency and RSS being the residual sum of squares.

Study No.	***EF***	***RSS***
	Iodosulfuron-methyl-sodium	
M-574865-01-1 (Design 2)	*0.92*	*3731*
	metabolite AE F075736	
M-600651-01-1	*0.96*	*3789*

M-200947-01-1	*0.87*	*15256*

According to a visual inspection of the model validation tests (Figure A 23 to Figure A 25), as well as the numeric evaluation for model efficiency (Table A 11), the calibrated model reliably predicted the effect of time-variable exposures to Iodosulfuron-methyl-sodium and metabolite AE F075736 on Lemna. Hence, the model is considered valid and robust, and can be furtheron applied for the purpose of risk assessment to simulate effects of any time-variable exposure to both active components

Reference:	***KCP 10.2.3/05***
Title:	*Lemna TK/TD modelling - Compound-specific parameterization and validation for mesosulfuron-methyl*
Report:	*Heine, S.; 2017; EnSa-17-0407; M-600766-01-1*
Authority registration No:	
Guideline(s):	*not applicable*
Deviations:	*none*
GLP/GEP:	*no*
Acceptability:	Have not been evaluated in this core document.
Duplication (if vertebrate study):	

Materials and Methods:

This report describes the compound specific preparation of the generic toxicokinetic and toxicodynamic (TK/TD) Lemna model to be used for mesosulfuron-methyl.

In a first step, toxicokinetic and toxicodynamic parameters of the model are calibrated on selected datasets in terms of adjusting them so that the model can describe the measured effects over time in all concentrations of the dataset. Toxicokinetic and toxicodynamic parameters are the uptake rate (P_up) and the internal concentration-response relationship that is based on an $EC(int)_{50}$ and a value defining the slope of the curve (b).

In a second step, the fully parameterized model is validated by testing the predictive power of the model with an independent (different from the datasets used for model calibration) dataset having a different exposure situation. If the calibration and validation are successful it is proven that the model can be used to extrapolate to untested exposure situations for mesosulfuron-methyl with its specific mechanism of action in Lemna.

Results and Discussion:

Model calibration:
Model calibration is the process of adjusting model parameters until optimal fit to the dataset is obtained.

The plant growths parts of the model were calibrated using the rates of exponential growth measured for the untreated control groups of all studies.

The TD and TK parts of the model were calibrated with the Lemna standard study Sowig & Weller, 2000 (M-195390-01-1, EU reviewed, see DAR KCA 8.2.7 /01) with seven days constant exposure, and with the Lemna peak exposure study (design 1) study of Kuhl (2016, M-577164-01-1; new study, see Appendix A 2.2.3 of this dRR). In this peak exposure study with a total duration of seven days, the effect of two peaks of 24h each on the growth of Lemna had been tested.
The calibration results are shown in Figure A 26 and Figure A 27.

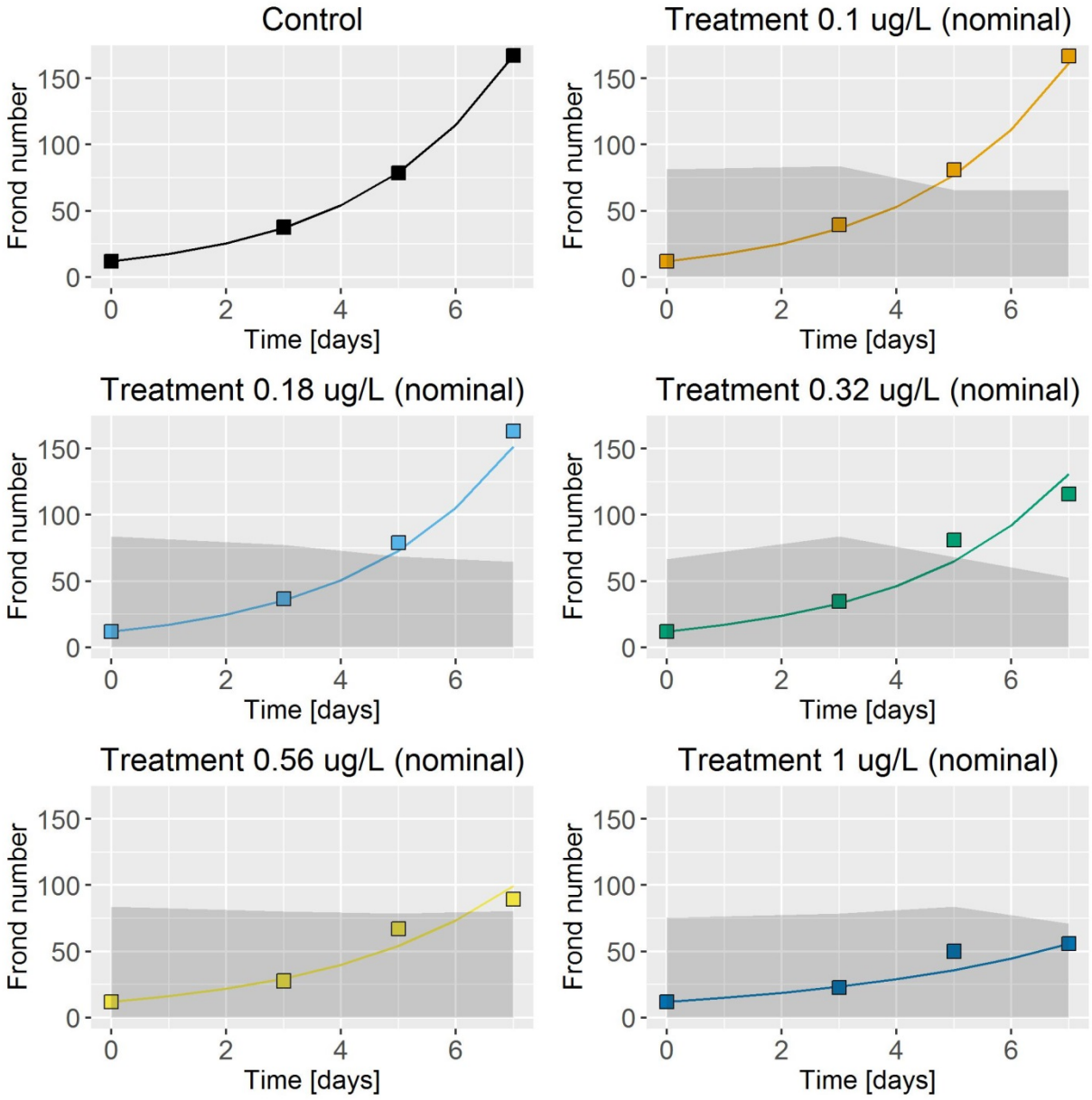


Figure A 26: ***Results of the model calibration for mesosulfuron-methyl with symbols representing experimental data and lines showing model results (grey areas illustrate the exposure situation): 7 days constant exposure situation, based on data from study KCA 8.2.7 /01, Sowig & Weller, 2000; M-195390-01-1***

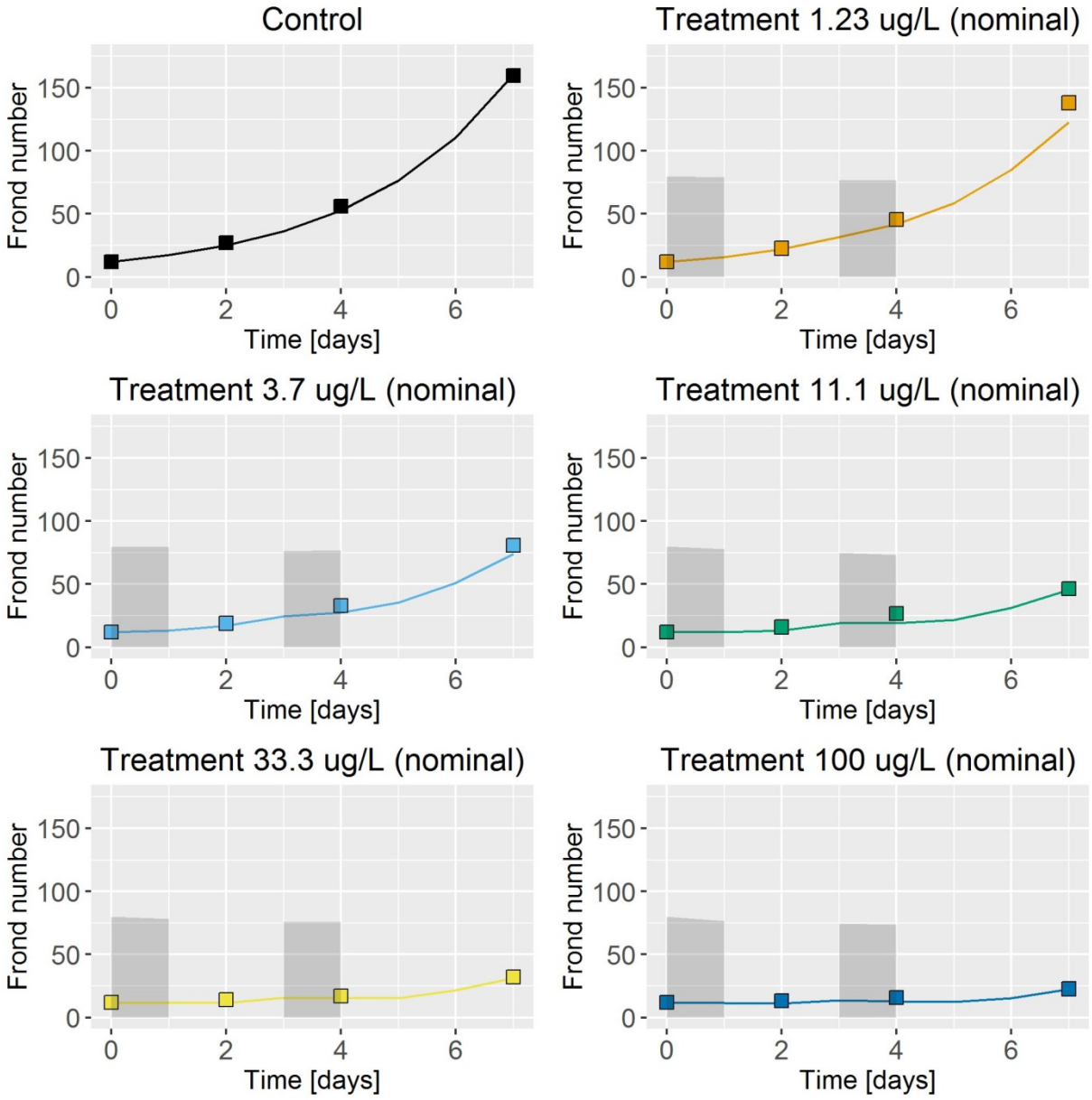


Figure A 27: ***Results of the model calibration for mesosulfuron-methyl with symbols representing experimental data and lines showing model results (grey areas illustrate the exposure situation): pulsed exposure with two 24 hours peak events at days 0 and 3 of a 7 days observation period, based on data from study Kuhl, 2016, M-577164-01-1; test series of 'design 1' study part***

Due to the number of available Lemna studies, the following robust model calibration could be generated:

Table A 12: Compound specific parameterization for mesosulfuron-methyl

Parameter	***Description***	***Value***	***Unit***	***Remark***
$EC_{50(int)}$	*Effective internal concentration at which 50% response is observed*	*1.5 [1.44 – 1.6]*	*µg/L*	*Calibrated*
b	*Value defining the slope of the dose-response function*	*1.7 [1.6 – 1.8]*	*-*	*Calibrated*
E_{max}	*Maximum effect*	*1*	*-*	*Set to 1 to enables effect of up to100%*
P_up	*Cuticular permeability*	*0.036 [0.03 – 0.042]*	*cm/d*	*Calibrated*
Kbm	*Plant/water partition coefficient*	*0.73*	*-*	*Estimated*

Model validation:
Exposure situations that were considered for the validation were short-term peaks (Figure A 28), time variable exposure of 46 days (Figure A 29) as well as nearly constant exposure for seven or five days with a subsequent recovery phase of seven days (Figure A 30 and Figure A 31). Overall, the model parameterization for mesosulfuron-methyl can be deemed acceptable considering the excellent visual fit of the validation as shown in the figures below. Besides the visual assessment, the model efficiency (EF) was calculated according FOCUS kinetics (2006) report procedures. EF ranges from minus infinity to +1 with larger values indicating better agreement. EF compares the sum of squared differences between calculated and observed data. For EF > 0, the value gives an indication of the fraction of the dataset that can be explained by the model.

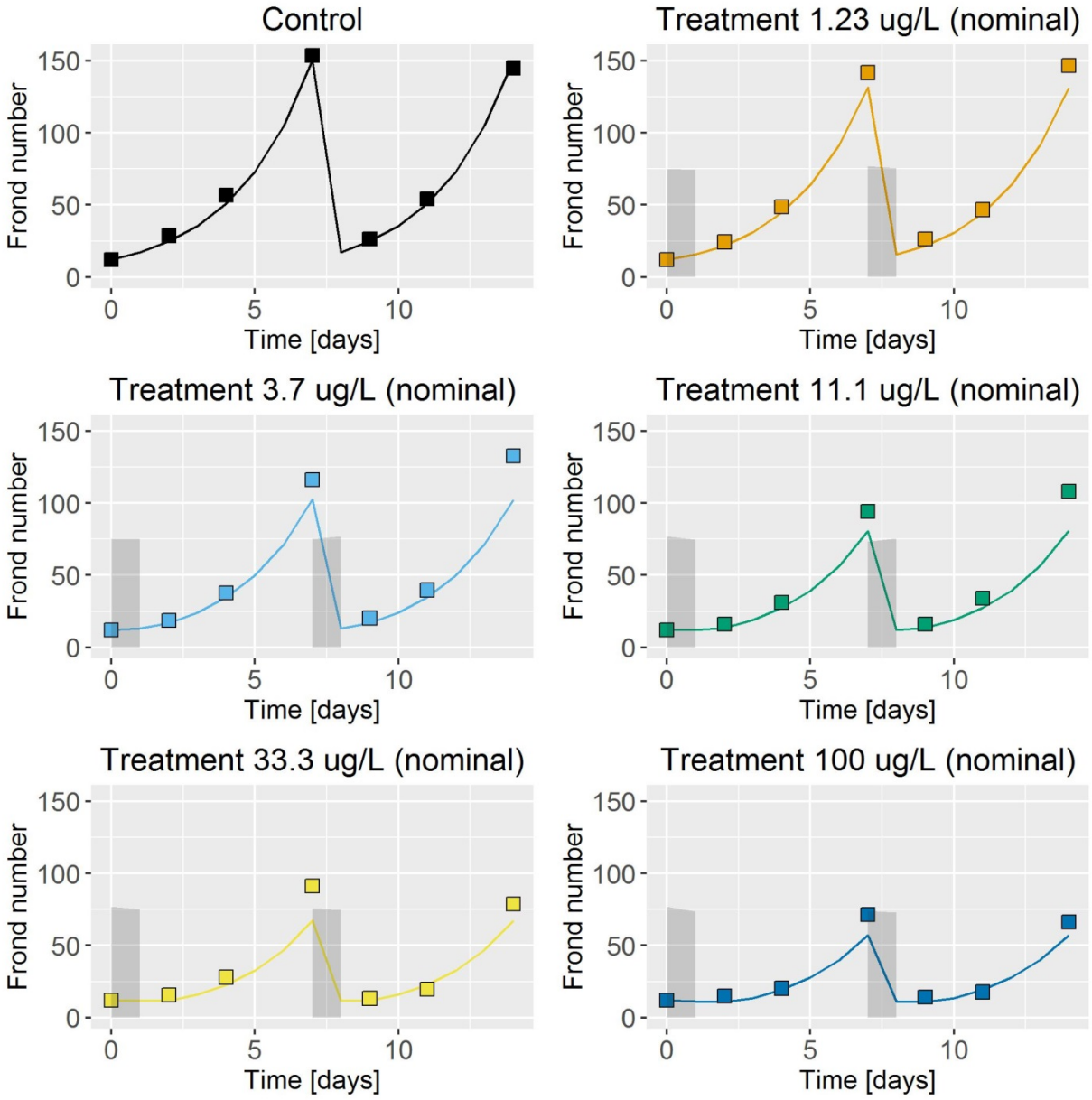


Figure A 28: ***Validation of the calibrated Lemna model for mesosulfuron-methyl with symbols representing experimental data and lines showing predictions of the model (grey areas illustrate the exposure situation): pulsed exposure with two 24 hours peak events at days 0 and 7 of a 14 days observation period, based on data from study Kuhl, 2016, M-577164-01-1; test series of 'design 2' study part***

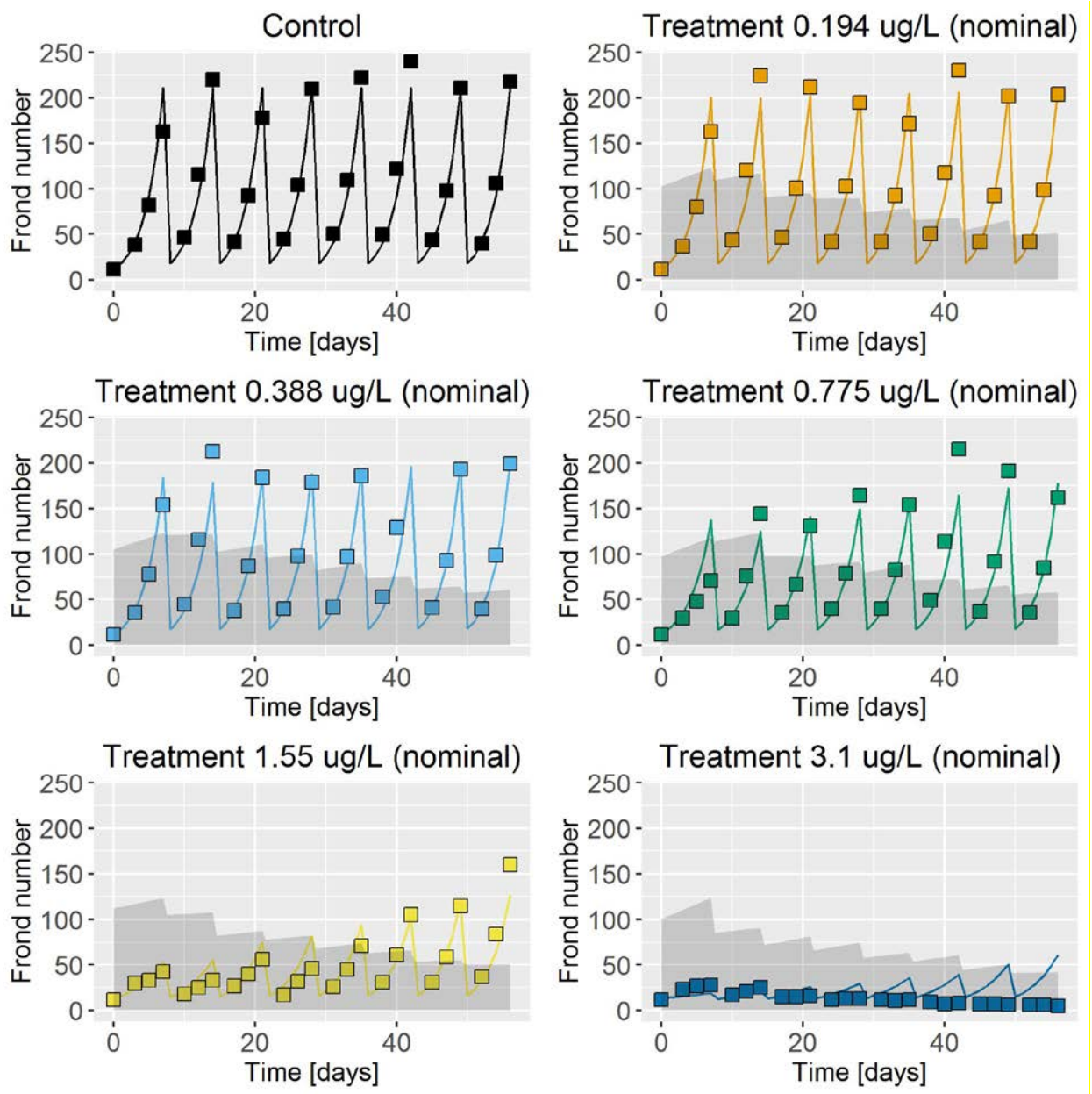


Figure A 29: ***Results of the validation of the parameterized model for mesosulfuron-methyl with lines representing model output and symbols representing experimental data from study M-445139-01-1 (the grey shaded area illustrates the concentration of mesosulfuron-methyl in water)***

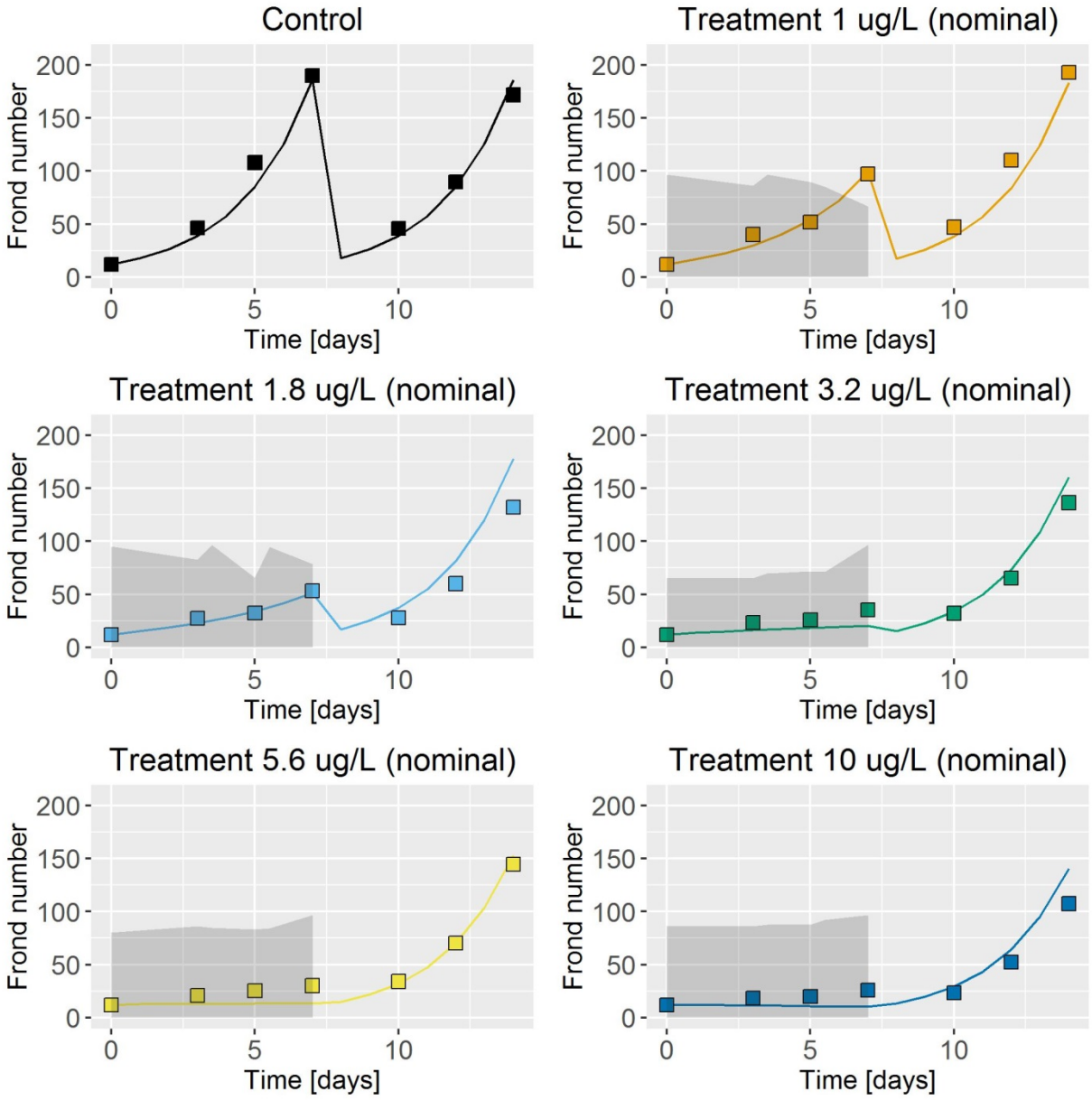


Figure A 30: ***Validation of the calibrated Lemna model for mesosulfuron-methyl with symbols representing experimental data and lines showing predictions of the model (grey areas illustrate the exposure situation): 7 days constant exposure + 7 days recovery period situation, based on data from study KCA 8.2.7 /07; Sowig, P.; Gosch, H.; 2002; M-206814-01-1***

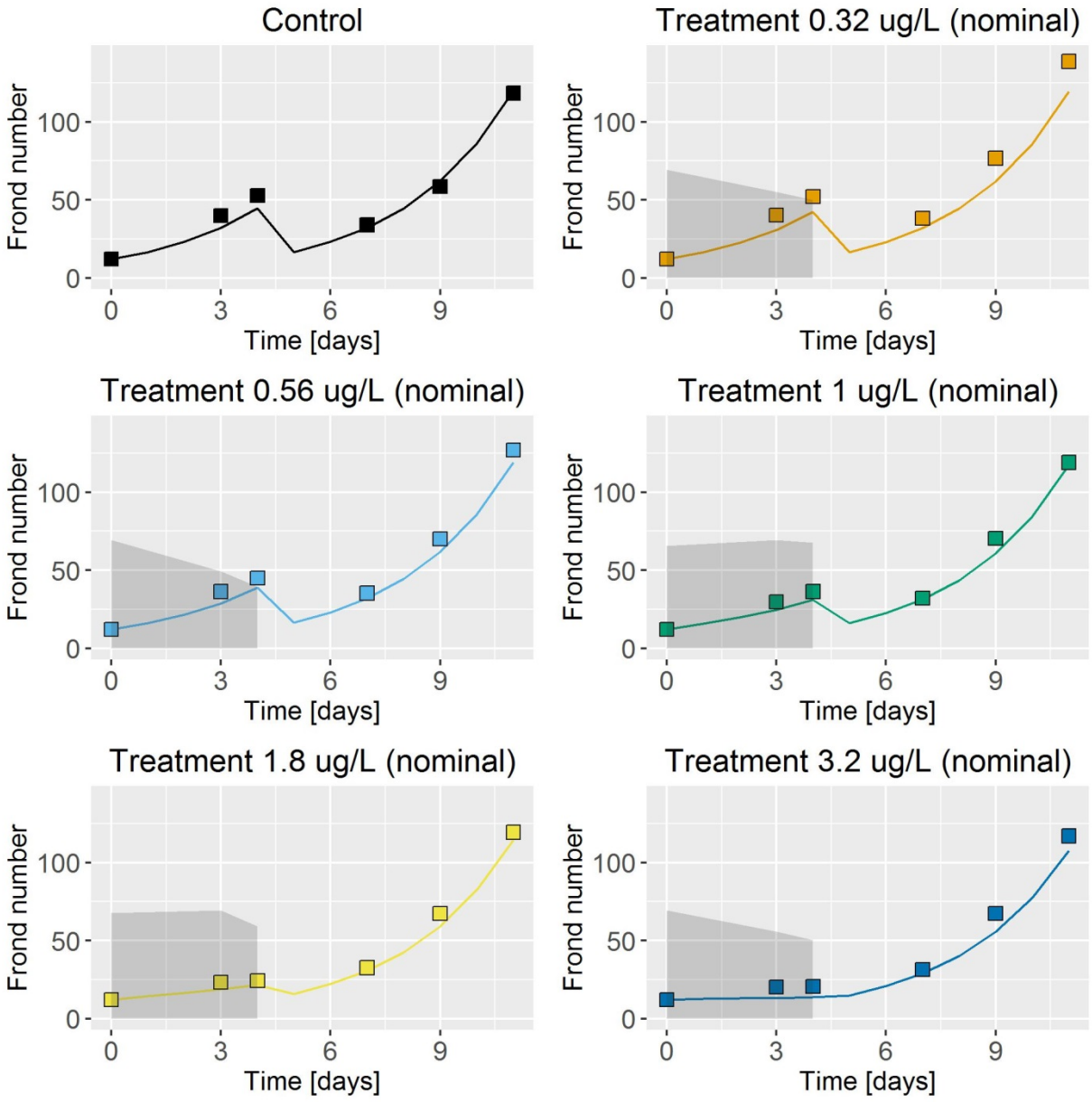


Figure A 31: ***Validation of the calibrated Lemna model for mesosulfuron-methyl with symbols representing experimental data and lines showing predictions of the model (grey areas illustrate the exposure situation): 4 days constant exposure + 7 days recovery period situation, based on data from study KCA 8.2.7/06; Sowig, P.; 2001; M-201731-01-1***

Table A 13: Numeric description of validation of the compound specific parameterization with EF being the model efficiency and RSS being the residual sum of squares.

Study No.	***EF***	***RSS***
M-577164-01-1 (Design 2)	*0.95*	*3725*
M-455139-01-1	*0.93*	*47488*
M-206814-01-1	*0.93*	*7742*
M-201731-01-1	*0.96*	*1754*

According to a visual inspection of the model validation tests (Figure A 28 to Figure A 31), as well as the numeric evaluation for model efficiency (Table A 13) , the calibrated model reliably predicted the effect of time-variable exposures to Mesosulfuron-methyl on Lemna. Hence, the model is considered valid and robust, and can be furtheron applied for the purpose of risk assessment to simulate effects of any time-variable exposure to Mesosulfuron-methyl.

(e) Model application for risk assessment of the product

For risk assessment of the present product, the successfully calibrated and validated Lemna models were applied in two ways, referring to AGD levels Tier 2C, and Tier 3:

In-silico time-variable exposure testing of Lemna, for derivation of $RAC_{pattern}$ of FOCUSsw scenarios: *'Virtual laboratory tests' on Lemna were simulated to address $FOCUS_{sw}$ exposure patterns of particular interest for the risk assessment, applying the model confirmatory to the assessments made before at Tier 2C (Section 9.5.2.5). Starting from the condensed exposure pattern representations previously derived via EPAT tool analysis of the FOCUSsw output (number, duration, maximum concentration, and interval of events exceeding the Tier 1 RAC), the biological effect of such patterns was simulated for a Lemna population assumed to grow under constant environmental conditions representing an 'in-silico laboratory'. To investigate on the dose-response relationship, the simulation was repeated multiple times with arbitrarily scaled concentration dimension of the exposure pattern, while keeping constant all further parameters. Based on the so generated data set, an $EC_{50pattern}$ could be derived in analogy to the procedures of a standard laboratory experiment. This $EC_{50pattern}$ is a descriptor which specifically reflects macrophyte sensitivity for the exposure timecourse experienced in the regarded FOCUSsw scenario of interest, and can be compared to the $PEC_{sw,max}$ predicted for this scenario.*

Population effect modelling for outdoor FOCUSsw water bodies: *Dynamics of a Lemna population growing outdoors in an edge-of-field surface water body were simulated for each of the crop relevant $FOCUS_{sw}$ exposure scenarios, for the critical GAP situations of the present product. To realistically simulate the biological impact of the predicted exposure patterns, the model environmental scenarios were constructed to reflect the properties of each associated FOCUS surface water body[23]. Additionally, to generate information on the margin of safety, Lemna population dynamics were simulated as well for exaggerated exposure situations, generated via a multiplication of the concentration dimension of the exposure patterns with exemplary scaling factors of either 10 or 100. Scaling the exposure supports the assessment and is intended to demonstrate that the model is able to predict considerable inhibitions of population dynamics. Following the standard concept of concentration addition, the population modelling approach can consider and combine the effect contributions by all biologically active components relevant to a product, i.e. can directly provide a combined risk assessment for the detailed and potentially complex exposure sitution of macrophytes in surface water bodies.*

A detailed description of both approaches and their results is provided in the following report:

[23] To account for the uncertainty resp. natural variation in some model relevant parameters, e.g. waterbody's nutrient concentrations , a stochastic simulation was performed varying those parameters in a Monte-Carlo approach. Therefore, actually 100 model runs were made per scenario, yielding output ranges.

Reference:	***KCP 10.2.3/06***
Title:	*Lemna TK/TD modelling - Assessing the impact of Atlantis OD applications on Lemna in Europe (FOCUSsw)*
Report:	*Heine, S.; 2018; EnSa-18-0974; M-637990-01-1*
Authority registration No:	
Guideline(s):	*none*
Deviations:	*none*
GLP/GEP:	*no*
Acceptability:	Have not been evaluated in this core document.
Duplication (if vertebrate study):	

The before described, calibrated and validated, Lemna TK/TD-population model was applied to establish higher tier risk assessments for the product IMS+MSM+MPR OD 42 (2+10+30). Two critical use patterns were addressed:

Table A 14: GAP translation for Lemna population effect modelling purposes

Critical use No. (in dRR)	*GAP No. (in report)*	*Crop*	*Growth stage & use timing*	*Max. apps*	*Interval (days)*	*Rate (kg a.s./ha)*
B	*I*	*winter cereals*	*BBCH 13-32, end of winter to spring use*	*1*	*-*	*MSM: 0.015 IMS: 0.003*
D	*II*	*winter cereals*	*BBCH 13-32, autumn use*	*1*	*-*	*MSM: 0.010 IMS: 0.002*

Aquatic exposure for these use patterns was described based on standard FOCUSsw exposure simulations, see summarised previously in the E-Fate section to this dRR (for iodosulfuron-methyl-sodium and its metabolite AE F075736: Heine et al. 2017 a, b; [M-602706-01-1, M-617758-01-1]; for mesosulfuron-methyl: Bolekhan et al. 2017a,b; [M-602229-01-1, M-602215-01-1]).

*For the assessment at **Tier 2C**, **in-silico time-variable exposure testing of Lemna,** $RAC_{pattern}$ determinations were confined to the active substance mesosulfuron-methyl, and FOCUS scenarios R3 stream and R4 stream, for the reasons outlined in Section 9.5.2.7 (a):*

Table A 15: FOCUS scenarios and compounds that are evaluated by Lemna virtual laboratory modelling for deriving $RAC_{pattern}$

GAP No	*FOCUS scenario*	*Exposure pattern characteristic*				*Effect modelling based on:*
		PECmax	*No. events**	*Duration*	*Interval*	
I	*R3 (stream)*	*0.3099*	*1*	*0.5*	*-*	*mesosulfuron-methyl*
	R4 (stream)	*0.2646*	*1*	*0.75*	*-*	*mesosulfuron-methyl*
II	*R3 (stream)*	*0.5158*	*1*	*0.625*	*-*	*mesosulfuron-methyl*
	R4 (stream)	*0.2641*	*1*	*0.541*	*-*	*mesosulfuron-methyl*

**An event is defined as a concentration that exceeds the regulatory acceptable concentration*

*For the assessment at **Tier 3, population effect modelling for outdoor FOCUSsw water bodies**, all three biologically active components of relevance to the product were considered in a combined toxicity approach based on centration addition, for all crop relevant FOCUSsw scenarios:*

Table A 16: FOCUS scenarios and compounds that are evaluated by Lemna population modelling

GAP No	FOCUS scenario	Effect modelling based on:
I	D1 (ditch)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D1 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D2 (ditch)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D2 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D3 (ditch)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D4 (pond)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D4 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D5 (pond)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D5 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D6 (ditch)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	R1 (pond)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	R1 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	R3 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	R4 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
II	D1 (ditch)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D1 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D2 (ditch)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D2 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D3 (ditch)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D4 (pond)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D4 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D5 (pond)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D5 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	D6 (ditch)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	R1 (pond)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	R1 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	R3 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl
	R4 (stream)	iodosulfuron-methyl-sodium, AE F075736, mesosulfuron-methyl

Methods & Results:

(f) In-silico time-variable exposure testing of Lemna, for derivation of RACpattern to FOCUSsw scenarios:

To derive $RAC_{pattern}$ for specific exposure patterns, the Lemna model was used to simulate virtual laboratory tests. The setting of the virtual laboratory simulation was designed in accordance to standard Lemna studies. Due to optimum growth conditions in standard Lemna studies, maximum growth rate was considered and the other parameters that influence growth (e.g. nutrition and temperature) were neglected. An initial biomass of 0.0012 g corresponding to a frond number of 12 and the compound specific parameters of mesosulfuron-methyl were used. The duration of the virtual laboratory test was set to seven days as a standard[24], in analogy to a laboratory test.

[24] Duration could be expanded for cases where exposure patterns exceed seven days, e.g. to 14 or, if necessary, to 21 days with a transfer of 12 fronds into a new virtual vessel after each week. This reflects the experimental practice

The virtual laboratory simulations were used to establish a dose-response relationship for the exposure patterns of interest, via performing several simulation runs with arbitrarily scaled concentration dimension of the exposure pattern while keeping constant all other pattern characteristics such as the duration and the interval between events. From the so generated dose-effect curves, $EC_{50pattern}$ was derived via standard Probit analysis:

$EC_{50pattern}$ determination and risk assessment for use group B (≡ GAP I):

*For **use group B** (winter cereals – end of winter to spring application), the exposure patterns predicted for mesosulfuron-methyl in FOCUS scenarios R3s and R4s were both characterised by a single dominant exposure event only, with a duration of 0.5 or 0.75 days, respectively (cf. Figures of Section 9.5.2.5) . In a virtual laboratory test on such exposure pattern, to achieve an inhibition of the relative growth rate by 50% ($EC_{50pattern}$), the concentrations had to be increased to 4166 and 1838 µg/L for the two scenarios, respectively. In agreement with an assessment factor of 10 the $RAC_{pattern}$ were therefore both > 100 µg/L for the specific exposure situation predicted for mesosulfuron-methyl in scenarios R3 stream and R4 stream, for end of winter to spring application to winter cereals.*

For risk assessment, these $RAC_{pattern}$ can be compared to the $PEC_{sw,max}$ concentrations of 0.3099 µg/L or 0.2646 µg/L for these scenarios, respectively, indicating again very large margins of safety and confirming the conclusions drawn before at Tier 1 (considering TWA) and Tier 2C (experimental).

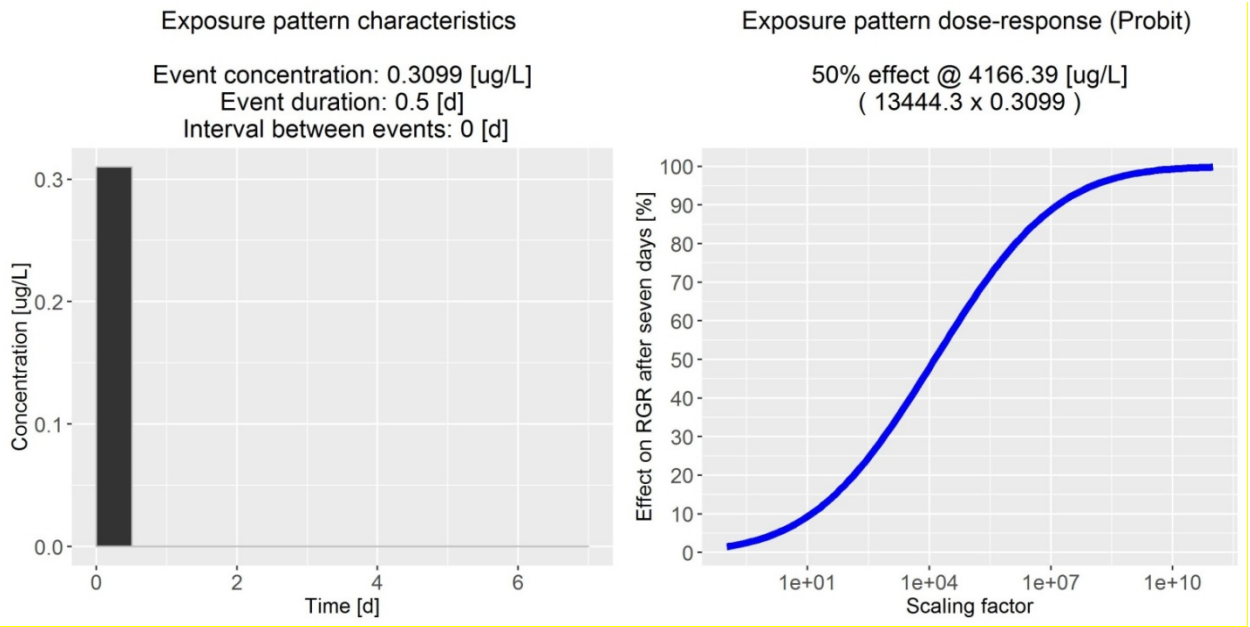


Figure A 32: Illustration of the evaluated exposure pattern and the corresponding dose-response relationship for scenario R3 stream, for use group B

where periodic transfers into fresh medium are done to ensure exponential growth. Effects on *Lemna* would then be described as inhibition of relative biomass growth rate at the end of the week showing the strongest growth inhibition.

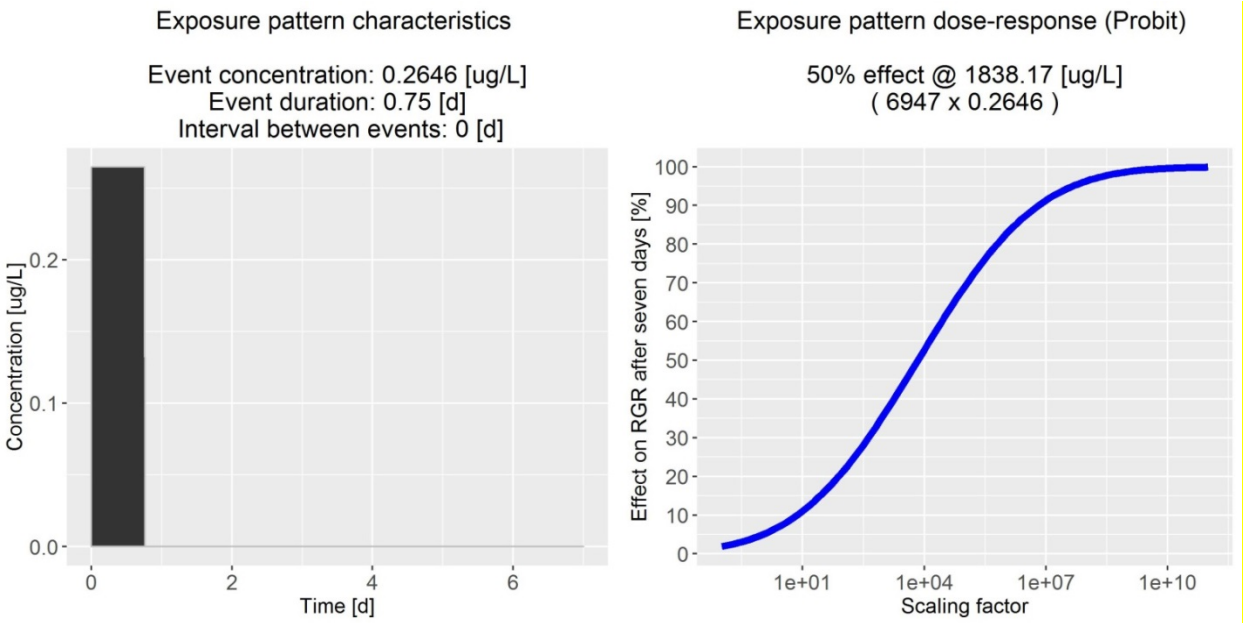


Figure A 33: ***Illustration of the evaluated exposure pattern and the corresponding dose-response relationship for scenario R4 stream, for use group B***

Table A 17: ***Assessing exposure patterns derived from FOCUS$_{sw}$ calculation to determine the corresponding exposure pattern that causes 50% effect by increasing the event[1)] concentration and keeping all other pattern characteristics - for use group B***

Scenario	***Pattern characteristics***				***Event conc. causing 50% effect [µg/L]***	***RAC$_{pattern}$ [µg/L]***	***RQ = PECmax / RAC$_{pattern}$)***
	Event concentration [µg/L] (PECmax)	***Number of events***	***Event duration [d]***	***Interval between events [d]***			
R3 stream	*0.3099*	*1*	*0.5*	*-*	*4166*	*416.6*	*0.0007*
R4 stream	*0.2646*	*1*	*0.75*	*-*	*1838*	*183.8*	*0.0014*

1) An event is defined as a concentration exceeding the tier 1 regulatory acceptable concentration (RAC)

Overall conclusion: *For overall conclusions, please refer to the dRR main part.*

(g) Population effect modelling for FOCUSsw water bodies

The impact of FOCUS predicted exposure pattern on Lemna population dynamics is assessed by calculating the inhibition of the total biomass for each day of a year, considering all biologically active components of relevance to the product. This provides a realistic estimation of the impact over the entire year covering typical growing phases in spring and phases with low or no growth in winter. As the simulation should also account for uncertainty, the confidence intervals of some parameters have been considered. For each FOCUS scenario 100 simulations were conducted, each having randomly chosen parameters in the specified ranges as shown in the table below. For the initial biomass a variability of ± 20% was assumed as the data is derived from measurements in summer. For the density dependence a variability of only ± 10% was assumed due to the high reliability of the data source.

Table A 18: Uncertainty of model parameters and their range that is considered during simulations.

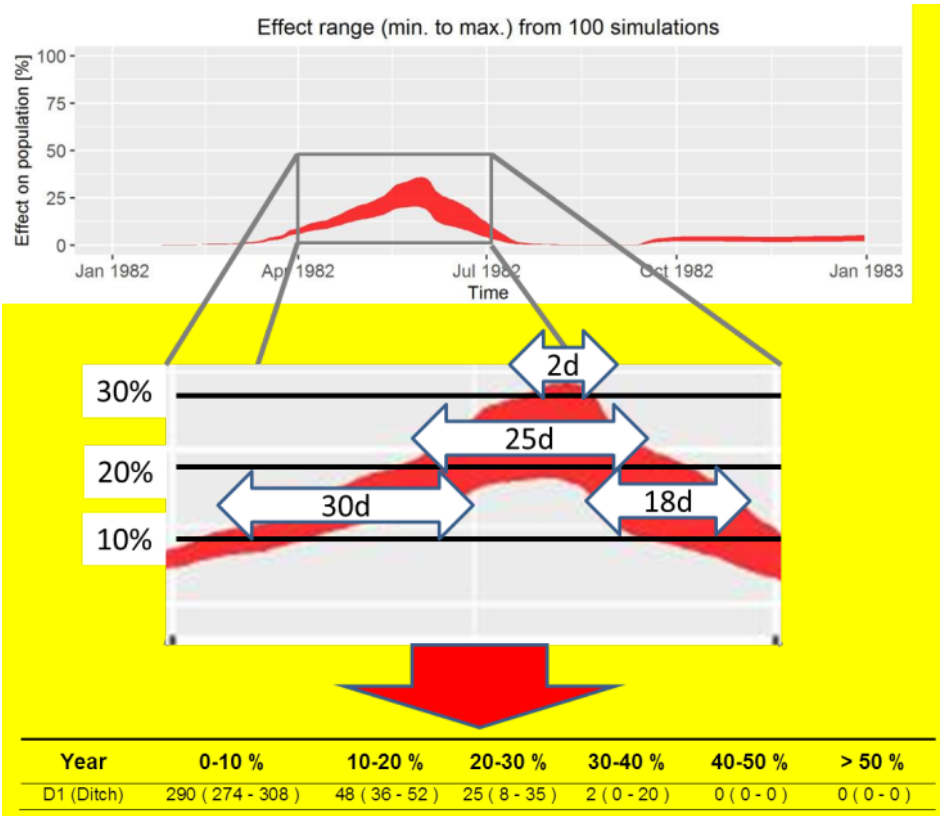
General Parameter	Description	Value	Unit	SE	CI
BM	*Initial biomass*	*28*	*g/m²*	*-*	*22-34*
Density	*Maximum biomass density*	*176*	*g/m²*	*-*	*158-194*
k_phot_max	*Maximum growth rate*	*0.42*	*1/d*	*0.0044*[1)]	*0.41-0.43*
Compound specific parameter (iodosulfuron-methyl-sodium)					
EC50(int)	*Effective internal concentration at which 50% response is observed*	*1.3*	*µg/L*	*0.053*	*1.2-1.4*
b	*Value defining the slope of the dose-response function*	*3.5*	*-*	*0.3*	*2.9-4.1*
P_up	*Cuticular permeability*	*0.032*	*cm/d*	*0.0024*	*0.027-0.036*
Compound specific parameter (metsulfuron-methyl)					
EC50(int)	*Effective internal concentration at which 50% response is observed*	*0.43*	*µg/L*	*0.021*	*0.38-0.47*
b	*Value defining the slope of the dose-response function*	*5.0*	*-*	*0.089*	*4.8-5.2*
P_up	*Cuticular permeability*	*0.017*	*cm/d*	*0.002*	*0.013-0.021*
Compound specific parameter (mesosulfuron-methyl)					
EC50(int)	*Effective internal concentration at which 50% response is observed*	*1.5*	*µg/L*	*0.029*	*1.4-1.6*
b	*Value defining the slope of the dose-response function*	*1.7*	*-*	*0.028*	*1.6-1.8*
P_up	*Cuticular permeability*	*0.036*	*cm/d*	*0.0029*	*0.03-0.042*

[1)] Largest value during the model preparation for mesosulfuron-methyl

The impact was quantified as effects on standing crop (total biomass) per day. To provoke effects and gain information about exposure patterns that would have an impact on Lemna population two additional

simulations were conducted for each GAP. In these simulations the Step 3 FOCUSsw exposure patterns were multiplied by a factor of either 10 or 100.

To link the model outcome to the specific protection goals the following criteria were applied. According to EFSA Aquatic Guidance Document (2013) the NOEC is equivalent to the EC_{10}. Therefore negligible effects were defined as effects < 10%. For small and medium effects no clear thresholds are given in the EFSA AGD. Nevertheless in Table 31 (page 118) for the MDD calculations small effects are defined < 50% and medium effects <70%. According to the EFSA Opinion on the development of specific protection goal options (EFSA, 2010) the effect levels should be linked to ecological relevance. This is missing for macrophytes at the moment. Due to the lack of guidance a pragmatic and conservative approach was taken in this study to define small and medium effects by means of 20 % increment steps. Since negligible effects are defined by EFSA as <10%, we defined small effect as <30% and medium effects as <50%. To compare model output to the specific protection goals, effects over time were summarized into tables as demonstrated in Figure A 36.



Year	0-10 %	10-20 %	20-30 %	30-40 %	40-50 %	> 50 %
D1 (Ditch)	290 (274 - 308)	48 (36 - 52)	25 (8 - 35)	2 (0 - 20)	0 (0 - 0)	0 (0 - 0)

Figure A 34: Summary of effects over time into effect table.

The effects were calculated daily as the deviation between treatment and control expressed in percent. Effects were investigated in bands with a resolution of 10%. All days within one effect band are added up and the respective sum of days within this effect class is entered in the respective column.

As the simulation should also account for uncertainty, the confidence intervals of some model parameters have been considered. For each FOCUS scenario 100 simulations were conducted, each having randomly chosen parameters only limited by pre-defined boundaries. Due to this the results of the population modelling are given in ranges.

Simulation results and discussion:

Original exposure patterns of product IMS+MSM+MPR OD 42 (2+10+30)
FOCUS Step 3 results - no scaling factor

The detailed simulation results are summarised in tabular form below, showing number of days with biomass deviations (mean (minimum - maximum)) divided into effect classes and years based on 100 simulations and FOCUS exposure patterns.

Whereas for the original (non-scaled) use pattern most FOCUS scenarios do not inhibit Lemna population dynamics to a notable extent (<10%), FOCUS scenarios D2 ditch and stream cause inhibitions up to 30% for a period of 62 days (D2 ditch) and up to 20% for period of 16 days (D2 stream). The application in autumn does not inhibit Lemna population dynamics at all.

Table A 19: Detailed simulation results for use group B (winter cereals – end of winter to spring application) - original exposure situation: 3 g/ha IMS + 15 g/ha MSM

Scenario	<10 %	≥ 10 < 20 %	≥ 20 < 30 %	≥ 30 < 40 %	≥ 40 < 50 %	> 50 %
D1 (Ditch)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D1 (Stream)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D2 (Ditch)	**304 (301 - 308)**	**30 (22 - 53)**	**32 (4 - 41)**	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D2 (Stream)	**349 (332 - 365)**	**16 (0 - 33)**	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D3 (Ditch)	366 (366 - 366)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D4 (Pond)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D4 (Stream)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D5 (Pond)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D5 (Stream)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
D6 (Ditch)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
R1 (Pond)	366 (366 - 366)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
R1 (Stream)	366 (366 - 366)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
R3 (Stream)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
R4 (Stream)	366 (366 - 366)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)

Exaggerated exposure patterns – concentration scaled by factor 10

Increasing the FOCUS exposure patterns by a factor of 10 also increases the magnitude of population inhibition. However, it is interesting to note that even for such exaggerated exposure situation, all run-off scenarios (R) still do not show any population inhibitions at all, while drainage (D) scenarios cause considerable inhibitions > 50% in some cases. The application in autumn shows more inhibition of population dynamics than the applications in spring.

Table A 20: Detailed simulation results for use group B (winter cereals – end of winter to spring application) - Exaggerated exposure situation: Concentration scaled by factor 10

Scenario	<10 %	≥ 10 < 20 %	≥ 20 < 30 %	≥ 30 < 40 %	≥ 40 < 50 %	> 50 %
D1 (Ditch)	**255 (251 - 258)**	**27 (25 - 29)**	**15 (13 - 17)**	**14 (13 - 15)**	**9 (8 - 11)**	**44 (23 - 74)**
D1 (Stream)	**309 (295 - 315)**	**36 (32 - 45)**	**21 (17 - 25)**	**0 (0 - 0)**	**0 (0 - 0)**	**0 (0 - 0)**
D2 (Ditch)	**79 (77 - 81)**	**89 (64 - 95)**	**26 (19 - 51)**	**39 (18 - 46)**	**18 (13 - 33)**	**114 (91 - 149)**
D2 (Stream)	**235 (229 - 240)**	**14 (12 - 16)**	**17 (15 - 19)**	**12 (10 - 15)**	**10 (8 - 12)**	**76 (63 - 93)**
D3 (Ditch)	*366 (366 - 366)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
D4 (Pond)	*365 (365 - 365)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
D4 (Stream)	*365 (365 - 365)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
D5 (Pond)	*365 (365 - 365)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
D5 (Stream)	*365 (365 - 365)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
D6 (Ditch)	*365 (365 - 365)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
R1 (Pond)	*366 (366 - 366)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
R1 (Stream)	*366 (366 - 366)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
R3 (Stream)	*365 (365 - 365)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*
R4 (Stream)	*366 (366 - 366)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*	*0 (0 - 0)*

Exaggerated exposure patterns – concentration scaled by fator 100

Increasing the FOCUS exposure patterns by an even higher factor of 100 again increases the magnitude of population inhibition. However, still all run-off scenarios (R) do not show any population inhibitions at all, hereby demonstrating a very large margin of safety for such substance exposure situation, while drainage (D) scenarios cause considerable inhibitions > 50% now in most of the D scenarios, for both use patterns relevant to the present product.

Table A 21: Detailed simulation results for use group B (winter cereals – end of winter to spring application) - Exaggerated exposure situation: Concentration scaled by factor 100

Scenario	<10 %	≥ 10 < 20 %	≥ 20 < 30 %	≥ 30 < 40 %	≥ 40 < 50 %	> 50 %
D1 (Ditch)	106 (72 - 132)	74 (59 - 93)	21 (16 - 37)	19 (17 - 22)	14 (12 - 16)	131 (117 - 149)
D1 (Stream)	228 (224 - 232)	36 (32 - 39)	16 (14 - 19)	18 (17 - 20)	14 (12 - 18)	52 (38 - 69)
D2 (Ditch)	12 (12 - 13)	7 (6 - 7)	20 (13 - 38)	33 (16 - 38)	8 (7 - 10)	284 (276 - 295)
D2 (Stream)	13 (13 - 14)	8 (7 - 9)	43 (42 - 46)	12 (10 - 12)	8 (7 - 8)	281 (268 - 295)
D3 (Ditch)	7 (6 - 8)	9 (8 - 12)	22 (21 - 23)	7 (5 - 52)	30 (11 - 128)	289 (57 - 900)
D4 (Pond)	81 (79 - 84)	18 (13 - 80)	27 (11 - 94)	22 (6 - 87)	25 (10 - 89)	191 (109 - 401)
D4 (Stream)	235 (221 - 248)	43 (40 - 49)	20 (15 - 26)	16 (10 - 22)	12 (9 - 17)	39 (20 - 60)
D5 (Pond)	191 (187 - 197)	23 (17 - 26)	15 (12 - 20)	10 (7 - 13)	13 (9 - 15)	114 (73 - 153)
D5 (Stream)	243 (239 - 247)	22 (20 - 33)	25 (18 - 27)	20 (14 - 41)	51 (26 - 60)	3 (0 - 32)
D6 (Ditch)	302 (297 - 313)	59 (46 - 66)	4 (0 - 22)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
R1 (Pond)	366 (366 - 366)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
R1 (Stream)	366 (366 - 366)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
R3 (Stream)	365 (365 - 365)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)
R4 (Stream)	366 (366 - 366)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)	0 (0 - 0)

**Values > 365 are possible because the maximum value (number of days) for all effect ranges (≥50 < 60 %; ≥60 < 70 %; ≥70 < 80 %; ≥80 < 90 %; ≥90 %) from 100 simulations are summarized and the single values might not originate from the same simulation*

Overall conclusion: *For overall conclusions, please refer to the dRR main part.*

Detailed information to Section 9.5.2.8:

Ecological modelling approaches, and their use in higher-tier risk assessment for the present product –considering multiyear exposure simulations

In response to concerns over the representativeness of the FOCUS model inherent weather year in the context of refined exposure assessment, additional FOCUS exposure simulations have been conducted for an extended period of 20 years (multi-year calculations). The present summary details the use of this multi-year exposure information in the context of Lemna population modelling, based on the general methodology outlined before.

For information on the methodology applied and results for exposure modelling, reference is made to the corresponding PEC_{sw} FOCUS Multiyear reports found presented in the E-fate section to this dRR.

Reference:	***KCP 10.2.3/07***
Title:	*Lemna TK/TD modelling - Assessing the impact of Atlantis OD applications on Lemna in Europe (FOCUSsw multiyear)*
Report:	*Heine, S.; 2018; EnSa-18-0973; M-637995-01-1*
Authority registration No:	
Guideline(s):	*none*
Deviations:	*none*
GLP/GEP:	*no*
Acceptability:	Have not been evaluated in this core document.
Duplication (if vertebrate study):	

For general information about the ecological modelling approaches, as well as model calibration, validation, and use in risk assessment. In analogy to the procedures for the standard FOCUS year, the successfully calibrated and validated Lemna models were applied in two ways, referring to AGD levels Tier 2C, and Tier 3:

(a) In-silico time-variable exposure testing of Lemna, for derivation of $RAC_{pattern}$ to FOCUSsw scenarios:

'Virtual laboratory tests' on Lemna were simulated to address $FOCUS_{sw}$ exposure patterns of particular interest for the risk assessment, applying the model confirmatory to the assessments made before at Tier 2C (Section 9.5.2.6 / Appendix A3.3). Starting from the condensed realistic worst case exposure pattern representations previously derived via percentile analysis of the FOCUSsw-multiyear output (80th percetile number, duration, maximum concentration, and 20^{th} percentile interval of events exceeding the Tier 1 RAC; cf. A3.3), the biological effect of such patterns was simulated for a Lemna population assumed to grow under constant environmental conditions representing an 'in-silico laboratory'. To investigate the dose-response relationship, the simulation was repeated multiple times with arbitrarily scaled concentration dimension of the exposure pattern, while keeping constant all further parameters. Based on the so generated data set, an $EC_{50pattern}$ could be derived in analogy to the procedures of a standard laboratory experiment. This $EC_{50pattern}$ is a descriptor which specifically reflects macrophyte sensitivity for the exposure timecourse experienced in the regarded FOCUSsw scenario of interest, and can be compared to the $PEC_{sw,max}$ predicted for this scenario.

For the assessment at Tier 2C, $RAC_{pattern}$ determinations were confined to the active substance

mesosulfuron-methyl, and FOCUS scenarios[25] R3 stream and R4 stream, for the reasons outlined in Section 9.5.2.7 (a):

Table A 22: FOCUS scenarios and compounds that are evaluated by Lemna virtual laboratory modelling for deriving $RAC_{pattern}$

Critical use No. (in dRR)	GAP No. (in report)	FOCUS scenario	Exposure pattern characteristic				Effect modelling based on:
			PECmax 80^{th} perc.	No. events 80^{th} perc.	Duration 80^{th} perc.	Interval 20^{th} perc.	
B	I	R3 (stream)	0.4524	2	0.8	7.3	mesosulfuron-methyl
		R4 (stream)	0.4918	2	0.6	4.4	mesosulfuron-methyl
D	II	R3 (stream)	0.3601	1	0.6	not relevant	mesosulfuron-methyl
		R4 (stream)	0.3484	1	0.8	not relevant	mesosulfuron-methyl

**An event is defined as a concentration that exceeds the regulatory acceptable concentration*

$EC_{50pattern}$ determination and risk assessment for use group B (≡ GAP I):

*For **use group B** (winter cereals – end of winter to spring application), the 80^{th} percentile worst case exposure patterns derived from multi-year (20 years) exposure simulations for mesosulfuron-methyl in FOCUS scenarios R3 stream was characterised by two dominant exposure events, with a duration of 0.8 days, and a peak intervals of 7.3 days. In virtual laboratory tests on such exposure pattern, to achieve an inhibition of the relative growth rate by 50% ($EC_{50pattern}$) the concentration had to be increased to 1743 µg/L. Applying an assessment factor of 10, the $RAC_{pattern}$ for R3 stream therefore is 174.3 µg/L.*

For scenario R4 stream, characterised by two exposure events of 0.6 days each at an interval of 4.4 days, the model predicts an $EC_{50\ pattern}$ of 56.7 µg/L, leading to a $RAC_{pattern}$ of 5.7 µg/L.

For risk assessment, these $RAC_{pattern}$ can be compared to the PEC_{sw} (multiyear 80^{th} percentile) concentrations of 0.4524 µg/L or 0.4918 µg/L for these scenarios, respectively, indicating again large margins of safety and confirming the conclusions drawn before at Tier 1 (considering TWA) and Tier 2C (experimental).

[25] In the original modelling report assessment is found presented for R1 stream in addition; however has not been summarised here as no refinement was triggered for this scenario in the present product context.

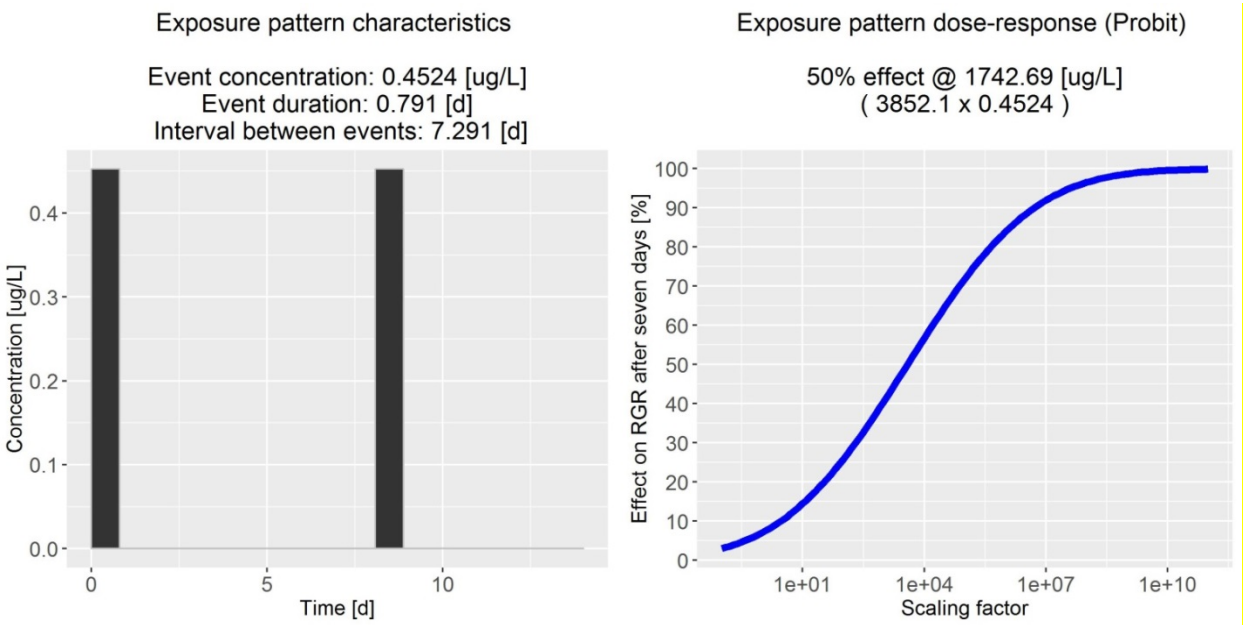


Figure A 35: ***Illustration of the evaluated 20-year surrogate exposure pattern and the corresponding dose-response relationship for scenario R3 stream, for use group B***

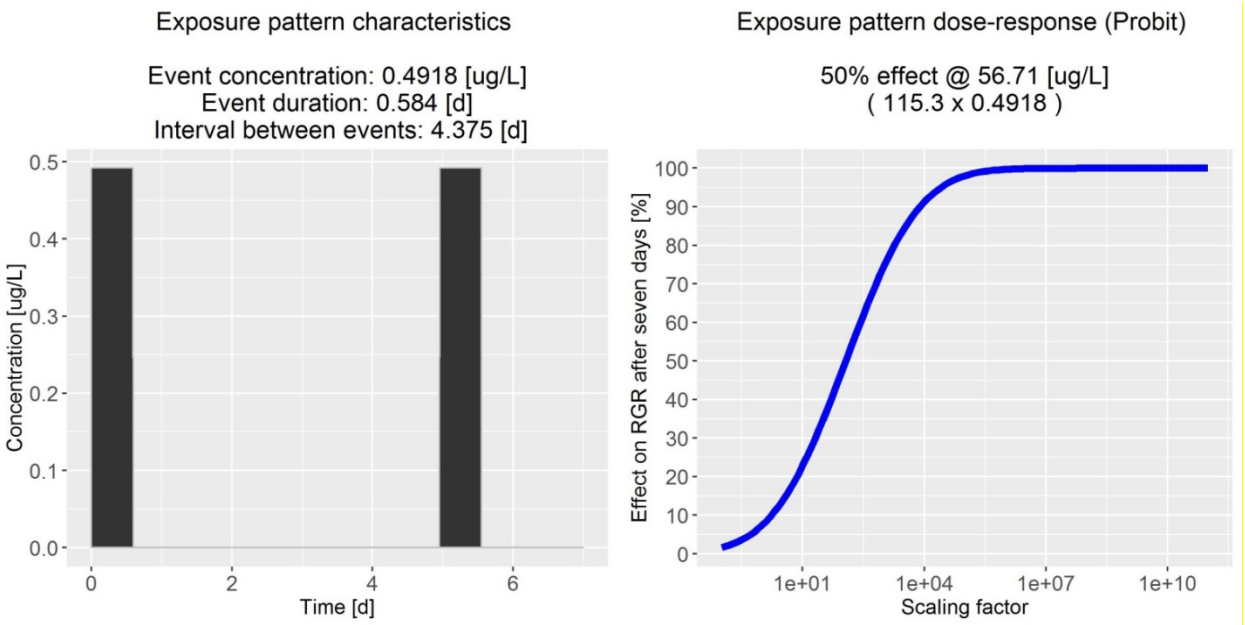


Figure A 36: ***Illustration of the evaluated 20-year surrogate exposure pattern and the corresponding dose-response relationship for scenario R4 stream, for use group B***

Table A 23: ***Assessing exposure patterns derived from FOCUS$_{sw}$ multiyear calculation to determine the corresponding exposure pattern that causes 50% effect by increasing the even concentration and keeping all other pattern characteristics - Use group B (winter cereals – end of winter to spring application / rate = 15 g/ha MSM)***

Scenario	***Pattern characteristics***				***Event conc. causing 50% effect [µg/L]***	***RAC$_{pattern}$ [µg/L]***	***RQ = PECmax / RAC$_{pattern}$)***
	80th perc. PECmax [µg/L]	***80th perc. events above Tier 1 RAC***	***80th perc. event duration above Tier 1 RAC [d]***	***20th per. interval betw. events above Tier 1 RAC [d]***			
R3 stream	*0.4524*	*2*	*0.8*	*7.3*	*1743*	*174*	*0.003*
R4 stream	*0.4918*	*2*	*0.6*	*4.4*	*56.7*	*5.7*	*0.086*

(b) Population effect modelling for FOCUSsw water bodies

Dynamics of a Lemna population growing outdoors in an edge-of-field surface water body were simulated for each of the crop relevant FOCUS$_{sw}$ exposure scenarios, for the critical GAP situations of the present product. The simulations and data interpretations were held identical to those previously reported for the standard FOCUS year, however were extended in the time dimension to consider the hourly prediction of exposure over a 20 years period of scenario weather data, resulting from the multi-year PECsw simulation (cf. summary in dRR E-Fate section).

Again, to generate supportive information on the margin of safety, Lemna population dynamics were simulated as well for exaggerated exposure situations, generated via a multiplication of the concentration dimension of the exposure patterns with exemplary scaling factors of either 10 or 100.

Results for use group B:

Only a condensed result overview is provided here for the sake of dRR length; for the full detailed simulation results reference is made to the original modelling report provided with this submission.

Table A 24: Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***					
Scaling factor ►	***1***					
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*					
Scenario ►	***D1d***	***D1s***	***D2d***	***D2s***	***D3d***	***D4p***
1975	*Neg.*	*Neg.*	*>30%<40% (62d)*	*>10%<20% (38d)*	*Neg.*	*Neg.*
1976	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1977	*>10%<20% (15d)*	*Neg.*	*>20%<30% (51d)*	*Neg.*	*Neg.*	*Neg.*
1978	*>40%<50% (37d)*	*>10%<20% (20d)*	*>20%<30% (47d)*	*>10%<20% (14d)*	*Neg.*	*Neg.*
1979	*Neg.*	*Neg.*	*>20%<30% (77d)*	*>10%<20% (44d)*	*Neg.*	*Neg.*
1980	*Neg.*	*Neg.*	*>20%<30% (59d)*	*>10%<20% (6d)*	*Neg.*	*Neg.*
1981	*Neg.*	*Neg.*	*>20%<30% (62d)*	*Neg.*	*Neg.*	*Neg.*
1982	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1983	*>40%<50% (48d)*	*>20%<30% (27d)*	*>20%<30% (53d)*	*>10%<20% (4d)*	*Neg.*	*Neg.*
1984	*Neg.*	*Neg.*	*>10%<20% (23d)*	*Neg.*	*Neg.*	*Neg.*
1985	*Neg.*	*Neg.*	*>30%<40% (68d)*	*>10%<20% (14d)*	*Neg.*	*Neg.*
1986	*Neg.*	*Neg.*	*>20%<30% (62d)*	*>10%<20% (19d)*	*Neg.*	*Neg.*
1987	*>50%<60% (64d)*	*>20%<30% (43d)*	*>20%<30% (66d)*	*>10%<20% (29d)*	*Neg.*	*Neg.*
1988	*Neg.*	*Neg.*	*>20%<30% (75d)*	*>10%<20% (4d)*	*Neg.*	*Neg.*
1989	*Neg.*	*Neg.*	*>20%<30% (46d)*	*Neg.*	*Neg.*	*Neg.*
1990	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1991	*>10%<20% (12d)*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1992	*>40%<50% (33d)*	*>10%<20% (14d)*	*>10%<20% (34d)*	*Neg.*	*Neg.*	*Neg.*
1993	*Neg.*	*Neg.*	*>10%<20% (38d)*	*Neg.*	*Neg.*	*Neg.*
1994	*Neg.*	*Neg.*	*>10%<20% (40d)*	*Neg.*	*Neg.*	*Neg.*

Neg. = negligible; d = days

Table (contd.): Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***					
Scaling factor ►	***1***					
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*					
Scenario ►	***D4s***	***D5p***	***D5s***	***D6d***	***R1p***	***R1s***
1975	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1976	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1977	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1978	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1979	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1980	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1981	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1982	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1983	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1984	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1985	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1986	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1987	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1988	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1989	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1990	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1991	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1992	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1993	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1994	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*

Neg. = negligible; d = days

Table (contd.): Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***	
Scaling factor ►	***1***	
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*	
Scenario ►	***R3s***	***R4s***
1975	*Neg.*	*Neg.*
1976	*Neg.*	*Neg.*
1977	*Neg.*	*Neg.*
1978	*Neg.*	*Neg.*
1979	*Neg.*	*Neg.*
1980	*Neg.*	*Neg.*
1981	*Neg.*	*Neg.*
1982	*Neg.*	*Neg.*
1983	*Neg.*	*Neg.*
1984	*Neg.*	*Neg.*
1985	*Neg.*	*Neg.*
1986	*Neg.*	*Neg.*
1987	*Neg.*	*Neg.*
1988	*Neg.*	*Neg.*
1989	*Neg.*	*Neg.*
1990	*Neg.*	*Neg.*
1991	*Neg.*	*Neg.*
1992	*Neg.*	*Neg.*
1993	*Neg.*	*Neg.*
1994	*Neg.*	*Neg.*

Neg. = negligible; d = days

Table (contd.): Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***					
Scaling factor ►	***10***					
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*					
Scenario ►	***D1d***	***D1s***	***D2d***	***D2s***	***D3d***	***D4p***
1975	*>60%<70% (278d)*	*>30%<40% (153d)*	*>90% (283d)*	*>90% (153d)*	*Neg.*	*Neg.*
1976	*>60%<70% (330d)*	*>30%<40% (160d)*	*>90% (332d)*	*>70%<80% (133d)*	*Neg.*	*Neg.*
1977	*>90% (289d)*	*>60%<70% (160d)*	*>90% (247d)*	*>80%<90% (149d)*	*Neg.*	*>10%<20% (50d)*
1978	*>90% (209d)*	*>70%<80% (112d)*	*>90% (299d)*	*>80%<90% (178d)*	*Neg.*	*Neg.*
1979	*>90% (179d)*	*>60%<70% (67d)*	*>90% (252d)*	*>90% (144d)*	*Neg.*	*Neg.*
1980	*>80%<90% (97d)*	*>20%<30% (53d)*	*>90% (302d)*	*>80%<90% (175d)*	*Neg.*	*Neg.*
1981	*>80%<90% (282d)*	*>20%<30% (58d)*	*>90% (309d)*	*>80%<90% (151d)*	*Neg.*	*>20%<30% (59d)*
1982	*>80%<90% (113d)*	*>30%<40% (67d)*	*>90% (284d)*	*>70%<80% (157d)*	*Neg.*	*>10%<20% (38d)*
1983	*>90% (258d)*	*>80%<90% (118d)*	*>90% (173d)*	*>80%<90% (119d)*	*Neg.*	*>20%<30% (52d)*
1984	*>90% (195d)*	*>30%<40% (123d)*	*>90% (291d)*	*>70%<80% (138d)*	*Neg.*	*Neg.*
1985	*>70%<80% (84d)*	*>10%<20% (28d)*	*>90% (240d)*	*>90% (152d)*	*Neg.*	*Neg.*
1986	*>80%<90% (122d)*	*>30%<40% (56d)*	*>90% (288d)*	*>80%<90% (135d)*	*>10%<20% (10d)*	*>10%<20% (35d)*
1987	*>90% (265d)*	*>70%<80% (194d)*	*>90% (300d)*	*>90% (151d)*	*Neg.*	*Neg.*
1988	*>60%<70% (296d)*	*>20%<30% (194d)*	*>90% (303d)*	*>90% (178d)*	*>20%<30% (60d)*	*>20%<30% (57d)*
1989	*>70%<80% (222d)*	*>40%<50% (125d)*	*>90% (329d)*	*>80%<90% (153d)*	*>10%<20% (39d)*	*Neg.*
1990	*>70%<80% (333d)*	*>30%<40% (105d)*	*>90% (231d)*	*>50%<60% (85d)*	*Neg.*	*Neg.*
1991	*>90% (295d)*	*>50%<60% (125d)*	*>90% (302d)*	*>70%<80% (157d)*	*Neg.*	*Neg.*
1992	*>90% (216d)*	*>70%<80% (123d)*	*>90% (223d)*	*>80%<90% (141d)*	*Neg.*	*Neg.*
1993	*>90% (179d)*	*>60%<70% (68d)*	*>90% (311d)*	*>80%<90% (146d)*	*Neg.*	*Neg.*
1994	*>90% (181d)*	*>60%<70% (83d)*	*>90% (293d)*	*>80%<90% (137d)*	*Neg.*	*>30%<40% (86d)*

Neg. = negligible; d = days

Table (contd.): Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***					
Scaling factor ►	***10***					
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*					
Scenario ►	***D4s***	***D5p***	***D5s***	***D6d***	***R1p***	***R1s***
1975	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (17d)*	*Neg.*	*Neg.*
1976	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1977	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1978	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1979	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1980	*Neg.*	*>50%<60% (96d)*	*>10%<20% (30d)*	*Neg.*	*Neg.*	*Neg.*
1981	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (16d)*	*Neg.*	*Neg.*
1982	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (27d)*	*Neg.*	*Neg.*
1983	*Neg.*	*>50%<60% (84d)*	*>10%<20% (20d)*	*>10%<20% (12d)*	*Neg.*	*Neg.*
1984	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1985	*Neg.*	*>20%<30% (44d)*	*Neg.*	*>10%<20% (29d)*	*Neg.*	*Neg.*
1986	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1987	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (33d)*	*Neg.*	*Neg.*
1988	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (29d)*	*Neg.*	*Neg.*
1989	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (18d)*	*Neg.*	*Neg.*
1990	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (10d)*	*Neg.*	*Neg.*
1991	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (8d)*	*Neg.*	*Neg.*
1992	*Neg.*	*Neg.*	*Neg.*	*>10%<20% (19d)*	*Neg.*	*Neg.*
1993	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*
1994	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*	*Neg.*

Neg. = negligible; d = days

Table (contd.): Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***	
Scaling factor ►	***10***	
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*	
Scenario ►	***R3s***	***R4s***
1975	*Neg.*	***Neg.***
1976	*Neg.*	*Neg.*
1977	*Neg.*	*Neg.*
1978	*Neg.*	*Neg.*
1979	*Neg.*	*Neg.*
1980	*Neg.*	*Neg.*
1981	*Neg.*	*Neg.*
1982	*Neg.*	*Neg.*
1983	*Neg.*	*Neg.*
1984	*Neg.*	*Neg.*
1985	*Neg.*	*Neg.*
1986	*Neg.*	*Neg.*
1987	*Neg.*	*Neg.*
1988	*Neg.*	*Neg.*
1989	*Neg.*	*Neg.*
1990	*Neg.*	*Neg.*
1991	*Neg.*	*Neg.*
1992	*Neg.*	*Neg.*
1993	*Neg.*	*Neg.*
1994	*Neg.*	*Neg.*

Neg. = negligible; d = days

Table (contd.): Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***					
Scaling factor ►	***100***					
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*					
Scenario ►	***D1d***	***D1s***	***D2d***	***D2s***	***D3d***	***D4p***
1975	*>90% (350d)*	*>80%<90% (235d)*	*>90% (358d)*	*>90% (360d)*	*>90% (356d)*	*>90% (340d)*
1976	*>90% (345d)*	*>80%<90% (259d)*	*>90% (360d)*	*>90% (361d)*	*>70%<80% (177d)*	*>90% (161d)*
1977	*>90% (322d)*	*>80%<90% (232d)*	*>90% (346d)*	*>90% (344d)*	*>90% (340d)*	*>90% (329d)*
1978	*>90% (351d)*	*>80%<90% (167d)*	*>90% (354d)*	*>90% (354d)*	*>90% (349d)*	*>90% (334d)*
1979	*>90% (344d)*	*>80%<90% (163d)*	*>90% (335d)*	*>90% (333d)*	*>90% (321d)*	*>90% (288d)*
1980	*>90% (276d)*	*>50%<60% (75d)*	*>90% (346d)*	*>90% (346d)*	*>90% (337d)*	*>90% (307d)*
1981	*>90% (325d)*	*>40%<50% (206d)*	*>90% (358d)*	*>90% (359d)*	*>90% (350d)*	*>90% (335d)*
1982	*>90% (292d)*	*>80%<90% (137d)*	*>90% (360d)*	*>90% (362d)*	*>90% (361d)*	*>90% (321d)*
1983	*>90% (354d)*	*>90% (188d)*	*>90% (361d)*	*>90% (361d)*	*>90% (359d)*	*>90% (357d)*
1984	*>90% (275d)*	*>70%<80% (159d)*	*>90% (357d)*	*>90% (358d)*	*>90% (354d)*	*>90% (343d)*
1985	*>90% (277d)*	*>60%<70% (85d)*	*>90% (338d)*	*>90% (336d)*	*>90% (335d)*	*>90% (300d)*
1986	*>90% (288d)*	*>80%<90% (104d)*	*>90% (353d)*	*>90% (352d)*	*>90% (351d)*	*>90% (332d)*
1987	*>90% (274d)*	*>80%<90% (238d)*	*>90% (343d)*	*>90% (344d)*	*>90% (328d)*	*>90% (287d)*
1988	*>90% (346d)*	*>70%<80% (317d)*	*>90% (363d)*	*>90% (362d)*	*>90% (363d)*	*>90% (360d)*
1989	*>90% (350d)*	*>80%<90% (196d)*	*>90% (360d)*	*>90% (358d)*	*>90% (359d)*	*>80%<90% (189d)*
1990	*>90% (345d)*	*>80%<90% (220d)*	*>90% (358d)*	*>90% (322d)*	*>90% (354d)*	*>90% (325d)*
1991	*>90% (323d)*	*>80%<90% (199d)*	*>90% (358d)*	*>90% (357d)*	*>90% (362d)*	*>90% (354d)*
1992	*>90% (351d)*	*>80%<90% (164d)*	*>90% (364d)*	*>90% (362d)*	*>90% (360d)*	*>90% (265d)*
1993	*>90% (344d)*	*>80%<90% (161d)*	*>90% (357d)*	*>90% (356d)*	*>90% (355d)*	*>90% (310d)*
1994	*>90% (345d)*	*>80%<90% (162d)*	*>90% (357d)*	*>90% (355d)*	*>90% (355d)*	*>90% (351d)*

Neg. = negligible; d = days

Table (contd.): Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***					
Scaling factor ►	***100***					
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*					
Scenario ►	***D4s***	***D5p***	***D5s***	***D6d***	***R1p***	***R1s***
1975	*>80%<90% (174d)*	*>70%<80% (152d)*	*>40%<50% (130d)*	*>60%<70% (94d)*	*Neg.*	*Neg.*
1976	*>40%<50% (112d)*	*>50%<60% (138d)*	*>10%<20% (28d)*	*>10%<20% (33d)*	*>20%<30% (34d)*	*Neg.*
1977	*>80%<90% (149d)*	*>50%<60% (133d)*	*>10%<20% (2d)*	*>30%<40% (38d)*	*Neg.*	*Neg.*
1978	*>70%<80% (135d)*	*>60%<70% (120d)*	*Neg.*	*>60%<70% (130d)*	*>20%<30% (30d)*	*Neg.*
1979	*>70%<80% (99d)*	*>70%<80% (245d)*	*>10%<20% (118d)*	*>50%<60% (125d)*	*>50%<60% (62d)*	*Neg.*
1980	*>50%<60% (177d)*	*>90% (357d)*	*>60%<70% (179d)*	*>50%<60% (113d)*	*>10%<20% (27d)*	*Neg.*
1981	*>70%<80% (217d)*	*>90% (345d)*	*>50%<60% (208d)*	*>70%<80% (133d)*	*>60%<70% (115d)*	*Neg.*
1982	*>70%<80% (203d)*	*>90% (254d)*	*>40%<50% (124d)*	*>80%<90% (167d)*	*>20%<30% (30d)*	*Neg.*
1983	*>90% (195d)*	*>90% (361d)*	*>70%<80% (141d)*	*>80%<90% (167d)*	*>70%<80% (90d)*	*>10%<20% (14d)*
1984	*>50%<60% (240d)*	*>90% (266d)*	*>40%<50% (157d)*	*>80%<90% (124d)*	*>10%<20% (3d)*	*Neg.*
1985	*>80%<90% (129d)*	*>90% (342d)*	*>50%<60% (114d)*	*>80%<90% (154d)*	*>10%<20% (1d)*	*Neg.*
1986	*>70%<80% (153d)*	*>90% (213d)*	*>40%<50% (136d)*	*>80%<90% (129d)*	*>20%<30% (23d)*	*>10%<20% (3d)*
1987	*>40%<50% (272d)*	*>60%<70% (190d)*	*>10%<20% (1d)*	*>90% (184d)*	*Neg.*	*Neg.*
1988	*>70%<80% (160d)*	*>90% (205d)*	*>30%<40% (107d)*	*>90% (169d)*	*Neg.*	*Neg.*
1989	*>60%<70% (181d)*	*>70%<80% (141d)*	*>20%<30% (60d)*	*>70%<80% (111d)*	*>70%<80% (106d)*	*Neg.*
1990	*>70%<80% (177d)*	*>70%<80% (155d)*	*>20%<30% (56d)*	*>40%<50% (61d)*	*Neg.*	*Neg.*
1991	*>70%<80% (282d)*	*>90% (352d)*	*>40%<50% (90d)*	*>90% (162d)*	*Neg.*	*Neg.*
1992	*>70%<80% (151d)*	*>80%<90% (173d)*	*>10%<20% (72d)*	*>70%<80% (97d)*	*Neg.*	*Neg.*
1993	*>50%<60% (232d)*	*>90% (333d)*	*>20%<30% (185d)*	*>10%<20% (31d)*	*Neg.*	*Neg.*
1994	*>90% (218d)*	*>90% (266d)*	*>50%<60% (121d)*	*>30%<40% (29d)*	*Neg.*	*Neg.*

Neg. = negligible; d = days

Table (contd.): Effect magnitude and duration caused by FOCUS multiyear exposure patterns from GAP I (1x3 g/ha iodosulfuron-methyl-sodium & 1x15 g/ha mesosulfuron-methyl). Columns highlighted in grey are results of the original FOCUSsw multiyear exposure patterns.

Level ►	***Step3***	
Scaling factor ►	***100***	
Year ▼	***GAP I = use group B*** *(end of winter-spring use on winter cereals, 1 x 3 g/ha IMS with consideration of metabolite AE F075736 & 15 g/ha MSM)*	
Scenario ►	***R3s***	***R4s***
1975	*Neg.*	*>10%<20% (3d)*
1976	*Neg.*	*Neg.*
1977	*>10%<20% (16d)*	*Neg.*
1978	*>10%<20% (10d)*	*Neg.*
1979	*>10%<20% (23d)*	*>10%<20% (3d)*
1980	*>10%<20% (1d)*	*Neg.*
1981	*Neg.*	*Neg.*
1982	*>10%<20% (1d)*	*Neg.*
1983	*>20%<30% (31d)*	*Neg.*
1984	*Neg.*	*Neg.*
1985	*Neg.*	*>10%<20% (20d)*
1986	*Neg.*	*Neg.*
1987	*Neg.*	*Neg.*
1988	*Neg.*	*Neg.*
1989	*Neg.*	*Neg.*
1990	*Neg.*	*Neg.*
1991	*Neg.*	*>10%<20% (11d)*
1992	*>10%<20% (13d)*	*Neg.*
1993	*Neg.*	*Neg.*
1994	*Neg.*	*>10%<20% (1d)*

Neg. = negligible; d = days

*Overall, the population simulation showed that consistently negligible effects on Lemna are expected for the exposure situation arising for all FOCUS multiyear exposure **run-off (R) scenarios**, for both critical uses assessed. A large margin of safety applies, as predicted effects were still negligible even when exploratively assuming a 10-fold exaggerated exposure situation; and only a 100-fold increase of the exposure patterns would result in a notable expression of effects in R1 stream, R3 stream and R4 stream water bodies for the application in spring and in autumn.*

*For drainage **scenarios D1 & D2 stream and ditch**, small (≤ 30%) to medium (≤ 50%) effects were predicted for the original exposure situation in some simulation years, reaching in maximum >50 / ≤60% for a single year in scenario D1 ditch.*
*For **all further drainage scenarios**, effects were negligible for the original exposure patterns representing the critical uses assessed.*

Explained by their longer-lasting (non-peak) exposure characteristics, drainage scenarios were found more responsive to explorative overdosing, and showed notable predicted effects at the 10x scaling factor, already.

***Tier 1 – considering mitigation measures:* Accurate GAP assessment based on FOCUS Step 4, all active substances and metabolite AE F075736**

As outlined under point 9.5.2.4, aquatic macrophyte risk assessment could in most parts be resolved on FOCUS Step 3 level. A FOCUS Step 4-based risk assessment was not deemed profitable for the remaining scenarios, as FOCUS Landscape & Mitigation procedures by definition do not foresee mitigation options for drainage route. For formal dossier completeness, RQ calculations at FOCUS Step 4 level are nevertheless provided as an appendix here in the following:

Iodosulfuron-methyl-sodium

Table A 25: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: winter cereals, 1 × 3 g iodosulfuron-methyl-sodium/ha, end of winter use

Winter cereals, end of winter-spring use, 3 g a.s./ha	***Scenario***	***PECsw STEP 4 - iodosulfuron-methyl-sodium***								***PECsw / RAC*** *RAC = 0.108 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D1 Ditch*	*0.0197*	*0.0058*	*0.0031*	*0.0018*	*0.0031*	*0.0018*	*0.0027*	*0.0016*	*0.182*	*0.054*	*0.029*	*0.017*	*0.029*	*0.017*	*0.025*	*0.015*
50 %		*0.0101*	*0.0031*	*0.0018*	*0.0011*	*0.0018*	*0.0011*	*0.0016*	*0.0010*	*0.094*	*0.029*	*0.017*	*0.010*	*0.017*	*0.010*	*0.015*	*0.009*
75 %		*0.0053*	*0.0018*	*0.0011*	*0.0011*	*0.0011*	*0.0011*	*0.0010*	*0.0010*	*0.049*	*0.017*	*0.010*	*0.010*	*0.010*	*0.010*	*0.009*	*0.009*
90 %		*0.0024*	*0.0011*	*0.0011*	*0.0011*	*0.0011*	*0.0011*	*0.0010*	*0.0010*	*0.022*	*0.010*	*0.010*	*0.010*	*0.010*	*0.010*	*0.009*	*0.009*
None	*D1 Stream*	*0.0165*	*0.0063*	*0.0034*	*0.0019*	*0.0034*	*0.0019*	*0.0006*	*0.0006*	*0.153*	*0.058*	*0.031*	*0.018*	*0.031*	*0.018*	*0.006*	*0.006*
50 %		*0.0084*	*0.0033*	*0.0019*	*0.0011*	*0.0019*	*0.0011*	*0.0006*	*0.0006*	*0.078*	*0.031*	*0.018*	*0.010*	*0.018*	*0.010*	*0.006*	*0.006*
75 %		*0.0043*	*0.0018*	*0.0011*	*0.0007*	*0.0011*	*0.0007*	*0.0006*	*0.0006*	*0.040*	*0.017*	*0.010*	*0.006*	*0.010*	*0.006*	*0.006*	*0.006*
90 %		*0.0019*	*0.0009*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0006*	*0.0006*	*0.018*	*0.008*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*
None	*D2 Ditch*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.0639*	*0.0639*	***1.426***	***1.426***	***1.426***	***1.426***	***1.426***	***1.426***	*0.591*	*0.591*
50 %		*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.0639*	*0.0639*	***1.426***	***1.426***	***1.426***	***1.426***	***1.426***	***1.426***	*0.591*	*0.591*
75 %		*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.0639*	*0.0639*	***1.426***	***1.426***	***1.426***	***1.426***	***1.426***	***1.426***	*0.591*	*0.591*
90 %		*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.1540*	*0.0639*	*0.0639*	***1.426***	***1.426***	***1.426***	***1.426***	***1.426***	***1.426***	*0.591*	*0.591*
None	*D2 Stream*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0332*	*0.0332*	*0.891*	*0.891*	*0.891*	*0.891*	*0.891*	*0.891*	*0.308*	*0.308*
50 %		*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0332*	*0.0332*	*0.891*	*0.891*	*0.891*	*0.891*	*0.891*	*0.891*	*0.308*	*0.308*
75 %		*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0332*	*0.0332*	*0.891*	*0.891*	*0.891*	*0.891*	*0.891*	*0.891*	*0.308*	*0.308*
90 %		*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0962*	*0.0332*	*0.0332*	*0.891*	*0.891*	*0.891*	*0.891*	*0.891*	*0.891*	*0.308*	*0.308*

Winter cereals, end of winter-spring use, 3 g a.s./ha	***Scenario***	***PECsw STEP 4 - iodosulfuron-methyl-sodium***								***PECsw / RAC*** *RAC = 0.108 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D3 Ditch*	*0.0191*	*0.0053*	*0.0026*	*0.0013*	*0.0026*	*0.0013*	*0.0003*	*0.0002*	*0.177*	*0.049*	*0.024*	*0.012*	*0.024*	*0.012*	*0.003*	*0.002*
50 %		*0.0095*	*0.0026*	*0.0013*	*0.0007*	*0.0013*	*0.0007*	*0.0002*	*<0.0001*	*0.088*	*0.024*	*0.012*	*0.006*	*0.012*	*0.006*	*0.002*	*<0.001*
75 %		*0.0048*	*0.0013*	*0.0007*	*0.0003*	*0.0007*	*0.0003*	*<0.0001*	*<0.0001*	*0.044*	*0.012*	*0.006*	*0.003*	*0.006*	*0.003*	*<0.001*	*<0.001*
90 %		*0.0019*	*0.0005*	*0.0003*	*0.0001*	*0.0003*	*0.0001*	*<0.0001*	*<0.0001*	*0.018*	*0.005*	*0.003*	*0.001*	*0.003*	*0.001*	*<0.001*	*<0.001*
None	*D4 Pond*	*0.0007*	*0.0006*	*0.0004*	*0.0003*	*0.0004*	*0.0003*	*0.0004*	*0.0003*	*0.006*	*0.006*	*0.004*	*0.003*	*0.004*	*0.003*	*0.003*	*0.003*
50 %		*0.0003*	*0.0003*	*0.0002*	*0.0002*	*0.0002*	*0.0002*	*0.0002*	*0.0001*	*0.003*	*0.003*	*0.002*	*0.002*	*0.002*	*0.002*	*0.002*	*0.001*
75 %		*0.0002*	*0.0002*	*0.0001*	*<0.0001*	*0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*0.002*	*0.002*	*0.001*	*<0.001*	*0.001*	*<0.001*	*<0.001*	*<0.001*
90 %		*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*
None	*D4 Stream*	*0.0144*	*0.0054*	*0.0028*	*0.0014*	*0.0028*	*0.0014*	*<0.0001*	*<0.0001*	*0.133*	*0.050*	*0.026*	*0.013*	*0.026*	*0.013*	*<0.001*	*<0.001*
50 %		*0.0072*	*0.0027*	*0.0014*	*0.0007*	*0.0014*	*0.0007*	*<0.0001*	*<0.0001*	*0.067*	*0.025*	*0.013*	*0.006*	*0.013*	*0.006*	*<0.001*	*<0.001*
75 %		*0.0036*	*0.0014*	*0.0007*	*0.0004*	*0.0007*	*0.0004*	*<0.0001*	*<0.0001*	*0.033*	*0.013*	*0.006*	*0.004*	*0.006*	*0.004*	*<0.001*	*<0.001*
90 %		*0.0014*	*0.0005*	*0.0003*	*0.0001*	*0.0003*	*0.0001*	*<0.0001*	*<0.0001*	*0.013*	*0.005*	*0.003*	*0.001*	*0.003*	*0.001*	*<0.001*	*<0.001*
None	*D5 Pond*	*0.0007*	*0.0006*	*0.0004*	*0.0003*	*0.0004*	*0.0003*	*0.0004*	*0.0001*	*0.006*	*0.006*	*0.004*	*0.003*	*0.004*	*0.003*	*0.003*	*0.001*
50 %		*0.0003*	*0.0003*	*0.0002*	*0.0002*	*0.0002*	*0.0002*	*0.0002*	*0.0001*	*0.003*	*0.003*	*0.002*	*0.002*	*0.002*	*0.002*	*0.002*	*0.001*
75 %		*0.0002*	*0.0002*	*0.0001*	*<0.0001*	*0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*0.002*	*0.002*	*0.001*	*<0.001*	*0.001*	*<0.001*	*<0.001*	*<0.001*
90 %		*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*
None	*D5 Stream*	*0.0149*	*0.0055*	*0.0029*	*0.0015*	*0.0029*	*0.0015*	*<0.0001*	*<0.0001*	*0.138*	*0.051*	*0.027*	*0.014*	*0.027*	*0.014*	*<0.001*	*<0.001*
50 %		*0.0074*	*0.0028*	*0.0015*	*0.0007*	*0.0015*	*0.0007*	*<0.0001*	*<0.0001*	*0.069*	*0.026*	*0.014*	*0.006*	*0.014*	*0.006*	*<0.001*	*<0.001*
75 %		*0.0037*	*0.0014*	*0.0007*	*0.0004*	*0.0007*	*0.0004*	*<0.0001*	*<0.0001*	*0.034*	*0.013*	*0.006*	*0.004*	*0.006*	*0.004*	*<0.001*	*<0.001*
90 %		*0.0015*	*0.0006*	*0.0003*	*0.0001*	*0.0003*	*0.0001*	*<0.0001*	*<0.0001*	*0.014*	*0.006*	*0.003*	*0.001*	*0.003*	*0.001*	*<0.001*	*<0.001*
None	*D6 Ditch*	*0.0190*	*0.0053*	*0.0027*	*0.0014*	*0.0027*	*0.0014*	*0.0003*	*0.0002*	*0.176*	*0.049*	*0.025*	*0.013*	*0.025*	*0.013*	*0.002*	*0.002*
50 %		*0.0095*	*0.0027*	*0.0014*	*0.0007*	*0.0014*	*0.0007*	*0.0002*	*0.0001*	*0.088*	*0.025*	*0.013*	*0.006*	*0.013*	*0.006*	*0.002*	*0.001*

Winter cereals, end of winter-spring use, 3 g a.s./ha	***Scenario***	***PECsw STEP 4 - iodosulfuron-methyl-sodium***								***PECsw / RAC*** *RAC = 0.108 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
75 %		*0.0048*	*0.0014*	*0.0007*	*0.0004*	*0.0007*	*0.0004*	*0.0001*	*0.0001*	*0.044*	*0.013*	*0.006*	*0.004*	*0.006*	*0.004*	*0.001*	*0.001*
90 %		*0.0020*	*0.0006*	*0.0004*	*0.0002*	*0.0004*	*0.0002*	*0.0001*	*0.0001*	*0.019*	*0.006*	*0.004*	*0.002*	*0.004*	*0.002*	*0.001*	*0.001*
None	*R1 Pond*	*0.0007*	*0.0006*	*0.0005*	*0.0004*	*0.0004*	*0.0003*	*0.0004*	*0.0003*	*0.006*	*0.006*	*0.005*	*0.004*	*0.004*	*0.003*	*0.003*	*0.003*
50 %		*0.0005*	*0.0004*	*0.0004*	*0.0004*	*0.0002*	*0.0002*	*0.0002*	*0.0001*	*0.005*	*0.004*	*0.004*	*0.004*	*0.002*	*0.002*	*0.002*	*0.001*
75 %		*0.0004*	*0.0004*	*0.0003*	*0.0003*	*0.0002*	*0.0001*	*0.0002*	*<0.0001*	*0.004*	*0.004*	*0.003*	*0.003*	*0.002*	*0.001*	*0.001*	*<0.001*
90 %		*0.0003*	*0.0003*	*0.0003*	*0.0003*	*0.0001*	*<0.0001*	*0.0001*	*<0.0001*	*0.003*	*0.003*	*0.003*	*0.003*	*0.001*	*<0.001*	*0.001*	*<0.001*
None	*R1 Stream*	*0.0139*	*0.0139*	*0.0139*	*0.0139*	*0.0057*	*0.0029*	*0.0003*	*0.0002*	*0.129*	*0.129*	*0.129*	*0.129*	*0.053*	*0.027*	*0.003*	*0.002*
50 %		*0.0139*	*0.0139*	*0.0139*	*0.0139*	*0.0057*	*0.0029*	*0.0003*	*0.0002*	*0.129*	*0.129*	*0.129*	*0.129*	*0.053*	*0.027*	*0.003*	*0.002*
75 %		*0.0139*	*0.0139*	*0.0139*	*0.0139*	*0.0057*	*0.0029*	*0.0003*	*0.0002*	*0.129*	*0.129*	*0.129*	*0.129*	*0.053*	*0.027*	*0.003*	*0.002*
90 %		*0.0139*	*0.0139*	*0.0139*	*0.0139*	*0.0057*	*0.0029*	*0.0003*	*0.0002*	*0.129*	*0.129*	*0.129*	*0.129*	*0.053*	*0.027*	*0.003*	*0.002*
None	*R3 Stream*	*0.0428*	*0.0428*	*0.0428*	*0.0428*	*0.0189*	*0.0098*	*0.0013*	*0.0007*	*0.396*	*0.396*	*0.396*	*0.396*	*0.175*	*0.091*	*0.012*	*0.006*
50 %		*0.0428*	*0.0428*	*0.0428*	*0.0428*	*0.0189*	*0.0098*	*0.0013*	*0.0007*	*0.396*	*0.396*	*0.396*	*0.396*	*0.175*	*0.091*	*0.012*	*0.006*
75 %		*0.0428*	*0.0428*	*0.0428*	*0.0428*	*0.0189*	*0.0098*	*0.0013*	*0.0007*	*0.396*	*0.396*	*0.396*	*0.396*	*0.175*	*0.091*	*0.012*	*0.006*
90 %		*0.0428*	*0.0428*	*0.0428*	*0.0428*	*0.0189*	*0.0098*	*0.0013*	*0.0007*	*0.396*	*0.396*	*0.396*	*0.396*	*0.175*	*0.091*	*0.012*	*0.006*
None	*R4 Stream*	*0.0292*	*0.0292*	*0.0292*	*0.0292*	*0.0133*	*0.0070*	*0.0016*	*0.0008*	*0.270*	*0.270*	*0.270*	*0.270*	*0.123*	*0.065*	*0.015*	*0.008*
50 %		*0.0292*	*0.0292*	*0.0292*	*0.0292*	*0.0133*	*0.0070*	*0.0016*	*0.0008*	*0.270*	*0.270*	*0.270*	*0.270*	*0.123*	*0.065*	*0.015*	*0.008*
75 %		*0.0292*	*0.0292*	*0.0292*	*0.0292*	*0.0133*	*0.0070*	*0.0016*	*0.0008*	*0.270*	*0.270*	*0.270*	*0.270*	*0.123*	*0.065*	*0.015*	*0.008*
90 %		*0.0292*	*0.0292*	*0.0292*	*0.0292*	*0.0133*	*0.0070*	*0.0016*	*0.0008*	*0.270*	*0.270*	*0.270*	*0.270*	*0.123*	*0.065*	*0.015*	*0.008*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Table A 26: ***Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: winter cereals, 1 × 2 g iodosulfuron-methyl-sodium/ha, autumn use***

Winter cereals, autumn use, 2 g a.s./ha	***Scenario***	***PECsw STEP 4 - iodosulfuron-methyl-sodium***								***PECsw / RAC*** *RAC = 0.108 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D1 Ditch*	*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0766*	*0.0766*	*0.831*	*0.831*	*0.831*	*0.831*	*0.831*	*0.831*	*0.709*	*0.709*
50 %		*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0766*	*0.0766*	*0.831*	*0.831*	*0.831*	*0.831*	*0.831*	*0.831*	*0.709*	*0.709*
75 %		*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0897*	*0.0766*	*0.0765*	*0.831*	*0.831*	*0.831*	*0.831*	*0.831*	*0.831*	*0.709*	*0.708*
90 %		*0.0897*	*0.0897*	*0.0897*	*0.0896*	*0.0897*	*0.0896*	*0.0765*	*0.0765*	*0.831*	*0.831*	*0.831*	*0.830*	*0.831*	*0.830*	*0.708*	*0.708*
None	*D1 Stream*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0506*	*0.0506*	*0.531*	*0.531*	*0.531*	*0.531*	*0.531*	*0.531*	*0.469*	*0.469*
50 %		*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0506*	*0.0506*	*0.531*	*0.531*	*0.531*	*0.531*	*0.531*	*0.531*	*0.469*	*0.469*
75 %		*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0506*	*0.0506*	*0.531*	*0.531*	*0.531*	*0.531*	*0.531*	*0.531*	*0.469*	*0.469*
90 %		*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0573*	*0.0506*	*0.0506*	*0.531*	*0.531*	*0.531*	*0.531*	*0.531*	*0.531*	*0.469*	*0.469*
None	*D2 Ditch*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0312*	*0.0312*	*0.743*	*0.743*	*0.743*	*0.743*	*0.743*	*0.743*	*0.289*	*0.289*
50 %		*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0312*	*0.0312*	*0.743*	*0.743*	*0.743*	*0.743*	*0.743*	*0.743*	*0.289*	*0.289*
75 %		*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0312*	*0.0312*	*0.743*	*0.743*	*0.743*	*0.743*	*0.743*	*0.743*	*0.289*	*0.289*
90 %		*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0802*	*0.0312*	*0.0312*	*0.743*	*0.743*	*0.743*	*0.743*	*0.743*	*0.743*	*0.289*	*0.289*
None	*D2 Stream*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0176*	*0.0176*	*0.466*	*0.466*	*0.466*	*0.466*	*0.466*	*0.466*	*0.163*	*0.163*
50 %		*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0176*	*0.0176*	*0.466*	*0.466*	*0.466*	*0.466*	*0.466*	*0.466*	*0.163*	*0.163*
75 %		*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0176*	*0.0176*	*0.466*	*0.466*	*0.466*	*0.466*	*0.466*	*0.466*	*0.163*	*0.163*
90 %		*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0503*	*0.0176*	*0.0176*	*0.466*	*0.466*	*0.466*	*0.466*	*0.466*	*0.466*	*0.163*	*0.163*
None	*D3 Ditch*	*0.0128*	*0.0033*	*0.0020*	*0.0010*	*0.0020*	*0.0010*	*0.0002*	*0.0001*	*0.119*	*0.031*	*0.019*	*0.009*	*0.019*	*0.009*	*0.002*	*0.001*
50 %		*0.0064*	*0.0016*	*0.0010*	*0.0005*	*0.0010*	*0.0005*	*0.0001*	*<0.0001*	*0.059*	*0.015*	*0.009*	*0.005*	*0.009*	*0.005*	*0.001*	*0.001*
75 %		*0.0032*	*0.0008*	*0.0005*	*0.0003*	*0.0005*	*0.0003*	*<0.0001*	*<0.0001*	*0.030*	*0.007*	*0.005*	*0.003*	*0.005*	*0.003*	*0.001*	*0.001*
90 %		*0.0013*	*0.0003*	*0.0002*	*<0.0001*	*0.0002*	*<0.0001*	*<0.0001*	*<0.0001*	*0.012*	*0.003*	*0.002*	*<0.001*	*0.002*	*<0.001*	*0.001*	*0.001*

Winter cereals, autumn use, 2 g a.s./ha	***Scenario***	***PECsw STEP 4 - iodosulfuron-methyl-sodium***								***PECsw / RAC*** *RAC = 0.108 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D4 Pond*	*0.0039*	*0.0039*	*0.0039*	*0.0038*	*0.0039*	*0.0038*	*0.0038*	*0.0038*	*0.036*	*0.036*	*0.036*	*0.035*	*0.036*	*0.035*	*0.035*	*0.035*
50 %		*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0037*	*0.035*	*0.035*	*0.035*	*0.035*	*0.035*	*0.035*	*0.035*	*0.034*
75 %		*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0037*	*0.0037*	*0.035*	*0.035*	*0.035*	*0.035*	*0.035*	*0.035*	*0.034*	*0.034*
90 %		*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0038*	*0.0037*	*0.0037*	*0.035*	*0.035*	*0.035*	*0.035*	*0.035*	*0.035*	*0.034*	*0.034*
None	*D4 Stream*	*0.0103*	*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0043*	*0.0043*	*0.095*	*0.051*	*0.051*	*0.051*	*0.051*	*0.051*	*0.040*	*0.040*
50 %		*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0043*	*0.0043*	*0.051*	*0.051*	*0.051*	*0.051*	*0.051*	*0.051*	*0.040*	*0.040*
75 %		*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0043*	*0.0043*	*0.051*	*0.051*	*0.051*	*0.051*	*0.051*	*0.051*	*0.040*	*0.040*
90 %		*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0055*	*0.0043*	*0.0043*	*0.051*	*0.051*	*0.051*	*0.051*	*0.051*	*0.051*	*0.040*	*0.040*
None	*D5 Pond*	*0.0008*	*0.0008*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.007*	*0.007*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*
50 %		*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*
75 %		*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*
90 %		*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0007*	*0.0006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*	*0.006*
None	*D5 Stream*	*0.0117*	*0.0045*	*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0014*	*0.0014*	*0.108*	*0.042*	*0.027*	*0.027*	*0.027*	*0.027*	*0.013*	*0.013*
50 %		*0.0059*	*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0014*	*0.0014*	*0.055*	*0.027*	*0.027*	*0.027*	*0.027*	*0.027*	*0.013*	*0.013*
75 %		*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0014*	*0.0014*	*0.027*	*0.027*	*0.027*	*0.027*	*0.027*	*0.027*	*0.013*	*0.013*
90 %		*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0029*	*0.0014*	*0.0014*	*0.027*	*0.027*	*0.027*	*0.027*	*0.027*	*0.027*	*0.013*	*0.013*
None	*D6 Ditch*	*0.0127*	*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0028*	*0.0028*	*0.118*	*0.101*	*0.101*	*0.101*	*0.101*	*0.101*	*0.026*	*0.026*
50 %		*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0028*	*0.0028*	*0.101*	*0.101*	*0.101*	*0.101*	*0.101*	*0.101*	*0.026*	*0.026*
75 %		*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0028*	*0.0028*	*0.101*	*0.101*	*0.101*	*0.101*	*0.101*	*0.101*	*0.026*	*0.026*
90 %		*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0109*	*0.0028*	*0.0028*	*0.101*	*0.101*	*0.101*	*0.101*	*0.101*	*0.101*	*0.026*	*0.026*
None	*R1 Pond*	*0.0004*	*0.0004*	*0.0003*	*0.0002*	*0.0003*	*0.0002*	*0.0003*	*0.0002*	*0.004*	*0.004*	*0.003*	*0.002*	*0.003*	*0.002*	*0.003*	*0.002*
50 %		*0.0002*	*0.0002*	*0.0002*	*0.0001*	*0.0002*	*0.0001*	*0.0001*	*<0.0001*	*0.002*	*0.002*	*0.002*	*0.001*	*0.002*	*0.001*	*0.001*	*<0.001*
75 %		*0.0001*	*0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*0.001*	*0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*

Winter cereals, autumn use, 2 g a.s./ha	**Scenario**	**PECsw STEP 4 - iodosulfuron-methyl-sodium**								**PECsw / RAC** RAC = 0.108 µg/L							
		PEC gl-max						**7-d PECtwa**		**PEC gl-max**						**7-d PECtwa**	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
90 %		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
None	R1 Stream	0.0107	0.0107	0.0107	0.0107	0.0043	0.0022	<0.0001	<0.0001	0.099	0.099	0.099	0.099	0.040	0.020	0.001	0.001
50 %		0.0107	0.0107	0.0107	0.0107	0.0043	0.0022	<0.0001	<0.0001	0.099	0.099	0.099	0.099	0.040	0.020	0.001	0.001
75 %		0.0107	0.0107	0.0107	0.0107	0.0043	0.0022	<0.0001	<0.0001	0.099	0.099	0.099	0.099	0.040	0.020	0.001	0.001
90 %		0.0107	0.0107	0.0107	0.0107	0.0043	0.0022	<0.0001	<0.0001	0.099	0.099	0.099	0.099	0.040	0.020	0.001	0.001
None	R3 Stream	0.0925	0.0925	0.0925	0.0925	0.0416	0.0217	0.0033	0.0017	0.856	0.856	0.856	0.856	0.385	0.201	0.031	0.016
50 %		0.0925	0.0925	0.0925	0.0925	0.0416	0.0217	0.0032	0.0017	0.856	0.856	0.856	0.856	0.385	0.201	0.030	0.016
75 %		0.0925	0.0925	0.0925	0.0925	0.0416	0.0217	0.0032	0.0017	0.856	0.856	0.856	0.856	0.385	0.201	0.030	0.016
90 %		0.0925	0.0925	0.0925	0.0925	0.0416	0.0217	0.0032	0.0017	0.856	0.856	0.856	0.856	0.385	0.201	0.030	0.016
None	R4 Stream	0.0242	0.0242	0.0242	0.0242	0.0109	0.0057	0.0010	0.0005	0.224	0.224	0.224	0.224	0.101	0.053	0.009	0.005
50 %		0.0242	0.0242	0.0242	0.0242	0.0109	0.0057	0.0010	0.0005	0.224	0.224	0.224	0.224	0.101	0.053	0.009	0.005
75 %		0.0242	0.0242	0.0242	0.0242	0.0109	0.0057	0.0010	0.0005	0.224	0.224	0.224	0.224	0.101	0.053	0.009	0.005
90 %		0.0242	0.0242	0.0242	0.0242	0.0109	0.0057	0.0010	0.0005	0.224	0.224	0.224	0.224	0.101	0.053	0.009	0.005

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Table A 27: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: spring cereals, 1 × 2 g iodosulfuron-methyl-sodium/ha, spring use

Spring cereals, spring use, 2 g a.s./ha	**Scenario**	**PECsw STEP 4 - iodosulfuron-methyl-sodium**								**PECsw / RAC** RAC = 0.108µg/L							
		PEC gl-max						**7-d PECtwa**		**PEC gl-max**						**7-d PECtwa**	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
None	D1 Ditch	0.0130	0.0034	0.0021	0.0011	0.0021	0.0011	0.0009	0.0005	0.120	0.031	0.019	0.010	0.019	0.010	0.008	0.005
50 %		0.0066	0.0018	0.0011	0.0006	0.0011	0.0006	0.0005	0.0003	0.061	0.017	0.010	0.006	0.010	0.006	0.005	0.003
75 %		0.0034	0.0009	0.0006	0.0004	0.0006	0.0004	0.0003	0.0002	0.031	0.008	0.006	0.004	0.006	0.004	0.003	0.002
90 %		0.0014	0.0004	0.0003	0.0002	0.0003	0.0002	0.0002	0.0002	0.013	0.004	0.003	0.002	0.003	0.002	0.002	0.002
None	D1 Stream	0.0102	0.0039	0.0022	0.0010	0.0022	0.0010	0.0001	0.0001	0.094	0.036	0.020	0.009	0.020	0.009	0.001	0.001
50 %		0.0051	0.0020	0.0011	0.0005	0.0011	0.0005	0.0001	0.0001	0.047	0.019	0.010	0.005	0.010	0.005	0.001	0.001
75 %		0.0026	0.0011	0.0006	0.0003	0.0006	0.0003	0.0001	0.0001	0.024	0.010	0.006	0.003	0.006	0.003	0.001	0.001
90 %		0.0011	0.0005	0.0003	0.0002	0.0003	0.0002	0.0001	0.0001	0.010	0.005	0.003	0.002	0.003	0.002	0.001	0.001
None	D3 Ditch	0.0128	0.0033	0.0020	0.0010	0.0020	0.0010	0.0003	0.0001	0.119	0.031	0.019	0.009	0.019	0.009	0.003	0.001
50 %		0.0064	0.0016	0.0010	0.0005	0.0010	0.0005	0.0001	<0.0001	0.059	0.015	0.009	0.005	0.009	0.005	0.001	<0.001
75 %		0.0032	0.0008	0.0005	0.0003	0.0005	0.0003	<0.0001	<0.0001	0.030	0.007	0.005	0.003	0.005	0.003	<0.001	<0.001
90 %		0.0013	0.0003	0.0002	<0.0001	0.0002	<0.0001	<0.0001	<0.0001	0.012	0.003	0.002	<0.001	0.002	<0.001	<0.001	<0.001
None	D4 Pond	0.0004	0.0004	0.0003	0.0002	0.0003	0.0002	0.0003	0.0002	0.004	0.004	0.003	0.002	0.003	0.002	0.003	0.002
50 %		0.0002	0.0002	0.0002	0.0001	0.0002	0.0001	0.0001	<0.0001	0.002	0.002	0.002	0.001	0.002	0.001	0.001	<0.001
75 %		0.0001	0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
90 %		<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
None	D4 Stream	0.0103	0.0039	0.0021	0.0009	0.0021	0.0009	<0.0001	<0.0001	0.095	0.036	0.019	0.008	0.019	0.008	<0.001	<0.001
50 %		0.0051	0.0020	0.0011	0.0005	0.0011	0.0005	<0.0001	<0.0001	0.047	0.019	0.010	0.005	0.010	0.005	<0.001	<0.001
75 %		0.0026	0.0010	0.0005	0.0002	0.0005	0.0002	<0.0001	<0.0001	0.024	0.009	0.005	0.002	0.005	0.002	<0.001	<0.001
90 %		0.0010	0.0004	0.0002	<0.0001	0.0002	<0.0001	<0.0001	<0.0001	0.009	0.004	0.002	<0.001	0.002	<0.001	<0.001	<0.001

Spring cereals, spring use, 2 g a.s./ha	***Scenario***	***PECsw STEP 4 - iodosulfuron-methyl-sodium***								***PECsw / RAC*** *RAC = 0.108µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D5 Pond*	*0.0004*	*0.0004*	*0.0003*	*0.0002*	*0.0003*	*0.0002*	*0.0003*	*0.0002*	*0.004*	*0.004*	*0.003*	*0.002*	*0.003*	*0.002*	*0.003*	*0.002*
50 %		*0.0002*	*0.0002*	*0.0002*	*0.0001*	*0.0002*	*0.0001*	*0.0001*	*<0.0001*	*0.002*	*0.002*	*0.002*	*0.001*	*0.002*	*0.001*	*0.001*	*<0.001*
75 %		*0.0001*	*0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*0.001*	*0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*
90 %		*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*
None	*D5 Stream*	*0.0100*	*0.0038*	*0.0021*	*0.0009*	*0.0021*	*0.0009*	*<0.0001*	*<0.0001*	*0.093*	*0.035*	*0.019*	*0.008*	*0.019*	*0.008*	*<0.001*	*<0.001*
50 %		*0.0050*	*0.0019*	*0.0010*	*0.0004*	*0.0010*	*0.0004*	*<0.0001*	*<0.0001*	*0.046*	*0.018*	*0.009*	*0.004*	*0.009*	*0.004*	*<0.001*	*<0.001*
75 %		*0.0025*	*0.0010*	*0.0005*	*0.0002*	*0.0005*	*0.0002*	*<0.0001*	*<0.0001*	*0.023*	*0.009*	*0.005*	*0.002*	*0.005*	*0.002*	*<0.001*	*<0.001*
90 %		*0.0010*	*0.0004*	*0.0002*	*<0.0001*	*0.0002*	*<0.0001*	*<0.0001*	*<0.0001*	*0.009*	*0.004*	*0.002*	*<0.001*	*0.002*	*<0.001*	*<0.001*	*<0.001*
None	*R4 Stream*	*0.0083*	*0.0032*	*0.0017*	*0.0007*	*0.0017*	*0.0007*	*<0.0001*	*<0.0001*	*0.077*	*0.030*	*0.016*	*0.006*	*0.016*	*0.006*	*<0.001*	*<0.001*
50 %		*0.0041*	*0.0016*	*0.0009*	*0.0004*	*0.0009*	*0.0004*	*<0.0001*	*<0.0001*	*0.038*	*0.015*	*0.008*	*0.004*	*0.008*	*0.004*	*<0.001*	*<0.001*
75 %		*0.0021*	*0.0008*	*0.0004*	*0.0002*	*0.0004*	*0.0002*	*<0.0001*	*<0.0001*	*0.019*	*0.007*	*0.004*	*0.002*	*0.004*	*0.002*	*<0.001*	*<0.001*
90 %		*0.0008*	*0.0003*	*0.0002*	*<0.0001*	*0.0002*	*<0.0001*	*<0.0001*	*<0.0001*	*0.007*	*0.003*	*0.002*	*<0.001*	*0.002*	*<0.001*	*<0.001*	*<0.001*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Metabolite AE F075736 of Iodosulfuron-methyl-sodium

Table A 28: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F075736 based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: winter cereals, 1 × 3 g iodosulfuron-methyl-sodium/ha, end of winter use

Winter cereals, end of winter-spring use, 3 g a.s./ha	Scenario	PECsw STEP 4 - AE F075736								PECsw / RAC							
		PEC gl-max						7-d PECtwa		RAC = 0.057 µg/L PEC gl-max						RAC = 0.073µg/L 7-d PECtwa	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
None	D1 Ditch	0.0348	0.0348	0.0348	0.0348	0.0348	0.0348	0.0342	0.0342	0.611	0.611	0.611	0.611	0.611	0.611	0.468	0.468
50 %		0.0348	0.0348	0.0348	0.0348	0.0348	0.0348	0.0342	0.0342	0.611	0.611	0.611	0.611	0.611	0.611	0.468	0.468
75 %		0.0348	0.0348	0.0348	0.0348	0.0348	0.0348	0.0342	0.0342	0.611	0.611	0.611	0.611	0.611	0.611	0.468	0.468
90 %		0.0348	0.0348	0.0348	0.0348	0.0348	0.0348	0.0342	0.0342	0.611	0.611	0.611	0.611	0.611	0.611	0.468	0.468
None	D1 Stream	0.0282	0.0282	0.0282	0.0282	0.0282	0.0282	0.0201	0.0201	0.495	0.495	0.495	0.495	0.495	0.495	0.275	0.275
50 %		0.0282	0.0282	0.0282	0.0282	0.0282	0.0282	0.0201	0.0201	0.495	0.495	0.495	0.495	0.495	0.495	0.275	0.275
75 %		0.0282	0.0282	0.0282	0.0282	0.0282	0.0282	0.0201	0.0201	0.495	0.495	0.495	0.495	0.495	0.495	0.275	0.275
90 %		0.0282	0.0282	0.0282	0.0282	0.0282	0.0282	0.0201	0.0201	0.495	0.495	0.495	0.495	0.495	0.495	0.275	0.275
None	D2 Ditch	0.1583	0.1583	0.1583	0.1583	0.1583	0.1583	0.1122	0.1122	**2.777**	**2.777**	**2.777**	**2.777**	**2.777**	**2.777**	**1.537**	**1.537**
50 %		0.1583	0.1583	0.1583	0.1583	0.1583	0.1583	0.1122	0.1122	**2.777**	**2.777**	**2.777**	**2.777**	**2.777**	**2.777**	**1.537**	**1.537**
75 %		0.1583	0.1583	0.1583	0.1583	0.1583	0.1583	0.1122	0.1122	**2.777**	**2.777**	**2.777**	**2.777**	**2.777**	**2.777**	**1.537**	**1.537**
90 %		0.1583	0.1583	0.1583	0.1583	0.1583	0.1583	0.1122	0.1122	**2.777**	**2.777**	**2.777**	**2.777**	**2.777**	**2.777**	**1.537**	**1.537**
None	D2 Stream	0.1302	0.1302	0.1302	0.1302	0.1302	0.1302	0.0697	0.0697	**2.284**	**2.284**	**2.284**	**2.284**	**2.284**	**2.284**	0.954	0.954
50 %		0.1302	0.1302	0.1302	0.1302	0.1302	0.1302	0.0697	0.0697	**2.284**	**2.284**	**2.284**	**2.284**	**2.284**	**2.284**	0.954	0.954
75 %		0.1302	0.1302	0.1302	0.1302	0.1302	0.1302	0.0697	0.0697	**2.284**	**2.284**	**2.284**	**2.284**	**2.284**	**2.284**	0.954	0.954
90 %		0.1302	0.1302	0.1302	0.1302	0.1302	0.1302	0.0697	0.0697	**2.284**	**2.284**	**2.284**	**2.284**	**2.284**	**2.284**	0.954	0.954
None	D3 Ditch	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.093	0.093	0.093	0.093	0.093	0.093	0.073	0.073

Winter cereals, end of winter-spring use, 3 g a.s./ha	**Scenario**	**PECsw STEP 4 - AE F075736**								**PECsw / RAC**							
		PEC gl-max						**7-d PECtwa**		RAC = 0.057 µg/L **PEC gl-max**						RAC = 0.073µg/L **7-d PECtwa**	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
50 %		0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.093	0.093	0.093	0.093	0.093	0.093	0.073	0.073
75 %		0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.093	0.093	0.093	0.093	0.093	0.093	0.073	0.073
90 %		0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.0053	0.093	0.093	0.093	0.093	0.093	0.093	0.073	0.073
None	D4 Pond	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.216	0.216	0.216	0.216	0.216	0.216	0.169	0.169
50 %		0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.216	0.216	0.216	0.216	0.216	0.216	0.169	0.169
75 %		0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.216	0.216	0.216	0.216	0.216	0.216	0.168	0.168
90 %		0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.0123	0.216	0.216	0.216	0.216	0.216	0.216	0.168	0.168
None	D4 Stream	0.0065	0.0065	0.0065	0.0065	0.0065	0.0065	0.0062	0.0062	0.114	0.114	0.114	0.114	0.114	0.114	0.085	0.085
50 %		0.0065	0.0065	0.0065	0.0065	0.0065	0.0065	0.0062	0.0062	0.114	0.114	0.114	0.114	0.114	0.114	0.085	0.085
75 %		0.0065	0.0065	0.0065	0.0065	0.0065	0.0065	0.0062	0.0062	0.114	0.114	0.114	0.114	0.114	0.114	0.085	0.085
90 %		0.0065	0.0065	0.0065	0.0065	0.0065	0.0065	0.0062	0.0062	0.114	0.114	0.114	0.114	0.114	0.114	0.085	0.085
None	D5 Pond	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.042	0.042	0.042	0.042	0.042	0.042	0.033	0.032
50 %		0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.042	0.042	0.042	0.042	0.042	0.042	0.032	0.032
75 %		0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.042	0.042	0.042	0.042	0.042	0.042	0.032	0.032
90 %		0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.0024	0.042	0.042	0.042	0.042	0.042	0.042	0.032	0.032
None	D5 Stream	0.0013	0.0013	0.0013	0.0013	0.0013	0.0013	0.0011	0.0011	0.023	0.023	0.023	0.023	0.023	0.023	0.016	0.016
50 %		0.0013	0.0013	0.0013	0.0013	0.0013	0.0013	0.0011	0.0011	0.023	0.023	0.023	0.023	0.023	0.023	0.016	0.016
75 %		0.0013	0.0013	0.0013	0.0013	0.0013	0.0013	0.0011	0.0011	0.023	0.023	0.023	0.023	0.023	0.023	0.016	0.016
90 %		0.0013	0.0013	0.0013	0.0013	0.0013	0.0013	0.0011	0.0011	0.023	0.023	0.023	0.023	0.023	0.023	0.016	0.016
None	D6 Ditch	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.018	0.018	0.018	0.018	0.018	0.018	0.013	0.013
50 %		0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.018	0.018	0.018	0.018	0.018	0.018	0.013	0.013
75 %		0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.018	0.018	0.018	0.018	0.018	0.018	0.013	0.013

Winter cereals, end of winter-spring use, 3 g a.s./ha	**Scenario**	**PECsw STEP 4 - AE F075736**								**PECsw / RAC**							
		PEC gl-max						**7-d PECtwa**		RAC = 0.057 µg/L **PEC gl-max**						RAC = 0.073µg/L **7-d PECtwa**	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
90 %		0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.0010	0.018	0.018	0.018	0.018	0.018	0.018	0.013	0.013
None	R1 Pond	0.0003	0.0003	0.0002	0.0002	0.0001	<0.0001	0.0001	<0.0001	0.005	0.005	0.004	0.004	0.002	<0.002	0.002	<0.001
50 %		0.0002	0.0002	0.0002	0.0002	<0.0001	<0.0001	<0.0001	<0.0001	0.004	0.004	0.004	0.004	<0.002	<0.002	<0.001	<0.001
75 %		0.0002	0.0002	0.0002	0.0002	<0.0001	<0.0001	<0.0001	<0.0001	0.004	0.004	0.004	0.004	<0.002	<0.002	<0.001	<0.001
90 %		0.0002	0.0002	0.0002	0.0002	<0.0001	<0.0001	<0.0001	<0.0001	0.004	0.004	0.004	0.004	<0.002	<0.002	<0.001	<0.001
None	R1 Stream	0.0071	0.0071	0.0071	0.0071	0.0029	0.0015	0.0002	<0.0001	0.125	0.125	0.125	0.125	0.051	0.026	0.002	<0.001
50 %		0.0071	0.0071	0.0071	0.0071	0.0029	0.0015	0.0002	<0.0001	0.125	0.125	0.125	0.125	0.051	0.026	0.002	<0.001
75 %		0.0071	0.0071	0.0071	0.0071	0.0029	0.0015	0.0002	<0.0001	0.125	0.125	0.125	0.125	0.051	0.026	0.002	<0.001
90 %		0.0071	0.0071	0.0071	0.0071	0.0029	0.0015	0.0002	<0.0001	0.125	0.125	0.125	0.125	0.051	0.026	0.002	<0.001
None	R3 Stream	0.0133	0.0133	0.0133	0.0133	0.0059	0.0030	0.0004	0.0002	0.233	0.233	0.233	0.233	0.104	0.053	0.006	0.003
50 %		0.0133	0.0133	0.0133	0.0133	0.0059	0.0030	0.0004	0.0002	0.233	0.233	0.233	0.233	0.104	0.053	0.006	0.003
75 %		0.0133	0.0133	0.0133	0.0133	0.0059	0.0030	0.0004	0.0002	0.233	0.233	0.233	0.233	0.104	0.053	0.006	0.003
90 %		0.0133	0.0133	0.0133	0.0133	0.0059	0.0030	0.0004	0.0002	0.233	0.233	0.233	0.233	0.104	0.053	0.006	0.003
None	R4 Stream	0.0111	0.0111	0.0111	0.0111	0.0050	0.0026	0.0006	0.0003	0.195	0.195	0.195	0.195	0.088	0.046	0.008	0.004
50 %		0.0111	0.0111	0.0111	0.0111	0.0050	0.0026	0.0006	0.0003	0.195	0.195	0.195	0.195	0.088	0.046	0.008	0.004
75 %		0.0111	0.0111	0.0111	0.0111	0.0050	0.0026	0.0006	0.0003	0.195	0.195	0.195	0.195	0.088	0.046	0.008	0.004
90 %		0.0111	0.0111	0.0111	0.0111	0.0050	0.0026	0.0006	0.0003	0.195	0.195	0.195	0.195	0.088	0.046	0.008	0.004

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Table A 29: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F075736 based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: winter cereals, 1 × 2 g iodosulfuron-methyl-sodium/ha, autumn use

Winter cereals, autumn use, 2 g a.s./ha	**Scenario**	**PECsw STEP 4 - AE F075736**								**PECsw / RAC**							
		PEC gl-max						**7-d PECtwa**		*RAC = 0.057 µg/L* **PEC gl-max**						*RAC = 0.073µg/L* **7-d PECtwa**	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D1 Ditch*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1374*	*0.1374*	***2.851***	***2.851***	***2.851***	***2.851***	***2.851***	***2.851***	***1.882***	***1.882***
50 %		*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1374*	*0.1374*	***2.851***	***2.851***	***2.851***	***2.851***	***2.851***	***2.851***	***1.882***	***1.882***
75 %		*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1374*	*0.1374*	***2.851***	***2.851***	***2.851***	***2.851***	***2.851***	***2.851***	***1.882***	***1.882***
90 %		*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1625*	*0.1374*	*0.1374*	***2.851***	***2.851***	***2.851***	***2.851***	***2.851***	***2.851***	***1.882***	***1.882***
None	*D1 Stream*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.0954*	*0.0954*	***1.921***	***1.921***	***1.921***	***1.921***	***1.921***	***1.921***	***1.307***	***1.307***
50 %		*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.0954*	*0.0954*	***1.921***	***1.921***	***1.921***	***1.921***	***1.921***	***1.921***	***1.307***	***1.307***
75 %		*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.0954*	*0.0954*	***1.921***	***1.921***	***1.921***	***1.921***	***1.921***	***1.921***	***1.307***	***1.307***
90 %		*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.1095*	*0.0954*	*0.0954*	***1.921***	***1.921***	***1.921***	***1.921***	***1.921***	***1.921***	***1.307***	***1.307***
None	*D2 Ditch*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.0826*	*0.0826*	***2.230***	***2.230***	***2.230***	***2.230***	***2.230***	***2.230***	***1.132***	***1.132***
50 %		*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.0826*	*0.0826*	***2.230***	***2.230***	***2.230***	***2.230***	***2.230***	***2.230***	***1.132***	***1.132***
75 %		*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.0826*	*0.0826*	***2.230***	***2.230***	***2.230***	***2.230***	***2.230***	***2.230***	***1.132***	***1.132***
90 %		*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.1271*	*0.0826*	*0.0826*	***2.230***	***2.230***	***2.230***	***2.230***	***2.230***	***2.230***	***1.132***	***1.132***
None	*D2 Stream*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0525*	*0.0525*	***1.516***	***1.516***	***1.516***	***1.516***	***1.516***	***1.516***	*0.719*	*0.719*
50 %		*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0525*	*0.0525*	***1.516***	***1.516***	***1.516***	***1.516***	***1.516***	***1.516***	*0.719*	*0.719*
75 %		*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0525*	*0.0525*	***1.516***	***1.516***	***1.516***	***1.516***	***1.516***	***1.516***	*0.719*	*0.719*
90 %		*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0864*	*0.0525*	*0.0525*	***1.516***	***1.516***	***1.516***	***1.516***	***1.516***	***1.516***	*0.719*	*0.719*
None	*D3 Ditch*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.246*	*0.246*	*0.246*	*0.246*	*0.246*	*0.246*	*0.192*	*0.192*
50 %		*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.246*	*0.246*	*0.246*	*0.246*	*0.246*	*0.246*	*0.192*	*0.192*
75 %		*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.246*	*0.246*	*0.246*	*0.246*	*0.246*	*0.246*	*0.192*	*0.192*
90 %		*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.0140*	*0.246*	*0.246*	*0.246*	*0.246*	*0.246*	*0.246*	*0.192*	*0.192*

Winter cereals, autumn use, 2 g a.s./ha	***Scenario***	***PECsw STEP 4 - AE F075736***								***PECsw / RAC***							
		PEC gl-max						***7-d PECtwa***		*RAC = 0.057 µg/L* ***PEC gl-max***						*RAC = 0.073µg/L* ***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D4 Pond*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0459*	*0.0459*	*0.807*	*0.807*	*0.807*	*0.807*	*0.807*	*0.807*	*0.629*	*0.629*
50 %		*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0459*	*0.0459*	*0.807*	*0.807*	*0.807*	*0.807*	*0.807*	*0.807*	*0.629*	*0.629*
75 %		*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0459*	*0.0459*	*0.807*	*0.807*	*0.807*	*0.807*	*0.807*	*0.807*	*0.629*	*0.629*
90 %		*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0460*	*0.0459*	*0.0459*	*0.807*	*0.807*	*0.807*	*0.807*	*0.807*	*0.807*	*0.629*	*0.629*
None	*D4 Stream*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0292*	*0.0292*	*0.640*	*0.640*	*0.640*	*0.640*	*0.640*	*0.640*	*0.400*	*0.400*
50 %		*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0292*	*0.0292*	*0.640*	*0.640*	*0.640*	*0.640*	*0.640*	*0.640*	*0.400*	*0.400*
75 %		*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0292*	*0.0292*	*0.640*	*0.640*	*0.640*	*0.640*	*0.640*	*0.640*	*0.400*	*0.400*
90 %		*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0365*	*0.0292*	*0.0292*	*0.640*	*0.640*	*0.640*	*0.640*	*0.640*	*0.640*	*0.400*	*0.400*
None	*D5 Pond*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0358*	*0.0358*	*0.632*	*0.632*	*0.632*	*0.632*	*0.632*	*0.632*	*0.490*	*0.490*
50 %		*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0358*	*0.0358*	*0.632*	*0.632*	*0.632*	*0.632*	*0.632*	*0.632*	*0.490*	*0.490*
75 %		*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0358*	*0.0358*	*0.632*	*0.632*	*0.632*	*0.632*	*0.632*	*0.632*	*0.490*	*0.490*
90 %		*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0360*	*0.0358*	*0.0358*	*0.632*	*0.632*	*0.632*	*0.632*	*0.632*	*0.632*	*0.490*	*0.490*
None	*D5 Stream*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0183*	*0.0183*	*0.386*	*0.386*	*0.386*	*0.386*	*0.386*	*0.386*	*0.251*	*0.251*
50 %		*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0183*	*0.0183*	*0.386*	*0.386*	*0.386*	*0.386*	*0.386*	*0.386*	*0.251*	*0.251*
75 %		*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0183*	*0.0183*	*0.386*	*0.386*	*0.386*	*0.386*	*0.386*	*0.386*	*0.251*	*0.251*
90 %		*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0220*	*0.0183*	*0.0183*	*0.386*	*0.386*	*0.386*	*0.386*	*0.386*	*0.386*	*0.251*	*0.251*
None	*D6 Ditch*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0141*	*0.0141*	*0.702*	*0.702*	*0.702*	*0.702*	*0.702*	*0.702*	*0.193*	*0.193*
50 %		*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0141*	*0.0141*	*0.702*	*0.702*	*0.702*	*0.702*	*0.702*	*0.702*	*0.193*	*0.193*
75 %		*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0141*	*0.0141*	*0.702*	*0.702*	*0.702*	*0.702*	*0.702*	*0.702*	*0.193*	*0.193*
90 %		*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0400*	*0.0141*	*0.0141*	*0.702*	*0.702*	*0.702*	*0.702*	*0.702*	*0.702*	*0.193*	*0.193*
None	*R1 Pond*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.001*	*<0.001*
50 %		*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.001*	*<0.001*
75 %		*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.001*	*<0.001*

Winter cereals, autumn use, 2 g a.s./ha	***Scenario***	***PECsw STEP 4 - AE F075736***								***PECsw / RAC***							
		PEC gl-max						***7-d PECtwa***		*RAC = 0.057 µg/L* ***PEC gl-max***						*RAC = 0.073µg/L* ***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
90 %		*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.0001*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.002*	*<0.001*	*<0.001*
None	*R1 Stream*	*0.0006*	*0.0006*	*0.0006*	*0.0006*	*0.0002*	*0.0001*	*<0.0001*	*<0.0001*	*0.011*	*0.011*	*0.011*	*0.011*	*0.004*	*0.002*	*<0.001*	*<0.001*
50 %		*0.0006*	*0.0006*	*0.0006*	*0.0006*	*0.0002*	*0.0001*	*<0.0001*	*<0.0001*	*0.011*	*0.011*	*0.011*	*0.011*	*0.004*	*0.002*	*<0.001*	*<0.001*
75 %		*0.0006*	*0.0006*	*0.0006*	*0.0006*	*0.0002*	*0.0001*	*<0.0001*	*<0.0001*	*0.011*	*0.011*	*0.011*	*0.011*	*0.004*	*0.002*	*<0.001*	*<0.001*
90 %		*0.0006*	*0.0006*	*0.0006*	*0.0006*	*0.0002*	*0.0001*	*<0.0001*	*<0.0001*	*0.011*	*0.011*	*0.011*	*0.011*	*0.004*	*0.002*	*<0.001*	*<0.001*
None	*R3 Stream*	*0.0250*	*0.0250*	*0.0250*	*0.0250*	*0.0113*	*0.0059*	*0.0009*	*0.0005*	*0.439*	*0.439*	*0.439*	*0.439*	*0.198*	*0.104*	*0.012*	*0.007*
50 %		*0.0250*	*0.0250*	*0.0250*	*0.0250*	*0.0113*	*0.0059*	*0.0009*	*0.0005*	*0.439*	*0.439*	*0.439*	*0.439*	*0.198*	*0.104*	*0.012*	*0.007*
75 %		*0.0250*	*0.0250*	*0.0250*	*0.0250*	*0.0113*	*0.0059*	*0.0009*	*0.0005*	*0.439*	*0.439*	*0.439*	*0.439*	*0.198*	*0.104*	*0.012*	*0.007*
90 %		*0.0250*	*0.0250*	*0.0250*	*0.0250*	*0.0113*	*0.0059*	*0.0009*	*0.0005*	*0.439*	*0.439*	*0.439*	*0.439*	*0.198*	*0.104*	*0.012*	*0.007*
None	*R4 Stream*	*0.0130*	*0.0130*	*0.0130*	*0.0130*	*0.0059*	*0.0031*	*0.0005*	*0.0003*	*0.228*	*0.228*	*0.228*	*0.228*	*0.104*	*0.054*	*0.007*	*0.004*
50 %		*0.0130*	*0.0130*	*0.0130*	*0.0130*	*0.0059*	*0.0031*	*0.0005*	*0.0003*	*0.228*	*0.228*	*0.228*	*0.228*	*0.104*	*0.054*	*0.007*	*0.004*
75 %		*0.0130*	*0.0130*	*0.0130*	*0.0130*	*0.0059*	*0.0031*	*0.0005*	*0.0003*	*0.228*	*0.228*	*0.228*	*0.228*	*0.104*	*0.054*	*0.007*	*0.004*
90 %		*0.0130*	*0.0130*	*0.0130*	*0.0130*	*0.0059*	*0.0031*	*0.0005*	*0.0003*	*0.228*	*0.228*	*0.228*	*0.228*	*0.104*	*0.054*	*0.007*	*0.004*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Table A 30: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for iodosulfuron-methyl-sodium metabolite AE F075736 based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: spring cereals, 1 × 2 g iodosulfuron-methyl-sodium/ha, spring use

Spring cereals, spring use, 2 g a.s./ha	**Scenario**	**PECsw STEP 4 - AE F075736**								**PECsw / RAC**							
		PEC gl-max						**7-d PECtwa**		RAC = 0.057 µg/L **PEC gl-max**						RAC = 0.073µg/L **7-d PECtwa**	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
None	D1 Ditch	0.0364	0.0364	0.0364	0.0364	0.0364	0.0364	0.0349	0.0349	0.639	0.639	0.639	0.639	0.639	0.639	0.478	0.478
50 %		0.0364	0.0364	0.0364	0.0364	0.0364	0.0364	0.0349	0.0349	0.639	0.639	0.639	0.639	0.639	0.639	0.478	0.478
75 %		0.0364	0.0364	0.0364	0.0364	0.0364	0.0364	0.0349	0.0349	0.639	0.639	0.639	0.639	0.639	0.639	0.478	0.478
90 %		0.0364	0.0364	0.0364	0.0364	0.0364	0.0364	0.0349	0.0349	0.639	0.639	0.639	0.639	0.639	0.639	0.478	0.478
None	D1 Stream	0.0234	0.0234	0.0234	0.0234	0.0234	0.0234	0.0213	0.0213	0.411	0.411	0.411	0.411	0.411	0.411	0.292	0.292
50 %		0.0234	0.0234	0.0234	0.0234	0.0234	0.0234	0.0213	0.0213	0.411	0.411	0.411	0.411	0.411	0.411	0.292	0.292
75 %		0.0234	0.0234	0.0234	0.0234	0.0234	0.0234	0.0213	0.0213	0.411	0.411	0.411	0.411	0.411	0.411	0.292	0.292
90 %		0.0234	0.0234	0.0234	0.0234	0.0234	0.0234	0.0213	0.0213	0.411	0.411	0.411	0.411	0.411	0.411	0.292	0.292
None	D3 Ditch	0.0046	0.0046	0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.081	0.081	0.079	0.079	0.079	0.079	0.062	0.062
50 %		0.0046	0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.081	0.079	0.079	0.079	0.079	0.079	0.062	0.062
75 %		0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.079	0.079	0.079	0.079	0.079	0.079	0.062	0.062
90 %		0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.0045	0.079	0.079	0.079	0.079	0.079	0.079	0.062	0.062
None	D4 Pond	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.156	0.156	0.156	0.156	0.156	0.156	0.122	0.122
50 %		0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.156	0.156	0.156	0.156	0.156	0.156	0.122	0.122
75 %		0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.156	0.156	0.156	0.156	0.156	0.156	0.122	0.122
90 %		0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.0089	0.156	0.156	0.156	0.156	0.156	0.156	0.122	0.122
None	D4 Stream	0.0046	0.0046	0.0046	0.0046	0.0046	0.0046	0.0044	0.0044	0.081	0.081	0.081	0.081	0.081	0.081	0.060	0.060
50 %		0.0046	0.0046	0.0046	0.0046	0.0046	0.0046	0.0044	0.0044	0.081	0.081	0.081	0.081	0.081	0.081	0.060	0.060
75 %		0.0046	0.0046	0.0046	0.0046	0.0046	0.0046	0.0044	0.0044	0.081	0.081	0.081	0.081	0.081	0.081	0.060	0.060
90 %		0.0046	0.0046	0.0046	0.0046	0.0046	0.0046	0.0044	0.0044	0.081	0.081	0.081	0.081	0.081	0.081	0.060	0.060

Spring cereals, spring use, 2 g a.s./ha	**Scenario**	**PECsw STEP 4 - AE F075736**								**PECsw / RAC**							
		PEC gl-max						**7-d PECtwa**		RAC = 0.057 µg/L **PEC gl-max**						RAC = 0.073µg/L **7-d PECtwa**	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
None	D5 Pond	0.0017	0.0017	0.0017	0.0016	0.0017	0.0016	0.0016	0.0016	0.030	0.030	0.030	0.028	0.030	0.028	0.022	0.022
50 %		0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.028	0.028	0.028	0.028	0.028	0.028	0.022	0.022
75 %		0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.028	0.028	0.028	0.028	0.028	0.028	0.022	0.022
90 %		0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.0016	0.028	0.028	0.028	0.028	0.028	0.028	0.022	0.022
None	D5 Stream	0.0009	0.0009	0.0009	0.0009	0.0009	0.0009	0.0008	0.0008	0.016	0.016	0.016	0.016	0.016	0.016	0.011	0.011
50 %		0.0009	0.0009	0.0009	0.0009	0.0009	0.0009	0.0008	0.0008	0.016	0.016	0.016	0.016	0.016	0.016	0.011	0.011
75 %		0.0009	0.0009	0.0009	0.0009	0.0009	0.0009	0.0008	0.0008	0.016	0.016	0.016	0.016	0.016	0.016	0.011	0.011
90 %		0.0009	0.0009	0.0009	0.0009	0.0009	0.0009	0.0008	0.0008	0.016	0.016	0.016	0.016	0.016	0.016	0.011	0.011
None	R4 Stream	0.0006	0.0006	0.0006	0.0006	0.0003	0.0001	<0.0001	<0.0001	0.011	0.011	0.011	0.011	0.005	0.002	<0.001	<0.001
50 %		0.0006	0.0006	0.0006	0.0006	0.0003	0.0001	<0.0001	<0.0001	0.011	0.011	0.011	0.011	0.005	0.002	<0.001	<0.001
75 %		0.0006	0.0006	0.0006	0.0006	0.0003	0.0001	<0.0001	<0.0001	0.011	0.011	0.011	0.011	0.005	0.002	<0.001	<0.001
90 %		0.0006	0.0006	0.0006	0.0006	0.0003	0.0001	<0.0001	<0.0001	0.011	0.011	0.011	0.011	0.005	0.002	<0.001	<0.001

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Mesosulfuron-methyl

Table A 31: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: winter cereals, 1 × 15 g mesosulfuron-methyl /ha, end of winter use

Winter cereals, end of winter-spring use, 15 g a.s./ha	***Scenario***	***PECsw STEP 4 - mesosulfuron-methyl***								***PECsw / RAC*** *RAC = 0.129 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D1 Ditch*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.1926*	*0.1926*	***1.695***	***1.695***	***1.695***	***1.695***	***1.695***	***1.695***	***1.493***	***1.493***
50 %		*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.1926*	*0.1926*	***1.695***	***1.695***	***1.695***	***1.695***	***1.695***	***1.695***	***1.493***	***1.493***
75 %		*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.1926*	*0.1926*	***1.695***	***1.695***	***1.695***	***1.695***	***1.695***	***1.695***	***1.493***	***1.493***
90 %		*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.2187*	*0.1926*	*0.1926*	***1.695***	***1.695***	***1.695***	***1.695***	***1.695***	***1.695***	***1.493***	***1.493***
None	*D1 Stream*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1264*	*0.1264*	***1.093***	***1.093***	***1.093***	***1.093***	***1.093***	***1.093***	*0.980*	*0.980*
50 %		*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1264*	*0.1264*	***1.093***	***1.093***	***1.093***	***1.093***	***1.093***	***1.093***	*0.980*	*0.980*
75 %		*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1264*	*0.1264*	***1.093***	***1.093***	***1.093***	***1.093***	***1.093***	***1.093***	*0.980*	*0.980*
90 %		*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1410*	*0.1264*	*0.1264*	***1.093***	***1.093***	***1.093***	***1.093***	***1.093***	***1.093***	*0.980*	*0.980*
None	*D2 Ditch*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*0.9150*	*0.9150*	***12.434***	***12.434***	***12.434***	***12.434***	***12.434***	***12.434***	***7.093***	***7.093***
50 %		*1.6040*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*0.9150*	*0.9150*	***12.434***	***12.434***	***12.434***	***12.434***	***12.434***	***12.434***	***7.093***	***7.093***
75 %		*1.6040*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*0.9150*	*0.9150*	***12.434***	***12.434***	***12.434***	***12.434***	***12.434***	***12.434***	***7.093***	***7.093***
90 %		*1.6040*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*1.6040*	*0.9150*	*0.9150*	***12.434***	***12.434***	***12.434***	***12.434***	***12.434***	***12.434***	***7.093***	***7.093***
None	*D2 Stream*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*0.5414*	*0.5414*	***7.930***	***7.930***	***7.930***	***7.930***	***7.930***	***7.930***	***4.197***	***4.197***
50 %		*1.0230*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*0.5414*	*0.5414*	***7.930***	***7.930***	***7.930***	***7.930***	***7.930***	***7.930***	***4.197***	***4.197***
75 %		*1.0230*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*0.5414*	*0.5414*	***7.930***	***7.930***	***7.930***	***7.930***	***7.930***	***7.930***	***4.197***	***4.197***
90 %		*1.0230*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*1.0230*	*0.5414*	*0.5414*	***7.930***	***7.930***	***7.930***	***7.930***	***7.930***	***7.930***	***4.197***	***4.197***
None	*D3 Ditch*	*0.0982*	*0.0289*	*0.0171*	*0.0105*	*0.0171*	*0.0105*	*0.0051*	*0.0042*	*0.761*	*0.224*	*0.133*	*0.081*	*0.133*	*0.081*	*0.039*	*0.033*

Winter cereals, end of winter-spring use, 15 g a.s./ha	**Scenario**	**PECsw STEP 4 - mesosulfuron-methyl**								**PECsw / RAC** RAC = 0.129 µg/L							
		PEC gl-max						**7-d PECtwa**		**PEC gl-max**						**7-d PECtwa**	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
50 %		0.0507	0.0161	0.0102	0.0069	0.0102	0.0069	0.0042	0.0039	0.393	0.125	0.079	0.053	0.079	0.053	0.032	0.030
75 %		0.0270	0.0097	0.0067	0.0051	0.0067	0.0051	0.0039	0.0039	0.209	0.075	0.052	0.040	0.052	0.040	0.030	0.030
90 %		0.0128	0.0058	0.0046	0.0040	0.0046	0.0040	0.0039	0.0039	0.099	0.045	0.036	0.031	0.036	0.031	0.030	0.030
None	D4 Pond	0.0412	0.0412	0.0411	0.0411	0.0411	0.0411	0.0409	0.0409	0.319	0.319	0.319	0.319	0.319	0.319	0.317	0.317
50 %		0.0411	0.0411	0.0411	0.0411	0.0411	0.0411	0.0409	0.0409	0.319	0.319	0.319	0.319	0.319	0.319	0.317	0.317
75 %		0.0411	0.0411	0.0411	0.0411	0.0411	0.0411	0.0409	0.0409	0.319	0.319	0.319	0.319	0.319	0.319	0.317	0.317
90 %		0.0411	0.0411	0.0411	0.0411	0.0411	0.0411	0.0409	0.0409	0.319	0.319	0.319	0.319	0.319	0.319	0.317	0.317
None	D4 Stream	0.0770	0.0385	0.0385	0.0385	0.0385	0.0385	0.0306	0.0306	0.597	0.298	0.298	0.298	0.298	0.298	0.237	0.237
50 %		0.0408	0.0385	0.0385	0.0385	0.0385	0.0385	0.0306	0.0306	0.316	0.298	0.298	0.298	0.298	0.298	0.237	0.237
75 %		0.0385	0.0385	0.0385	0.0385	0.0385	0.0385	0.0306	0.0306	0.298	0.298	0.298	0.298	0.298	0.298	0.237	0.237
90 %		0.0385	0.0385	0.0385	0.0385	0.0385	0.0385	0.0306	0.0306	0.298	0.298	0.298	0.298	0.298	0.298	0.237	0.237
None	D5 Pond	0.0198	0.0193	0.0185	0.0179	0.0185	0.0179	0.0182	0.0176	0.153	0.150	0.143	0.139	0.143	0.139	0.141	0.137
50 %		0.0181	0.0179	0.0175	0.0172	0.0175	0.0172	0.0173	0.0170	0.140	0.139	0.136	0.133	0.136	0.133	0.134	0.132
75 %		0.0173	0.0172	0.0170	0.0168	0.0170	0.0168	0.0168	0.0167	0.134	0.133	0.132	0.130	0.132	0.130	0.130	0.130
90 %		0.0168	0.0168	0.0168	0.0168	0.0168	0.0168	0.0167	0.0167	0.130	0.130	0.130	0.130	0.130	0.130	0.130	0.130
None	D5 Stream	0.0827	0.0352	0.0223	0.0153	0.0223	0.0153	0.0097	0.0097	0.641	0.273	0.173	0.119	0.173	0.119	0.075	0.075
50 %		0.0452	0.0215	0.0150	0.0121	0.0150	0.0121	0.0097	0.0097	0.350	0.167	0.116	0.094	0.116	0.094	0.075	0.075
75 %		0.0265	0.0146	0.0121	0.0121	0.0121	0.0121	0.0097	0.0097	0.205	0.113	0.094	0.094	0.094	0.094	0.075	0.075
90 %		0.0152	0.0121	0.0121	0.0121	0.0121	0.0121	0.0097	0.0097	0.118	0.094	0.094	0.094	0.094	0.094	0.075	0.075
None	D6 Ditch	0.1009	0.0323	0.0206	0.0141	0.0206	0.0141	0.0083	0.0083	0.782	0.250	0.160	0.109	0.160	0.109	0.065	0.065
50 %		0.0540	0.0197	0.0138	0.0106	0.0138	0.0106	0.0083	0.0083	0.419	0.153	0.107	0.082	0.107	0.082	0.065	0.065
75 %		0.0305	0.0133	0.0104	0.0104	0.0104	0.0104	0.0083	0.0083	0.236	0.103	0.081	0.081	0.081	0.081	0.065	0.065

Winter cereals, end of winter-spring use, 15 g a.s./ha	***Scenario***	***PECsw STEP 4 - mesosulfuron-methyl***								***PECsw / RAC*** *RAC = 0.129 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
90 %		*0.0164*	*0.0104*	*0.0104*	*0.0104*	*0.0104*	*0.0104*	*0.0083*	*0.0083*	*0.127*	*0.081*	*0.081*	*0.081*	*0.081*	*0.081*	*0.065*	*0.065*
None	*R1 Pond*	*0.0063*	*0.0059*	*0.0054*	*0.0050*	*0.0030*	*0.0018*	*0.0028*	*0.0017*	*0.049*	*0.046*	*0.042*	*0.039*	*0.023*	*0.014*	*0.022*	*0.013*
50 %		*0.0052*	*0.0050*	*0.0047*	*0.0045*	*0.0023*	*0.0013*	*0.0022*	*0.0012*	*0.040*	*0.039*	*0.036*	*0.035*	*0.018*	*0.010*	*0.017*	*0.009*
75 %		*0.0046*	*0.0045*	*0.0044*	*0.0043*	*0.0020*	*0.0011*	*0.0019*	*0.0010*	*0.036*	*0.035*	*0.034*	*0.033*	*0.016*	*0.009*	*0.014*	*0.008*
90 %		*0.0043*	*0.0042*	*0.0042*	*0.0042*	*0.0018*	*0.0009*	*0.0017*	*0.0009*	*0.033*	*0.033*	*0.033*	*0.033*	*0.014*	*0.007*	*0.013*	*0.007*
None	*R1 Stream*	*0.1008*	*0.1008*	*0.1008*	*0.1008*	*0.0415*	*0.0210*	*0.0043*	*0.0022*	*0.781*	*0.781*	*0.781*	*0.781*	*0.322*	*0.163*	*0.033*	*0.017*
50 %		*0.1008*	*0.1008*	*0.1008*	*0.1008*	*0.0415*	*0.0210*	*0.0043*	*0.0022*	*0.781*	*0.781*	*0.781*	*0.781*	*0.322*	*0.163*	*0.033*	*0.017*
75 %		*0.1008*	*0.1008*	*0.1008*	*0.1008*	*0.0415*	*0.0210*	*0.0043*	*0.0022*	*0.781*	*0.781*	*0.781*	*0.781*	*0.322*	*0.163*	*0.033*	*0.017*
90 %		*0.1008*	*0.1008*	*0.1008*	*0.1008*	*0.0415*	*0.0210*	*0.0043*	*0.0022*	*0.781*	*0.781*	*0.781*	*0.781*	*0.322*	*0.163*	*0.033*	*0.017*
None	*R3 Stream*	*0.3099*	*0.3099*	*0.3099*	*0.3099*	*0.1370*	*0.0710*	*0.0095*	*0.0049*	***2.402***	***2.402***	***2.402***	***2.402***	***1.062***	*0.550*	*0.073*	*0.038*
50 %		*0.3099*	*0.3099*	*0.3099*	*0.3099*	*0.1370*	*0.0710*	*0.0095*	*0.0049*	***2.402***	***2.402***	***2.402***	***2.402***	***1.062***	*0.550*	*0.073*	*0.038*
75 %		*0.3099*	*0.3099*	*0.3099*	*0.3099*	*0.1370*	*0.0710*	*0.0095*	*0.0049*	***2.402***	***2.402***	***2.402***	***2.402***	***1.062***	*0.550*	*0.073*	*0.038*
90 %		*0.3099*	*0.3099*	*0.3099*	*0.3099*	*0.1370*	*0.0710*	*0.0095*	*0.0049*	***2.402***	***2.402***	***2.402***	***2.402***	***1.062***	*0.550*	*0.073*	*0.038*
None	*R4 Stream*	*0.2646*	*0.2646*	*0.2646*	*0.2646*	*0.1203*	*0.0631*	*0.0146*	*0.0076*	***2.051***	***2.051***	***2.051***	***2.051***	*0.933*	*0.489*	*0.113*	*0.059*
50 %		*0.2646*	*0.2646*	*0.2646*	*0.2646*	*0.1203*	*0.0631*	*0.0146*	*0.0076*	***2.051***	***2.051***	***2.051***	***2.051***	*0.933*	*0.489*	*0.113*	*0.059*
75 %		*0.2646*	*0.2646*	*0.2646*	*0.2646*	*0.1203*	*0.0631*	*0.0146*	*0.0076*	***2.051***	***2.051***	***2.051***	***2.051***	*0.933*	*0.489*	*0.113*	*0.059*
90 %		*0.2646*	*0.2646*	*0.2646*	*0.2646*	*0.1203*	*0.0631*	*0.0146*	*0.0076*	***2.051***	***2.051***	***2.051***	***2.051***	*0.933*	*0.489*	*0.113*	*0.059*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Table A 32: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: winter cereals, 1 × 10 g mesosulfuron-methyl /ha, autumn use

Winter cereals, autumn use, 10 g a.s./ha	***Scenario***	***PECsw STEP 4 - mesosulfuron-methyl***								***PECsw / RAC*** *RAC = 0.129 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D1 Ditch*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.2640*	*1.2640*	***10.527***	***10.527***	***10.527***	***10.527***	***10.527***	***10.527***	***9.798***	***9.798***
50 %		*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.2640*	*1.2640*	***10.527***	***10.527***	***10.527***	***10.527***	***10.527***	***10.527***	***9.798***	***9.798***
75 %		*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.2640*	*1.2640*	***10.527***	***10.527***	***10.527***	***10.527***	***10.527***	***10.527***	***9.798***	***9.798***
90 %		*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.3580*	*1.2640*	*1.2640*	***10.527***	***10.527***	***10.527***	***10.527***	***10.527***	***10.527***	***9.798***	***9.798***
None	*D1 Stream*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.7944*	*0.7944*	***6.570***	***6.570***	***6.570***	***6.570***	***6.570***	***6.570***	***6.158***	***6.158***
50 %		*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.7944*	*0.7944*	***6.570***	***6.570***	***6.570***	***6.570***	***6.570***	***6.570***	***6.158***	***6.158***
75 %		*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.7944*	*0.7944*	***6.570***	***6.570***	***6.570***	***6.570***	***6.570***	***6.570***	***6.158***	***6.158***
90 %		*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.8475*	*0.7944*	*0.7944*	***6.570***	***6.570***	***6.570***	***6.570***	***6.570***	***6.570***	***6.158***	***6.158***
None	*D2 Ditch*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*0.5944*	*0.5944*	***10.837***	***10.837***	***10.837***	***10.837***	***10.837***	***10.837***	***4.608***	***4.608***
50 %		*1.3980*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*0.5944*	*0.5944*	***10.837***	***10.837***	***10.837***	***10.837***	***10.837***	***10.837***	***4.608***	***4.608***
75 %		*1.3980*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*0.5944*	*0.5944*	***10.837***	***10.837***	***10.837***	***10.837***	***10.837***	***10.837***	***4.608***	***4.608***
90 %		*1.3980*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*1.3980*	*0.5944*	*0.5944*	***10.837***	***10.837***	***10.837***	***10.837***	***10.837***	***10.837***	***4.608***	***4.608***
None	*D2 Stream*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.3500*	*0.3500*	***6.818***	***6.818***	***6.818***	***6.818***	***6.818***	***6.818***	***2.713***	***2.713***
50 %		*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.3500*	*0.3500*	***6.818***	***6.818***	***6.818***	***6.818***	***6.818***	***6.818***	***2.713***	***2.713***
75 %		*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.3500*	*0.3500*	***6.818***	***6.818***	***6.818***	***6.818***	***6.818***	***6.818***	***2.713***	***2.713***
90 %		*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.8795*	*0.3500*	*0.3500*	***6.818***	***6.818***	***6.818***	***6.818***	***6.818***	***6.818***	***2.713***	***2.713***
None	*D3 Ditch*	*0.0662*	*0.0200*	*0.0121*	*0.0075*	*0.0121*	*0.0075*	*0.0039*	*0.0034*	*0.513*	*0.155*	*0.094*	*0.058*	*0.094*	*0.058*	*0.031*	*0.027*
50 %		*0.0346*	*0.0115*	*0.0075*	*0.0052*	*0.0075*	*0.0052*	*0.0034*	*0.0032*	*0.268*	*0.089*	*0.058*	*0.040*	*0.058*	*0.040*	*0.027*	*0.025*
75 %		*0.0188*	*0.0072*	*0.0052*	*0.0041*	*0.0052*	*0.0041*	*0.0032*	*0.0031*	*0.146*	*0.056*	*0.040*	*0.032*	*0.040*	*0.032*	*0.025*	*0.024*
90 %		*0.0093*	*0.0046*	*0.0039*	*0.0034*	*0.0039*	*0.0034*	*0.0030*	*0.0030*	*0.072*	*0.036*	*0.030*	*0.026*	*0.030*	*0.026*	*0.024*	*0.023*

Winter cereals, autumn use, 10 g a.s./ha	**Scenario**	**PECsw STEP 4 - mesosulfuron-methyl**								**PECsw / RAC** RAC = 0.129 µg/L							
		PEC gl-max						**7-d PECtwa**		**PEC gl-max**						**7-d PECtwa**	
Nozzle red.	Vegetated strip (m)	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*	None	None	None	None	10 m low*	20 m high*	10 m low*	20 m high*
	No spray buffer (m)	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m	0 m	5 m	10 m	20 m	10 m	20 m	10 m	20 m
None	D4 Pond	0.1414	0.1413	0.1411	0.1409	0.1411	0.1409	0.1409	0.1407	**1.096**	**1.095**	**1.094**	**1.092**	**1.094**	**1.092**	**1.092**	**1.091**
50 %		0.1410	0.1409	0.1408	0.1407	0.1408	0.1407	0.1406	0.1405	**1.093**	**1.092**	**1.091**	**1.091**	**1.091**	**1.091**	**1.090**	**1.089**
75 %		0.1408	0.1408	0.1407	0.1407	0.1407	0.1407	0.1405	0.1404	**1.091**	**1.091**	**1.091**	**1.091**	**1.091**	**1.091**	**1.089**	**1.088**
90 %		0.1407	0.1406	0.1406	0.1406	0.1406	0.1406	0.1404	0.1404	**1.091**	**1.090**	**1.090**	**1.090**	**1.090**	**1.090**	**1.088**	**1.088**
None	D4 Stream	0.1678	0.1678	0.1678	0.1678	0.1678	0.1678	0.1339	0.1339	**1.301**	**1.301**	**1.301**	**1.301**	**1.301**	**1.301**	**1.038**	**1.038**
50 %		0.1678	0.1678	0.1678	0.1678	0.1678	0.1678	0.1339	0.1339	**1.301**	**1.301**	**1.301**	**1.301**	**1.301**	**1.301**	**1.038**	**1.038**
75 %		0.1678	0.1678	0.1678	0.1678	0.1678	0.1678	0.1339	0.1339	**1.301**	**1.301**	**1.301**	**1.301**	**1.301**	**1.301**	**1.038**	**1.038**
90 %		0.1678	0.1678	0.1678	0.1678	0.1678	0.1678	0.1339	0.1339	**1.301**	**1.301**	**1.301**	**1.301**	**1.301**	**1.301**	**1.038**	**1.038**
None	D5 Pond	0.1018	0.1017	0.1016	0.1015	0.1016	0.1015	0.1005	0.1004	0.789	0.788	0.788	0.787	0.788	0.787	0.779	0.778
50 %		0.1015	0.1015	0.1014	0.1014	0.1014	0.1014	0.1003	0.1003	0.787	0.787	0.786	0.786	0.786	0.786	0.778	0.778
75 %		0.1014	0.1014	0.1013	0.1013	0.1013	0.1013	0.1003	0.1002	0.786	0.786	0.785	0.785	0.785	0.785	0.778	0.777
90 %		0.1013	0.1013	0.1013	0.1013	0.1013	0.1013	0.1002	0.1002	0.785	0.785	0.785	0.785	0.785	0.785	0.777	0.777
None	D5 Stream	0.1450	0.1450	0.1450	0.1450	0.1450	0.1450	0.0692	0.0692	**1.124**	**1.124**	**1.124**	**1.124**	**1.124**	**1.124**	0.536	0.536
50 %		0.1450	0.1450	0.1450	0.1450	0.1450	0.1450	0.0692	0.0692	**1.124**	**1.124**	**1.124**	**1.124**	**1.124**	**1.124**	0.536	0.536
75 %		0.1450	0.1450	0.1450	0.1450	0.1450	0.1450	0.0692	0.0692	**1.124**	**1.124**	**1.124**	**1.124**	**1.124**	**1.124**	0.536	0.536
90 %		0.1450	0.1450	0.1450	0.1450	0.1450	0.1450	0.0692	0.0692	**1.124**	**1.124**	**1.124**	**1.124**	**1.124**	**1.124**	0.536	0.536
None	D6 Ditch	0.3850	0.3850	0.3850	0.3850	0.3850	0.3850	0.1168	0.1168	**2.984**	**2.984**	**2.984**	**2.984**	**2.984**	**2.984**	0.905	0.905
50 %		0.3850	0.3850	0.3850	0.3850	0.3850	0.3850	0.1168	0.1168	**2.984**	**2.984**	**2.984**	**2.984**	**2.984**	**2.984**	0.905	0.905
75 %		0.3850	0.3850	0.3850	0.3850	0.3850	0.3850	0.1168	0.1168	**2.984**	**2.984**	**2.984**	**2.984**	**2.984**	**2.984**	0.905	0.905
90 %		0.3850	0.3850	0.3850	0.3850	0.3850	0.3850	0.1168	0.1168	**2.984**	**2.984**	**2.984**	**2.984**	**2.984**	**2.984**	0.905	0.905
None	R1 Pond	0.0022	0.0019	0.0014	0.0009	0.0014	0.0009	0.0013	0.0008	0.017	0.015	0.011	0.007	0.011	0.007	0.010	0.007
50 %		0.0011	0.0009	0.0007	0.0005	0.0007	0.0004	0.0007	0.0004	0.009	0.007	0.005	0.004	0.005	0.003	0.005	0.003
75 %		0.0006	0.0005	0.0005	0.0004	0.0003	0.0002	0.0003	0.0002	0.005	0.004	0.004	0.003	0.002	0.002	0.003	0.002

Winter cereals, autumn use, 10 g a.s./ha	***Scenario***	***PECsw STEP 4 - mesosulfuron-methyl***								***PECsw / RAC*** *RAC = 0.129 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
90 %		*0.0004*	*0.0004*	*0.0003*	*0.0003*	*0.0002*	*0.0001*	*0.0002*	*0.0001*	*0.003*	*0.003*	*0.002*	*0.002*	*0.002*	*0.001*	*0.001*	*0.001*
None	*R1 Stream*	*0.0474*	*0.0474*	*0.0474*	*0.0474*	*0.0191*	*0.0096*	*0.0002*	*0.0001*	*0.367*	*0.367*	*0.367*	*0.367*	*0.148*	*0.074*	*0.002*	*0.001*
50 %		*0.0474*	*0.0474*	*0.0474*	*0.0474*	*0.0191*	*0.0096*	*0.0002*	*0.0001*	*0.367*	*0.367*	*0.367*	*0.367*	*0.148*	*0.074*	*0.002*	*0.001*
75 %		*0.0474*	*0.0474*	*0.0474*	*0.0474*	*0.0191*	*0.0096*	*0.0002*	*0.0001*	*0.367*	*0.367*	*0.367*	*0.367*	*0.148*	*0.074*	*0.002*	*0.001*
90 %		*0.0474*	*0.0474*	*0.0474*	*0.0474*	*0.0191*	*0.0096*	*0.0002*	*0.0001*	*0.367*	*0.367*	*0.367*	*0.367*	*0.148*	*0.074*	*0.002*	*0.001*
None	*R3 Stream*	*0.5158*	*0.5158*	*0.5158*	*0.5158*	*0.2319*	*0.1211*	*0.0182*	*0.0095*	***3.998***	***3.998***	***3.998***	***3.998***	***1.798***	*0.939*	*0.141*	*0.074*
50 %		*0.5158*	*0.5158*	*0.5158*	*0.5158*	*0.2319*	*0.1211*	*0.0180*	*0.0094*	***3.998***	***3.998***	***3.998***	***3.998***	***1.798***	*0.939*	*0.140*	*0.073*
75 %		*0.5158*	*0.5158*	*0.5158*	*0.5158*	*0.2319*	*0.1211*	*0.0179*	*0.0094*	***3.998***	***3.998***	***3.998***	***3.998***	***1.798***	*0.939*	*0.139*	*0.073*
90 %		*0.5158*	*0.5158*	*0.5158*	*0.5158*	*0.2319*	*0.1211*	*0.0179*	*0.0093*	***3.998***	***3.998***	***3.998***	***3.998***	***1.798***	*0.939*	*0.139*	*0.072*
None	*R4 Stream*	*0.2641*	*0.2641*	*0.2641*	*0.2641*	*0.1192*	*0.0623*	*0.0112*	*0.0059*	***2.047***	***2.047***	***2.047***	***2.047***	*0.924*	*0.483*	*0.087*	*0.045*
50 %		*0.2641*	*0.2641*	*0.2641*	*0.2641*	*0.1192*	*0.0623*	*0.0112*	*0.0059*	***2.047***	***2.047***	***2.047***	***2.047***	*0.924*	*0.483*	*0.087*	*0.045*
75 %		*0.2641*	*0.2641*	*0.2641*	*0.2641*	*0.1192*	*0.0623*	*0.0112*	*0.0059*	***2.047***	***2.047***	***2.047***	***2.047***	*0.924*	*0.483*	*0.087*	*0.045*
90 %		*0.2641*	*0.2641*	*0.2641*	*0.2641*	*0.1192*	*0.0623*	*0.0112*	*0.0059*	***2.047***	***2.047***	***2.047***	***2.047***	*0.924*	*0.483*	*0.087*	*0.045*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux*

Table A 33: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for mesosulfuron-methyl based on FOCUS Step 4 calculations and toxicity data for aquatic plants with mitigation of spray drift and run-off for the use of IMS+MSM+MPR OD 42 (2+10+30) in cereals – Use: spring cereals, 1 × 10 g mesosulfuron-methyl /ha, spring use

Spring cereals, spring use, 10 g a.s./ha	***Scenario***	***PECsw STEP 4 - mesosulfuron-methyl***								***PECsw / RAC*** *RAC = 0.129 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D1 Ditch*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2003*	*0.2003*	***1.616***	***1.616***	***1.616***	***1.616***	***1.616***	***1.616***	***1.553***	***1.553***
50 %		*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2003*	*0.2003*	***1.616***	***1.616***	***1.616***	***1.616***	***1.616***	***1.616***	***1.553***	***1.553***
75 %		*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2003*	*0.2003*	***1.616***	***1.616***	***1.616***	***1.616***	***1.616***	***1.616***	***1.553***	***1.553***
90 %		*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2085*	*0.2003*	*0.2003*	***1.616***	***1.616***	***1.616***	***1.616***	***1.616***	***1.616***	***1.553***	***1.553***
None	*D1 Stream*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1236*	*0.1236*	***1.342***	***1.342***	***1.342***	***1.342***	***1.342***	***1.342***	*0.958*	*0.958*
50 %		*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1236*	*0.1236*	***1.342***	***1.342***	***1.342***	***1.342***	***1.342***	***1.342***	*0.958*	*0.958*
75 %		*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1236*	*0.1236*	***1.342***	***1.342***	***1.342***	***1.342***	***1.342***	***1.342***	*0.958*	*0.958*
90 %		*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1731*	*0.1236*	*0.1236*	***1.342***	***1.342***	***1.342***	***1.342***	***1.342***	***1.342***	*0.958*	*0.958*
None	*D3 Ditch*	*0.0657*	*0.0194*	*0.0115*	*0.0069*	*0.0115*	*0.0069*	*0.0036*	*0.0030*	*0.509*	*0.150*	*0.089*	*0.053*	*0.089*	*0.053*	*0.028*	*0.023*
50 %		*0.0340*	*0.0109*	*0.0069*	*0.0046*	*0.0069*	*0.0046*	*0.0030*	*0.0028*	*0.264*	*0.084*	*0.053*	*0.036*	*0.053*	*0.036*	*0.023*	*0.022*
75 %		*0.0182*	*0.0066*	*0.0046*	*0.0035*	*0.0046*	*0.0035*	*0.0028*	*0.0028*	*0.141*	*0.051*	*0.036*	*0.027*	*0.036*	*0.027*	*0.022*	*0.022*
90 %		*0.0087*	*0.0040*	*0.0032*	*0.0028*	*0.0032*	*0.0028*	*0.0028*	*0.0028*	*0.067*	*0.031*	*0.025*	*0.022*	*0.025*	*0.022*	*0.022*	*0.022*
None	*D4 Pond*	*0.0288*	*0.0288*	*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0286*	*0.0286*	*0.223*	*0.223*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*
50 %		*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0286*	*0.0286*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*
75 %		*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0285*	*0.0285*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*	*0.221*	*0.221*
90 %		*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0287*	*0.0285*	*0.0285*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*	*0.222*	*0.221*	*0.221*
None	*D4 Stream*	*0.0545*	*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0216*	*0.0216*	*0.422*	*0.205*	*0.205*	*0.205*	*0.205*	*0.205*	*0.167*	*0.167*
50 %		*0.0285*	*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0216*	*0.0216*	*0.221*	*0.205*	*0.205*	*0.205*	*0.205*	*0.205*	*0.167*	*0.167*
75 %		*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0216*	*0.0216*	*0.205*	*0.205*	*0.205*	*0.205*	*0.205*	*0.205*	*0.167*	*0.167*
90 %		*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0265*	*0.0216*	*0.0216*	*0.205*	*0.205*	*0.205*	*0.205*	*0.205*	*0.205*	*0.167*	*0.167*

Spring cereals, spring use, 10 g a.s./ha	***Scenario***	***PECsw STEP 4 - mesosulfuron-methyl***								***PECsw / RAC*** *RAC = 0.129 µg/L*							
		PEC gl-max						***7-d PECtwa***		***PEC gl-max***						***7-d PECtwa***	
Nozzle red.	*Vegetated strip (m)*	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**	*None*	*None*	*None*	*None*	*10 m low**	*20 m high**	*10 m low**	*20 m high**
	No spray buffer (m)	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*	*0 m*	*5 m*	*10 m*	*20 m*	*10 m*	*20 m*	*10 m*	*20 m*
None	*D5 Pond*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0117*	*0.0117*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*
50 %		*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0116*	*0.0116*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.090*	*0.090*
75 %		*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0116*	*0.0116*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.090*	*0.090*
90 %		*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0118*	*0.0116*	*0.0116*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.091*	*0.090*	*0.090*
None	*D5 Stream*	*0.0541*	*0.0221*	*0.0133*	*0.0121*	*0.0133*	*0.0121*	*0.0057*	*0.0057*	*0.419*	*0.171*	*0.103*	*0.094*	*0.103*	*0.094*	*0.044*	*0.044*
50 %		*0.0289*	*0.0129*	*0.0121*	*0.0121*	*0.0121*	*0.0121*	*0.0057*	*0.0057*	*0.224*	*0.100*	*0.094*	*0.094*	*0.094*	*0.094*	*0.044*	*0.044*
75 %		*0.0163*	*0.0121*	*0.0121*	*0.0121*	*0.0121*	*0.0121*	*0.0057*	*0.0057*	*0.126*	*0.094*	*0.094*	*0.094*	*0.094*	*0.094*	*0.044*	*0.044*
90 %		*0.0121*	*0.0121*	*0.0121*	*0.0121*	*0.0121*	*0.0121*	*0.0057*	*0.0057*	*0.094*	*0.094*	*0.094*	*0.094*	*0.094*	*0.094*	*0.044*	*0.044*
None	*R4 Stream*	*0.0418*	*0.0171*	*0.0171*	*0.0171*	*0.0080*	*0.0041*	*0.0009*	*0.0005*	*0.324*	*0.133*	*0.133*	*0.133*	*0.062*	*0.032*	*0.007*	*0.004*
50 %		*0.0209*	*0.0171*	*0.0171*	*0.0171*	*0.0077*	*0.0040*	*0.0009*	*0.0005*	*0.162*	*0.133*	*0.133*	*0.133*	*0.060*	*0.031*	*0.007*	*0.004*
75 %		*0.0171*	*0.0171*	*0.0171*	*0.0171*	*0.0077*	*0.0040*	*0.0009*	*0.0005*	*0.133*	*0.133*	*0.133*	*0.133*	*0.060*	*0.031*	*0.007*	*0.004*
90 %		*0.0171*	*0.0171*	*0.0171*	*0.0171*	*0.0077*	*0.0040*	*0.0009*	*0.0005*	*0.133*	*0.133*	*0.133*	*0.133*	*0.060*	*0.031*	*0.007*	*0.004*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** low and high fractional reduction in the runoff and erosion through volume, mass and flux.*