Bayer CropScience

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Document Title

Summary of the ecotoxicological studies Iodosulfuron-methyl-sodium + Mesosulfuron-methyl +Mefenpyr-diethyl OD 42 (2+10+30 g/L)

Data Requirements

EU Regulation 1107/2009 & EU Regulation 284/2013
Document MCP
Section 10: Ecotoxicological studies

According to the guidance document, SANCO 10181/2013, for preparing dossiers for the approval of a chemical active substance

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[1] Amendments or additions are presented using the approach outlined in SANCO/10180 Chapter 4: How to revise an Assessment Report.

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Covers the point required in SANCO 10181/2013 format shown below

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In agreement with the Rapporteur Member State, the product dossier is submitted following the dRR format. All points required under the SANCO 10181/2013 are covered, although their naming might differ slightly.

IIIA 10 ECOTOXICOLOGICAL STUDIES

This document reviews risk assessment for Non-Target Organisms for the plant protection product IMS + MSM + MPR OD 42 which contains the active substances iodosulfuron-methyl-sodium (IMS) and mesosulfuron-methyl (MSM), and the crop safener mefenpyr-diethyl (MPR).

This product is the representative formulation for the inclusion of mesosulfuron-methyl at European level. In its function as Document MCP for the EU review process, the assessment will focus on only the active substance mesosulfuron-methyl. A complete assessment to cover all active substances of the formulation will be provided at a later stage, as part of the post-AIR process for renewal of authorisations at member state level, once mesosulfuron-methyl is re-approved under Regulation (EU) 1107/2009.

In general, formulants (inactive ingredients) present in a product do not influence to a relevant extent the behaviour of the active substances in the environment. An exemption is for slow release formulations but this is not the case for the present product. Therefore, data derived from tests with the individual active substances are considered representative for the behaviour of these substances in product IMS+MSM+MPR OD 42. This assumption has been supported by testing as well the formulated product on a selection of organisms.

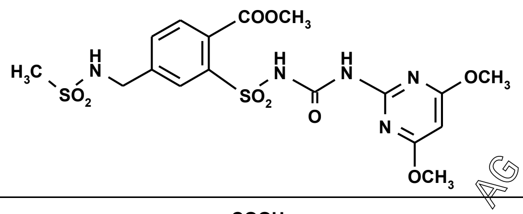
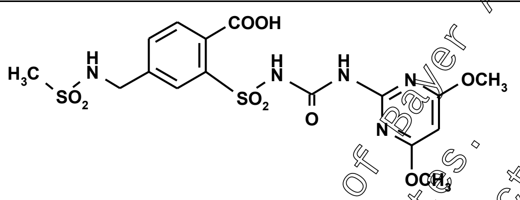
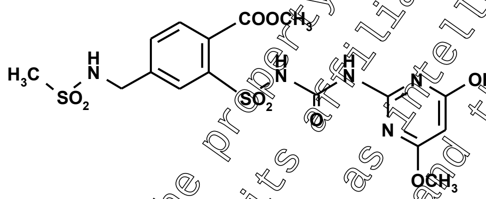
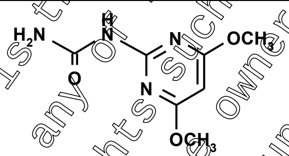
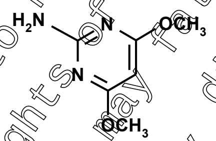
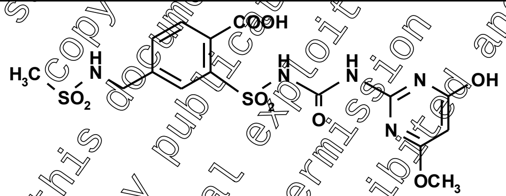
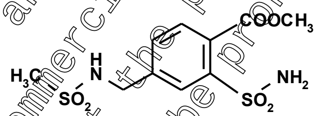
Intended application pattern

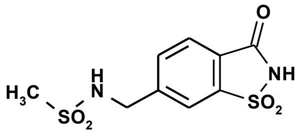
The formulation is intended for use as a post-emergent herbicide to control weeds in winter and spring cereals. The critical use pattern for this formulation is summarised as follows. A detailed use pattern can be found in Document D-1 of this dossier.

Table 10- 1: Intended application pattern for the representative uses of mesosulfuron-methyl in product IMS+MSM+MPR OD 42

Crop	Timing of application	Number of applications	Application interval [days]	Maximum label rate [L/ha]	Maximum application rate, individual treatment [g a.s./ha]	
					iodosulfuron-methyl-sodium	mesosulfuron-methyl
Winter wheat	BBCH 20-32 end of winter, beginning of vegetation	1	-	1.5	3	15
Winter rye	BBCH 20-32 end of winter, beginning of vegetation	1	-	0.6	1.2	6

Table 10- 2: Mesosulfuron-methyl: Active substance and metabolites addressed in this document

Compound / Codes	Chemical Structure	Explanation for Consideration	Considered for
Mesosulfuron-methyl / AE F130060		active substance	PEC_{soil} PEC_{gw} PEC_{sw} & PEC_{sed}
AE F154851		**aerobic soil:** **>10%** anaerobic soil: < 5% soil photolysis: n.d. water/sediment: <5% hydrolysis: <5% aqu. photolysis: n.d.	PEC_{soil} PEC_{gw} PEC_{sw} & PEC_{sed}
AE F160459		**aerobic soil:** **>5%** **anaerobic soil:** **>10%** soil photolysis: n.d. **water/sediment:** **>10%** hydrolysis: n.d. aqu. photolysis: n.d.	PEC_{soil} PEC_{gw} PEC_{sw} & PEC_{sed}
AE F099095		**aerobic soil:** **>10%** anaerobic soil: <5% soil photolysis: n.d. water/sediment: <5% hydrolysis: n.d. aqu. photolysis: n.d.	PEC_{soil} PEC_{gw} PEC_{sw} & PEC_{sed}
AE F092944		**aerobic soil:** **>10%** anaerobic soil: <5% soil photolysis: n.d. water/sediment: <5% **hydrolysis:** **>10%** aqu. photolysis: n.d.	PEC_{soil} PEC_{gw} PEC_{sw} & PEC_{sed}
AE F160460		**aerobic soil:** **>5%** **anaerobic soil:** **>5%** soil photolysis: n.d. **water/sediment:** **>5%** hydrolysis: n.d. aqu. photolysis: n.d.	PEC_{soil} PEC_{gw} PEC_{sw} & PEC_{sed}
AE F140584		**aerobic soil:** **>5%** anaerobic soil: <5% soil photolysis: n.d. water/sediment: <5% **hydrolysis:** **>10%** aqu. photolysis: n.d.	PEC_{soil} PEC_{gw} PEC_{sw} & PEC_{sed}

Compound / Codes	Chemical Structure	Explanation for Consideration	Considered for
AE F147447		**aerobic soil:** ≥5% **anaerobic soil:** ≥5% soil photolysis: n.d. **water/sediment:** >10% **hydrolysis:** >10% aqu. photolysis: n.d.	PEC_{soil} PEC_{gw} PEC_{sw} & PEC_{sed}

IIIA 10.1 Effects on Birds

Ecotoxicological endpoints used in risk assessment

Table 10.1- 1: Endpoints of the formulation IMS + MSM + MPR OD 42 used in risk assessment

Test substance	Endpoint
IMS + MSM + MPR OD 42	Mesosulfuron-methyl is of low acute oral toxicity to Bobwhite quail and Mallard duck, with LD_{50} values in excess of 2000 mg a.s./kg bw. For animal welfare reason, acute oral studies with formulations are routinely not conducted for birds, where the individual active substance tests indicated low toxicity to birds. Based on the active ingredient data, the toxicity of the formulation can be reliably predicted. In the present case, considering that avian LD_{50} of iodosulfuron-methyl-sodium is >2000 mg a.s./kg bw[1]), and LD_{50} of mefenpyr-diethyl is >2000 mg a.s./kg bw[2]), it is reasonable to assume that the product would also be practically non-toxic to birds. Therefore, it is justified to waive an acute test with the formulation in birds.

[1]) EU list of endpoints for iodosulfuron-methyl-sodium [SANCO/10166/2003-Final]
[2] [redacted] (1991, amended 1994), M-129750-02-1, Mefenpyr DAR, June 2011, available on CIRCA (Archive individual substances – Mefenpyr-diethyl(safener)).

Table 10.1- 2: Endpoints for the active substance mesosulfuron-methyl used in risk assessment

Test substance	Test organism	Study type	Endpoint		Reference
Mesosulfuron-methyl	**Acute toxicity to bird**				
	Bobwhite quail, Mallard duck	acute, oral	LD_{50}	> 2000 mg as/kg bw	[redacted] (1998) M-180378-01-1 KCA 8.1.1.1 /01 [redacted] (1998) M-147788-01-1 KCA 8.1.1.1 /02
	Long-term toxicity to bird				
	Bobwhite quail	20-weeks feeding chronic, reproduction	NOEC = NOEL	1000 ppm 93 mg as/kg bw/d	[redacted] (2000) M-198082-01-1 KCA 8.1.1.3 /01

All above endpoints used in risk assessment are consistent with the *proposed* EU endpoints listed in Document N2 for mesosulfuron-methyl.

Risk assessment for birds

The risk assessment procedure follows the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009).
The risk assessment follows a tiered approach to assess the effects of plant protection products on birds based on current regulatory requirements. The risk is considered acceptable, if the 'Toxicity Exposure Ratio' (TER) value pass the trigger values of 10 for acute exposure and 5 for chronic

exposure. If the TER values are below the trigger values in certain areas, a refined risk assessment based on more relevant and realistic conditions is performed for those particular areas.

Calculation of Toxicity Exposure Ratio (TER)

According to the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009), the calculation of acute and long-term Toxicity to Exposure Ratio (TER) is defined as follows:

Acute risk: $TER_A = LD_{50}$ [mg as/kg bw] / DDD

Long-term risk: TER_{LT} = NO(A)EL [mg as/kg bw/d] / DDD

The endpoints for acute and long-term risk assessment derive from acute and reproductions studies respectively, and are expressed as dose [mg per kilogram body weight per day].

Calculation of Daily Dietary Dose (DDD)

Acute exposure:

The daily dietary dose for a single application is given by the following equation:

$DDD_{single\ application}$ = application rate [kg/ha] × shortcut value (SV_{90})

Long-term exposure:

For a single application the daily dietary dose is given by the following equation:

$DDD_{single\ application}$ = application rate [kg/ha] × shortcut value (SV_m) × TWA

Where

DDD	Daily dietary dose
TWA	Time weighted average factor (= f_{twa}) based on a default time window of 21 days and a DT_{50} of 10 days leading to a value of 0.53
Shortcut value	SV = FIR/bw x RUD: Value for exposure estimate based on species and crop.
RUD	Residue per unit dose: residues on feed items normalized on an application rate of 1 kg a.s./ha.
90	90^{th} percentile values for acute exposure, extension for RUD and SV
m	mean values for reproductive/long-term exposure, extension for RUD and SV

Standard exposure scenario for risk assessment on screening level

The main potential exposure route for birds is expected to be consumption of contaminated feed.

The risk assessment on screening level is based on standard scenarios, i.e. combination of indicator species and crop.
Default ("shortcut"-) values for the exposure estimate will be used as provided in Appendix A of the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009) representing a worst case assessment.

It is assumed that

- animals satisfy their entire food demand in the treated area (PT = 1),
- animals feed on a single food type only (PD = 1),
- over an acute time frame (hours) the animals feed on items containing maximum residues (90th percentile), whereas they would ingest food containing mean residues over a long-term period (days to weeks),
- long-term predicted environmental concentrations to be compared with chronic endpoints can be calculated as the time-weighted average concentration. Default assumptions are a time window of 21 days and a DT_{50} of 10 days leading to a time weighted average factor (= f_{twa}) of 0.53. This factor is equally valid for feed items consisting of vegetation as well as of arthropods.
- The 'indicator species' used on screening level is not a real species but, by virtue of its size and feeding habits is considered to have higher exposure than other species that occur in a particular crop at a particular time and is therefore protective for all other species in that particular crop.

Avian indicator species for risk assessment on screening level

The product IMS + MSM + MPR OD 42 is intended to be used in winter wheat for a single application between BBCH 20 and 32 at an application rate of 1.5 L/ha, corresponding to 0.015 kg mesosulfuron-methyl/ha, and in winter rye for a single application between BBCH 20 and 32 at an application rate of 0.6 L/ha, corresponding to 0.006 kg mesosulfuron-methyl/ha. According to the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009) the following indicator species have to be addressed in risk assessment on screening level.

Table 10.1- 3: Relevant avian indicator species for risk assessment on screening level

Crop	Indicator species	Shortcut value	
		For long-term RA based on RUD_m	For acute RA based on RUD_{90}
Cereals	Small omnivorous bird	64.8	158.8

Summary of calculated TER values for birds

Table 10.1- 4: Summary of all acute TER calculations as given under point 10.1.1

Crop / Compound	Indicator species	SV_{90}	TER_A	Trigger	Refinement used ?
Winter wheat, 1 × 15 g a.s./ha					
Mesosulfuron-methyl	Small omnivorous bird	158.8	>840	10	no
Winter rye, 1 × 6 g a.s./ha					
Mesosulfuron-methyl	Small omnivorous bird	158.8	>2105	10	no

Table 10.1- 5: Summary of all reproductive (long-term) TER calculations as given under point 10.1.2

Crop / Compound	Indicator species	SV_{mean}	TER_{LT}	Trigger	Refinement used ?
Winter wheat, 1 × 15 g a.s./ha					
Mesosulfuron-methyl	Small omnivorous bird	64.8	181	5	no
Winter rye, 1 × 6 g a.s./ha					
Mesosulfuron-methyl	Small omnivorous bird	64.8	451	5	no

Conclusion: According to the presented risk assessment, the risk to birds from the use of the product in cereals is acceptable.

IIIA 10.1.1 Acute toxicity exposure ratio (TER_A)

Acute toxicity exposure ratio on screening level for birds

Table 10.1.1- 1: Acute DDD and TER calculation (active substance mesosulfuron-methyl) on screening level for birds

Crop / Compound	Indicator species	LD_{50} [mg/kg bw]	DDD			DDD	TER_A	Trigger
			Appl. rate [kg/ha]	SV_{90}	MAF_{90}			
Winter wheat, 1 × 15 g a.s./ha								
Mesosulfuron-methyl	Small omnivorous bird	>2000	0.015	158.8	1	2.38	>840	10
Winter rye, 1 × 6 g a.s./ha								
Mesosulfuron-methyl	Small omnivorous bird	>2000	0.006	158.8	1	0.95	>2105	10

All TER values are above the required trigger of 10 for acute exposure. Acute risk to birds is therefore acceptable for the intended product uses.

Acute risk assessment for birds drinking contaminated water

An assessment of the risk potentially posed by consumption of contaminated drinking water is required according to the EFSA Guidance Document for Birds and Mammals (2009). For details see point 10.1.2 of this dossier.

As formulation IMS + MSM + MPR OD 42 is applied in cereals, no pools in leaf axils where an acute exposure possibly might occur are to be expected.

The acute risk from water in puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil is covered by the long-term risk assessment under Point 10.1.2 of this dossier.

IIIA 10.1.2 Short and long-term toxicity exposure ratio (TER_{ST}, TER_{LT})

Short-term toxicity exposure ratio for birds

According to the risk assessment scheme of EFSA GD birds and mammals (2009) a short-term risk assessment is not required. However, the endpoint from short-term dietary studies, e.g. 5-day dietary study in birds (OECD 205) should be used in an acute risk assessment when indicating a higher toxicity via the dietary exposure route (lower LDD_{50}).
Situation for mesosulfuron-methyl: Short term dietary studies for mesosulfuron-methyl gave no indication for higher toxicity via the dietary exposure route compared to one application via gavage in the acute oral studies.

Long-term toxicity exposure ratio on screening level for birds

Table 10.1.2-1: Long-term DDD and TER calculation (active substance mesosulfuron-methyl) on screening level for birds

Crop / Compound	Indicator species	NO(A)EL [mg/kg bw]	Appl. rate [kg/ha]	SV_m	MAF_m	f_{twa}	DDD	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha									
Mesosulfuron-methyl	Small omnivorous bird	93	0.015	64.8	1	0.53	0.52	181	5
Winter rye, 1 × 6 g a.s./ha									
Mesosulfuron-methyl	Small omnivorous bird	93	0.006	64.8	1	0.53	0.21	451	5

All TER values are above the required trigger of 5 for reproductive/long-term exposure. Long-term risk to birds is therefore acceptable for the intended product uses.

Long-term risk assessment for birds drinking contaminated water

An assessment of the risk potentially posed by consumption of contaminated drinking water is required according to the EFSA Guidance Document for Birds and Mammals (2009). Two scenarios were identified as relevant for assessing the risk of pesticides via drinking water to birds and mammals:

- Leaf scenario, only relevant for birds possibly drinking water from puddles in leaf whorls after application of a pesticide to a crop and subsequent rainfall or irrigation. This scenario is only relevant for acute exposure.
  As IMS + MSM + MPR OD 42 is applied in cereals, no pools in leaf axils where an acute exposure possibly might occur are to be expected.
- Puddle scenario. Birds and mammals taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. This scenario is relevant for acute and long-term exposure.

An "escape clause" recommended in the EFSA Guidance Document for Birds and Mammals (2009) allows for screening the need for a quantitative risk assessment by a comparison between the application rate and the toxicity of the respective substance. This escape clause specifies that *"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)."* [1].

Table 10.1.2- 2: Evaluation of potential concern for exposure of birds drinking water (escape clause)

Crop / Compound	Koc [L/kg]	Application rate [g as/ha]	NO(A)EL [mg as/ kg bw/d]	Ratio (Application rate) / NO(A)EL	"Escape clause" No concern if ratio	Conclusion
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	48[1]	15	93	0.16	≤ 50	No concern
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	48	6	93	0.06	≤ 50	No concern

[1] median value, MCA 7.1.3.1, mesosulfuron Review Report (SANCO/10298/2003 final)

This evaluation confirms that the risk for birds from drinking water that may contain residues from the use of IMS + MSM + MPR OD 42 is acceptable.

IIIA 10.1.3 Baits: Concentration of active ingredient in bait in mg/kg

Not applicable for spray application.

IIIA 10.1.4 Pellets, granules, prills or treated seed

Not applicable for spray application.

[1] EFSA (2009): Guidance Document on Risk Assessment for Birds & Mammals on request from EFSA, p. 66

IIIA 10.1.4.1 Amount of active ingredient in or on each item

Not applicable for spray application.

IIIA 10.1.4.2 Proportion of active ingredient LD_{50} per 100 items and per gram of items

Not applicable for spray application.

IIIA 10.1.5 Size and shape of pellet, granule or prill

Not applicable for spray application.

IIIA 10.1.6 Acute toxicity of the formulation

For animal welfare reason, acute oral studies with formulations are routinely not conducted for birds, when the individual active ingredients have been shown to clearly be devoid of relevant toxicity to birds.
Based on LD_{50} of both active substances and the safener contained in formulation IMS + MSM + MPR OD 42 consistently > 2000 a.s./kg bw, it is reasonable to assume that the product would not pose an unacceptable risk to birds. Therefore it is justified to waive the acute test with the formulation in birds.

IIIA 10.1.7 Supervised cage or field trials

The risk assessment based on the active substances indicates acceptable acute, short-term and long-term risks to birds (see Points 10.1.1 and 10.1.2 of this dossier). For this reason and also considering animal welfare, no supervised cage or field study with the preparation was deemed necessary.

IIIA 10.1.8 Acceptance of bait, granules or treated seeds (palatability testing)

Not applicable for spray application.

IIIA 10.1.9 Effects of secondary poisoning

Substances with a high bioaccumulation potential could theoretically bear a risk of secondary poisoning for birds if feeding on contaminated prey like fish or earthworms. For organic chemicals, a log P_{OW} > 3 is used to trigger an in-depth evaluation of the potential for bioaccumulation.

The log P_{OW} of mesosulfuron-methyl was determined to be significantly below that trigger (see Table 10.1.9-1).

Thus a risk assessment for a generic earthworm eating bird and a generic fish eating bird is not required since bioaccumulation of the substance is not to be expected.

Table 10.1.9- 1: Log P_{OW} values of mesosulfuron-methyl

Compound	log P_{OW}	Reference
Mesosulfuron-methyl	-0.48 (pH 7)*	[redacted] (1996) M-142043-02-1 CA 2.7

* mesosulfuron Review Report (SANCO/10298/2003 final)

IIIA 10.2 Effects on aquatic organisms

Ecotoxicological endpoints used in risk assessment

Table 10.2- 1: Endpoints of the formulation IMS + MSM + MPR OD 42 used in risk assessment

Test substance	Test organism	Study type	Endpoint [mg/L]		References
IMS + MSM + MPR OD 42	**Fish, acute**				
	Oncorhynchus mykiss (rainbow trout)	static acute, 96 h	LC_{50}	8.83	[redacted] (2003) C038744 M-225670-01-1 KIIIA 10.2.2.1/01
	Aquatic invertebrates, acute				
	Daphnia magna (water flea)	static acute, 48 h	EC_{50}	7.6	[redacted] (2003) C038151 M-224326-01-1 KIIIA 10.2.2.2/01
	Algae				
	Pseudokirchneriella subcapitata (green alga)	growth inhibition, 72 h	E_rC_{50}	6.71	[redacted] (2003) C038152 M-224329-01-1 KIIIA 10.2.2.3/01
	Aquatic macrophytes				
	Lemna gibba (duckweed)	growth inhibition, 7 d	E_rC_{50}	0.0884	[redacted] (2003) C037713 M-223377-01-1 KIIIA 10.8.2.1/01

Table 10.2- 2: Endpoints for the active substance mesosulfuron-methyl and metabolites used in risk assessment

Test substance	Test organism	Test system	Endpoint [mg/L]		References
Mesosulfuron-methyl	**Fish, acute**				
	Oncorhynchus mykiss (rainbow trout) *Lepomis macrochirus* (bluegill sunfish) *Cyprinodon variegates* (sheepshead minnow)	Acute, static, 96 h	LC_{50}	> 100	[redacted] et al. (1999) M-186666-01-1 KCA 8.2.1 /01 [redacted] et al. (1999) M-186597-01-1 KCA 8.2.1 /02 [redacted] (2001) M-238810-01-1 KCA 8.2.1 /02
	Fish, chronic				
	Oncorhynchus mykiss (rainbow trout)	chronic, 28d	NOEC	32	[redacted] et al. (2000) M-187567-01-1 KCA 8.2.2 /01
	Aquatic invertebrates, acute				

Test substance	Test organism	Test system	Endpoint [mg/L]		References
	Daphnia magna (water flea)	Acute, static, 48 h	EC_{50}	>100	[redacted] et al. (1999) M-186707-01-1 KCA 8.2.4.1 /01
	Mysidopsis bahia (mysid shrimp)	Acute, static, 96 h	LC_{50}	>100	Abedi et al. (2001) M-238811-01-1 KCA 8.2.4.2 /01
	Aquatic invertebrates, chronic				
	Daphnia magna (water flea)	chronic, semi static, 21 d	NOEC	1.8	[redacted] et al. (2000) M-197785-02-2 KCA 8.2.5.1 /01
	Algae				
	Pseudokirchneriella subcapitata (green alga)	~~Growth inhibition, 96 h~~	~~E_rC_{50}~~	~~>0.29~~	~~[redacted] et al. (1998) M-143500-01-1 KCA 8.2.6.1 /01~~
		Growth inhibition, 72 h	E_rC_{50}	3.99	[redacted] (2015) M-516540-01-1 KCA 8.2.6.1 /09
	Aquatic plant				
	Lemna gibba (duck weed)	Growth inhibition, 7 d	E_rC_{50}	0.00129	[redacted] (2013) M-445139-01-1 KCA 8.2.7 /09 [redacted], 2014 M-487405-01-1 KCA 8.2.7 /10
	Aquatic plants *(SSD analysis based on data for 10 species)*	Growth inhibition, 8 weeks	HC5 *based on ErC50*	0.0017	[redacted], (2009) M-329474-01-1 KCA 8.2.7 /08 [redacted] (2013) M-445139-01-1 KCA 8.2.7 /09
AE F154851	**Algae**				
	Pseudokirchnerilla subcapitata (green alga)	Growth inhibition, 72 h	E_rC_{50}	38.0	[redacted] (2005) M-255087-01-1 KCA 8.2.6.1 /04
	Aquatic plant				
	Lemna gibba (duck weed)	Growth inhibition, static, 7 d	E_rC_{50}	0.11	[redacted] (2005) M-255283-01-1 KCA 8.2.7 /11
AE F160459	**Algae**				
	Pseudokirchnerilla subcapitata (green alga)	Growth inhibition, 96 h	E_rC_{50}	> 100	[redacted] et al. (2000) M-198314-01-1 KCA 8.2.6.1 /02
	Aquatic plant				
	Lemna gibba (duck weed)	Growth inhibition, static, 7 d	E_rC_{50}	2.6	[redacted] (2000) M-198076-01-1 KCA 8.2.7 /03

Test substance	Test organism	Test system	Endpoint [mg/L]	References
AE F099095	**Algae**			
	Pseudokirchnerilla subcapitata (green alga)	Growth inhibition, 72 h	E_rC_{50} > 100	[redacted] (2005) M-254084-01-1 KCA 8.2.6.1 /05
	Aquatic plant			
	Lemna gibba (duck weed)	Growth inhibition, static, 7 d	E_rC_{50} > 100	[redacted] (2005) M-254496-01-1 KCA 8.2.7 /12
AE F092944	**Fish, acute**			
	Oncorhynchus mykiss (rainbow trout)	Acute, static, 96 h	LC_{50} 254	[redacted] (1993) M-131422-01-1 KCA 8.2.1 /04
	Aquatic invertebrates, acute			
	Daphnia magna (water flea)	Acute, static, 48 h	EC_{50} 233	[redacted] (1993) M-131382-01-1 KCA 8.2.4.1 /02
	Algae			
	Desmodesmus subspicatus (syn. *Scenedesmus subspicatus*) (green alga)	Growth inhibition, 72 h	E_rC_{50} > 560	[redacted] (1993) M-131421-01-1 KCA 8.2.6.1 /06
	Aquatic plant			
	Lemna gibba (duck weed)	Growth inhibition, static, 7 d	E_rC_{50} > 100	[redacted] [redacted] (2000) M-186916-01-1 KCA 8.2.7 /13
AE F160460	**Aquatic plant**			
	Lemna gibba (duck weed)	Growth inhibition, static, 7 d	E_rC_{50} > 100	[redacted] (2000) M-199266-01-1 KCA 8.2.7 /04
AE F140584	**Aquatic plant**			
	Lemna gibba (duck weed)	Growth inhibition, static, 7 d	E_rC_{50} > 10	[redacted] (2014) M-486658-01-1 KCA 8.2.7 /14
AE F147447	**Algae**			
	Pseudokirchnerilla subcapitata (green alga)	Growth inhibition, 96 h	E_rC_{50} > 100	[redacted] [redacted] (2000) M-199529-01-1 KCA 8.2.6.1 /03
	Aquatic plant			
	Lemna gibba (duck weed)	Growth inhibition, static, 7 d	E_rC_{50} > 100	[redacted] [redacted] (2000) M-198273-01-1 KCA 8.2.7 /05

All above endpoints used in risk assessment are consistent with the *proposed* EU endpoints listed in Document N2 for mesosulfuron-methyl.

IIIA 10.2.1 Toxicity exposure ratios

Predicted Environmental Concentrations used in risk assessment

Formulated product:

Spray drift represents the only route that might lead to exposure of surface water to the formulated product. Since integrity of the formulation will be lost upon soil contact, indirect entry routes such as run-off or drainage processes are not of relevance for a formulation risk assessment.

As a tier 1 approach, drift PECsw of the product is calculated considering standard drift rates and a standard water body, which is 30 cm deep and without riparian vegetation.

Table 10.2.1- 1: Initial maximum PEC_{sw} values of the formulation, considering spray drift after one application as route of entry relevant for the product

Compound	Scenario	Drift rate (arable crops)	Winter wheat, 1 x 1.5 L/ha	Winter rye, 1 x 0.6 L/ha
			$PEC_{sw,\,max}$ [µg/L]	$PEC_{sw,\,max}$ [µg/L]
IMS + MSM + MPR OD 42	small static ditch, at the edge of the treated field, water depth 0.3 m	2.77 % (no buffer)	**13.85**	**5.54**

PEC derived from calculation of entry in standard ditch via spray drift (water body of 30 cm depth), according to BBA (2006)[2], taking into account the specified density of the product (1.000 g/mL)
Bold values were used for risk assessment

Active substances and metabolites:

Predicted environmental concentrations for the active substance and its metabolites relevant for risk assessment were calculated in surface water (PEC_{SW}) and in sediment (PEC_{sed}) according to FOCUS surface water scenarios as described in detail in Point IIIA 9.7 (active substance) and IIIA 9.8 (metabolites) of this MCP document.

The relevant PEC values considered for TER calculations are summarised in the tables below. Maximum values are used for risk assessments.

[2] [redacted]., (2006) Bekanntmachung über die Abtrifteckwerte, die bei der Prüfung und Zulassung von Pflanzenschutzmitteln herangezogen werden, http://www.jki.bund.de/de/startseite/institute/anwendungstechnik/abdrift-eckwerte.html

Table 10.2.1- 2: Initial maximum PECsw values for mesosulfuron-methyl and its metabolites at FOCUS Steps 1 & 2

(a) originally submitted simulation – KIIIA 9.7/01 and KIIIA 9.7/01

Compound	FOCUS Scenario	Winter wheat, 1 × 15 g a.s./ha	Winter rye, 1 × 6 g a.s./ha
		$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
Mesosulfuron-methyl	**STEP 1**	4.837	1.935
	STEP 2 – Northern Scenario	**1.202**	**0.481**
	STEP 2 – Southern Scenario	0.986	0.395
AE F154851	**STEP 1**	0.728	0.291
	STEP 2 – Northern Scenario	**0.173**	**0.069**
	STEP 2 – Southern Scenario	0.140	0.056
AE F160459	**STEP 1**	0.449	0.180
	STEP 2 – Northern Scenario	**0.128**	**0.051**
	STEP 2 – Southern Scenario	0.108	0.043
AE F099095	**STEP 1**	0.326	0.130
	STEP 2 – Northern Scenario	**0.079**	**0.032**
	STEP 2 – Southern Scenario	0.063	0.025
AE F092944	**STEP 1**	0.099	0.040
	STEP 2 – Northern Scenario	**0.024**	**0.010**
	STEP 2 – Southern Scenario	0.020	0.008
AE F160460	**STEP 1**	0.410	0.164
	STEP 2 – Northern Scenario	**0.100**	**0.040**
	STEP 2 – Southern Scenario	0.082	0.033
AE F140584	**STEP 1**	0.229	0.092
	STEP 2 – Northern Scenario	**0.028**	**0.011**
	STEP 2 – Southern Scenario	0.023	0.009
AE F147447	**STEP 1**	0.195	0.078
	STEP 2 – Northern Scenario	**0.054**	**0.022**
	STEP 2 – Southern Scenario	0.045	0.018

Bold values were used for risk assessment

(b) alternative simulation using RMS requested modelling parameters– KIIIA 9.7/02 and KIIIA 9.8/02

Compound	FOCUS Scenario	Winter wheat, 1 × 15 g a.s./ha PEC$_{sw, max}$ [µg/L]	Winter rye, 1 × 6 g a.s./ha PEC$_{sw, max}$ [µg/L]
Mesosulfuron-methyl	STEP 1	4.745	1.898
	STEP 2 – Northern Scenario	**1.849**	**0.740**
	STEP 2 – Southern Scenario	1.504	0.602
AE F154851	STEP 1	0.731	0.293
	STEP 2 – Northern Scenario	**0.281**	**0.112**
	STEP 2 – Southern Scenario	0.226	0.090
AE F160459	STEP 1	0.451	0.180
	STEP 2 – Northern Scenario	**0.191**	**0.076**
	STEP 2 – Southern Scenario	0.158	0.063
AE F099095	STEP 1	0.392	0.157
	STEP 2 – Northern Scenario	**0.153**	**0.061**
	STEP 2 – Southern Scenario	0.122	0.049
AE F092944	STEP 1	0.109	0.044
	STEP 2 – Northern Scenario	**0.041**	**0.017**
	STEP 2 – Southern Scenario	0.033	0.013
AE F160460	STEP 1	0.411	0.164
	STEP 2 – Northern Scenario	**0.156**	**0.063**
	STEP 2 – Southern Scenario	0.127	0.051
AE F140584	STEP 1	0.229	0.092
	STEP 2 – Northern Scenario	**0.049**	**0.020**
	STEP 2 – Southern Scenario	0.040	0.016
AE F147447	STEP 1	0.175	0.070
	STEP 2 – Northern Scenario	**0.074**	**0.030**
	STEP 2 – Southern Scenario	0.061	0.024

Bold values were used for risk assessment

Table 10.2.1- 3: Initial maximum PECsw values for mesosulfuron-methyl at FOCUS Step 3

(a) originally submitted simulation – KIIIA 9.7/01 and KIIIA 9.7/01)

FOCUS scenario	Mesosulfuron-methyl	
	Winter wheat, 1 × 15 g a.s./ha	Winter rye, 1 × 6 g a.s./ha
	$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
Step 3		
D1 (ditch)	**0.161**	**0.063**
D1 (stream)	**0.118**	**0.047**
D2 (ditch)	**1.601**	**0.576**
D2 (stream)	**1.010**	**0.366**
D3 (ditch)	**0.096**	**0.038**
D4 (pond)	**0.024**	**0.008**
D4 (stream)	**0.079**	**0.031**
D5 (pond)	**0.011**	**0.004**
D5 (stream)	**0.078**	**0.031**
D6 (ditch)	**0.102**	**0.041**
R1 (pond)	**0.006**	**0.002**
R1 (stream)	**0.110**	**0.043**
R3 (stream)	**0.325**	**0.130**
R4 (stream)	**0.246**	**0.100**

Bold values were used for risk assessment.

(b) alternative simulation using RMS requested modelling parameters– KIIIA 9.7/02 and KIIIA 9.8/02

FOCUS scenario	Mesosulfuron-methyl	
	Winter wheat, 1 × 15 g a.s./ha	Winter rye, 1 × 6 g a.s./ha
	$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
Step 3		
D1 (ditch)	**0.187**	0.075
D1 (stream)	**0.132**	0.053
D2 (ditch)	**1.328**	0.510
D2 (stream)	**0.837**	0.322
D3 (ditch)	**0.096**	0.038
D4 (pond)	**0.035**	0.013
D4 (stream)	**0.080**	0.032
D5 (pond)	**0.016**	0.006
D5 (stream)	**0.081**	0.032
D6 (ditch)	**0.102**	0.041
R1 (pond)	**0.007**	0.003
R1 (stream)	**0.111**	0.045
R3 (stream)	**0.327**	0.130
R4 (stream)	**0.266**	0.108

Bold values were used for risk assessment.

Risk assessment

The risk assessment has been performed according to "Guidance Document on Aquatic Ecotoxicology in the context of the Directive 91/414/EEC" (Sanco/3268/2001 rev.4 (final) 17 October 2002). The "Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters" (EFSA Panel on Plant Protection Products and their Residues, 2013, EFSA Journal 2013;11(7):3290, 268 pp. doi:10.2903/j.efsa.2013.3290) has been considered where appropriate.

Toxicity exposure ratios (TER_A or TER_{LT} values) are calculated based on endpoints of the most sensitive species per organims group, and worst-case PEC_{SW} values.

Summary of TER values for aquatic organisms

Table 10.2.1- 4: TER overview summary for formulated product, as detailed under points 10.2.1.1 to 10.2.1.11

Crop / Compound	Organism group	Time-scale	FOCUS Step	TER	Trigger	Refinement used ?
Winter wheat, 1× 1.5 L product/ha						
IMS + MSM + MPR OD 42	Fish	acute	Tier 1 drift	638	100	No
	Invertebrates	acute	Tier 1 drift	549	100	No
	Green algae	long-term	Tier 1 drift	484	10	No
	Aquatic plants	long-term	Tier 1 drift	6.38#	10	No
Winter rye, 1× 0.6 L product/ha						
IMS + MSM + MPR OD 42	Fish	acute	Tier 1 drift	1 594	100	No
	Invertebrates	acute	Tier 1 drift	1 372	100	No
	Green algae	long-term	Tier 1 drift	1 211	10	No
	Aquatic plants	long-term	Tier 1 drift	15.96	10	No

#) no refined assessment conducted at product level; refinement at active substance level will cover the situation for product.

Table 10.2.1- 5: TER overview summary for active substance mesosulfuron-methyl and metabolites, as detailed under points 10.2.1.1 to 10.2.1.11

Crop / Compound	Organism group	Time-scale	FOCUS Step	TER	Trigger	Refinement used ?
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	Fish	acute	Step 2	> 83 195	100	No
		long-term	Step 2	26 622	10	No
	Invertebrates	acute	Step 2	> 83 195	100	No
		long-term	Step 2	1 498	10	No
	Green algae	long-term	Step 2	241	10	No
	Aquatic plants	long-term	Step 3	D1 (ditch) 7.27 D1 (stream) 9.92 D2 (ditch) **0.73** D2 (stream) **1.16** D3 (ditch) 12.19 D4 (pond) 48.75 D4 (stream) 14.81 D5 (pond) 106.36 D5 (stream) 15.00 D6 (ditch) 11.47 R1 (pond) 195.00 R1 (stream) 10.64 R3 (stream) 3.60 R4 (stream) 4.76	3	Yes
AE F154851	Green algae	long-term	Step 2	219 653	10	No
	Aquatic plants	long-term	Step 2	636	10	No
AE F160459	Green algae	long-term	Step 2	> 781 250	10	No
	Aquatic plants	long-term	Step 2	20 313	10	No
AE F099095	Green algae	long-term	Step 2	> 1 265 823	10	No
	Aquatic plants	long-term	Step 2	> 1 265 823	10	No
AE F092944	Fish	acute	Step 2	10 583 333	100	No
	Invertebrates	acute	Step 2	9 708 333	100	No
	Green algae	long-term	Step 2	> 23 333 333	10	No
	Aquatic plants	long-term	Step 2	> 4 166 667	10	No
AE F160460	Aquatic plants	long-term	Step 2	> 1 000 000	10	No
AE F140584	Aquatic plants	long-term	Step 2	> 357	10	No
AE F147447	Green algae	long-term	Step 2	> 1 851 852	10	No
	Aquatic plants	long-term	Step 2	> 1 851 852	10	No

Crop / Compound	Organism group	Time-scale	FOCUS Step	TER	Trigger	Refinement used?
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	Fish	acute	Step 2	> 207 900	100	No
		long-term	Step 2	66 528	10	No
	Invertebrates	acute	Step 2	> 207 900	100	No
		long-term	Step 2	3 742	10	No
	Green algae	long-term	Step 2	603	10	No
	Aquatic plants	long-term	Step 3	D1 (ditch) 18.57 D1 (stream) 24.89 D2 (ditch) **2.03** D2 (stream) 3.20 D3 (ditch) 30.79 D4 (pond) 146.25 D4 (stream) 37.74 D5 (pond) 292.50 D5 (stream) 37.74 D6 (ditch) 28.54 R1 (pond) 585.00 R1 (stream) 27.21 R3 (stream) 9.00 R4 (stream) 11.70	3	Yes
AE F154851	Green algae	long-term	Step 2	550 725	10	No
	Aquatic plants	long-term	Step 2	1 594	10	No
AE F160459	Green algae	long-term	Step 2	1 960 784	10	No
	Aquatic plants	long-term	Step 2	50 980	10	No
AE F099095	Green algae	long-term	Step 2	> 3 125 000	10	No
	Aquatic plants	long-term	Step 2	> 3 125 000	10	No
AE F092944	Fish	acute	Step 2	25 400 000	100	No
	Invertebrates	acute	Step 2	23 300 000	100	No
	Green algae	long-term	Step 2	> 56 000 000	10	No
	Aquatic plants	long-term	Step 2	> 10 000 000	10	No
AE F160460	Aquatic plants	long-term	Step 2	> 2 500 000	10	No
AE F140584	Aquatic plants	long-term	Step 2	909	10	No
AE F147447	Green algae	long-term	Step 2	> 4 545 455	10	No
	Aquatic plants	long-term	Step 2	> 4 545 455	10	No

IIIA 10.2.1.1 TER$_A$ for fish

Table 10.2.1.1- 1: TER$_A$ calculations (formulated product) for fish based on Tier 1 drift calculation

Crop / Compound	Species	Endpoint [µg/L]		PEC$_{sw,max}$ [µg/L]	TER$_A$	Trigger
Winter wheat, 1× 1.5 L product/ha						
IMS + MSM + MPR OD 42	*O. mykiss*	LC_{50}	8 830	13.85	638	100
Winter rye, 1 × 0.6 L product/ha						
IMS + MSM + MPR OD 42	*O. mykiss*	LC_{50}	8 830	5.54	1 594	100

Table 10.2.1.1- 2: TER$_A$ calculations (active substance mesosulfuron-methyl and metabolites) for fish based on FOCUS Step 2

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [µg/L]		PEC$_{sw,max}$ [µg/L]	TER$_A$	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*O. mykiss* *L. macrochirus* *C. variegates*	LC$_{50}$	> 100 000	1.202	> 83 195	100
AE F092944	*O. mykiss*	LC$_{50}$	254 000	0.024	10 583 333	100
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*O. mykiss* *L. macrochirus* *C. variegates*	LC$_{50}$	> 100 000	0.481	> 207 900	100
AE F092944	*O. mykiss*	LC$_{50}$	254 000	0.010	25 400 000	100

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [µg/L]		PEC$_{sw,max}$ [µg/L]	TER$_A$	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*O. mykiss* *L. macrochirus* *C. variegates*	LC$_{50}$	> 100 000	1.849	> 54 083	100
AE F092944	*O. mykiss*	LC$_{50}$	254 000	0.041	6 195 122	100
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*O. mykiss* *L. macrochirus* *C. variegates*	LC$_{50}$	> 100 000	0.740	> 135 135	100
AE F092944	*O. mykiss*	LC$_{50}$	254 000	0.017	14 941 177	100

All TER$_A$ values meet the required trigger of 100, indicating an acceptable acute risk to fish for the intended uses.

IIIA 10.2.1.2 TER$_{LT}$ for fish

Table 10.2.1.2- 1: TER$_{LT}$ calculations (active substance mesosulfuron-methyl) for fish based on FOCUS Step 2

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [µg/L]		PEC$_{sw,max}$ [µg/L]	TER$_{LT}$	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*O. mykiss*	NOEC	32 000	1.202	26 622	10
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*O. mykiss*	NOEC	32 000	0.481	66 528	10

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*O. mykiss*	NOEC	32 000	1.849	17.306	10
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*O. mykiss*	NOEC	32 000	0.740	43 243	10

The TER_{LT} values meet the required trigger of 10, indicating an acceptable long-term risk to fish for the intended uses.

IIIA 10.2.1.3 TER_A for Daphnia

Table 10.2.1.3- 1: TER_A calculations (formulated product) for aquatic invertebrates based on Tier 1 drift calculation

Crop / Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_A	Trigger
Winter wheat, 1× 1.5 L product/ha						
IMS + MSM + MPR OD 42	*D. magna*	EC_{50}	7 600	13.85	549	100
Winter rye, 1 × 0.6 L product/ha						
IMS + MSM + MPR OD 42	*D. magna*	EC_{50}	7 600	5.54	1 372	100

Table 10.2.1.3- 2: TER_A calculations (active substance mesosulfuron-methyl and metabolites) for aquatic invertebrates based on FOCUS Step 2

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_A	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*D. magna*	EC_{50}	> 100 000	1.202	> 83 195	100
AE F092944	*D. magna*	EC_{50}	233 000	0.024	9 708 333	100
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*D. magna*	EC_{50}	> 100 000	0.481	> 207 900	100
AE F092944	*D. magna*	EC_{50}	233 000	0.010	23 300 000	100

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_A	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*D. magna*	EC_{50}	> 100 000	1.849	> 54 083	100
AE F092944	*D. magna*	EC_{50}	233 000	0.041	5 682 927	100
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*D. magna*	EC_{50}	> 100 000	0.740	> 135 135	100
AE F092944	*D. magna*	EC_{50}	233 000	0.017	13 705 882	100

All TER_A values meet the required trigger of 100, indicating an acceptable acute risk to aquatic invertebrates for the intended uses.

IIIA 10.2.1.4 TER_{LT} for Daphnia

Table 10.2.1.4- 1: TER_{LT} calculations (active substance mesosulfuron-methyl and metabolites) for aquatic invertebrates based on FOCUS Step 2

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*D. magna*	NOEC	1 800	1.202	1 498	10
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*D. magna*	NOEC	1 800	0.481	3 742	10

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*D. magna*	NOEC	1 800	1.849	973	10
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*D. magna*	NOEC	1 800	0.740	2 432	10

The TER_{LT} values meet the required trigger of 10, indicating an acceptable long-term risk to aquatic invertebrates for the intended uses.

IIIA 10.2.1.5 TER_A for aquatic insect

No specific studies on the acute toxicity of the product to aquatic insect species were conducted. The product is not an insecticide.

IIIA 10.2.1.6 TER$_{LT}$ for aquatic insect

No specific studies on the long-term toxicity of the product to aquatic insect species were conducted. The product is not an insecticide.

IIIA 10.2.1.7 TER$_{A}$ for aquatic crustacean

No specific studies on the acute toxicity of the product to aquatic crustacean species were conducted.

IIIA 10.2.1.8 TER$_{LT}$ for aquatic crustacean

No specific studies on the long-term toxicity of the product to aquatic crustacean species were conducted.

IIIA 10.2.1.9 TER$_{A}$ for aquatic gastropod mollusc

No specific studies on the acute toxicity of the product to aquatic gastropod mollusc species were conducted.

IIIA 10.2.1.10 TER$_{LT}$ for aquatic gastropod mollusc

No specific studies on the long-term toxicity of the product to aquatic gastropod mollusc species were conducted.

IIIA 10.2.1.11 TER$_{LT}$ for algae

Table 10.2.1.11- 1: TER$_{LT}$ calculations (formulated product) for algae based on Tier 1 drift calculation

Crop / Compound	Species	Endpoint [µg/L]		PEC$_{sw,max}$ [µg/L]	TER$_{LT}$	Trigger
Winter wheat, 1× 1.5 L product/ha						
IMS + MSM + MPR OD 42	*P. subcapitata*	E_rC_{50}	6 710	13.85	484	10
Winter rye, 1 × 0.6 L product/ha						
IMS + MSM + MPR OD 42	*P. subcapitata*	E_rC_{50}	6 710	5.54	1 211	10

Table 10.2.1.11- 2: TER$_{LT}$ calculations (active substance mesosulfuron-methyl and metabolites) for algae based on FOCUS Step 2

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [µg/L]		PEC$_{sw,max}$ [µg/L]	TER$_{LT}$	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*P. subcapitata*	E_rC_{50}	~~>290~~ 3 990	1.202	~~>241~~ 3 319	10
AE F154851	*P. subcapitata*	E_rC_{50}	38 000	0.173	219 653	10
AE F160459	*P. subcapitata*	E_rC_{50}	> 100 000	0.128	> 781 250	10
AE F099095	*P. subcapitata*	E_rC_{50}	> 100 000	0.079	> 1 265 823	10
AE F092944	*P. subcapitata*	E_rC_{50}	> 560 000	0.024	> 23 333 333	10
AE F147447	*P. subcapitata*	E_rC_{50}	> 100 000	0.054	> 1 851 852	10
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*P. subcapitata*	E_rC_{50}	~~>290~~ 3 990	0.481	~~>603~~ 8 295	10
AE F154851	*P. subcapitata*	E_rC_{50}	38 000	0.069	550 725	10
AE F160459	*P. subcapitata*	E_rC_{50}	> 100 000	0.051	> 1 960 784	10
AE F099095	*P. subcapitata*	E_rC_{50}	> 100 000	0.032	> 3 125 000	10
AE F092944	*P. subcapitata*	E_rC_{50}	> 560 000	0.010	> 56 000 000	10
AE F147447	*P. subcapitata*	E_rC_{50}	> 100 000	0.022	> 4 545 455	10

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [µg/L]		PEC$_{sw,max}$ [µg/L]	TER$_{LT}$	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*P. subcapitata*	E_rC_{50}	3 990	1.849	3 319	10
AE F154851	*P. subcapitata*	E_rC_{50}	38 000	0.281	135 231	10
AE F160459	*P. subcapitata*	E_rC_{50}	> 100 000	0.191	> 523 560	10
AE F099095	*P. subcapitata*	E_rC_{50}	> 100 000	0.153	> 653 595	10
AE F092944	*P. subcapitata*	E_rC_{50}	> 560 000	0.041	> 13 658 537	10
AE F147447	*P. subcapitata*	E_rC_{50}	> 100 000	0.074	> 1 351 351	10
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*P. subcapitata*	E_rC_{50}	3 990	0.740	5 392	10
AE F154851	*P. subcapitata*	E_rC_{50}	38 000	0.112	339 286	10
AE F160459	*P. subcapitata*	E_rC_{50}	> 100 000	0.076	> 1 315 789	10
AE F099095	*P. subcapitata*	E_rC_{50}	> 100 000	0.061	> 1 639 344	10
AE F092944	*P. subcapitata*	E_rC_{50}	> 560 000	0.017	> 32 941 176	10
AE F147447	*P. subcapitata*	E_rC_{50}	> 100 000	0.030	> 3 333 333	10

The TER$_{LT}$ values meet the required trigger of 10, indicating an acceptable long-term risk to algae for the intended uses.

TER for aquatic plants

Table 10.2.1.11- 3: TER_{LT} calculations (formulated product) for aquatic plant based on Tier 1 drift calculation

Crop / Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1× 1.5 L product/ha						
IMS + MSM + MPR OD 42	*L. gibba*	E_rC_{50}	88.4	13.85	**6.38**	10
Winter rye, 1× 0.6 L product/ha						
IMS + MSM + MPR OD 42	*L. gibba*	E_rC_{50}	88.4	5.54	15.96	10

Bold values: trigger is not met and further refinement is required

Refined risk assessment for the formulated product

For the drift entry of the formulated product no higher tier exposure calculations are available. FOCUS surface water calculations can only be performed for the individual active substances.

PEC_{sw} calculations (tier 1 as well as FOCUS surface water) are based on the scenario of immediate equal distribution of the active substance in the water body. Under these conditions – instant and equal dilution in a big water volume - it can be assumed that the properties of the formulants will no longer influence the behaviour of the active substances. The same scenario is also reflected in laboratory tests on aquatic plants, where the test item is equally distributed in the test solution before test organisms are put in the system and where the formulation additionally decomposes over the test period of a 7-day static test.

Given the well-known exceptional toxicity of sulfonyl urea type (ALS inhibitor) herbicides to aquatic plants, especially to *Lemna gibba*, it is justified to assume that the toxicity of the formulated product originates exclusively from additive effects of its contained active substances mesosulfuron-methyl and iodosulfuron-methyl-sodium. For confirmation of this hypothesis, an expected endpoint for the fractional active substance composition of the product was calculated based on the individual substance endpoints, and found to be matching the actually measured formulation endpoint within natural biological variance (calculated expected E_rC_{50} = 98.4 µg/L vs. measured product E_rC_{50} =88.4 µg/L; cf. Table 10.2.1.11-4).

Table 10.2.1.11- 4: Calculation of the acute mixed toxicity of the formulation according to Finney

	Mesosulfuron-methyl	Iodosulfuron-methyl-sodium	IMS + MSM + MPR OD 42
Content within the product [%]	1.0	0.2	-
Effects on *Lemna* (*L. gibba*)			
E_rC_{50} [µg as/L]	1.29	0.83#	
E_rC_{50} – added toxicity [µg product/L]	Calculated expected E_rC_{50} 98.4		Measured E_rC_{50} 88.4

#) EU list of endpoints for iodosulfuron-methyl-sodium [SANCO/10166/2003-Final]

The risk assessment for aquatic plant can therefore safely be performed on individual active substance basis; any refinements made in these assessments will apply for the formulated product as well.

For the purpose of the present MCP document, however, assessments will only address the active substance mesosulfuron-methyl eligible for Approval renewal. Assessments for the second active substance, iodosulfuron-methyl-sodium, will be provided at a later stage, as part of the post-AIR process.

Table 10.2.1.11- 5: TER_{LT} calculations (active substance mesosulfuron-methyl and metabolites) for aquatic plant based on FOCUS Step 2

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*L. gibba*	E_rC_{50}	1.29	1.202	**1.07**	10
AE F154851	*L. gibba*	E_rC_{50}	110	0.173	636	10
AE F160459	*L. gibba*	E_rC_{50}	2 600	0.128	20 313	10
AE F099095	*L. gibba*	E_rC_{50}	> 100 000	0.079	> 1 265 823	10
AE F092944	*L. gibba*	E_rC_{50}	> 100 000	0.024	> 4 166 667	10
AE F160460	*L. gibba*	E_rC_{50}	> 100 000	0.100	> 1 000 000	10
AE F140584	*L. gibba*	E_rC_{50}	> 10	0.028	> 357	10
AE F147447	*L. gibba*	E_rC_{50}	> 100 000	0.054	> 1 851 852	10
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*L. gibba*	E_rC_{50}	1.29	0.481	**2.68**	10
AE F154851	*L. gibba*	E_rC_{50}	110	0.069	1 594	10
AE F160459	*L. gibba*	E_rC_{50}	2 600	0.051	50 980	10
AE F099095	*L. gibba*	E_rC_{50}	> 100 000	0.032	> 3 125 000	10
AE F092944	*L. gibba*	E_rC_{50}	> 100 000	0.010	> 10 000 000	10
AE F160460	*L. gibba*	E_rC_{50}	> 100 000	0.040	> 2 500 000	10
AE F140584	*L. gibba*	E_rC_{50}	> 10	0.011	> 909	10
AE F147447	*L. gibba*	E_rC_{50}	> 100 000	0.022	> 4 545 455	10

Bold values: trigger is not met and further refinement is required

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha					
Mesosulfuron-methyl	*L. gibba*	E_rC_{50} 1.29	1.849	**0.70**	10
AE F154851	*L. gibba*	E_rC_{50} 110	0.281	391	10
AE F160459	*L. gibba*	E_rC_{50} 2 600	0.191	13 613	10
AE F099095	*L. gibba*	E_rC_{50} > 100 000	0.153	653 595	10
AE F092944	*L. gibba*	E_rC_{50} > 100 000	0.041	2 439 024	10
AE F160460	*L. gibba*	E_rC_{50} > 100 000	0.156	641 026	10
AE F140584	*L. gibba*	E_rC_{50} > 10	0.049	204	10
AE F147447	*L. gibba*	E_rC_{50} > 100 000	0.074	1 351 351	10
Winter rye, 1 × 6 g a.s./ha					
Mesosulfuron-methyl	*L. gibba*	E_rC_{50} 1.29	0.740	**1.74**	10
AE F154851	*L. gibba*	E_rC_{50} 110	0.112	982	10
AE F160459	*L. gibba*	E_rC_{50} 2 600	0.076	34 211	10
AE F099095	*L. gibba*	E_rC_{50} > 100 000	0.061	1 639 344	10
AE F092944	*L. gibba*	E_rC_{50} > 100 000	0.017	5 882 353	10
AE F160460	*L. gibba*	E_rC_{50} > 100 000	0.063	1 587 302	10
AE F140584	*L. gibba*	E_rC_{50} > 10	0.020	500	10
AE F147447	*L. gibba*	E_rC_{50} > 100 000	0.030	3 333 333	10

Bold values: trigger is not met and further refinement is required

The TER_{LT} values for the parent active substance mesosulfuron-methyl do not meet the trigger of 10 based on FOCUS Step 2 PEC values. The trigger is met for all metabolites.

Therefore, in the next step, TER values are calculated based on more realistic **FOCUS Step 3** PEC values, for the parent active substance only.

Table 10.2.1.11- 6: TER_{LT} calculations (active substance mesosulfuron-methyl) for aquatic plant based on FOCUS Step 3

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [µg/L]	Focus scenario	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron -methyl	*L. gibba*	E_rC_{50} 1.29	D1 (ditch)	0.161	**8.01**	10
			D1 (stream)	0.118	10.93	
			D2 (ditch)	1.601	**0.81**	
			D2 (stream)	1.010	**1.28**	
			D3 (ditch)	0.096	13.44	
			D4 (pond)	0.024	53.75	
			D4 (stream)	0.079	16.33	
			D5 (pond)	0.011	117.27	
			D5 (stream)	0.078	16.54	
			D6 (ditch)	0.102	12.65	
			R1 (pond)	0.006	215.00	
			R1 (stream)	0.110	11.73	
			R3 (stream)	0.325	**3.97**	
			R4 (stream)	0.246	**5.24**	
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron -methyl	*L. gibba*	E_rC_{50} 1.29	D1 (ditch)	0.063	20.48	10
			D1 (stream)	0.047	27.45	
			D2 (ditch)	0.576	**2.24**	
			D2 (stream)	0.366	**3.52**	
			D3 (ditch)	0.038	33.95	
			D4 (pond)	0.008	161.25	
			D4 (stream)	0.031	41.61	
			D5 (pond)	0.004	322.50	
			D5 (stream)	0.031	41.61	
			D6 (ditch)	0.041	31.46	
			R1 (pond)	0.002	645.00	
			R1 (stream)	0.043	30.00	
			R3 (stream)	0.130	**9.92**	
			R4 (stream)	0.100	12.90	

Bold values: trigger is not met and further refinement is required

The following scenarios do not pass the risk assessment for mesosulfuron-methyl at FOCUS Step 3 and require a refined risk assessment:

- for intended use on winter wheat, 1× 1.5 L prod./ha ≡ 1 × 15 g a.s./ha
  - D1, ditch
  - D2, ditch & stream
  - R3, stream

- R4, stream

- for intended use on winter rye, 1× 0.6 L prod./ha ≡ 1 × 6 g a.s./ha
  - D2, ditch & stream
  - R3, stream

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [µg/L]		Focus scenario	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha							
Mesosulfuron-methyl	*L. gibba*	E_rC_{50}	1.29	D1 (ditch)	0.187	**6.90**	10
				D1 (stream)	0.132	**9.77**	
				D2 (ditch)	1.328	**0.97**	
				D2 (stream)	0.837	**1.54**	
				D3 (ditch)	0.096	13.44	
				D4 (pond)	0.035	36.86	
				D4 (stream)	0.080	16.13	
				D5 (pond)	0.016	80.63	
				D5 (stream)	0.081	15.93	
				D6 (ditch)	0.102	12.65	
				R1 (pond)	0.007	184.29	
				R1 (stream)	0.111	11.62	
				R3 (stream)	0.327	**3.94**	
				R4 (stream)	0.266	**4.85**	
Winter rye, 1 × 6 g a.s./ha							
Mesosulfuron-methyl	*L. gibba*	E_rC_{50}	1.29	D1 (ditch)	0.075	17.20	10
				D1 (stream)	0.053	24.34	
				D2 (ditch)	0.510	**2.53**	
				D2 (stream)	0.322	**4.01**	
				D3 (ditch)	0.038	33.95	
				D4 (pond)	0.013	99.23	
				D4 (stream)	0.032	40.31	
				D5 (pond)	0.006	215.00	
				D5 (stream)	0.032	40.31	
				D6 (ditch)	0.041	31.46	
				R1 (pond)	0.003	430.00	
				R1 (stream)	0.045	28.67	
				R3 (stream)	0.130	**9.92**	
				R4 (stream)	0.108	11.94	

Bold values: trigger is not met and further refinement is required

The following scenarios do not pass the risk assessment for mesosulfuron-methyl at FOCUS Step 3 and require a refined risk assessment:

- for intended use on winter wheat, 1× 1.5 L prod./ha ≡ 1 × 15 g a.s./ha
  - D1, ditch & stream
  - D2, ditch & stream
  - R3, stream
  - R4, stream

- for intended use on winter rye, 1× 0.6 L prod./ha ≡ 1 × 6 g a.s./ha
  - D2, ditch & stream
  - R3, stream

Refined aquatic risk assessment for active substance mesosulfuron-methyl: probabilistic assessment – species sensitivity distribution and HC_5 approach

In addition to the tier 1 laboratory 7-day endpoint for Lemna gibba (ErC50 of 1.29 µg a.s./L), further macrophyte endpoints have been generated for mesosulfuron-methyl:

- An outdoor growth inhibition study with nine macrophytes ([redacted] 2009; M-329474-01-1; KCA 8.2.7 /08) tested sensitivity to mesosulfuron-methyl over a period of 8 weeks in pond systems representing a typical static water body.
- Since for biological reason *Lemna* could not be grown in the outdoor-ponds of the before study, an analogous 8-week laboratory test under sterile conditions was conducted for this species ([redacted] 2013; M-445139-01-1; KCA 8.2.7 /09). Herein, the exposure situation in the pond systems was mimicked in the laboratory, to generate an 8-week endpoint for *Lemna* equivalent to the endpoints from the outdoor study.

The results of these two studies allow for species sensitivity distribution (SSD) analysis. E_rC_{50} values for the nine species tested in the outdoor ponds ranged from 2.1 µg a.s./L (*Pontederia cordata*) to > 25 µg a.s./L (*Nymphaea odorata, Cabomba caroliniana, Glyceria maxima)*. The lowest endpoint for week 8 in the *Lemna gibba* bioassay was 1.9 µg a.s./L (E_rC_{50} for frond number).
The complete data set from both studies was used for calculation of the EC_{50}-based median HC_5 value according to [redacted]. (2000)[3]. Endpoints that are not discrete numbers ("greater-than" figures for *Nymphaea odorata, Cabomba caroliniana, Glyceria maxima*) were thereby ignored.

Table 10.2.1.11- 7: Survey of aquatic plant endpoints used for the calculation of the HC_5

Species	ErC_{50} (µg/L)	
Lemna gibba (8 week)	1.9	**median HC_5 = 1.17 µg/L** n=7
Pontederia cordata	2.1	
Elodea canadensis	3.8	
Ceratophyllum demersum	5.3	
Potamogeton pectinatus	7.1	
Mentha aquatica	12	

[3] [redacted] (2000): Uncertainty of the hazardous concentration and fraction affected for normal species sensitivity distributions. Ecotoxicology and Environmental Safety, 46: 1-18.

Myriophyllum heterophyllum	22	
Nymphaea odorata	(>25)	(‘greater than’ figures were omitted from the calculation; the HC5 will increase if the ‘greater than’ figures are included)
Cabomba caroliniana	(>25)	
Glyceria maxima	(>25)	

Remark: as a conservative approach the lowest EC50-figure per species from the outdoor pond study was considered

Refined TER_{LT} calculations for aquatic plant based on this probabilistic endpoint are provided in Table 10.2.1.11-8. According to the new aquatic guidance document (EFSA, 2013, p. 100), an assessment factor of 3 should be applied in risk assessments based on median HC_5.

Table 10.2.1.11- 8: Refined TER_{LT} calculations (active substance mesosulfuron-methyl) for aquatic plant based on FOCUS Step 3 and median HC_5

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [µg/L]	Focus scenario	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*Aquatic macrophytes*	HC_5 1.17	D1 (ditch)	0.161	7.27	3
			D1 (stream)	0.118	9.92	
			D2 (ditch)	1.601	**0.73**	
			D2 (stream)	1.010	**1.16**	
			D3 (ditch)	0.096	12.19	
			D4 (pond)	0.024	48.75	
			D4 (stream)	0.079	14.81	
			D5 (pond)	0.011	106.36	
			D5 (stream)	0.078	15.00	
			D6 (ditch)	0.102	11.47	
			R1 (pond)	0.006	195.00	
			R1 (stream)	0.110	10.64	
			R3 (stream)	0.325	3.60	
			R4 (stream)	0.246	4.76	
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*Aquatic macrophytes*	HC_5 1.17	D1 (ditch)	0.063	18.57	3
			D1 (stream)	0.047	24.89	
			D2 (ditch)	0.576	**2.03**	
			D2 (stream)	0.366	3.20	
			D3 (ditch)	0.038	30.79	
			D4 (pond)	0.008	146.25	
			D4 (stream)	0.031	37.74	
			D5 (pond)	0.004	292.50	
			D5 (stream)	0.031	37.74	
			D6 (ditch)	0.041	28.54	
			R1 (pond)	0.002	585.00	
			R1 (stream)	0.043	27.21	
			R3 (stream)	0.130	9.00	
			R4 (stream)	0.100	11.70	

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	**Species**	**Endpoint [µg/L]**	**Focus scenario**	**PEC$_{sw,max}$ [µg/L]**	**TER$_{LT}$**	**Trigger**
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*Aquatic macrophytes*	HC_5 1.17	D1 (ditch)	0.187	6.26	3
			D1 (stream)	0.132	8.86	
			D2 (ditch)	1.328	**0.88**	
			D2 (stream)	0.837	**1.40**	
			D3 (ditch)	0.096	12.19	
			D4 (pond)	0.035	33.43	
			D4 (stream)	0.080	14.63	
			D5 (pond)	0.016	73.13	
			D5 (stream)	0.081	14.44	
			D6 (ditch)	0.102	11.47	
			R1 (pond)	0.007	167.14	
			R1 (stream)	0.111	10.54	
			R3 (stream)	0.327	3.58	
			R4 (stream)	0.266	4.40	
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*Aquatic macrophytes*	HC_5 1.17	D1 (ditch)	0.075	15.60	3
			D1 (stream)	0.053	22.08	
			D2 (ditch)	0.510	**2.29**	
			D2 (stream)	0.322	3.63	
			D3 (ditch)	0.038	30.79	
			D4 (pond)	0.013	90.00	
			D4 (stream)	0.032	36.56	
			D5 (pond)	0.006	195.00	
			D5 (stream)	0.032	36.56	
			D6 (ditch)	0.041	28.54	
			R1 (pond)	0.003	390.00	
			R1 (stream)	0.045	26.00	
			R3 (stream)	0.130	9.00	
			R4 (stream)	0.108	10.83	

The refined risk assessment of mesosulfuron-methyl passes all Focus Step 3 scenarios, except D2. Since the PEC values simulated for scenario D2 are driven by the entry route drainage (cf. Document MCP, Section 9.7), mitigation options as implemented in FOCUS Step 4 (e.g. drift buffer zones, vegetated filter strips) would not reduce the aquatic exposure to mesosulfuron-methyl for this particular scenario situation. Therefore, no further risk assessment based on FOCUS Step 4 calculations is presented. In the MSs concerned with the D2 scenario, a local restriction of product use on drained fields during drainage season will be proposed in the national dossiers submitted in the post Approval re-registration process.

<u>Supplemental information:</u> Comparison of predicted exposure profiles versus exposure regime tested in the higher tier studies

For the following GAP and FOCUSsw scenario situations, a refined endpoint (HC5) from higher tier studies on aquatic macrophytes was used to resolve the risk assessment:

- for intended use on winter wheat, 1× 1.5 L prod./ha ≡ 1 × 15 g a.s./ha
  - D1, ditch
  - R3, stream
  - R4, stream

- for intended use on winter rye, 1× 0.6 L prod./ha ≡ 1 × 6 g a.s./ha
  - D2, stream
  - R3, stream

Risk assessments for all other FOCUSsw scenarios were either passed already at a lower Tier (Lemna laboratory endpoint), or were left unresolved.

According to the Aquatic Guidance Document[4], "for a straightforward risk and effect assessment, the exposure regime of the PPP in the ecotoxicological test should be realistic to worst case relative to the predicted exposure regime in the edge-of-field surface water under consideration". An evaluation of this criterium for the higher approach used is made below.

<u>Exposure regime underlying the higher tier studies used for HC5 derivation:</u>
For mesosulfuron-methyl, an outdoor growth inhibition study with nine macrophytes over 8 weeks has been performed ([redacted] 2009; M-329474-01-1, KCA 8.2.7/08). The climatic conditions during the outdoor test at the site of Smithers Viscient (formerly Smithers Springborn) in Massachusetts resemble the conditions in middle Europe. Analytical measurements were made during the study and indicate a dissipation of mesosulfuron-methyl similar to that in water/sediment studies investigating the environmental fate and behavior of the compound. In order to also address the effects on *Lemna gibba*[5] for an analogous exposure regime, the dissipation of mesosulfuron-methyl observed during the outdoor growth inhibition study was mimicked on a weekly base under sterile conditions in the laboratory ([redacted] 2013; M-445139-01-1, KCA 8.2.7 /09).
For this test, the exposure regime was derived as follows: The mean percentage levels of mesosulfuron-methyl analytically determined for the three highest treatment levels of the pond study were 100 %, 70.70 %, 56.48 % and 35.31 % for day 0, day 14, day 28, and day 54, respectively. Based on these measured values, figures for days 7, 21, 35, 42, and 49 were interpolated, and a stepwise weekly reduction in test item concentration was used to mimic the outdoor dissipation of mesosulfuron-methyl in the laboratory study on *Lemna gibba* (cf. Table 10.2.1.11-9). After each 7-

[4] "Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters" (EFSA Panel on Plant Protection Products and their Residues, 2013, EFSA Journal 2013)

[5] For biological reason, this species could not be cultivated simultaneously in the pond systems of the above study.

day-period an aliquot of fronds were transferred to freshly prepared test medium of the subsequent concentration level. *Lemna* clearly represented the most sensitive of all macrophytes tested, cf. Table 10.2.1.11- 7.

Table 10.2.1.11- 9: Study exposure timecourse of mesosulfuron-methyl based on the analytical findings of the outdoor growth inhibition study, and weekly interpolated values used for laboratory test on *Lemna gibba*

day	%	comment
Day 0	100.00	Mean of measured recoveries at the three highest concentrations
Day 7	84.08	Geometric mean between day 0 and day 14 figure
Day 14	70.70	Mean of measured recoveries at the three highest concentrations
Day 21	63.19	Geometric mean between day 14 and day 28 figure
Day 28	56.48	Mean of measured recoveries at the three highest concentrations
Day 35	50.22	Geometric mean between day 28 and day 42 figure
Day 42	44.66	Geometric mean between day 28 and day 56 figure
Day 49	39.71	Geometric mean between day 42 and day 56 figure
Day 56	35.31	Mean of measured recoveries at the three highest concentrations

<u>Comparison of predicted surface water concentration profiles versus study exposure regime:</u>
To compare the predicted exposure profiles for the critical FOCUSsw scenarios with the exposure regime of the ecotoxicological tests, a graphical visualisation is provided in Figures 10.2.1.11-1 to 10.2.1.11-4 as follows:

red line: Simulated aquatic exposure profile: concentration over time resulting from Step 3 FOCUSsw calculation (cf. simulation reported in KIIIA 9.7 /01, plots reported in KIIIA 9.7 /02). The diagrams show a timeframe including 1 week before maximum to 8 weeks after maximum.

green dot: HC5 value = 1.17 µg/L (derived acc. Table 10.2.1.11-7)

violet square: RAC value = 0.39 µg/L (based on HC5 value divided by assessment factor of 3).

dashed green line: Relative illustration of the exposure regime in the studies used for derivation of the HC5 endpoint. For visualisation, a line is plotted starting at HC5 level at the time of $PEC_{sw,max}$, with stepwise decrease according to the percentual figures in Table 10.2.1.11-9, based on the analytical results of the pond study.

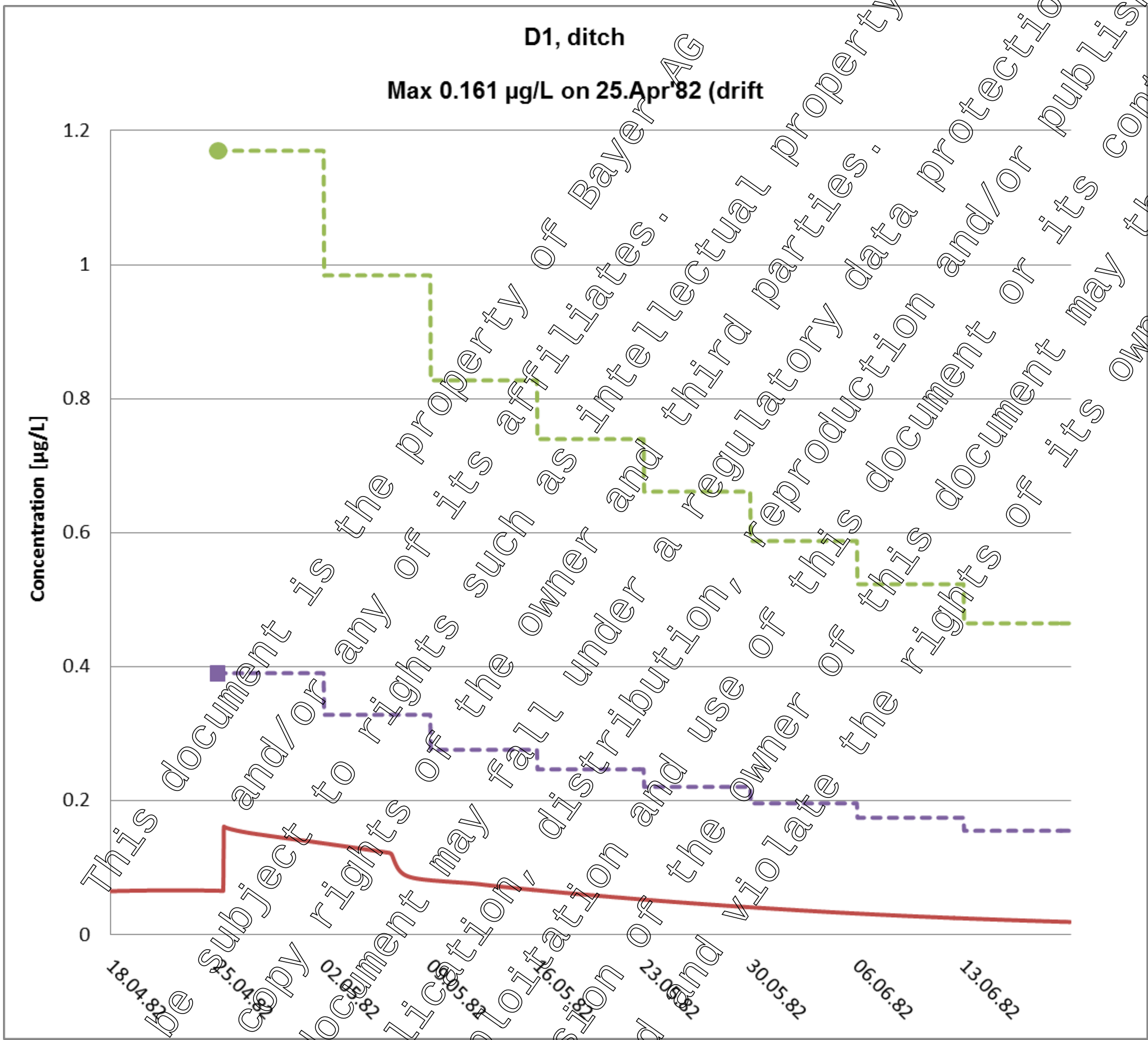
dashed violet line: Analogous to green dashed line, but relative to the RAC value.

Note that only the specific data point of the HC5 and/or RAC value is the relevant endpoint for use in straightforward risk assessment via comparison with $PEC_{sw,\ max}$.. Technically, these HC5 and/or RAC endpoints represent the integral exposure regime over an 8 week period that may be described as the area under the dotted line graphs. Therefore, the most relevant parameter for comparison of study exposure regime vs. predicted exposure profiles is the areas under the curves.

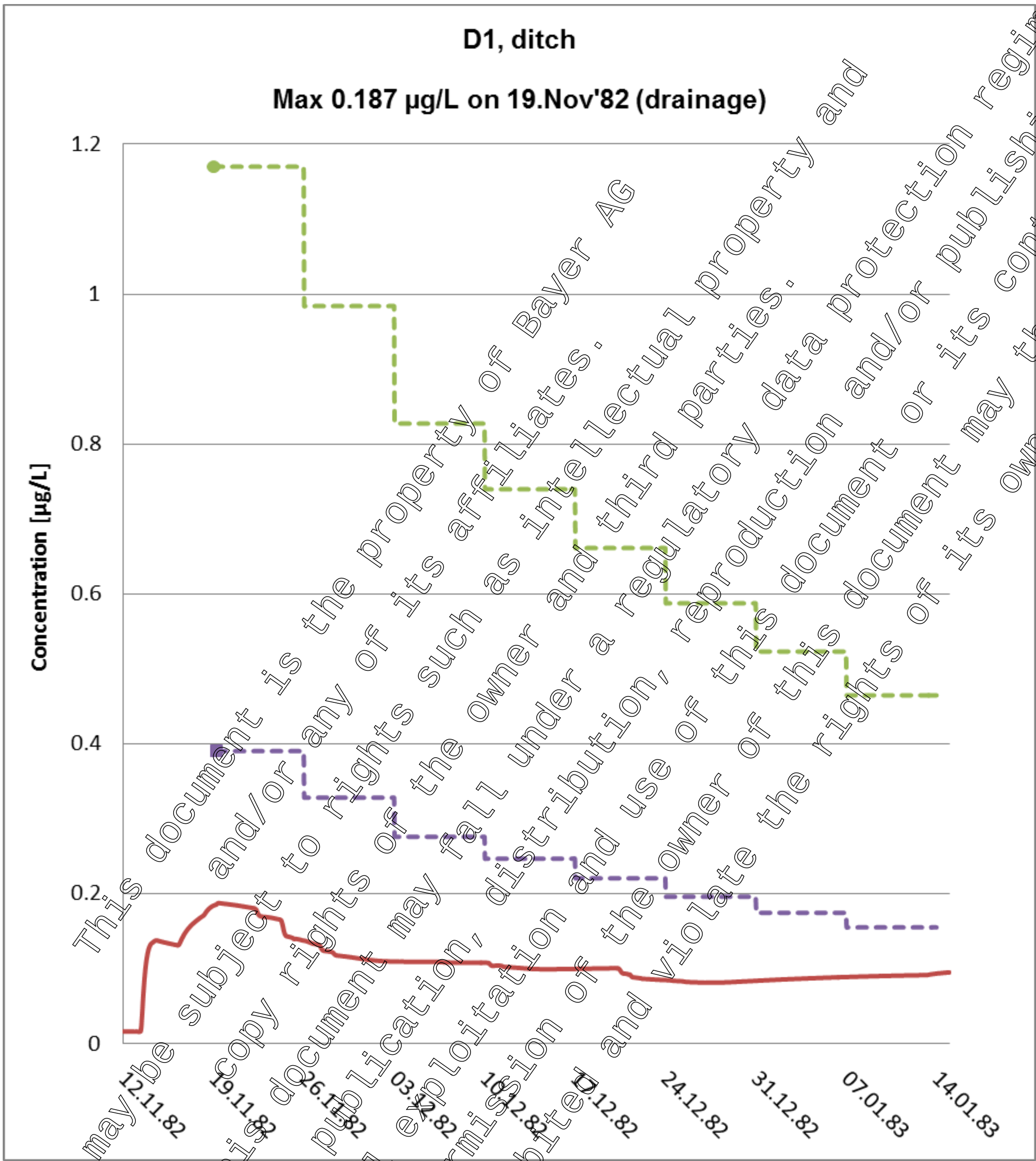
<u>**Intended use on winter wheat, 1× 1.5 L prod./ha ≡ 1 × 15 g a.s./ha:**</u>

Figure 10.2.1.11-1a: Illustration of predicted exposure profile for FOCUSsw scenario D1 (ditch), and exposure regimes represented by the higher tier endpoints HC5 / RAC [use on winter wheat,1 x 15 g/ha mesosulfuron-methyl]

a) based on PEC values of originally submitted simulation



b) based on PEC values of alternative simulation using RMS requested parameters



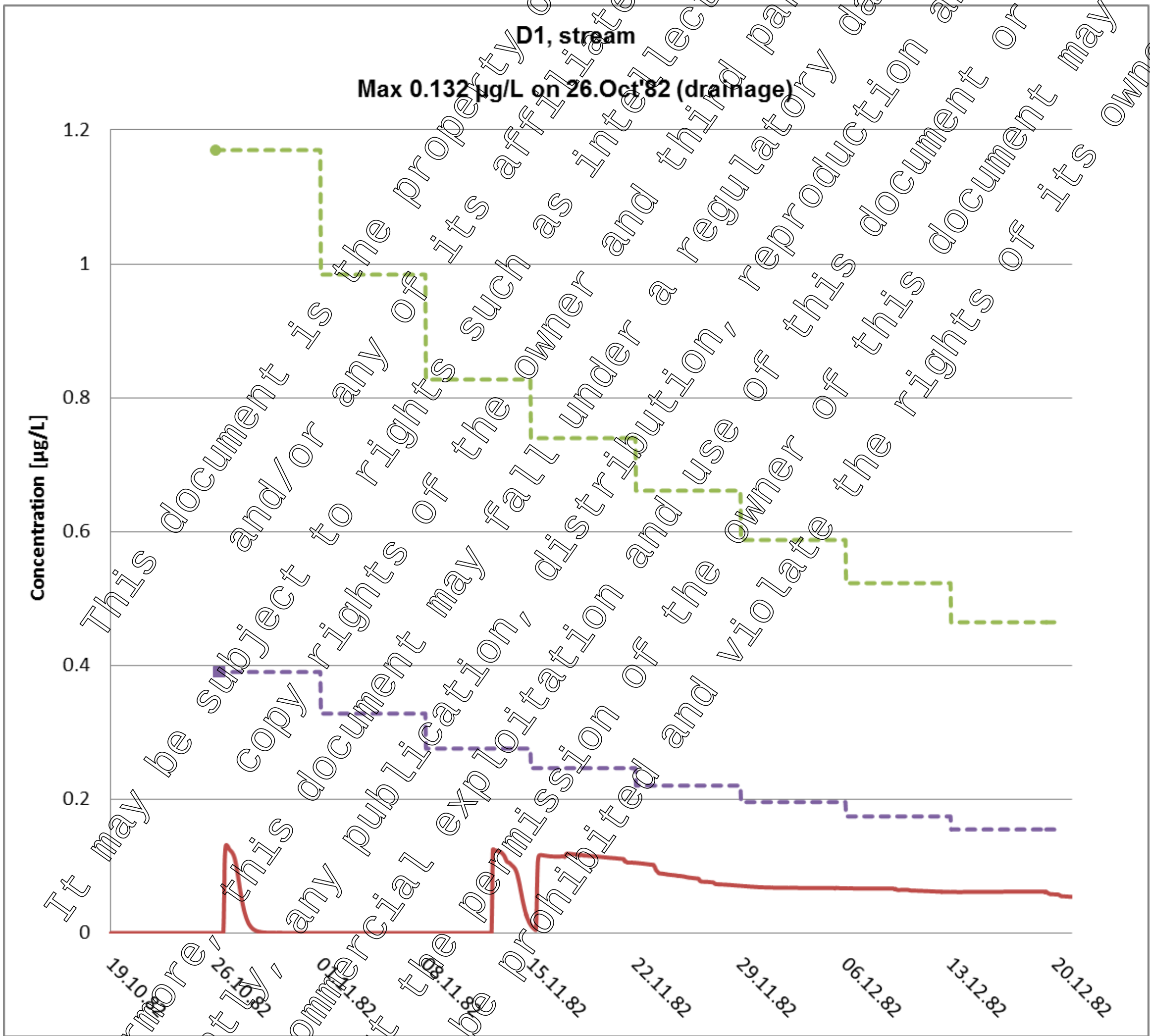
Interpretation: $PEC_{sw,\ max}$ is clearly below RAC (HC5 divided by AF=3). The integral of predicted exposure over time does clearly not exceed the exposure × time regime represented by the higher tier endpoints. Therefore, the ecotoxicological test exposure regime was worst case relative to the predicted exposure regime in the edge-of-field surface water under consideration for scenario D1 (ditch).

Figure 10.2.1.11-1b: Illustration of predicted exposure profile for FOCUSsw scenario D1 (stream), and exposure regimes represented by the higher tier endpoints HC5 / RAC [use on winter wheat,1 x 15 g/ha mesosulfuron-methyl]

a) based on PEC values of originally submitted simulation

No refinement based on pond study endpoint was needed to pass risk assessment for scenario D1 (stream) when using PEC values of the originally submitted simulation; a comparison of FOCUS exposure profile versus pond study exposure regime is therefore not required.

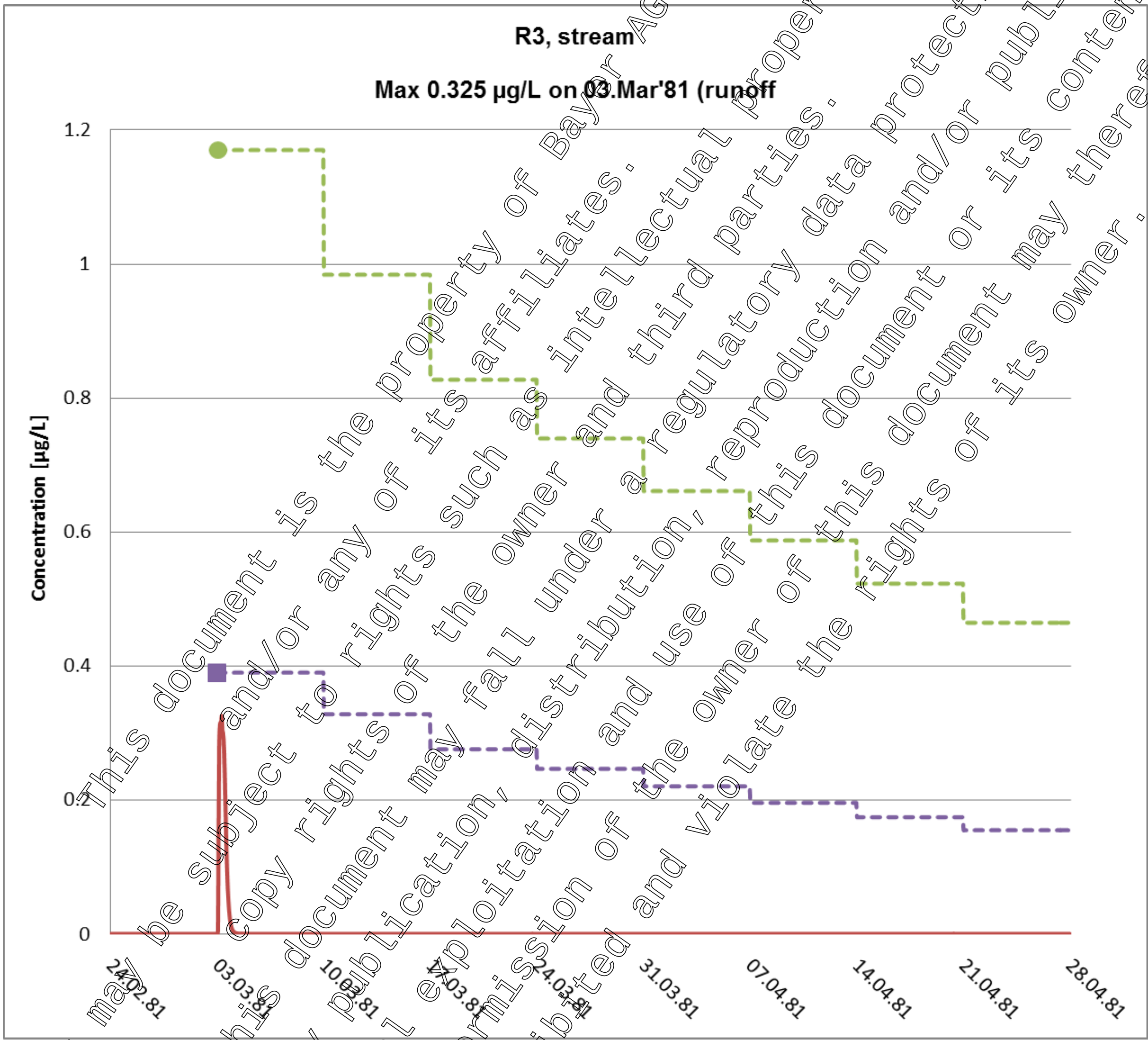
b) based on PEC values of alternative simulation using RMS requested parameters



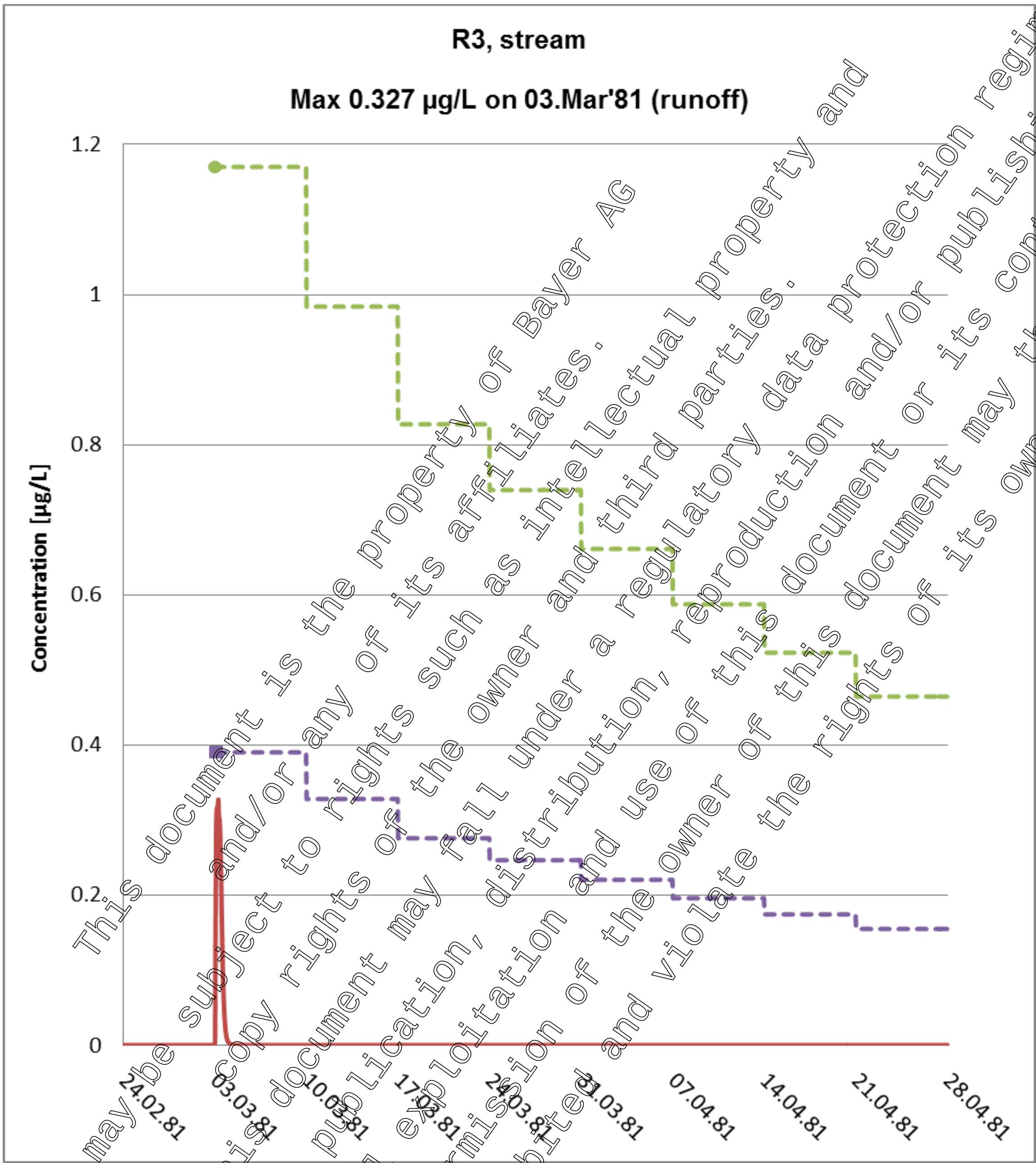
Interpretation: $PEC_{sw, max}$ is clearly below RAC (HC5 divided by AF=3). The integral of predicted exposure over time does clearly not exceed the exposure × time regime represented by the higher tier endpoints. Therefore, the ecotoxicological test exposure regime was worst case relative to the predicted exposure regime in the edge-of-field surface water under consideration for scenario D1 (stream).

Figure 10.2.1.11-2: Illustration of predicted exposure profile for FOCUSsw scenario R3 (stream), and concentration regimes represented by the higher tier endpoints HC5 / RAC [use on winter wheat,1 x 15 g/ha mesosulfuron-methyl]

a) based on PEC values of originally submitted simulation



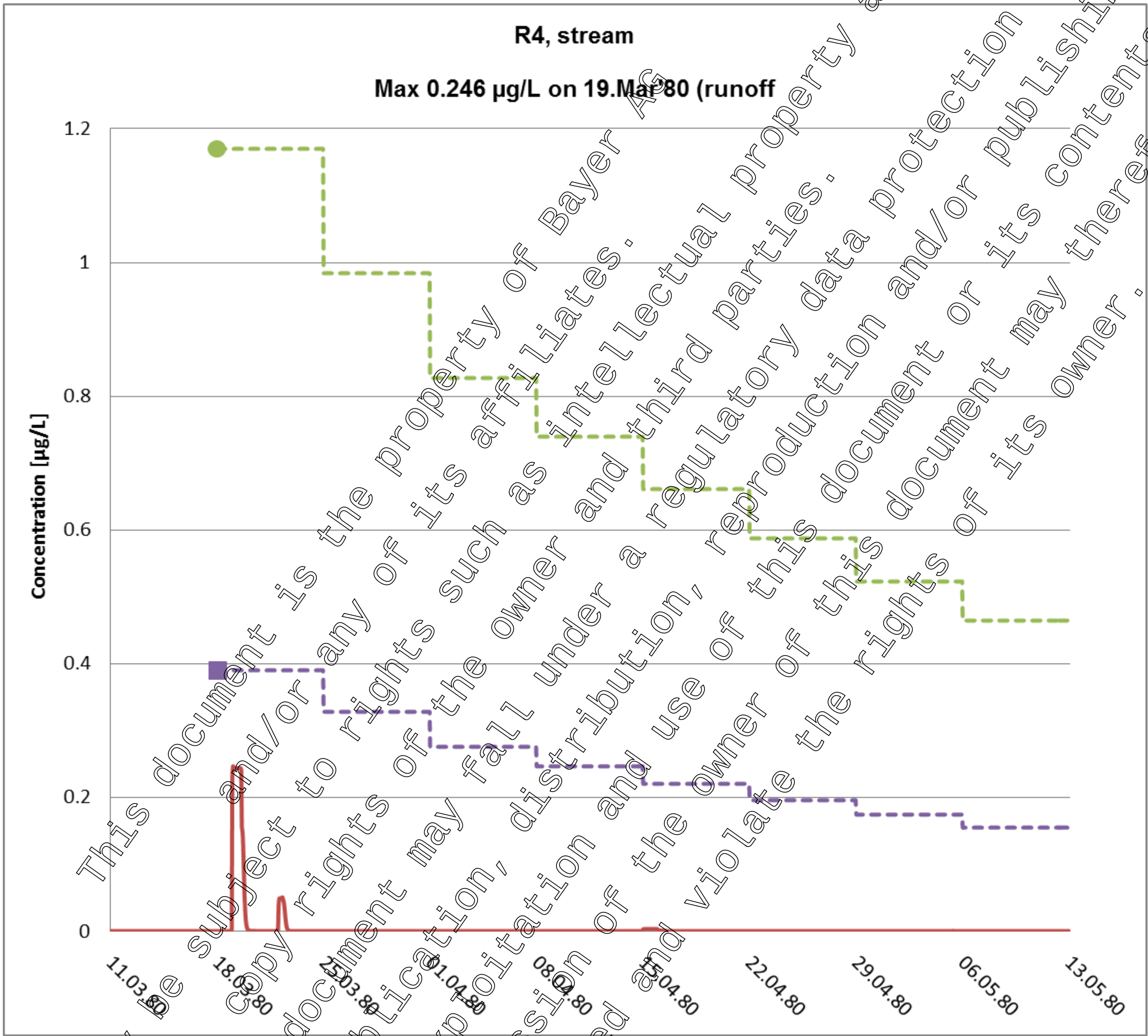
b) based on PEC values of alternative simulation using RMS requested parameters



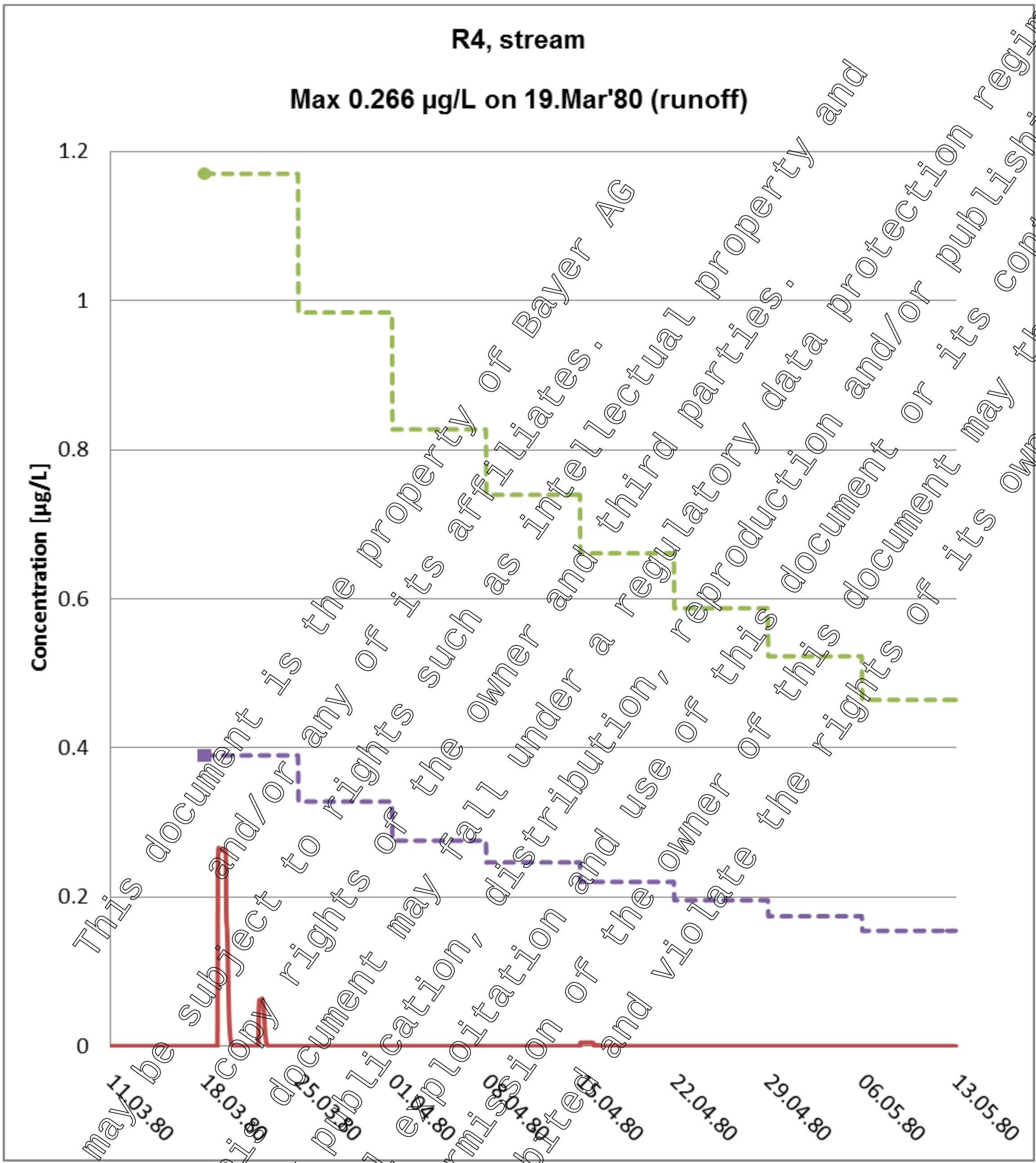
Interpretation: $PEC_{sw,\ max}$ is clearly below RAC (HC5 divided by AF=3). The integral of predicted exposure over time does clearly not exceed the exposure × time regime represented by the higher tier endpoints. It should be noted that in fact the predicted exposure in scenario R3 (stream) is confined to a very short pulse, below the RAC and lasting approximately a single day only. Therefore, the ecotoxicological test exposure regime was by far worst case relative to the predicted exposure regime in the edge-of-field surface water under consideration for scenario R3 (stream).

Figure 10.2.1.11-3: Illustration of predicted exposure profile for FOCUSsw scenario R4 (stream), and concentration regimes represented by the higher tier endpoints HC5 / RAC [use on winter wheat,1 x 15 g/ha mesosulfuron-methyl]

a) based on PEC values of originally submitted simulation



b) based on PEC values of alternative simulation using RMS requested parameters

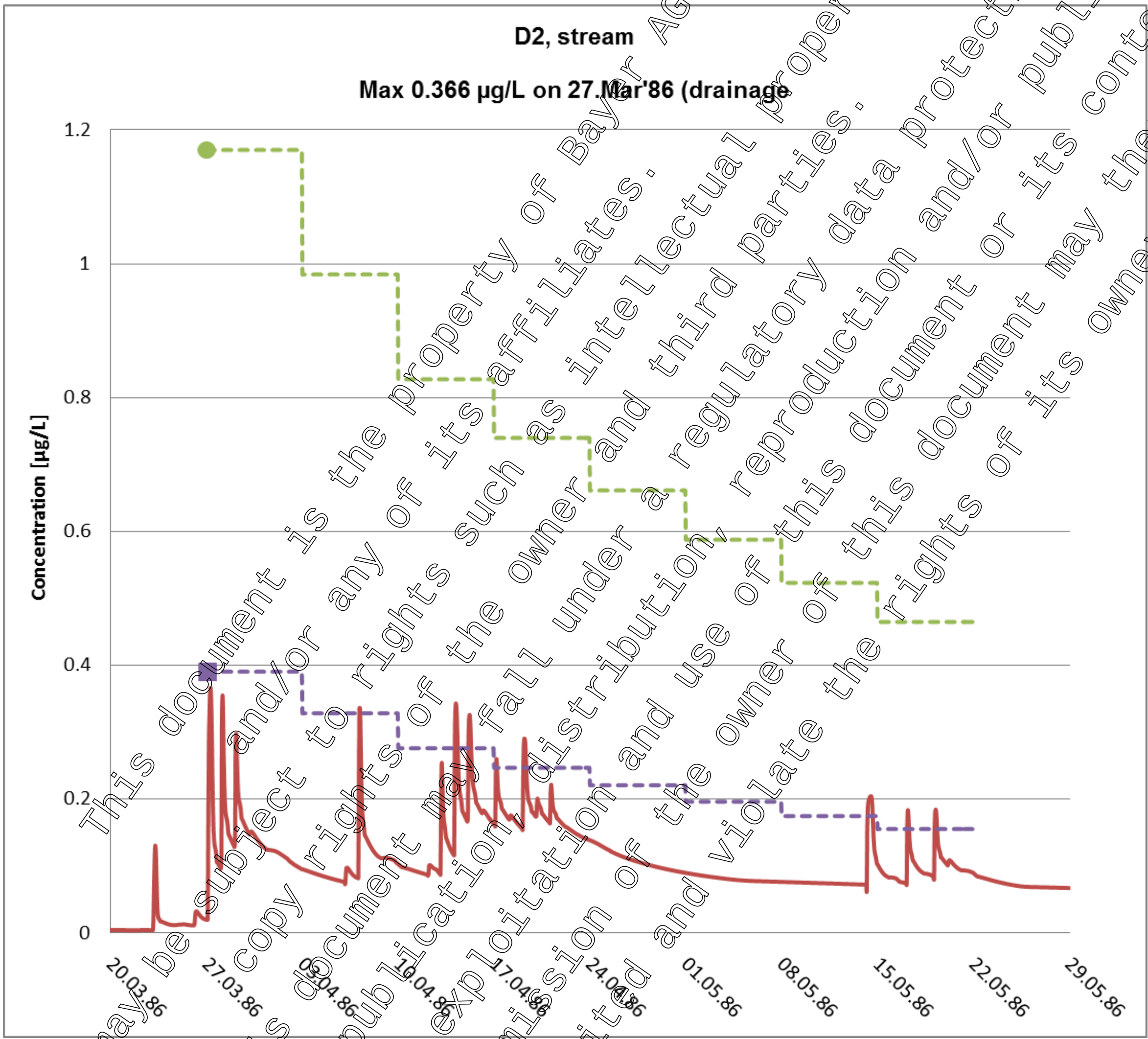


Interpretation: $PEC_{sw,\,max}$ is clearly below RAC (HC5 divided by AF=3). The integral of predicted exposure over time does clearly not exceed the exposure × time regime represented by the higher tier endpoints. In fact, it should be noted that the predicted exposure in scenario R4 (stream) is confined to a very short pulse followed by a lower second pulse, both below the RAC and each lasting approximately a single day only. Therefore, the ecotoxicological test exposure regime was by far worst case relative to the predicted exposure regime in the edge-of-field surface water under consideration for scenario R4 (stream).

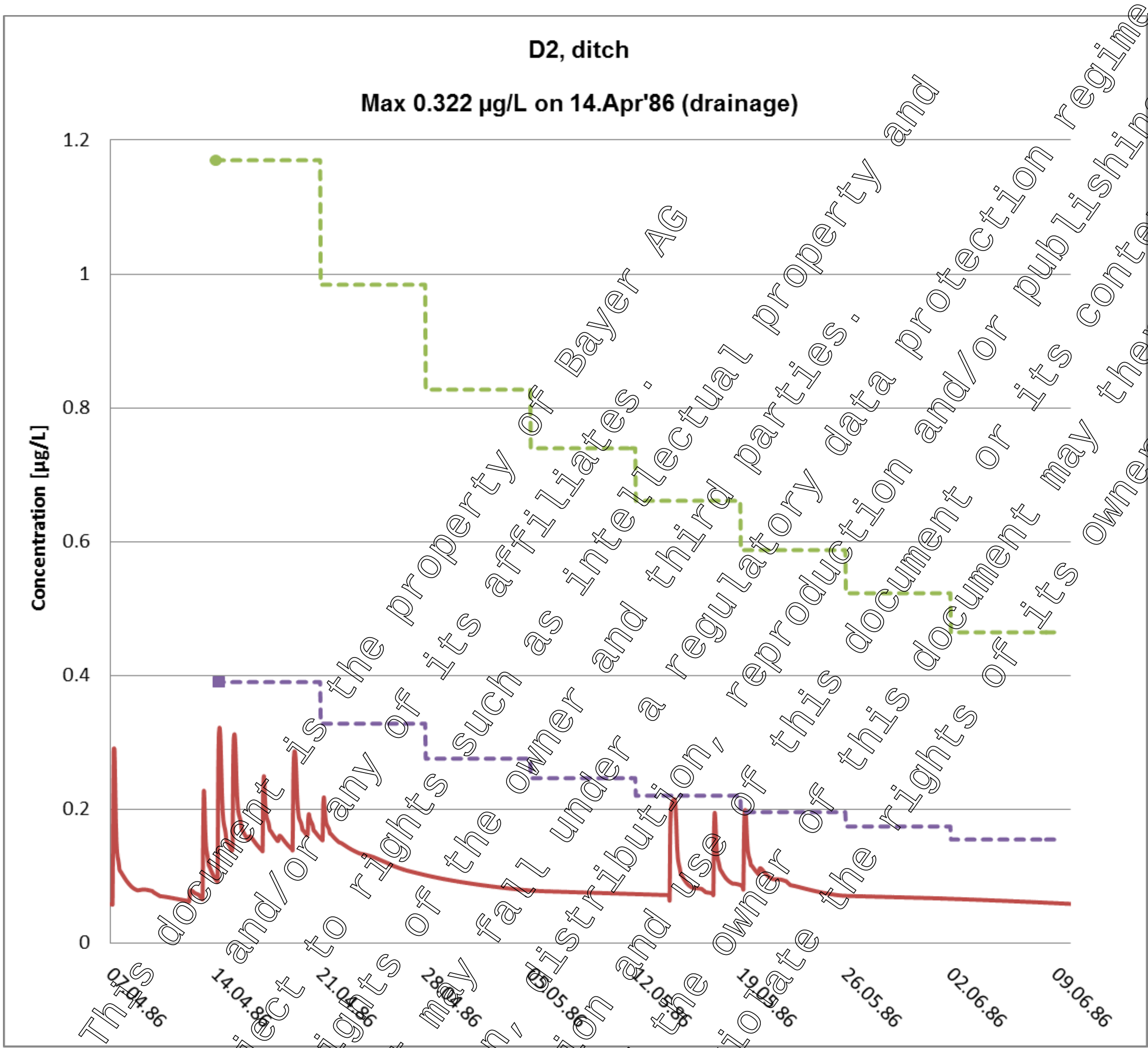
Intended use on winter rye, 1× 0.6 L prod./ha ≡ 1 × 6 g a.s./ha:

Figure 10.2.1.11-4: Illustration of predicted exposure profile for FOCUSsw scenario D2 (stream), and concentration regimes represented by the higher tier endpoints HC5 / RAC [use on winter rye, 1 x 6 g/ha mesosulfuron-methyl]

a) based on PEC values of originally submitted simulation



b) based on PEC values of alternative simulation using RMS requested parameters



Interpretation: $PEC_{sw,\,max}$ is below RAC (HC5 divided by AF=3). The integral of predicted exposure over time does not exceed the exposure × time regime represented by the higher tier endpoints. With regard to daily exposure levels, some slight and short-term breaches of the violet line are observed but for the most time the predicted exposure profile remains below the exposure regime underlying the RAC derivation, and is significantly below the exposure regime underlying the HC5 definition over the entire time period considered.

Despite these exceedances of the exposure regime underlying the RAC derivation it can be safely concluded that a risk assessment based on $PEC_{sw,\,max}$ versus RAC is protective for aquatic macrophytes in the FOCUS scenario situation of D2 (stream), due to the fact that

- the breaches are peak exposure events of only very short duration (≤ 1 day),
- their peak height only slightly breaches the equivalent concentration line projected from RAC and never reaches the equivalent concentration line projected from HC5, and
- the area under the predicted exposure curve is significantly below the area under the equivalent concentration line projected from HC5.

<u>R3 (stream):</u> Concerning exposure timecourse discussion for scenario R3 (stream), reference is made to the above assessment on the same scenario in context of the intended use on winter cereals, 1 × 15 g a.s./ha, which covers the situation as well for the intended use on winter rye, 1 × 6 g a.s./ha (see Figure 10.2.1.11-2).

Conclusion:

Overall, it can be concluded that the Guideline criteria for an acceptable risk assessment based on the higher tier endpoint is fulfilled, since the exposure regime in the ecotoxicological tests was realistic to worst case relative to the predicted exposure regime in the edge-of-field surface water under consideration for all FOCUS scenarios that were resolved via this higher tier assessment route.

IIIA 10.2.2 Acute toxicity of the formulation

IIIA 10.2.2.1 Fish

Report:	[redacted]6;[redacted];2003;M-225670-01
Title:	Acute toxicity of AE F130081 + Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 10 + 2 + 30 to fish (Oncorhynchus mykiss) (product code: AE F115008 06 OD04 A104)
Report No:	C038744
Document No(s):	M-225670-01-1
Guidelines:	**EU (=EEC): 92/69/EEC, C.1 (1992); OECD: 203 (rev.1992); USEPA (=EPA): 72-1/SEP-EPA-540/9-85-006 (1982/1985), OPPTS 850.1075 (public draft);Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the effects of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to *Oncorhynchus mykiss*. The study was designed to meet both, OECD and EPA criteria.

Material and Methods

The study was conducted under static conditions. Nominal concentrations were 0.94, 1.88, 3.75, 7.50, 15.0, and 30.0 mg product/L. In addition, an untreated control was tested. 10 fish were used per treatment level in a volume of 40 L test water. Mean weight was 0.7 g, mean length was 4.3 cm. Static biological loading was 0.18. The mean water temperature was 10.1 to 11.2 °C. The daily illumination period lasted 16 hours. pH varied between 6.9 and 7.1. Oxygen concentration varied between 97 and 102 %. At test start total hardness was 40 to 60 mg/L as $CaCO_3$.

Findings

Analytical measurements for mesosulfuron-methyl (sodium salt) resulted in concentrations between 95% and 101% of nominal treatment levels. Biological results are reported as nominal.

Percent mortality is summarised in the following table.

Table 10.2.2.1- 1: Acute toxicity to *Oncorhynchus mykiss* (based on nominal concentrations)

Nominal (mg product/L)	24 hrs	48 hrs	72 hrs	96 hrs
Untreated control	0	0	0	0
0.94	0	0	0	0
1.88	0	0	0	0
3.75	0	0	10	10
7.5	0	10	10	10
15	100	100	100	100
30	100	100	100	100

The following intoxication symptoms were observed in the surviving fish: swimming at the surface, lethargic behaviour, loss of equilibrium and enhanced respiration.

Conclusions:

The acute toxicity of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to *Oncorhynchus mykiss* under static conditions based on nominal figures are as follows:

24 h LC_{50} = 10.2 mg product/L (95% confidence limits 8.87 - 11.8 mg product/L)

48 h LC_{50} = 8.832 mg product/L (95% confidence limits 6.90 - 11.3 mg product/L)

96 h LC_{50} = 8.832 mg product/L (95% confidence limits 6.90 - 11.3 mg product/L)

96 h NOEC = 1.88 mg product/L

IIIA 10.2.2.2 Aquatic invertebrates (Daphnia)

Report:	;[redacted]b;[redacted];2003;M-224326-01
Title:	Acute toxicity of AE F130081 & iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 10 + 2 +30 to the waterflea Daphnia magna Code: AE F115008 06 OD04 A104
Report No:	C038151
Document No(s):	M-224326-01-1
Guidelines:	**OECD No. 202, 4 April 1984 and corresponding revised draft document, dated October 2000; EEC Directive 92/69/EWG, part C.2; U.S. EPA Pesticide Assessment Guidelines, Subdivision E, § 72 2; OPPTS Guideline 850.1010 public draft 1996 (modified);Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the effects of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to *Daphnia magna*. The study was designed to meet both, OECD and EPA criteria.

Material and Methods

The study was conducted under static conditions. Nominal concentrations were 0.13, 0.25, 0.50, 1.0, 2.0, 4.0, 8.0 and 16.0 mg product/L. In addition an untreated control was tested. 6 replicates with 5 individuals each were used per treatment level. Maximum age of test animals was 24 hours. The mean water temperature was 21 ± 1 °C. pH varied between 7.8 and 8.0. Oxygen concentration varied between 8.0 and 9.1 mg/L.

Findings

Analytical measurements for AE F130081 (mesosulfuron-methyl, sodium salt) resulted in concentrations between 91% and 103% of nominal treatment levels. Biological results are reported as nominal.

Mortality and intoxication symptoms are summarised in the following table.

Table 10.2.2.2- 1: Toxicity to *Daphnia magna* (based on nominal concentrations)

Nominal (mg product/L)	24 hrs	48 hrs
Untreated control	0	0
0.13	0	0
0.25	0	0
0.5	0	0
1	0	0
2	0	3
4	0	3
8	27	67
16	57	87

The following intoxication symptoms were observed in the surviving organisms: Dwelling near the bottom, lethargic behaviour and moving erratic or gyrating.

Conclusion

The acute toxicity endpoints of formulation IMS + MSM + MPR OD 42 (AE F115008 06 OD04 A104) to *Daphnia magna* under static conditions based on nominal figures are as follows:

24-h EC_{50} = 13.6 mg product/L (95% confidence limits 10.8 - 17.0 mg product/L)
48-h EC_{50} = 7.6 mg product/L (95% confidence limits 6.4 - 9.0 mg product/L)
48-h NOEC = 1.0 mg product/L

IIIA 10.2.2.3 Algae

Report:	[redacted];[redacted];2003;M-224329-01
Title:	Influence of mesosulfuron-methyl & iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 10 + 2 +30 (Atlantis liquid) on the growth of green alga, Pseudokirchneriella subcapitata Code: AE F115008 06 OD04 A104
Report No:	C038152
Document No(s):	M-224329-01-1
Guidelines:	**OECD: 201;Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the effects of formulation IMS + MSM + MPR OD 42 (Atlantis®OD,AE F115008 06 OD04 A104) to the growth of *Pseudokirchneriella subcapitata*. The study was designed to meet OECD criteria.

Material and Methods

Algal cultures with an initial cell density of 10,000 algal cells/mL were incubated in a synthetic medium for 72 hours at 1.56, 3.13, 6.25, 12.5 and 25.0 mg formulation/L. In addition an untreated control was tested. 3 replicates were used per treatment level, the replicate number in the control was twice as high. The mean water temperature was 22 ± 1 °C. pH varied between 7.8 and 8.6. The mean light intensity during the test was 7744 lux.

Findings

Analytical measurements for AE F130060 resulted in concentrations between 94% and 104% of nominal treatment levels at test start and between 92% and 102% of nominal treatment levels at test termination. Biological results are reported as nominal.

Inhibitory effects and intoxication symptoms are summarised in the following table.

Table 10.2.2.3- 1: Cell number, growth rates in *Pseudokirchneriella subcapitata* cultures treated with the test item and their % deviation relative to that of the control

Nominal (mg formulation/L)	72 hours (cell number)	72 hours (average growth rate)	72 hours (growth inhibition in %)
Control	398 000	1.225	--
1.56	435 000	1.257	-2.6
3.13	282 000	1.107	9.6
6.25	93 000	0.732	40.3
12.5	12 000	0.045	96.3
25	10 000	0.000	100

-% inhibition: increase in growth relative to the control

No cell deformation was observed.

Conclusion

The effect of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) on the growth inhibition of *Pseudokirchneriella subcapitata* based on nominal figures are as follows:

72-h E_rC_{50}= 6.71 mg formulation/L
72 h $E_{logb}C_{50}$= 6.25 mg formulation/L
72-h NOEC = 3.13 mg formulation/L

IIIA 10.2.2.4 Marine or estuarine organisms

This is not an EC data requirement / not required by Directive 91/414/EEC.

IIIA 10.2.2.5 Marine sediment invertebrates

This is not an EC data requirement / not required by Directive 91/414/EEC.

IIIA 10.2.3 Microcosm or mesocosm study

No microcosm or mesocosm studies were performed with the formulated product. Based on the toxicity data and application rate of the product, the risk assessment (TER calculations) presented above indicates acceptable risk to aquatic organisms. Therefore, microcosm or mesocosm studies with the formulated product are not deemed necessary.

IIIA 10.2.4 Residue data in fish

Based on the triggers stated in the Aquatic Guidance Document, a fish BCF-study for the product was not conducted.

The octanol / water partition coefficient Log P_{ow} of mesosulfuron-methyl and its metabolites are well below the trigger value of 3.
Therefore considerable accumulation (bioconcentration) of residues of the parent compounds and/or the metabolites in fish is unlikely, and a BCF-study is not required.

IIIA 10.2.5 Chronic toxicity to fish

Based on the triggers stated in the Aquatic Guidance Document, further chronic studies with the formulated product are not considered necessary, as the relevant information can be obtained from studies with the active ingredient.

IIIA 10.2.5.1 28 day study

Please refer to point IIIA 10.2.5.

IIIA 10.2.5.2 Fish early life stage test

Please refer to point IIIA 10.2.5.

IIIA 10.2.5.3 Fish life cycle test

Please refer to point IIIA 10.2.5.

IIIA 10.2.6 Chronic toxicity to aquatic invertebrates

Based on the triggers stated in the Aquatic Guidance Document, further chronic studies with the formulated product are not considered necessary, as the relevant information can be obtained from studies with the active ingredient.

IIIA 10.2.6.1 21 day test (Daphnia magna)

Please refer to point IIIA 10.2.6.

IIIA 10.2.6.2 Aquatic insect

Please refer to point IIIA 10.2.6.

IIIA 10.2.6.3 Aquatic gastropod mollusc

Please refer to point IIIA 10.2.6.

IIIA 10.2.7 Accumulation in aquatic non-target organisms

Based on the information given under Point IIIA 10.2.4, considerable accumulation of residues of the product and/or metabolites in aquatic organisms is unlikely to occur.

IIIA 10.3 Effects on terrestrial vertebrates other than birds

Ecotoxicological endpoints used in risk assessment

Table 10.3- 1: Endpoints of the formulation IMS + MSM + MPR OD 42 used in risk assessment

Test substance	Test organism	Study type	Endpoint	Reference
IMS + MSM + MPR OD 42	**Acute toxicity to mammals**			
	Rat	acute, oral	LD_{50} ≥ 5000 mg/kg bw	[redacted] (2003) M-225480-01-1 KIIIA 7.1.1 /01

Table 10.3- 2: Endpoints of the active substance mesosulfuron-methyl used in risk assessment

Test substance	Test organism	Study type	Endpoint	Reference
Mesosulfuron-methyl	**Acute toxicity to mammals**			
	Rat	acute, oral	LD_{50} > 5000 mg as/kg bw	[redacted] (1996) M-140405-01-1 KCA 5.2.1 /01
	Long-term toxicity to mammals			
	Rat	2-generation dietary reproduction study	NOEC 16000 ppm ≡ NOEL 1277 mg as/kg bw/d	[redacted] (2000) M-198366-01-1 KCA 5.6.1 /02

All above endpoints used in risk assessment are consistent with the *proposed* EU endpoints listed in Document N2 for mesosulfuron-methyl.

Risk Assessment for mammals

The risk assessment procedure for wild mammals follows the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009); principles see described under point 10.1 for birds.

Mammalian indicator species for risk assessment on screening level

The product IMS + MSM + MPR OD 42 is intended to be used in winter wheat for a single application between BBCH 20 and 32 at an application rate of 1.5 L/ha, corresponding to 0.015 kg mesosulfuron-methyl/ha and in winter rye for a single application between BBCH 20 and 32 at an application rate of 0.6 L/ha, corresponding to 0.006 kg mesosulfuron-methyl/ha. According to the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009) the following indicator species have to be addressed in risk assessment on screening level.

Table 10.3- 3: Relevant mammalian indicator species for risk assessment on screening level

Crop	Indicator species	Shortcut value	
		For long-term RA based on RUD mean	For acute RA based on RUD 90th perc.
Cereals	Small herbivorous mammal	48.3	118.4

IIIA 10.3.1 Toxicity exposure ratios

Summary of calculated TER values for mammals

Table 10.3.1- 1: Summary of TER values for acute toxicity

Crop / Compound	Indicator species	SV_{90}	TER_A	Trigger	Refinement used ?
Winter wheat, 1 × 15 g a.s./ha					
Mesosulfuron-methyl	Small herbivorous mammal	118.4	> 2809	10	no
Winter rye, 1 × 6 g a.s./ha					
Mesosulfuron-methyl	Small herbivorous mammal	118.4	> 7042	10	no

Table 10.3.1- 2: Summary of TER values for long-term toxicity

Crop / Compound	Indicator species	SV_{mean}	TER_{LT}	Trigger	Refinement used ?
Winter wheat, 1 × 15 g a.s./ha					
Mesosulfuron-methyl	Small herbivorous mammal	48.3	3361	5	no
Winter rye, 1 × 6 g a.s./ha					
Mesosulfuron-methyl	Small herbivorous mammal	48.3	8513	5	no

Conclusion: According to the presented risk assessment, the risk to mammals from the use of the product in cereals is acceptable.

IIIA 10.3.1.1 Acute toxicity exposure ratio (TER_A)

Acute toxicity exposure ratio on screening level for mammals

The risk assessment on screening level has been performed for cereals for an application rate of 1.5 L product/ha corresponding to 0.015 kg mesosulfuron-methyl/ha and for an application rate of 0.6 L product/ha corresponding to 0.006 kg mesosulfuron-methyl/ha.

Table 10.3.1.1- 1: Acute DDD and TER calculation (active substance mesosulfuron-methyl) on screening level for mammals

Crop / Compound	Indicator species	LD_{50} [mg/kg bw]	DDD			DDD	TER_A	Trigger
			Appl. rate [kg/ha]	SV_{90}	MAF_{90}			
Winter wheat, 1 × 15 g a.s./ha								
Mesosulfuron-methyl	Small herbivorous mammal	> 5000	0.015	118.4	1	1.78	> 2809	10
Winter rye, 1 × 6 g a.s./ha								
Mesosulfuron-methyl	Small herbivorous mammal	> 5000	0.006	118.4	1	0.71	> 7042	10

All TER values are above the required trigger of 10 for acute exposure. Acute risk to mammals is therefore acceptable for the intended product uses.

Acute risk assessment for mammals drinking contaminated water

For further details, reference is made to Point 10.1.1 of this dossier. However, according to EFSA Guidance Document for Birds and Mammals (2009), unlike for birds the scenario of pools formed in leaf axils is not relevant for mammals. Therefore the risk assessment for mammals is limited to the scenario of puddles formed on the ground after application.

The acute risk from water in puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil is covered by the long-term risk assessment under Point 10.3.1.3 of this dossier.

IIIA 10.3.1.2 Short-term toxicity exposure ratio (TER_{ST})

Not required according to current regulatory requirements.

IIIA 10.3.1.3 Long-term toxicity exposure ratio (TER_{LT})

Reproductive/long-term toxicity exposure ratio on screening level for mammals

The risk assessment on screening level has been performed for cereals for an application rate of 1.5 L product/ha corresponding to 0.015 kg mesosulfuron-methyl/ha and for an application rate of 0.6 L product/ha corresponding to 0.006 kg mesosulfuron-methyl/ha.

Table 10.3.1.3- 1: Long-term DDD and TER calculation (active substance mesosulfuron-methyl) on screening level for mammals

Crop / Compound	Indicator species	NO(A)EL [mg/kg bw]	Appl. rate [kg/ha]	SV_m	MAF_m	f_{twa}	DDD	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha									
Mesosulfuron-methyl	Small herbivorous mammal	1277	0.015	48.3	1	0.53	0.38	3361	5
Winter rye, 1 × 6 g a.s./ha									
Mesosulfuron-methyl	Small herbivorous mammal	1277	0.006	48.3	1	0.53	0.15	8513	5

All TER values are above the required trigger of 5 for reproductive/long-term exposure. Long-term risk to mammals is therefore acceptable for the intended product uses

Long-term risk assessment for mammals drinking contaminated water

For further details, reference is made to Point 10.1.1 of this dossier.

Table 10.3.1.3- 2: Evaluation of potential concern for exposure via drinking water of mammals (escape clause)

Crop / Compound	Koc [L/kg]	Application rate [g as/ha]	NO(A)EL [mg as/ kg bw/d]	Ratio (Application rate) / NO(A)EL	"Escape clause" No concern if ratio	Conclusion
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	48 [1]	15	1277	0.01	≤ 50	No concern
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	48	6	1277	0.005	≤ 50	No concern

[1] median value, MCA 7.1.3.1, mesosulfuron Review Report (SANCO/10298/2003 final)

This evaluation confirms that the risk for mammals from drinking water that may contain residues from the use of IMS + MSM + MPR OD 42 is acceptable.

IIIA 10.3.2 Other studies

IIIA 10.3.2.1 Acute oral toxicity of the preparation

Table 10.3.2.1- 1: Toxicological profile of IMS + MSM + MPR OD 42

Test system	Test species	LD_{50} [mg product/kg bw]	Reference (see IIIA, Point 7)
Acute oral	rat	≥ 5000	[redacted] (2003) M-225480-01-1

The study confirmed a low acute oral toxicity of the formulated product, reflecting the low toxicity of the active substances. It is therefore reasonable to assume that the product would not pose an unacceptable risk to mammals, as indicated by the risk assessment performed for the active substances (see Points 10.3.1.1 and 10.3.1.3).

IIIA 10.3.2.2 Acceptance of bait, granules or treated seed (palatability testing)

Not applicable for spray application.

IIIA 10.3.2.3 Effects of secondary poisoning

The log K_{OW} values for mesosulfuron-methyl (log K_{OW} = -0.48 at pH 7) is below the trigger value indicating a very low risk of secondary poisoning. For details regarding log K_{ow} of the active substance refer to IIIA 10.1.9.

IIIA 10.3.3 Supervised cage or field trials

The risk assessment based on the mesosulfuron-methyl indicates acceptable acute and long-term risks to mammals (see Points 10.3.1.1 and 10.3.1.3 of this dossier). For this reason and also considering animal welfare, no supervised cage or field study with the preparation was deemed necessary.

IIIA 10.4 Effects on bees

Ecotoxicological endpoints used in risk assessment

Table 10.4- 1: Endpoints of the formulation IMS + MSM + MPR OD 42

Test substance	Test organism	Study type	Endpoint		Reference
IMS + MSM + MPR OD 42	**Acute toxicity for honey bees**				
	Apis mellifera	oral, 48 h	LD_{50}	234 µg product/bee	[redacted] (2003) M-222991-01-1 KIIIA 10.4.2.1/01
		contact, 48 h	LD_{50}	498 µg product/bee	

Table 10.4- 2: Endpoints of/for the active substance mesosulfuron-methyl

Test substance	Test organism	Study type	Endpoint	Reference
Mesosulfuron-methyl	**Acute toxicity for honey bees**			
	Apis mellifera	oral, 96 h	LD_{50} > 105.6 µg a.s./bee (NOED) (≥ 105.6 µg a.s./bee)	[redacted] 2012 M-433998-01-1 KCA 8.3.1.1./01
		contact, 96 h	LD_{50} > 100 µg a.s./bee (NOED) (≥ 100 µg a.s./bee)	
	Chronic toxicity for honey bees			
	Apis mellifera	10 d chronic adult feeding study	LC_{50} > 120 mg a.s./kg NOEC ≥ 120 mg a.s./kg	[redacted] 2014 M-485655-01-1 KCA 8.3.1.2./01
Mesosulfuron-methyl WG 75	**Acute toxicity for bumble bees**			
	Bombus terrestris	contact, 96 h	LD_{50} > 100 µg a.s./bee (NOED) (≥ 100 µg a.s./bee)	[redacted], 2014 M-485279-01-1 KCA 8.3.1.1 /02
Mesosulfuron-methyl WG 75 (+Mefenpyr-diethyl WG 15)	**Honey bee brood feeding test**			
	Apis mellifera	Oomen *et al.*, 1992	No adverse effects on adult bee mortality, bee brood development (eggs, young larvae, old larvae, pupae), behaviour, colony strength and colony development, by feeding honey bee colonies sugar syrup at a mesosulfuron-methyl concentration typically present in the spray tank (37.5 ppm)	[redacted], 2013 M-465325-01-1 KCA 8.3.1.3/01
	Apis mellifera	Semi-field honey bee brood study (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	[redacted], 2015 M-510267-01-1 KCA 8.3.1.3 /03

All above listed endpoints are considered for the risk assessment and are consistent with the *proposed* EU endpoints listed in Document N2 for mesosulfuron-methyl.

IIIA 10.4.1 Hazard quotients for bees

An indication of hazard (Hazard Quotient or Q_H) can be derived according to the EPPO risk assessment scheme, by calculating the ratio between the application rate (expressed in g a.s./ha or in g product/ha) and the laboratory contact and oral LD_{50} (expressed in µg a.s./bee or in µg product/bee).

Q_H values can be calculated using data from the studies performed with the active substance and with the formulation. Q_H values higher than 50 indicate the need of higher tiered activities to clarify the actual risk to honey bees.

Hazard Quotient, oral: $$Q_{HO} = \frac{\text{maximum application rate}}{LD_{50}\ \text{oral}} = \frac{[\text{g a.s./ha or g product/ha}]}{[\mu\text{g a.s./bee or }\mu\text{g product/bee}]}$$

Hazard Quotient, contact: $$Q_{HC} = \frac{\text{maximum application rate}}{LD_{50}\ \text{contact}} = \frac{[\text{g a.s./ha or g product/ha}]}{[\mu\text{g a.s./bee or }\mu\text{g product/bee}]}$$

IIIA 10.4.1.1 Oral exposure Q_{HO}

Table 10.4.1.1- 1: Hazard quotients (formulated product) for bees – oral exposure

Test item	Oral LD_{50} [µg product/bee]	Max. application rate [g product/ha][#]	Hazard quotient Q_{HO}	Trigger	*A-priori* acceptable risk for adult bees
Winter wheat, 1× 1.5 L product/ha					
IMS + MSM + MPR OD 42	234	1500	6.4	50	yes
Winter rye, 1× 0.6 L product/ha					
IMS + MSM + MPR OD 42	234	600	2.6	50	yes

[#]) specified density for product IMS + MSM + MPR OD 42: 1.000 g/mL

Table 10.4.1.1- 2: Hazard quotients (active substance mesosulfuron-methyl) for bees – oral exposure

Test item	Oral LD_{50} [µg a.s./bee]	Max. application rate [g a.s./ha]	Hazard quotient Q_{HO}	Trigger	*A-priori* acceptable risk for adult bees
Winter wheat, 1 × 15 g a.s./ha					
Mesosulfuron-methyl	> 105.6	15	< 0.1	50	yes
Winter rye, 1 × 6 g a.s./ha					
Mesosulfuron-methyl	> 105.6	6	< 0.1	50	yes

The hazard quotient for oral exposure is below the validated trigger value for higher tier testing (i.e. $Q_{HO} < 50$). Risk to bees from oral exposure is therefore acceptable for the intended product uses.

IIIA 10.4.1.2 Contact exposure Q_{HC}

Table 10.4.1.2- 1: Hazard quotients (formulated product) for bees – contact exposure

Test item	Contact LD_{50} [µg product/bee]	Max. application rate [g product/ha]#	Hazard quotient Q_{HO}	Trigger	*A-priori* acceptable risk for adult bees
Winter wheat, 1× 1.5 L prod./ha					
IMS + MSM + MPR OD 42	498	1500	3.0	50	yes
Winter rye, 1× 0.6 L prod./ha					
IMS + MSM + MPR OD 42	498	600	1.2	50	yes

#) specified density for product IMS + MSM + MPR OD 42: 1.000 g/mL

Table 10.4.1.2- 2: Hazard quotients (active substance mesosulfuron-methyl) for bees – contact exposure

Test item	Contact LD_{50} [µg a.s./bee]	Max. application rate [g a.s./ha]	Hazard quotient Q_{HO}	Trigger	*A-priori* acceptable risk for adult bees
Winter wheat, 1 × 15 g a.s./ha					
Mesosulfuron-methyl	>100	15	<0.2	50	yes
Winter rye, 1 × 6 g a.s./ha					
Mesosulfuron-methyl	>100	6	<0.1	50	yes

The hazard quotient for contact exposure is below the validated trigger value for higher tier testing (i.e. $Q_{HC} < 50$). Risk to bees from contact exposure is therefore acceptable for the intended product uses.

Further considerations for the risk assessment

In addition to acute laboratory studies with adult honey bees, mesosulfuron-methyl was further subjected to topical acute bumble bee testing [**KCA 8.3.1.1 /02**]. The study did not reveal sensitivity differences between honey bee and bumble bee foragers.

In addition, mesosulfuron-methyl was subjected to chronic laboratory testing with adult honey bees **[KCA 8.3.1.2 /01]**. This chronic study was designed as a limit test by exposing adult honey bees for 10 consecutive days to a concentration of nominally 120 mg mesosulfuron-methyl per kg aqueous sugar solution (120 ppm). Thus, the nominal employed test concentration exceeded the concentration of mesosulfuron-methyl as usually present in the spray tank. No adverse lethal-, sub-lethal, behavioural or delayed effects were found by exposing adult honey bees for ten consecutive days exclusively to sugar solution, containing 120 ppm mesosulfuron-methyl (nominal).

In order to reveal whether mesosulfuron-methyl poses a risk to immature honey bee life stages, a bee brood feeding study [**KCA 8.3.1.3/01**] has been conducted by following the provisions/method of Oomen P.A., de Ruijter, A. & van der Steen, J. (OEPP/EPPO Bulletin 22:613-616 (1992)), which require, amongst other parameters to "*...use formulated products only... products are fed at a concentration recommended for high-volume use...*". The honey bee brood feeding test is a worst-case screening test, by feeding the honey bees directly in the hive with a treated sugar solution which contains the test substance at a concentration typically present in the spray tank (and as such at a very high concentration) and by investigating the development of eggs, young & old larvae by employing digital photo imaging technology.

This particular study tested formulated mesosulfuron-methyl (via Mesosulfuron-methyl WG 75) together with formulated crop safener mefenpyr-diethyl (as Mefenpyr-diethyl WG 15). The actual test concentration of mesosulfuron-methyl was 37.5 mg/L (37.5 ppm), which corresponds to a typical concentration of mesosulfuron-methyl present in the spray tank when using product IMS + MSM + MPR OD 42. The administration of 1 litre sugar solution per colony, containing 37.5 ppm mesosulfuron-methyl, has not resulted in adverse effects. There were neither adverse acute or chronic effects on adult honey bees nor adverse effects on immature honey bee life stages (eggs, young larvae, old larvae, pupae) or on the colony itself. Neither mortality of worker bees and pupae (as assessed via dead bee traps) nor the termination rate of eggs, young larvae and old larvae (as assessed via digital imaging of individual marked cells) was statistically significantly different from the untreated control.

In order to investigate brood development under actual use conditions of mesosulfuron-methyl, a higher tier semi-field honey bee brood study [**KCA 8.3.1.3/03**] (according to the provisions of the OECD Guidance Document 75) was conducted under forced/confined exposure conditions, by applying the rate of 20.11 g Mesosulfuron-methyl WG 75 per hectare, corresponding to 15 g mesosulfuron-methyl/ha, under tunnel conditions to the full flowering and highly bee attractive surrogate crop *Phacelia tanacetifolia*.
The test was designed as a replicated tunnel study to assess potential effects of mesosulfuron-methyl to honey bee colonies, including a very detailed assessment of brood development. Tunnels (25 m length x 5 m width x 2.5 m height) were set up on a ca. 80 m² plot of *Phacelia tanacetifolia*. Small bee colonies were introduced to the tunnels 4 days before the application. One honey bee colony was used per tunnel. The test item, water and a reference item was applied during honey bees actively foraging on the crop. The trial was carried out using four tunnels (i.e. replicates) for the test item treatment, the control and the reference item treatment (Insegar, 250 g/kg fenoxycarb), respectively. The confined exposure phase of the honey bees inside the treated crop was 4 days following the test item application. At the end of the 4th day after application, due to the herbicide mode of action of them test item, the *Phacelia*-crop was no longer attractive to bees (faded crop) and did not longer support the confined colonies. Thus, all bee colonies (i.e. the colonies from the test item, the water and the reference item group, respectively) were relocated after 4 complete days of confined exposure from their respective tunnels and placed in an area with no main flowering, bee attractive crops. The test item was applied under optimum foraging conditions. After foliar (spray) application of the water (control), test item (Mesosulfuron-methyl WG 75) and the reference item (fenoxycarb), ontogenesis of a defined number of honey bee eggs was observed for each group and colony. Mortality of adult bees and pupae/larvae as well as foraging activity of the adult bees was also assessed. The condition of the colonies was assessed in regular intervals until the end of the trial. Ontogenesis of the bees from egg to adult workers was observed for a period of 22 days (i.e. one complete honey bee brood cycle). This was done one day before the application by taking out a brood comb and taking a digital picture of the

brood comb. After saving the file on a computer, 200 eggs per colony were marked at this first brood area fixing day BFD0 (BFD = Brood Area Fixing Day). For each subsequent brood assessment (BFDn), again, the respective comb was taken out of the hive and another digital photo was taken in order to investigate the progress of the brood development until day 21 following the application (BFD22 following BFD0). Statistical evaluation was done for mortality, foraging activity, colony strength and the brood termination rate using Shapiro-Wilk`s test (check for normal distribution), Levene`s test (check for homogeneity of variance), Student or Welch t- test (pairwise comparison. No adverse effects on mortality of worker or pupae, foraging activity, behaviour, nectar- and pollen storage as well as on queen survival were observed. No effects on colony development, colony strength or bee brood were observed. Based on the results of this study, it can be concluded that Mesosulfuron-methyl WG 75 (750 g/kg) does not adversely affect honey bees and honey bee brood when applied at a rate of 20.11 g product/ha (corresponding to 15 g mesosulfuron-methyl/ha) in 400 L tap water/ha, during honey bees actively foraging on a bee-attractive, flowering crop. The observed, characteristic brood effects of the reference item Insegar (a.s. fenoxycarb) in terms of typicality, time of occurrence and extent, showed that the prevailing test conditions allowed for a profound detection of effects on immature honey bee life stages.

Synopsis

Mesosulfuron-methyl has a low acute toxicity to honey bees, with LD_{50} (oral and contact) above the highest tested dose level (oral: LD_{50} > 105.6 µg a.s./bee, contact: LD_{50} > 100 µg a.s./bee). The calculated Hazard Quotients for both, mesosulfuron-methyl as well as for IMS + MSM + MPR OD 42 are well below the validated trigger value which would indicate the need for a refined risk assessment; no adverse effects on honey bee mortality are to be expected. This conclusion is confirmed by the results of the bee brood feeding study.

The acute laboratory study conducted with bumble bees revealed no sensitivity differences between honey bee and bumble bee foragers.

Regarding potential side effects of mesosulfuron-methyl on immature honey bee life stages as well as on colony development, 37.5 ppm mesosulfuron-methyl, a concentration which corresponds to a typical concentration of mesosulfuron-methyl via IMS + MSM + MPR OD 42 present in the spray tank, has not resulted in adverse/statistical significant effects on mortality of worker bees and pupae nor in adverse/statistically significant effects on the termination rate of eggs, young larvae and old larvae (as assessed via digital imaging of individually marked cells) in the bee brood feeding study on colony level. Even at this very high concentration under the worst case conditions of the honey bee brood feeding test, no adverse effects on immature honey bee life stages were found; the findings in this study regarding the absence of chronic/delayed effects on adults honey bees are in line with the absence of adverse chronic effects on adult bees in the chronic 10 day laboratory feeding test with adult honey bees under laboratory conditions (at 120 ppm).

In order to investigate potential effects of mesosulfuron-methyl under confined semi-field testing conditions (according to the provisions of OECD Guidance Document No. 75), Mesosulfuron-methyl WG 75 (750 g/kg) was applied at a rate corresponding to 15 g a.s./ha in 400 L water/ha to full-flowering *Phacelia* during honey bees actively foraging on the crop. This study design, although being conservative for an actual exposure situation of honey bees in cereals, is from an apidological and apicultural point of view more realistic than an in-hive feeding of the test compound via a treated sugar solution, which contains the test substance at a concentration typically present in the spray tank (and as such at a very high concentration). The results of this higher tier semi-field study confirmed the conclusions made above on the basis of the outcome of the lower-tiered studies, as no adverse direct or delayed effects on mortality of worker bees or pupae, foraging activity, behaviour, nectar- and pollen storage, queen survival, colony strength, colony development as well as the development of bee brood were observed, even under aggravated, forced exposure conditions and by digitally following-up in a very detailed manner the fate of individually marked brood cells (digital photographic assessment) from egg stage until emergence.

Overall, it can be concluded that mesosulfuron-methyl, when applied at the maximum application rate of 15 g a.s./ha even during the flowering period of potentially bee-attractive weeds inside the cereal cropping area, does not pose an unacceptable risk to honey bees and honey bee colonies.

IIIA 10.4.2 Acute toxicity of the formulation to bees

IIIA 10.4.2.1 Oral

Report:	[redacted]9;[redacted];2003;M-222991-01
Title:	Effects of AE F115008 06 OD04 A104 (acute contact and oral) on honey bees (Apis mellifera L.) in the laboratory
Report No:	C037487
Document No:	M-222991-01-1
Guidelines:	**OECD: 213, 214;Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the oral and contact toxicity of IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to *Apis mellifera*. The study was designed to meet OECD criteria.

Material and Methods

Acute oral test

Worker bees, 4-6 weeks old were treated with 63, 127, 245, 495 and 986 µg product/bee. Test duration was 48 hrs. In addition an untreated control was tested. Moreover, Perfekthion EC was tested as a toxic standard. 3 replicates with 30 bees were used per treatment level. Bees starved during a period of 0.5 hours prior to test start. The temperature was 25 °C. Relative air humidity varied between 60 and 76 %. The bees were maintained at dark during the test.

Acute contact test

Worker bees, 4-6 weeks old were treated with 116, 232, 463, 926 and 1389 µg product/bee. Test duration was 96 hrs. In addition, an untreated control was tested. Moreover, Perfekthion EC was tested as a toxic standard. 3 replicates with 10 bees each were used per treatment level. The temperature was 25°C. Relative air humidity varied between 60 and 76 %.

Findings

Acute oral test: Mortality and intoxication symptoms were observed as follows:

Actual intake (µg product/bee)	4 hrs (% mortality)	24 hrs (% mortality)	48 hrs (% mortality)
Control	0	0	0
63	0	6.7	6.7
127	0	10.0	10.0
245	0	43.3	46.7
495	0	93.3	96.7
986	0	90.0	96.7
Toxic standard			
0.04	0	0	3.3
0.08	0	23.3	30.0
0.16	3.3	36.7	70.0
0.33	40.0	56.7	96.7

Acute contact test: Mortality and intoxication symptoms were observed as follows:

µg product/bee	24 hrs (% mortality)	48 hrs (% mortality)	96 hrs (% mortality)
Control	3.3	3.3	6.7
116	3.3	3.3	33.3
232	10	13.3	20.0
463	6.7	6.7	16.7
926	40.0	63.3	90.0
1389	63.3	63.3	96.7
Toxic standard			
0.1	16.7	43.3	70.0
0.2	90.0	93.3	96.7
0.3	93.3	93.3	96.7

The following observations were made: apathy and discoordinated movement.

Conclusion

The effect of of IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) after oral and contact exposure on the mortality of *Apis mellifera* based on nominal figures are as follows:

Acute oral test:

24h LD_{50} = 262 µg product/bee (95% confidence limits 213 - 319 µg product/bee)
48h LD_{50} = 234 µg product/bee (95% confidence limits 197 - 280 µg product/bee)

Acute contact test

48h LD_{50} = 970 µg product/bee (95% confidence limits 771 - 1220 µg product/bee)
96h LD_{50} = 498 µg product/bee (95% confidence were not determined)

IIIA 10.4.2.2 Contact

The acute contact toxicity studies on honey bees with the product are summarised in Point 10.4.2.1.

IIIA 10.4.3 Effects on bees of residues on crops

A honey bee brood feeding study according to the provisions of [redacted] *et al.* ([redacted], L., 2013; M-465325-01) as well as a semi-field brood tunnel study according to the provisions of the OECD Guidance Document 75 ([redacted], 2015, M-510267-01-1) have been conducted. These studies are summarized under KCA 8.3.1.3 /01 and KCA 8.3.1.3 /03, respectively.

IIIA 10.4.4 Cage tests

A semi-field brood tunnel study according to the provisions of the OECD Guidance Document 75 ([redacted], 2015, M-510267-01-1) has been conducted. The study is summarized under KCA 8.3.1.3 /03.

IIIA 10.4.5 Field tests

Not necessary considering the outcome of the risk assessment and the results of lower-tiered studies.

IIIA 10.4.6 Investigation into special effects

Please refer to point IIIA 10.4.3.

IIIA 10.4.6.1 Larval toxicity

Please refer to point IIIA 10.4.3.

IIIA 10.4.6.2 Long residual effects

Please refer to point IIIA 10.4.3.

IIIA 10.4.6.3 Disorienting effects on bees

Please refer to point IIIA 10.4.3.

IIIA 10.4.7 Tunnel tests

Not necessary considering the outcome of the risk assessment and the results of lower-tiered studies.

IIIA 10.5 Effects on arthropods other than bees

Toxicity tests on non-target arthropods were conducted with IMS + MSM + MPR OD 42 on the sensitive standard species *Typhlodromus pyri* and *Aphidius rhopalosiphi* and on *Chrysoperla carnea*. A summary of the results is provided in Table 10.5- 1.

Table 10.5- 1: Endpoints of the formulation IMS + MSM + MPR OD 42 used in risk assessment

Test species Reference	Tested formulation, study type, duration, exposure	Ecotoxicological endpoint	
Aphidius rhopalosiphi [redacted] (2003) C036547 M-220929-01-1 KIIIA 10.5.1/01	IMS + MSM + MPR OD 42 lab., glass plates, [mL/ha] 375 530 750 1061 1500	LR_{50} = 877.3 mL/ha corr. Mortality [%] 0.0 2.6 56.4 59.0 87.2	 Effect on Parasitation Efficiency[A] [%] -2.2 5.0 - - -
Aphidius rhopalosiphi [redacted](2003) C037712 M-223374-01-1 KIIIA 10.5.2/01	IMS + MSM + MPR OD 42 ext. lab., barley seedlings [mL/ha] 750 1500	LR_{50} > 1500 mL/ha corr. Mortality [%] 0.0 13.3	 Effect on Parasitation Efficiency [%] 25.8 8.7
Typhlodromus pyri [redacted] (2003) C036098 M-219955-01-1 KIIIA 10.5.1/02	IMS + MSM + MPR OD 42 lab., glass plates, [mL/ha] 150 267 474 844 1500	LR_{50} > 1500 mL/ha corr. Mortality [%] 13.5 8.4 33.9 40.7 32.1	 Effect on Reproduction[B] [%] -1.2 4.9 -4.9 19.8 12.3
Chrysoperla carnea [redacted] (2003) C038055 M-224105-02-1 KIIIA 10.5.2/02	IMS + MSM + MPR OD 42 ext. lab., maize leaves [mL/ha] Control 750 1500	LR_{50} > 1500 mL/ha corr. Mortality [%] - 0.0 0.0	 Eggs/Female/Day — Hatching [%] 30.7 — 87.7 32.6 — 90.6 34.4 — 89.4

[A] negative value means increased parasitation efficiency compared to the control
[B] negative value indicates increased reproduction compared to the control

All above endpoints used in risk assessment are consistent with the *proposed* EU endpoints listed in Document N2 for mesosulfuron-methyl.

Risk assessment procedures

The risk assessment was performed according to Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002) and to the Guidance Document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods (ESCORT 2, Candolfi et al. 2000[6]).

In-field hazard quotient (HQ) tier 1 risk assessment

The following equation was used to calculate the hazard quotient (HQ) for the in-field scenario:

In field-HQ = max. single application rate * MAF / LR_{50}

IMS + MSM + MPR OD 42 is intended to be applied once with an application rate of 1500 mL/ha in winter wheat and with an application rate of 600 mL/ha in winter rye. Resulting HQ values are presented in the following table. The risk is considered acceptable if the calculated HQ is < 2.

Table 10.5- 2: HQ for terrestrial non-target arthropods for the in-field scenario

Crop / Compound	Species	Appl. rate [mL/ha]	MAF	LR_{50} [mL/ha]	HQ	Trigger
Winter wheat, 1× 1.5 L product/ha						
IMS + MSM + MPR OD 42	*T. pyri*	1500	1	> 1500	< 1	2
	A. rhopalosiphi	1500	1	877.3	1.71	2
Winter rye, 1 × 0.6 L product/ha						
IMS + MSM + MPR OD 42	*T. pyri*	600	1	> 1500	< 0.4	2
	A. rhopalosiphi	600	1	877.3	0.68	2

Conclusion: For the standard species, the in-field HQ values are below the trigger of concern, indicating an acceptable risk for non-target arthropods.

Off-field hazard quotient (HQ) tier 1 risk assessment

The following equation was used to calculate the hazard quotient (HQ) for the off-field scenario:

Off-field HQ = max. single application rate * MAF * (drift factor/VDF)*correction factor / LR_{50}

MAF = multiple application factor
Drift factor = i.e 0.0277, 90th percentile for one application (according to Ganzelmeier)
VDF = vegetation distribution factor
Vegetation distribution factor = 10

[6] Candolfi et al.: Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods; ESCORT 2 workshop (European Standard Characteristics Of Non-Target Arthropod Regulatory Testing), Wageningen, NL, March 21-23, 2000, SETAC Europe; SETAC publication August 2001

Correction factor = 10 (uncertainty factor for the extrapolation from indicator species to other off-field non-target arthropods; default value for tier 1 risk assessment according to the Terrestrial Guidance Document)

The risk is considered acceptable if the calculated HQ is < 2.

Table 10.5- 3: HQ for terrestrial non-target arthropods for the off-field scenario

Crop / Compound	Species	Appl. rate [mL/ha]	MAF	Drift [%]	VDF	Corr. factor	LR_{50} / [g/ha]	HQ	Trigger
Winter wheat, 1× 1.5 L product/ha									
IMS + MSM + MPR OD 42	*T. pyri*	1500	1	2.77	10	10	>1500	<0.03	2
	A. rhopalosiphi	1500	1	2.77	10	10	877.3	0.05	2
Winter rye, 1 × 0.6 L product/ha									
IMS + MSM + MPR OD 42	*T. pyri*	600	1	2.77	10	10	> 1500	< 0.01	2
	A. rhopalosiphi	600	1	2.77	10	10	877.3	0.02	2

Conclusion: The estimated HQ is below the trigger of concern, indicating no unacceptable risk for non-target arthropods.

IIIA 10.5.1 Using artificial substrates

Report:	[redacted];[redacted];[redacted];2003;M-220929-01
Title:	Effects of AE F115008 06 OD04 A104 on the parasitoid Aphidius rhopalosiphi in the laboratory - dose response test Code: AE F115008 06 OD04 A104
Report No:	C036547
Document No:	M-220929-01-1
Guidelines:	**IOBC; WPRS 2000;Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the effects of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to mortality and parasitisation efficiency of parasitoid wasps (*Aphidius rhopalosiphi*). The standard laboratory study was designed to meet IOBC criteria.

Material and Methods

Wasps were treated with 375, 530, 750, 1061 and 1500 mL product/ha with an application volume of 200 L/ha on glass plates. Moreover, Perfekthion EC was tested as a toxic standard with a dosage of 0.3 mL/ha. The exposure duration was 48 hours. In the course of the exposure phase 4 replicates with 10 (7 females and 3 males) were used per treatment level. The wasps were introduced into the test systems 20 to 60 minutes after the application.
A consecutive parasitisation test was performed at treatment levels with mortality rates less than 50%. Untreated pots with barley seedlings infested with aphids (*Rhopalosiphum padi*) served as post-exposure units. 20 replicates with one female each were used during the post-exposure period. The 24-hour-parasitation period was followed by a post- parasitisation period of 12 days.

The temperature varied between 20 to 24°C during the whole study period. Relative air humidity varied between 60 to 88% and 60 to 67 % during the exposure and the post-exposure period, respectively. The test systems were exposed to 1370 to 1800 lux during the exposure period and 4000 to 10000 lux over the post-exposure period. The light period during the whole test was 16 hours.

Findings

All validity criteria according to control mortality, effects of the toxic reference and the parasitisation rates are fulfilled.

Mortality and parasitisation rate are summarised in the following table.

Table 10.5.1- 1: Percent mortality and parasitisation efficiency of *Aphidius rhopalosiphi*

mL product/ha	48 h % corrected mortality	Significance	% reduction of parasitisation	p-value
Control				
375	0.0	n.s.	-2.2	n.s.
530	2.6	n.s.	5.0	n.s.
750	56.4	*	n.a.	*
1061	59.0	*	n.a.	*
1500	87.2	*	n.a.	*
Toxic standard	100.0	*	n.a.	*

n.s. = not significant
n.a. = not applicable

The following observations were made: affected and moribund individuals were observed after 2 hours at treatment levels between 750 and 1500 mL product/ha.

Conclusion

The effect of the formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) on mortality and the parasitisation rate of *Aphidius rhopalosiphi* are as follows:

48 h LD_{50} = 877.3 mL product /ha (95% confidence limits 791.6 - 972.3 mL/ha)
NOEC = 530 mL product /ha

Report:	[redacted]n;[redacted];2003;M-219955-01
Title:	Effects of AE F115008 06 OD04 A104 on the predatory mite Typhlodromus pyri in the laboratory dose response test
Report No:	C036098
Document No:	M-219955-01-1
Guidelines:	**IOBC: ESCORT 1994;Deviation not specified**
GLP/GEP:	**yes**

Objective
The aim of the study was to determine the effects of the formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to mortality and reproduction of predatory mites (*Typhlodromus pyri*). The standard laboratory study was designed to meet IOBC criteria.

Material and Methods
Mites were treated with 150, 267, 474, 844 and 1500 mL product/ha with an application volume of 200 L/ha on glass plates. Moreover, Perfekthion EC was tested as a toxic standard with a dosage of 8 mL product/ha. Test duration was 14 days. 3 replicates with 20 protonymphs were used per treatment level. The protonymphs were introduced into the test systems 25 to 40 minutes after the application. The temperature varied between 24°C and 26°C. Relative air humidity varied between 61% and 89 %. The test systems were exposed to 250 to 590 lux. The light period during the whole test was 16 hours.

Findings
All validity criteria according to control mortality, effects of the toxic reference and the reproduction rates in the control are fulfilled.

Mortality and reproduction are summarised in the following table:

Table 10.5.1- 2: Mortality and reproduction of *Typhlodromus pyri*

mL product/ha	Day 7 (% corrected mortality)	Significance	Day 7 to 14 (% reduction of reproduction)	Significance
Control				
150	13.5	n.s.	-1.2	n.s.
267	8.4	n.s.	4.9	n.s.
474	33.9	*	-4.9	n.s.
844	40.7	*	19.8	n.s.
1500	32.1	*	12.3	n.s.
Toxic reference	91.6	*	n.a.	n.a.

No intoxication symptom was observed.

Conclusion
The effect of IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) on mortality and the reproduction rate of *Typhlodromus pyri* are as follows:

7 day LD_{50} > 1500 mL product/ha
21 day NOEC ≥ 1500 mL product/ha

IIIA 10.5.2 Extended laboratory studies

Report:	[redacted]p;[redacted];2003;M-223374-01
Title:	Effects of AE F115008 06 OD04 A104 on the parasitoid Aphidius rhopalosiphi - extended laboratory study
Report No:	C037712
Document No:	M-223374-01-1
Guidelines:	**IOBC: Mead-Briggs et al. 2000;Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the effects of the formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to mortality and parasitisation efficiency of parasitoid wasps (*Aphidius rhopalosiphi*). The extended laboratory study was designed to meet IOBC criteria.

Material and Methods

Wasps were treated with 750 and 1500 mL product/ha with an application volume of 400 L/ha on barley seedlings. Moreover, Perfekthion EC was tested as a toxic standard with a dosage of 10.0 mL product/ha. The exposure duration was 48 hours. In the course of the exposure phase 6 replicates with 5 females were used per treatment level. The wasps were introduced into the test systems 15 to 20 minutes after the application.

A consecutive parasitisation test was performed at treatment levels with mortality rates less than 50%. Untreated pots with barley seedlings infested with aphids (*Rhopalosiphum padi*) served as post-exposure units. 20 replicates with one female each were used during the post-exposure period. The 24-hour parasitisation period was followed by a post- parasitisation period of 11 days.

The temperature varied between 18 - 22°C during the whole study period. Relative air humidity varied between 60 to 83% and 66% during the exposure and the post-exposure period, respectively. The test systems were exposed to 1230 - 1960 lux during the exposure period and 6830 - 11500 lux over the post-exposure period. The light period during the whole test was 16 hours.

Findings

All validity criteria according to control mortality, effects of the toxic reference and the parasitation rates are fulfilled.

Mortality and parasitisation rate are summarised in the following table.

Table 10.5.2- 1: Percent mortality and parasitisation efficiency of *Aphidius rhopalosiphi*

	48 h % mortality	Mummies per female	% reduction of parasitisation
Control	0.0	28.7	
750 mL product/ha	0.0 n.s.	21.3 n.s.	25.8
1500 mL product/ha	13.3 n.s.	26.2 n.s.	8.7
Toxic standard	100.0	n.a.	n.a.

No sigificant mortality compared to the control and no repellent effects were observed.

Conclusion

The effect of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) on mortality and the parasitisation rate of *Aphidius rhopalosiphi* are as follows:

48 h LD_{50} > 1500 mL product/ha
NOEC≥1500 mL product/ha

Report:	[redacted];[redacted];2003;M-224105-03; Amended: 2004-02-19
Title:	Effects of AE F115008 06 OD04 A104 on the lacewing Chrysoperla carnea, extended laboratory study Revised final report no. 1
Report No:	C040071
Document No:	M-224105-03-1
Guidelines:	**IOBC: Vogt et al. 2000;Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the effects of the formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to larval mortality and reproduction of lacewings (*Chrysoperla carnea*). The extended laboratory study was designed to meet IOBC criteria.

Material and Methods

2 to 3 days old larvae were treated with 750 and 1500 mL product/ha with an application volume of 200 L/ha on maize leaves. Moreover, Perfekthion EC was tested as a toxic standard with a dosage of 60 mL product/ha. 50 replicates were used per treatment level. The larvae were introduced into the test systems 50 to 55 minutes after the application. The larvae were fed with UV-sterilised eggs of *Sitotroga cerealella*. The duration of the exposure phase was 12 to 17 days.
The reproduction phase lasted 7 to 12 days (pre-oviposition) and 1 week with 2 checks (oviposition period). The temperature varied between 23°C and 26°C. Relative air humidity varied between 61% and 88 %. The test systems were exposed to 1070 to 2230 lux. The light period during the whole test was 16 hours.

Findings

All validity criteria according to control mortality, effects of the toxic reference and the reproduction rates in the control are fulfilled.

Mortality and reproduction are summarised in the following table.

Table 10.5.2- 2: Mortality and reproduction of adult *Chrysoperla carnea*

	% corrected mortality	Mean number of eggs/female/day	Mean larval hatching rate
Control		30.7	87.7
750 mL product/ha	0.0	32.6	90.6
1500 mL product/ha	0.0	34.4	89.4
Toxic reference	57.4		

No mortality and reproduction effects were observed.

Conclusion

The effect of the formulation IMS + MSM + MPR OD 42 (Atlantis® OD, AE F115008 06 OD04 A104) on mortality and the reproduction rate of *Chrysoperla carnea* is as follows:

LD_{50} > 1500 mL product/ha
NOEC ≥ 1500 mL product/ha

IIIA 10.5.3 Semi-field tests

In view of the findings reported under 10.5.1, and based on current data requirements, no semi-field studies with the preparation have been conducted.

IIIA 10.5.4 Field tests

In view of the findings reported under 10.5.1, and based on current data requirements, no field studies with the preparation have been conducted.

IIIA 10.6 Effects on earthworms and other soil non-target macro-organisms

Ecotoxicological endpoints used in risk assessment

Table.10.6- 1: Endpoints of the formulation IMS + MSM + MPR OD 42 used in risk assessment

Test substance	Test organism	Study type	Endpoint [mg/kg dws]		References
	Earthworm, chronic				
IMS + MSM + MPR OD 42	*Eisenia fetida*	reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC	76	[redacted] (2014) M-483205-01-1 KIIIA 10.6.3/01

dws = dry weight soil

Table.10.6- 2: Endpoints of the active substance mesosulfuron-methyl and metabolites used in risk assessment

Test substance	Test organism	Study type	Endpoint [mg/kg dws]		References
Earthworm, chronic					
Mesosulfuron-methyl	*Eisenia fetida*	reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC	125	[redacted] (2010) M-392544-01-1 KCA 8.4.1 /02
AE F154851	*Eisenia fetida*	reproduction, 56 d (5% peat in test soil), test item mixed into soil	NOEC	≥93.9*	[redacted] (2012) M-425013-01-1 KCA 8.4.1 /03
AE F160459	*Eisenia fetida*	reproduction, 56 d (5% peat in test soil), test item mixed into soil	NOEC	90	[redacted] (2012) M-429097-01-1 KCA 8.4.1 /04
AE F099095	*Eisenia fetida*	reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC	≥100	[redacted] (2013) M-473217-01-1 KCA 8.4.1 /05
AE F092944	*Eisenia fetida*	reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC	10	[redacted] (2013) M-461051-01-1 KCA 8.4.1 /06
AE F160460	*Eisenia fetida*	reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC	≥100	[redacted] (2013) M-468911-01-1 KCA 8.4.1 /07
AE F140584	*Eisenia fetida*	reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC	≥117	[redacted] (2013) M-468921-01-1 KCA 8.4.1 /08
AE F147447	*Eisenia fetida*	reproduction, 56 d (5% peat in test soil), test item mixed into soil	NOEC	90	[redacted] (2012) M-428651-01-1 KCA 8.4.1 /09

* corrected to an analysed purity of 93.9 %
dws = dry weight soil

All above endpoints used in risk assessment are consistent with the *proposed* EU endpoints listed in Document N2 for mesosulfuron-methyl.

IIIA 10.6.1 Toxicity exposure ratios, TER_A and TER_{LT}

Predicted Environmental Concentrations used in risk assessment

Formulated product:

Predicted environmental concentrations in soil (PEC_{soil}) values were calculated for the formulation based on the standard assumptions of distribution in a soil layer of 5 cm with a bulk density of 1.5 g/cm^3; a crop interception of 50% was taken into account.

Table 10.6.1- 1: Initial PECsoil values of the formulation

Crop / Compound	Scenario	Winter wheat, 1 x 1.5 L/ha	Winter rye, 1 x 0.6 L/ha
		$PEC_{soil, max}$ [mg/kg]	$PEC_{soil, max}$ [mg/kg]
IMS + MSM + MPR OD 42	soil layer: 5 cm soil density: 1.5 g/mL product density: 1.000 g/mL# crop interception: 50%	**1.000**	**0.400**

Bold values: worst case considered in risk assessment
#) specified density for product IMS + MSM + MPR OD 42: 1.000 g/mL

Active substance and metabolites:

Predicted environmental concentrations for the active substance and its metabolites were calculated in Point IIIA 9.4 (active substance) and IIIA 9.5 (metabolites) of this MCP document. The relevant PEC values considered for TER calculations are summarised in the tables below. Maximum values are used for risk assessments.

Table 10.6.1- 2: Maximum PECsoil for the active substance mesosulfuron-methyl and its metabolites
a) originally submitted simulation – KIIIA 9.4/01 and KIIIA 9.5/01)

Crop / Compound	Winter wheat, 1 x 1.5 L/ha		Winter rye, 1 x 0.6 L/ha	
	$PEC_{soil, initial}$ [mg/kg]	$PEC_{soil, accu}$ [mg/kg]	$PEC_{soil, initial}$ [mg/kg]	$PEC_{soil, accu}$ [mg/kg]
Mesosulfuron-methyl	0.010	**0.011**	0.004	**0.004**
AE F154851	**0.002**	-	**<0.001**	**-**
AE F160459	<0.001	**0.001**	<0.001	**<0.001**
AE F099095	0.001	**0.002**	<0.001	**<0.001**
AE F092944	**<0.001**	-	**<0.001**	**-**
AE F160460	**<0.001**	-	**<0.001**	**-**
AE F140584	**<0.001**	-	**<0.001**	**-**
AE F147447	<0.001	**<0.001**	<0.001	**<0.001**

Bold values: worst case considered in risk assessment

b) alternative simulation using RMS requested modelling parameters– KIIIA 9.4/02 and KIIIA 9.5/02

Crop / Compound	Winter wheat, 1 x 1.5 L/ha		Winter rye, 1 x 0.6 L/ha	
	$PEC_{soil, initial}$ [mg/kg]	$PEC_{soil, accu}$ [mg/kg]	$PEC_{soil, initial}$ [mg/kg]	$PEC_{soil, accu}$ [mg/kg]
Mesosulfuron-methyl	0.016	**0.020**	0.006	**0.008**
AE F154851	0.003	**0.004**	0.001	**0.001**
AE F160459	0.001	**0.002**	<0.001	**<0.001**
AE F099095	0.002	**0.003**	<0.001	**0.001**
AE F092944	**<0.001**	-	**<0.001**	**-**
AE F160460	**0.001**	-	**<0.001**	**-**
AE F140584	**<0.001**	-	**<0.001**	**-**
AE F147447	<0.001	**0.002**	<0.001	**<0.001**

Bold values: worst case considered in risk assessment

Risk Assessment

The risk assessment procedure follows the requirements as given in the EU Regulation 1107/2009 and the Guidance Document on Terrestrial Ecotoxicology.

Based on the endpoints in the table above the TER values are calculated using the following equations:

TER_{LT} = NOEC / PEC_{soil}

The risk is considered acceptable if the TER_{LT} is >5.

For lipophilic substances (log P_{OW} > 2) all results from the laboratory studies are corrected by a factor 2 even when the organic matter is less than 10 %.

However, for none of the components logP_{OW} exceeds this trigger (refer to Section 2 of the MCA document, CA 2.7), hence an additional assessment factor is not required.

Table 10.6.1- 3: TER$_{LT}$ calculations (formulated product) for earthworms

Crop / Compound	Species	Endpoint [mg/kg soil]	PEC$_{max}$ [mg/kg soil]	TER$_{LT}$	Trigger
Winter wheat, 1× 1.5 L prod./ha					
IMS + MSM + MPR OD 42	*Eisenia fetida*	NOEC 76	1.000	76	5
Winter rye, 1× 0.6 L prod./ha					
IMS + MSM + MPR OD 42	*Eisenia fetida*	NOEC 76	0.400	190	5

Table 10.6.1- 4: TER$_{LT}$ calculations (active substance mesosulfuron-methyl and metabolites) for earthworms

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [mg/kg soil]	PEC$_{soil,max/accu}$ [mg/kg]	TER$_{LT}$	Trigger
Winter wheat, 1 × 15 g a.s./ha					
Mesosulfuron-methyl	*Eisenia fetida*	NOEC 125	0.011	11 364	5
AE F154851	*Eisenia fetida*	NOEC ≥ 93.9	0.002	≥ 46 950	
AE F160459	*Eisenia fetida*	NOEC 90	0.001	90 000	
AE F099095	*Eisenia fetida*	NOEC ≥ 100	0.002	≥ 50 000	
AE F092944	*Eisenia fetida*	NOEC 10	< 0.001	> 10 000	
AE F160460	*Eisenia fetida*	NOEC ≥ 100	< 0.001	≥ 100 000	
AE F140584	*Eisenia fetida*	NOEC ≥ 117	< 0.001	≥ 117 000	
AE F147447	*Eisenia fetida*	NOEC 90	< 0.001	> 90 000	
Winter rye, 1 × 6 g a.s./ha					
Mesosulfuron-methyl	*Eisenia fetida*	NOEC 125	0.004	31 250	5
AE F154851	*Eisenia fetida*	NOEC ≥ 93.9	<0.001	≥ 93 900	
AE F160459	*Eisenia fetida*	NOEC 90	<0.001	> 90 000	
AE F099095	*Eisenia fetida*	NOEC ≥ 100	<0.001	≥ 100 000	
AE F092944	*Eisenia fetida*	NOEC 10	<0.001	> 10 000	
AE F160460	*Eisenia fetida*	NOEC ≥ 100	<0.001	≥ 100 000	
AE F140584	*Eisenia fetida*	NOEC ≥ 117	<0.001	≥ 117 000	
AE F147447	*Eisenia fetida*	NOEC 90	<0.001	> 90 000	

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [mg/kg soil]		PEC$_{soil,max/accu}$ [mg/kg]	TER$_{LT}$	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*Eisenia fetida*	NOEC	125	0.020	6 250	5
AE F154851	*Eisenia fetida*	NOEC	≥ 93.9	0.004	≥ 23 475	
AE F160459	*Eisenia fetida*	NOEC	90	0.002	45 000	
AE F099095	*Eisenia fetida*	NOEC	≥ 100	0.003	≥ 33 333	
AE F092944	*Eisenia fetida*	NOEC	10	<0.001	> 10 000	
AE F160460	*Eisenia fetida*	NOEC	≥ 100	0.001	≥ 100 000	
AE F140584	*Eisenia fetida*	NOEC	≥ 117	<0.001	≥ 117 000	
AE F147447	*Eisenia fetida*	NOEC	90	0.002	45 000	
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*Eisenia fetida*	NOEC	125	0.008	15 625	5
AE F154851	*Eisenia fetida*	NOEC	≥ 93.9	0.001	≥ 93 900	
AE F160459	*Eisenia fetida*	NOEC	90	<0.001	> 90 000	
AE F099095	*Eisenia fetida*	NOEC	≥ 100	0.001	≥ 100 000	
AE F092944	*Eisenia fetida*	NOEC	10	<0.001	> 10 000	
AE F160460	*Eisenia fetida*	NOEC	≥ 100	<0.001	≥ 100 000	
AE F140584	*Eisenia fetida*	NOEC	≥ 117	<0.001	≥ 117 000	
AE F147447	*Eisenia fetida*	NOEC	90	<0.001	> 90 000	

Conclusion: The TER$_{LT}$ values meet the required trigger of 5, indicating an acceptable long-term risk to earthworms for the intended uses.

IIIA 10.6.2 Acute toxicity

Under the Regulation (EC) No. 1107/2009 acute earthworm toxicity tests are no longer data requirements.

IIIA 10.6.3 Sublethal effects

Report:	[redacted];[redacted];2014;M-483205-01
Title:	Iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl OD 42 (2+10+30) G: Sublethal toxicity to the earthworm Eisenia fetida in artificial soil
Report No:	13 10 48 182 S
Document No:	M-483205-01-1
Guidelines:	**OECD 222 (2004), ISO 11268-2 (1998);none**
GLP/GEP:	**yes**

Objective:

The purpose of this study was to determine the sublethal effects of formulation IMS + MSM + MPR OD 42 on reproduction, mortality and growth of the earthworm *Eisenia fetida* by dermal and alimentary uptake using an artificial soil in a laboratory test. The test was performed according to the recommendations of the OECD Guideline 222 (2004) and the International Standard ISO 11268-2 (1998).

Material and Methods:

Test item: Iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl OD 42 (2+10+30) G, Short name: IMS+MSM+MPR OD 42 (2+10+30) G, BCS Codes: BCS-BB66887, BSC-AK65185, BCS-AF80757, Sample description: TOX10332-00, Specification No.: 102000008429, Material No.: 06268129, Batch ID: EFKM002637, active ingredients (analysed content): 0.218 % w/w (2.174 g/L) iodosulfuron-methyl-sodium (AE F115008); 1.04 % w/w (10.33 g/L) mesosulfuron-methyl (AE F130060), 2.98 % w/w (29.71 g/L) mefenpyr-diethyl (AE F107892), density (20 °C): 0.966 g/mL; water solubility: dispersible.

Adult earthworms (*Eisenia fetida,* about 4 months old) were exposed to 10 – 17 – 28 – 46 – 76 – 127 – 211 - 350 mg test item/kg dry weight (d.w.) of soil containing 68.5% quartz sand, 20% kaolin clay, 10% sphagnum peat, 1% food and 0.5% $CaCO_3$, at 18.0 – 21.7 °C and a photoperiod: light : dark = 16 h : 8 h (530 lx) and were fed with horse manure. Mortality and biomass change were determined after 4 weeks and reproduction was determined after 8 weeks.

Toxic standard: 5 and 10 mg Nutdazim 50 FLOW/kg soil d.w.; control: untreated, solvent control: none.

Dates of work: November 19, 2013 – January 14, 2014

Findings:

Table 10.6.3- 1: Effects on mortality, growth and reproduction of the earthworms

Test item **Test object** **Exposure**	Iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl OD 42 (2+10+30) G *Eisenia fetida* Artificial soil		
	Mortality	**Biomass change**	**Reproduction**
	[mg test item/kg d.w.]		
NOEC LOEC	≥ 350 > 350	≥ 350 > 350	76 127
EC_{10} [1)] (95% confidence limits)	-	-	60 (52 – 69)
EC_{20} [1)] (95% confidence limits)	-	-	87 (78 – 96)

[1)] based on Probit analysis

Observations:

Table 10.6.3- 2: Effects on mortality, growth and reproduction of the earthworms

Iodosulfuron-methyl-sodium + mesosulfuron-methyl + mefenpyr-diethyl OD 42 (2+10+30) G [mg test item/kg d.w.]									
	Control	**10**	**17**	**28**	**46**	**76**	**127**	**211**	**350**
Mortality of adult worms after 4 weeks									
Mortality	1.3	0.0	0.0	5.0	0.0	2.5	0.0	2.5	2.5
Biomass change (change in fresh weight after 4 weeks relative to initial fresh weight)									
Mean (mg)	139.6	149.9	141.0	127.7	145.0	140.4	137.6	134.1	121.3
Mean (%)	33.9	36.5	34.1	31.1	35.3	34.2	33.4	32.8	29.3
Number of juveniles per surviving adult worm after 8 weeks									
Mean	13.3	13.3	13.7	13.0	12.7	11.4	8.5	5.7	2.6
Number of juveniles per replicate after 8 weeks									
Mean	131.8	132.5	136.5	123.8	127.0	110.8	85.3*	55.3*	25.8*
Reproduction compared to control (%)									
% to control	100	100.6	103.6	93.9	96.4	84.1	64.7	41.9	19.5

No statistically significant differences between the control and test item were calculated for mortality and biomass (Fisher's Exact Binomial Test with Bonferroni Correction, α = 0.05, one-sided greater)
* statistically significantly different compared to control for reproduction (Williams-t-test, α = 0.05, one-sided smaller)

Validity criteria:

- Adult mortality: ≤ 10 % (being 1.3 % after 4 weeks)
- Number of juveniles per replicate: ≥ 30 (being 126, 148, 111, 165, 102, 151, 132 and 119 for replicate 1, 2, 3, 4, 5, 6, 7 and 8)
- Coefficient of variation of reproduction: ≤ 30 % (being 16.4 %)

In a reference test, the number of juveniles was reduced by 39 and 100 % by the toxic standard Nutdazim 50 FLOW (Carbendazim, SC 500) at concentrations of 5 and 10 mg product/kg soil dws in comparison to the control. Therefore, the observed effects assure a high sensitivity of the test system.

Conclusion:

Formulation IMS + MSM + MPR OD 42 showed no statistically significantly adverse effects on mortality and biomass of the earthworm *Eisenia fetida* in artificial soil up to and including 350 mg test item/kg soil dry weight, i.e. the highest concentration tested. The test item showed statistically significantly adverse effects on reproduction at 127, 211 and 350 mg test item/kg soil d.w. Therefore, the overall No-Observed-Effect-Concentration (NOEC) was determined to be 76 mg test item/kg soil d.w., and the overall Lowest-Observed-Effect-Concentration (LOEC) was determined to be 127 mg test item/kg soil d.w.

IIIA 10.6.4 Field tests

Considering the findings reported above no further studies are required.

IIIA 10.6.5 Residue content of earthworms

According to the "Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC", SANCO/4145/2000 (2002) a log $P_{ow} > 3$ is used to indicate that there might be a potential for bioaccumulation. For information on the residue content of earthworms please refer to IIIA 10.1.9.

IIIA 10.6.6 Effects on other non-target macro-organisms

Ecotoxicological endpoints used in risk assessment

Table 10.6.6- 1: Endpoints of the formulation IMS + MSM + MPR OD 42 used in risk assessment

Test substance	Test organism	Study type	Endpoint [mg/kg dws]	Reference
	Other non-target macro-organisms, chronic			
IMS + MSM + MPR OD 42	*Hypoaspis aculeifer*	reproduction, 14 d (5% peat in test soil) test item mixed into soil	NOEC 316	[redacted] (2011) M-404679-01-1 KIIIA 10.6.6/01
	Folsomia candida	reproduction, 28 d (5% peat in test soil) test item mixed into soil	NOEC 17	[redacted] (2011) M-407706-01-1 KIIIA 10.6.6/02

dws = dry weight soil

Table 10.6.6- 2: Endpoints of the active substance mesosulfuron-methyl and metabolites used in risk assessment

Test substance	Test organism	Study type	Endpoint [mg/kg dws]	References
Other non-target macro-organisms, chronic				
Mesosulfuron-methyl	*Hypoaspis aculeifer*	reproduction, 14 d (5% peat in test soil), test item mixed into soil	NOEC ≥1000	[redacted] (2012) M-429376-01-1 KCA 8.4.2.1/01
	Folsomia candida	reproduction, 28 d (5% peat in test soil), test item mixed into soil	NOEC ≥1000	[redacted] (2012) M-426538-01-1 KCA 8.4.2.1/02
AE F154851	*Folsomia candida*	reproduction, 28 d (5% peat in test soil), test item mixed into soil	NOEC ≥ 100	[redacted] (2013) M-462785-01-1 KCA 8.4.2.1/03
AE F160459	*Folsomia candida*	reproduction, 28 d (5% peat in test soil), test item mixed into soil	NOEC ≥ 100	[redacted] (2013) M-462786-01-1 KCA 8.4.2.1/04
AE F092944	*Hypoaspis aculeifer*	reproduction, 14 d (5% peat in test soil), test item mixed into soil	NOEC ≥ 100	[redacted] 2013) M-454043-01-1 KCA 8.4.2.1/05
	Folsomia candida	reproduction, 28 d (5% peat in test soil), test item mixed into soil	NOEC ≥ 100	[redacted] (2013) M-451142-01-1 KCA 8.4.2.1/06
AE F147447	*Folsomia candida*	reproduction, 28 d (5% peat in test soil), test item mixed into soil	NOEC ≥ 100	[redacted] (2013) M-462782-01-1 KCA 8.4.2.1/07

dws = dry weight soil

All above endpoints used in risk assessment are consistent with the *proposed* EU endpoints listed in Document N2 for mesosulfuron-methyl.

Predicted Environmental Concentrations used in risk assessment

Please refer to Point IIIA 10.6.1

Toxicity exposure ratios for non-target soil meso- and macrofauna (other than earthworms)

Ecotoxicological endpoints and PEC_{soil} values used for TER calculations for soil non-target macro-organisms are summarised below. TER values were calculated using the equation:

$$TER = NOEC / PEC_{soil}$$

The risk is considered acceptable if the TER is >5.

Table 10.6.6- 3: TER_{LT} calculations (formulated product) for soil macro-organisms other than earthworms

Crop / Compound	Species	Endpoint [mg/kg soil]		PEC_{max} [mg/kg soil]	TER_{LT}	Trigger
Winter wheat, 1× 1.5 L prod./ha						
IMS + MSM + MPR OD 42	*Hypoaspis aculeifer*	NOEC	316	1.00	316	5
	Folsomia candida	NOEC	17	1.00	17	
Winter rye, 1× 0.6 L prod./ha						
IMS + MSM + MPR OD 42	*Eisenia fetida*	NOEC	316	0.400	790	5
	Folsomia candida	NOEC	17	0.400	42.5	

Table 10.6.6- 4: TER_{LT} calculations (active substance mesosulfuron-methyl and metabolites) for soil macro-organisms other than earthworms

a) risk assessment based on PEC values of originally submitted simulation

Crop / Compound	Species	Endpoint [mg/kg dws]		$PEC_{soil,max/accu}$ [mg/kg]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*Hypoaspis aculeifer*	NOEC	≥ 1000	0.011	≥ 90 909	5
	Folsomia candida	NOEC	≥ 1000	0.011	≥ 90 909	
AE F154851	*Folsomia candida*	NOEC	≥ 100	0.002	≥ 50 000	
AE F160459	*Folsomia candida*	NOEC	≥ 100	0.001	≥ 100 000	
AE F092944	*Hypoaspis aculeifer*	NOEC	≥ 100	< 0.001	> 100 000	
	Folsomia candida	NOEC	≥ 100	< 0.001	> 100 000	
AE F147447	*Folsomia candida*	NOEC	≥ 100	< 0.001	> 100 000	
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*Hypoaspis aculeifer*	NOEC	≥ 1000	0.004	≥ 250 000	5
	Folsomia candida	NOEC	≥ 1000	0.004	≥ 250 000	
AE F154851	*Folsomia candida*	NOEC	≥ 100	< 0.001	> 100 000	
AE F160459	*Folsomia candida*	NOEC	≥ 100	< 0.001	> 100 000	
AE F092944	*Hypoaspis aculeifer*	NOEC	≥ 100	< 0.001	> 100 000	
	Folsomia candida	NOEC	≥ 100	< 0.001	> 100 000	
AE F147447	*Folsomia candida*	NOEC	≥ 100	< 0.001	> 100 000	

b) risk assessment based on PEC values of alternative simulation using RMS requested parameters

Crop / Compound	Species	Endpoint [mg/kg dws]		$PEC_{soil,max/accu}$ [mg/kg]	TER_{LT}	Trigger
Winter wheat, 1 × 15 g a.s./ha						
Mesosulfuron-methyl	*Hypoaspis aculeifer*	NOEC	≥ 1000	0.020	≥ 50 000	5
	Folsomia candida	NOEC	≥ 1000	0.020	≥ 50 000	
AE F154851	*Folsomia candida*	NOEC	≥ 100	0.004	≥ 25 000	
AE F160459	*Folsomia candida*	NOEC	≥ 100	0.002	≥ 50 000	
AE F092944	*Hypoaspis aculeifer*	NOEC	≥ 100	< 0.001	> 100 000	
	Folsomia candida	NOEC	≥ 100	< 0.001	> 100 000	
AE F147447	*Folsomia candida*	NOEC	≥ 100	0.002	> 50 000	
Winter rye, 1 × 6 g a.s./ha						
Mesosulfuron-methyl	*Hypoaspis aculeifer*	NOEC	≥ 1000	0.008	≥ 125 000	5
	Folsomia candida	NOEC	≥ 1000	0.008	≥ 125 000	
AE F154851	*Folsomia candida*	NOEC	≥ 100	0.001	≥ 100 000	
AE F160459	*Folsomia candida*	NOEC	≥ 100	< 0.001	> 100 000	
AE F092944	*Hypoaspis aculeifer*	NOEC	≥ 100	< 0.001	> 100 000	
	Folsomia candida	NOEC	≥ 100	< 0.001	> 100 000	
AE F147447	*Folsomia candida*	NOEC	≥ 100	< 0.001	> 100 000	

Conclusion: The TER_{LT} values meet the required trigger of 5, indicating an acceptable long-term risk for soil non-target macro-organisms other than earthworms, i.e. collembola and soil mites.

Effects on other soil non-target macro-organisms

Report:	[redacted] b; [redacted] ;2011;M-404679-01
Title:	Iodosulfuron-methyl-sodium + mesosulfuron-methyl-sodium + mefenpyr-diethyl OD 42 (2+10+30) G: Influence on mortality and reproduction on the soil mite species Hypoaspis aculeifer tested in artifical soil
Report No:	KRA-HR-48/11
Document No:	M-404679-01-1
Guidelines:	**OECD 226 from October 03, 2008; OECD guideline for the Testing of Chemicals - Predatory mite (Hypoaspis (Geolaelaps) aculeifer) reproduction test in soil;none**
GLP/GEP:	**yes**

Objective:

The purpose of the study was to assess the effects of formulation IMS + MSM + MPR OD 42 (2+10+30) G on mortality and reproduction on the soil mite species *Hypoaspis aculeifer* tested during an exposure of 14 days in artificial soil comparing control and treatment. The test was performed according to the recommendations of the OECD Guideline 226 (2008).

Material and methods:

Test item: Iodosulfuron-methyl-sodium + mesosulfuron-methyl-sodium + mefenpyr-diethyl OD 42 (2+10+30) G; (Bach ID: 2009-009105; Specification No.: 102000008429 - 07; Sample description: TOX 08886-00; Master recipe ID: 0102735-001; content: 1.985 g iodosulfuron-methyl-sodium/L (0.198 %w/w); 10.55 g mesosulfuron-methyl-sodium/L (1.05 %w/w); 29.80 g mefenpyr-diethyl/L (2.97 %w/w); density: 1.002 g/mL.
Ten adult, fertilized, female *Hypoaspis aculeifer* per replicate (8 control replicates and 4 replicates for each test item concentration) were exposed to control and treatments. Concentrations of 100, 178, 316, 562 and 1000 mg test item/kg dry weight artificial soil were tested. In each test vessel 20 g dry weight artificial soil were weighed in. The *Hypoaspis aculeifer* were of a uniform age not differing more than three days (28 days after start of egg laying). During the test, they were fed with cheese mites bred on brewer's yeast and with nematodes bred on watered oat flakes. During the study a temperature of 20 ± 2 °C and light regime of 400 – 800 Lux, 16 h light : 8 h dark was applied. The artificial soil was prepared according to the guideline with the following constituents (percentage distribution on dry weight basis): 74.8 % fine quartz sand, 5% *Sphagnum* peat, air dried and finely ground, 20 % Kaolin clay and approximately 0.17 % Calcium carbonate ($CaCO_3$).
After a period of 14 days, the surviving adults and the living juveniles were extracted by applying a temperature gradient using a MacFadyen-apparatus. Extracted mites were collected in a fixing solution (20 % ethylene glycol, 80 % deionised water; 2 g detergent/L fixing solution were added). All *Hypoaspis aculeifer* were counted under a binocular.

Findings:

Table 10.6.6- 5: Percent mortality and reproduction of adult, female *Hypoaspis aculeifer* after 14 days

Test item Test object Exposure	Iodosulfuron-methyl-sodium + mesosulfuron-methyl-sodium + mefenpyr-diethyl OD 42 (2+10+30) G *Hypoaspis aculeifer* Artificial soil		
	% mortality (Adults)	Mean number of juveniles per test vessel ± standard dev.	Reproduction (% of control)
Control	2.5	345.3 ± 30.8	-
100	17.5	300.0 ± 81.2	86.9
178	0.0	385.7 ± 12.2	111.7
316	0.0	292.7 ± 24.9	84.8
562	35.0	28.8 * ± 12.6	8.3
1000	100	0.0 * ± 0.0	0
			Reproduction
NOEC (mg test item/kg dry weight artificial soil)			316
LOEC (mg test item/kg dry weight artificial soil)			562

* statistical significance (Welch-t test for inhomogeneous variances with Bonferroni-Holm adjustment one-sided smaller, α = 0.05)

Observations:

Validity of the study:

Table 10.6.6- 6: Validity criteria

Validity criteria	Recommended by the guideline	Obtained in this study
Mean adult mortality	≤ 20%	2.5%
Mean number of juveniles per replicate (with 10 adult females introduced)	≥ 50	345.3
Coefficient of variation calculated for the number of juvenile mites per replicate	≤ 30%	8.9%

All validity criteria were met. Therefore this study is valid.

Mortality

In the control group 2.5 % of the adult *Hypoaspis aculeifer* died which is below the allowed maximum of ≤ 20 % mortality. The LC_{50} was calculated to be 609 mg test item/kg dry weight artificial soil. Confidence limits could not be calculated.

Reproduction

Concerning the number of juveniles statistical analysis (Welch-t test for inhomogeneous variances with Bonferroni-Holm adjustment, one-sided smaller, α = 0.05) revealed no significant difference between control and all concentrations up to 316 mg test item/kg dry weight artificial soil. Therefore the No-Observed-Effect-Concentration (NOEC) for reproduction is 316 mg test item/kg dry weight artificial soil. The Lowest-Observed-Effect-Concentration (LOEC) for reproduction is 562 mg test item/kg dry weight artificial soil. Probit analysis revealed an EC_{50}-value of 404 mg test item/kg dry weight artificial soil with 95 % confidence limits of 317 and 646 mg test item/kg dry weight artificial soil.

Conclusions:

NOEC: 316 mg test item/kg dry weight artificial soil.
LOEC: 562 mg test item/kg dry weight artificial soil.

Report:	[redacted] g; [redacted] ;2011;M-407706-01
Title:	Iodosulfuron-methyl-sodium + mesosulfuron-methyl-sodium + mefenpyr-diethyl OD 42 (2+10+30) G: Influence on the reproduction of the collembolan species Folsomia candida tested in artificial soil
Report No:	FRM-COLL-113/11
Document No:	M-407706-01-1
Guidelines:	**OECD 232 adopted, September 07, 2009: OECD Guidelines for Testing Chemicals - Collembolan Reproduction Test in Soil;minor deviations**
GLP/GEP:	**yes**

Objective:

The purpose of this study was to assess the effect of formulation IMS + MSM + MPR OD 42 (2+10+30) G on survival and reproduction of the collembolan species *Folsomia candida* during an exposure of 28 days in an artificial soil comparing control and treatment. The test was performed according to the recommendations of the OECD Guideline 232 (2009).

Material and methods:

Iodosulfuron-methyl-sodium + mesosulfuron-methyl-sodium + mefenpyr-diethyl OD 42 (2+10+30) G (analytical findings: iodosulfuron-methyl-sodium 1.985 g/L corresponding to 0.198 % w/w, mesosulfuron-methyl-sodium 10.55 g/L corresponding to 1.05 % w/w, mefenpyr-diethyl 29.80 g/L corresponding to 2.97 % w/w, density: 1.002 g/mL, batch ID.: 2009-009105, master recipe ID: 0102735-001, specification no.: 102000008429-07, sample description: TOX08886-00.
Since the first test run on the test item did not provide a final result, a second test run was performed studying lower test concentrations. 10 collembolans (10-12 days old) per replicate (8 replicates for the control group and 4 replicates for the treatment group) were exposed to control (water treated), 100, 178, 316, 562 and 1000 mg test item/kg artificial soil dry weight in the 1st test run and 10, 17, 30, 52 and 90 mg test item/kg artificial soil dry weight in the 2nd test run at 20 ± 2°C, 400 – 800 lux, 16h light: 8h dark. During the study, they were fed with granulated dry yeast.
Mortality and reproduction were determined after 29 days (1st run) and 28 days (2nd run).

Findings

Table 10.6.6- 7: Percent mortality and reproduction of adult *Folsomia candida* after 4 weeks treatment

Test item Test object Exposure	**Iodosulfuron-methyl-sodium + mesosulfuron-methyl-sodium + mefenpyr-diethyl OD 42 (2+10+30) G *Folsomia candida* Artificial soil**		
mg test item/kg soil dry weight	Adult mortality (%)	Mean number of juveniles±SD	Reproduction (% of control)
1st test run			
Control	5	1432.4 ± 159.6	
1000	100	0 ± 0	0 *B
562	100	0 ± 0	0 *B
316	100	0 ± 0	0 *B
178	55	180.8 ± 32.6	13 *B
100	7.5	1189.3 ± 68.0	83 *B
2nd test run			
Control	2.5	1567 ± 166	
90	2.5	1295 ± 63	83 *W
52	2.5	1336 ± 160	85 *W
30	17.5	1369 ± 59	87 *W
17	7.5	1498 ± 48	96 n.s.
10	0	1585 ± 73	101 n.s.
$NOEC_{reproduction}$ (mg test item/kg soil dry weight) $LOEC_{reproduction}$ (mg test item/kg soil dry weight)			17 30

The calculations were performed with un-rounded values
*B = statistically significant (Bonferroni-U test one-sided-smaller, α = 0.05)
*W = statistically significant (William's-t test one-sided-smaller, α = 0.05)
n.s. = statistically not significant (William's-t test one-sided-smaller, α = 0.05)

Observations:

Validity of the study:

Validity Criteria for the untreated control of the study according OECD 232 from September 07, 2009.

Table 10.6.6- 8: Validity criteria

Validity criteria	**Recommended by the guideline**	**Obtained in this study**	
		1st run	2nd run
Mean adult mortality	≤ 20%	5%	2.5%
Mean number of juveniles per replicate (with 10 collembolans introduced)	≥ 100	1432	1567
Coefficient of variation calculated for the number of juveniles per replicate	≤ 30%	11.1%	10.6%

All validity criteria were met. Therefore this study is valid.

Mortality:

In the control group 5 % (1st run) and 2.5 % (2nd run) of the adult *Folsomia candida* died which is below the allowed maximum of ≤ 20 % mortality. The highest mortality rate of 100 % was observed in the treatment group from 316 up to 1000 mg test item/kg artificial soil dry weight.

Reproduction:
Concerning the number of juveniles statistical analysis (Bonferroni-U test, one-sided smaller, α = 0.05) revealed statistically significant differences between the control and all treatment groups in the 1st test run. In the 2nd test run statistical analysis (William's-t Test, one sided smaller, α = 0.05) revealed statistically significant differences from 30 up to 90 mg test item/kg artificial soil dry weight. Therefore the No-Observed-Effect-Concentration (NOEC) for reproduction is 17 mg test item/kg artificial soil dry weight. The Lowest-Observed-Effect-Concentration (LOEC) for reproduction is 30 mg test item/kg artificial soil dry weight.

Conclusions:

$NOEC_{reproduction}$: 17 mg test item/kg artificial soil dry weight.
$LOEC_{reproduction}$: 30 mg test item/kg artificial soil dry weight.

IIIA 10.6.7 Effects on organic matter breakdown

A study on the organic matter breakdown is not required based on the DT_{90f} value of the active substance and acceptable TER values for earthworms, soil macro-organisms and/or soil micro-organisms.

IIIA 10.7 Effects on soil microbial activity

Ecotoxicological endpoints used in risk assessment

Table 10.7- 1: Endpoints of the formulation IMS + MSM + MPR OD 42 used in risk assessment

Test item	Test design	Ecotoxicological endpoint		Reference
	N-transformation			
IMS + MSM + MPR OD 42	42 d	no unacceptable effects	≥ 7.5 L prod./ha ≥ 10 µL prod./kg dws	[redacted] (2003) M-222656-01-1 KIIIA 10.7.1/01

dws = dry weight soil

Table 10.7- 2: Endpoints of the active substance mesosulfuron-methyl and metabolites used in risk assessment

Test item	Test design	Ecotoxicological endpoint		Reference
N-transformation				
Mesosulfuron-methyl	28 d	no unacceptable effects	≥0.1 mg a.s./kg dws	[redacted] (1998) M-143358-01-1 KCA 8.5/01
AE F154851	28 d	no unacceptable effects	≥0.1 mg/kg dws	[redacted] (2002) M-214090-01-1 KCA 8.5/02
AE F160459	28 d	no unacceptable effects	≥0.1 mg/kg dws	[redacted] (2002)

				M-214086-01-1 KCA 8.5/03
AE F099095	28 d	no unacceptable effects	≥0.1 mg/kg dws	[redacted] (2002) M-214088-01-1 KCA 8.5/04
AE F092944	28 d	no unacceptable effects	≥0.137 mg/kg dws	[redacted] (2013) M-453511-01-1 KCA 8.5/09
AE F147447	28 d	no unacceptable effects	≥0.057 mg/kg dws	[redacted] (2013) M-460668-01-1 KCA 8.5/10

dws = dry weight soil

All above endpoints used in risk assessment are consistent with the *proposed* EU endpoints listed in Document N2 for mesosulfuron-methyl.

Predicted Environmental Concentrations used in risk assessment

Please refer to Point IIIA 10.6.1

Risk assessment for soil nitrogen transformation

According to current regulatory requirements the risk is considered acceptable if the effect on nitrogen mineralisation at the recommended application rate of a compound/product is ≤ 25% after 100 days.

In no case did deviations from the control exceed the threshold level of 25% at 28 days after application. The tested concentrations by far exceeded the maximum predicted environmental concentrations in soil of the respective components. This indicates acceptable risk to soil micro-organisms for the intended uses of formulation IMS + MSM + MPR OD 42.

IIIA 10.7.1 Laboratory testing

Report:	[redacted]d; [redacted];2003;M-222656-01
Title:	Mesosulfuron-methyl & iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 10 + 2 + 30 (AE F115008 06 OD04 A104): Determination of effects on nitrogen transformation in soil
Report No:	C037340
Document No(s):	M-222656-01-1
Guidelines:	**OECD: 216;Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the effects of formulation IMS + MSM + MPR OD 42 (Atlantis® OD, AE F115008 06 OD04 A104) on microbial nitrogen-turnover in soil. The study was designed to meet OECD criteria.

Material and Methods

A silty sand with 57 % sand content, 0.6 % organic carbon and a microbial biomass of 8.7 % of organic carbon was amended with 5 g lucerne meal per kg dry soil with a C/N ratio of 16/1. The soil was stored at 20 ± 1°C. The pH before test start was 5.5. The following treatment levels were tested: 1.5 and 7.5 L product/ha with addition of an untreated control. 3 replicates were used per treatment level.

Findings

Although deviations from the control were < 25% at day 28, the test was inadvertently prolonged up to day 42. pH varied between 5.5 and 5.7 during the test. Percentual deviations from the control were observed as follows:

Table 10.7.1- 1: Rates of nitrogen transformation / day: % difference between nitrate-N rates per day of control and treated soil samples

L product/ha	Day 0 - 7	Day 7 - 14	Day 14 - 28	Day 28 - 42
1.5	+2	-7	+4	-3
7.5	+23	+5	+7	+5

Conclusion

The formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) has no impact on microbial nitrogen turnover in soil when applied at field rate and has no impact on microbial nitrogen turnover in soil when applied at 5-times field rate.

IIIA 10.7.2 Additional testing

According to the previous results (see Point 10.7.), no further laboratory testing on soil non-target micro-organisms was considered necessary.

IIIA 10.8 Effects on non-target plants

IIIA 10.8.1 Terrestrial plants

Ecotoxicological endpoints used in risk assessment

For herbicides and plant growth regulators, it is considered unprofitable to conduct tier 1 studies as it is inevitable that these will lead to tier 2 or dose response studies in order to generate data suitable for deterministic or probabilistic risk assessments, i.e. ER_{50} values for 6-10 species, representing a broad range of plant species. The endpoints from the tier 2 studies on formulation IMS + MSM + MPR OD 42 are summarised in following table.

Table 10.8.1- 1: Endpoints of the formulation IMS + MSM + MPR OD 42 used in risk assessment

Number of species tested (species)	Test method Test substance Application rate	Effects	Reference
Dicotyledoneae: 7 (sugar beet, oilseed rape, radish, cucumber, sunflower, soybean, tomato) Monocotyledoneae: 3 (onion, oat, corn)	Tier 2 vegetative vigour IMS + MSM + MPR OD 42 0 (control), 1.5, 0.75, 0.375, 0.188 and 0.094 L prod./ha for corn and oats 0 (control), 0.188, 0.094, 0.047, 0.023 and 0.011 L prod./ha for sugar beet, oilseed rape, radish, cucumber, sunflower, soybean, tomato and onion with visual phytotoxicity ratings and assessments of mortality on Days 7, 14 and 21, dry weight measurements on Day 21	most sensitive species: sunflower; **lowest EC_{50}: 0.027 L prod./ha**	[redacted] (2004) M-226821-01-1 KIIIA 10.8.1.2/01
Dicotyledoneae: 7 (sugar beet, oilseed rape, radish, cucumber, sunflower, soybean, tomato) Monocotyledoneae: 3 (onion, oat, corn)	Tier 2 seedling emergence IMS + MSM + MPR OD 42 0 (control), 1.5, 0.75, 0.375, 0.188 and 0.094 L prod./ha for corn and oats 0 (control), 0.375, 0.188, 0.094, 0.047 and 0.023 L prod./ha for sugar beet, oilseed rape, radish, cucumber, sunflower, soybean, tomato and onion with daily assessments of germination until 65% emergence of control seedlings, visual phytotoxicity ratings and assessments of number of plants on Days 7 and 14 and 19-21 after emergence of 50% of control seeds; assessments of mortality and measurement of dry weight on Day 21	most sensitive species: onion; **lowest EC_{50}: 0.064 L prod./ha**	[redacted] (2004) M-226820-01-1 KIIIA 10.8.1.3/01

Exposure situation considered for risk assessment

Effects on non-target plants are of concern in the off-field environment, where they may be exposed to spray drift. The amount of spray drift reaching off-crop habitats is calculated using the 90th percentile estimates derived by the *BBA (2000)*[7] from the spray-drift predictions of *Ganzelmeier & Rautmann*

[7] BBA (2000) Bundesanzeiger Jg. 52 (Official Gazette), Nr 100, S. 9879-9880 (25.05.2000) Bekanntmachung über die Abtrifteckwerte, die bei der Prüfung und Zulassung von Pflanzenschutzmitteln herangezogen werden. Public domain.

(2000)[8]. For a single application to cereals, 2.77% of the application rate was assumed to reach areas at the edge of the crop (0 meter buffer zone; worst-case scenario). For a 5 m buffer zone a drift rate of 0.57% is assumed. For a 10 m buffer zone a drift rate of 0.29% is assumed.
According Table 10-1, the maximum label rate of IMS + MSM + MPR OD 42 is 1.5L product/ha for use in winter wheat, or 0.6 L product/ha for use in winter rye.

Risk assessment for Terrestrial Non-Target Higher Plants

The risk assessment is based on the "Guidance Document on Terrestrial Ecotoxicology", (SANCO/10329/2002 rev2 final, 2002). It is restricted to off-field situations, as non-target plants are non-crop plants located outside the treated area. Spray drift from the treated areas may lead to residues of a product in off-crop areas.

Deterministic Risk assessment
According to the Terrestrial Guidance Document[9], the risk to non-target plants is evaluated by comparing the lowest ER_{50} observed in the laboratory studies with the drift rates ($PER_{off\text{-}field}$) inclosing a safety factor of 5. In addition, the usage of drift reducing nozzles is considered.

Table 10.8.1- 2: Deterministic risk assessment for the formulation IMS + MSM + MPR OD 42 based on effects on seedling emergence

Distance	Drift	PER	Endpoint	TER [trigger = 5]			
[m]	(%)	no drift reduction [mL product/ha]	lowest ER_{50} [mL product/ha]	No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
Winter wheat, 1× 1500 mL prod./ha							
1	2.77	41.55	64	**1.54**	**3.08**	6.16	15.40
5	0.57	8.55	64	7.49	14.97	29.94	74.85
10	0.29	4.35	64	14.71	29.43	58.85	147.13
Winter rye, 1× 600 mL prod./ha							
1	2.77	16.62	64	**3.85**	7.70	15.40	38.51
5	0.57	3.42	64	18.71	37.43	74.85	187.13
10	0.29	1.74	64	36.78	73.56	147.13	367.82

[8] Ganzelmeier H., Rautmann D. (2000) Drift, drift-reducing sprayers and sprayer testing. Aspects of Applied Biology 57, 2000, Pesticide Application. Public domain.
[9] Anonymous (2002b). Guidance Document on terrestrial ecotoxicology under council directive 91/414/EEC. SANCO/10329/2002. 17 October 2002.

Table 10.8.1- 3: Deterministic risk assessment for the formulation IMS + MSM + MPR OD 42 based on effects on vegetative vigour

Distance	Drift	PER	Endpoint	TER [trigger = 5]			
[m]	(%)	no drift reduction [mL product/ha]	lowest ER_{50} [mL product/ha]	No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
Winter wheat, 1× 1500 mL prod./ha							
1	2.77	41.55	27	**0.65**	**1.30**	**2.60**	6.50
5	0.57	8.55	27	**3.16**	6.32	12.63	31.58
10	0.29	4.35	27	6.21	12.41	24.83	62.07
Winter rye, 1× 600 mL prod./ha							
1	2.77	16.62	27	**1.62**	**3.25**	6.50	16.25
5	0.57	3.42	27	7.89	15.79	31.58	78.95
10	0.29	1.74	27	15.52	31.03	62.07	155.17

According to the results of the deterministic approach involving the most sensitive endpoint in the vegetative vigour study (shoot dry weight of sunflower) the following conclusions can be drawn:

- For one application of 1.5 L product/ha to winter wheat, the trigger of 5 at 1 m distance is only exceeded if nozzles with at least 90% drift reduction are used. Alternatively, 50% drift reduction and a 5 m buffer zone could be applied to mitigate the risk. Considering a distance of 10 m, no drift reducing nozzles are necessary.

- For one application of 0.6 L product/ha to winter rye, the trigger of 5 at 1 m distance is only exceeded if nozzles with at least 75% drift reduction are used. Considering a distance of 5 m, no drift reducing nozzles are necessary.

The results of the deterministic risk assessment for vegetative vigour indicate the necessity of mitigation measures. However, as an alternative approach a probabilistic risk assessment has been conducted.

Probabilistic Risk assessment

In addition to the deterministic risk assessment the Terrestrial Guidance Document recommends the use of the HC_5 (the concentration below which less than 5% of the species will be harmed above the EC_{50} level) which can be calculated from the data sets of ER_{50} growth inhibition levels. The EU guidance document for terrestrial ecotoxicology states: "If the ED_{50} 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 HC_5 itself (TER =1) can be regarded to be protective.
The HC_5 was calculated according to

HC_5 = 10 exp(avg-ks*std)

With
avg = mean of log10 transformed EC_{50} values
std = standard deviation of log10 transformed EC_{50} values
ks = extrapolation factor

Although there is no common agreement whether to exclude "greater-than"- figures from the HC_5-calculation or to include them as "equal to"-figures, the exclusion of "greater than"-figures can be regarded as a very conservative approach. Moreover, it has to be decided, whether the HC_5 is calculated with EC_{50} for dry weight only (the lowest endpoint in most species) or with the lowest EC_{50}.

Table 10.8.1- 4: HC_5-figures obtained from different calculation modes for seedling-emergence and vegetative vigour. Lowest figures are printed in bold

HC_5	Seedling emergence [L product/ha]	Vegetative vigour [L product/ha]
HC_5 based on dry weight data from all species	0.079	0.021
HC_5 based on dry weight data after exclusion of greater-than-figures	0.072	0.018
HC_5 based on lowest endpoint from all species	0.071[1)]	0.021[3)]
HC_5 based on lowest endpoint from all species after exclusion of greater-than-figures	0.057[2)]	**0.016**[4)]

1) With the exception of corn and oats (EC_{50} for survival) and onion (EC_{50} of emergence) same figures as for dry weight, since the dryweight-EC_{50} was the lowest endpoint for all other species than corn, oats and onion.

2) With the exception of corn and oats (EC_{50} for survival) and onion (EC_{50} of emergence) same figures as for dry weight, since the dryweight-EC_{50} was the lowest endpoint for all other species than corn, oats and onion. As the EC_{50} of corn and oats (EC_{50} for survival) and soybean (EC_{50} for shoot dry weight) are "greater than"-figures, these figures were excluded for calculation.

3) With the exception of cucumber (EC_{50} for survival) same figures as for dry weight, since the dryweight-EC_{50} was the lowest endpoint for all other species than cucumber.

4) With the exception of cucumber same figures as for dry weight, since the dryweight-EC_{50} was the lowest endpoint for all other species than cucumber. As the EC_{50} of cucumber (EC_{50} for survival) and onion (EC_{50} for shoot dry weight) are "greater than"-figures, these figures were excluded for calculation.

Based on the calculations presented in Table 10.8.1- 4 the lowest HC_5-levels were taken as a most conservative approach. The following probabilistic risk assessment has been conducted with the vegetative vigour data only, since the HC_5 is considerably lower than for seedling emergence. The TER calculation is summarised in the following table; a trigger value of 1 is applied for acceptable risk in case of the HC_5.

Table 10.8.1- 5: Probabilistic risk assessment for the formulation IMS + MSM + MPR OD 42 based on effects on vegetative vigour

Distance	Drift	PER	Endpoint	TER [trigger = 1]			
[m]	(%)	no drift reduction [mL product/ha]	HC5 based on ER_{50} [mL product/ha]	No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
Winter wheat, 1× 1500 mL prod./ha							
1	2.77	41.55	16	**0.39**	**0.77**	1.54	3.85
5	0.57	8.55	16	1.87	3.74	7.49	18.71
10	0.29	4.35	16	3.68	7.36	14.71	36.78
Winter rye, 1× 600 mL prod./ha							
1	2.77	16.62	16	**0.96**	1.93	3.85	9.63
5	0.57	3.42	16	4.68	9.36	18.71	46.78
10	0.29	1.74	16	9.20	18.39	36.78	91.95

Based on the results of the probabilistic risk assessment involving the lowest endpoints of all species (after exclusion of all greater-than figures) of the vegetative vigour test the following conclusions can be drawn:

- For one application of 1.5 L product/ha to winter wheat, the trigger of 1 at 1 m distance is exceeded if nozzles with at least 75% drift reduction are used. Considering a distance of 5 m, no drift reducing nozzles are necessary.

- For one application of 0.6 L product/ha to winter rye, the trigger of 1 at 1 m distance is exceeded if nozzles with at least 50% drift reduction are used. Considering a distance of 5 m, no drift reducing nozzles are necessary.

Conclusion

Overall, it can be concluded that terrestrial non-target plants are not at risk when the product is applied in winter wheat and winter rye at rates recommended according to good agricultural practice provided that a 5 m buffer zone is applied. Alternatively, 1 m distance is required when 75% drift reduced spray nozzles are used for the use in winter wheat and when 50% drift reduced spray nozzles are used for the use in winter rye.

IIIA 10.8.1.1 Seed germination

Please refer to Point IIIA 10.8.1.3.

IIIA 10.8.1.2 Vegetative vigour

Report:	[redacted]0;[redacted];[redacted];2004;M-226821-01
Title:	Iodosulfuron-methyl-sodium + mefenpyr-diethyl + AE F130081: oil based suspension concentrate; 2 + 30 + 10.44 g/l (Code: AE F115008 06 OD04 A104): Effects on vegetative vigour of ten species of non-target plants
Report No:	C039372
Document No:	M-226821-01-1
Guidelines:	**OECD: 208 B, (draft 2000);Deviation not specified**
GLP/GEP:	**yes**

Objective

The purpose of this specific study was to evaluate the effect of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104), a formulation of iodosulfuron-methyl-sodium, mesosulfuron-methyl and mefenpyr-diethyl on the vegetative vigour of ten plant species representing a broad range of both dicotyledonous and monocotyledonous plant families.

Material and Methods

Plants from ten species; corn (*Zea mays*), cucumber (*Cucumis sativus*), oats (*Avena sativa*), oilseed rape (*Brassica napus*), onion (*Allium cepa*), radish (*Raphanus sativus*), soybean (*Glycine max*), sugar beet (*Beta vulgaris*), sunflower (*Helianthus annuus*) and tomato (*Lycopersicum esculentum*) were sprayed with Atlantis®OD (AE F115008 06 OD04 A104) at the 2-4 leaf stage. Solutions of the product and serial dilutions were sprayed with doses of the product ranging from the maximum use rate of 1.5 L/ha down to 0.011 L/ha using a laboratory track sprayer. There were five dose rates that differed with each species. For oats and corn these were 1.5, 0.75, 0.375, 0.188 and 0.094 L/ha. For sunflower these were 0.375, 0.188, 0.094, 0.047 and 0.023 L/ha. For cucumber, oilseed rape, onion, radish, soybean, sugar beet and tomato these were 0.188, 0.094, 0.047, 0.023 and 0.011 L/ha. Plants were grown and maintained under glasshouse conditions with a temperature 23 ± 5° C during day, 18 ± 5° C at night. Assessments were made 21 days after application against the untreated controls. Statistical analysis of data was performed to obtain NOEC and EC_{50} values for survival and biomass (shoot dry weight), using probit analysis with maximum likelihood regression.

Findings

All species showed the relevant phytotoxic symptoms for the product visible as chlorosis, stunting and necrosis.
Phytotoxicity due to Atlantis®OD (AE F115008 06 OD04 A104) resulted in a suppression of growth leading to a reduction in growth as measured by growth stage in all species, except for onion, where only marginal effects were seen at the highest dose tested. In all species except for cucumber, onion and soybean, the higher dose rates tested resulted in mortality.
Radish was the most sensitive species where Atlantis®OD (AE F115008 06 OD04 A104) biomass measured as shoot dry weight was the most sensitive endpoint.
Biomass was also the most sensitive endpoint for all other species.
The table below summarises the NOEC, and where determined the EC_{25} and EC_{50} values for survival, the NOEC, and where determined the EC_{25} and EC_{50} for shoot dry weight.

Table 10.8.1.2- 1: The effect of IMS + MSM + MPR OD 42 on ten species: survival and biomass (shoot dry weight)

	Survival (L product/ha)			Shoot dry weight (L product/ha)		
	NOEC	**EC_{25}**	**EC_{50}**	**NOEC**	**EC_{25}**	**EC_{50}**
Corn	0.375	0.472	0.775	0.188	0.230	0.385
Cucumber	0.188	>0.188	>0.188	0.047	0.084	0.221
Oats	0.188	0.280	0.328	0.094	0.195	0.287
Oilseed rape	0.047	0.106	0.138	0.023	0.032	0.056
Onion	0.188	>0.188	>0.188	0.188	>0.188	>0.188
Radish	0.011	0.028	0.041	<0.011	0.011	0.038
Soybean	0.188	>0.188	>0.188	0.047	0.073	0.136
Sugar beet	0.094	0.153	0.212	0.047	0.067	0.144
Sunflower	0.047	0.080	0.099	<0.023	0.007	**0.027**
Tomato	0.188	>0.188	>0.188	0.023	0.024	0.036

Conclusion

Based on the results of this study in which formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) was tested under glasshouse conditions significant adverse effects were observed in all plant species tested, except onion. **The most sensitive species was sunflower with the lowest EC_{50} of 0.027 L product/ha for shoot dry weight.**

IIIA 10.8.1.3 Seedling emergence

Report:	[redacted];2004;M-226820-01
Title:	Iodosulfuron-methyl-sodium + mefenpyr-diethyl + AE F130081; oil based suspension concentrate: 2 + 30 + 10.44 g/l (Code: AE F115008 06 OD04 A104): Effects on seedling emergence and growth in ten species of non-target plants
Report No:	C039371
Document No:	M-226820-01-1
Guidelines:	**OECD: 208A, (2000);Deviation not specified**
GLP/GEP:	**yes**

Objective

The purpose of this specific study was to evaluate the effect of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104), a formulation of iodosulfuron-methyl-sodium, mesosulfuron-methyl and mefenpyr-diethyl on the seedling emergence and seedling growth of ten plant species representing a broad range of both dicotyledonous and monocotyledonous plant families.

Material and Methods

Seeds of ten plant species corn (*Zea mays*), cucumber (*Cucumis sativus*), oats (*Avena sativa*), oilseed rape (*Brassica napus*), onion (*Allium cepa*), radish (*Raphanus sativus*) soybean (*Glycine max*), sugar beet (*Beta vulgaris*), sunflower (*Helianthus annuus*) and tomato (*Lycopersicum esculentum*) were treated after sowing with Atlantis®OD (AE F115008 06 OD04 A104). Solutions of the product and serial dilutions were sprayed at doses ranging from the maximum use rate of 1.5 L/ha down to 0.023 L/ha using a laboratory track sprayer. There were five dose rates that differed with each species. For oats and corn these were 1.5, 0.75, 0.375, 0.188 and 0.094 L/ha. For sugar beet, oilseed rape, radish, cucumber, sunflower, soybean, tomato and onion these were 0.375, 0.188, 0.094, 0.047 and 0.023 L/ha. Plants were grown and maintained under glasshouse conditions with a temperature 23 ± 5° C day, 18 ± 5° C night.

Assessments were made 21 days after 50% emergence of control seedlings and evaluated against the untreated controls. Statistical analysis of data was performed to obtain NOEC and EC_{50} values for emergence, survival and biomass (shoot dry weight), using probit analysis with maximum likelihood regression.

Findings

All species showed the relevant phytotoxic symptoms for the product visible as chlorosis, stunting and necrosis.

Phytotoxicity due to Atlantis®OD (AE F115008 06 OD04 A104) resulted in a suppression of growth leading to a decrease in growth stage at the higher rates tested for oats, oilseed rape, onion, radish, sugar beet, sunflower and tomato. There were no reductions in growth for corn, cucumber and soybean.

Onion was the most sensitive species where Atlantis®OD (AE F115008 06 OD04 A104) also impacted emergence and survival with emergence being the most sensitive endpoint. In all other species biomass was the most sensitive endpoint. In corn, oats, oilseed rape, onion, radish, sugar beet, sunflower and tomato, EC_{50} values for biomass were obtained that were within the dose range selected for these species. For the less sensitive cucumber and soybean the calculated EC_{50} values were higher than their dose ranges.

The table below summarises the NOEC and where determined the EC_{25} and EC_{50} values for emergence and survival, and the NOEC and where determined the EC_{25} and EC_{50} for shoot dry weight.

Table 10.8.1.3- 1: The effect of IMS + MSM + MPR OD 42 on ten species:seedling emergence, survival and biomass (shoot dry weight)

	Emergence (L product/ha)			Survival (L product/ha)			Shoot dry weight (L product/ha)		
Plant species	**NOEC**	**EC_{25}**	**EC_{50}**	**NOEC**	**EC_{25}**	**EC_{50}**	**NOEC**	**EC_{25}**	**EC_{50}**
Corn	1.5	>1.5	>1.5	0.375	>0.375	>0.375	0.188	0.256	0.631
Cucumber	0.375	>0.375	>0.375	0.375	>0.375	>0.375	0.188	0.174	0.327
Oats	0.75	>0.75	>0.75	0.375	>0.375	>0.375	0.375	0.457	0.760
Oilseed rape	0.375	>0.375	>0.375	0.375	>0.375	>0.375	0.094	0.122	0.229
Onion	0.047	0.019	**0.064**	0.047	0.064	0.091	n.d.	0.117	0.133
Radish	0.375	>0.375	>0.375	0.188	>0.375	>0.375	0.047	0.074	0.136
Soybean	0.375	>0.375	>0.375	0.375	>0.375	>0.375	0.094	0.259	>0.375
Sugar beet	0.375	>0.375	>0.375	0.375	>0.375	>0.375	0.047	0.083	0.155
Sunflower	0.375	>0.375	>0.375	0.375	>0.375	>0.375	0.047	0.044	0.098
Tomato	0.375	>0.375	>0.375	0.375	>0.375	>0.375	0.188	0.269	0.326

Conclusion

Based on the results of this study in which formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) was tested under glasshouse conditions adverse effects were observed in all plant species tested. The most sensitive species was onion with the lowest EC_{50} of 0.064 L/ha for seedling emergence.

IIIA 10.8.1.4 Field testing

Further studies were not considered necessary.

IIIA 10.8.2 Aquatic plants

The toxicological spectrum of the product as well as the single active substances towards aquatic plants is presented under the Point 10.2. The risk assessment for *Lemna* is presented under point 10.2.1.11.

IIIA 10.8.2.1 Lemna growth test

Report:	[redacted]ü;[redacted];2003;M-223377-01
Title:	Influence of mesosulfuron-methyl & iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 10 + 2 + 30 - influence on the growth of Lemna gibba G3 in a static test Code: AE F115008 06 OD04 A104
Report No:	C037713
Document No(s):	M-223377-01-1
Guidelines:	**OECD: 221;Deviation not specified**
GLP/GEP:	**yes**

Objective

The aim of the study was to determine the effects of formulation IMS + MSM + MPR OD 42 (Atlantis®OD, AE F115008 06 OD04 A104) to the growth of *Lemna gibba*. The study was designed to meet OECD criteria.

Material and Methods

Lemna cultures with an initial frond number of 12 were cultivated in 20X AAP-medium for 7 days at 2.98, 9.53, 30.5, 97.7, 313 and 1000 µg product/L under static conditions. In addition an untreated control was tested. 3 replicates were used per treatment level. The mean water temperature was 23.3 ± 0.1 °C. pH varied between 7.9 and 8.7. The light intensity during the test was 7579 lux (mean).

Findings

Analytical measurements for AE F130081 (mesosulfuron-methyl, sodium salt form) resulted in concentrations between 86% and 110% of nominal treatment levels in fresh water samples and between 92% and 104% of nominal treatment levels in samples from aged water. Biological results are reported as nominal.

Inhibitory effects and intoxication symptoms are summarised in the following table.

Table 10.8.2.1- 1: Frond counts, dry weights of plants and percent inhibition of their average growth rate

Nominal (µg product/L)	7 days frond #	7 days dry weight (mg)	7 days % inhibition (growth rate for frond #)	14 days % inhibition (log biomass)
Untreated control	87	11.7		
2.98	91	13.2	-2.4	-4.8
9.53	99	14.3	-7.0	-7.9
30.5	83	11.5	2.1	0.5
97.7	29	7.5	56.0	16.9
313	22	6.7	69.4	20.8
1000	20	6.6	75.1	21.6

Clustered fronds were observed as intoxication symptoms.

Conclusion

The effect of formulation IMS + MSM + MPR OD 42 on the growth inhibition of *Lemna gibba* based on nominal figures are as follows:

7 day E_rC_{50}= 88.4 µg product/L (95% confidence limits 30.5 - 97.7 µg product/L)
7 day $E_{logb}C_{50}$> 1000 µg product/L
7 day NOEC= 30.5 µg product/L

IIIA 10.8.2.2 Field tests

The spectrum of the biological activity of the product is well represented by the results and the risk assessments in Point 10.2. Therefore, further studies are not considered necessary.

IIIA 10.9 Other non-target species (flora and fauna)

The spectrum of the biological activity of the product is well represented by the results and the risk assessments in Point 10.2 to 10.8 of this dossier. Therefore, further data from biological primary screening or other preliminary tests are not considered relevant for the risk assessment.

IIIA 10.9.1 Available preliminary data on other non-target species (flora and fauna)

Not relevant. See statement provided under Point 10.9.

IIIA 10.9.2 Critical assessment of relevance of preliminary test data

Not relevant. See statement provided under Point 10.9.

IIIA 10.10 Other/special studies

The spectrum of the biological activity of the product is well represented by the results and the risk assessments in Point 10.2 to 10.8 of this dossier. Therefore, further data from biological primary screening or other preliminary tests are not considered relevant for the risk assessment.

IIIA 10.10.1 Laboratory studies

Not relevant. See statement provided under Point 10.10.

IIIA 10.10.2 Field studies

Not relevant. See statement provided under Point 10.10.

IIIA 10.11 Summary and evaluation of Points 9 and 10.1-10.10

IIIA 10.11.1 Predicted distribution and fate in the environment and time courses involved

The distribution and fate of the active substance in the environment is found summarised in Document MCP, Section 9.

IIIA 10.11.2 Non-target species at risk and extent of potential exposure

A summary of the respective document chapters, conclusions and potential risk mitigation measures is given in the following text:

Terrestrial vertebrates

All toxicity-to-exposure-ratios (TER) for birds and mammals meet the regulatory requirements in a risk assessment at screening level. Thus, no unacceptable risk is to be expected for birds and mammals for the intended uses of the product.

Aquatic organisms

TER values for fish, invertebrates and algae meet the regulatory trigger in a tier 1 risk assessment based on FOCUS Step 2 PECsw values. Thus, no unacceptable risk is to be expected for these aquatic organisms for the intended uses of the product.

For aquatic plant, a refined risk assessment is presented comparing PECsw at FOCUS Step 3 versus HC_5 based on EC_{50} data from 10 aquatic macrophyte species. The regulatory trigger is met for all scenario situations except D2. Since exposure in this scenario is drainage-driven and cannot be reduced by the mitigation options implemented in FOCUS Step 4, no further refinement was made. . In the MSs concerned with the D2 scenario, a local restriction of product use on drained fields during drainage season will be proposed in the national dossiers submitted in the post Approval re-registration process.

Honey bees

A tier 1 risk assessment showed that the hazard quotients (oral and contact) are below the EU-trigger value. Thus, no unacceptable risk is to be expected for bees for the intended uses of the product.

Terrestrial non-target arthropods

A tier 1 risk assessment indicated no unacceptable adverse effects on non-target arthropods for the in- or off-field habitats following the use of the product according to the proposed use pattern. No mitigation measures are needed.

Earthworms and other soil non-target macro-organisms

A tier 1 risk assessment indicated no unacceptable chronic effects on earthworms. Tests with collembola and *Hypoaspis* also indicate no unacceptable risk for other soil non-target macro-organisms are from the intended uses of the product.

Non-target soil micro-organisms

No adverse effects on soil micro-organisms are to be expected for the intended uses of the product.

Terrestrial non-target plants

Based on a probabilistic risk assessment, the risk to non-target plants in the off-field environment is acceptable provided that a 5 m buffer zone is applied. Alternatively, 1 m distance is required when 75% drift reduced spray nozzles are used for the use in winter wheat and when 50% drift reduced spray nozzles are used for the use in winter rye.

IIIA 10.11.3 Short and long term risks for non-target species, populations, communities and processes

Please refer to point 10.11.2.

IIIA 10.11.4 Risk of fish kills and fatalities in large vertebrates or terrestrial predators

According to the risk assessments presented, a large margin of safety applies for fish and terrestrial vertebrates, and there is no risk of bioaccumulation in the food chain.

IIIA 10.11.5 Precautions necessary to avoid/minimise environmental contamination and to protect non-target species

No specific precautionary measures apply other than the mitigation imposed by the risk assessments for aquatic macrophytes, and non-target terrestrial plants.