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Document Title

Summary of the ecotoxicological studies iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 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

Date

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Author(s)

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Bayer CropScience

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Version history

Date	Data points containing amendments or additions[1] and brief description	Document identifier and version number

[1] It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report

Table of Contents

CP 10 ECOTOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCT

Use pattern considered in this risk assessment

Table10- 1: Intended application pattern

Crop	Timing of application (range)	Number of applications	Application interval [days]	Maximum label rate [L/ha]	Maximum application rate, individual treatment (ranges) [g/ha]	
					Iodosulfuron-methyl-sodium	Mefenpyr-diethyl
Winter wheat	BBCH 13-32	1	-	0.1	10	30
Winter barley	BBCH 20-32	1	-	0.075	7.5	225

Definition of the residue for risk assessment

Justification for the residue definition for risk assessment is provided in MCA Sec.7, Point 7.4.1 and MCA Sec. 6, Point 6.7.1.

Table10- 2: Definition of the residue for risk assessment

Compartment	Compound / Code
Soil	Iodosulfuron-methyl-sodium AE F075736 AE F145741 AE F145740 AE 0002166 AE F161778 BCS-CW81253 AE 0000119 AE F059411
Groundwater	same as soil
Surface Water	Iodosulfuron-methyl-sodium AE F075736 AE F145741 AE F145740 AE 0002166 AE F161778 BCS-CW81253 AE 0000119 AE F059411 AE 0014966 AE 0034855 AE 1234964 AE F159737 AE F154781
Air	Iodosulfuron-methyl-sodium
Plant	Iodosulfuron-methyl-sodium

CP 10.1 Effects on birds and other terrestrial vertebrates

The risk assessment has been performed according to "European Food Safety Authority; Guidance Document on Risk Assessment for Birds & Mammals on request from EFSA" (EFSA Journal 2009; 7(12):1438. doi:10.2903/j.efsa.2009.1438).

CP 10.1.1 Effects on birds

Table CP 10.1.1- 1 Endpoints used in risk assessment

Test substance		species/origin	Endpoint	Reference
Iodosulfuron-methyl-sodium	Acute risk assessment	Lowest LD_{50} from Bobwhite quail, Mallard duck, Japanese quail	LD_{50} > 2000 mg as/kg bw	[redacted], 1998 M-181334-01-1 KCA 8.1.1.1 /02 [redacted], 1997 M-142450-01-1 KCA 8.1.1.1.03 [redacted], 1996 M-140780-01-1 KCA 8.1.1.1 /01
	Long-term risk assessment	Lowest NO(A)EL from Bobwhite quail	NO(A)EC ≡ NO(A)EL ≥ 1077 ppm ≥ 78 mg as/kg bw/d	[redacted], 2004 M-242537-01-1 KCA 8.1.1.3 /04

Toxicity of the formulation

Iodosulfuron-methyl-sodium is of low acute oral toxicity to Bobwhite quail, Mallard duck and Japanese quail with LD_{50} values in excess of 2000 mg a.s./kg bw.
With regard to animal welfare reason, acute oral studies with formulations are routinely not conducted for birds, but only with the active ingredients, if toxic substances are nontoxic to birds. From the LD_{50} data of the active ingredients the toxicity of the formulation can be reliably be predicted.
Taking into consideration that the LD_{50} of all ingredients of the formulation are non-toxic (LD_{50} of mefenpyr-diethyl > 2000 mg a.s./kg bw; [redacted] & [redacted] (1991, amended 1994); M-129750-02-1), it is safe to assume that the product is also non-toxic to birds. Therefore it is justified to waive the acute test with the formulation in birds.

Table CP 10.1.1- 2: Relevant generic avian focal species for Tier 1 risk assessment

Crop	Scenario	Generic focal species	Representative species	Shortcut value	
				For long-term RA based on RUD_m	For acute RA based on RUD_{90}
Cereals	Early (shoots) autumn-winter BBCH 10 – 29	Large herbivorous bird "goose"	Pink-foot goose (*Anser brachyrhynchus*)	**16.2**	**30.5**
Cereals	BBCH 10 – 29	Small omnivorous bird "lark"	Woodlark (*Lullula arborea*)	**10.9**	**24.0**
Cereals	BBCH 30 – 39	Small omnivorous bird "lark"	Woodlark (*Lullula arborea*)	5.4	12.0

BOLD: Species considered in risk assessment (only worst case for each species)

ACUTE DIETARY RISK ASSESSMENT

Table CP 10.1.1- 3 Tier 1 acute DDD and TER calculation for birds

Crop	Generic focal species	DDD			DDD	LD_{50} [mg/kg bw]	TER_A	Trigger
		Appl. rate [kg/ha]	SV_{90}	MAF_{90}				
Iodosulfuron-methyl-sodium								
Cereals	Large herbivorous bird "goose" <Pink-foot goose>	0.01	30.5	1	0.3	≥ 2000	≥ 6557	10
Cereals	Small omnivorous bird "lark" <Woodlark>		24.9		0.2	≥ 2000	≥ 8333	10

Acute risk assessment for birds drinking contaminated water from pools in leaf whorls

As the formulated product is applied on winter 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.

LONG-TERM REPRODUCTIVE RISK ASSESSMENT

Table CP 10.1.1- 4 Tier 1 long-term DDD and TER calculation for birds

Crop	Generic focal species	DDD				DDD	NO(A)EL [mg/kg bw/d]	TER_{LT}	Trigger
		Appl. rate [kg/ha]	SV_m	MAF_m	f_{twa}				
Iodosulfuron-methyl-sodium									
Cereals	Large herbivorous bird "goose" <Pink-foot goose>	0.01	16.2	1	0.53	0.1	≥ 78	≥ 909	5
Cereals	Small omnivorous bird "lark" <Woodlark>		10.9			0.1	≥ 78	≥ 1350	5

Long-term risk assessment for birds drinking contaminated water in puddles

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 the formulated product is applied on 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* (= application rate x MAF) *(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 CP 10.1.1- 5 Evaluation of potential concern for exposure of birds drinking water (escape clause)

Crop	Koc [L/kg]	Application rate * MAF [g as/ha]	NO(A)EL [mg as/ kg bw/d]	Ratio (Application rate * MAF) / NO(A)EL	"Escape clause" No concern if ratio	Conclusion
Iodosulfuron-methyl-sodium						
Cereals, 1 x 10 g a.s./ha[1)]	50.8	10 * 1.0 [1)]	≥ 78	≤ 0.1	≤ 50	No concern

[1)] Use in winter wheat covering the use in winter barley with an application rate of 1 x 7.5 g as/ha

RISK ASSESSMENT 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.

As the log P_{OW} of the active substance iodosulfuron-methyl-sodium and its metabolites is below the trigger (<3), no evaluation of secondary poisoning is needed (see Sec.2, CA2.7)).

CP 10.1.1.1 Acute oral toxicity

Acute oral studies with formulations are routinely not conducted for birds, but only with the active ingredients. From the LD_{50} data of the active ingredients the toxicity of the formulation can be reliably be predicted.
Taking into consideration that the LD_{50} of all ingredients of the formulation are non-toxic, it is safe to assume that the product is also non-toxic to birds. Therefore it is justified to waive the acute test with the formulation in birds.

CP 10.1.1.2 Higher tier data on birds

Since iodosulfuron-methyl-sodium is of low toxicity to birds, no higher tier data are needed.

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

CP 10.1.2 Effects on terrestrial vertebrates other than birds

Table CP 10.1.2- 1 Endpoints used in risk assessment

Test substance		species/origin	Endpoint		Reference
Iodosulfuron-methyl-sodium	Acute risk assessment	Rat	LD_{50}	2678 mg as/kg bw	[redacted], 1993 M-132162-01-1 KCA 5.2.1/01
	Long-term risk assessment	Rat	NOAEC ≡ NOAEL	500 ppm ≥ 50 mg as/kg bw/d	[redacted], 1998 M-182825-01-1 KCA 5.6.1/02

[1)] Mean of male and female

Toxicity of the formulated product

Iodosulfuron-methyl-sodium showed low toxicity to small mammals, as LD_{50} of the active substance for rats was 2678 mg /kg bw.

The acute oral toxicity of the formulated product was determined in a study on rats.

Table CP 10.1.2- 2 Toxicity of Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 400 (100 + 300 g/L) to mammals

Test species	Test design	Ecotoxicological endpoint			Reference
Rat	acute, oral	LD_{50}	> 2000	mg product/kg bw	[redacted], 2003 C038943 M-226073-01-1 KCP 7.1.1 /01
		$LD_{50\ cut\text{-}off}$	≥ 5000	mg product/kg bw	

The study results show a low acute oral toxicity of the formulated product with a study endpoint ≥5000 mg/kg bw which reflects the low toxicity of the active substance. As the risk assessment based on the active substance revealed TER values above the respective triggers demonstrating a safe use (see Point 10.1.2 of this dossier, Table CP 10.1.2- 4 and Table CP 10.1.2- 5), also on a safe use of the formulation can be conducted.

Table CP 10.1.2- 3: Relevant mammalian generic species for Tier 1 risk assessment

Crop	Scenario	Generic focal species	Representative species	Shortcut value	
				For long-term RA based on RUD_{in}	For acute RA based on RUD_{90}
Cereals	BBCH 10-19	Small insectivorous mammal "shrew"	Common shrew (*Sorex araneus*)	**4.2**	**7.6**
Cereals	BBCH ≥ 20	Small insectivorous mammal "shrew"	Common shrew (*Sorex araneus*)	1.9	5.4
Cereals	Early (shoots)	Large herbivorous mammal "lagomorph"	Rabbit (*Oryctolagus cuniculus*)	**22.3**	**42.1**
Cereals	BBCH 10-29	Small herbivorous mammal "mouse"	Wood mouse (*Apodemus sylvaticus*)	**7.8**	**17.2**
Cereals	BBCH 30-39	Small omnivorous mammal "mouse"	Wood mouse (*Apodemus sylvaticus*)	3.9	8.6

BOLD: Species considered in risk assessment (only worst case for each species)

ACUTE DIETARY RISK ASSESSMENT

Table CP 10.1.2- 4 Tier 1 acute DDD and TER calculation for mammals

Crop	Generic focal species	DDD			DDD	LD_{50} [mg/kg bw]	TER_A	Trigger
		Appl. rate [kg/ha]	SV_{90}	MAF_{90}				
Iodosulfuron-methyl-sodium								
Cereals	Small insectivorous mammal "shrew" <Common shrew>	0.01	7.6	1	0.1	2678	35 237	10
Cereals	Large herbivorous mammal "lagomorph" <Rabbit>		42.1		0.4	2678	6361	10
Cereals	Small omnivorous mammal "mouse" <Wood mouse>		17.2		0.2	2678	15 570	10

LONG-TERM REPRODUCTIVE ASSESSMENT

Table CP 10.1.2- 5 Tier 1 long-term DDD and TER calculation for mammals

Crop	Generic focal species	DDD				DDD	NO(A)EL [mg/kg bw/d]	TER_{LT}	Trigger
		Appl. rate [kg/ha]	SV_m	MAF_m	f_{twa}				
Iodosulfuron-methyl-sodium									
Cereals	Small insectivorous mammal "shrew" <Common shrew>	0.01	4.2	1.0	0.53	0.02	≥ 50	≥ 2500	5
Cereals	Large herbivorous mammal "lagomorph" <Rabbit>		22.3			0.12	≥ 50	≥ 417	5
Cereals	Small omnivorous mammal "mouse" <Wood mouse>		7.8			0.04	≥ 50	≥ 1250	5

Long-term risk assessment for mammals drinking contaminated water

The puddle scenario is relevant for the long-term risk assessment.

Table CP 10.1.2- 6 Evaluation of potential concern for exposure of mammals drinking water

Crop	Koc [L/kg]	Application rate x MAF [g as/ha]	NO(A)EL [mg as/kg bw/d]	Ratio (Application rate x MAF) / NO(A)EL	"Escape clause" No concern if ratio	Conclusion
Iodosulfuron-methyl-sodium						
Cereals, 1 x 10 g a.s./ha [1)]	50.8	10 * 1.0 [1)]	≥ 50	0.2	≤ 50	No concern

[1)] Use in winter wheat covering the use in winter barley with an application rate of 1 x 7.5 g as/ha

RISK ASSESSMENT OF SECONDARY POISONING

Substances with a high bioaccumulation potential could theoretically bear a risk of secondary poisoning for mammals 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.

As the log P_{ow} of the active substance iodosulfuron-methyl-sodium and its metabolites is below the trigger (<3), no evaluation of secondary poisoning is needed (see Sec.2, CA2.7)

CP 10.1.2.1 Acute oral toxicity to mammals

Refer to KCP 7.1.1.1.01: The Endpoint is $LD_{50} \geq 5000$ mg/kg.

CP 10.1.2.2 Higher tier data on mammals

Since iodosulfuron-methyl-sodium is of low toxicity in mammals, no higher tier data are needed.

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

Not required according to 1107/2009. Since iodosulfuron-methyl-sodium is of low toxicity in birds and laboratory rodents, no risk for reptiles and amphibians is to be expected.

CP 10.2 Effects on aquatic organisms

Risk assessment for aquatic organisms

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.

Ecotoxicological endpoints used in risk assessment

Table CP 10.2- 1 Endpoints of the formulation used in risk assessment

Test organism	Study type	Test duration	LC/EC_{50} [mg/L]	NOEC [mg/L]	References
Acute toxicity to fish					
Oncorhynchus mykiss (rainbow trout)	static renewal acute	96 h	7.75	1.56	[redacted], 2004 C040810 M-229600-01-1 KCP 10.2.1 /01
Acute toxicity to aquatic invertebrates					
Daphnia magna (water flea)	static renewal acute	48 h	8.3	4.0	[redacted], 2004 C040690 M-229361-01-1 KCP 10.2.1 /02
Effects on algal growth					
Pseudokirchneriella subcapitata (green alga)	growth inhibition	72 h	E_rC_{50}: 6.71	< 0.1	[redacted], 2004 C040808 M-229597-01-1 KCP 10.2.1 /03
Effects on aquatic macrophytes					
Lemna gibba (duck weed)	growth inhibition	7d	E_rC_{50} (frond#): 0.0084	0.00123	[redacted], 2004 C040808 M-229602-01-1 KCP 10.2.1 /04

Table CP 10.2- 2 Endpoints of iodosulfuron-methyl-sodium and metabolites used in risk assessment

Test organism	Test system	Test duration	Endpoint [mg/L]		Reference
Iodosulfuron-methyl-sodium					
Fish, acute *Oncorhynchus mykiss* *Lepomis macrochirus* *Cyprinodon variegates*	Acute, static	96 h	LC_{50}	> 100	[redacted], 1998 M-143096-01-1 KCA 8.2.1 /01 [redacted], 1998 M-143095-01-1 KCA 8.2.1 /02 [redacted] & [redacted], 2000 M-238449-02-1 KCA 8.2.1 /03
Invertebrate, acute *Daphnia magna* *Mysidopsis bahia*	Acute, static Acute, static	48 h 96 h	EC_{50} >100 LC_{50}		[redacted], 1998 M-143098-01-1 KCA 8.2.4.1 /01 [redacted], 2000 M-238447-02-1 KCA 8.2.4.2 /01
Fish, chronic *Oncorhynchus mykiss*	Juvenile growth	28d	NOEC	10	[redacted] & [redacted] 1998 M-143097-01-1 KCA 8.2.2.1 /01
Invertebrate, chronic *Daphnia magna*	Static renewal	21 d	NOEC	10	[redacted] & [redacted], 1998 M-143099-01-1 KCA 8.2.5.1 /01
Algae, chronic *Pseudokirchneriella subcapitata*	Growth inhibition	96 h	E_rC_{50}	0.152	[redacted], 1998 M-143094-01-1 KCA 8.2.6.1 /01
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, mimicking exposure of outdoor study	7 d 6 weeks	E_rC_{50} E_rC_{50} NOEC	0.00108 0.000609 0.0004	[redacted], 2013 M-469584-01-1 KCA 8.2.7 /07
Macrophytes in outdoor ponds, 9 macrophytes	Growth inhibition, recovery	6 weeks 2 d + 5.5 weeks	NOEC NOEC	0.00027 0.00072	[redacted], 2011 M-407716-01-1 KCA 8.2.7 /06
Aquatic plants (probabilistic risk assessment: outdoor data from 9 macrophyte species plus 6-week Lemna)	Growth inhibition	42 d	HC5 (from E_rC_{50} of 9 species)	0.000385	KCA 8.2.7 /06 KCA 8.2.7 /07
AE F075736					
Algae, chronic *Pseudokirchneriella subcapitata*	Growth inhibition	72 h / 96 h	E_rC_{50}	>0.56	[redacted], [redacted] & [redacted], 1998 M-181569-01-1 KCA 8.2.6.1 /03
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50}	0.000511	[redacted] & [redacted], 1998 M-182336-01-1 KCA 8.2.7 /03

Test organism	Test system	Test duration	Endpoint [mg/L]	Reference
AE F145741				
Algae, chronic *Pseudokirchnerilla subcapitata*	Growth inhibition	72 h	E_rC_{50} 10.9	[redacted], 2013 M-470687-01-1 KCA 8.2.6.1 /04
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} 3.84	[redacted], 2013 M-462128-01-1 KCA 8.2.7 /10
AE F145740				
Algae, chronic *Pseudokirchnerilla subcapitata*	growth inhibition	72 h	E_rC_{50} >10	[redacted], 2013 M-465388-01-1 KCA 8.2.6.1 /05
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} >10	[redacted], 2013 M-462121-01-1 KCA 8.2.7 /11
AE 0002166				
Algae, chronic *Pseudokirchnerilla subcapitata*	growth inhibition	72 h	E_rC_{50} >10	[redacted], 2013 M-470669-01-1 KCA 8.2.6.1 /06
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} 0.023	[redacted], 2002 M-205481-01-1 KCA 8.2.7 /12
AE F161778				
Algae, chronic *Pseudokirchnerilla subcapitata*	growth inhibition	72 h	E_rC_{50} >10	[redacted], 2013 M-468872-01-1 KCA 8.2.6.1 /07
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} 0.0281	[redacted], 2001 M-197639-01-1 KCA 8.2.7 /13
BCS-CW81253				
Algae, chronic *Pseudokirchnerilla subcapitata*	growth inhibition	72 h	E_rC_{50} >10	[redacted], 2013 M-465389-01-1 KCA 8.2.6.1 /08
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} >10	[redacted], 2013 M-462125-01-1 KCA 8.2.7 /14
AE 0000119				
Algae, chronic *Pseudokirchnerilla subcapitata*	growth inhibition	72 h / 96 h	E_rC_{50} >100	[redacted] & [redacted], 2002 M-205698-01-1 KCA 8.2.6.1 /09
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} >100	[redacted], 2002 M-210320-01-1 KCA 8.2.7 /15
AE F059411				
Invertebrate, acute *Daphnia magna*	Acute, static	48 h	EC_{50} >100	[redacted] et al., 1998 M-181330-01-1 KCA 8.2.4.1 /02
Algae, chronic *Pseudokirchnerilla subcapitata*	Growth inhibition	72 h / 96 h	E_rC_{50} >100	[redacted], [redacted] & [redacted]; 1998 M-181379-01-1 KCA 8.2.6.1 /02

Test organism	Test system	Test duration	Endpoint [mg/L]	Reference
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} >100	[redacted], 2002 M-203638-01-1 KCA 8.2.7 /16 [redacted] & [redacted], 1998 M-181177-01-1 KCA 8.2.7 /02
AE 0014966				
Algae, chronic *Pseudokirchnerilla subcapitata*	Growth inhibition	72 h / 96 h	E_rC_{50} 47.5	[redacted] & [redacted], 2002 M-203681-01-1 KCA 8.2.6.1 /10
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} 0.575	[redacted], 2002 M-186853-01-1 KCA 8.2.7 /17
AE 0034855				
Algae, chronic *Pseudokirchnerilla subcapitata*	Growth inhibition	72 h / 96 h	E_rC_{50} >109	[redacted] & [redacted], 2002 M-210624-01-1 KCA 8.2.6.1 /11
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} >100	[redacted], 2002 M-210318-01-1 KCA 8.2.7 /18
AE 1234964				
Fish, acute *Oncorhynchus mykiss*	Acute, static	96 h	LC_{50} > 100	[redacted] & [redacted], 2006 M-278097-01-1 KCA 8.2.1 /04
Invertebrate, acute *Daphnia magna*	Acute, static	48 h	EC_{50} >100	[redacted] & [redacted], 2006 M-278971-01-1 KCA 8.2.4.1 /03
Algae, chronic *Pseudokirchnerilla subcapitata*	growth inhibition	72 h	E_rC_{50} >100	[redacted] & [redacted], 2006 M-293396-01-1 KCA 8.2.6.1 /12
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} >100	[redacted], 2006 M-281240-01-1 KCA 8.2.7 /19
AE F159737				
Fish, acute *Oncorhynchus mykiss*	Acute, static	96 h	LC_{50} > 100	[redacted] & [redacted], 2006 M-278099-01-1 KCA 8.2.1 /05
Invertebrate, acute *Daphnia magna*	Acute, static	48 h	EC_{50} >100	[redacted] & [redacted], 2006 M-278973-01-1 KCA 8.2.4.1 /04
Algae, chronic *Pseudokirchnerilla subcapitata*	Growth inhibition	72 h	E_rC_{50} >100	[redacted] & [redacted], 2006 M-281243-01-1 KCA 8.2.6.1 /13
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} >100	[redacted], 2006 M-281250-01-1 KCA 8.2.7 /20
AE F154781				
Algae, chronic *Pseudokirchneriella subcapitata*	Growth inhibition	72 h	E_rC_{50} >10	[redacted], 2013 M-476160-01-1 KCA 8.2.6.1 /14

Test organism	Test system	Test duration	Endpoint [mg/L]	Reference
Aquatic plant, chronic *Lemna gibba*	Growth inhibition, static	7 d	E_rC_{50} >10	[redacted], 2013 M-470494-01-1 KCA 8.2.7/21

For most metabolites measured endpoints are available only for the most sensitive species of the parent compound, algae and *Lemna*. In accordance to the guidance in section 6.6 and section 6.7 of the Aquatic guidance document (Sanco 3268/2001) in the risk assessment for daphnia and fish – as a worst case – it is assumed that the toxicity is 10 times higher (i.e. the endpoint 10 times lower) than that of the parent compound iodosulfuron-methyl-sodium.

Remark on the 7-day Lemna endpoint (see also the statement by [redacted] (2013; M-479697-01-1, KCA 8.2.7/05)
Two *Lemna*-studies have been conducted with iodosulfuron-methyl-sodium a.i (see Table CP 10.2-2). The first one is a 14-day study conducted in 1997 by [redacted] according to EPA Guideline 122-2. In this study(, KCA 8.2.7/01) only frond number was determined on days 2, 5, 7, 9, 11 and 14. A second endpoint like frond dry weight or frond area, which is mandatory according to OECD 221 (2006), has not been determined. Moreover, inhibition percentages were calculated by using the absolute frond counts in the treatments compared to the control, while nowadays a 7-day ErC50 based on growth rate inhibition is used for risk assessments.

The second study ([redacted] 2013, KCA 8.2.7/07) was performed according to the currently valid guideline OECD 221 (2006) measuring two endpoints, frond number and frond area. This study can be considered as fully valid study without restrictions. This 6-week study was designed to mimic the exposure of an outdoor-pond study and to obtain 6-week effect data for *Lemna* – a species that could not be kept in outdoor ponds. Beside the 6-week endpoints, effect data were calculated on a weekly basis. The endpoints obtained from the first 7-day period can be used for tier-1 risk assessments. The NOEC determined by Christ & Ruff was 0.4 µg/L. In the new *Lemna*-study 7-day ErC10-figures were 0.449 and 0.501 µg/L for frond counts and frond area, respectively.

The new *Lemna* study ([redacted] 2013; M-469584-01-1, KCA 8.2.7/07) shall replace the old study mentioned above for the following reasons:

1. In the new study two endpoints, frond number and frond area, where measured.
2. The new study has been conducted on the currently valid guideline OECD 221 (2006).
3. The growth rate related endpoints have been used already in the past but a lot of regulators were using the biomass related values because they are lower. Nevertheless the scientific community in Europe was already convinced since a long time that the focus should be on the growth rate related endpoints. This is as well reflected in the current versions of the OECD guidelines for algae and *Lemna*. In these guidelines it is stated that the growth rate related endpoints are preferred. Within a risk assessment sensitivities of different plant species are compared. As their growth, the test durations and the test designs are different a comparison of sensitivities only makes sense when growth rate related endpoints are used.
4. The fact, that the NOEC from the old study is very close to the 7day ErC10-figures from the new study indicates, that the test organisms were of equal sensitivity.

Overall, it can be concluded that the new fully valid and according to current state of the science performed 7-day *Lemna*-study supersedes the old 14-day Lemna study, based on frond counts solely.

Consequently, the EU-agreed endpoint of 0.83 µg/L, based on frond counts shall be replaced by the new 7-day E_rC_{50} of 1.08 µg/L based on growth rate.

Predicted Environmental Concentrations used in risk assessment

Formulated product:

For the formulated product PEC values can only be calculated for drift exposure. The formulants are assumed to be rapidly degraded in soil, and the only exposure route that is considered relevant for the entry of the formulated product into surface water is via spray drift from treated fields. Run-off and drainage entry of the formulants can be excluded. Therefore, experimental endpoints from the product are to be compared with the drift exposure PECs of the product. These are calculated in a simple tier 1 approach, considering standard drift rates and a standard water body, which is 30 cm deep and without riparian vegetation.

Table CP 10.2- 3: Initial maximum PEC_{sw} values of the formulation, considering spray drift after one application as only route of entry relevant for the product

Compound	Scenario	Drift rate (arable crops)	Winter wheat, 1 x 0.1 L/ha	Winter barley, 1 x 0.075 L/ha
			$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
IMS+MPR OD 400 (100+300)	small static ditch, at the edge of the treated field, water depth 0.3 m	2.77 % (no buffer)	**1.06**	**0.79**

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 relative density of the product (1.144 g/mL)
Bold values were used for risk assessment

Active ingredient and metabolites

Table CP 10.2- 4: Initial max PEC_{sw} values of iodosulfuron-methyl-sodium and metabolites – FOCUS Step 2 (KCP 9.2.5/01, 02; Tables CP 9.2.5-10 to 14)

Compound	FOCUS Scenario	Winter cereals, 1 x 10 g/ha	Winter cereals, 1 x 7.5 g/ha
		$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
Iodosulfuron-methyl-sodium	**STEP 1**	3.214	2.411
	STEP 2 – North Single	**0.389**	**0.214**
	STEP 2 – South Single	0.327	0.183
AE F075736	**STEP 1**	2.136	1.602
	STEP 2 – North Single	**0.745**	**0.383**
	STEP 2 – South Single	0.604	0.313
AE F145741	**STEP 1**	0.222	0.166
	STEP 2 – North Single	**0.070**	**0.037**
	STEP 2 – South Single	0.057	0.030

2 [redacted] D., (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

Compound	FOCUS Scenario	Winter cereals, 1 x 10 g/ha	Winter cereals, 1 x 7.5 g/ha
		$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
AE F145740	**STEP 1**	0.274	0.206
	STEP 2 – North Single	**0.104**	**0.054**
	STEP 2 – South Single	0.085	0.045
AE 0002166	**STEP 1**	0.518	0.388
	STEP 2 – North Single	**0.147**	**0.078**
	STEP 2 – South Single	0.121	0.065
AE F161778	**STEP 1**	0.324	0.243
	STEP 2 – North Single	**0.091**	**0.046**
	STEP 2 – South Single	0.073	0.037
BCS-CW81253	**STEP 1**	0.723	0.543
	STEP 2 – North Single	**0.249**	**0.124**
	STEP 2 – South Single	0.199	0.100
AE F154781	**STEP 1**	0.002	0.001
	STEP 2 – North Single	**0.002**	**0.001**
	STEP 2 – South Single	0.002	0.001
AE F059411	**STEP 1**	0.333	0.250
	STEP 2 – North Single	**0.125**	**0.064**
	STEP 2 – South Single	0.101	0.052
AE 0014966	**STEP 1**	0.010	0.007
	STEP 2 – North Single	**0.010**	**0.007**
	STEP 2 – South Single	0.010	0.007
AE 0000119	**STEP 1**	0.197	0.148
	STEP 2 – North Single	**0.061**	**0.032**
	STEP 2 – South Single	0.050	0.027
AE 0034855	**STEP 1**	0.007	0.005
	STEP 2 – North Single	**0.007**	**0.005**
	STEP 2 – South Single	0.007	0.005
AE 1234964	**STEP 1**	0.003	0.002
	STEP 2 – North Single	**0.003**	**0.002**
	STEP 2 – South Single	0.003	0.002
AE F159737	**STEP 1**	0.003	0.002
	STEP 2 – North Single	**0.003**	**0.002**
	STEP 2 – South Single	0.003	0.002

Bold values were used for risk assessment

Table CP 10.2- 5: Initial maximum PEC_{sw} values of iodosulfuron-methyl-sodium and metabolite AE F075736, FOCUS Step 3, using laboratory and field soil degradation data (KCP 9.2.5/03, 04; Tables CP 9.2.5-15 to 18)

FOCUS Scenario STEP 3	Laboratory soil DT_{50}			Field soil DT_{50}	
	Iodosulfuron-methyl-sodium		AE F075736	Iodosulfuron-methyl-sodium	AE F075736
	Entry route*	$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
Winter cereals, 1 x 10 g/ha					
D1 (ditch)	S	0.064	0.051	0.065	0.020
D1 (stream)	S	0.055	0.034	0.055	0.014
D2 (ditch)	D	0.143	0.787	0.247	0.439
D2 (stream)	D	0.092	0.495	0.162	0.288
D3 (ditch)	S	0.063	0.004	0.063	<0.001
D4 (pond)	S	0.002	0.021	0.002	0.002
D4 (stream)	S	0.050	0.014	0.050	0.001
D5 (pond)	S	0.002	0.005	0.002	0.001
D5 (stream)	S	0.050	0.003	0.050	<0.001
D6 (ditch)	S	0.063	0.004	0.063	0.002
R1 (pond)	S	0.002	0.001	0.002	0.001
R1 (stream)	S	0.042	0.025	0.045	0.013
R3 (stream)	R	0.133	0.042	0.159	0.021
R4 (stream)	R	0.088	0.040	0.111	0.020
Winter cereals, 1 x 7.5 g/ha					
D1 (ditch)	S	0.048	0.038	0.048	0.015
D1 (stream)	S	0.041	0.026	0.041	0.010
D2 (ditch)	D	0.097	0.589	0.169	0.328
D2 (stream)	D	0.064	0.370	0.113	0.217
D3 (ditch)	S	0.048	0.003	0.048	<0.001
D4 (pond)	S	0.002	0.016	0.002	0.001
D4 (stream)	S	0.038	0.010	0.038	<0.001
D5 (pond)	S	0.002	0.004	0.002	<0.001
D5 (stream)	S	0.037	0.002	0.037	<0.001
D6 (ditch)	S	0.047	0.003	0.048	0.002
R1 (pond)	S	0.002	0.001	0.002	0.001
R1 (stream)	S	0.031	0.019	0.033	0.010
R3 (stream)	R	0.100	0.032	0.119	0.016
R4 (stream)	R	0.066	0.030	0.083	0.015

* Letters S, D, and R correspond to the dominant entry path – spray drift, drainage, and runoff

ACUTE RISK ASSESSMENT FOR AQUATIC ORGANISMS

Table CP 10.2- 6: TER_A calculations based on drift entry for the formulation and on FOCUS Step 2 for iodosulfuron-methyl-sodium and metabolites

Compound	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_A	Trigger
Winter cereals, 1 x 10 g a.s./ha					
IMS + MPR OD 400 (100+300)	Fish, acute	LC_{50} 7750	1.06	7 311	100
	Invertebrate, acute	EC_{50} 8300	1.06	7 830	100
Iodosulfuron-methyl-sodium	Fish, acute	LC_{50} > 100 000	0.389	> 257 069	100
	Invertebrate, acute	EC_{50} > 100 000	0.389	> 257 069	100
AE F075736	Fish, acute	LC_{50} > 10 000	0.745	> 13 423	100
	Invertebrate, acute	EC_{50} > 10 000	0.745	> 13 423	100
AE F145741	Fish, acute	LC_{50} > 10 000	0.070	> 142 857	100
	Invertebrate, acute	EC_{50} > 10 000	0.070	> 142 857	100
AE F145740	Fish, acute	LC_{50} > 10 000	0.104	> 96 154	100
	Invertebrate, acute	EC_{50} > 10 000	0.104	> 96 154	100
AE 0002166	Fish, acute	LC_{50} > 10 000	0.147	> 68 027	100
	Invertebrate, acute	EC_{50} > 10 000	0.147	> 68 027	100
AE F161778	Fish, acute	LC_{50} > 10 000	0.091	> 109 890	100
	Invertebrate, acute	EC_{50} > 10 000	0.091	> 109 890	100
BCS-CW81253	Fish, acute	LC_{50} > 10 000	0.249	> 40 161	100
	Invertebrate, acute	EC_{50} > 10 000	0.249	> 40 161	100
AE 0000119	Fish, acute	LC_{50} > 10 000	0.061	> 163 934	100
	Invertebrate, acute	EC_{50} > 10 000	0.061	> 163 934	100
AE F059411	Fish, acute	LC_{50} > 10 000	0.125	> 80 000	100
	Invertebrate, acute	EC_{50} > 100 000	0.125	> 800 000	100
AE 0014966	Fish, acute	LC_{50} > 10 000	0.010	> 1 000 000	100
	Invertebrate, acute	EC_{50} > 10 000	0.010	> 1 000 000	100
AE 0034855	Fish, acute	LC_{50} > 10 000	0.007	> 1 428 571	100
	Invertebrate, acute	EC_{50} > 10 000	0.007	> 1 428 571	100
AE 1234964	Fish, acute	LC_{50} > 100 000	0.003	> 33 333 333	100
	Invertebrate, acute	EC_{50} > 100 000	0.003	> 33 333 333	100
AE F159737	Fish, acute	LC_{50} > 100 000	0.003	> 33 333 333	100
	Invertebrate, acute	EC_{50} > 100 000	0.003	> 33 333 333	100
AE F154781	Fish, acute	LC_{50} > 10 000	0.002	> 5 000 000	100
	Invertebrate, acute	EC_{50} > 10 000	0.002	> 5 000 000	100

(Continued: TER$_A$ calculations based on drift entry for the formulation and on FOCUS Step 2 for iodosulfuron-methyl-sodium and metabolites)

Compound	Species	Endpoint [µg/L]	PEC$_{sw,max}$ [µg/L]	TER$_A$	Trigger
Winter cereals, 1 x 7.5 g a.s./ha					
IMS + MPR OD 400 (100+300)	Fish, acute	LC_{50} 7750	0.79	9 810	100
	Invertebrate, acute	EC_{50} 8300	0.79	10 506	100
Iodosulfuron-methyl-sodium	Fish, acute	LC_{50} > 100 000	0.214	> 467 290	100
	Invertebrate, acute	EC_{50} > 100 000	0.214	> 467 290	100
AE F075736	Fish, acute	LC_{50} > 10 000	0.383	> 26 110	100
	Invertebrate, acute	EC_{50} > 10 000	0.383	> 26 110	100
AE F145741	Fish, acute	LC_{50} > 10 000	0.037	> 270 270	100
	Invertebrate, acute	EC_{50} > 10 000	0.037	> 270 270	100
AE F145740	Fish, acute	LC_{50} > 10 000	0.054	> 185 185	100
	Invertebrate, acute	EC_{50} > 10 000	0.054	> 185 185	100
AE 0002166	Fish, acute	LC_{50} > 10 000	0.078	> 128 205	100
	Invertebrate, acute	EC_{50} > 10 000	0.078	> 128 205	100
AE F161778	Fish, acute	LC_{50} > 10 000	0.046	> 217 391	100
	Invertebrate, acute	EC_{50} > 10 000	0.046	> 217 391	100
BCS-CW81253	Fish, acute	LC_{50} > 10 000	0.124	> 80 645	100
	Invertebrate, acute	EC_{50} > 10 000	0.124	> 80 645	100
AE 0000119	Fish, acute	LC_{50} > 10 000	0.032	> 312 500	100
	Invertebrate, acute	EC_{50} > 10 000	0.032	> 312 500	100
AE F059411	Fish, acute	LC_{50} > 10 000	0.064	> 156 250	100
	Invertebrate, acute	EC_{50} > 100 000	0.064	> 1 562 500	100
AE 0014966	Fish, acute	LC_{50} > 10 000	0.007	> 1 428 571	100
	Invertebrate, acute	EC_{50} > 10 000	0.007	> 1 428 571	100
AE 0034855	Fish, acute	LC_{50} > 10 000	0.005	> 2 000 000	100
	Invertebrate, acute	EC_{50} > 10 000	0.005	> 2 000 000	100
AE 1234964	Fish, acute	LC_{50} > 100 000	0.002	> 50 000 000	100
	Invertebrate, acute	EC_{50} > 100 000	0.002	> 50 000 000	100
AE F159737	Fish, acute	LC_{50} > 100 000	0.002	> 50 000 000	100
	Invertebrate, acute	EC_{50} > 100 000	0.002	> 50 000 000	100
AE F154781	Fish, acute	LC_{50} > 10 000	0.001	> 10 000 000	100
	Invertebrate, acute	EC_{50} > 10 000	0.001	> 10 000 000	100

CHRONIC RISK ASSESSMENT FOR AQUATIC ORGANISMS

Table CP 10.2- 7: TER_{LT} calculations based on drift entry for the formulation and on FOCUS Step 2 for iodosulfuron-methyl-sodium and metabolites

Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter cereals, 1 x 10 g a.s./ha						
IMS + MPR OD 400 (100+300)	Green algae, chronic	E_rC_{50}	6710	1.06	6 330	10
	Aquatic plants, chronic	E_rC_{50}	8.4	1.06	**7.92**	10
Iodosulfuron-methyl-sodium	Fish, chronic	NOEC	10 000	0.389	25 707	10
	Invertebrate, chronic	NOEC	10 000	0.389	25 707	10
	Green algae, chronic	E_rC_{50}	152	0.389	391	10
	Aquatic plants, chronic	E_rC_{50}	1.08	0.389	**2.77**	10
AE F075736	Fish, chronic	NOEC	1 000	0.745	1 342	10
	Invertebrate, chronic	NOEC	1 000	0.745	1 342	10
	Green algae, chronic	E_rC_{50}	560	0.745	752	10
	Aquatic plants, chronic	E_rC_{50}	0.511	0.745	**0.69**	10
AE F145741	Fish, chronic	NOEC	1 000	0.070	14 286	10
	Invertebrate, chronic	NOEC	1 000	0.070	14 286	10
	Green algae, chronic	E_rC_{50}	10 900	0.070	155 714	10
	Aquatic plants, chronic	E_rC_{50}	3 840	0.070	54 857	10
AE F145740	Fish, chronic	NOEC	1 000	0.104	9 615	10
	Invertebrate, chronic	NOEC	1 000	0.104	9 615	10
	Green algae, chronic	E_rC_{50}	> 10 000	0.104	> 96 154	10
	Aquatic plants, chronic	E_rC_{50}	> 10 000	0.104	> 96 154	10
AE 0002166	Fish, chronic	NOEC	1 000	0.147	6 803	10
	Invertebrate, chronic	NOEC	1 000	0.147	6 803	10
	Green algae, chronic	E_rC_{50}	> 10 000	0.147	> 68 027	10
	Aquatic plants, chronic	E_rC_{50}	23	0.147	156	10
AE F161778	Fish, chronic	NOEC	1 000	0.091	10 989	10
	Invertebrate, chronic	NOEC	1 000	0.091	10 989	10
	Green algae, chronic	E_rC_{50}	> 10 000	0.091	> 109 890	10
	Aquatic plants, chronic	E_rC_{50}	28.1	0.091	309	10
BCS-CW81253	Fish, chronic	NOEC	1 000	0.249	4 016	10
	Invertebrate, chronic	NOEC	1 000	0.249	4 016	10
	Green algae, chronic	E_rC_{50}	> 10 000	0.249	> 40 161	10
	Aquatic plants, chronic	E_rC_{50}	> 10 000	0.249	> 40 161	10
AE 0000119	Fish, chronic	NOEC	1 000	0.061	16 393	10
	Invertebrate, chronic	NOEC	1 000	0.061	16 393	10
	Green algae, chronic	E_rC_{50}	> 100 000	0.061	> 1 639 344	10
	Aquatic plants, chronic	E_rC_{50}	> 100 000	0.061	> 1 639 344	10

(Continued: TER_{LT} calculations based on drift entry for the formulation and on FOCUS Step 2 for iodosulfuron-methyl-sodium and metabolites)

Compound	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
AE F059411	Fish, chronic	NOEC 1 000	0.125	8 000	10
	Invertebrate, chronic	NOEC 1 000	0.125	8 000	10
	Green algae, chronic	E_rC_{50} > 100 000	0.125	> 800 000	10
	Aquatic plants, chronic	E_rC_{50} 100 000	0.125	800 000	10
AE 0014966	Fish, chronic	NOEC 1 000	0.010	100 000	10
	Invertebrate, chronic	NOEC 1 000	0.010	100 000	10
	Green algae, chronic	E_rC_{50} 47 500	0.010	4 750 000	10
	Aquatic plants, chronic	E_rC_{50} 575	0.010	57 500	10
AE 0034855	Fish, chronic	NOEC 1 000	0.007	142 857	10
	Invertebrate, chronic	NOEC 1 000	0.007	142 857	10
	Green algae, chronic	E_rC_{50} > 109 000	0.007	15 571 428	10
	Aquatic plants, chronic	E_rC_{50} > 100 000	0.007	> 15 571 428	10
AE 1234964	Fish, chronic	NOEC 1 000	0.003	333 333	10
	Invertebrate, chronic	NOEC 1 000	0.003	333 333	10
	Green algae, chronic	E_rC_{50} > 100 000	0.003	> 33 333 333	10
	Aquatic plants, chronic	E_rC_{50} > 100 000	0.003	> 33 333 333	10
AE F159737	Fish, chronic	NOEC 1 000	0.003	333 333	10
	Invertebrate, chronic	NOEC 1 000	0.003	333 333	10
	Green algae, chronic	E_rC_{50} > 100 000	0.003	> 33 333 333	10
	Aquatic plants, chronic	E_rC_{50} > 100 000	0.003	> 33 333 333	10
AE F154781	Fish, chronic	NOEC 1 000	0.002	200 000	10
	Invertebrate, chronic	NOEC 1 000	0.002	200 000	10
	Green algae, chronic	E_rC_{50} > 10 000	0.002	> 5 000 000	10
	Aquatic plants, chronic	E_rC_{50} 10 000	0.002	> 5 000 000	10
Winter cereals, 1 x 7.5 g a.s./ha					
IMS + MPR OD 400 (100+300)	Green algae, chronic	E_rC_{50} 6710	0.79	8 494	10
	Aquatic plants, chronic	E_rC_{50} 84	0.79	10.63	10
Iodosulfuron-methyl-sodium	Fish, chronic	NOEC 10 000	0.214	46 729	10
	Invertebrate, chronic	NOEC 10 000	0.214	46 729	10
	Green algae, chronic	E_rC_{50} 152	0.214	710	10
	Aquatic plants, chronic	E_rC_{50} 1.08	0.214	**5.05**	10
AE F075736	Fish, chronic	NOEC 1 000	0.383	2 611	10
	Invertebrate, chronic	NOEC 1 000	0.383	2 611	10
	Green algae, chronic	E_rC_{50} 560	0.383	1 462	10
	Aquatic plants, chronic	E_rC_{50} 0.511	0.383	**1.33**	10

(Continued: TER_{LT} calculations based on drift entry for the formulation and on FOCUS Step 2 for iodosulfuron-methyl-sodium and metabolites)

Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
AE F145741	Fish, chronic	NOEC	1 000	0.037	27 027	10
	Invertebrate, chronic	NOEC	1 000	0.037	27 027	10
	Green algae, chronic	E_rC_{50}	10 900	0.037	294 595	10
	Aquatic plants, chronic	E_rC_{50}	3 840	0.037	103 784	10
AE F145740	Fish, chronic	NOEC	1 000	0.054	18 519	10
	Invertebrate, chronic	NOEC	1 000	0.054	18 519	10
	Green algae, chronic	E_rC_{50}	10 000	0.054	185 185	10
	Aquatic plants, chronic	E_rC_{50}	> 10 000	0.054	> 185 185	10
AE 0002166	Fish, chronic	NOEC	1 000	0.078	12 821	10
	Invertebrate, chronic	NOEC	1 000	0.078	12 821	10
	Green algae, chronic	E_rC_{50}	> 10 000	0.078	> 128 205	10
	Aquatic plants, chronic	E_rC_{50}	23	0.078	295	10
AE F161778	Fish, chronic	NOEC	1 000	0.046	21 739	10
	Invertebrate, chronic	NOEC	1 000	0.046	21 739	10
	Green algae, chronic	E_rC_{50}	> 10 000	0.046	> 217 391	10
	Aquatic plants, chronic	E_rC_{50}	28.1	0.046	611	10
BCS-CW81253	Fish, chronic	NOEC	1 000	0.124	8 065	10
	Invertebrate, chronic	NOEC	1 000	0.124	8 065	10
	Green algae, chronic	E_rC_{50}	> 10 000	0.124	> 80 645	10
	Aquatic plants, chronic	E_rC_{50}	> 10 000	0.124	> 80 645	10
AE 0009119	Fish, chronic	NOEC	1 000	0.032	31 250	10
	Invertebrate, chronic	NOEC	1 000	0.032	31 250	10
	Green algae, chronic	E_rC_{50}	> 100 000	0.032	> 3 125 000	10
	Aquatic plants, chronic	E_rC_{50}	100 000	0.032	> 3 125 000	10
AE F059411	Fish, chronic	NOEC	1 000	0.064	15 625	10
	Invertebrate, chronic	NOEC	1 000	0.064	15 625	10
	Green algae, chronic	E_rC_{50}	100 000	0.064	> 1 562 500	10
	Aquatic plants, chronic	E_rC_{50}	> 100 000	0.064	> 1 562 500	10
AE 0014966	Fish, chronic	NOEC	1 000	0.007	142 857	10
	Invertebrate, chronic	NOEC	1 000	0.007	142 857	10
	Green algae, chronic	E_rC_{50}	47 500	0.007	6 785 714	10
	Aquatic plants, chronic	E_rC_{50}	575	0.007	82 143	10
AE 0034855	Fish, chronic	NOEC	1 000	0.005	200 000	10
	Invertebrate, chronic	NOEC	1 000	0.005	200 000	10
	Green algae, chronic	E_rC_{50}	> 109 000	0.005	> 21 800 000	10
	Aquatic plants, chronic	E_rC_{50}	> 100 000	0.005	> 21 800 000	10

(Continued: TER_{LT} calculations based on drift entry for the formulation and on FOCUS Step 2 for iodosulfuron-methyl-sodium and metabolites)

Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
AE 1234964	Fish, chronic	NOEC	1 000	0.002	500 000	10
	Invertebrate, chronic	NOEC	1 000	0.002	500 000	10
	Green algae, chronic	E_rC_{50}	> 100 000	0.002	> 50 000 000	10
	Aquatic plants, chronic	E_rC_{50}	> 100 000	0.002	> 50 000 000	10
AE F159737	Fish, chronic	NOEC	1 000	0.002	500 000	10
	Invertebrate, chronic	NOEC	1 000	0.002	500 000	10
	Green algae, chronic	E_rC_{50}	> 100 000	0.002	> 50 000 000	10
	Aquatic plants, chronic	E_rC_{50}	> 100 000	0.002	> 50 000 000	10
AE F154781	Fish, chronic	NOEC	1 000	0.001	1 000 000	10
	Invertebrate, chronic	NOEC	1 000	0.001	1 000 000	10
	Green algae, chronic	E_rC_{50}	> 10 000	0.001	> 10 000 000	10
	Aquatic plants, chronic	E_rC_{50}	> 10 000	0.001	> 10 000 000	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 active substance(s).

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 substance(s). 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.

Iodosulfuron-methyl-sodium is the only active substance in the representative formulation IMS + MPR OD 400 (100+300) which contains 100 g Iodosulfuron-methyl-sodium /L corresponding to 8.7 % w/w. Given the well-known exceptional toxicity of sulfonyl urea herbicides to aquatic plants, especially to *Lemna gibba*, it is justified to consider that the toxicity of the formulated product originates from the iodosulfuron-methyl-sodium content only.

This is confirmed when the toxicity of the formulated product and technical iodosulfuron-methyl-sodium are compared (both endpoints determined in 7-day static tests, with proven stability of the active substance iodosulfuron-methyl-sodium).

The *Lemna*- E_rC_{50} of this product of 8.4 µg /L is clearly within the expected biological variance to the endpoint obtained for the active ingredient (E_rC_{50} = 1.08 µg a.s./L).

As obviously the toxicity to aquatic plants is driven by the active ingredient iodosulfuron-methyl-sodium the risk assessment can safely be performed for the active substance only. Thus, the risk assessment for the formulated product is covered by the refined risk assessment for the active substance iodosulfuron-methyl-sodium.

Table CP 10.2- 8: TER_{LT} calculations based on FOCUS Step 3 (laboratory soil DT_{50})

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
Iodosulfuron-methyl-sodium, winter cereals, 1 x 10 g/ha					
Aquatic plants, chronic	E_rC_{50} 1.08	0.064	D1 (ditch)	16.9	10
		0.055	D1 (stream)	19.6	10
		0.143	D2 (ditch)	**7.6**	10
		0.092	D2 (stream)	11.7	10
		0.063	D3 (ditch)	17.1	10
		0.002	D4 (pond)	540.0	10
		0.050	D4 (stream)	21.6	10
		0.002	D5 (pond)	540.0	10
		0.050	D5 (stream)	21.6	10
		0.063	D6 (ditch)	17.1	10
		0.002	R1 (pond)	540.0	10
		0.042	R1 (stream)	25.7	10
		0.133	R3 (stream)	**8.1**	10
		0.088	R4 (stream)	12.3	10
AE F075736, winter cereals, 1 x 10 g/ha					
Aquatic plants, chronic	E_rC_{50} 0.511	0.051	D1 (ditch)	10.02	10
		0.034	D1 (stream)	15.0	10
		0.787	D2 (ditch)	**0.6**	10
		0.495	D2 (stream)	**1.0**	10
		0.004	D3 (ditch)	127.8	10
		0.021	D4 (pond)	24.3	10
		0.014	D4 (stream)	36.5	10
		0.005	D5 (pond)	102.2	10
		0.003	D5 (stream)	170.3	10
		0.004	D6 (ditch)	127.8	10
		0.001	R1 (pond)	511.0	10
		0.025	R1 (stream)	20.4	10
		0.042	R3 (stream)	12.2	10
		0.040	R4 (stream)	12.8	10
Iodosulfuron-methyl-sodium, winter cereals, 1 x 7.5 g/ha					
Aquatic plants, chronic	E_rC_{50} 1.08	0.048	D1 (ditch)	22.5	10
		0.041	D1 (stream)	26.3	10
		0.097	D2 (ditch)	11.1	10
		0.064	D2 (stream)	16.9	10
		0.048	D3 (ditch)	22.5	10
		0.002	D4 (pond)	540.0	10
		0.038	D4 (stream)	28.4	10
		0.002	D5 (pond)	540.0	10
		0.037	D5 (stream)	29.2	10

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
		0.047	D6 (ditch)	23.0	10
		0.002	R1 (pond)	540.0	10
		0.031	R1 (stream)	34.8	10
		0.100	R3 (stream)	10.8	10
		0.066	R4 (stream)	16.4	10
AE F075736, winter cereals, 1 x 7.5 g/ha					
Aquatic plants, chronic	E_rC_{50} 0.511	0.038	D1 (ditch)	13.4	10
		0.025	D1 (stream)	20.4	10
		0.589	D2 (ditch)	**0.9**	10
		0.370	D2 (stream)	**1.4**	10
		0.003	D3 (ditch)	170.3	10
		0.016	D4 (pond)	31.9	10
		0.010	D4 (stream)	51.1	10
		0.004	D5 (pond)	127.8	10
		0.002	D5 (stream)	255.5	10
		0.003	D6 (ditch)	170.3	10
		0.001	R1 (pond)	511.0	10
		0.019	R1 (stream)	26.9	10
		0.032	R3 (stream)	16.0	10
		0.030	R4 (stream)	17.3	10

***** Refinement using a drift rate of 0.57 % (5 m buffer) for arable crops (see Formulated product, Table CP 10.2-3)
Bold values: trigger is not met and further refinement is required

Table CP 10.2- 9: TER_{LT} calculations based on FOCUS Step 3 (field soil DT_{50})

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
Iodosulfuron-methyl-sodium, winter cereals, 1 x 10 g/ha					
Aquatic plants, chronic	E_rC_{50} 1.08	0.065	D1 (ditch)	16.6	10
		0.055	D1 (stream)	19.6	10
		0.247	D2 (ditch)	**4.4**	10
		0.162	D2 (stream)	**6.7**	10
		0.063	D3 (ditch)	17.1	10
		0.002	D4 (pond)	540	10
		0.050	D4 (stream)	21.6	10
		0.002	D5 (pond)	540	10
		0.050	D5 (stream)	21.6	10
		0.063	D6 (ditch)	17.1	10
		0.002	R1 (pond)	540	10
		0.045	R1 (stream)	24	10
		0.159	R3 (stream)	**6.8**	10

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
		0.111	R4 (stream)	**9.7**	10
AE F075736, winter cereals, 1 x 10 g/ha					
Aquatic plants, chronic	E_rC_{50} 0.511	0.020	D1 (ditch)	25.6	10
		0.014	D1 (stream)	36.5	10
		0.439	D2 (ditch)	**1.2**	10
		0.288	D2 (stream)	**1.8**	10
		<0.001	D3 (ditch)	511	10
		0.002	D4 (pond)	256	10
		0.001	D4 (stream)	511	10
		<0.001	D5 (pond)	511	10
		<0.001	D5 (stream)	511	10
		0.002	D6 (ditch)	256	10
		0.001	R1 (pond)	511	10
		0.013	R1 (stream)	39.3	10
		0.021	R3 (stream)	24.3	10
		0.020	R4 (stream)	25.6	10
Iodosulfuron-methyl-sodium, winter cereals, 1 x 7.5 g/ha					
Aquatic plants, chronic	E_rC_{50} 1.08	0.048	D1 (ditch)	22.5	10
		0.041	D1 (stream)	26.3	10
		0.169	D2 (ditch)	**6.4**	10
		0.113	D2 (stream)	**9.6**	10
		0.048	D3 (ditch)	22.5	10
		0.002	D4 (pond)	540	10
		0.038	D4 (stream)	28.4	10
		0.002	D5 (pond)	540	10
		0.037	D5 (stream)	29.2	10
		0.048	D6 (ditch)	22.5	10
		0.002	R1 (pond)	540	10
		0.033	R1 (stream)	32.7	10
		0.119	R3 (stream)	**9.07**	10
		0.083	R4 (stream)	13.0	10
AE F075736, winter cereals, 1 x 7.5 g/ha					
Aquatic plants, chronic	E_rC_{50} 0.511	0.015	D1 (ditch)	34.1	10
		0.010	D1 (stream)	51.1	10
		0.328	D2 (ditch)	**1.6**	10
		0.217	D2 (stream)	**2.4**	10
		<0.001	D3 (ditch)	511	10
		0.001	D4 (pond)	511	10
		<0.001	D4 (stream)	511	10
		<0.001	D5 (pond)	511	10
		<0.001	D5 (stream)	511	10

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
		0.002	D6 (ditch)	256	10
		0.001	R1 (pond)	511	10
		0.010	R1 (stream)	51.1	10
		0.016	R3 (stream)	31.9	10
		0.015	R4 (stream)	34.1	10

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

The following scenarios do not pass the risk assessment at step 3 (based on DT_{50} of field dissipation studies) and require a refined risk assessment:
Iodosulfuron-methyl-sodium:
D2 (ditch and stream), R3 (stream) and R4 (stream) for 1 x 10 g a.s./ha;
D2 (ditch and stream) and R3 (stream) for 1 x 7.5 g a.s./ha.
AE F075736: D2 (ditch and stream) for 1 x 10 g a.s./ha and 1 x 7.5 g a.s./ha.

REFINED CHRONIC RISK ASSESSMENT FOR AQUATIC PLANTS

In addition to the tier 1 test with *Lemna gibba*, resulting in the E_rC_{50} of 1.08 µg a.s./L, two further macrophyte studies have been conducted with iodosulfuron-methyl-sodium technical and the formulation iodosulfuron-methyl-sodium WG 50, respectively.

- In the macrophyte pond study ([redacted] 2011; M-407716-01-1, KCA 8.2.7 /06), ten different macrophyte species were exposed to iodosulfuron-methyl-sodium applied as WG 50 formulation under outdoor conditions. This formulation was created for the only purpose to ensure the full solubility of the test substance in the application solutions. The aim of the study was to deliver an appropriate number of endpoints for an HC_5 calculation. The study included two different exposure regimes:
  1) Constant exposure over 6 weeks with natural degradation of the compound in the ponds; this part was conducted in an EC_x design and can be regarded as representative for a static water body. The dissipation of the parent substance over a six week period was quantified by analytical measurements. In parallel to the decrease of the parent substance iodosulfuron-methyl-sodium, the increase of the metabolite AE F075736 was measured (see Figure 10.2-1). The 6-week endpoints derived from the outdoor macrophyte growth inhibition study are based on initial measured concentrations of iodosulfuron-methyl-sodium.
  2) 2-day peak exposure (two peak concentrations 0.27 and 0.72 µg a.s./L, initial measured) with subsequent replacement of the test solutions with untreated dilution water in the ponds. This second regime aimed at mimicking short runoff or drift peaks in flowing water bodies and their effects on macrophytes.
- Since *Lemna* could not be tested in the outdoor-ponds due to the low nutrient levels in the pond water, and since the parallel *Lemna* test with enriched pond water was considered less reliable due to strong algae infestation, *Lemna* was tested under sterile conditions in the laboratory ([redacted] 2013; M-469584-01-1, KCA 8.2.7 /07). As the concentration of iodosulfuron-methyl-sodium in the water column of the outdoor-ponds decreased by about 50% within four weeks after the application, laboratory tests were set in that way that the concentration of the test substances

mimicked the decrease of iodosulfuron-methyl-sodium and the simultaneous increase of AE F075736 over time.

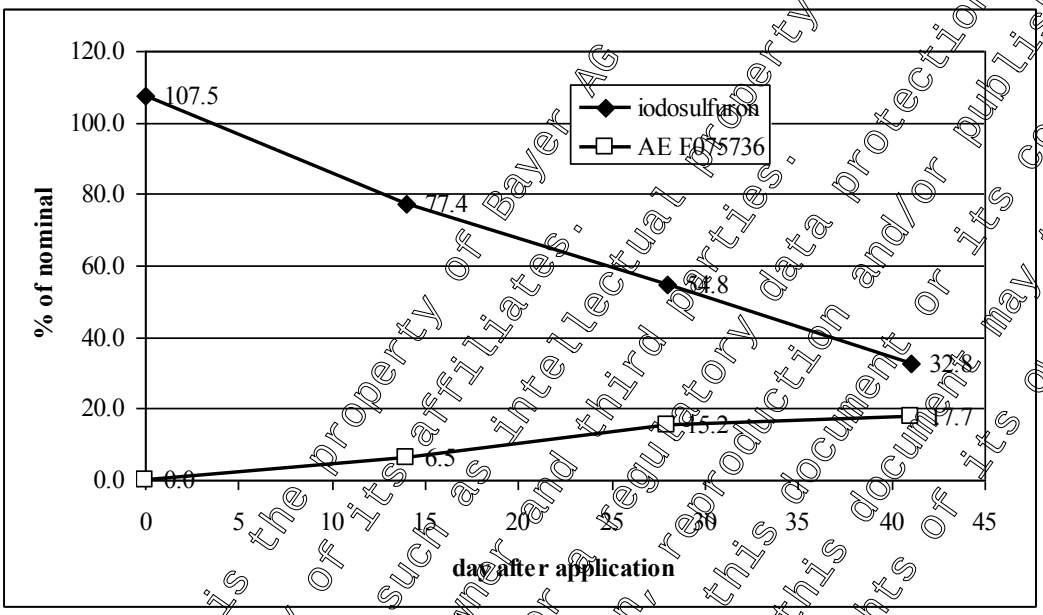

Figure 10.2-1: Dissipation of iodosulfuron-methyl-sodium and formation of its main metabolite AE F075736 in the ponds of the outdoor macrophyte growth inhibition study ([redacted] 2011). Data points are mean % nominal values per day from all treatment levels.

The exposure pattern described in the tested ponds including the relation of iodosulfuron-methyl-sodium to AE F075736 is representative e.g. for drift entry of iodosulfuron-methyl-sodium in static water bodies. In this case, where only the parent compound enters the water body, so that exposure to AE F075736 occurs only due to degradation the parent, the toxicity of AE F075736 is covered with the endpoint of the parent compound. A separate risk assessment for AE F075736 is not deemed necessary. However, if AE F075736 enters the water body independently from parent, e.g. via to run-off and drainage after formation in the soil, a separate risk assessment based on an own endpoint has to be performed.

Probabilistic risk assessment: SSD and HC_5 calculation for iodosulfuron-methyl-sodium

The refined risk assessment for iodosulfuron-methyl-sodium is mainly based on the results of the multispecies outdoor pond study ([redacted] 2011, M-407716-01-1, KCA 8.2.7 /06) and the associated 6-weeks laboratory bioassay with *Lemna gibba*. ([redacted] 2013, M-469584-01-1, KCA 8.2.7 /07). The data of the two studies have been used to generate a species sensitivity distribution (SSD) and calculate an HC_5.

Although the multispecies outdoor pond study had been started with ten species, *Glyceria maxima* was removed from the study on exposure day 29 due to generally poor health in all treated and control ponds. The evaluation was done with the remaining nine species. For more information on the study and further endpoints, see study the summary in document M, point CA 8.2.7.

All endpoints listed in Table CP 10.2- 10 are based on initial concentrations of iodosulfuron-methyl-sodium at the start of the 6-week test period. The outdoor pond study yielded EC_{50} values for the variable dry weight growth rate for all nine species, ranging from 0.54 µg a.s./L to > 61 µg a.s./L. The EC50 > 61 µg/L obtained for *Cabomba carolinea* has been omitted from the HC5-calculation according to Aldenberg, T. & Jaworska, J.S. (2000)[3].
As mentioned above the lowest endpoint from the 6-weeks *Lemna* bioassay is 0.609 µg a.s./L (E_rC_{50} for frond number). This endpoint was added to the overall eight endpoints from the pond study. The complete data set used for generating the SSD is shown in the table below.

Table CP 10.2- 10: Refined species included in the SSD and their relevant EC_{50} value

Species	**Endpoint** [µg a.s./L]
Salvinia minima	E_rC_{50} 0.54
Lemna gibba (6 weeks)	E_rC_{50} 0.609
Elodea canadensis	E_rC_{50} 1.4
Potamogeton pectinatus	E_rC_{50} 1.5
Mentha aquatica	E_rC_{50} 6
Ceratophyllum demersum	E_rC_{50} 6.2
Myriophyllum heterophyllum	E_rC_{50} 6.7
Sagittaria latifolia	E_rC_{50} 7.9
Nymphaea cordorata	EC_{50} 14
HC_5	**0.385**

The HC_5 calculation is based on the method of Aldenberg & Jaworska (2000)[3]. A median HC_5 of 0.385 µg a.s./L was calculated (cf. Table CP 10.2- 10).

Refined aquatic risk assessment for iodosulfuron-methyl-sodium

For the refined risk assessment **long-term exposure scenarios** and **peak exposure scenarios** may be considered separately. In order to distinguish long-term exposure from peak exposure the temporal patterns of PEC-figures ([redacted] & [redacted] 2014, M-477282-01-1, KCP 9.2.5 /04) were analysed.
Run-off scenarios R3 and R4 show a dominant and very sharp peak that lasted less than 1 day. This primary peak may be followed or preceded by one or a few significantly smaller secondary peaks. These scenarios are considered as peak exposure scenarios in the refined risk assessment.
Drainage scenarios D2 (ditch and stream) show high exposure over a long time period, with many entry events and slow dissipation after the entry. These scenarios are considered as long-term exposure scenarios in the refined risk assessment.

For **the long-term exposure scenarios**, the calculated HC_5 is compared to FOCUS Step 3 max. PEC_{sw} values. The results of these calculations are provided in Table CP 10.2- 11. An assessment factor of 3

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

should be applied in conjunction with the median HC_5 to derive the regulatory acceptable concentration.

For **the peak exposure scenarios**, the overall-NOEC of 0.72 µg a.s./L derived from the 48-hour peak exposure experiment of the multispecies outdoor pond study ([redacted] 2011, M-407716-01-1, KCA 8.2.7 /06) is considered appropriate. As this is the overall-NOEC out of 9 macrophyte species, it is considered justified to apply an assessment factor not higher than 3.

Table CP 10.2- 11: Refined risk assessment for aquatic macrophytes using refined endpoints for iodosulfuron-methyl-sodium

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER	Trigger
Iodosulfuron-methyl-sodium, winter cereals, 1 x 10 g/ha					
Aquatic plants, chronic	HC_5 0.385	0.247	D2 (ditch)	**1.6**	3
		0.162	D2 (stream)	**2.4**	3
Aquatic plants, chronic	NOEC 0.72	0.159	R3 (stream)	4.5	3
		0.111	R4 (stream)	6.5	3
Iodosulfuron-methyl-sodium, winter cereals, 1 x 7.5 g/ha					
Aquatic plants, chronic	HC_5 0.385	0.169	D2 (ditch)	**2.3**	3
		0.113	D2 (stream)	3.4	3
Aquatic plants, chronic	NOEC 0.72	0.119	R3 (stream)	6.1	3

With the refined endpoints the risk assessment for the run-off scenarios R3 and R4 is passed for both use rates.
For scenarios D2 (ditch and stream) TER values are still below the relevant trigger value of 3. For these scenarios, also the risk assessment for AE F075736 is not passed (see Table CP 10.2- 9). As D2 scenarios are driven by drainage entry mitigation measures such as buffer zones or drift reducing nozzles will not reduce the concentration of the compounds in the water body. Therefore, no further risk assessment based on FOCUS Step 4 calculations in presented.

In conclusion, for all FOCUS scenarios except of D2 (ditch and stream) the application of iodosulfuron-methyl-sodium + mefenpyr-diethyl OD400 at recommended application rates does not cause a risk to aquatic macrophytes. No mitigation measures are needed.

CP 10.2.1 Acute toxicity to fish, aquatic invertebrates, or effects on aquatic algae and macrophytes

Report:	[redacted];2004;M-229600-01
Title:	Acute toxicity of iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 100 + 300 to fish (Oncorhynchus mykiss) (product code: AE F115008 02 OD35 A202)
Report No:	C040810
Document No(s):	M-229600-01-1
Guidelines:	**EU (=EEC): 92/69/EEC, C.1.; OECD: 203; USEPA (=EPA): 72-1/SEP-EPA-540/9-85-006, OPPTS 850.1075;Deviation not specified**
GLP/GEP:	**yes**

Executive summary:

The aim of the study was to determine the acute toxicity of the test item to Rainbow trout *(Oncorhynchus mykiss),* expressed as 96h-LC_{50} for mortality.
Oncorhynchus mykiss (10 fish in each test level) were exposed in a static system over a period of 96 hours to nominal concentrations of 1.56, 3.13, 6.25, 12.5 and 25.0 mg test item/L against a water control.
Mortality and sublethal behavioural effects were used to determine the endpoints. Based on analytical findings the biological endpoints are reported as nominal figures. The 96-hour-LC_{50} was 7.75 mg test item/L (95% confidence limits 6.43 – 9.33 mg/L), the 96-hour-NOEC was determined to be 1.56 mg test item/L.

Material and Methods:

Test item: Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100 + 300; Product code: AE F115008 02 OD35 A202; Analysed content: Iodosulfuron-methyl-sodium (AE F115008): 8.82%, Mefenpyr-diethyl (AE F107892): 26.0%; Batch No.: AAIM01665; Analysis ref. code: AZ 11073; Development/product No.: 300035317.

Rainbow trout *(Oncorhynchus mykiss*) were exposed for 96 h under static conditions to nominal concentrations of 1.56, 3.13, 6.25, 12.5, and 25.0 mg test item / L against a control. The mean body wet weight of the fish at the beginning of the test was 1.4 ± 0.2 g (mean ± SD), mean body total length was 5.3 ± 0.3 cm (mean ± SD). The biomass loading was 0.35 g fish/L test medium. Each vessel (aquaria made of glass; 32×36×38 cm (l×d×h)) served as one replicate filled with 40 L. Reconstituted water was used for the test. It was prepared by adding salt stock solutions to demineralized water (conductivity < 0.2 µS/cm) to yield ionic concentrations according to ISO. The water was then aerated to reach the oxygen saturation point.
Dissolved oxygen concentrations ranged from 95 to 100 % oxygen saturation, the pH values ranged from 6.9 to 7.1, the hardness ranged from 40 to 60 mg $CaCO_3$/L and the water temperature ranged from 12.1 °C to 12.4 °C in all aquaria over the whole testing period. Iodosulfuron-methyl-sodium was analyzed in all test levels after 0 h, on day 2 and on day 4 of the exposure period.

Dates of experimental work: January 26, 2004 to March 11, 2004

Results:

The analytical findings for AE F115008 (iodosulfuron-methyl-sodium) reflect the expected nominal concentrations. Based on analytical determination of iodosulfuron-methyl-sodium (in water by LC-MS/MS) mean measured values between 103 % and 105 % of nominal were found in all exposure levels over the whole testing period of 96 hours.
Given that the toxicity cannot be attributed to the active ingredient but to the formulation as a whole, the LC_{50} values have been calculated based on nominal test concentrations of the formulation only. Therefore all results are given as nominal values. There were neither any adverse effects nor any mortality in the control group. There were behavioral observations on fish caused by the test item over the whole exposure period in all test levels ≥ 3.13 mg test item /L. At the test level with 3.13 mg test item/L fish showed the following symptoms after 96h: remained for unusually long periods at the water surface; showed labored respiration.
Cumulative mortality was observed as follows (with a total number of 10 fish tested in each test level):

Table CP 10.2.1-1: Cumulative mortality

Exposure time	4 h		24 h		48 h		72 h		96 h	
Test level (mg test item / L)	No. of dead	% dead	No. of dead	% dead	No. of dead	% dead	No. of dead	% dead	No. of dead	% dead
Control	0	0	0	0	0	0	0	0	0	0
1.56	0	0	0	0	0	0	0	0	0	0
3.13	0	0	0	0	0	0	0	0	0	0
6.25	0	0	0	0	0	0	1	10	1	10
12.5	2	20	10	100	10	100	10	100	10	100
25.0	10	100	10	100	10	100	10	100	10	100

Conclusions:

Based on nominal concentrations, the 96 h – LC_{50} was calculated by probit analysis to be 7.75 mg test item / L (c.l.95%: 6.43 - 9.33 mg /L). The NOEC was considered to be 1.56 mg test item / L, the highest concentration without lethal or sublethal effects. The minimum concentration causing 100% mortality (96h) was 12.5 mg test item /L. The maximum concentration causing no number of dead fish (96h) was 3.13 mg test item/L.

Report:	[redacted], 2004;M-229361-01
Title:	Acute toxicity of Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 400 to the waterflea Daphnia magna Code: AE F115008 02 OD35 A202
Report No:	C040690
Document No(s):	M-229361-01-1
Guidelines:	**EU (=EEC): 92/69/EEC, part C2; OECD: 202; USEPA (=EPA): OPPTS 850.1010, subdivision E, §72-2;Deviation not specified**
GLP/GEP:	**yes**

Executive Summary:

The aim of the study was to determine the influence of the test item on mobility of *Daphnia magna* over 48 hours in a static exposure, expressed as EC_{50} for immobilisation.

Young *Daphnia magna* (1st instars <24 hour old, 6 x 5 animals per concentration) were exposed in a static system over a period of 48 hours to nominal concentrations of 2.0, 4.0, 8.0, 16.0 and 32.0 mg formulation/L without feeding. In addition an untreated dilution water control was tested.
After 24 and 48 hours, behaviour of the water fleas was visually evaluated by counting mobile daphnids. Additionally all possible signs on sublethal effects had to be recorded. Based on nominal concentrations of the mixed formulation, the EC_{50} for immobilisation after 48 hours (24 hours) of static exposure was 8.3 mg formulation/L (11.8 mg formulation/L). Based on nominal concentrations of the mixed formulation, the EC_{50} for immobilisation after 48 hours of static exposure was 8.3 mg form./L (95 % confidence limits 7.3 to 9.5 mg formulation/L). The corresponding EC_{50} for immobilisation after 24 hours of static exposure was 11.8 mg formulation/L (95 % confidence limits 10.4 to 13.5 mg form./L). Statistical results confirm the observed NOEC of 4.0 mg formulation/L after 24 and 48 hours of exposure on a 5 % level of significance (significantly treatment related immobilisation at 8.0 mg formulation/L after 24 and 48 hours of exposure).

Materials and Methods:

Test item: Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 400; Content: 8.82 % w/w Iodosulfuron-methyl-sodium + 26.0 % w/w Mefenpyr-diethyl; Product code: AE F115008 02 OD35 A202; Specification: Batch AAIM01665; BCS-Development No.: 30 00353917; Physical-density: 1.144 g/mL; Analysis ref. code: AZ 11073.

Young *Daphnia magna* (unfed first instars, <24 hour old, from laboratory stock breeding) were exposed in a static test system for 48 hours to nominal concentrations of 2.0, 4.0, 8.0, 16.0 and 32.0 mg formulation/L without feeding. In addition an untreated dilution water control was tested. Each vessel (glass beakers; 100 mL) served as one replicate filled with 50 mL artificial mineral medium M7 (similar to the M4 medium, Elendt 1990). Six vessels (replicates), each provided with five daphnids, were used per treatment group and control (= 30 animals per study group). After 24 and 48 hours, behaviour of the water fleas was visually evaluated by counting mobile daphnids, defined as animals with swimming movements (slight movements of antennae were not interpreted as swimming movement) within approximately 15 seconds after gentle agitation of the test vessel. Additionally all possible signs on sublethal effects had to be recorded and physical-chemical water parameters were assessed.

For analytical verification of the test item concentrations and the control sample were taken at 0 and 48 hours. High-performance liquid chromatography (HPLC) was used as analytical method.

An acute non-GLP toxicity test was performed on September 04, 2003 ([redacted] report No.: DOM 23074) under the same conditions using the reference substance $K_2Cr_2O_7$, p.a. grade (test concentrations: 0.75, 1.00, 1.33, 1.78, 2.37 and 3.16 mg/L). The 24 hour EC_{50} of 1.28 mg/L (95% confidence limits 1.17-1.39 mg/L) determined in this test matched well data obtained during previous studies with the same test substance. The slope function for the regression line (after Litchfield & Wilcoxon (4)) was = 1.40, based on a calculated probit slope of 6.835 (DOM 23074).

Dates of experimental work: December 01, 2003 – March 11, 2004

Results:

Study quality:
Since no immobilisation of untreated control animals occurred, the quality limit of 10 % control immobility was met. As the physical chemical measurements show, the composition of the test water corresponds to the nominal values, and the EC_{50} of the reference substance is located within the required range. Thus, the study conditions and breeding quality met the required quality criteria.

Analytical findings:
The measured concentrations of a.s.-component iodosulfuron-methyl-sodium in the freshly prepared test solutions at test initiation ranged between 97% and 101% (mean: 99%) of the corresponding nominal concentrations.
The measured concentrations of the aged test solutions at the end of the 48 hours exposure period ranged between 95% to 102% (mean: 97%) of nominal, demonstrating stability in the test system.
Given that the toxicity cannot be attributed to the active substance component but to the tested formulation as a whole, the EC_{50} values have been calculated based on nominal test concentrations only. Detailed analytical results are presented in the following table:

Table CP 10.2.1-2: Analysed concentrations of iodosulfuron-methyl-sodium in test solutions

Nominal test concentrations		Analysed concentrations of the freshly prepared solutions		Analysed concentrations of the freshly prepared	
mg form./L	µg a.s./L[1]	µg a.s./L	% of nominal	µg a.s./L	% of nominal
Control		< 4.9	--	< 4.9	--
2.0	176	174	99 %	167	95 %
4.0	353	347	98 %	347	98 %
8.0	706	687	97 %	674	96 %
16.0	1410	1402	99 %	1360	96 %
32.0	2820	2857	101 %	2874	102 %
		Mean: 99 % of nominal		Mean: 97 % of nominal	

[1] = measured a.s.-component AE F115008

Biological findings:
Observations on immobilisation are listed as follows:

Table CP 10.2.1-3: Toxicity to Daphnia magna (based on nominal concentrations)

Nominal Test Concentration Mg form./L	Exposed Daphnids (=100%)	Immobilised Daphnids			
		24 h.		48 h.	
		n	% ± SD	n	% ± SD
Control	30	0	0	0	0
2.0	30	0	0	0	0
4.0	30	0	0	0	0
8.0	30	4	13 ± 10	16	53 ± 21
16.0	30	24	80 ± 22	28	93 ± 10
32.0	30	30	100	30	100

Biological endpoints derived:
From the results presented above the following biological endpoints can be derived:

Table CP 10.2.1-4: Statistical results of Probit Analysis conducted for determination of EC50 values

Probit Analysis for data obtained after	Slope Function (after Litchfield & Wilcoxon)	EC_{50} mg form./L nominally	Lower 95 % cl mg form./L nominally	Upper 95 % cl mg form./L nominally
24 hours	1.415	**11.8**	10.4	13.5
48 hours	1.453	**8.3**	7.3	9.5

Conclusions:

Based on nominal concentrations of the mixed formulation Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 400, the EC_{50} for immobilisation after 48 hours of static exposure was 8.3 mg formulation/L (95 % confidence limits 7.3 to 9.5 mg formulation/L).
The corresponding EC_{50} for immobilisation after 24 hours of static exposure was 11.8 mg formulation/L (95 % confidence limits 10.4 to 13.5 mg form./L).
Statistical results confirm the observed NOEC of 4.0 mg formulation/L after 24 and 48 hours of exposure on a 5% level of significance (significantly treatment related immobilisation at 8.0 mg formulation/L after 24 and 48 hours of exposure).

Report;	[redacted]; [redacted];2004;M-229597-01
Title:	Influence of Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300 on the growth of the green alga, Pseudokirchneriella subcapitata (formerly named Selenastrum capricornutum)
Report No:	C040808
Document No:	M-229597-01-1
Guidelines:	**OECD; 201;Deviation not specified**
GLP/GCP:	**yes**

Executive Summary:

The aim of the study was to determine the toxicity of the test item to *Pseudokirchneriella subcapitata*, expressed as EC_{50} for growth.

Cultures of *Pseudokirchneriella subcapitata* (green alga) with an initial cell density of 10 000 cells/mL per test concentration were exposed in a chronic multigeneration test for 3 days under static test conditions to the nominal concentrations of 0.10, 0.31, 1.0, 3.1 and 10.0 mg formulation/L. In addition an untreated medium control was tested. (Potassium dichromate as positive control was tested once a year.)
24, 48 and 72 hour growth rates based on cell numbers were used to determine the endpoints. Given that the toxicity cannot be attributed to one of the active ingredients but to the test material as a whole, the calculations are based on nominal concentrations only. The (0-72h) E_rC_{50} is 6.71 mg formulation/L, the (0-72h) NOE_rC is < 0.1 mg formulation/L.

Materials and Methods:

Test material: Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300; Analysed content: AE F115008: 8.82 % w/w and AE F107892: 26.0 % w/w; Batch No.: AAIM01665; Product code: AE F115008 02 OD35 A202; Physical-density: 1.144 g/mL; Certificate of Analysis: AZ 11073.
Green alga (*Pseudokirchneriella subcapitata*) were exposed in a chronic multigeneration test for 3 days under static test conditions to the nominal concentrations of 0.10, 0.31, 1.0, 3.1 and 10.0 mg formulation/L. In addition a untreated medium control was tested. At test initiation the cell density was 10 000 cells/mL per test concentration. Aliquots each 150 g of the untreated medium were filled into the 6 controls and of the treated medium into the 3 treatment vessels per treatment level. The pH values ranged from 7.9 to 8.7 in the controls and the incubation temperature ranged from 23.0°C to 23.3°C (measured in an additional incubated glass vessel) over the whole period of testing.
Concentrations of iodosulfuron-methyl-sodium were measured in all test levels on day 0 and day 3 of the exposure period.
OD-measurements, pH-measurements, temperature measurements (hourly by the data logger) and morphological examination of cells were made on study days 0, 1, 2 and 3. Cell numbers were estimated photometrically.

Dates of experimental work: January 23, 2004 - March 16, 2004

Results:

Validity criteria:
The validity criterion of cell density increase >16x in the control is fulfilled. A factor of 96.8 was determined for the present study.

Analytical findings:
Concentrations of iodosulfuron-methyl-sodium in the treatment levels found on day 0 were 82.6 to 108 % of nominal (average 102 %). On day 3 recoveries of 77.1 to 107 % (average 99.0 %) of nominal were found. Given that the toxicity cannot be attributed to the active ingredient but to the test material as a whole, the calculations are based on nominal concentrations only. Detailed analytical results are presented in the following table:

Table CP 10.2.1-5: Comparison of nominal and analytically determined concentrations of iodosulfuron-methyl-sodium on Day 0 and Day 3

Nominal concentration in mg formulation/L (µg Iodosulfuron-methyl-sodium /L)		Day 0		Day 3	
		Actual concentration (µg Iodosulfuron-methyl-sodium/L) Average	%	Actual concentration (µg Iodosulfuron-methyl-sodium/L) Average	%
Control		<0.882	--	<0.882	--
0.10	(8.82) A	7.98	82.6	6.25	77.1
	B	6.59		7.35	
0.31	(27.3)	29.6	108	29.3	107
1.0	(88.2)	92.5	105	91.4	104
3.1	(273)	292	107	292	107
10.0	(882)	931	106	880	99.8
Stock solution 100	(8820)	8169	92.6	--	--
Mean (without stock solution)			102		99.0

Biological findings:
A static 72 h algal growth test was conducted to determine the effects of the test substance on the growth of the green alga, *Pseudokirchneriella subcapitata*. Observations on growth rates are listed as follows:

Table CP 10.2.1-6: Test initiation with 10,000 cells/mL

Nominal concentration (mg formulation/L)	Cell number after 72 h (mean)	Average growth rate in µ [1/*d*] (0 h → 72 h)	% inhibition of average growth rate
control	968,000	1.529	--
0.10	843,000	1.483	3.0
0.31	731,000	1.436	6.1
1.0	430,000	1.259	17.7
3.1	208,000	1.017	33.5
10.0	65,000	0.631	58.8

Growth rate values are preferred, because the validity criteria concerning the exponential algal growth are fulfilled within this test.

Conclusions:

The (0 - 72h) E_rC_{50} for iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300 is 6.71 mg formulation/L (CI 95%: 5.80-7.91) and the (0 - 72h) NOE_rC is <0.1 mg formulation/L.

Report:	KCP 10.2.1 /04; [redacted], M.;2004;M-229602-03
Title:	Iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 100 + 300 - Influence on the growth of Lemna gibba G3 Code: AE F115008 02 OD35 A202
Report No:	C040811
Document No(s):	M-229602-03-1
Guidelines:	**OECD: 221;Deviation not specified**
GLP/GEP:	**yes**

Executive summary:

The aim of the study was to determine the toxicity of the test item to *Lemna gibba* G3 as a representative aquatic macrophyte, expressed as EC_{50} for 50 percent inhibition of growth rate. 3x12 fronds per test concentration were exposed in a chronic multigeneration test for 7 days under static test conditions to nominal concentrations of 0.41, 1.23, 3.70, 11.1, 33.3 and 100 µg formulation/L against a control. Counting of fronds and pH-measurements were made on study days 0, 2, 5 and 7. The dry weight was determined only on day 7. Recoveries of iodosulfuron-methyl-sodium were measured in all freshly prepared test vessels on day 0 and in all aged test vessels on day 7, except the lowest test level. Given that the toxicity cannot be attributed to the active ingredient but to the test material as a whole, the calculations are based on nominal concentrations of the formulation only. The E_rC_{50} for frond numbers (based on average growth rates) was 8.4 µg formulation/L (95% confidence limits: 0.3 to 239 µg/L) and the E_rC_{50} for dry weights (based on average growth rates) was > 100 µg formulation/L. The NOE_rC for frond numbers (based on average growth rates) was 1.23 µg formulation/L and the NOE_rC for dry weights (based on average growth rates) was 3.70 µg formulation/L.

Material and Methods:

Test item: Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 100+300; Product code: AE F115008 02 OD35 A202; active ingredients: AE F115008, content: 8.82 % w/w, AE F107892, content: 26.0 % w/w; Formulation-batch No.: AAIM01665; Certificate of analysis: AZ 11073.

3x12 fronds per test concentration were exposed in a chronic multigeneration test for 7 days under static test conditions to nominal concentrations of 0.41, 1.23, 3.70, 11.1, 33.3, and 100 µg formulation/L against a control. The pH values ranged from 7.6 to 8.7 in all test levels and the incubation temperature ranged from 23.3 °C to 23.4 °C measured in an additional incubated glass vessel over the whole period of testing (mean 23.3 °C). The incubator was illuminated with a light intensity of 7717 lux (mean of total of 5 measurements on day 0: 6837, 7314, 8109, 8162, and 8162 lux). Recoveries of AE F115008 were measured in all freshly prepared test levels on day 0 and in all aged test levels on day 7, except the lowest test level.

Dates of experimental work: November 26, 2003 to March 11, 2004

Results:

Validity criteria:
The following validity criterion is met: the frond number in the controls increased by a factor of 10 corresponding to a doubling time (T_d) of about 2.1 days (minimum requirement: T_d = 2.5 days).

Analytical findings:

The quantities of AE F115008 found in all freshly prepared test levels on day 0 in reference to nominal concentrations ranged between 81 and 105 % (average 89 %). In 7 d-aged test levels there were analytical findings between 80 and 110 % (average 91 %) of nominal. The lowest test concentration of 0.41 ug formulation/L has not been analysed because this concentration was below the NOEC. Given that the toxicity cannot be attributed to only one of the active ingredients but to the test material as a whole, the calculations are based on nominal concentrations of the formulation only.

Table CP 10.2.1-7: Nominal and measured concentrations of AE F115008

Nominal concentration in µg formulation/L (µg AE F130081/L)	Day	Detection 1	Detection 2	Mean	% of nominal
Control	0 7	< 0.0196[1] < 0.0196	< 0.0196 < 0.0196	< 0.0196 < 0.0196	- -
0.41 (0.036)	0 7	not determined not determined	not determined not determined	- -	- -
1.23 (0.11)	0 7	0.117 0.121	0.114 0.121	0.115 0.121	105 110
3.70 (0.33)	0 7	0.299 0.302	0.293 0.306	0.296 0.304	90 92
11.1 (0.98)	0 7	0.797 0843	0.788 0.841	0.792 0.842	81 86
33.3 (2.94)	0 7	2.55 2.07	2.47 3.15	2.51 2.61	85 89
100 (8.82)	0 7	7.39 7.05	7.35 7.02	7.37 7.03	84 80

[1] lowest standard concentration used for determination

Biological findings:

Growth inhibition was observed as listed below.

Table CP 10.2.1-8: Frond counts, dry weight and percent inhibition of the average growth rate (12 fronds correspond to 1.1 mg dry weight at test initiation

Test levels (µg formulation/L)	Final frond no. (day 7, means)	Final dry weight of plants (day 7, means) [mg]	% inhibition	
			Average growth rate for frond no.	Average growth rate for dry weight of plants
Control	122	13.1	-	-
0.41	107	12.2	5.5	3.1
1.23	108	12.7	5.0	1.3
3.70	92	10.9	12.3	7.3
11.1	23	5.7	71.5	33.3
33.3	18	4.8	82.6	40.7
100	19	5.0	80.4	38.6

Conclusions:

The inhibitory effect of the formulation to duckweed, *Lemna gibba* was determined as follows:

Table CP 10.2.1-9: The inhibitory effect of the formulation to *Lemna gibba*

	Average growth rate for fronds numbers (µg formulation/L)	Average growth rate for dry weights of plants (µg formulation/L)
E_rC_{50} (Cl 95%)	8.4 (0.3 – 239)	> 100
LOE_rC	3.70	11.1
NOE_rC	1.23	3.70

The LOE_rC determination is based on statistical data analysis.

CP 10.2.2 Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms

No additional long-term and chronic toxicity study on fish, aquatic invertebrates and sediment dwelling organisms was conducted.

CP 10.2.3 Further testing on aquatic organisms

No further testing on aquatic organisms was conducted.

CP 10.3 Effects on arthropods

CP 10.3.1 Effects on bees

The ecotoxicological endpoints of honey bee laboratory studies are provided in the following tables. Details of the honeybee testing with the active substance iodosulfuron-methyl sodium are presented in MCA, Section 6, Point 8.3.1.

Table CP 10.3.1- 1: Bee toxicity data generated with technical iodosulfuron-methyl sodium

Test substance	Ecotoxicological endpoint		Reference
Acute oral and contact toxicity (laboratory) in honey bees			
Iodosulfuron-methyl sodium, tech.	LD_{50}-oral, 48/72 h	LD_{50} > 80 µg a.s./bee	[redacted], 1996 M-141821-01-1 KCA 8.3.1.1 /01
Iodosulfuron-methyl sodium, tech.	LD_{50}-contact, 48/72 h	LD_{50} > 150 µg a.s./bee	[redacted], 1996 M-141225-01-1 KCA 8.3.1.2 /01
Iodosulfuron-methyl sodium, tech.	LD_{50}-oral, 48 h LD_{50}-contact, 48 h	**LD_{50} > 107.6 µg a.s./bee** **LD_{50} > 100 µg a.s./bee**	[redacted], 2012 M-436273-01-1 KCA 8.3.1.1 /01
Acute contact toxicity (laboratory) in bumble bees			
Iodosulfuron-methyl sodium, tech.	LD_{50}-contact, 48 h	LD_{50} > 100 µg a.s./bee	[redacted], 2014 M-477331-01-1 KCA 8.3.1.1 /02
Chronic toxicity in adult honey bees (laboratory)			
Iodosulfuron-methyl sodium, tech.	10 d chronic adult feeding study	LC_{50} > 120 mg a.s./kg NOEC ≥ 120 mg a.s./kg	[redacted], 2014 M-479390-01-1 KCA 8.3.1.2 /01

Bold values: endpoints used for risk assessment

Table CP 10.3.1- 2: Honey bee toxicity data generated with formulated iodosulfuron-methyl sodium

Test substance	Ecotoxicological endpoint		Reference
Acute oral and contact toxicity (laboratory)			
Iodosulfuron-methyl sodium + mefenpyr-diethyl OD 400 (100 + 300)	LD_{50}-oral, 48 h LD_{50}-contact, 48 h	LD_{50} 180.98 µg product/bee LD_{50} 317.59 µg product/bee	[redacted], 2004 M-227123-01-1 KCP 10.3.1.1.1/01
Bee brood feeding test			
Iodosulfuron-methyl sodium WG 10 (+Mefenpyr-diethyl WG 15)	Honey bee brood feeding (Oomen *et al.*, 1992)	Slightly, but statistically significantly increased termination rate of eggs, young and old larvae, identical (better) brood nest development than in the control; brood index and brood compensation indices displayed a continuous increase, indicating a successful development of the brood. No ecologically adverse effects on the survival of adult bees and pupae, behaviour, colony strength and overall colony conditions by feeding honey bee colonies sugar syrup at a iodosulfuron-methyl sodium concentration typically present in the spray tank (25 ppm)	[redacted], 2013 M-465335-01-1 KCA 8.3.1.3 /01
Cage and tunnel studies			
Iodosulfuron-methyl sodium + mefenpyr-diethyl OD 400 (100+300 g/L)	Semi-field honey bee brood study (according to OECD 75; forced exposure conditions) in *Phacelia*; application during full-bloom and bees actively foraging	No adverse effects on mortality, flight intensity, behaviour, brood development (brood termination rate, brood index, compensation index) as well as on colony vitality at maximum application rate (0.1 L product/ha)	[redacted], 2014 M-477913-01-1 KCA 8.3.1.3 /02

Risk assessment for bees

Hazard Quotients

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

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

The maximum label rate of Iodosulfuron-methyl sodium + Mefenpyr-diethyl OD 400 (100 + 300) is 0.1 L (100 mL) product/ha in winter wheat (BBCH 13 - 32). With the content of iodosulfuron-methyl sodium and mefenpyr-diethyl within the formulation being 100 g iodosulfuron-methyl sodium/L and 300 g mefenpyr-diethyl/L, respectively, this accounts to a maximum application rate of 10 g iodosulfuron-methyl sodium a.s./ha. Considering a realistic worst case density of 1.15 g/mL of Iodosulfuron-methyl sodium + Mefenpyr-diethyl OD 400, 100 mL product/ha corresponds to 115 g product/ha.

Table CP 10.3.1- 3: Hazard quotients for bees – oral exposure

Test item	Oral LD_{50} [µg a.s./bee] / *[µg product/bee]*	Max. application rate [g a.s./ha] / *[g product/ha]*	Hazard quotient Q_{HO}	Trigger	*A-priori* acceptable risk for adult bees
Max. application rate = 10 g iodosulfuron a.s. / ha via 0.1 L Iodosulfuron+Mefenpyr-diethyl OD 400 / ha, which corresponds to 115 g product / ha					
Iodosulfuron-methyl-sodium, tech.	> 107.6	10	< 0.1	50	yes
Iodosulfuron-methyl sodium + Mefenpyr-diethyl OD 400 (100 + 300 g/L)	*180.98*	*115*	*0.6*	50	yes

The hazard quotient for oral exposure is below the validated trigger value for higher tier testing (i.e. QHO < 50).

Table CP 10.3.1- 4: Hazard quotients for bees – contact exposure

Test item	Contact LD_{50} [µg a.s./bee] / *[µg product/bee]*	Max. application rate [g a.s./ha] / *[g product/ha]*	Hazard quotient Q_{HO}	Trigger	*A-priori* acceptable risk for adult bees
Max. application rate = 10 g iodosulfuron a.s. / ha via 0.1 L Iodosulfuron+Mefenpyr-diethyl OD 400 / ha, which corresponds to 115 g product / ha					
Iodosulfuron-methyl-sodium, tech.	> 100	10	< 0.1	50	yes
Iodosulfuron-methyl sodium + Mefenpyr-diethyl OD 400 (100 + 300 g/L)	*317.59*	*115*	*0.4*	50	yes

The hazard quotient for contact exposure is below the validated trigger value for higher tier testing (i.e. QHC < 50).

Further considerations for the risk assessment

In addition to acute laboratory studies with adult honey bees, iodosulfuron-methyl sodium was further subjected to topical acute bumble bee testing. The study did not reveal sensitivity differences between honey bee and bumble bee foragers.

Moreover, iodosulfuron-methyl sodium was subjected to chronic laboratory testing with adult honey bees. 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 iodosulfuron-methyl sodium per kg aqueous sugar solution (120 ppm). Thus, the nominal employed test concentration exceeded the concentration of iodosulfuron-methyl sodium 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 iodosulfuron-methyl sodium (nominal).

In order to reveal whether iodosulfuron-methyl sodium poses a risk to immature honey bee life stages, a bee brood feeding study 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 was conducted by mixing formulated iodosulfuron-methyl sodium via Iodosulfuron-methyl sodium WG 10 (together with formulated mefenpyr-diethyl, as Mefenpyr-diethyl WG 15), and the tested concentration corresponded to about the concentration of iodosulfuron-methyl sodium in the spray tank of a high-volume use. The actual test concentration of iodosulfuron-methylsodium was 25 mg/L. The administration of 1 litre sugar solution per colony, containing 25 ppm iodosulfuron-methyl sodium, resulted in a slightly-moderately, but statistically significantly

increased termination rate of eggs, young and old larvae, however, there was concurrently an identical or even better brood nest development than in the control. The brood index and the brood compensation indices displayed a continuous increase, indicating a successful development of the brood. There were no ecologically adverse effects on the survival of adult bees and pupae, behaviour, colony strength and overall colony conditions.

In order to clarify whether the observations in the honey bee brood feeding study, conducted under worst-case exposure conditions, are relevant for actual use conditions of iodosulfuron-methyl sodium, a higher tier semi-field honey bee brood study (according to the provisions of the OECD Guidance Document 75) was conducted under forced/confined exposure conditions, by applying the maximum rate (0.1 L) of Iodosulfuron-methyl sodium + mefenpyr-diethyl OD 400 (100+300 g/L) 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 iodosulfuron-methyl-sodium to honey bee colonies, including a very detailed assessment of brood development. Tunnels (20 m length x 5.5 m width x 2.5 m height) were set up on a ca. 75 m² plot of *Phacelia* (2 x 36 m²). Small bee colonies were introduced to the tunnels 3 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 the test item, the *Phacelia*-crop was no longer attractive to bees (faded) 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 (Iodosulfuron-methyl sodium + mefenpyr-diethyl OD 400 (100+300 g/L)) 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, 220 - 270 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 Iodosulfuron-methyl sodium + mefenpyr-diethyl OD 400 (100+300 g/L) does not adversely affect honey bees and honey bee brood when applied at a rate of 0.1 L product/ha (corresponding to 10 g iodosulfuron-methyl sodium a.s./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

Iodosulfuron-methyl sodium has a low acute toxicity to honey bees, with LD50 (oral and contact) above the highest tested dose level (oral: LD50 > 107.6 µg a.s./bee, contact: LD50 > 100 µg a.s./bee). The calculated Hazard Quotients for iodosulfuron-methyl sodium 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 as well as by the results of the semi-field study, which covered the maximum application rates of 10 g iodosulfuron-methyl sodium a.s./ha.

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

Regarding potential side effects of iodosulfuron-methyl sodium on immature honey bee life stages, the conducted bee brood feeding study (Oomen et al., 1992) found slightly-moderately, but statistically significantly increased termination rates of eggs, young and old larvae. Despite of this observation, there was concurrently an identical (better) brood nest development than in the control; in addition, the brood index and brood compensation indices displayed a continuous increase, indicating a successful development of the brood; overall the study revealed no ecologically adverse effects on the survival of adult bees and pupae, behaviour, colony strength and overall colony conditions. Thus, when considering the severity of the exposure situation in this worst-case screening test in combination with the absence of effects on both, colony level parameters and also on the overall development of bee brood, it can be concluded even on the basis of this worst-case screening study that the use of iodosulfuron-methyl sodium as a post-emergence (until early stem elongation) herbicide in cereals - a crop which poses for bees not a profitable feeding and foraging area for nectar and pollen - does not pose an unacceptable risk for adult honey bees, immature honey bee life stages and honey bee colonies.

Nonetheless, in order to clarify whether the conclusions on the basis of lower tiered honey bee studies are correct, iodosulfuron-methyl sodium was subjected to confined semi-field testing (according to the provisions of OECD Guidance Document No. 75), by applying the maximum rate of Iodosulfuron-methyl sodium + mefenpyr-diethyl OD 400 (100+300 g/L) 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 iodosulfuron-methyl sodium, when applied at the maximum application rate of 10 g a.s./ha in cereals, 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.

CP 10.3.1.1 Acute toxicity to bees

CP 10.3.1.1.1 Acute oral toxicity to bees

Report:	[redacted];[redacted];2004;M-227123-01
Title:	Assessment of side effects of AE F115008 02 OD35 A202 to the honey bee, Apis mellifera L., in the laboratory
Report No:	C039689
Document No:	M-227123-01-1
Guidelines:	**OECD: 213, 214;Deviation not specified**
GLP/GEP:	**no**

Executive summary:

The objective of this study was to determine the oral and contact toxicity of the test item AE F115008 02 OD35 A202 (= Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 400 (100 + 300 g/L)) on the honey bee, *Apis mellifera* L, in a dose response test according to the OECD guideline No. 213 and 214 (1998).
In the laboratory, the bees were exposed to the doses of 70.86, 141.72, 283.45, 566.89 and 1133.79 µg product/bee (equivalent to 6.25, 12.5, 25.0, 50.0 and 100.0 µg a.s./bee) of the test item AE F115008 02 OD35 A202 by feeding and topical application. The nominal test levels of 70.86, 141.72, 283.45, 566.89 and 1133.79 µg product/bee corresponded to an actual intake of 85.20, 162.84, 303.85, 485.29 and 864.02 µg product/bee. Perfekthion (active ingredient: dimethoate, nominal content: 400 g/L) was tested as a toxic standard. 5 replicates with 50 bees were used per treatment level. The number of dead bees in the individual test cages was recorded after 4 h, 24 h and 48 h. In case of symptoms of poisoning the behavioural differences between the bees of the control group and those of the test item treatment were noted at each observation interval.

According to the results of this study it can be stated the oral LD_{50}/48h of AE F115008 02 OD35 A202 (=Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 400 (100 + 300 g/L)) is 180.98 µg product/bee and the contact LD_{50}/48h of is 317.59 µg product/ bee.

Material and Methods:

Test item: AE F115008 02 OD35 A202; Batch/ Lot. No.: AAIM01665; GAB-code: 20031404; Purity: 1. AE F107892 (mefenpyr-diethyl): 26.0% (w/w) (300 g/L nominal) 2. AE F115008 (iodosulfuron-methylsodium): 8.82% (w/w) (100 g/L nominal).

In the laboratory, the bees were exposed to the doses of 70.86, 141.72, 283.45, 566.89 and 1133.79 µg product/bee (equivalent to 6.25, 12.5, 25.0, 50.0 and 100.0 µg a.s./bee) of the test item AE F115008 02 OD35 A202 by feeding and tropical application. Perfekthion (active ingredient: dimethoate, nominal content: 400 g/L) was tested as a toxic standard. In the oral toxicity test a 50 % (w/v) aqueous sucrose solution was used as control, in the contact toxicity test tap water was used for the control group. 5 replicates with 50 bees were used per treatment level.

For the oral toxicity test, the test item was dissolved in tap water and mixed with a defined amount of a 50 % aqueous sucrose solution such that the intended nominal dose which was calculated for one bee was found in 20 µL. The bees starved during a period of 2 hours prior to test start. 250 µL of the test solution per bee was offered during a period of 6 hours. The amount of solution consumed (mean value of 10 bees) was determined by weighing the feeders before and after feeding. After the feeding period, the bees in the test cages were supplied ad libitum with a pure untreated 50 % aqueous sucrose solution.
For the contact toxicity test, the test item was dissolved in tap water. After the bees had been anaesthetised with carbon dioxide they were treated individually by topical application to the ventral thorax. 2 µL of test item or reference item solution were applied to the thorax of each bee. A 2 µL droplet was chosen in deviation to the guideline recommendation of 1 µL since a higher volume ensured a more reliable dispersion of the test item. After application the bees were returned to the test cages and fed with a 50 % aqueous sucrose solution ad libitum.
The number of dead bees in the individual test cages was recorded after 4 h, 24 h and 48 h. In case of symptoms of poisoning the behavioural differences between the bees of the control group and those of the test item treatment were noted at each observation interval.
The temperature varied between 24.5 and 26.0 °C. Relative air humidity varied between 45 and 75 %. The bees were maintained at dark during the test.

Dates of work: January 27, 2004 - January 29, 2004

Results:

Validity criteria:
The results are considered to be valid. The mean mortality of the control in the oral and contact toxicity test was < 10%. The 24h LD_{50} of the reference item in the oral toxicity test was within the range of 0.10 to 0.35 µg a.s. / bee. The 24h LD_{50} of the reference item in the contact toxicity test was within the range of 0.10 to 0.30 µg a.s. / bee.

Oral toxicity test:
In the oral toxicity the nominal test level of 1133.79 µg product/bee (100.0 µg a.s./bee) corresponded to an actual intake of 864.02 µg product/bee (76.21 µg a.s./bee). At this dose a mortality of 98.0 % (corrected mortality 98.0 %) was observed after 48 hours. The mortality in the reference item was determined to be 88.0 % (corrected mortality 87.8 %) in the highest concentration at test termination.

Contact toxicity test:
Contact toxicity test at the dose of 1133.79 µg product/bee (100.0 µg a.s./bee) which was tested in the contact toxicity test with AE F115008 02 OD35 A202 a mortality of 100.0 % (corrected mortality 100.0 %) was observed after 48 hours. The mortality in the reference item was determined to be 76.0 % (corrected mortality 75.5 %) in the highest concentration after 48 hours.

In the control group fed with 50 % (w/v) sugar solution a mortality of 2.0 % occurred after 48 hours as well as in the control group of the contact toxicity test. In both tests no behavioural differences were observed between the test item treated bees and the control bees during the entire test period.

Table CP 10.3.1.1.1- 1: LD_{50} values in the oral and contact toxicity test of AE F115008 02 OD35 A202

AE F1 1 5008 02 OD35 A202	LD_{50}/24h	LD_{50}/48h
	[µg product/bee]	
Oral toxicity test	192.72	180.98
Contact toxicity test	328.62	317.59

Table CP 10.3.1.1.1- 2: LD_{50} values in the oral and contact toxicity test of the reference item (dimethoate)

Perfekthion	LD_{50}/24h	LD_{50}/48h
	[µg a.s./bee]	
Oral toxicity test	0.16	0.14
Contact toxicity test	0.20	0.19

The effect of AE F115008 02 OD35 A202 (= Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 400 (100 + 300 g/L)) after oral exposure on the mortality of Apis mellifera based on nominal figures are as follows:
24h LD_{50} = 192.72 µg product/bee (95% confidence limits 167.99 - 219.04 µg product/bee)
48h LD_{50} = 180.98 µg product/bee (95% confidence limits 158.69 - 204.35 µg product/bee)
The effect of AE F115008 02 OD35 A202 (= Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 400 (100 + 300 g/L)) after contact exposure on the mortality of Apis mellifera based on nominal figures are as follows:
24h LD_{50} = 328.62 µg product/bee (95% confidence limits 276.15 – 392.53 µg product/bee)
48h LD_{50} = 317.59 µg product/bee (95% confidence limits 254.01 – 380.34 µg product/bee)

Conclusions:

According to the results of this study it can be stated the oral LD_{50}/48h of AE F115008 02 OD35 A202 (=Iodosulfuron-methyl-sodium + Mefenpyr-diethyl OD 400 (100 + 300 g/L)) is 180.98 µg product/bee and the contact LD_{50}/48h of is 317.59 µg product/ bee.

CP 10.3.1.1.2 Acute contact toxicity to bees

See point 10.3.1.1.1

CP 10.3.1.2 Chronic toxicity to bees

A 10 day chronic oral toxicity study was conducted with technical iodosulfuron-methyl sodium, the corresponding summary is filed under KCA, point 8.3.1.2/01.

CP 10.3.1.3 Effects on honey bee development and other honey bee life stages

A honey bee brood feeding study according to the provisions of Oomen *et al*. ([redacted] 2013; M-465335-01) as well as a semi-field brood tunnel study according to the provisons of the OECD Guidance Document 75 ([redacted] 2014; M-477913-01-1) have been conducted. These studies are summarized under KCA 8.3.1.3 /01 and KCA 10.3.1.3 /02, respectively.

CP 10.3.1.4 Sub-lethal effects

There is no particular study design / test guideline to assess "sub-lethal effects" in honey bees. However, in each laboratory study as well as in any higher-tier study, sub-lethal effects, if occurring, are described and reported.

CP 10.3.1.5 Cage and tunnel tests

A honey bee brood feeding study according to the provisions of Oomen *et al*. ([redacted] 2013; M-465335-01) as well as a semi-field brood tunnel study according to the provisons of the OECD Guidance Document 75 ([redacted] 2014; M-477913-01-1) have been conducted. These studies are summarized under KCA 8.3.1.3 /01 and KCA 10.3.1.3 /02, respectively.

CP 10.3.1.6 Field tests with honeybees

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

CP 10.3.2 Effects on non-target arthropods other than bees

Toxicity tests on non-target arthropods were conducted with IMS + MPR OD 400 on the sensitive standard species *Typhlodromus pyri* and *Aphidius rhopalosiphi*. A summary of the results is provided in Table CP 10.3.2- 1.

Table CP 10.3.2- 1: IMS + MPR OD 400: Ecotoxicological endpoints for arthropods other than bees

Test species	Tested Formulation, study type, exposure	Ecotoxicological Endpoint		Reference Dossier-file-No.
Aphidius rhopalosiphi	IMS + MPR OD 400	LR_{50} > 300 mL prod./ha		[redacted] & [redacted], 2004
		Corr. Mortality [%]	Effect on Reproduction [%]	C039343
	Laboratory, glass plates			M-226797-01-1
	3.7 mL prod./ha	2.6	29.2	KCA 8.3.2.1 /03
	11.1 mL prod./ha	-2.6[A]	0.6	KCP 10.3.2.1 /01
	33.3 mL prod./ha	-2.6[A]	13.3	
	100.0 mL prod./ha	-2.6[A]	20.8	
	300.0 mL prod./ha	2.6	18.1	
Typhlodromus pyri	IMS + MPR OD 400	LR_{50} > 300 mL prod./ha		[redacted], 2004
		Corr. Mortality [%]	Effect on Reproduction [%]	C039089
	Laboratory, glass plates			M-226371-01-1
	3.7 mL prod./ha	5.0	-11.5[B]	KCA 8.3.2.2 /03
	11.1 mL prod./ha	11.7	5.1	KCP 10.3.2.1 /02
	33.3 mL prod./ha	10.0	15.4	
	100.0 mL prod./ha	10.0	26.9	
	300.0 mL prod./ha	13.3	11.5	

A: A negative value indicates a lower mortality in the treatment than in the control.
B: A negative value indicates a higher reproduction rate in the treatment than in the control.

Risk assessment procedures

The risk assessment was performed according to the 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[4]).

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}

Use pattern:
Please note that for the risk assessment on non-target arthropods, the worst-case application rate of 1 x 0.1 L product/ha in winter wheat has been taken into account. This use pattern is considered to cover also the single application in winter barley as given in the intended use pattern for this product (1 x 0.075 L product/ha; see Table 10-1).

IMS + MPR OD 400 is intended to be applied once with an application rate of 0.1 L product/ha. Therefore, the multiple application factor (MAF) was set at 1.0. Resulting HQ values are presented in the following table. The risk is considered acceptable if the calculated HQ is < 2.

Table CP 10.3.2- 2: HQ for terrestrial non-target arthropods for the in-field scenario

Crop	Species	Appl. rate [mL product/ha]	MAF	LR_{50} [mL product/ha]	HQ	Trigger
Cereals	*T. pyri*	100	1	> 300	<0.3	2
	A. rhopalosiphi			> 300	<0.3	2

The in-field HQ values for *Typhlodromus pyri* and *Aphidius rhopalosiphi* are below the trigger of concern, indicating that **no unacceptable risk is to be expected for non-target arthropods in the in-field area** from the use of IMS + MPR OD 400 according to the proposed use pattern.

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) = 1 (single application)
Drift factor = 0.0277 (90^{th} percentile for 1 application in field crops, 1m distance; ESCORT 2)
VDF (vegetation distribution factor) = 10

[4] 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 CP 10.3.2- 3: HQ for terrestrial non-target arthropods for the off-field scenario

Crop	Species	Appl. rate [mL product/ha]	MAF	Drift [%]	VDF	Corr. factor	LR_{50} [mL product/ha]	HQ	Trigger
Cereals	*T. pyri*	100	1	2.77	10	10	> 300	< 0.009	2
	A. rhopalosiphi				10	10	> 300	< 0.009	2

The calculated HQ values are below the trigger of concern, indicating that **no unacceptable risk is to be expected for non-target arthropods in the off-field area** from the use of IMS + MPR OD 400 according to the proposed use pattern.

CP 10.3.2.1 Standard laboratory testing for non-target arthropods

Report:	[redacted];[redacted];[redacted];2004;M-226797-01
Title:	Effects of AE F115008 02 OD35 A202 on the parasitoid Aphidius rhopalosiphi in the laboratory - dose-response test -
Report No:	C039343
Document No:	M-226797-01-1
Guidelines:	**IOBC: WPRS 2000;Deviation not specified**
GLP/GEP:	**yes**

Executive Summary:

The purpose of this study was to produce a concentration-response curve for mortality effects seen over 48 h of exposure. Adult *Aphidius rhopalosiphi* (approximately 48 h old; 7 females and 3 males per replicate) were exposed on glass plates to application rates of 3.7, 11.1, 33.3, 100 and 300 ml product/ha (diluted in 200 L deionized water/ha) and were compared to those of deionized water treated controls (200 L/ha). Perfekthion (0.3 mL product/ha diluted in 200 L deionized water/ha) was used as reference treatment. The duration of the mortality part was 48 hours. The reproductive performance of the survivors was examined for another 24 hour period using females from the control and from those test item concentrations where corrected mortality was < 50.0 %.
Under laboratory conditions the LR_{50} could not be calculated. It is estimated to be higher than 300 mL product/ha. The reproductive capacity of *A. rhopalosiphi* was not statistically significantly reduced up to 300 mL product/ha (the highest rate tested) compared to the control. All validity criteria according to the guideline were met.

Materials and Methods:

Test item. AE F115008 02 OD35 A202 (code for: IMS + MPR OD 400); active ingredients: AE F107892, content: 26.0 % w/w, AE F115008, content: 8.82 % w/w; Batch No.: AAIM01665; Density: 1.144 g/mL; Certificate of Analysis Ref. Code: AZ 11073.

Under laboratory conditions approximately 48 h old adult *Aphidius rhopalosiphi* (7 females and 3 males per replicate) were exposed to dried spray deposits of 3.7, 11.1, 33.3, 100 and 300 mL product/ha in 200 L deionised water/ha (corresponding to 0.0212, 0.0635, 0.190, 0.572 and 1.72 g product/L) on glass surfaces (4 replicates per treatment group). Deionised water was used as a control treatment and Perfekthion (0.3 ml product/ha diluted in 200 L deionised water/ha, containing nominally 400 g dimethoate/L) as a reference treatment. The duration of the mortality part was 48 hours. The reproductive performance of the survivors was examined for another 24 hour period using females from the control and from those test item concentrations where corrected mortality was < 50.0 %.

Toxic standard: Perfekthion (containing nominally (analysed) 400 g (401.2 g) dimethoate/L) 0.3 mL in 200 L deionised water/ha (corresponding to 1.5 µL Perfekthion/L); control: deionised water only (200 L/ha).

Dates of work: November 17, 2003 – December 15, 2003

Results:

Table CP 10.3.2.1- 1: Validity criteria

Validity criteria	Recommended	Obtained
Control mortality	≤ 13 %	2.5 %
Control reproduction rate	≥ 5 mummies per female	36.6 mummies per female (mean value)
	≤ 2 parasitoids producing zero values	1 parasitoid producing zero values
Toxic standard mortality	≥ 50 %	100 %

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

Table CP 10.3.2.1- 2: Effects on mortality and parasitisation efficiency of *Aphidius rhopalosiphi*, laboratory testing-dose response test

Test item	**AE F115008 02 OD35 A202 (IMS + MPR OD 400)**					
Test organism	*Aphidius rhopalosiphi*					
Exposure on	treated glass surfaces					
Treatment	**Mortality after 48 h[a] [%]**		**Corrected mortality after 48 h [%]**	**Mummies per female[b]**		**Reduction of parasitisation efficiency relative to the control [%]**
Control	2.5			36.6		
3.7 mL product/ha	5.0	n.s.	2.6	25.9	n.s.	29.2
11.1 mL product/ha	0.0	n.s.	-2.6	36.3	n.s.	0.6
33.3 mL product/ha	0.0	n.s.	-2.6	31.7	n.s.	13.3
100 mL product/ha	0.0	n.s.	-2.6	28.9	n.s.	20.8
300 mL product/ha	5.0	n.s.	2.6	29.9	n.s.	18.1
0.3 mL Perfekthion/ha (Toxic reference)	100.0	*	100.0	n.a.		-

[a] n.s. = not significant, * = significant, Fisher Exact Test, $\alpha = 0.05$
[b] n.s. = not significant; Dunnett-Test, $\alpha = 0.05$
n.a. = not assessed

Conclusions:

Under laboratory conditions the LR_{50} could not be calculated due to the low effects of AE F115008 02 OD35 A202 (IMS + MPR OD 400). It is estimated to be higher than 300 mL product/ha.
The reproductive capacity of *A. rhopalosiphi* was not statistically significantly reduced up to 300 mL product/ha (the highest rate tested) compared to the control.

Report:	[redacted]; [redacted]; 2004; M-226371-01
Title:	Effects of AE F115008 02 OD35 A202 on the predatory mite Typhlodromus pyri in the laboratory dose response test
Report No:	C039079
Document No:	M-226371-01-1
Guidelines:	**EU (=EEC): Bluemel et al. (2000); Deviation not specified**
GLP/GEP:	**yes**

Executive Summary:

The purpose of this study was to produce a dose response curve for mortality effects seen after 7 days of exposure. Mites were exposed on glass plates to application rates of 3.7, 11.1, 33.3, 100 and 300 ml product/ha (diluted in 200 L deionized water/ha) and were compared to those of deionized water treated controls (200 L/ha). Perfekthion (10 mL product/ha diluted in 200 L deionized water/ha) was used as reference treatment. Assessment of the number of living, escaped and dead mites was conducted 2 and 7 days after application. For the reproduction assessment surviving mites from the control and from all test item groups displaying less than 50 % corrected mortality were sexed and the number of eggs per females was recorded at 4 assessment days within one week. Under worst case laboratory conditions the LR50 for Typhlodromus pyri was estimated to be > 300 mL product/ha in

200 L deionized water/ha. The reproduction of *Typhlodromus pyri* was not affected up to 300 ml product/ha in 200 L deionized water/ha. All validity criteria according to the guideline were met.

Materials and Methods:

Test item. AE F115008 02 OD35 A202 (code for IMS + MPR OD 400); active ingredients: AE F107892, content: 26.0 % w/w, AE F115008, content: 8.82 % w/w; Batch No.: AAIM01665; Density: 1.144 g/mL; Certificate of Analysis Ref. Code: AZ 11073.

Protonymphs (< 24 hours old) of *Typhlodromus pyri* (20 mites per replicate) were exposed to air dried spray deposits of 3.7, 11.1, 33.3, 100 and 300 mL product/ha in 200 L deionised water/ha (corresponding to 0.0212, 0.0635, 0.190, 0.572 and 1.72 g product/L) on glass plates (3 replicates per treatment group) under laboratory conditions. Deionised water (200 L/ha) was used as a control treatment and Perfekthion (10 mL product/ha diluted in 200 L deionised water/ha, containing nominally 400 g dimethoate/L) as a reference treatment. Initial evaluation of the test item was conducted in a range finding test. Based on these results a main test was designed. Assessment of the number of living, escaped and dead mites was conducted 2 and 7 days after application. For the reproduction assessment surviving mites from the control and from all test item groups displaying less than 50 % corrected mortality were sexed and the number of eggs per females was recorded at 4 assessment days within one week. The toxic standard treatment caused a 100 % corrected mortality.

Toxic standard: Perfekthion (containing nominally (analysed) 400 g (401.2 g) dimethoate/L): 10 mL in 200 L deionised water/ha (corresponding to 50 µL Perfekthion/L); control: deionised water only (200 L/ha).

Dates of work: December 02, 2003 – December 16, 2003

Results:

Table CP 10.3.2.1- 3: Validity criteria

Validity criteria	Recommended	Obtained
Control mortality	≤ 20 %	0 %
Control reproduction: Number of eggs per female for the second week	> 4 eggs	7.8 eggs
Toxic standard mortality (control corrected) at day 7 after test initiation	> 50 % (preferably < 100 %)	100 %

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

Mortality

There were no significant differences compared to the control up to 3.7 ml product/ha (Fisher Exact Test, a = 0.05). Significantly increased mortality to the control was observed at 11.1 mL up to and including 300 mL product/ha. The statistically significant differences occurring at these rates are not considered to be a test item effect, because mortality was below 20 % and is thus within the limit of the accepted range for the control mortality. The LR_{50} value could not be calculated due to the low effects of the product for the tested rates. Therefore, the LR_{50} was determined to be: LR_{50} > 300 mL AE F115008 02 OD35 A202/ha, the highest rate tested in the study. No abnormal behaviour or conditions were observed with the surviving mites.

Reproduction

There were no significant differences compared to the control in all rates tested (Bonferroni t-Test (inhomog. Var.), a = 0.05).

Table CP 10.3.2.1- 4: Effects on mortality and reproduction of *Typhlodromus pyri*, laboratory testing, dose response test

Test item	AE F115008 02 OD35 A202 (IMS + MPR OD 400)					
Test organism	*Typhlodromus pyri*					
Exposure on	Dried spray deposits on glass plates					
Treatment	**Mortality[a] [%]**		**Corrected mortality [%]**	**Reproduction[b] [eggs/female]**		**Effect on reproduction[c] [%]**
Control	0.0			7.8		
3.7 mL product/ha	5.0	n.s.	5.0	8.7	n.s.	-11.5
11.1 mL product/ha	11.7	*	11.7	7.4	n.s.	5.1
33.3 mL product/ha	10.0		10.0	6.6	n.s.	15.4
100 mL product/ha	10.0	*	10.0	5.7	n.s.	26.9
300 mL product/ha	13.3	*	13.3	6.9	n.s.	11.5
10 mL Perfekthion/ha (Toxic reference)	100	*	100	n.a.		n.a.
LR_{50}	**> 300 mL product/ha**					

[a] n.s. = not significant, * = significant; Fisher Exact Test, α = 0.05
[b] n.s. = not significant; Bonferroni-t-Test (inhomog. Var.), α = 0.05
[c] negative value indicates increased reproduction compared to the control
n.a. not applicable

Conclusions:

Under worst case laboratory conditions the LR_{50} of AE F115008 02 OD35 A202 (IMS + MPR OD 400) on artificial substrate (glass) on *Typhlodromus pyri* was determined to be LR_{50} > 300 ml product/ha in 200 L deionised water/ha. The reproduction of *T. pyri* was not affected up to 300 mL AE F115008 02 OD35 A202/ha in 200 L deionised water/ha.

CP 10.3.2.2 Extended laboratory testing, aged residue studies with non-target arthropods

No extended laboratory testing, aged residue studies were deemed necessary.

CP 10.3.2.3 Semi-field studies with non-target arthropods

No semi field studies were deemed necessary.

CP 10.3.2.4 Field studies with non-target arthropods

No field studies were deemed necessary.

CP 10.3.2.5 Other routes of exposure for non-target arthropods

No relevant exposure of non-target arthropods is expected by other routes of exposure than by contact.

CP 10.4 Effects on non-target soil meso- and macrofauna

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

Predicted environmental concentrations used in risk assessment

Predicted environmental concentrations in soil (PEC_{soil}) values were calculated for the active substance and its respective metabolites as described in detail in MCP Sec 9, CP 9.1.3.

The maximum PEC_{soil} values are summarised in the following table.

Table CP 10.4- 1 Maximum PEC_{soil} of the product IMS + MPR OD 400 for the uses assessed, considering a standard mixing depth of 5 cm, a bulk density of 1.5 g/mL soil ; and a product density: 1.144 g/mL

Use pattern	Winter cereals, 1 × 10 g a.s./ha (25% interception) [mg/kg]	Winter cereals, 1 × 7.5 g a.s./ha (50% interception) [mg/kg]
IMS + MPR OD 400	**0.1144**	0.0572

Bold values: worst case considered in risk assessment

Table CP 10.4- 2 Maximum PEC_{soil} of iodosulfuron-methyl-sodium and its metabolites for the uses assessed.

Use pattern	Winter cereals, 1 × 10 g a.s./ha (25% interception) [mg/kg]	Winter cereals, 1 × 7.5 g a.s./ha (50% interception) [mg/kg]
Iodosulfuron-methyl-sodium	**0.010**	0.005
AE F075736	**0.006**	0.003
AE F161778	**0.001**	<0.001
AE F059411	**0.001**	<0.001
AE F145740	**<0.001**	<0.001
AE F145741	**<0.001**	<0.001
AE 0000119	<0.001	<0.001
BCS-CW81253	0.002	0.001
AE 0002166	0.002	<0.001

Bold values: worst case considered in risk assessment

Table CP 10.4- 3: PEC_{soil} of metabolites AE F059411, AE 0000119 and BCS-CW81253 for the uses assessed, taking the effect of accumulation into account (standard mixing depth of 5 cm)

Use Pattern	PEC_{soil}	AE F059411 [mg/kg]	AE 0000119 [mg/kg]	BCS-CW81253 [mg/kg]
Winter cereals 1 × 10 g a.s./ha, 25% interception	plateau	<0.001	<0.001	<0.001
	total*	**0.002**	**<0.001**	**0.003**
Winter cereals 1 × 7.5 g a.s./ha, 50% interception	plateau	<0.001	<0.001	<0.001
	total*	<0.001	<0.001	0.001

* total = plateau (background concentration after multi-year use) + max. PEC_{soil} (see Table CP 10.4- 2)
Bold values: worst case considered in risk assessment

CP 10.4.1 Earthworms

The summary of the toxicity of IMS + MPR OD 400, iodosulfuron-methyl-sodium and its soil metabolites to earthworms is provided in Tables 10.4.1- 1-3. Details of the studies with the active substance and the metabolites are presented in the document M, Point CA 8.4.

Chronic toxicity of iodosulfuron-methyl-sodium to earthworms

Table CP 10.4.1- 1 Endpoints used in risk assessment

Test substance	Test species, Test design	Endpoint	Reference
IMS + MPR OD 400	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC ≥ 100 mg prod./kg dws	[redacted], 2013 M-465323-01-1 KCP 10.4.1.1 /01
Iodosulfuron-methyl-sodium	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC 9.3 mg a.s./kg dws[1)]	[redacted] & [redacted], 2010 10P29RR M-397577-01-1 KCA 8.4.1 /02
AE F075736	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item sprayed on soil surface	NOEC ≥0.216 mg/kg dws[2)]	[redacted], 1998 CE98/092 M-182339-01-1 KCA 8.4.1 /01
AE F145741	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC ≥100 mg/kg dws	[redacted], 2013 82101022 M-457891-01-1 KCA 8.4.1 /03
AE F145740	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC ≥100 mg/kg dws	[redacted], 2013 82091022 M-457334-01-1 KCA 8.4.1 /04
AE 0002166	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC ≥100 mg/kg dws	[redacted], 2013 82111022 M-457338-01-1 KCA 8.4.1 /05

Test substance	Test species, Test design	Endpoint	Reference
BCS-CW81253	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC ≥100 mg/kg dws	[redacted], 2013 13 10 48 091 S M-462824-01-1 KCA 8.4.1 /06
AE 0000119	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC ≥100 mg/kg dws	[redacted], 2011 LRT-RG-R-104/11 M-404685-01-1 KCA 8.4.1 /07
AE F059411	*Eisenia fetida* reproduction, 56 d, (5% peat in test soil)	NOEC 30 mg/kg dws	[redacted] (2011) LRT-RG-R-100/11 M-410920-01-1 KCA 8.4.1 /08

[1)] corrected to an analysed purity of 93.0%
[2)]No observed effects at 10 g/ha and 50 g/ha; conversion from g/ha to mg as/kg dws with the following assumptions: calculated based on actual test rate, analysed purity of 92.2%, test vessel surface of 283.4 cm2 and test substrate of 850 g wet weight with moisture content of 28.8% per test vessel
dws = dry weight soil

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

Table CP 10.4.1- 2 TER calculations for earthworms

Compound, test design	Endpoint	$PEC_{soil,max/accu}$ [mg/kg]	TER_{LT}	Trigger
IMS + MPR OD 400 reproduction	NOEC ≥100 mg prod./kg dws	0.1144	≥ 874	5
Iodosulfuron reproduction	NOEC 9.3 mg/kg dws	0.010	930	5
AE F075736 reproduction	NOEC 0.216 mg/kg dws	0.006	36	5
AE F145741 reproduction	NOEC ≥100 mg/kg dws	<0.001	≥ 100 000	5
AE F145740 reproduction	NOEC ≥100 mg/kg dws	<0.001	≥ 100 000	5
AE 0002166 reproduction	NOEC ≥100 mg/kg dws	0.002	≥ 50 000	5
BCS-CW81253 reproduction	NOEC ≥100 mg/kg dws	0.003	≥ 33 333	5
AE 0000119 reproduction	NOEC ≥100 mg/kg dws	<0.001	≥ 100 000	5
AE F059411 reproduction	NOEC 30 mg/kg dws	0.002	15 000	5

Conclusion: The TER_{LT} values are above the trigger, indicating no unacceptable risk for earthworms.

CP 10.4.1.1 Earthworms sub-lethal effects

Report:	[redacted]; [redacted];2013;M-465323-01
Title:	Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G: Effects on survival, growth and reproduction of the earthworm Eisenia fetida tested in artificial soil
Report No:	kra/Rg-R-151/13
Document No:	M-465323-01-1
Guidelines:	**EU Directive 91/414/EEC** **Regulation (EC) No. 1107/2009** **US EPA OCSPP Not Applicable;none**
GLP/GEP:	**yes**

Executive Summary:

The purpose of this study was to assess the effect of Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100 + 300) G on survival, growth, and reproduction of the earthworm *Eisenia fetida* during an exposure in an artificial soil (10% peat content) with 5 different test concentrations.
Adult *Eisenia fetida* (with clitellum and weight range 0.36 to 0.56 g, approximately 8 months old, 8 x 10 animals for the control group and 4 x 10 animals for each treatment group) were exposed in artificial soil (with 10 % peat content) to an untreated control and to the nominal concentrations of 10, 18, 32, 56 and 100 mg test item/kg dry weight artificial soil. The test item was mixed into the soil. After 28 days the surviving animals and their weight alteration was determined. After additional 28 days the number of offspring was assessed. The test was performed according to the guideline ISO 11268-2 (1998) and the OECD Guideline 222 (2004). The NOEC and LOEC (based on reproduction) for this study were determined to be 56 mg and 100 mg test item/kg dry weight artificial soil, respectively.

Material and methods:

Test item: Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100 + 300) G; Sample description: TOX09939-00; Batch code: EFT000452; Material No.: 06352286; Specification No.: 102000011563-06; Content: 93.84 g iodosulfuron-methyl-sodium/L and 302.3 g mefenpyr-diethyl/L; Density: 1.135 g/mL.

Adult Eisenia fetida (approx. 8 months old, 8 x 10 animals for the control group and 4 x 10 animals per test concentration of the treatment group) were exposed in an artificial soil (with 10% peat content) to the nominal test concentrations of 10, 18, 32, 56 and 100 mg test item/kg dry weight artificial soil. The test item was mixed into the soil. After 28 days the number of surviving animals and their weight alteration was determined. They were then removed from the artificial soil. After further 28 days, the number of offspring was determined. The test was performed according to the guideline ISO 11268-2 (1998) and the OECD Guideline 222 (2004). Mortality, weight change, feeding activity and reproduction rate were determined as endpoints. The artificial soil contained 69 % industrial quartz sand, 20 % kaolin clay, 10 % sphagnum peat, shredded, 1 % food, dried ground cow manure, and $CaCO_3$ for the adjustment to pH to 6.0 ± 0.5 according to OECD 222; the pH was 5.55 to 5.64 at experimental start and 6.32 to 6.48 at experimental end; the water content at experimental start was 33.08% to 34.49% (54.44% to 57.96% of the maximum water holding capacity) and at experimental end 33.10% to 35.00% (54.49% to 59.29% of the maximum water holding capacity); temperature was

within the range of 18°C to 22°C; the illumination was 16 h light : 8 h dark, light intensity was within the range of 400 to 800 lux.

Toxic standard (Carbendazim EC 360 G): 0 – 1.25 – 2.50 – 5.00 mg a.s./kg soil d.w.; control: untreated artificial soil moistened with deionised water, solvent control: none.

Dates of experimental work: January 10, 2013 to March 15, 2013

Results:

Validity Criteria:

Table CP 10.4.1.1- 1: Validity criteria

Validity criteria	Recommended	Obtained
Mortality of the adults in the control	≤ 10%	0%
Rate of reproduction of juveniles (earthworms per control vessel)	≥ 30	361.6
Coefficient of variance of reproduction in the control	≤ 30%	6.5%

The validity criteria of the test according to the guideline were fulfilled.

In the most recent toxic standard reference test with the reference item Carbendazim EC 360 G (Study No.: Rg-R-Ref 19/12; Report No. kra-Rg-R-Ref 19/12; NON-GLP, performed from September 21 2012 to November 28, 2012), no mortality of the adult earthworms was observed 28 days after application. The change of body weight of the adult earthworms of the test concentration of 5.0 mg a.s./kg dry weight soil was statistically significant reduced in comparison to the control. The number of juveniles per test vessel of the two highest test concentrations of 2.50 and 5.00 mg a.s./kg dry weight artificial soil were statistically significant reduced in comparison to the control. EC_{10}, EC_{20} and EC_{50} for reproduction were calculated to be 3.06, 3.22 and 3.54 mg a.s./kg dry weight artificial soil, respectively.

Mortality:
After 28 days of exposure no worms died in the control group and no mortality was observed at any test item concentration.

Effect on growth:
Statistically significant different values for the growth relative to the control were not observed.
Therefore, based on biological and statistical significance:
NOEC related to growth: ≥ 100 mg test item/kg dry weight artificial soil
LOEC related to growth: > 100 mg test item/kg dry weight artificial soil

Reproduction:
No statistically significant different values for the number of juveniles per test vessel relative to the control were observed at the test concentrations of 10, 18, 32 and 56 mg test item/kg dry weight artificial soil. Statistically significant different values for the number of juveniles per test vessel relative to the control were observed at the highest test concentration of 100 mg test item/kg dry weight artificial soil.
Therefore, based on biological and statistical significance:

NOEC related to reproduction: 56 mg test item/kg dry weight artificial soil
LOEC related to reproduction: 100 mg test item/kg dry weight artificial soil

Table CP 10.4.1.1- 2: Effects on mortality and changes in body weight of the adults after an exposure period of 28 days and the number of offspring per test vessel after 56 days are shown in the following table (values in this table are rounded values).

Test object	*Eisenia fetida*					
Test item	**Control**	**IMS+MPR OD 400 (100+300) G**				
mg test item/kg dry weight artificial soil	---	10	18	32	56	100
Mortality of adult earthworms [%] after 28 days	0	0	0	0	0	0
Mean change of body weight of the adults from day 0 to day 28 [%] *	38.22	32.45	40.38	40.13	41.40	37.70
Standard Deviation	4.81	5.34	3.25	7.68	3.84	2.49
Mean number of offspring per test vessel after 56 days **	361.6	368.5	359.8	365.8	351.3	324.3 **
Standard Deviation	25.6	40.3	41.7	41.5	14.6	39.4
Coefficient of variance (%)	6.5	10.9	11.6	11.3	4.2	12.1
% of control	---	101.9	99.5	101.1	97.1	89.7
					Reproduction	
EC_{10} (mg test item/kg dry weight soil [1)]) (95% confidence limits)					n. d.	
EC_{20} (mg test item/kg dry weight soil [1)]) (95% confidence limits)					n. d.	
EC_{50} (mg test item/kg dry weight soil [1)]) (95% confidence limits)					n. d.	

* no statistical significance compared to the control (Williams' Multiple Sequential t-test, two-sided, $\alpha = 0.05$)
** statistical significance compared to the control (Williams' Multiple Sequential t-test, one-sided smaller, $\alpha = 0.05$)
1) Probit analysis
n. d. not determinded due to mathematical reasons or inappropriate data

Conclusions:

Overall, based on the biological and statistical significance of the effects observed on growth and reproduction, it was concluded that the NOEC for this study is 56 mg test item/kg dry weight artificial soil. Thus, the overall LOEC was determined to be 100 mg test item/kg dry weight artificial soil.

CP 10.4.1.2 Earthworms field studies

Considering the findings reported above no further studies are required.

CP 10.4.2 Effects on non-target soil meso- and macrofauna (other than earthworms)

A summary of the toxicity of IMS + MPR OD 400, Iodosulfuron-methyl-sodium and its soil metabolites to other soil non-target macro-organisms is provided in Table CP 10.4.2- 1. For details of the studies conducted with the active substance and metabolites, please refer to the M document, point CA 8.4.2.1.

Table CP 10.4.2- 1 Endpoints used in risk assessment

Test substance	Test species	Endpoint	Reference
IMS + MPR OD 400	*Hypoaspis aculeifer*	NOEC 56 mg prod./kg dws	[redacted], 2011 M-411284-01-1 KCP 10.4.2.1/01
	Folsomia candida	NOEC ≥ 100 mg prod./kg dws	[redacted], 2011 M-411346-01-1 KCP 10.4.2.1/02
Iodosulfuron-methyl-sodium	*Hypoaspis aculeifer*	NOEC ≥ 1000 mg a.s./kg dws	[redacted], 2012 M-438590-01-1 KCA 8.4.2.1/01
	Folsomia candida	NOEC 316 mg a.s./kg dws	[redacted], 2012 M-438498-01-1 KCA 8.4.2.1/02
AE F075736	*Hypoaspis aculeifer*	NOEC ≥ 10 mg/kg dws	[redacted], 2013 M-456338-01-1 KCA 8.4.2.1/03
	Folsomia candida	NOEC ≥ 10 mg/kg dws	[redacted], 2013 M-464404-01-1 KCA 8.4.2.1/04
AE F145741	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	[redacted], 2013 M-462732-01-1 KCA 8.4.2.1/05
AE F145740	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	[redacted], 2013 M-459885-01-1 KCA 8.4.2.1/06
AE 0002166	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	[redacted], 2013 M-470489-01-1 KCA 8.4.2.1/07
BCS-CW81253	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	[redacted], 2013 M-453497-01-1 KCA 8.4.2.1/08
	Folsomia candida	NOEC ≥ 100 mg/kg dws	[redacted], 2013 M-462821-01-1 KCA 8.4.2.1/09
AE F059411	*Hypoaspis aculeifer*	NOEC 100 mg/kg dws	[redacted], 2010 M-452258-01-1 KCA 8.4.2.1/10
	Folsomia candida	NOEC ≥ 100 mg/kg dws	[redacted], 2011 M-400027-01-1 KCA 8.4.2.1/11
AE 0000119	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	[redacted], 2010 M-386844-01-1 KCA 8.4.2.1/12
	Folsomia candida	NOEC ≥ 100 mg/kg dws	[redacted], 2010

Test substance	Test species	Endpoint	Reference
			M-384229-01-1 KCA 8.4.2.1/13

dws = dry weight soil

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 CP 10.4.2- 2 TER calculations for other non-target soil meso- and macrofauna

Compound	Species	Endpoint	$PEC_{soil,max,accu}$ [mg/kg]	TER	Trigger
IMS + MPR OD 400	*Hypoaspis aculeifer*	NOEC 56 mg product/kg dws	0.1144	490	5
	Folsomia candida	NOEC ≥ 100 product/kg dws	0.1144	≥ 874	5
Iodosulfuron-methyl-sodium	*Hypoaspis aculeifer*	NOEC ≥ 1000 mg a.s./kg dws	0.010	≥ 100 000	5
	Folsomia candida	NOEC 316 mg a.s./kg dws	0.010	31 600	5
AE F075736	*Hypoaspis aculeifer*	NOEC ≥ 10 mg/kg dws	0.006	≥ 167	5
	Folsomia candida	NOEC ≥ 10 mg/kg dws	0.006	≥ 167	5
AE F145741	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	<0.001	≥ 100 000	5
AE F145740	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	<0.001	≥ 100 000	5
AE 0002166	*Hypoaspis aculeifer*	NOEC ≥ 100 mg a.s./kg dws	0.002	≥ 50 000	5
BCS-CW81253	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	0.003	≥ 33 333	5
	Folsomia candida	NOEC ≥ 100 mg/kg dws	0.003	≥ 33 333	5
AE F059411	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	0.002	≥ 50 000	5
	Folsomia candida	NOEC ≥ 100 mg/kg dws	0.002	≥ 50 000	5
AE 0000119	*Hypoaspis aculeifer*	NOEC ≥ 100 mg/kg dws	<0.001	≥ 100 000	5
	Folsomia candida	NOEC ≥ 100 mg a.s./kg dws	<0.001	≥ 100 000	5

Conclusion: The TER values are above the trigger, indicating no unacceptable risk for soil non-target macro-organisms, i.e. collembola and soil mites.

CP 10.4.2.1 Species level testing

Report:	[redacted];2011;M-411284-01
Title:	Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G: Effects on the reproduction of the predatory mite Hypoaspis aculeifer
Report No:	11 10 48 064 S
Document No:	M-411284-01-1
Guidelines:	**OECD 226 (2008): Predatory mite (Hypoaspis (Geolaelaps) aculeifer) reproduction test in soil;none**
GLP/GEP:	**yes**

Executive Summary:

The purpose of this study was to determine potential effects of the test item on the mortality and the reproductive output of the soil mite species *Hypoaspis aculeifer* (CANESTRINI) as a representative of soil micro-arthropods during a test period of 14 days.
10 adult soil mites (females) per replicate (8 replicates for the control group and 4 replicates for each treatment group) were exposed to untreated control and to 56, 100, 180, 320, 560 and 1000 mg test item/kg soil dry weight (d.w.). Two weeks after start of exposure, the number of juveniles and surviving parental mites were determined. The test was performed in accordance with the OECD Guideline 226 (2008).
The EC_{50} was determined to be 165.5 mg test item/kg soil d.w.. The No-Observed-Effect-Concentration (NOEC) and the Lowest-Observed-Effect-Concentration (LOEC) for mortality were determined to be 560 and 1000 mg test item/kg soil d.w., respectively. The No-Observed-Effect-Concentration (NOEC) and the Lowest-Observed-Effect-Concentration (LOEC) for reproduction were determined to be 56 and 100 mg test item/kg soil d.w., respectively.

Materials and Methods:

Test item. Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G; Sample description: TOX 09374-00, Batch ID: EFKP000788; Specification No.: 102000011563-05; Analysed active ingredients: 99.07 g/L iodosulfuron-methyl-sodium (AE F115008), 301.7 g/L mefenpyr-diethyl (AE F107892); Density (20°C): 1.138 g/mL; Water solubility: dispersible.

10 adult soil mites (females) were exposed to 56 - 100 - 180 - 320 - 560 - 1000 mg test item/kg d.w. of soil containing 74.8 % quartz sand, 20 % kaolin clay, 5 % sphagnum peat and 0.2 % CaCO3, at 19.5 - 20.9 °C and a photoperiod light : dark = 16 h : 8 h (604 lx) and were fed every 2 days with *Tyrophagus putrescentiae* (SCHRANK). Mortality and reproduction were determined after 14 days.

Toxic standard (Dimethoate EC 400): 4.10 – 5.12 – 6.40 – 8.00 – 10.00 mg a.s./kg soil d.w.; control: quartz sand, solvent control: none.

Dates of work: April 29, 2011 – May 23, 2011

Results:

Table CP 10.4.2.1- 1: Validity criteria

Validity criteria	Recommended	Obtained
Mean mortality of adult females	≤ 20 %	5.0 %
Mean number of juveniles per replicate	≥ 50	246.4

Coefficient of variation (mean number of juveniles per replicate)	≤ 30 %	17.6 %

All validity criteria for the study were met.

In a separate study (BioChem project No. R 11 10 48 003 S, dated March 29, 2011), the EC_{50} (reproduction) of the reference item Dimethoate EC 400 was calculated to be 5.4 mg a.i./ kg soil d.w. The results of the reference test demonstrate the sensitivity of the test system.

Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G caused no statistically significant mortality (Fisher`s Exact Binomial Test, $p > 0.05$) of adult mites up to a test concentration of 560 mg/kg soil dry weight at the end of the 14-day exposure period. At the tested concentration of 1000 mg test item/kg soil d.w. a statistically significant mortality of adult mites of 80.0 % was observed (Fisher`s Exact Binomial Test, $p \le 0.05$).
In the control group a parental mortality of 5.0 % observed. The mortality in the test item treatment groups ranged between 0 and 80.0 %.
The number of juveniles 14 days after having introduced the parental mites into the test vessels was on average 246.4 in the control and 261.0, 187.0, 102.3, 41.3, 37.0 and 0.0 at the test concentrations of 56, 100, 180, 320, 560 and 1000 mg test item/kg soil d.w. The test item caused no statistically significant reduction of reproduction up to and including a test concentration of 56 mg/kg soil dry weight. At the tested concentrations of 100, 180, 320, 560 and 1000 mg test item/kg soil dry weight statistically significant reductions (William's t-test, $p \le 0.05$) of 58.5, 83.3, 85.0 and 100.0 % were observed, respectively.

Table CP 10.4.2.1- 2: Effects on mortality and reproduction of *Hypoaspis aculeifer*

Test item **Test object** **Exposure**	**Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G** ***Hypoaspis aculeifer*** **Artificial soil**	
	Adult mortality	Reproduction
	(mg test item/kg soil d.w.)	
LOEC	1000	100
EC_{10}	-	66.2
EC_{20}	-	90.7
LC_{50}/EC_{50}	612.8	165.5
95 % confidence limit	471.3-779.8	129.3-210.9
NOEC	560	56

Table CP 10.4.2.1- 3: Effects on mortality and reproduction of *Hypoaspis aculeifer*

Endpoint	**Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G (mg metabolite/kg soil d.w.)**						
	control	**56**	**100**	**180**	**320**	**560**	**1000**
Mortality of soil mites after 14 days (%)	5.0	5.0	5.0	7.5	2.5	2.5	80.0*
Mean number of juveniles after 14 days	264.4	261.0	187.0*	102.3*	41.3*	37.0*	0.0*
CV %	17.6	25.5	10.7	74.2	58.7	73.3	-
Reduction of reproduction (% to control)	-	-5.9	24.1	58.5	83.3	85.0	100.0

* statistically significant difference compared to control (Fisher`s Exact Binomial Test for mortality, $p \leq 0.05$; Williams t-test for reproduction; $p \leq 0.05$)
Calculations were done using non-rounded values
Percent reduction: $(1 - R_t / R_c) * 100$ %
Rt = the reproduction observed in the treated group(s)
Rc = the reproduction observed in the control group
Negative values indicate a higher reproductive performance compared to control.

Conclusions:

In a 14-day Hypoaspis aculeifer reproduction study with Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G, the LC50 was determined to be 612.8 mg test item/kg soil d.w. (95 % confidence limits: 471.3 - 779.8 mg test item/kg soil d.w.) and the EC50 was determined to be 165.5 mg test item/kg soil d.w. (95 % confidence limits: 129.3 - 210.9 mg test item/kg soil d.w.) The No-Observed-Effect-Concentration (NOEC) and the Lowest-Observed-Effect-Concentration (LOEC) for mortality were determined to be 560 and 1000 mg test item/kg soil d.w., respectively. The No-Observed-Effect-Concentration (NOEC) and the Lowest-Observed-Effect-Concentration (LOEC) for reproduction were determined to be 56 and 100 mg test item/kg soil d.w., respectively.

Report:	[redacted];[redacted];2011;M-411346-01
Title:	Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G: Effects on the reproduction of the collembolans Folsomia candida
Report No:	11 10 48 065 S
Document No:	M-411346-01-1
Guidelines:	**OECD 232 (2009): OECD Guideline for testing of chemicals No. 232 (adopted 7 September 2009): Collembolan reproduction test in soil ISO 11267 (1999): Soil quality – Inhibition of reproduction of Collembola (Folsomia candida) by soil pollutants;none**
GLP/GEP:	**yes**

Executive Summary:

The purpose of this study was to determine potential effects of the test item on the reproductive output of the collembolans *Folsomia candida* as a representative of soil micro-arthropods during a test period of 28 days.
10 collembolans (9-12 days old) per replicate (8 replicates for the control group and 4 replicates for each treatment group) were exposed to untreated control and to 5.6, 10, 18, 32, 56, 100 mg test item/kg soil dry weight. After 4 weeks the number of offspring (juveniles) and surviving parental collembolans were counted. The test was performed as a limit test in accordance with the OECD Guideline 232 (2009) and the International Standard ISO 11267 (1999).
The overall No-Observed-Effect-Concentration (NOEC) was determined to be ≥ 100 mg test item/kg soil dry weight. The Lowest-Observed-Effect-Concentration (LOEC) was determined to be > 100 mg test item/kg soil dry weight. The validity criteria for the control group of the study were accomplished.

Materials and Methods:

Test item: Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G; Sample description: TOX 09374-00; Batch ID: EFKP000788; Specification No.: 102000011563-05; Analysed active ingredients: 8.71 % w/w, 99.07 g/L iodosulfuron-methyl-sodium (AE F115008), 26.5 % w/w, 301.7 g/L mefenpyr-diethyl (AE F107892); Density (20°C): 1.138 g/mL; Water solubility: dispersable.

10 *Collembola* (9-12 days old) were exposed to 5.6 - 10 - 18 - 32 - 56 – 100 mg test item/kg soil dry weight containing 74.7 % quartz sand, 20 % kaolin clay, 5 % sphagnum peat and 0.3 % $CaCO_3$, at 18.7 – 21.5 °C and a photoperiod: light : dark = 16 h : 8 h (710 lx) and were fed weekly with granulated dry yeast. Mortality and reproduction were determined after 28 days.

Toxic standard: 44 – 67 – 100 – 150 – 225 mg boric acid/kg soil d.w.; control: quartz sand, solvent control: none.

Dates of work: May 02, 2011 – May 30, 2011

Results:

Table CP 10.4.2.1- 4: Validity criteria

Validity criteria (for the control group)	Recommended	Obtained
Mean adult mortality	≤ 20 %	5.0 %
Mean number of juvenile per replicate	≥ 100	893
Coefficient of variation (mean number of juveniles per replicate)	≤ 30 %	11.5 %

The requirement of the ISO guideline concerning the precision of the counting method (average error <10 %) was fulfilled, the determined overall error of counting amounted to 4.4 %.

In a separate study (BioChem project No. R 11 10 48 004 S, dated May 05, 2011), the EC_{50} (reproduction) of the reference item boric acid was calculated to be 107 mg a.s./kg soil dry weight. The results of the reference test demonstrate the sensitivity of the test system.

The test item caused 2.5, 7.5, 2.5, 7.5, 0.0 and 2.5 % parental mortality at the test concentrations of 5.6, 10, 18, 32, 56 and 100 mg test item/kg soil d.w., respectively. 5.0 % parental mortality was observed in the control.
No statistically significant effect (Fisher's Exact Binomial Test, $p > 0.05$) on parental mortality was found for any concentration tested. No effects on behaviour of the collembolans were observed during the test.
The number of juvenile springtails counted four weeks after having introduced the parental collembolans into the test vessels was on average 893 in the control and 850, 857, 971, 872, 940 and 866 at the test concentrations 5.6, 10, 18, 32, 56 and 100 mg test item/kg soil d.w., respectively.
No statistically significant effects on the number of juveniles compared to the control group were found was found for any concentration tested.

The no-observed-effect-concentration (NOEC) was determined to be ≥ 100 mg test item/kg dry weight.

Table CP 10.4.2.1-5: Effects on mortality and reproduction of *Folsomia candida*

Test item Test object Exposure	Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G *Folsomia candida* Artificial soil	
	Adult mortality	Reproduction
	(mg test item/kg soil d.w.)	
LOEC	> 100	> 100
LC_{10}/ EC_{10}	> 100	> 100
LC_{20}/ EC_{20}	> 100	> 100
LC_{50}/ EC_{50}	> 100	> 100
NOEC	≥ 100	≥ 100

Table CP 10.4.2.1- 6: Effects on mortality and reproduction of *Folsomia candida*

Endpoint	Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G (mg test item/kg soil d.w.)						
	control	5.6	10	18	32	56	100
Mortality of parental collembolans after 4 weeks (%)	5.0	2.5	7.5	2.5	7.5	0.0	2.5
Mean number of juveniles after 4 weeks	893	850	857	971	872	940	866
CV %	11.5	15.8	13.4	15.8	15.9	10.5	10.1
% Reduction of reproduction compared to control	-	5	4	-9	2	-5	3

No statistically significant differences between the control and test item were calculated for mortality and reproduction (Fisher's Exact Binomial Test with Bonferroni Correction, Williams Multiple Sequential t-test)
Calculations were done using non-rounded values
Percent reduction: $(1 - R_t / R_c) * 100$ %
R_t = the reproduction observed in the treated group(s)
R_c = the reproduction observed in the control group
Negative values indicate a higher reproductive performance compared to control.

Conclusions:

The test item Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300) G showed no statistically significantly adverse effects on adult mortality and reproduction of the collembolans *Folsomia candida* in artificial soil up to and including 100 mg test item/kg soil d.w.
Therefore, the overall No-Observed-Effect-Concentration (NOEC) was determined to be ≥ 100 mg test item/kg soil d.w., and the Lowest-Observed-Effect-Concentration (LOEC) was determined to be > 100 mg test item/kg soil d.w.

CP 10.4.2.2 Higher tier testing

In view of the findings above, no higher tier testing is required.

CP 10.5 Effects on soil nitrogen transformation

The toxicity of iodosulfuron on soil non-target micro-organisms is summarised in Table CP 10.5- 1. For details of the studies conducted with the active substance and metabolites, please refer to the document M, point CA 8.4.2.1.

Table CP 10.5- 1: Effects on soil nitrogen transformation

Test item	Test design	Ecotoxicological endpoint	Reference
N-transformation			
IMS + MPR OD 400	Study duration 28 d	no unacceptable effects ≥0.67 µL prod./ha ≥0.0673mg prod./mg dws	[redacted] 2004 M-226312-01-1 KCP 10.5/01
Iodosulfuron-methyl-sodium	Study duration 28 d	no unacceptable effects ≥0.0586 mg a.s./kg dws [1]	[redacted] (1996) M-141782-01-1 KCA 8.5/01
AE F075736	Study assumably duration 28 d	no effect 0.2 mg/kg	SANCO 7593/VI/97-final from 14 Aug 2000
AE F145741	Study duration 28 d	no unacceptable effects ≥0.059 mg/kg dws	[redacted] (2013) M-457273-01-1 KCA 8.5/02
AE F145740	Study duration 28 d	no unacceptable effects ≥0.063 mg/kg dws	[redacted] (2013) M-457344-01-1 KCA 8.5/03
AE 0002166	Study duration 28 d	no unacceptable effects ≥0.053 mg/kg dws	[redacted] (2013) M-464391-01-1 KCA 8.5/04
AE F161778	Study duration 28 d	no unacceptable effects ≥0.046 mg/kg dws	[redacted] (2013) M-464817-01-1 KCA 8.5/05
BCS-CW81253	Study duration 28 d	no unacceptable effects ≥0.043 mg/kg dws	[redacted] (2013) M-459899-01-1 KCA 8.5/06
AE 0000119	Study duration 28 d	no unacceptable effects ≥0.4 mg/kg dws	[redacted] (2010) M-395864-01-1 KCA 8.5/07
AE F059411	Study duration 42 d	no unacceptable effects ≥0.204 mg/kg dws	[redacted] (2003) M-448838-01-1 KCA 8.5/08

dws = dry weight soil; a.s. = active substance; prod. = product
[1] Corrected to an analysed purity of 87.4%

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 25% 28 days after application, indicating low risk to soil micro-organisms.

Report:	[redacted];[redacted];2004;M-226312-01
Title:	Iodosulfuron-methyl-sodium & mefenpyr-diethyl OD 100 + 300 (AE F115008 02 OD35 A202): Determination of effects on nitrogen transformation in soil
Report No:	C039050
Document No(s):	M-226312-01-1
Guidelines:	**OECD: 216, (2000);Deviation not specified**
GLP/GEP:	**no**

Executive Summary:

The objective of the experiment was to determine the influence of 0.13 and 0.67 µL Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300/kg dry weight soil on nitrogen transformation in an agricultural soil. The test was performed in accordance with OECD guideline No. 216, adopted 21st January 2000.
A silty sand soil was exposed for 28 d to concentrations of 0.13 and 0.67 µL test item/kg soil dry weight. Application rates were equivalent to 0.1 and 0.5 L test item/ha, which is equivalent to 1x and 5x recommended field rate, respectively. Lucerne-grass-green meal was added to the soil (5 g/kg dry weight soil) to stimulate nitrogen transformation. During the 28-day experiments, the recommended field rate of Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300 (0.1 L test item/ha) and the 5-fold overdose of the test item caused a temporary stimulation of the daily nitrate rates at the time interval 0-7 and 7-14 days after treatment, respectively, in a silty sand soil amended with Lucerne-grass-green meal. At the end of the experiment (14-28 day interval), differences in the nitrate-N rates between the control soil samples and treated soil samples are < 25 % and meet the trigger values of above mentioned guideline for a termination of the study.

Material and methods:

Test item. Iodosulfuron & Mefenpyr-diethyl OD 100+300; Analytical findings: AE F115008, 8.82 % w/w; AE F107892, 26.0 % w/w; Development No.: 0309260; Batch No.: AAIM01665; Density: 1.144 g/mL.

A silty sand soil was exposed for 28 d to concentrations of 0.13 and 0.67 µL lodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300/kg dry weight soil. Application rates were equivalent to 0.1 and 0.5 L lodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300/ha, which is equivalent to 1x and 5x recommended field rate, respectively. Lucerne-grass-green meal was added to the soil (5 g/kg dry weight soil) to stimulate nitrogen transformation. Sodium chloride was used as a reference standard in the experiments.

Dates of work: November 06, 2003 – December 09, 2003

Results:

Validity Criteria:
In this study, the highest coefficient of variation (CV) between nitrate-N concentration in replicate control samples was 24 % (7 days after treatment). This difference of the recommended limit of ± 15 % was only found on day 7 and is not considered to be relevant for the validity of the study.

In the most recent non-GLP-test (LKC-N-Ref-01/03, [redacted], C., 2003) with the reference item Sodium chloride and the agricultural soil described above, 16 g NaCl/kg dry weight soil had distinct and long-term (> 28 days) influence on microbial mineralization of nitrogen.

<u>Nitrogen transformation:</u>
During the 28-day experiment, the recommended field rate of Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300 and the 5-fold overdose of the test item caused a temporary stimulation of the daily nitrate rates at the time interval 0-7 and 7-14 days after treatment, respectively, in a silty sand soil amended with luceme-grass-green meal. At the end of the experiment (14-28 day interval), differences in the nitrate-N rates between control soil samples and treated soil samples are < 25 % and meet the trigger values of above mentioned guideline for a termination of the study.

Table CP 10.5- 2: Effects on non-target soil micro-organisms

Test item	Iodosulfuron & Mefenpyr-diethyl OD 100+300	
Test object	Soil Microorganisms Nitrogen-Transformation (silty sand soil)	
Exposure	28 days	
µL test item/kg dry weight soil	0.13	0.67
L test item/ha (equivalent)	0.1 (recommended field rate)	0.5 (5x recommended field rate)
Final Result after 28 days	Difference to control < 25 %	Difference to control < 25 %

Conclusions:

When used as recommended, Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300 should not have an impact on nitrogen transformation in soils.

CP 10.6 Effects on terrestrial non-target higher plants

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.

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.

Seedling emergence and vegetative vigour studies have been conducted with the plant protection product with the product code AE F115008 02 OD35 A202, which contains the active substance iodosulfuron (100 g/L) and the safener mefenpyr-dithyl (300 g/L) solved in an OD-formulation, following OECD testing guideline 208 (see Point 10.6.2).

Ecological endpoints
The endpoints from the tier 2 studies used for the risk assessment are summarised in following table.

Table CP 10.6- 1: Survey of non-target plant tests performed with IMS + MPR OD 400

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 + MPR OD 400 0 (control), 1.56, 3.13, 6.25, 12.5, 25 and 50 mL prod./ha for corn and oats 0 (control), 0.39, 0.78, 1.56, 3.13, 6.25 and 12.5 mL prod./ha for cucumber and onion 0 (control), 0.1, 0.2, 0.39, 0.78, 1.56 and 3.13 mL prod./ha for sugar beet, oilseed rape, radish, sunflower, soybean and tomato with visually observations on Days 7, 14 and 21, dry weight measurements on Day 21	most sensitive species: sunflower; **lowest EC_{50}: 2.43 mL prod./ha**	[redacted] & [redacted]; 2004; C042604 M-232956-01-1 KCP 10.6.2/01
Dicotyledoneae: 7 (sugar beet, oilseed rape, radish, cucumber, sunflower, soybean, tomato) Monocotyledoneae: 2 (oat, corn)	Tier 2 seedling emergence IMS + MPR OD 400 0 (control), 1.56, 3.13, 6.25, 12.5, 25 and 50 mL prod./ha with daily assessments of germination until 65% emergence of control seedlings, and assessments of number of plants and mortality on Days 7 and 14 after this time, measurement of dry weight on Day 14	most sensitive species: sugar beet; **lowest EC_{50}: 5.62 mL prod./ha**	[redacted] & [redacted], 2004; C042664 M-233058-01-1 KCP 10.6.2/02

Exposure

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)*[5] from the spray-drift predictions of *Ganzelmeier & Rautmann (2000)*[6]. 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. The highest single application rate of iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) is 0.1 L product/ha.

Deterministic Risk assessment

According to the Terrestrial Guidance Document[7], 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.

[5] 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.

[6] Ganzelmeier H., Rautmann D. (2000) Drift, drift-reducing sprayers and sprayer testing. Aspects of Applied Biology 57, 2000, Pesticide Application. Public domain.

[7] Anonymous (2002b). Guidance Document on terrestrial ecotoxicology under council directive 91/414/EEC. SANCO/10329/2002. 17 October 2002.

Table CP 10.6- 2: Deterministic risk assessment for iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) based on effects on seedling emergence

arable field crops, one application, 100 mL product/ha; lowest ER_{50} = 5.62 mL product/ha						
Distance	Drift	PER	TER			
[m]	(%)	no drift reduction [mL product/ha]	No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
1	2.77	2.77	2.03	4.06	**8.12**	**20.30**
5	0.57	0.57	**9.86**	**19.72**	**39.44**	**98.60**
10	0.29	0.29	**19.38**	**38.76**	**77.52**	**193.80**

Table CP 10.6- 3: Deterministic risk assessment for iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) based on effects on vegetative vigour

arable field crops, one application, 100 mL product/ha; lowest ER_{50} = 2.43 mL product/ha						
Distance	Drift	PER	TER			
[m]	(%)	no drift reduction [mL product/ha]	No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
1	2.77	2.77	0.88	1.76	3.52	**8.80**
5	0.57	0.57	4.26	**8.52**	**17.04**	**42.60**
10	0.29	0.29	**8.38**	**16.76**	**33.52**	**83.80**

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

Table CP 10.6- 4: HC5-calculation for seedling-emergence with iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L).

species	input values	LOG_{10}	mean of log10 transformed EC_{50} values	extrapolation factor for n=9
corn	19.55	1.2911	1.0858	1.7091
Oat	24.59	1.3908		
Oilseed rape	7.34	0.8657		
Radish	9.06	0.9571		
Sugar beet	**5.62**	0.7497		
cumber	5.69	0.7551		
Sunflower	6.35	0.8028		
Tomato	12.29	1.0896		
soybean	74.11	1.8699		

The HC_5 calculation for the shoot dry weight-EC_{50}-values from the seedling emergence study leads to HC_5 values of **2.799.** In case of the vegetative vigor study only three ER50-figures are available. The others are greater-than-figures. Thus, no HC5 could be calculated for vegetative vigour. The TER calculation is summarised in the following tables.

Table CP 10.6- 5: Probabilistic risk assessment for iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) based on effects on seedling emergence

arable field crops, one application, 100 mL product/ha, HC_5 = 2.799 mL product/ha						
Distance	Drift	PER	TER			
[m]	(%)	no drift reduction [g sum of a.i./ha]	No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
1	2.77	2.77	**1.01**	**2.02**	**4.04**	**10.1**
5	0.57	0.57	**4.91**	**9.82**	**19.64**	**49.1**
10	0.29	0.29	**9.65**	**19.30**	**38.60**	**96.50**

Since iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) has stronger effects on the vegetative vigour of young plants than on the seedling emergence, the vegetative vigour data determine the risk assessment. From Tables 10.6.1- 3 it becomes obvious, that a 5m buffer zone is sufficient to protect terrestrial non-target plants if 50% drift reducing spraying equipment is used. With the use of 90% drift reducing nozzles no buffer zone is required.

Iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) poses no unacceptable risk to terrestrial non-target plants in off-crop areas following the proposed uses.

CP 10.6.1 Summary of screening data

Report:	[redacted]; [redacted];2004;M-229488-01
Title:	Soil mix crop screening tests Compounds used: AE F115008 OD35 A1 (iodosulfuron + mefenpyr-diethyl 100 + 300 g/l, oil dispersion)
Report No:	C040757
Document No:	M-229488-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**no**

Objective
The test reported here was designed to determine the sensitivity of various crops to soil incorporated AE F115008 02 OD35 A1 under standardised glasshouse conditions.

Material and Methods
EC10 values were calculated based on % visual damage and % fresh weight reduction. The results are reported below as both in concentration of µg formulated product per kg of soil (use rate 70 µg/kg) and with the corresponding dose rate in ml formulated product per ha (use rate 100 ml/ha).

Findings
Cereal crops were the most insensitive although some phytotoxicity was recorded from the highest rates used. No statistically significant reduction in fresh weight was recorded at any dose on the cereal crops.

EC_{10} Values (**in µg/kg formulated product mixed in soil**) for HUSSAR®OD based on % phyto ratings and fresh weight harvest at 21 DAT (Log dose vs % effect linear regression)													
	HORVS	SECCW	TRZAS	TRZAW	ZEAMA	LOLMU	BEAVA	BRSNW	**HELAN**	LIUUT	PHSVN	PIBST	SINAL
% Phyto	40.6	40.2	31.2	21.0	6.9	7.5	8.9	**1.6**	6.8	27.8	26.5	6.8	
Fresh Wt.	27.8	52.0	18.2	6.6	9.0	2.3	3.1	**0.6**	2.7			15.3	
EC_{10} Values (**in ml/ha formulated product**) for AE F115008 02 OD35 A1 based on % phyto ratings and fresh weight harvest at 21 DAT (Log dose vs % effect linear regression)													
% Phyto	57.7	57.1	44.3	34.1	9.8	10.7	12.6	**2.3**	9.7	39.5	37.6	9.7	
Fresh Wt.	39.5	73.8	25.8	9.4	12.8	3.3	4.4	**0.9**			3.8	21.7	

Conclusion
Dicot crops are more sensitive, with sunflowers the most sensitive one.

CP 10.6.2 Testing on non-target plants

Report:	[redacted];2004;M-232956-01
Title:	Iodosulfuron-methlyl sodium and Mefenpyr-diethyl 100 + 300 g/L, oil based suspension concentrate (AE F115008 02 OD35 A202) Effects on vegetative vigour of ten species of non-target plants
Report No:	C042604
Document No:	M-232956-01-1
Guidelines:	**OECD: 208B (July 2000, draft);Deviation not specified**
GLP/GEP:	**yes**

Executive summary:

The purpose of this specific study was to evaluate the effect of Iodosulfuron-methyl sodium & Mefenpyr-diethyl 100 + 300 g/L, oil based suspension concentrate (AE F115008 02 OD35 A202) on the vegetative vigour of ten plant species representing a broad range of both dicotyledonous and monocotyledonous plant families.
A total of ten species were tested in this vegetative vigour test under glasshouse conditions including seven dicotyledonous and three monocotyledonous species representing eight different plant families. At the 2-4 leaf stage, plants were sprayed once with doses of AE F115008 02 OD35 A202 ranging from 50 mL product/ha down to 0.10 mL product/ha. There were five dose rates that differed with each species. For oats and corn these were 50, 25, 12.5, 6.25, 3.13 and 1.56 ml product/ha. For cucumber and onion these were 12.5, 6.25, 3.13, 1.56, 0.78 and 0.39 ml product/ha. For sugar beet, oilseed rape, radish, sunflower, soybean and tomato these were 3.13, 1.56, 0.78, 0.39, 0.2 and 0.1 mL product/ha. Each pot (replicate) contained 5 plants and there were 40 plants treated (i.e. 8 replicates). Control pots were treated with de-ionized water. Plants were grown and maintained under glasshouse conditions with a temperature control set at 23 ± 5°C during day, and 18 ± 5°C at night.
Visually observations were made on test days 7, 14 and 21. 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.
Significant adverse effects were observed in all plant species tested, except onion. Based on the results of this study in which AE F115008 02 OD35 A202 was tested under glasshouse conditions the most sensitive species was sunflower with the lowest EC_{50} of 2.43 mL product/ha for shoot dry weight.

Material and Methods:

Test item: Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300 (Code: AE F115008 02 OD35 A202); Batch/Fl.-No.: AAIM01665; contents of a.s.: 8.82 % w/w Iodosulfuron-methylsodium, 26.0 % w/w Mefenpyr-diethyl; Certificate of analysis: AZ 11073.

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 AE F115008 02 OD35 A202 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 50 mL product/ha down to 0.10 ml product/ha using a laboratory track sprayer. The control was treated with deionized water. There were five dose rates that differed with each species. For oats and corn these were 50, 25, 12.5, 6.25, 3.13 and 1.56 ml product/ha. For cucumber and onion these were 12.5, 6.25, 3.13, 1.56, 0.78 and 0.39 ml product/ha. For sugar beet, oilseed rape, radish, sunflower, soybean and

tomato these were 3.13, 1.56, 0.78, 0.39, 0.2 and 0.1 mL product/ha. Plants were grown and maintained under glasshouse conditions with a temperature control set at 23 ± 5°C during day, and 18 ± 5°C at night.
Visually observations were made on test days 7, 14 and 21. 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.

Dates of experimental work: January 29, 2004 - February 26, 2004

Results:

Validity criteria:
This study can be considered valid as the validity criteria of 90% survival during the study period of the untreated controls and the absence of any phytotoxic symptoms was achieved for all species.

Table CP 10.6.2- 1: Validity criteria in the untreated control for the vegetative vigour test with iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L)

Validity criteria	Survival of untreated controls	Phytotoxicity in untreated controls
	>90%	0 %
Corn	100 %	0 %
Oat	100 %	0 %
Onion	95 %	0 %
Oilseed rape	100 %	0 %
Radish	100 %	0 %
Sugar beet	100 %	0 %
Cucumber	100 %	0 %
Sunflower	100 %	0 %
Tomato	100 %	0 %
soybean	100 %	0 %

Biological findings:
All species except onion showed the relevant phytotoxic symptoms within the dose rates tested visible as chlorosis, bleaching, necrosis, leaf deformation, delayed growth, ramification and stunting.
The dose range chosen proved to be too low in most of the species. EC_x figures for mortality and/or biomass could only be obtained for oilseed rape, radish and sunflower.
The table below summarises the NOEC, and where determined the EC_{25}, EC_{50} values for survival, the growth stages at the final assessment and the NOEC, and EC50 for shoot dry weight. Endpoints are expressed as ml product/ha AE F115008 02 OD35 A202.

Table CP 10.6.2- 2: The effect of iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) on ten species

Plant species	Survival			Shoot dry weight			Remark
	NOEC	EC_{25}	EC_{50}	NOEC	EC_{25}	EC_{50}	
corn	50	> 50	> 50	50	> 50	> 50	1; 2
Oats	50	> 50	> 50	50	> 50	> 50	1; 2
Onion	12.5	> 12.5	> 12.5	6.25	> 50	> 50	1; 2
Oilseed rape	3.13	> 3.13	> 3.13	0.78	3.49	20.82	1; 2; 3
Radish	1.56	1.43	2.93	0.78	1.28	4.92	
Sugar beet	3.13	> 3.13	> 3.13	3.13	> 3.13	> 3.13	1; 2
Cucumber	12.5	> 12.5	> 12.5	12.5	12.5	> 12.5	1; 2
Sunflower	3.13	> 3.13	> 3.13	0.78	1.17	**2.43**	1; 2
Tomato	3.13	> 3.13	> 3.13	3.13	> 3.13	> 3.13	1; 2
soybean	3.13	> 3.13	> 3.13	3.13	> 3.13	> 3.13	1; 2

remark 1: EC_{25} and EC_{50} > highest dose rate since no mortality or inhibition > 25% was observed
remark 2: NOEC for survival set to the highest dose rate since mortality was not dose-related
remark 3: in case of shoot dry weight toxrat calculated EC_{25} and EC_{50} figures of 3.49 and 20.82 mL product/ha, respectively. Since the EC_{50} level is far above the highest dose rate this figure has to be treated with care.

Conclusions:

Significant adverse effects were observed in all plant species tested, except onion. Based on the results of this study in which iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) was tested under glasshouse conditions the most sensitive species was sunflower with the lowest EC_{50} of 2.43 mL product/ha for shoot dry weight.

Report:	[redacted]; [redacted]; [redacted]; 2004; M-233058-01
Title:	Iodosulfuron-methyl sodium & mefenpyr-diethyl 100 + 300 g/l, oil based suspension concentrate (AE F115008 02 OD35 A202): Effects on seedling emergence of nine species of non target plants
Report No:	C042664
Document No:	M-233058-01-1
Guidelines:	**OECD: 208A, (draft 2000);Deviation not specified**
GLP/GEP:	**yes**

Executive summary:

The purpose of this specific study was to evaluate the effect of Iodosulfuron-methyl sodium & Mefenpyr-diethyl 100 + 300 g/L oil based suspension concentrate (AE F115008 02 OD35 A202) on the seedling emergence of nine plant species representing a broad range of both dicotyledonous and monocotyledonous plant families.
A total of nine species were tested in this seedling emergence test under glasshouse conditions including seven dicotyledonous and two monocotyledonous species representing seven different plant families. The seeds of the nine species were treated after sowing with the test item. Solutions of the product and serial dilutions were sprayed with doses of the product ranging from 50 mL/ha down to 1.56 mL/ha. Each pot (replicate) contained 5 plants and there were 40 plants treated (i.e. 8 replicates). Control pots were treated with de-ionized water. Plants were grown and maintained under glasshouse conditions with a temperature control set at 23 ± 5°C during day and 18 ± 5°C at night.

Assessments were made daily until 65% emengence of control seedlings, and 7 and 14 days after this time and evaluated against the untreated controls. Statistical analysis of data was performed to obtain NOEC, EC_{25} and EC_{50} values for emergence, survival and biomass (shoot dry weight), for the final assessment using probit analysis with maximum likelihood regression.
The most sensitive species was sugar beet with the lowest EC_{50} of 5.62 mL product/ha for shoot dry weight.

Material and Methods:

Test item: Iodosulfuron-methyl-sodium & Mefenpyr-diethyl OD 100+300 (Code: AE F115008 02 OD35 A202), contents of a.s.: 8.82 % w/w Iodosulfuron-methylsodium, 26.0 % w/w Mefenpyr-diethyl; Batch/Fl.-No.: AAIM01665; Certificate of analysis: AZ 11073.

Seeds of nine species; corn (*Zea mays*), oat *(Avena sativa),* oilseed rape *(Brassica napus)* radish *(Raphanus sativus),* sugar beet *(Beta vulgaris),* cucumber *(Cucumis sativus),* sunflower *(Helianthus annuus),* tomato *(Lycopersicum esculentum)* and soybean *(Glycine max)* were treated after sowing with AE F115008 02 OD35 A202. Solutions of the product and serial dilutions were sprayed with doses of the product ranging from 50 mL/ha down to 1.56 mL/ha using a laboratory track sprayer. The control was treated with deionized water. Onion *(Allium cepa)* was intended to be tested as a tenth species, but was terminated since the validity criteria were not met. Plants were grown and maintained under glasshouse conditions with a temperature control set at 23 ± 5°C during day and 18 ± 5°C at night.
Assessments were made daily until 65% emergence of control seedlings, and 7 and 14 days after this time and evaluated against the untreated controls. Statistical analysis of data was performed to obtain NOEC, EC_{25} and EC_{50} values for emergence, survival and biomass (shoot dry weight), for the final assessment using probit analysis with maximum likelihood regression.

Dates of experimental work: January 20, 2004 - May 21, 2004

Results:

Validity criteria:
This study can be considered valid as the validity criteria of 90% survival during the study period of the untreated controls and the absence of any phytotoxic symptoms was achieved for all species.

Table CP 10.6.2- 3: Validity criteria in the untreated control for the vegetative vigour test with iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L)

	Emergence (% of sown)	Mortality (%)
Validity criteria	>65%	< 10 %
corn	100 %	0 %
Oat	95 %	0 %
Oilseed rape	95 %	0 %
Radish	100 %	0 %
Sugar beet	90 %	2.6 %
Cucumber	90 %	2.8 %
Sunflower	90 %	2.9 %
Tomato	90 %	0 %
soybean	100 %	0 %

Biological findings:
All species showed the relevant phytotoxic symptoms visible as chlorosis, necrosis, leaf deformation and stunting.
Phytotoxicity due to iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) resulted in a suppression of growth leading to a reduction in growth as measured by growth stage in all species. Biomass was the most sensitive endpoint for all species.
The table below summarises the NOEC and where determined the EC_{25} and EC_{50} values for emergence and survival, the growth stages at the final assessment and the NOEC, EC_{25} and EC_{50} for shoot dry weight. Endpoints are related to the product and given as mL product/ha.

Table CP 10.6.2- 4: The effect of iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L)on nine species.

Plant sp.	Emergence			Survival			Shoot dry weight		
	NOEC	EC_{25}	EC_{50}	NOEC	EC_{25}	EC_{50}	NOEC	EC_{25}	EC_{50}
corn	50	> 50	> 50	50	> 50	> 50	3.13	6.15	19.55
Oat	50	> 50	> 50	50	> 50	> 50	3.13	8.77	24.59
Oilseed rape	50	> 50	> 50	6.25	> 50	> 50	3.13	4.41	7.34
Radish	50	> 50	> 50	50	> 50	> 50	1.56	4.39	9.06
Sugar beet	50	> 50	> 50	50	> 50	> 50	1.56	2.82	**5.62**
Cucumber	50	> 50	> 50	50	> 50	> 50	< 1.56	2.28	5.69
Sunflower	50	> 50	> 50	50	> 50	> 50	1.56	0.62	6.35
Tomato	25	19.6	52.8	12.5	32.9	58.7	1.56	4.22	12.29
soybean	50	> 50	> 50	50	> 50	> 50	12.5	29.3	74.11

Conclusions:

Based on the results of this study in which the effect of iodosulfuron-methyl-sodium + mefenpyr-diethyl OD 400 (100+300 g/L) to seedling emergence and survival of nine plant species was tested under glasshouse conditions the most sensitive species was sugar beet with the lowest EC_{50} of 5.62 mL product/ha for shoot dry weight.

CP 10.6.3 Extended laboratory studies on non-target plants

Considering the findings reported above no further studies are required.

CP 10.6.4 Semi-field and field tests on non-target plants

Considering the findings reported above no further studies are required.

CP 10.7 Effects on other terrestrial organisms (flora and fauna)

Studies on effects on other terrestrial organisms are neither available nor required.

CP 10.8 Monitoring data

Reliable monitoring data on iodosulfuron-methyl-sodium are not available.