Bayer CropScience

Document Title

Summary of the ecotoxicological studies foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L)

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Version history

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

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

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CP 10 ECOTOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCT

Comments with respect to the Annex I renewal of approval process

This dossier contains study reports already submitted by Bayer CropScience for the Annex I inclusion of foramsulfuron, as well as new data, not yet evaluated at EU level and that was considered by the applicant to be necessary for the renewal of approval of foramsulfuron. In order to distinguish these, reference to studies in the original dossier are depicted in grey.

For summaries of studies submitted during the frame of the first Annex I inclusion, please refer to the corresponding section in the Monograph. Copies of the study reports are provided in the baseline dossier provided by Bayer CropScience. Additional studies which were not submitted during the Annex I inclusion process are provided in the dossier and summarized in this document.

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 (range) [L/ha]	Maximum application rate, individual treatment (ranges) [g/ha] Foramsulfuron	Isoxadifen-ethyl
Maize	BBCH 12-18	1	-	2.6	60	60
Maize	BBCH 12-18	2	7	1.3	30	30

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	Foramsulfuron AE F092944 AE F130619 AE F153745
Groundwater	Foramsulfuron AE F092944 AE F130619 AE F153745
Surface water	Foramsulfuron AE F092944 AE F130619 AE F153745 AE 0338795 AE F099095 4-Amino-N-methylbenzamide 4-Formamido-N-methylbenzamide Foramsulfuron sulfamic acid
Plant material	Foramsulfuron

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 10.1.1-1 Endpoints used in risk assessment

Test substance		species/origin	Endpoint		Reference
Foramsulfuron	Acute risk assessment	Lowest LD_{50} from Bobwhite quail, Mallard duck	LD_{50}	≥ 2000 mg as/kg bw	XXXXXX1998 M-143541-01-1 KCA 8.1.1.1 /01 XXXXXX 1997 M-142752-01-1 KCA 8.1.1.1 /02
	Long-term risk assessment	Bobwhite quail	NOEC ≡ NO(A)EL	≥ 1000 ppm ≥ 104 mg as/kg bw/d	XXXXXX1999 M-194248-01-1 KCA 8.1.1.3 /01

Toxicity of the formulation

Foramsulfuron is of low acute oral toxicity to Bobwhite quail and Mallard duck with LD_{50} values in excess of 2000 mg a.s./kg bw.
The acute oral toxicity of the formulated product was determined in a study on Bobwhite quail.

Table 10.1.1- 2: Avian toxicity data of the formulated FSN + IDF OD 45 (22.5 + 22.5)

Test species	Test design	Ecotoxicological endpoint	Reference
Bobwhite quail *Colinus virginianus*	acute, oral	LD_{50} ≥ 2000 mg product/kg bw	XXXXXX(2000) M-192635-01-1 KCP 10.1.1.1.01

The results of the study with FSN + IDF OD 45 (22.5 + 22.5) (see) show a low toxicity 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. 1.1 of this dossier, Table 10.1.1- 4 and Table 10.1.1- 5 for foramsulfuron), also on a safe use of the formulation can be concluded.

Table 10.1.1- 3: 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}
Maize	BBCH 10 – 29	Medium granivorous bird "gamebird"	Partridge (*Perdix perdix*)	**3.0**	**6.6**
Maize	BBCH 10 – 29	Small omnivorous bird "lark"	Woodlark (*Lulula arborea*)	**10.9**	**24.0**
Maize	BBCH 10 – 29	Medium herbivorous/ granivorous bird "pigeon"	Wood pigeon (*Columba palumbus*)	**22.7**	**55.6**
Maize	BBCH 10 – 19	Small insectivorous bird "wagtail"	Yellow wagtail (*Motacilla flava*)	**11.3**	**26.8**
Maize	Leaf development BBCH 10 – 19	Small insectivorous/ worm feeding species "thrush"	Robin (*Erithakus rubecula*)	**5.7**	**10.5**

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

ACUTE DIETARY RISK ASSESSMENT

Table 10.1.1- 4 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}				
Foramsulfuron								
Maize	Medium granivorous bird "gamebird" <Partridge>	0.06	6.6	1	0.4	> 2000	> 5051	10
Maize	Small omnivorous bird "lark" <Woodlark>		24.0		1.4	> 2000	> 1389	10
Maize	Medium herbivorous/ granivorous bird "pigeon" <Wood pigeon>		55.6		3.3	> 2000	> 600	10
Maize	Small insectivorous bird "wagtail" <Yellow wagtail>		26.8		1.6	> 2000	> 1244	10
Maize	Small insectivorous/ worm feeding species "thrush" <Robin>		10.5		0.6	> 2000	> 3175	10

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

As the formulated product is applied on maize, 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 10.1.1- 5 Tier 1 long-term DDD and TER calculation for birds

Crop	Generic focal species	DDD					NO(A)EL [mg/kg bw/d]	TER_{LT}	Trigger
		Appl. rate [kg/ha]	SV_m	MAF_m	f_{twa}	DDD			
Foramsulfuron									
Maize	Medium granivorous bird "gamebird" <Partridge>	0.06	3.0	1	0.53	0.1	≥ 104	≥ 1090	5
Maize	Small omnivorous bird "lark" <Woodlark>		10.9			0.3	≥ 104	≥ 300	5
Maize	Medium herbivorous/ granivorous bird "pigeon" <Wood pigeon>		22.7			0.7	≥ 104	≥ 144	5
Maize	Small insectivorous bird "wagtail" <Yellow wagtail>		11.3			0.4	≥ 104	≥ 289	5
Maize	Small insectivorous/ worm feeding species "thrush" <Robin>		5.7			0.2	≥ 104	≥ 574	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 maize, 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 10.1.1- 6 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
Foramsulfuron						
Maize, 1 x 60 g a.s./ha[1)]	38 - 151	60 * 1.0 [1)]	≥ 104	≤ 0.6	≤ 50	No concern

[1)] Covering the double application with an application rate of 30 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 foramsulfuron and its metabolites is below the trigger (<3), no evaluation of secondary poisoning is needed (see Table 10.1.1- 7).

Table 10.1.1- 7 Log P_{ow} values

Compound	Log K_{OW}	Reference
Foramsulfuron-sodium	1.44 (pH 2) - 0.78 (pH 7)	SANCO/10324/2002-Final; M-195233-01-1 MCA, Sec.2, Point 2.7
AE F130619	1.57 (pH 6)	M-192883-01-1 MCA, Sec.2, Point 2.7
AE 0338795	- 2.33 (pH 7)	M-236158-01-1 MCA, Sec.2, Point 2.7
AE F092944	-0.92	M-194629-01-1 MCA, Sec.2, Point 2.7
AE F153745	-0.62	M-194736-01-1 MCA, Sec.2, Point 2.7

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

CP 10.1.1.1 Acute oral toxicity

Report:	K[redacted]o;[redacted];;2000;M-192635-01
Title:	Bobwhite quail acute oral toxicity (LD50) AE F130360 + AE 122006 flowable oil 22.5 + 22.5 g/l Code: AE F130360 01 1K05 A3
Report No:	C005783
Document No(s):	Report includes Trial Nos.: Tox99230 M-192635-01-1
Guidelines:	**USEPA (=EPA): E§ 71-1;Deviation not specified**
GLP/GEP:	**yes**

Endpoint is LD_{50} ≥2 000 mg product/kg bw.

CP 10.1.1.2 Higher tier data on birds

Since foramsulfuron is of low toxicity to birds, no higher tier data are needed.

CP 10.1.2 Effects on terrestrial vertebrates other than birds

Table 10.1.2- 1 Endpoints used in risk assessment

Test substance		species/origin	Endpoint	Reference
Foramsulfuron	Acute risk assessment	Rat	LD_{50} > 5000[1)] mg as/kg bw	[redacted]1997 M-141959-01-1 KCA 5.2.1 /01
	Long-term risk assessment	Rat	NO(A)EC ≡ NO(A)EL ≥ 1218[2)] mg as/kg bw/d 15 000 ppm	[redacted] 1999 M-187748-01-1 KCA 5.6.1 /01

[1)] 10 rats per group, no mortality occurred
[2)] Geometric mean of male and female

Toxicity of the formulated product

Foramsulfuron showed low toxicity to small mammals, as LD_{50} of the active substance for rats was higher than 5000 mg /kg bw.
The acute oral toxicity of the formulated product was determined in a study on rats.

Table 10.1.2- 2 Toxicity of the formulated product FSN + IDF OD 45 (22.5 + 22.5) to mammals

Test species	Test design	Ecotoxicological endpoint		Reference
Rat	acute, oral	LD_{50} > 5000	mg product /kg bw	[redacted] 1999 M-192928-01-1 KCP 7.1.1 /01

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 10.1.2- 4 and Table 10.1.2- 5), also on a safe use of the formulation can be conducted.

Table 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_m	For acute RA based on RUD_{90}
Maize	BBCH 10-19	Small insectivorous mammal "shrew"	Common shrew (*Sorex araneus*)	**4.2**	**2.6**
Maize	BBCH 10-29	Small herbivorous mammal "vole"	Common vole (*Microtus arvalis*)	**72.3**	**136.4**
Maize	BBCH 10-29	Small omnivorous mammal "mouse"	Wood mouse (*Apodemus sylvaticus*)	**7.8**	**17.2**

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

ACUTE DIETARY RISK ASSESSMENT

Table 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}				
Foramsulfuron								
Maize	Small insectivorous mammal "shrew" <Common shrew>	0.06	7.6	1	0.5	> 5000	> 10 965	10
Maize	Small herbivorous mammal "vole" <Common vole>		136.4		8.2	> 5000	> 611	10
Maize	Small omnivorous mammal "mouse" <Wood mouse>		17.2		1.0	> 5000	> 4 845	10

LONG-TERM REPRODUCTIVE ASSESSMENT

Table 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}				
Foramsulfuron									
Maize	Small insectivorous mammal "shrew" <Common shrew>	0.06	4.2	1.0	0.53	0.1	≥ 1218	≥ 9120	5
Maize	Small herbivorous mammal "vole" <Common vole>		72.3			2.3	≥ 1218	≥ 530	5
Maize	Small omnivorous mammal "mouse" <Wood mouse>		7.8			0.2	≥ 1218	≥ 4911	5

Long-term risk assessment for mammals drinking contaminated water

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

Table 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
Foramsulfuron						
Maize, 1 x 60 g a.s./ha [1)]	38 - 151	60 * 1.0 [1)]	≥ 1218	≤ 0.05	≤ 50	No concern

[1)] Covering the double application with an application rate of 30 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 foramsulfuron and its metabolites is below the trigger (<3), no evaluation of secondary poisoning is needed (see Table 10.1.1- 7).

CP 10.1.2.1 Acute oral toxicity to mammals

Refer to KCP 7.1.1/01: The Endpoint is LD_{50} > 5000 mg/kg.

CP 10.1.2.2 Higher tier data on mammals

Since foramsulfuron 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 foramsulfuron 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 10.2- 1 Endpoints of the formulation used in risk assessment

Test organism	Study type	Test duration	LC/EC$_{50}$[1] [mg/L]	NOEC[2] [mg/L]	References
Acute toxicity to fish					
Oncorhynchus mykiss (rainbow trout)	static renewal acute	96 h	14	3.9	XXXXXX, 2000 B002796 M-238518-01-2 KCP 10.2.1 /01
Lepomis macrochirus (bluegill sunfish)	static renewal acute	96 h	7.8	3.9	XXXXXX, 2000 B002795 M-238517-01-2 KCP 10.2.1 /02
Prolonged toxicity to fish					
Oncorhynchus mykiss (rainbow trout)	Flow through	28 d	-	1.8	XXXXXX, 2000 B002764 M-238492-01-2 KCP 10.2.2 /01
Acute toxicity to aquatic invertebrates					
Daphnia magna (water flea)	static renewal acute	48 h	6.9	3.6	[redacted], 2000 B002797 M-238519-01-2 KCP 10.2.1 /03
Chronic toxicity to aquatic invertebrates					
Daphnia magna (water flea)	static renewal	21 d	-	0.4	[redacted], 2000 B002760 M-238488-01-2 KCP 10.2.2 /02
Effects on algal growth					
Selenastrum capricornutum (green alga)	static	72 h	E_rC_{50}[3]: >5.0	N/C	[redacted], 2000 B002798 M-238520-01-2 KCP 10.2.1 /04
		96 h	E_rC_{50}: >5.0	1.3	
Effects on aquatic macrophytes					
Lemna gibba (duck weed)	static-renewal	7d	E_rC_{50} (frond#): 45 *µg* prod./L (corresponds to 1.01 *µg a.s.*/L)	10 *µg* prod./L	[redacted], 2000 B002845 M-238581-01-1 KCP 10.2.1 /05
Lemna gibba (duck weed)	static-renewal	7d	E_rC_{50}: 1.1 *µg a.s.*/L	0.2 *µg a.s.*/L	[redacted], 2002 B003893 M-240877-01-1 KCP 10.2.1 /08
Lemna gibba (duck weed)	static-renewal	7d	E_rC_{50} (frond#): 1.56 *µg a.s.*/L E_rC_{50} (weight): >3.08 *µg a.s.*/L	<0.10 *µg a.s.*/L	[redacted] et al., 2008 EBFSX011 M-296352-01-1 KCP 10.2.1 /09
Lemna gibba (duck weed)	static-renewal	7d	**Geomean E_rC_{50}:** 1.20 µg a.s./L corresponding to **53.3 µg prod./L**		KCP 10.2.1 /05 KCP 10.2.1 /08 KCP 10.2.1 /09

[1] LC = lethal concentration, EC = effect concentration
[2] NOEC = No Observed Effects Concentration
[3] E_rC_{50} = effect concentration calculated as rate from cell densities (numbers)
N/C = not calculated
Bold figures are used for risk assessments
µg a.s./L refers to µg foramsulfuron/L

According to the new aquatic guidance document (EFSA 2013)[2] endpoints based on growth rates are regarded as relevant for risk assessments. In case of Lemna the three E_rC_{50}-figures for frond numbers (1.01, 1.1, and 1.56), obtained from studies with the formulation as test substance, result in a geometric mean of 1.20 µg foramsulfuron/L.
This endpoint is very close to the Lemna endpoint of 1.01 µg a.s./L, obtained from the study with the active substance foramsulfuron as test substance. Therefore, for the refined risk assessment only the figure of 1.01 µg a.s./L will be used.

[2] EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013;11(7):3290, 268 pp. doi:10.2903/j.efsa.2013.3290.

Table 10.2- 2 Endpoints of foramsulfuron and metabolites used in risk assessment

Test substance	Test species	Endpoint		Reference
Foramsulfuron	Fish, acute *Oncorhynchus mykiss, Lepomis macrochirus*	LC_{50}	> 100 mg as/L	XXXXXX[redacted] 1997 A57725, A57751 (Amendment) M-141405-02-1 KCA 8.2.1 /01 XXXXXX, 1997 A57726, A57752 (Amendment) M-141406-02-1 KCA 8.2.1 /02
	Fish, chronic *Pimephales promelas*	NOEC	10.5 mg as/L	XXXXXX 2004 B004606 M-241508-01-1 KCA 8.2.2.1 /02
	Invertebrate, acute *Daphnia magna*	EC_{50}	> 100 mg as/L	[redacted], (1997) A57724, A57750 (Amendment) M-141404-02-1 KCA 8.2.4.1 /01
	Invertebrate, chronic *Daphnia magna*	NOEC	> 100 mg as/L	[redacted], 1999 B002180 M-237962-01-2 KCA 8.2.5.1 /01
	Algae *Anabaena flos-aquae*	E_rC_{50}	8.1 mg as/L	[redacted], 1999 C003699 M-186627-01-1 KCA 8.2.6.2 /02
	Aquatic plant *Lemna gibba*	E_rC_{50}	0.00101 mg as/L	[redacted], 1998 A67514 , C002148 (Amendment) M-147891-02-1 KCA 8.2.7 /01
	Aquatic plant *Myriophyllum spicatum*	EC_{50}	>0.084 mg as/L	[redacted] et al., 2012; M-431270-01-1 KCA 8.2.7 /09
	Aquatic plant macrophyte outdoor growth inhibition study; ten species	NOEC (6 weeks) NOEC (48h peak)	0.1 µg as/L 4.1 µg as/L	[redacted], 2012; M-429538-01-1 KCA 8.2.7 /07
	Aquatic plant *Lemna gibba* (6 week study; mimicking exposure of outdoor study)	E_rC_{50} (frond number)	0.00118 mg a.s./L	[redacted], 2013; M-464150-01-1 KCA 8.2.7 /08
	Aquatic plants (probabilistic risk assessment: macrophyte outdoor data plus 6-week Lemna)	HC5	0.000652 mg a.s./L	KCA 8.2.7 /07 KCA 8.2.7 /08
	Aquatic plant *Lemna gibba* peak exposure; 24 h	E_rC_{50}	>0.0567 mg as/L	[redacted], 2013; M-462569-01-1 KCA 8.2.7 /06

Test substance	Test species	Endpoint		Reference
AE F153745	Aquatic plant *Lemna gibba*	EC_{50}	> 100 mg/L	[redacted], 2000 B002765 M-240924-01-2 KCA 8.2.7 /02
AE 0338795	Aquatic plant *Lemna gibba*	E_rC_{50}	27.2 mg/L	[redacted], 2000 B002774 M-238498-01-2 KCA 8.2.7 /03
AE F092944	Fish, acute *Oncorhynchus mykiss*	LC_{50}	254 mg a.s/L	[redacted]1993 A50396 M-131422-01-1 KCA 8.2.1 /04
	Invertebrate, acute *Daphnia magna*	EC_{50}	233 mg a.s/L	[redacted], 1993 A50353 M-131382-01-1 KCA 8.2.4.1 /02
	Algae *Desmodesmus subspicatus*	E_rC_{50}	> 560 mg/L	[redacted], 1993 A50395 M-131421-01-1 KCA 8.2.6.1 /02
	Aquatic plant *Lemna gibba*	E_rC_{50}	> 100 mg/L	[redacted], 2000 C003865 M-186916-01-1 KCA 8.2.7 /10
AE F099095	Algae *Pseudokirchneriella subcapitata*	E_rC_{50}	> 100 mg/L	[redacted], 2005 EBMMX092 M-254084-01-1 KCA 8.2.6.1 /03
	Aquatic plant *Lemna gibba*	E_rC_{50}	> 100 mg/L	[redacted], 2005 EBMMX091 M-254496-01-1 KCA 8.2.7 /11
AE F130619	Aquatic plant *Lemna gibba*	E_rC_{50}	0.000889 mg a.s./L	[redacted], 2013; M-452669-01-1 KCA 8.2.7 /12
4-amino-N-methylbenzamide	Aquatic plant *Lemna gibba*	E_rC_{50}	>10 mg a.s./L	[redacted], 2013; M-464163-01-1 KCA 8.2.7 /13
4-formamido-N-methylbenzamide	Aquatic plant *Lemna gibba*	E_rC_{50}	>10 mg a.s./L	[redacted], 2013; M-464321-01-1 KCA 8.2.7 /14
Foramsulfuron-sulfamic acid	Aquatic plant *Lemna gibba*	E_rC_{50}	>10 mg a.s./L	[redacted], 2013; M-464386-01-1 KCA 8.2.7 /15

Predicted Environmental Concentrations used in risk assessment

Table 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 (no buffer)	Maize, 1 x 2.6 L/ha $PEC_{sw, max}$ [µg/L]	Maize, 2 x 1.3 L/ha $PEC_{sw, max}$ [µg/L]
FSN+IDF OD 45 (22.5+22.5)	small static ditch, at the edge of the treated field, water depth 0.3 m	2.77 % (arable crops)	**23.17**	**11.59**

Bulk density of the product: 0.9652 g/cm³ at 20 °C
Bold values were used for risk assessment

Table 10.2- 4: Initial max PEC_{sw} values of foramsulfuron and metabolites – FOCUS Step 2 (KCP 9.2.5/02)

Compound	FOCUS Scenario	Maize, 1 x 60 g/ha $PEC_{sw, max}$ [µg/L]	Maize, 2 x 30 g/ha $PEC_{sw, max}$ [µg/L]
Foramsulfuron	**STEP 1**	18.85	18.85
	STEP 2 – North Multi		2.291
	STEP 2 – South Multi	-	**4.189**
	STEP 2 – North Single	2.713	1.357
	STEP 2 – South Single	**4.948**	2.474
AE F130619	**STEP 1**	5.071	5.071
	STEP 2 – North Multi	-	0.149
	STEP 2 – South Multi	-	**0.276**
	STEP 2 – North Single	0.255	0.128
	STEP 2 – South Single	**0.481**	0.241
AE F092944	**STEP 1**	0.682	0.682
	STEP 2 – North Multi	-	0.090
	STEP 2 – South Multi	-	**0.172**
	STEP 2 – North Single	0.099	0.049
	STEP 2 – South Single	**0.189**	0.094
AE F153745	**STEP 1**	0.961	0.961
	STEP 2 – North Multi	-	0.068
	STEP 2 – South Multi	-	**0.070**
	STEP 2 – North Single	0.081	0.041
	STEP 2 – South Single	**0.087**	0.044
AE 0338795	**STEP 1**	0.127	0.127
	STEP 2 – North Multi	-	0.107
	STEP 2 – South Multi	-	**0.107**
	STEP 2 – North Single	0.127	0.063
	STEP 2 – South Single	**0.127**	0.063
AE F099095	**STEP 1**	0.085	0.085
	STEP 2 – North Multi	-	0.066
	STEP 2 – South Multi	-	**0.066**
	STEP 2 – North Single	0.085	0.043
	STEP 2 – South Single	**0.085**	0.043

Compound	FOCUS Scenario	Maize, 1 x 60 g/ha	Maize, 2 x 30 g/ha
		$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
4-Amino-N-methylbenzamide	**STEP 1**	0.024	0.024
	STEP 2 – North Multi	-	0.021
	STEP 2 – South Multi	-	**0.021**
	STEP 2 – North Single	0.023	0.012
	STEP 2 – South Single	**0.023**	0.012
4-Formylamido-N-methylbenzamide	**STEP 1**	0.043	0.043
	STEP 2 – North Multi	-	0.038
	STEP 2 – South Multi	-	**0.038**
	STEP 2 – North Single	0.043	0.021
	STEP 2 – South Single	**0.043**	0.021
Foramsulfuron-sulfamic acid	**STEP 1**	0.060	0.060
	STEP 2 – North Multi	-	0.053
	STEP 2 – South Multi	-	**0.053**
	STEP 2 – North Single	0.060	0.030
	STEP 2 – South Single	**0.060**	0.030

Bold values were used for risk assessment

Table 10.2- 5: Initial maximum PEC_{sw} values of foramsulfuron and metabolite – FOCUS Step 3 (KCP 9.2.5/02)

FOCUS Scenario STEP 3	Foramsulfuron			AE F130619	
	Entry route*	$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
Maize, 1 x 60 g/ha		**Single application**	**Multiple applications**	**Single application**	**Multiple applications**
D3 (ditch)	S	**0.314**	-	**0.032**	-
D4 (pond)	S	**0.013**	-	**0.001**	-
D4 (stream)	S	**0.271**	-	**0.001**	-
D5 (pond)	S	**0.015**	-	**0.002**	-
D5 (stream)	S	**0.251**	-	**<0.001**	-
D6 (ditch)	S	**0.316**	-	**0.032**	-
R1 (pond)	R	**0.025**	-	**0.004**	-
R1 (stream)	R	**1.284**	-	**0.081**	-
R2 (stream)	R	**0.972**	-	**0.106**	-
R3 (stream)	R	**2.225**	-	**0.178**	-
R4 (stream)	R	**2.341**	-	**0.202**	-
Maize, 2 x 30 g/ha		**Single application**	**Multiple applications**	**Single application**	**Multiple applications**
D3 (ditch)	S	**0.157**	0.136	**0.016**	0.014
D4 (pond)	S	0.006	**0.010**	**<0.001**	<0.001
D4 (stream)	S	**0.136**	0.118	<0.001	**0.001**
D5 (pond)	S	0.007	**0.013**	0.001	**0.001**
D5 (stream)	S	**0.126**	0.117	<0.001	**0.001**
D6 (ditch)	S	**0.158**	0.138	**0.016**	0.014
R1 (pond)	R	0.013	**0.062**	0.002	**0.010**
R1 (stream)	R	0.622	**1.281**	0.040	**0.099**
R2 (stream)	R	0.456	**0.456**	**0.052**	0.052
R3 (stream)	R	1.084	**1.084**	**0.089**	0.089
R4 (stream)	R	1.151	**1.315**	0.101	**0.121**

* Letters S, D, and R correspond to the dominant entry path - spray drift, drainage, and runoff
Bold values were used for risk assessment (worst-case from single and multiple applications for each scenario)

Table 10.2- 6: Initial maximum PEC_{sw} values of foramsulfuron and metabolites – FOCUS Step 4 (KCP 9.2.5/02)

Compound	FOCUS Scenario	Buffer [m]	Maize, 1 x 60 g/ha	Maize, 2 x 30 g/ha	
			$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]	
				Single application	Multiple applications
Foramsulfuron	D3 (ditch)	10m SD + RO	0.055	**0.027**	0.022
	D4 (pond)		0.008	0.004	**0.006**
	D4 (stream)		0.061	**0.030**	0.025
	D5 (pond)		0.010	0.005	**0.009**
	D5 (stream)		0.057	**0.028**	0.026
	D6 (ditch)		0.058	0.029	**0.034**
	R1 (pond)		0.012	0.006	**0.059**
	R1 (stream)		0.547	0.265	**0.580**
	R2 (stream)		0.426	0.200	**0.200**
	R3 (stream)		1.006	0.490	**0.490**
	R4 (stream)		1.065	0.523	**0.598**
	D3 (ditch)	20m SD + RO	0.028	**0.014**	0.012
	D4 (pond)		0.006	0.003	**0.004**
	D4 (stream)		0.032	**0.016**	0.013
	D5 (pond)		0.008	0.004	**0.007**
	D5 (stream)		0.030	**0.015**	0.014
	D6 (ditch)		0.032	0.016	**0.034**
	R1 (pond)		0.007	0.004	**0.014**
	R1 (stream)		0.279	0.135	**0.303**
	R2 (stream)		0.224	0.104	**0.104**
	R3 (stream)		0.526	0.256	**0.256**
	R4 (stream)		0.558	0.274	**0.313**
AE F130619	D3 (ditch)	10m SD + RO	<0.001	<0.001	**<0.001**
	D4 (pond)		<0.001	<0.001	**<0.001**
	D4 (stream)		0.001	<0.001	**0.001**
	D5 (pond)		<0.001	<0.001	**0.001**
	D5 (stream)		<0.001	<0.001	**0.001**
	D6 (ditch)		0.008	0.004	**0.008**
	R1 (pond)		<0.001	<0.001	**0.002**
	R1 (stream)		0.035	0.017	**0.045**
	R2 (stream)		0.046	0.023	**0.023**
	R3 (stream)		0.080	0.040	**0.040**
	R4 (stream)		0.092	0.046	**0.055**
	D3 (ditch)	20m SD + RO	<0.001	<0.001	**<0.001**
	D4 (pond)		<0.001	<0.001	**<0.001**
	D4 (stream)		0.001	<0.001	**0.001**
	D5 (pond)		<0.001	<0.001	**0.001**
	D5 (stream)		<0.001	<0.001	**0.001**
	D6 (ditch)		0.008	0.004	**0.008**
	R1 (pond)		<0.001	<0.001	**<0.001**
	R1 (stream)		0.018	0.009	**0.024**
	R2 (stream)		0.024	0.012	**0.012**
	R3 (stream)		0.042	0.021	**0.021**
	R4 (stream)		0.048	0.024	**0.029**

SD = spray drift buffer; RO = runoff buffer
Bold values are worst-case from single and multiple applications for each scenario

ACUTE RISK ASSESSMENT FOR AQUATIC ORGANISMS

Table 10.2- 7 TER_A calculations based on drift entry for the formulation and on FOCUS Step 2 for foramsulfuron and AE F092944

Compound	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_A	Trigger
Maize, 1 x 60 g a.s./ha					
FSN + IDF OD 45 (22.5+22.5)	Fish, acute	LC_{50} 7 800	23.17	337	100
	Invertebrate, acute	LC_{50} 6 900	23.17	298	100
Foramsulfuron	Fish, acute	LC_{50} > 100 000	4.948	> 20 210	100
	Invertebrate, acute	LC_{50} > 100 000	4.948	> 20 210	100
AE F092944	Fish, acute	LC_{50} 254 000	0.189	1 343 915	100
	Invertebrate, acute	LC_{50} 223 000	0.189	1 179 894	100
Maize, 2 x 30 g a.s./ha					
FSN + IDF OD 45 (22.5+22.5)	Fish, acute	LC_{50} 7 800	11.59	673	100
	Invertebrate, acute	LC_{50} 6 900	11.59	595	100
Foramsulfuron	Fish, acute	LC_{50} > 100 000	4.189	> 23 872	100
	Invertebrate, acute	LC_{50} > 100 000	4.189	> 23 872	100
AE F092944	Fish, acute	LC_{50} 254 000	0.172	1 476 744	100
	Invertebrate, acute	LC_{50} 223 000	0.172	1 296 512	100

CHRONIC RISK ASSESSMENT FOR AQUATIC ORGANISMS

Table 10.2- 8 TER_{LT} calculations based on drift entry for the formulation and on FOCUS Step 2 for foramsulfuron and metabolites

Compound	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Maize, 1 x 60 g a.s./ha					
FSN + IDF OD 45 (22.5+22.5)	Fish, chronic	NOEC 1 800	23.17	78	10
	Invertebrate, chronic	NOEC 400	23.17	17	10
	Green algae, chronic	E_rC_{50} > 5 000	23.17	216	10
	Aquatic plants, chronic	E_rC_{50} 53.23	23.17	2.30	10
Foramsulfuron	Fish, chronic	NOEC 10 500	4.948	2 122	10
	Invertebrate, chronic	NOEC > 100 000	4.948	> 20 210	10
	Green algae, chronic	E_rC_{50} 8100	4.948	1637	10
	Aquatic plants, chronic	E_rC_{50} 1.01	4.948	0.20	10
AE F092944	Green algae, chronic	E_rC_{50} > 560 000	0.189	2 962 962	10
	Aquatic plants, chronic	EC_{50} > 100 000	0.189	> 529 101	10
AE F099095	Green algae, chronic	E_bC_{50} > 100 000	0.085	> 1 176 471	10
	Aquatic plants, chronic	EC_{50} > 100 000	0.085	> 1 176 471	10
AE F153745	Aquatic plants, chronic	EC_{50} > 100 000	0.087	> 1 149 425	10
AE 0338795	Aquatic plants, chronic	E_rC_{50} 27 200	0.127	214 173	10
AE F130619	Aquatic plants, chronic	EC_{50} 0.889	0.481	1.85	10
4-Amino-N-methylbenzamide	Aquatic plants, chronic	E_rC_{50} > 10 000	0.023	> 434 783	10
4-Formylamido-N-methylbenzamide	Aquatic plants, chronic	E_rC_{50} > 10 000	0.043	> 232 558	10
Foramsulfuron sulfamic acid	Aquatic plants, chronic	E_rC_{50} > 10 000	0.060	> 166 667	10
Maize, 2 x 30 g a.s./ha					
FSN + IDF OD 45 (22.5+22.5)	Fish, chronic	NOEC 1 800	11.59	155	10
	Invertebrate, chronic	NOEC 400	11.59	35	10
	Green algae, chronic	E_rC_{50} > 5 000	11.59	431	10
	Aquatic plants, chronic	E_rC_{50} 53.23	11.59	4.60	10
Foramsulfuron	Fish, chronic	NOEC 10 500	4.189	2 507	10
	Invertebrate, chronic	NOEC > 100 000	4.189	> 23 872	10
	Green algae, chronic	E_rC_{50} 8100	4.189	1933	10
	Aquatic plants, chronic	E_rC_{50} 1.01	4.189	0.24	10
AE F092944	Green algae, chronic	E_rC_{50} > 560 000	0.172	3 255 813	10
	Aquatic plants, chronic	EC_{50} > 100 000	0.172	> 581 395	10
AE F099095	Green algae, chronic	E_bC_{50} > 100 000	0.066	> 1 515 152	10
	Aquatic plants, chronic	EC_{50} > 100 000	0.066	> 1 515 152	10
AE F153745	Aquatic plants, chronic	EC_{50} > 100 000	0.070	> 1 428 571	10
AE 0338795	Aquatic plants, chronic	E_rC_{50} 27 200	0.107	254 205	10
AE F130619	Aquatic plants, chronic	EC_{50} 0.889	0.276	3.22	10
4-Amino-N-methylbenzamide	Aquatic plants, chronic	E_rC_{50} > 10 000	0.021	> 476 190	10

Compound	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
4-Formylamido-N-methylbenzamide	Aquatic plants, chronic	E_rC_{50} > 10 000	0.038	> 263 158	10
Foramsulfuron sulfamic acid	Aquatic plants, chronic	E_rC_{50} > 10 000	0.053	>188 679	10

Table 10.2- 9 TER_{LT} calculations based on FOCUS Step 3

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
Foramsulfuron, Maize, 1 x 60 g/ha					
Aquatic plants, chronic	E_rC_{50} 1.01	0.314	D3 (ditch)	**3.2**	10
		0.013	D4 (pond)	77.7	10
		0.271	D4 (stream)	**3.7**	10
		0.015	D5 (pond)	67.3	10
		0.254	D5 (stream)	**4.0**	10
		0.316	D6 (ditch)	**3.2**	10
		0.025	R1 (pond)	40.4	10
		1.284	R1 (stream)	**0.8**	10
		0.972	R2 (stream)	**1.0**	10
		2.225	R3 (stream)	**0.5**	10
		2.341	R4 (stream)	**0.4**	10
AE F130619, Maize, 1 x 60 g/ha					
Aquatic plants, chronic	E_rC_{50} 0.889	0.032	D3 (ditch)	27.8	10
		0.001	D4 (pond)	889	10
		0.001	D4 (stream)	889	10
		0.002	D5 (pond)	445	10
		<0.001	D5 (stream)	>889	10
		0.032	D6 (ditch)	27.8	10
		0.004	R1 (pond)	222	10
		0.081	R1 (stream)	11.0	10
		0.106	R2 (stream)	**8.4**	10
		0.178	R3 (stream)	**5.0**	10
		0.202	R4 (stream)	**4.4**	10

Table 10.2- 9 (continued): TER_{LT} calculations based on FOCUS Step 3

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
Foramsulfuron, Maize, 2 x 30 g/ha					
Aquatic plants, chronic	E_rC_{50} 1.01	0.157	D3 (ditch)	**6.4**	10
		0.010	D4 (pond)	101.0	10
		0.136	D4 (stream)	**7.4**	10
		0.013	D5 (pond)	77.7	10
		0.126	D5 (stream)	**8.0**	10
		0.158	D6 (ditch)	**6.4**	10
		0.062	R1 (pond)	16.3	10
		1.281	R1 (stream)	**0.8**	10
		0.456	R2 (stream)	**2.2**	10
		1.084	R3 (stream)	**0.9**	10
		1.315	R4 (stream)	**0.8**	10
AE F130619, Maize, 2 x 30 g/ha					
Aquatic plants, chronic	E_rC_{50} 0.889	0.016	D3 (ditch)	55.6	10
		0.001	D4 (pond)	>889	10
		0.001	D4 (stream)	889	10
		0.001	D5 (pond)	889	10
		0.001	D5 (stream)	889	10
		0.016	D6 (ditch)	55.6	10
		0.010	R1 (pond)	88.9	10
		0.099	R1 (stream)	**9.0**	10
		0.052	R2 (stream)	17.1	10
		0.089	R3 (stream)	**10.0**	10
		0.121	R4 (stream)	**7.3**	10

Bold values require further refinement

REFINED CHRONIC RISK ASSESSMENT FOR AQUATIC PLANTS

Foramsulfuron

In addition to the tier 1 test with *Lemna gibba*, resulting in the E_rC_{50} of 1.01 µg a.s./L four further macrophyte studies have been conducted with foramsulfuron technical and the formulation Foramsulfuron WG 50, respectively.

- Aim of the 14 d laboratory study with *Myriophyllum spicatum* ([redacted] et al., 2012; M-431270-01-1, KCA 8.2.7/09) was to investigate the sensitivity of a dicotyledonous macrophyte species to foramsulfuron. In this study *Myriophyllum spicatum* showed low sensitivity to the compound with maximum inhibitions of the growth parameters (shoot length, wet weight, dry weight) being less than 20% up to the maximum test concentration (88 µg a.s./L).
- The 6 weeks (42 d) bioassay with *Lemna gibba* ([redacted], 2013; M-464150-01-1, KCA 8.2.7/ 08) has been performed to generate an endpoint which can be compared to the macrophyte species tested in the outdoor pond study (see below). Since *Lemna gibba* insufficiently growths under the mesotrophic conditions in outdoor ponds, decreasing concentrations of foramsulfuron as observed

in the pond study were mimicked in the laboratory in 20 x APP nutrient medium under sterile conditions. Every week, duckweed plants were transferred to new test vessels with a stepwise lower foramsulfuron content. The total test duration of the bioassay was equal to the duration of the pond study. As the most sensitive response variable frond number, a 42 d E_rC_{50} of 1.18 µg a.s./L was obtained.

- The 24h- peak exposure study with *Lemna gibba* ([redacted], 2013; M-462569-01-1, KCA 8.2.7 /06) has been conducted to specifically address peak exposure patterns as predicted e.g. for runoff scenarios. The study should reveal expected differences in the magnitude and duration of effects between a constant exposure as given in a *Lemna* standard test and an exposure for a very limited time span. *Lemna gibba* was exposed to the compound for 24 h. Afterward the plants were transferred to untreated growth medium in which they were kept for further six days. The E_rC_{50} was greater than 56.7 µg a.s./L, the NOEC of growth rates in the period between day 2 and day 7 (post-exposure after the peak) was 2.42 µg a.s./L. These endpoints refer to growth rates of both parameters, frond number and total frond area.
- In the macrophyte pond study ([redacted], 2012; M-429538-01-1, KCA 8.2.7 /07), ten different macrophyte species were exposed to foramsulfuron applied as WG 50 formulation under outdoor conditions. 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.
  2) 48 h peak exposure (two peak concentrations 1.6 and 3.9 µg a.s./L, measured) with subsequent replacement of the test solutions with untreated dilution water in the ponds. As with the *Lemna* peak exposure study, this second regime aimed at mimicking short runoff or drift peaks and their effects on macrophytes.

Endpoints relevant for the refined risk assessment are presented in Table 10.2- 2. Although the study has been started with ten species, the data for *Nymphaea odorata* were omitted from the analysis due to poor emergence even in the controls. The evaluation was done with the remaining nine species. For more information on the studies and further endpoints, see study summaries in document M, CA 8.2.7.

Probabilistic risk assessment: SSD and HC_5 calculation for foramsulfuron

The refined risk assessment for foramsulfuron is mainly based on the results of the multispecies outdoor pond study and the associated 6-weeks laboratory bioassay with *Lemna gibba*. The data of the two studies have been used to generate a species sensitivity distribution (SSD) and calculate an HC_5. Since endpoints in the *Lemna* bioassay have been calculated based on nominal concentrations, also from the pond study the nominal endpoints were used.
The outdoor pond study yielded EC_{50} values ranging from 1.5 µg a.s./L to > 61 µg a.s./L. For the variable shoot length growth rate, definitive EC_{50} values could be calculated only for two of the ten species tested. However, for the variable dry weight growth rate definitive EC_{50} figures were obtained for seven species. According to the new aquatic guidance document (EFSA, 2013, p. 93) greater-than figures should be included in an SSD calculation, if they are outside the range of already available endpoints. In the present case this applies to *Mentha aquatica* and *Cabomba caroliniana* which both delivered E_rC_{50} values of > 61 µg a.s./L. The highest definitive endpoint was 60 µg a.s./L and was obtained for *Glyceria maxima*. As a pragmatic and conservative approach, the E_rC_{50} of > 61 µg a.s./L was included in the SSD only once.

As mentioned above the lowest endpoint from the 6-weeks *Lemna* bioassay is 1.18 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 10.2- 10).

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

Species	**Endpoint** [µg a.s./L]	
Lemna gibba	E_rC_{50}	1.18
Elodea canadensis	E_rC_{50}	1.5
Salvinia minima	E_rC_{50}	2.8
Sagittaria latifolia	E_rC_{50}	4.6
Stuckenia pectinata	E_rC_{50}	7.7
Ceratophyllum demersum	E_rC_{50}	21.0
Myriophyllum heterophyllum	E_rC_{50}	41.0
Glyceria maxima	E_rC_{50}	60.0
Mentha aquatica / Cabomba caroliniana	E_rC_{50}	61.0
HC_5		**0.652**

The HC_5 calculation is based on the method of [redacted] (2000)[3]. A median HC_5 of 0.652 µg a.s./L was calculated (cf. Table 10.2- 10).

Refined aquatic risk assessment for foramsulfuron

For the refined risk assessment **long-term exposure scenarios** and **peak exposure scenarios** were considered separately. In order to distinguish long-term exposure scenarios from peak exposure scenarios the temporal patterns of PEC-figures ([redacted] 2013; M-468841-02-1) were analysed. Peak scenarios showed a dominant peak (primary peak) that lasted not longer than 24 hours. In some scenarios this primary peak was followed by one or a few smaller peaks called secondary peaks in the following text. The following scenarios were considered as peak-scenarios: D4 stream, D5 stream, D6 ditch, R1 stream, R2 stream, R3 stream and R4 stream.

Report:	[redacted]*; [redacted] 2013; M-468841-02; Amended: 2013-11-18
Title:	Foramsulfuron (FSN) and metabolite: PECsw,sed FOCUS EUR (graphical outputs) - Use in maize in Europe
Report No:	EnSa-13-0880
Document No:	M-468841-02-1
Guidelines:	**not applicable;not applicable**
GLP/GEP:	**no**

Predicted environmental concentrations of the active substance foramsulfuron and its metabolites for the use in maize in Europe were calculated and reported in the study report KCP 9.2.5/02.

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

This report KCP 10.2/ 01 supplements the original document and provides graphical representation of time evolution of PECsw concentrations for all calculated uses and scenarios at Step3 level for parent and its metabolite AE F130619.

For **the long-term scenarios**, the calculated HC_5 was compared to Focus Step 3 max. PEC_{sw} figures. The results of these calculations are provided in Table 10.2- 11. According to the new aquatic guidance document (EFSA, 2013a, p. 100), an assessment factor of 3 should be applied in conjunction with the median HC_5 to derive the regulatory acceptable concentration.
In case that further refinement is required as the risk assessment based on the median HC_5 combined with FOCUS Step 3 PECvalues is not passed in a second step a risk assessment is performed with Focus Step 4 max. PEC_{sw} figures considering a 10 m buffer zone to mitigate spray drift and run-off entry.

The **peak scenarios** were considered separately. For the TER calculations the peak E_rC_{50} >56.7 µg a.s./L from the *Lemna* peak study was taken into account. Regarding the derivation of a regulatory acceptable concentration from a refined exposure laboratory test, the new aquatic guidance document (EFSA, 2013a, p. 110) proposes an assessment factor of 10 in conjunction with the EC_{50} for plants. This approach is reasonable because:

1. *Lemna* is the most sensitive aquatic macrophyte species,
2. *Lemna* is also most sensitive to peak exposures. The peak NOEC of 3.9 µg a.s./L from the pond study is higher than the NOEC of 2.42 µg a.s./L obtained from the *Lemna*-peak study.

A refined risk assessment based on the comparison of the 24 h *Lemna*-peak study with primary peak (PECmax) from peak exposure patterns described by [redacted] (2013; M-468841-02-1) can be justified for the following reasons:

1. The primary peak lasted not longer than 24 hours.
2. The secondary peaks (if they occurred at all) did not exceed the NOEC of 2.42 µg a.s./L.
3. The temporal distance between primary and secondary peaks was greater or equal than three days (with exception of the R2 stream scenarios, where a slight peak (<0.1 µg a.s./L) occurred after two days already). Figures 1 and 3 in the *Lemna* peak study ([redacted] 2013; M-462569-01-1, KCA 8.2.7 /06) reveal that the growth curves ("growth lines" in the semi-logarithmic plots) even between day 2 and 5 are running parallel to the control at concentrations up to 2.42 µg a.s./L indicating a rapid recovery within a few days. Taking into account that the secondary peaks are far less than 2.42 µg/L and a fast recovery of Lemna-growth after a preceding exposure has been observed, it can be concluded that the secondary peaks can be neglected.

It can be concluded that for all FOCUS Step 3 scenarios which are characterised by peak exposure the risk of foramsulfuron to aquatic plants is acceptable.

AE F130619

No higher tier-data are available for AE F130619. Both compounds, AE F130619 and its parent compound foramsulfuron, have a very similar molecular structure, and it has been shown that the *Lemna*-E_rC_{50} of AE F130619 is very close to the respective endpoint of the parent. Although no peak-exposure study has been conducted with AE F130619, it can be assumed, that the result would be similar. It is therefore reasonable to use the endpoint of foramsulfuron from the *Lemna* peak exposure study, the E_rC_{50} of >56.7 µg/L also to evaluate peak exposure scenarios of AE F130619. In order to address the higher uncertainty resulting from the fact that only a similar but not the exact chemical structure was tested, an increased assessment factor of 20 is proposed.

Summary: Rationale for setting of assessment factors for refined risk assessment

Endpoint	Proposed assessment factor	Reference and further comments
Foramsulfuron		
HC_5 of 0.652 µg/L derived from EC_{50}-levels obtained in the outdoor macrophyte study and the 6-week *Lemna* study. *Lemna* is the most sensitive species. The HC_5 is used for the risk assessments of **long-term exposure scenarios**.	3	The HC_5 is calculated from a total of nine endpoints obtained from a wide variety of different aquatic macrophytes. The AF of 3 is proposed on page 100 in new aquatic guidance document (EFSA 2013).
E_rC_{50} > 56.7 µg/L obtained from *Lemna*-peak exposure study. The short-term exposure is comparable to **peak exposures scenarios.**	10	The peak exposure study has been done with the most sensitive species (*Lemna*). Regarding the derivation of a regulatory acceptable concentration from a refined exposure laboratory test, the new aquatic guidance document (EFSA, 2013a, p. 110) proposes an assessment factor of 10 in conjunction with the EC_{50} for plants.
AE F130619		
E_rC_{50} > 56.7 µg/L obtained from *Lemna*-peak exposure study with foramsulfuron The short-term exposure is comparable to peak exposure scenarios.	20	The similar molecular structure of this metabolite compared to the parent and the similar endpoint obtained from the standard *Lemna*-growth inhibition study justifies the use of the same endpoint for peak exposure as for the parent. In order to address the additional uncertainty an assessment factor of 20 instead of 10 is proposed

Table 10.2- 11 Refined TER_{LT} calculations based on FOCUS Step 3 and refined ecotox endpoints

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
Foramsulfuron, Maize, 1 x 60 g/ha					
Aquatic plants, chronic	**long-term exposure** HC_5: 0.652	0.314	D3 (ditch)	**2.1**	3
		0.013	D4 (pond)	50.2	3
		0.015	D5 (pond)	43.5	3
		0.025	R1 (pond)	26.1	3
	peak exposure peak E_rC_{50}: >56.7	0.271	D4 (stream)	209	10
		0.251	D5 (stream)	226	10
		0.316	D6 (ditch)	179	10
		1.284	R1 (stream)	44.1	10
		0.972	R2 (stream)	58.3	10
		2.225	R3 (stream)	25.5	10
		2.341	R4 (stream)	24.2	10
AE F130619, Maize, 1 x 60 g/ha					
Aquatic plants, chronic	**peak exposure** peak E_rC_{50}: >56.7	0.106	R2 (stream)	535	20
		0.178	R3 (stream)	319	20
		0.202	R4 (stream)	281	20
Foramsulfuron, Maize, 2 x 30 g/ha					
Aquatic plants, chronic	**long-term exposure** HC_5: 0.652	0.157	D3 (ditch)	4.2	3
		0.010	D4 (pond)	65.2	3
		0.013	D5 (pond)	50.2	3
		0.062	R1 (pond)	10.5	3
	peak exposure peak E_rC_{50}: >56.7	0.156	D4 (stream)	417	10
		0.126	D5 (stream)	450	10
		0.158	D6 (ditch)	359	10
		1.281	R1 (stream)	44.3	10
		0.456	R2 (stream)	124.3	10
		1.084	R3 (stream)	52.3	10
		1.315	R4 (stream)	43.1	10
AE F130619, Maize, 2 x 30 g/ha					
Aquatic plants, chronic	**peak exposure** peak E_rC_{50}: >56.7	0.052	R1 (stream)	1090	20
		0.089	R3 (stream)	637	20
		0.121	R4 (stream)	469	20

Bold TER values require further refinement

Scenario D3 ditch for foramsulfuron, Maize, 1 x 60 g/ha is the only scenario that requires a further refinement.

Higher-tier risk assessment based on Focus Step 4

Table 10.2- 12 TER_{LT} calculations based on FOCUS Step 4

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	FOCUS scenario	TER_{LT}	Trigger
Foramsulfuron, Maize, 1 x 60 g/ha; 10 m spray drift & runoff buffer					
Aquatic plants, chronic	**long-term exposure** HC_5: 0.652	0.053	D3 (ditch)	11.9	3

The outcome of the aquatic risk assessment can be summarized as follows:

	Step 3 standard RA based on *Lemna* E_rC_{50}	Step 3 higher-tier RA based on differenciated endpoints for long-term and peak exposure	Step 4 higher-tier RA based on differenciated endpoints for long-term and peak exposure	conclusion
Maize, 1 x 60 g/ha				
D3 (ditch)			✔ (10 m)	10 m buffer
D4 (pond)	✔	✔		no buffer
D4 (stream)		✔		no buffer
D5 (pond)	✔	✔		no buffer
D5 (stream)		✔		no buffer
D6 (ditch)		✔		no buffer
R1 (pond)	✔	✔		no buffer
R1 (stream)		✔		no buffer
R2 (stream)		✔		no buffer
R3 (stream)		✔		no buffer
R4 (stream)		✔		no buffer
Maize, 2 x 30 g/ha				
D3 (ditch)		✔		no buffer
D4 (pond)	✔	✔		no buffer
D4 (stream)		✔		no buffer
D5 (pond)	✔	✔		no buffer
D5 (stream)		✔		no buffer
D6 (ditch)		✔		no buffer
R1 (pond)	✔	✔		no buffer
R1 (stream)		✔		no buffer
R2 (stream)		✔		no buffer
R3 (stream)		✔		no buffer
R4 (stream)		✔		no buffer

In conclusion, no mitigation measure is required to pass the aquatic risk assessment in case of the 2-fold application in maize (2 x 30 g a.s./ha), while in case of the single application (1 x 60 g a.s./ha) a 10 m drift buffer is necessary to pass scenario D3.

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

Report:	K[redacted]§;[redacted];;2000;M-238518-01
Title:	Static renewal toxicity with the rainbow trout, Oncorhynchus mykiss: AE F130360 + AE F122006: AE F130360 01 1K05 A304
Report No:	B002796
Document No(s):	Report includes Trial Nos.: 1889-AG CF00W543 M-238518-01-2
Guidelines:	**OECD: 203;Deviation not specified**
GLP/GEP:	**yes**

Report:	K[redacted]g;[redacted];2000;M-238517-01
Title:	Static renewal toxicity with the bluegill sunfish, Lepomis macrochirus: AE F130360 + AE F122006: AE F130360 01 1K05 A304
Report No:	B002795
Document No(s):	Report includes Trial Nos.: 1888-AG CF00W542 M-238517-01-2
Guidelines:	**OECD: 203;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]§;[redacted];[redacted];2000;M-238519-02
Title:	Static renewal toxicity test with the Daphnid *Daphnia magna*: AE F130360 + AE F122006: AE F130360 01 1K05 A304
Report No:	B002797
Document No(s):	Report includes Trial Nos.: 1890-AG CF00W544 M-238519-01-2
Guidelines:	**OECD: 202;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];2000;M-238520-02
Title:	Growth and reproduction toxicity test with the freshwater alga, *Selenastrum capricornutum*: AE F130360 + AE F122006: AE F130360 01 1K05 A304
Report No:	B002798
Document No(s):	Report includes Trial Nos.: 1891-AG CF00W545 M-238520-01-2
Guidelines:	**OECD: 201;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]b; [redacted]; [redacted]; [redacted];2000;M-238581-01
Title:	Toxicity to the Duckweed, *Lemna gibba*: AE F130360 + AE F122006 flowable: AE F130360 01 1K05
Report No:	B002845
Document No(s):	Report includes Trial Nos.: 1928-AG CF99W571 M-238581-01-1
Guidelines:	**USEPA (=EPA): 123-3;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]b; [redacted]; [redacted];2000;M-238567-01
Title:	Toxicity of AE F130360 + AE F122006 + AE F115698, water dispersible granule, 30 + 30 + 2% w/w including a methylated rapeseed oil surfactant to duckweed, *Lemna gibba* G3 determined under static renewal test conditions: AE F130360 02 WG62 A10
Report No:	B002838
Document No(s):	Report includes Trial Nos.: 45737 M-238567-01-1
Guidelines:	**OECD:;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]; [redacted]; [redacted];2000;M-238536-01
Title:	Toxicity of AE F130360 + AE F122006 + AE F115698, water dispersible granule, 30 + 30 + 2% w/w code: AE F130360 02 WG62 A104 to duckweed, *Lemna gibba* G3, determined under static renewal test conditions: AE F130360 02 WG62 A104
Report No:	B002837
Document No(s):	Report includes Trial Nos.: CF99W571 M-238536-01-1
Guidelines:	**OECD: Draft (test (2009));Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]; [redacted];2002;M-240877-01
Title:	Foramsulfuron Oil Flowable 22.5 g/L Formulation (AE F130360 01 1K05 A304) - Toxicity To Duckweed, *Lemna gibba*
Report No:	B003892
Document No(s):	Report includes Trial Nos.: 13726.6166 M-240877-01-1
Guidelines:	**USEPA (=EPA): OPPTS 850.4400;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]q;[redacted];[redacted];[redacted];2008;M-296352-01
Title:	Toxicity of foramsulfuron + isoxadifen-ethyl OD 22.5+22.5 g/L (AE F130360 01 1K05 A9) to duckweed (*Lemna gibba* G3) under static-renewal conditions
Report No:	EBFSX011
Document No:	M-296352-01-1
Guidelines:	**FIFRA Guideline 123-2 (1982)** **OPPTS Guideline 850.4400 (2006 draft)** **OECD Guideline 221 (2006);none**
GLP/GEP:	**yes**

Executive Summary

A 7-day static-renewal duckweed growth test was conducted to determine the growth effects of Foramsulfuron + Isoxadifen-Ethyl OD 22.5+22.5 g/L (AE F130360 01 1K05 A9) on *Lemna gibba* G3. The duckweed *Lemna gibba* G3 was exposed for 7 days under static-renewal (Day 3 and Day 5 renewal) conditions. Nominal (mean measured) concentrations were control (<0.01), 0.094 (0.10), 0.19 (0.19), 0.38 (0.41), 0.75 (0.77), 1.5 (1.53), and 3.0 (3.08) µg a.s./L. Concentrations were based on the amount of Foramsulfuron in the Foramsulfuron + Isoxadifen-Ethyl OD 22.5+22.5 g/L (AE F130360 01 1K05 A9). Growth was determined by frond counts on days 0, 3, 5 and 7 and frond dry weights from day 0 and day 7. Results are reported as mean measured recoveries of foramsulfuron as measured on Day 0, Day 3 (old and new solutions), Day 5 (old and new solutions) and Day 7.
The NOEC and LOEC for the endpoint of growth rate for frond dry weight were 0.77 µg a.s./L and 1.5 µg a.s./L, respectively. For all other endpoints the NOEC and LOEC was < 0.10 µg a.s./L and 0.10 µg a.s./L, respectively. The endpoint with the most sensitive EC_{10} was day 7 frond dry weight yield with an E_yC_{10} value of 0.14 µg a.s./L. The endpoint with the most sensitive EC_{50} value was day 7 frond yield with an E_yC_{50} value of 0.75 µg a.s./L.

Material and Methods:

Test item: Foramsulfuron + Isoxadifen-Ethyl OD 22.5+22.5 g/L (AE F130360 01 1K05 A9); Batch number: EFKM001398; Tox-No: 08077-00; purity: 2.32 % Foramsulfuron, 2.40 % Isoxadifen-Ethyl.

The duckweed *Lemna gibba* G3 was exposed for 7 days under static-renewal (Day 3 and Day 5 renewal) conditions. Nominal (mean measured) concentrations were control (<0.01), 0.094 (0.10), 0.19 (0.19), 0.38 (0.41), 0.75 (0.77), 1.5 (1.53), and 3.0 (3.08) µg a.s./L. Concentrations were based on the amount of Foramsulfuron in the Foramsulfuron + Isoxadifen-Ethyl OD 22.5+22.5 g/L (AE F130360 01 1K05 A9). Growth was determined by frond counts on days 0, 3, 5 and 7 and frond dry weights from day 0 and day 7. Results are reported as mean measured recoveries of foramsulfuron as measured on Day 0, Day 3 (old and new solutions), Day 5 (old and new solutions) and Day 7.
The test system consisted of three replicates per level. Each replicate contained three plants and twelve fronds for a total of 9 plants per level. Conductivity and pH value were measured on days 0, 3 (old and new solutions), 5 (old and new solutions) and 7 from all test levels. Visual observations were conducted on day 0, 3, 5 and 7.
Growth rate for frond counts and cumulative biomass for frond counts (as area under the growth curve) were measured. The variable used to calculate these response parameters was frond number as determined by direct frond counts. Frond dry weights measured at study initiation from representative samples and dry weights measured at study termination from the test samples were used to calculate response parameters for 7 day frond dry weight yield and growth rate for frond dry weight. Temperature during the test ranged between 23.3 and 23.8°C (recorded hourly), pH was 7.7 to 8.89,

the photoperiod was 24 hours light and the light intensity was 5040 to 6450 lux. All test dishes were placed in an environmentally controlled chamber.

Dates of work: November 01, 2007 (study initiation) – November 09, 2007 (in-life termination)

Results:

Validity Criteria:
All biological validity criteria for this study were met.

Biological findings:
On study Day 7 small fronds were noted in the 0.77 and 1.53 µg a.s. /L test vessels. Also noted on Day 7 in the 3.08 µg a.s./L was the appearance of brown fronds. All other plants in all test concentrations and controls appeared normal throughout the study period.

Table 8.2.7-16: Toxicity to *Lemna gibba* G3

Test Substance	Foramsulfuron + Isoxadifen-Ethyl OD 22.5+22.5 g/L (AE F130360 01 1K05 A9)
Test Object	*Lemna gibba* G3
Exposure	7-Day, static-renewal
7-day E_yC_{10} – frond count	0.26 µg foramsulfuron/L
7-day E_yC_{50} – frond count	0.75 µg foramsulfuron/L
7-day E_rC_{10} – growth rate for frond numbers	0.32 µg foramsulfuron/L
7-day E_rC_{50} – growth rate for frond numbers	1.56 µg foramsulfuron/L
7-day E_bC_{10} – cumulative biomass for frond numbers	0.22 µg foramsulfuron/L
7-day E_bC_{50} – cumulative biomass for frond numbers	0.86 µg foramsulfuron/L
7-day E_yC_{10} – frond dry weight	0.14 µg foramsulfuron/L
7-day E_yC_{50} – frond dry weight	2.1 µg foramsulfuron/L
7-day NOEC – growth rate for frond dry weight	0.77 µg foramsulfuron/L
7-day E_rC_{50} – growth rate for frond dry weight	>3.08 µg foramsulfuron/L (greater than highest test concentration)
Lowest Concentration With an Effect (LOEC)	0.10 µg foramsulfuron/L
Highest Concentration Without Toxic Effect (NOEC)	< 0.10 µg foramsulfuron/L
Toxic Threshold/Effect Concentration, TEC (Geometric mean of NOEC and LOEC)	NA

Conclusions:

The NOEC and LOEC in the 7-day exposure of *Lemna gibba* G3 to Foramsulfuron + Isoxadifen-Ethyl OD 22.5+22.5 g/L (AE F130360 01 1K05 A9) for the endpoint of growth rate for frond dry weight were 0.77 µg a.s./L and 1.5 µg a.s./L, respectively. For all other endpoints the NOEC and LOEC was < 0.10 µg a.s./L and 0.10 µg a.s./L, respectively. Additionally, following the recommendations in OECD 221, EC_{10}s were calculated for all endpoints. The endpoint with the most sensitive EC_{10} was

day 7 frond dry weight yield with an E_yC_{10} value of 0.14 µg a.s./L. The endpoint with the most sensitive EC_{50} value was day 7 frond yield with an E_yC_{50} value of 0.75 µg a.s./L.

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

Report:	K[redacted]d;[redacted];;2000;M-238492-01
Title:	Prolonged toxicity to the rainbow trout, Oncorhynchus mykiss, in a flow through system: AE F130360 + AE F122006 oil flowable 22.5 + 22.5 g/L; AE F130360 01-1K05 A304
Report No:	B002764
Document No(s):	Report includes Trial Nos.: CF99W541 M-238492-01-2
Guidelines:	**OECD: 204;Deviation not specified**
GLP/GEP:	**yes**

Report:	KCP 10.2.2 /02;[redacted];;2000;M-238488-02
Title:	Effects on life cycle of the water flea (*Daphnia magna*) in a static renewal system: AE F130360 + AE F122006, oil flowable 22.5 + 22.5 g/L; AE F130360 01-1K05 A304
Report No:	B002760
Document No(s):	Report includes Trial Nos.: CF99W548 M-238488-01-2
Guidelines:	**USEPA: EPA 72-4(b);Deviation not specified**
GLP/GEP:	**yes**

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.

Toxicity of foramsulfuron to bees

Details of the honeybee testing with the active substance foramsulfuron are presented in MCA, Section 6, Point 8.3.1.

Table 10.3.1- 1: Acute toxicity of foramsulfuron (tech.) to bees

Test substance	Test organism	Ecotoxicological endpoint		Reference
Foramsulfuron, tech.	Honey bee	48/72 h-LD_{50}-oral	LD_{50} > 163 µg a.s./bee	[redacted], 1998 M-143626-01-1 KCA 8.3.1.1.1 /01
Foramsulfuron, tech.	Honey bee	48/72 h-LD_{50}-contact	LD_{50} > 1.9 µg a.s./bee	[redacted], 1997 M-143705-01-1 KCA 8.3.1.1.2 /01
Foramsulfuron, tech.	Honey bee	48 h-LD_{50}-oral 48 h-LD_{50}-contact	**LD_{50} > 110.1 µg a.s./bee** **LD_{50} > 100 µg a.s./bee**	[redacted], 2012 M-444765-01-1 KCA 8.3.1.1.2 /02

Bold values: Endpoints considered relevant for risk assessment

Table 10.3.1- 2: Honey bee toxicity data generated with formulated foramsulfuron

Test substance	Ecotoxicological endpoint		Reference
Acute oral and contact toxicity (laboratory)			
Foramsulfuron + Isoxadifen-ethyl (oil-flowable) 45 (22.5 + 22.5)	48 h-LD_{50}-oral 72 h-LD_{50}-oral	230.5 µg product/bee 226.3 µg product/bee	[redacted] (1999) M-187293-01-1 List of Endpoints (EU review report, 2002)
Foramsulfuron + Isoxadifen-ethyl (oil-flowable) 45 (22.5 + 22.5)	48 h-LD_{50}-contact	> 392.2 µg product/bee	[redacted] (1999) M-187293-01-1 List of Endpoints (EU review report, 2002)
Foramsulfuron + Isoxadifen-ethyl OD (oil-dispersion) 45 (22.5 + 22.5)	48 h-LD_{50}-oral 48 h-LD_{50}-contact	**LD_{50} > 214.4 µg product/bee** **LD_{50} > 200 µg product/bee**	[redacted], 2013 M-465361-01-1 KCP 10.3.1.1/01
Chronic toxicity to adult bees (laboratory)			
Foramsulfuron WG 50	10 d chronic adult feeding study	LC_{50} > 120 mg a.s./kg NOEC ≥ 120 mg a.s./kg	[redacted], (2013) M-470839-01-1 KCA 8.3.1.2/01
In vitro honey bee larvae (laboratory)			
Foramsulfuron WG 50	In vitro honey bee larvae laboratory study, single exposure test design	LD_{50} > 100 µg a.s./larva NOED ≥ 100 µg a.s./larva	[redacted], (2013) M-470485-01-1 KCA 8.3.1.3/01
Bee brood feeding test			
Foramsulfuron WG 50	Honey bee brood feeding (Oomen *et al*., 1992)	Slightly, but statistically significantly increased termination rate of young and old larvae, which is not biologically relevant; no adverse effects on the survival of adult bees and pupae, behaviour, colony strength, condition of the colonies, brood index and brood compensation index by feeding honey bee colonies sugar syrup at a foramsulfuron-concentration at a concentration typically present in the spray tank (100 ppm)	[redacted], (2013) M-465326-01-1 KCA 8.3.1.3/02
Cage and tunnel studies			
Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5 + 22.5)	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 (2.67 L product/ha)	[redacted] (2013) M-468794-01-1 KCA 8.3.1.3/03

Bold values: Endpoints considered relevant for risk assessment

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 Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5 + 22.5) is 2.67 L product/ha in maize (BBCH 12 - 18). With the content of foramsulfuron and isoxadifen-ethyl within the formulation being 22.5 g substance/L, respectively, this accounts to a maximum application rate of 60 g foramsulfuron a.s./ha. Based on a density of 0.961 g/cm³, 2.67 L product/ha corresponds to 2566 g product/ha.

Table 10.3.1- 4: 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
Maximum application rate = 60 g foramsulfuron a.s./ha via 2.67 L (≈2566 g) Foramsulfuron + Isoxadifen-ethyl OD 45 / ha					
Foramsulfuron tech.	> 110.1	60	< 1	50	yes
Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5 + 22.5 g/L)	> 214.4	*2566*	*< 12*	50	yes

The hazard quotient for oral exposure is below the validated trigger value for higher tier testing (i.e. $Q_{HO} < 50$).

Table 10.3.1- 5: 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
Maximum application rate = 60 g foramsulfuron a.s./ha via 2.67 L (≈2566 g) Foramsulfuron + Isoxadifen-ethyl OD 45 / ha					
Foramsulfuron, tech.	> 100	60	< 1	50	yes
Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5 + 22.5 g/L)	*>200*	*2566*	< 13	50	yes

The hazard quotient for contact exposure is below the validated trigger value for higher tier testing (i.e. $Q_{HC} < 50$).

Further considerations for the risk assessment

In addition to acute laboratory studies with adult honey bees, foramsulfuron 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 foramsulfuron a.s./kg in aqueous sugar solution. As technical foramsulfuron is - at least under certain circumstances - not readily soluble in water (e.g. 37.2 mg/L at pH 5) and because difficulties occurred by dissolving technical foramsulfuron in a pre-test, the actual test was conducted by using the formulated product Foramsulfuron WG 50. The nominal employed test concentration corresponded to about the concentration of foramsulfuron in the spray tank of a high-volume use. 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 foramsulfuron (nominal).

In order to reveal whether foramsulfuron poses a risk to immature honey bee life stages, a bee brood feeding study has been conducted by following the provisions/method of [redacted] (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 in June 2012 by mixing formulated foramsulfuron via Foramsulfuron WG 50 (together with formulated safener cyprosulfamide, as Cyprosulfamide SC 500), and the tested concentration corresponded to about the concentration of foramsulfuron in the spray tank of a high-volume use. The actual test concentration of foramsulfuron was 100 mg/L. The administration of 1 litre sugar solution per colony, containing 100 ppm foramsulfuron, resulted in a slightly, but statistically significantly increased termination rate of young and old larvae. No adverse effects on the survival of adult bees and pupae, behaviour, colony strength, condition of the colonies, colony development, brood index and brood compensation index was observed. The observed slightly elevated termination rate of larvae - if at all test item related - was in absolute terms low and as such biologically not relevant.

Nonetheless, in order to clarify whether the observations in the honey bee brood feeding study are due to natural variability or test-item related, foramsulfuron was subjected to *in-vitro* larval testing. The study was conducted in June 2013 by following the OECD Draft Test Guideline on Honey Bee (*Apis mellifera*) Larval Toxicity Test, Single Exposure (Version of 21 February 2013) and the current draft version of the Post-WNT25 Approved Larval Honey Bee Test, dated April 2013, which is the Draft-version of the OECD 237-guideline (Adopted: 26 July 2013).
The *in-vitro* larvae study was conducted with Foramsulfuron WG 50, as technical foramsulfuron was not well soluble in water. The potential effects on larval development were investigated at a level of 100 µg a.s./larva, i.e. the (highest) dose recommended for a limit test. In order to achieve this dose, the foramsulfuron concentration in the larval diet was about 3000 ppm. No adverse effects on mortality were observed. The mortality in both, in the control and in the foramsulfuron treatment group was max. 2.1%, respectively; the toxic reference treatment resulted in at least 89.6 % larval mortality.

Based on these findings, the observations in the honey bee brood feeding study are rather to be attributed to natural variability than being test-item related.

In parallel to the *in-vitro* larval test, a higher tier semi-field honey bee brood study (according to the provisions of the OECD Guidance Document 75) was conducted in June/July 2013 under forced/confined exposure conditions, by applying the maximum rate (2.68 L) of Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5 + 22.5 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 foramsulfuron 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 (Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5 + 22.5 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 Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L) does not adversely affect honey bees and honey bee brood when applied at a rate of 2.68 L product/ha (corresponding to 60 g foramsulfuron 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

The calculated Hazard Quotients for foramsulfuron 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, which covered the maximum application rates of 60 g foramsulfuron a.s./ha.
Regarding potential side effects of foramsulfuron on immature honey bee life stages, the conducted bee brood feeding study ([redacted] *et al.*, 1992) found a slightly, but statistically significantly increased termination rate of young and old larvae; as the observed slightly elevated termination rate of larvae was in absolute terms low; this observation - if at all test item related - was as such biologically not relevant. The bee brood feeding study further did not reveal adverse effects on the survival of adult bees and pupae, behaviour, colony strength, colony development as well as the condition of the colonies. Nonetheless, to clarify whether the observations in the honey bee brood feeding study are due to natural variability or test-item related, foramsulfuron was subjected to *in-vitro* larval testing. The potential effects on larval development were investigated at a level of 100 µg a.s./larva, i.e. the (highest) dose recommended for a limit test and revealed no adverse effects on larval mortality: the performance of the test item groups was identical as in the control group whereas the toxic reference performance was fully in line with the guideline specification. Based on the findings of the *in-vitro* larvae study, the observations in the honey bee brood feeding study are rather to be attributed to natural variability than being test-item related (intrinsic).
In parallel, foramsulfuron was subjected to confined semi-field testing (according to the provisions of OECD Guidance Document No. 75) by applying the maximum rate of Foramsulfuron + Isoxadifen-ethyl OD 45 (i.e. 2.68 L) to full-flowering *Phacelia* during honey bees actively foraging on the crop.
The results of this higher tier study confirmed all 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 foramsulfuron, when applied at the maximum application rate of 60 g a.s./ha even during the flowering period of potentially bee-attractive weeds inside the 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]u; [redacted];1999;M-187295-01
Title:	Oral toxicity (LD50) to honey bees (*Apis mellifera* L.) AE F130360 + AE F122006 oil flowable 22.5 + 22.5 g/L Code: AE F130360 01 1K05 A3 01
Report No:	C004077
Document No:	M-187295-01-1
Guidelines:	**EPPO: 170;Deviation not specified**
GLP/GEP:	**yes**

Endpoint according to the Review Report for foramsulfuron (SANCO/10324/2002-Final):
LD_{50} = 226.3 µg/bee

Report:	[redacted]; [redacted];2013;M-465361-01
Title:	Effects of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory
Report No:	79092035
Document No:	M-465361-01-1
Guidelines:	**OECD 213 and 214 (1998);none**
GLP/GEP:	**no**

Executive Summary:

The purpose of this study was to determine the acute contact and oral toxicity of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G to the honey bee (*A. mellifera* L.) under laboratory conditions. For this purpose female worker bees (*Apis mellifera*) were exposed for 48 hours to a single dose of 200.0 µg product/bee by topical application (contact limit test) and to a single dose of 214.4 µg product/bee by feeding (oral limit test, value based on the actual intake of the test item). Mortality of the bees was used as the toxic endpoint. Sublethal effects, such as changes in behaviour, were also assessed.

The contact LD_{50} (48 h) was > 200.0 µg product/bee. The oral LD_{50} (48 h) was > 214.4 µg product/bee.

Material and methods:

Test item. Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G; Foramsulfuron (AE F130360): 2.33 % w/w, 22,41 g/L; isoxadifen-ethyl (AE F122006): 2.29 % w/w, 21.96 g/L, (all values analytical); Batch ID: EFKM002442; Sample description: TOX10129-00; Material No.: 06321801; Specification No.: 102000011304-06; Workorder: 13005744; density: 0.961 g/mL (20°C).

Test units were stainless steel cages of 10 cm x 8.5 cm x 5.5 cm (length x height x width). 10 bees were used per test unit. 5 test units were used per test item dose level, control and reference item dose level, respectively. 50 female worker bees (*Apis mellifera*) were exposed for 48 hours to a single dose of 200.0 µg product/bee by topical application (contact limit test) and 50 female worker bees (*Apis mellifera*) were exposed for 48 hours to a single dose of 214.4 µg product/bee by feeding (oral limit test, value based on the actual intake of the test item).

For the contact test a single 5 µL droplet of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G, dissolved in tap water with 0.5 % Adhäsit, was placed on the dorsal bee thorax, likewise for the toxic reference (dimethoate) and the control (tap water). For the oral test aqueous stock solutions of the test item and reference item were prepared and mixed with ready-to-use sugar syrup (30 % sucrose, 31 %

glucose, 39 % fructose) at a concentration of 50 % (w/w). For the control, tap water and sugar syrup was used at the same ratio 50% (w/w) tap water, 50% (w/w) ready-to-use sugar syrup. The treated food was offered in syringes, which were weighed before and after introduction into the cages. After a maximum 55 minutes, the uptake was complete and the syringes containing the treated food were removed, weighed and replaced by ones containing fresh, untreated food.
The number of dead bees was determined after 4 (± 0.5 h) hours (first day), 24 and 48 (± 2 h) hours. Behavioural abnormalities (e.g. vomiting, apathy, intensive cleaning) were assessed after 4 (± 0.5 h) hours (first day), 24 and 48 (± 2 h) hours. Temperature during the test was 24 - 25 °C; relative humidity was 51 - 77%. Bees were kept in darkness (except during observation).

Dates of experimental work: May 14, 2013 – May 23, 2013 (contact and oral limit test)

Results:

Validity Criteria:

Table 10.3.1.1.1-1: Validity criteria

Validity Criteria		Recommended	Obtained
Control Mortality	Contact Test		
	CO_2/water control	10%	0.0 %
	Oral Test		
	water/sugar syrup control	10%	0.0 %
LD_{50} of Reference Item (24 h)	Contact Test		
		0.10 - 0.30 µg a.s./bee	0.19 µg a.s./bee
	Oral Test		
		0.10 - 0.35 µg a.s./bee	0.13 µg a.s./bee

All validity criteria for the study were met

Biological results:

Contact test:

At the end of the contact toxicity test (48 hours after application), there was 2.0 % mortality at 200.0 µg product/bee. No mortality occurred in the control group (water + 0.5 % Adhäsit). After the first 4 hours one single bee at the 200.0 µg/bee dose level showed cramp (before dying). During 24 and 48 hours after application one single bee in the test item treated group was apathetic.

Oral test:

In the oral toxicity test, the maximum nominal test level of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (i.e. 200 µg product/bee) corresponded to an actual intake of 214.4 µg product/bee. This dose level led to 2.0 % mortality after 48 hours. No mortality occurred in the control group (50 % aqueous sugar syrup solution). No test item induced behavioural effects were observed at any time in the oral toxicity test.

Table 10.3.1.1.1-2: Toxicity to honey bees; laboratory tests

Test Item	Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G

Test Object	*Apis mellifera*	
Exposure	contact (solution in Adhäsit (0.5 %)/water)	oral (sugar syrup solution)
Application rate µg product/bee	200.0	214.4
LD_{50} µg product/bee	> 200.0	> 214.4
LD_{20} µg product /bee	> 200.0	> 214.4
LD_{10} µg product /bee	> 200.0	> 214.4
NOED µg product /bee*	≥ 200.0	≥ 214.4

* The NOED was estimated using Fisher Exact Test (pairwise comparison, one-sided greater, α = 0.05).

The contact and oral LD_{50} (24 h) values of the reference item (dimethoate) were calculated to be 0.19 and 0.13 µg a.si./bee, respectively.

Conclusions:

The toxicity of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G was tested in both, an acute contact and an acute oral toxicity test on honey bees.
The contact LD_{50} (48 h) was > 200.0 µg product/bee. The oral LD_{50} (48 h) was > 214.4 µg product/bee.

CP 10.3.1.1.2 Acute contact toxicity to bees

Report:	[redacted]d; [redacted];1999;M-187293-01
Title:	Contact toxicity (LD50) to honey bees (Apis mellifera L.) AE F130360 + AE F122006 oil dispersible 22.5 + 22.5 g/L Code: AE F130360 01 1K0 A301
Report No:	1004076
Document No:	M-187293-01-1
Guidelines:	**EPPO: 170;Deviation not specified**
GLP/GEP:	**yes**

Endpoint according to the Review Report for foramsulfuron (SANCO/10324/2002-Final):
LD_{50} > 392.2 µg/bee

Report:	[redacted]d; [redacted];2013;M-465361-01
Title:	Effects of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (acute contact and oral) on honey bees (Apis mellifera L.) in the laboratory
Report No:	79092035
Document No:	M-465361-01-1
Guidelines:	**OECD 213 and 214 (1998);none**
GLP/GEP:	**no**

The study is summarised in detail in KCP 10.3.1.1.1/02. The endpoint from this study is:
48 h-LD_{50}-contact > 200.0 µg product/bee
48 h-LD_{50}-oral > 214.4 µg product/bee

CP 10.3.1.2 Chronic toxicity to bees

A 10 day chronic oral toxicity study was conducted with Foramsulfuron WG 50, 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 was conducted with Foramsulfuron WG 50, the corresponding summary is filed under KCA, point 8.3.1.3/02.

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 tunnel study to assess potential effects of foramsulfuron to honey bee colonies, including a very detailed assessment of brood development with FSN + IDF OD 45 was conducted, the corresponding summary is filed under KCA, point 8.3.1.2/03.

CP 10.3.1.6 Field tests with honeybees

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

CP 10.3.2 Effects on non-target arthropods other than bees

Toxicity tests on non-target arthropods were conducted with FSN + IDF OD 45 on the sensitive standard species *Typhlodromus pyri* and *Aphidius rhopalosiphi*. In addition, tests on further species are available (*Chrysoperla carnea*, *Aleochara bilineata*, *Poecilus cupreus*, *Pardosa* sp.). A summary of the results is provided in Table 10.3.2- 1.

Table 10.3.2- 1: FSN + IDF OD 45: Ecotoxicological endpoints for arthropods other than bees

Test species, Dossier-file-No. Reference	**Tested Formulation, study type, exposure**	**Ecotoxicological Endpoint**	
Typhlodromus pyri M-457360-01-1 Rep.No: 13 10 48 031 A [redacted], 2013	FSN + IDF OD 45 Laboratory, glass plate 267 mL prod./ha 475 mL prod./ha 844 mL prod./ha 1501 mL prod./ha 2670 mL prod./ha	LR_{50} > 2670 mL prod./ha Corr. Mortality [%] 1.0 5.1 38.8 36.7 48.0	
Typhlodromus pyri M-191384-01-1 Rep.No: CW99/003 [redacted], 1999	FSN + IDF OD 45 Laboratory, glass plate 267 mL prod./ha 2667 mL prod./ha	Corr. Mortality [%] -8.5 ^{A} 53	Effect on Reproduction [%] -0.8 ^{B} 33.9
Typhlodromus pyri M-192822-01-1 Rep.No: CW99/092 [redacted], 1999	FSN + IDF OD 45 Extended lab., exposure on detached *Polygonum convolvulus* leaves 2000 mL prod./ha 4000 mL prod./ha	LR_{50} > 4000 mL prod./ha Corr. Mortality [%] -1.3 ^{A} 20.0	Effect on Reproduction [%] 9.4 -10.4 ^{B}

Test species, Dossier-file-No. Reference	Tested Formulation, study type, exposure	Ecotoxicological Endpoint
Aphidius rhopalosiphi M-461455-01-1 Rep.No: 13 10 48 030 A [redacted], 2013	FSN + IDF OD 45 Laboratory, glass plate 2nd test run: 35 mL prod./ha 62 mL prod./ha 111 mL prod./ha 197 mL prod./ha 350 mL prod./ha 1st test run: 267 mL prod./ha 475 mL prod./ha 844 mL prod./ha 1501 mL prod./ha 2670 mL prod./ha	LR_{50} 241 mL prod./ha Corr. Mortality [%] 0 0 7.5 50.0 57.5 61.5 89.7 100 100 100
Aphidius rhopalosiphi M-191908-01-1 Rep.No: 991048029 [redacted], 1999	FSN + IDF OD 45 Laboratory, glass plate 160 mL prod./ha 2000 mL prod./ha 4000 mL prod./ha	 Corr. Mortality [%] Effect on Reproduction [%] 26 25.3 100 n.a. 100 n.a.
Aphidius rhopalosiphi M-198973-01-1 Rep.No: 001048067 [redacted], 2000	FSN + IDF OD 45 Aged residues, spray deposits on potted maize plants 107 mL prod./ha Residues aged for 0 days: Residues aged for 3 days: Residues aged for 7 days: 2000 mL prod./ha Residues aged for 0 days: Residues aged for 3 days: Residues aged for 7 days: 2670 mL prod./ha Residues aged for 0 days: Residues aged for 3 days: Residues aged for 7 days:	LR_{50} > 2670 mL prod./ha Corr. / Effect on / Repellency / Repellency Mortality [%] / Repr. [%] / (30 min) [%] / (2h) [%] 0 -3[B] 32 39 0 2 -7[C] 6 0 -3[B] 11 -24[C] 0 5 6 70 0 0 13 6 0 -6[B] 5 -13[C] 0 3 5 21 5 6 -12[C] 7 0 -2[B] 5 -4[C]
Chrysoperla carnea M-194627-01-1 Rep.No: 991048098 [redacted], 2000	FSN + IDF OD 45 Laboratory, glass plate Control 160 mL prod./ha 2000 mL prod./ha 4000 mL prod./ha	LR_{50} > 4000 mL prod./ha Corr. Mortality [%] Eggs/Female/Day Hatching [%] - 17.8 81.3 13 15.7 81.7 2 15.0 80.8 35 15.4 81.7
Aleochara bilineata M-193482-01-1 Rep.No: 991048095 [redacted], 1999	FSN + IDF OD 45 Laboratory, spray deposits on quartz sand 160 mL prod./ha 2000 mL prod./ha 4000 mL prod./ha	ER_{50} > 4000 mL prod./ha Effect on Reproduction [%] 0 10 15
Poecilus cupreus M-186968-01-1 Rep.No: CW98/112 [redacted], 1999	FSN + IDF OD 45 Laboratory, spray deposits on quartz sand 2667 mL prod./ha 5333 mL prod./ha	LR_{50} > 5333 mL prod./ha Corr. Mortality [%] Effect on Feeding Rate [%] 0 -22.5[D] 0 -12.4[D]

Test species, Dossier-file-No. Reference	Tested Formulation, study type, exposure	Ecotoxicological Endpoint
Pardosa sp. M-188675-01-1 Rep.No: 991048030 [redacted], 1999	FSN + IDF OD 45 Laboratory, spray deposits on quartz sand 160 mL prod./ha 2000 mL prod./ha 4000 mL prod./ha	LR_{50} > 4000 mL prod./ha Corr. Mortality [%] Effect on Feeding Rate [%] 0 8 5 3 0 2

[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.
[C]: A negative value indicates a higher percentage of wasps found on plants in the treatment than in the control.
[D]: A negative value indicates a higher feeding rate in the treatment than in the control.
prod.: product
n.a.: not assessed

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:

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

Use pattern:

Please note that for the risk assessment on non-target arthropods, the worst-case application rate of 1 x 2.6 L product/ha has been taken into account. This use pattern is considered to cover also the multiple applications as given in the intended use pattern for this product (2 x 1.3 L product/ha; see Table 10-1).

FSN + IDF OD 45 is intended to be applied once with an application rate of 2.6 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.

[4] [redacted] 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

Table 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
Maize	*T. pyri*	2600	1	> 2670	1.0	2
	A. rhopalosiphi			241	**10.8**	2

The in-field HQ value for *Typhlodromus pyri* is below the trigger of concern. However, the in-field HQ value for *Aphidius rhopalosiphi* is above the trigger of 2, indicating a need for refinement.

In-field tier 2 risk assessment:

The risk is considered acceptable if effects on mortality and reproduction are < 50% at the in-field PEC_{max} (application rate x MAF).

Table 10.3.2- 4: Tier 2 in-field risk assessment (based on study results from extended laboratory studies with the standard species *Typhlodromus pyri* and *Aphidius rhopalosiphi* and laboratory studies with additional species)

Test Species	in-field PEC_{max} [mL product/ha]	LR_{50}/ER_{50} [mL/ha]	Risk acceptable if:	Refined assessment required?
Aphidius rhopalosiphi	2600	>2670	Effects are < 50%	no
Typhlodromus pyri	2600	>4000	Effects are < 50%	no
Chrysoperla carnea	2600	>4000	Effects are < 50%	no
Aleochara bilineata	2600	>4000	Effects are < 50%	no
Poecilus cupreus	2600	>5333	Effects are < 50%	no
Pardosa sp.	2600	>4000	Effects are < 50%	no

An extended laboratory aged residue study has been performed on *Aphidius rhopalosiphi* ([redacted], 2000; M-198973-01-1). In this study, FSN + IDF OD 45 was applied on potted maize plants. Bioassays with freshly dried residues and residues aged for 3 and 7 days resulted in a corrected mortality of 0%, 5% and 0%, respectively, at a rate of 2670 mL product/ha. Effects on reproduction were < 7% in all bioassays. At the highest tested rate of 2670 mL product/ha no repellent effects of the test item were observed. This study indicates that no unacceptable effects on mortality or reproduction of *Aphidius rhopalosiphi* are to be expected, even directly after application.

The extended laboratory study with *Typhlodromus pyri* ([redacted], 1999; M-192822-01-1) resulted in 20% corrected mortality at a rate of 4000 mL product/ha and a higher reproduction rate than in the control, confirming the results of the tier 1 assessment and showing that no adverse effects on reproduction of *Typhlodromus pyri* are to be expected.

Further tests on additional arthropod species resulted in LR_{50} and ER_{50} values above the intended application rate of 2600 mL product/ha (see Tables 10.3.2- 1 and 10.3.2- 4 above).

It can be concluded that **no unacceptable in-field risk for non-target arthropods has to be expected** from the use of FSN + IDF OD 45 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 (90th percentile for 1 application in field crops, 1m distance; ESCORT 2)
VDF (vegetation distribution factor) = 10
Correction factor = 10 (uncertainty factor for the extrapolation from indicator species to other off-field non-target arthropods; default value for tier 1 risk assessment according to the Terrestrial Guidance Document)

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

Table 10.3.2- 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
Maize	*T. pyri*	2600	1	2.77	10	10	>2670	0.03	2
	A. rhopalosiphi				10	10	241	0.3	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 FSN + IDF OD 45 according to the proposed use pattern.

CP 10.3.2.1 Standard laboratory testing for non-target arthropods

Report:	[redacted];[redacted];1999;M-191908-01
Title:	Toxicity to the parasitoid *Aphidius rhopalosiphi* (Destefani-Perez) / adults under laboratory conditions according to IOBC Guidelines ([redacted] 1992/1997) Code: AE F130360 01 1K05 A3G
Report No:	C005351
Document No:	M-191908-01-1
Guidelines:	**IOBC.;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]*;[redacted];1999;M-191384-01
Title:	Toxicity to the predatory mite *Typhlodromus pyri* SCHEUTEN (Acari, Phytoseiidae) in the laboratory AE F130360 + AE F122006 oil flowable 22.5 + 22.5 g/L Code: AE F130360 01 1K05 A3G
Report No:	C005311
Document No:	M-191384-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]k; [redacted];1999;M-188675-01
Title:	Toxicity to the ground dwelling predator *Pardosa* spp. (laboratory) according to IOBC Guideline ([redacted] et al. 1998) Code: AE F130360 01 1K05 A304
Report No:	C004831
Document No:	M-188675-01-1
Guidelines:	**IOBC: Wehling et al. 1998;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]t; [redacted];1999;M-186968-01
Title:	Toxicity to the ground dwelling predator *Poecilus cupreus* L. (Coleoptera, Carabidae) in the laboratory AE F130360 + AE F122006 oil flowable 22.5 + 22.5 g/L Code: AE F130360 01 1K05 A301
Report No:	C003899
Document No:	M-186968-01-1
Guidelines:	**BBA: VI 23-2.1.8;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]g; [redacted];1999;M-193482-01
Title:	Toxicity to the ground dwelling predator *Aleochara bilineata* Gyll. (laboratory) according to IOBC Guideline ([redacted]1998) Code: AE F130360 01 1K05 A304
Report No:	C006202
Document No:	M-193482-01-1
Guidelines:	**IOBC: Morath & Nelson, 1992;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]o; [redacted];2000;M-194627-01
Title:	Toxicity to the foliage dwelling predator *Chrysoperla carnea* STEPH. (laboratory) following the IOBC Guideline ([redacted]1988) ringtest method ([redacted] et al. 1997) and OECD Guideline proposal ([redacted] et al. 1999) Code: AE F130360 01 1K05 A304
Report No:	C006101
Document No:	M-194627-01-1
Guidelines:	**IOBC: 1988; 1992;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]6; [redacted];2000;M-194770-01
Title:	Effectivity of the herbicide AE F130360 on entomology screening species
Report No:	C006603
Document No:	M-194770-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**no**

This last study was in the baseline dossier and has been included here for completeness; however please note that this study is not relevant for this data point.

Report:	[redacted]d; [redacted];2013;M-457360-01
Title:	Effects of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L) on the predatory mite *Typhlodromus pyri* SCHEUTEN in a laboratory test
Report No:	13 10 48 031 A
Document No:	M-457360-01-1
Guidelines:	**IOBC (BLUEMEL et al. 2000);none**
GLP/GEP:	**yes**

Executive Summary:

The purpose of this study was to determine a rate-response relationship for mortality of the predatory mite *Typhlodromus pyri* SCHEUTEN in a worst-case laboratory test. Mites were exposed on glass plates to application rates of 267, 475, 844, 1501 and 2670 ml product/ha in 200 L deionized water/ha and effects on mortality were compared to those of deionized water treated controls (200 L/ha). Dimethoate (applied at 15 mL product/ha, nominally equivalent to 6 g a.s./ha, in 200 L deionized water/ha) was used as reference item. Survival of the predatory mites was used as test endpoint with the aim to calculate the LR_{50} if possible. The test was performed according to the IOBC Guideline ([redacted] et al. 2000) taking account of the recommendations given by [redacted] et al. (2001), but without performance of a reproduction assessment. The LR_{50} for *Typhlodromus pyri* was estimated to be > 2670 mL product/ha in 200 L water/ha, the highest rate tested. All validity criteria according to the guideline were met.

Materials and Methods:

Test item. Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5+22.5 g/L); analysed active ingredients: 2.33 % w/w (22.41 g/L) foramsulfuron (AE F130360), 2.29 % w/w (21.96 g/L) isoxadifen-ethyl (AE F122006); Specification No.: 102000011304-06; Batch ID: EFKM002442, Sample description: TOX10129-00, Material No.: 06321801, Density: 0.961 g/mL (according to Certificate of Analysis).

The test item was tested under laboratory conditions after contact exposure of protonymphs of the predatory mite *Typhlodromus pyri* SCHEUTEN to dried spray residues of the test item with rates of 267 – 475 – 844 – 1501 – 2670 mL product/ha in 200 L deionised water/ha applied on glass plates. The control was treated with deionised water (200 L/ha). Dimethoate EC 400 (15 mL product/ha, nominally equivalent to 6 g a.s./ha, in 200 L deionised water/ha) was used as a toxic reference item.
Protonymphs of the predatory mite *Typhlodromus pyri* SCHEUTEN were exposed in 5 replicates per treatment group and 20 mites per replicate to the residues of the test item, reference item and control treatments, respectively. During the assessments the mites were fed with a mix of pine (*Pinus nigra*) and birch (*Betula pendula*) pollen, 1:1. The number of surviving, dead, trapped and escaped predatory mites was recorded over a period of 7 days. From these data the endpoint mortality was calculated.

Toxic standard: (Dimethoate EC 400): 15 mL product/ha (nominally equivalent to 6 g a.s./ha) in 200 L/ha of deionised water; control: deionised water only (200 L/ha).

Dates of work: May 21, 2013 – May 28, 2013

Results:

Table 10.3.2.1-1: Validity criteria

Validity criteria	
Mortality in the control group	≤ 20 % (dead, trapped and escaped mites) on day 7
Corrected mortality in the reference group	50 – 100 % on day 7

All validity criteria were met.

The results of the control group indicated that the test organisms were in a good condition (mortality: 2.0 %). The results of the reference item group indicated that the test system was sensitive to harmful

substances (corrected mortality: 85.7 %). Concerning mortality in the control group and as well the susceptibility of the test organisms to the reference item the study is proved to be valid.
After 7 days, the mortality in the test item treatments ranged between 3.0 % and 49.0 % in comparison to 2.0 % in the control. Based on these results the corrected mortality for the different rates ranged between 1.0 % and 48.0 %. The LR_{50} for Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5+22.5 g/L) was estimated to be > 2670 mL product/ha in 200 L water/ha.

Table 10.3.2.1-2: Effects on mortality of *Typhlodromus pyri* Scheuten

Test item	**Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5 + 22.5 g/L)**	
Test organism	*Typhlodromus pyri* SCHEUTEN	
Exposure on	Dried spray deposits on glass plates	
Treatment	**Mortality[2] [%]**	**Corrected mortality[3] [%]**
Control	2.0	-
Application rate[1] [mL product/ha]		
267	3.0 (n.s.)	1.0
475	7.0 (n.s.)	5.1
844	40.0*	38.8
1501	38.0*	36.7
2670	49.0*	48.0
LR_{50}	**>2670 mL product/ha**	
Reference item Dimethoate EC 400 150 mL product/ha	86.0*	85.7

[1] Application rate in 200 L water/ha.
[2] Mortality after exposure to residues on treated glass plates. The results for mortality in individual treatments were compared to that in the control using Fisher`s Exact Binomial test (α = 0.05).
[3] Corrected mortality according to [redacted] (1925)
(n.s.) not statistically significantly different compared to the control: Fisher`s Exact Binomial test with Bonferroni correction (α = 0.05).
* statistically significantly different compared to the control: Fisher`s Exact Binomial test with Bonferroni correction (α = 0.05) for test item and Fisher`s Exact Binomial test (α = 0.05) for reference item

No unusual observations regarding behaviour were noted in the control and the test item treatment groups at any observation point during the test.

Conclusions:

In a worst-case laboratory study with Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5+22.5 g/L) the LR_{50} for *Typhlodromus pyri* was estimated to be > 2670 mL product/ha in 200 L water/ha, the highest rate tested.

Report:	[redacted]3;[redacted];2013;M-461455-01
Title:	Effects of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L) on the parasitic wasp *Aphidius rhopalosiphi* (DESTEFANI-PEREZ) in a laboratory test
Report No:	13 10 48 030 A
Document No:	M-461455-01-1
Guidelines:	**IOBC (MEAD-BRIGGS et al. 2000);none**
GLP/GEP:	**yes**

Executive Summary:

The purpose of this study was to determine a rate-response relationship for mortality of the parasitic wasp *Aphidius rhopalosiphi* (DESTEFANI-PEREZ) in a laboratory test. Adult wasps (used within 48 hours after hatching, 4 x 7 females and 4 x 3 males for the control groups and the treatment groups) were exposed to control (deionised water) and dried spray residues of the test item with rates of 267, 475, 844, 1501 and 2670 mL product/ha (1st test run) and 35, 62, 111, 197 and 350 mL product/ha (2nd test run) in 200 L deionised water/ha applied on glass plates. Dimethoate EC 400 (0.3 mL product/ha in 200 L deionised water/ha) was used as a toxic reference item. Survival of the parasitic wasps was used as test endpoint with the aim to calculate the LR_{50}, if possible. The LR_{50} for *Aphidius rhopalosiphi* was calculated to be 241 mL product/ha in 200 L water/ha based on the results of the 1st and 2nd test run.
The test was performed following the IOBC Guideline ([redacted] *et al.* 2000) taking account of the recommendations given by [redacted] *et al.* (2001), but without performance of a reproduction assessment.

Material and Methods:

Test item: Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5+22.5 g/L); analysed active ingredients: 2.33 % w/w (22.41 g/L) Foramsulfuron (AE F130360) and 2.29 % w/w (21.96 g/L) Isoxadifen-ethyl (AE F122006); Specification No.: 102000011304 - 06, Batch ID: EFKM002442, Sample description: TOX10129-00, Material No.: 06321801, density: 0.961 g/mL (according to Certificate of Analysis)

The test item was tested under laboratory conditions after contact exposure of adults of the parasitic wasp *Aphidius rhopalosiphi* (DESTEFANI-PEREZ) to dried spray residues of the test item with rates of 267, 475, 844, 1501 and 2670 mL product/ha (1st test run) and 35, 62, 111, 197 and 350 mL product/ha (2nd test run) in 200 L deionised water/ha applied on glass plates. The control was treated with deionised water (200 L/ha). Dimethoate EC 400 (0.3 mL product/ha in 200 L deionised water/ha) was used as a toxic reference item.
Adults of the parasitic wasp *Aphidius rhopalosiphi* (DESTEFANI-PEREZ) were exposed in 4 replicates per treatment group and 7 females and 3 males per replicate to the residues of the test item, reference item and control treatments, respectively. During the exposure phase the adult wasps were fed with 25 % w/w aqueous fructose solution. The number of surviving, affected, moribund and dead wasps was recorded over a period of 48 hours. From these data the endpoint mortality was calculated.

Climatic conditions:	Temperature:	1st test run:	19-21°C
		2nd test run:	19-21°C
	Relative humidity:	1st test run:	67-73%
		2nd test run:	68-71%
	Light – dark – cycle:	16 hours light, 8 hours dark	

Dates of work: 1st test run: June 03, 2013 – June 05, 2013
2nd test run: June 24, 2013 – June 26, 2013

Results:

Table 10.3.2.1-3: Validity criteria

Validity criteria	Recommended	Obtained 1st run	Obtained 2nd run
Mortality in the control group	≤ 13 % (48 hours)	2.5 %	0 %
Corrected mortality in the reference item group	> 50% (48 hours)	100 %	100 %

All validity criteria according to [redacted] et al. (2000) were met.

The results of the control group indicated that the test organisms were in a good condition (mortality: 2.5 % in the 1st test run and 0 % in the 2nd test run). The results of the reference item group indicated that the test system was sensitive to harmful substances (corrected mortality: 100 %, both test runs). Concerning mortality in the control group and as well the susceptibility of the test organisms to the reference item the study is proved to be valid.

Mortality:

1st test run

After 48 hours, the mortality in the test item treatments ranged between 62.5 % and 100 % in the test item groups in comparison to 2.5 % in the control. Based on these results the corrected mortality for the different rates was between 61.5 % and 100 %.

2nd test run

After 48 hours, the mortality in the test item treatments ranged between 0 % and 57.5 % in the test item groups in comparison to 0 % in the control. Based on these results the corrected mortality for the different rates was between 0 % and 57.5 %.

Table 10.3.2.1-4: Effects on mortality of *Aphidius rhopalosiphi* (DESTEFANI-PEREZ)

Test item	**Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5+22.5 g/L)**	
Test object	*Aphidius rhopalosiphi* (DESTEFANI-PEREZ)	
Exposure	dried spray deposits on glass plates	
Treatment	**Mortality [2] [%]**	**Corrected mortality [3] [%]**
Application rate [1] [mL product/ha]		
1[st] test run		
Control	2.5	
267	62.5*	61.5
475	90.0*	89.7
844	100*	100
1501	100*	100
2670	100*	100
2[nd] test run		
Control	0	-
35	0 (n.s.)	0
62	0 (n.s.)	0
111	7.5 (n.s.)	7.5
197	50.0*	50.0
350	57.5*	57.5
LR_{50} [4] [95 % CL][5]	**241 mL product/ha** [216 – 269 mL product/ha]	
Reference item Dimethoate EC 400 0.3 mL product/ha (1[st] and 2[nd] test run)	100*	100

[1] Application rate in 200 L water/ha
[2] Mortality after exposure to residues on treated glass plates. The results for mortality in individual treatments were compared to that in the control using FISHER´s Exact Binomial test (α = 0.05).
[3] Corrected mortality according to [redacted] (1925)
[4] LR_{50} = lethal rate over 1[st] and 2[nd] test run
[5] 95 % CL means lower and upper 95 % confidence limits
(n.s.) not statistically significantly different compared to the control
* statistically significantly different compared to the control

No unusual observations were noted in the control and all test item treatment groups at any observation point during the test.

Conclusions

In a worst-case laboratory study with Foramsulfuron + Isoxadifen-ethyl OD 45 (22.5+22.5 g/L) the LR_{50} for *Aphidius rhopalosiphi* was calculated to be 241 mL product/ha in 200 L water/ha based on the results of the 1[st] and 2[nd] test run.
All validity criteria according to [redacted] et al. (2000) were met.

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

Report:	[redacted]h; [redacted];1999;M-192822-01
Title:	Toxicity to the predatory mite *Typhlodromus pyri* SCHEUTEN (Acari, Phytoseiidae) using an extended laboratory test AE F130360 + AE F122006 SC flowable 225 + 225 g/L Code: AE F130360 01 1K05 A301
Report No:	C005863
Document No:	M-192822-01-1
Guidelines:	**Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted]j; [redacted]2000;M-198973-01
Title:	Toxicity of AE F130360 01 1K05 A304 to the cereal aphid parasitoid *Aphidius rhopalosiphi* (Destefani-Perez) (extended laboratory test/aged residue test") Code: AE F130360 01 1K05 A304
Report No:	C010411
Document No:	M-198973-01-1
Guidelines:	**ESCORT: [redacted]et al. 1994; ATBC: Mead-Briggs & Longley 1997; Deviation not specified**
GLP/GEP:	**yes**

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 Point 9.1.3.
A soil layer of 5 cm with a bulk density of 1.5 g/cm^3, 25% interception and a DT_{50} of 82 days (maximum DT_{50} of laboratory studies normalized to 20°C and field capacity to FOCUS (2000)) for the parent compound foramsulfuron, 25.7 days for AE F130619, 3.68 days for AE F153745 and 147.6 days for AE F092944 were considered.

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

Table 10.4- 1 PEC_{soil} of foramsulfuron and its metabolites for the uses assessed, taking the effect of accumulation into account (standard mixing depth of 5 cm)

Compound	Maize 1 x 60 g a.s./ha			Maize 2 x 30 g a.s./ha		
	$PEC_{soil, max}$ [mg/kg]	$PEC_{soil, plateau}$ [mg/kg]	$PEC_{soil, accu}$ [1] [mg/kg]	$PEC_{soil, max}$ [mg/kg]	$PEC_{soil, plateau}$ [mg/kg]	$PEC_{soil, accu}$ [1] [mg/kg]
FSN + IDF OD 45	**2.499** [2]	--	--	2.499 [2]	--	--
Foramsulfuron	0.060	0.003	**0.063**	0.058	0.003	0.061
AE F130619	0.016	< 0.001	**0.016**	0.015	< 0.001	0.015
AE F153745	0.003	< 0.001	**0.003**	0.002	< 0.001	0.002
AE F092944	0.004	< 0.001	**0.004**	0.004	< 0.001	0.004

[1] $PEC_{soil, accu}$ = annual maximum ($PEC_{soil, max}$) + plateau concentration ($PEC_{soil, plateau}$) after multi-year use
[2] Calculated based on: application rate: 2.6 L prod./ha; interception: 25% ; product density: 0.961 g/mL
Bold values: worst case considered in risk assessment

CP 10.4.1 Earthworms

The summary of the toxicity of FSN + IDF OD 45, foramsulfuron and its soil metabolites to earthworms is provided in Table 10.4.1- 1. Details of the studies with the active substance and the metabolites are presented in the document M, Point CA 8.4.

Chronic toxicity of foramsulfuron to earthworms

Table 10.4.1- 1 Endpoints used in risk assessment

Test substance	Test species, test design	Endpoint	Reference
FSN + IDF OD 45	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC ≥ 370 mg prod./kg dws	[redacted], 2013 M-464888-01-1 KCP 10.4.1.1 /01
Foramsulfuron	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item sprayed on soil surface	NOEC ≥ 600 g a.s./ha ≥ 2.75 mg a.s./kg dws [1]	[redacted], 2000 M-193508-01-1 KCA 8.4.1 /01
AE F092944	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC 10 mg/kg dws	[redacted], 2013 M-461051-01-1 KCA 8.4.1 /02
AE F153745	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC ≥ 100 mg/kg dws	[redacted], 2013 M-459518-01-1 KCA 8.4.1 /04
AE F130619	*Eisenia fetida* reproduction, 56 d (10% peat in test soil), test item mixed into soil	NOEC 56 mg/kg dws	[redacted], 2013 M-461453-01-1 KCA 8.4.1 /03

[1] Considering a jar surface area of 283.4 cm^2 and an amount of 618 g dry soil per jar – BCS calculation results in 2.75 mg a.s./kg dws

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 10.4.1- 2 TER calculations for earthworms

Compound, test design	Endpoint		$PEC_{soil,max/accu}$ [mg/kg]	TER_{LT}	Trigger
FSN + IDF OD 45 reproduction	NOEC	≥ 370 mg prod./kg dws	2.499	≥ 148	5
Foramsulfuron reproduction	NOEC	≥ 2.75 mg a.s./kg dws	0.063	≥ 43.7	5
AE F092944 reproduction	NOEC	10 mg a.s./kg dws	0.004	≥ 2 500	5
AE F153745 reproduction	NOEC	≥ 100 mg a.s./kg dws	0.003	≥ 33 333	5
AE F130619 reproduction	NOEC	56 mg a.s./kg dws	0.016	≥ 3 500	5

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

Report:	[redacted];1999;M-193746-01
Title:	A 14-day acute toxicity test with the earthworm (*Eisenia fetida*) Code: AE F130360 01 JK05 4304
Report No:	006356
Document No:	M-193746-01-1
Guidelines:	**OECD: 207;Deviation not specified**
GLP/GEP:	**yes**

This study is part of the baseline dossier as it was part of the initial submission. However, as acute toxicity tests with earthworms are no longer required according to EEC 1107/2009, no risk assessment is based on results of this study.

CP 10.4.1.1 Earthworms sub-lethal effects

Report:	[redacted];2013;M-464888-01
Title:	Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G: Effects on reproduction and growth of earthworms *Eisenia fetida* in artificial soil
Report No:	83352022
Document No:	M-464888-01-1
Guidelines:	**OECD, Guideline for the testing of chemicals No. 222, Earthworm, Reproduction Test (adopted April 13, 2004)** **ISO-Guideline 11268-2, Soil quality - Effects of pollutants on earthworm (Eisenia fetida) - Part 2: Determination of effec;none**
GLP/GEP:	**yes**

Executive Summary:

The purpose of this study was to investigate the effects of foramsulfuron + isoxadifen-ethyl OD45 (22.5 + 22.5) G on the mortality, body weight, feeding activity and reproduction of adult *Eisenia fetida*.
Adult *Eisenia fetida* (with clitellum and weight range 300 to 600 mg, 9 to 10 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 13, 21, 34, 55, 88, 142, 229 and 370 mg test item/ kg dry weight artificial soil. The test item was incorporated into the soil. After 28 days exposure of adult worms the mortality, behavioural effects and biomass development was carried out. After additional 28 days the reproduction rate (number of offspring) was assessed. The test was performed according to the guideline ISO 11268-2 (1998) and the OECD Guideline 222 (2004).
The No Observed Effect Concentration (NOEC) for mortality, growth and feeding activity of the earthworm *Eisenia fetida* was determined to be ≥370 mg test item/kg soil, i.e. the highest concentration tested. The No Observed Effect Concentration (NOEC) for reproduction was determined to be the concentration of 229 mg test item/kg soil. The Lowest Observed Effect Concentration (LOEC) was determined to be 370 mg test item/kg soil and the EC_{10}, EC_{20} and EC_{50} values were determined to be 273.9 mg test item/kg soil, 305.8 mg test item/kg soil and 369.2 mg test item/kg soil.

Materials and Methods:

Test item. Foramsulfuron + isoxadifen-ethyl OD 45 (22.5 + 22.5) G (BCS-AH47626 + BCS-AI19578); Batch ID: EFKM002442; Material No.: 06321801; Specification No.: 102000011304-06; density: 0.961 g/mL (at 20°C); content of a.s.: foramsulfuron (AE F130360): 2.33% w/w, 22.41 g/L, isoxadifen-ethyl (AE F122006): 2.29% w/w, 21.96 g/L, Sample description: TOX10129-00.

Adult *Eisenia fetida* (with clitellum and weight range 300 to 600 mg, 9 to 10 months old, source: from an in-house culture, 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 13, 21, 34, 55, 88, 142, 229 and 370 mg test item/ kg dry weight artificial soil. The test item was incorporated into the soil. After 28 days exposure of adult worms in treated artificial soil the mortality, behavioural effects and biomass development was carried out. After additional 28 days the reproduction rate (number of offspring) was assessed (assessed 56 days after application). 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 69.6 % fine quartz sand, 20 % kaolin clay, 10 % sphagnum peat, air dried and finely ground, and 0.4 % $CaCO_3$ for the adjustment to pH to 6.0 ± 0.5 according to OECD 222; the pH was 5.9 to 6.1 at experimental start and 5.9 to 6.0 at experimental end; the water content at experimental start was 25.8% to 29.3% (49.6% to 56.4% of the maximum water holding capacity) and at experimental end 30.2% to 34.2% (58.1% to 65.8% 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 (Luxan Carbendazim 500 FC): 0.57 – 0.87 – 1.30 – 1.96 – 2.91 mg a.s./kg soil d.w. (corresponds to 1.3 – 2.0 – 3.0 – 4.5 – 6.7 mg test item/ kg soil d.w.); .; control: untreated artificial soil moistened with deionised water, solvent control: none.

Dates of experimental work: May 08, 2013 – July 24, 2013

Results:

Table 10.4.1.1- 1: Validity criteria

Validity criteria	Recommended	Obtained
Mortality of adults in the control	≤ 10 %	0 %
Reproduction of control (number of juvenile worms per replicate)	≥ 50	146 - 382
Coefficient of variation of reproduction in the control	≤ 30 %	29.1 %

All study validity criteria were met.

In the most recent GLP conducted experiment with the reference item Luxan Carbendazim 500 FC (performed under IBACON Project No. 46645022 from August 2012 to October 2012), there were statistically significant effects on reproduction at a concentration of 1.30 mg carbendazim/kg soil and higher. The EC_{10}, EC_{20} and EC_{50} (reproduction) were calculated to be 1.2, 1.4 or 1.7 mg a.s./kg artificial soil dry weight.

Mortality:
No mortality was observed in any treatment group.

Weight change:
The body weight changes of the earthworms after 4 weeks exposure to foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G were not statistically significantly different compared to the control up to and including the highest test concentration of 370 mg test item/kg soil (Williams t-test, $\alpha = 0.05$, two-sided).

Reproduction:
The reproduction rates were not significantly different compared to the control up to and including the test concentration of 229 mg test item/kg soil (Williams t-test, $\alpha = 0.05$, one-sided smaller). At the highest test concentration of 370 mg test item/kg soil a statistically significantly reduced reproduction was observed.

No behavioural abnormalities were observed in any of the treatment groups. The feeding activity in all the treated groups was comparable to the control (see table below).

Table 10.4.1.1- 2: Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G: Effect on earthworms (*Eisenia fetida*) in a 56-day reproduction study

Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G [mg/kg soil dry weight]	**Control**	**13**	**21**	**34**	**55**	**88**	**142**	**229**	**370**
Mortality (day 28) [%]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Significance	-	-	-	-	-	-	-	-	-
Weight change (day 28) [%]	26.3	24.1	23.6	25.0	24.4	20.2	21.5	25.4	31.6
Significance [1)]	-	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Mean No. of juveniles (day 56)	237	239	236	251	266	275	278	231	118
Significance [1)]	-	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	*
Reproduction in [%] of control (day 56)	-	100.8	99.5	105.6	112.2	115.6	117.2	97.1	49.6
Food consumption [g]	24.4	24.8	25.0	24.3	24.5	24.8	25.0	24.5	24.3
Endpoints [mg/kg soil dry weight]									
NOEC (day 28 mortality and weight)	**≥370**								
NOEC (day 56 reproduction)	**229**								
LOEC (day 56 reproduction)	**370**								
EC Values (reproduction) [2)]	EC_{10}			EC_{20}			EC_{50}		
	273.9 (269.3 to 278.1)			305.8 (302.5 to 308.8)			369.2 (368.2 to 370.3)		

- = not applicable
n.s. = not significantly different compared to the control
* = significantly different compared to the control
[1)] Williams t-test, $\alpha = 0.05$, two-sided for weight changes and one-sided smaller for reproduction
[2)] Logit Analysis

Conclusions:

In an earthworm reproduction and growth study with foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G the No Observed Effect Concentration (NOEC) for mortality, growth and feeding activity of the earthworm *Eisenia fetida* was determined to be ≥370 mg test item/kg soil, i.e. the highest concentration tested.
The No Observed Effect Concentration (NOEC) for reproduction was determined to be the concentration of 229 mg test item/kg soil. The Lowest Observed Effect Concentration (LOEC) was determined to be 370 mg test item/kg soil and the EC_{10}, EC_{20} and EC_{50} values were determined to be 273.9 mg test item/kg soil (95% confidence limits of 269.3 to 278.1 mg test item/kg soil), 305.8 mg test item/kg soil (95% confidence limits of 302.5 to 308.8 mg test item/kg soil) and 369.2 mg test item/kg soil (95% confidence limits of 368.2 to 370.3 mg test item/kg 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 FSN + IDF OD 45, foramsulfuron and its soil metabolites to other soil non-target macro-organisms is provided in Table 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 10.4.2- 1 Endpoints used in risk assessment

Test substance	Test species	Endpoint		Reference
FSN + IDF OD 45	*Folsomia candida*	NOEC	142 mg product/kg dws	[redacted], 2013 M-462827-01-1 KCP 10.4.2.1/01
	Hypoaspis aculeifer	NOEC	≥ 370 product/kg dws	[redacted], 2013 M-462835-01-1 KCP 10.4.2.1/02
Foramsulfuron	*Folsomia candida*	NOEC	178 mg a.s./kg dws	[redacted], 2012 M-443369-01-1 KCA 8.4.2/02
	Hypoaspis aculeifer	NOEC	≥ 1000 mg a.s./kg dws	[redacted], 2012 M-443308-01-1 KCA 8.4.2/01
AE F092944	*Folsomia candida*	NOEC	≥ 100 mg/kg dws	[redacted], 2013 M-451142-01-1 KCA 8.4.2/04
	Hypoaspis aculeifer	NOEC	≥ 100 mg/kg dws	[redacted], 2013 M-454043-01-1 KCA 8.4.2/03
AE F153745	*Folsomia candida*	NOEC	≥ 100 mg/kg dws	[redacted], 2013 M-450830-01-1 KCA 8.4.2/06
	Hypoaspis aculeifer	NOEC	≥ 100 mg/kg dws	[redacted], 2013 M-447606-01-1 KCA 8.4.2/05
AE F130619	*Folsomia candida*	NOEC	≥ 100 mg/kg dws	[redacted], 2013 M-450824-01-1 KCA 8.4.2/08
	Hypoaspis aculeifer	NOEC	≥ 100 mg/kg dws	[redacted], 2013 M-454051-01-1 KCA 8.4.2/07

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 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
FSN + IDF OD 45	*Folsomia candida*	NOEC 142 mg product/kg dws	2.499	56.8	5
	Hypoaspis aculeifer	NOEC ≥ 370 product /kg dws	2.499	≥ 148	5
Foramsulfuron	*Folsomia candida*	NOEC 178 mg a.s./kg dws	0.063	2 825	5
	Hypoaspis aculeifer	NOEC ≥ 1000 mg a.s./kg dws	0.063	≥ 15 873	5
AE F092944	*Folsomia candida*	NOEC ≥ 100 mg/kg dws	0.004	≥ 25 000	5
	Hypoaspis aculeifer	NOEC ≥ 100 mg/kg dws	0.004	≥ 25 000	5
AE F153745	*Folsomia candida*	NOEC ≥ 100 mg/kg dws	0.003	≥ 33 333	5
	Hypoaspis aculeifer	NOEC ≥ 100 mg/kg dws	0.003	≥ 33 333	5
AE F130619	*Folsomia candida*	NOEC ≥ 100 mg/kg dws	0.016	≥ 6 250	5
	Hypoaspis aculeifer	NOEC ≥ 100 mg/kg dws	0.016	≥ 6 250	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]p;[redacted];2013;M-462827-01
Title:	Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G): Effects on reproduction of the collembola *Folsomia candida* in artificial soil
Report No:	83353016
Document No:	M-462827-01-1
Guidelines:	**GLP compliant study based on OECD 232, 2009 and ISO 11267, 1999;none**
GLP/GEP:	**yes**

Executive Summary:

The purpose of the study was to determine the effects of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) on mortality and reproduction of the Collembola *Folsomia candida* in artificial soil.

10 collembolans (10-12 days old) per replicate (8 replicates for the control group, 4 replicates for each treatment group) were exposed to control (water treated), 13, 21, 34, 55, 88, 142, 229 and 370 mg test item/kg soil dry weight. After a period of 28 days, mortality, behavioural effects and reproduction were determined.

The overall No-Observed-Effect-Concentration (NOEC) was determined to be 142 mg test item/kg soil dry weight. The overall Lowest-Observed-Effect-Concentration (LOEC) was determined to be 229 mg test item/kg soil dry weight. All validity criteria for the untreated control of the study according to the OECD Guideline 232 have been fulfilled.

Material and Methods:

Test item: Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G); batch ID: EFKM002442; specification no.: 102000011304-06; sample description: TOX10129-00; density: 0.961 g/ml; content of a.s.: foramsulfuron (AE F130360): 2.33% w/w, 22.41 g/L, isoxadifen-ethyl (AE F122006): 2.29% w/w, 21.96 g/L.

10 Collembola (10-12 days old, from cultures held at the laboratory) per replicate (8 replicates for the control group, 4 replicates for each treatment group) were exposed 28 days in treated artificial soil. Different concentrations of the test item were mixed homogeneously into the soil which was placed into glass vessels before the Collembola were introduced on top of the soil; 8 concentrations (13, 21, 34, 55, 88, 142, 229 and 370 mg test item/kg soil) and one control (untreated) were tested. The collembolans were fed with approximately 2 mg dry yeast for each test vessel at the beginning of the test and on day 14. The assessments of adult mortality, behavioural effects and reproduction were performed after 28 d.
The artificial soil contained 74.8 % fine quartz sand, 20 % kaolin clay, 5 % sphagnum peat, air dried and finely ground, and 0.2 % $CaCO_3$ for the adjustment to pH to 6.0 ± 0.5 according to OECD 232; the pH was 5.7 to 5.8 at experimental start and 5.7 at experimental end; the water content at experimental start was 21.2% to 21.7% (55.8% to 57.1% of the maximum water holding capacity) and at experimental end 20.0% to 21.9% (52.7% to 57.6% 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 33.6 – 53.7 – 85.9 – 137.5 – 220.0 mg boric acid/kg soil d.w.; control: artificial soil with deionised water, solvent control: none.

Dates of experimental work: June 05, 2013 to July 04, 2013

Results:

Table 10.4.2.1-1: Validity criteria

Validity criteria	Recommended	Obtained
Control mortality (mean)	≤ 20 %	5 %
Control reproduction (mean number of juveniles per replicate)	≥ 100	423 - 555
Coefficient of variation of the control reproduction	≤ 30 %	10.7 %

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

In a separate GLP conducted study (study code 61403016) the reference item Boric acid showed statistically significant effects on mortality and reproduction at concentrations of ≥ 53.7 mg/kg soil dry weight; the EC_{50} for reproduction was calculated to be 59.9 mg/kg soil dry weight.

Mortality:
A mortality of 58% was observed in the highest test item treated group of 370 mg test item/kg soil dry weight, which was statistically significantly different compared to the control, where 5% of the Collembola died (Fisher's Exact test, $\alpha = 0.05$, one-sided greater). At the lower test concentrations no significant increased mortality was observed, except at the concentration of 21 mg test item/kg soil dry weight, which is not considered to be treatment related since at the higher concentrations up to and including 229 mg test item/kg soil dry weight no effects were observed.

Reproduction:
The reproduction of the Collembola exposed to foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) was not statistically significantly different compared to the control up to and including the test concentration of 142 mg test item/kg soil dry weight (Bonferroni-Welch t-test, $\alpha = 0.05$, one-sided smaller).

No behavioural abnormalities were observed in any of the treatment groups.

Table 10.4.2.1-2: Effect of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) on Collembola (*Folsomia candida)* in a 28-day reproduction study

Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) [mg/kg soil]	**Control**	**13**	**21**	**34**	**55**	**88**	**142**	**229**	**370**
Mortality (day 28) [%]	5	13	23	15	15	20	13	15	58
Statistical significance[1)]	-	n.s.	*	n.s.	n.s.	n.s.	n.s.	n.s.	*
No. of juveniles (day 28)	487	532	386	467	532	432	512	321	53
Reproduction in [%] of control (day 28)	-	109	79	96	109	89	105	66	11
Statistical significance [2)]	-	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	*	*
	Endpoints [mg/kg soil]								
NOEC (mortality)	229								
NOEC (reproduction)	142								
LOEC (reproduction)	229								
EC Values (reproduction) [3)]	EC_{10}			EC_{20}				EC_{50}	
	179.05			203.10				258.48	

n.s. = not significantly different compared to the control * = significantly different compared to the control
[1)] Fisher's Exact Test, α = 0.05, one-sided greater [2)] Bonferroni-Welch t-test, α = 0.05, one-sided smaller
[3)] Probit analysis

Conclusions:

Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) caused no significant effects on mortality of *Folsomia candida* up to and including the concentration of 229 mg test item/kg soil dry weight and no effects on reproduction up to and including the concentration of 142 mg test item/kg soil dry weight.
Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be 142 mg test item/kg soil dry weight. The overall Lowest Observed Effect Concentration (LOEC) was determined to be 229 mg test item/kg soil dry weight. The EC_{50} was determined to be 258.48 mg test item/kg soil dry weight.

Report:	[redacted]i;[redacted];2013;M-462835-01
Title:	Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G): Effects on reproduction of the predatory mite *Hypoaspis aculeifer* in artificial soil
Report No:	83351089
Document No:	M-462835-01-1
Guidelines:	**GLP compliant study according to OECD 226, 2008;none**
GLP/GEP:	**yes**

Executive summary:

The purpose of the study was to determine the effects of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) on mortality and reproduction of the Predatory Mite *Hypoaspis aculeifer*.
10 adult soil mites (females) per replicate (8 replicates for the control group and 4 replicates for each treatment group) were exposed to control (water treated), 13, 21, 34, 55, 88, 142, 229 and 370 mg test item/kg soil dry weight. Two weeks after start of exposure, the number of juveniles and surviving adult female mites were determined.

The overall No-Observed-Effect-Concentration (NOEC) was determined to be ≥ 370 mg test item/kg soil dry weight. The overall Lowest-Observed-Effect-Concentration (LOEC) and the EC_{50} were estimated to be greater than 370 mg test item/kg soil dry weight. The validity criteria for the control group of the study were accomplished.

Material and Methods:

Test item: Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G); batch ID: EFKM002442; specification no.: 102000011304-06; sample description: TOX10129-00; density: 0.961 g/ml; content of a.s.: foramsulfuron (AE F130360): 2.33% w/w, 22.41 g/L, isoxadifen-ethyl (AE F122006): 2.29% w/w, 21.96 g/L.

10 collembolans (adult females, approximately 9 days after reaching the adult stage) per replicate (8 replicates for the control group, 4 replicates for each treatment group) were exposed 14 days in treated artificial soil. Different concentrations of the test item were mixed homogeneously into the soil which was filled in glass vessels before the predatory mites were introduced on top of the soil; 8 concentrations (13, 21, 34, 55, 88, 142, 229 and 370 mg test item/kg soil dry weight) and one control (untreated) were tested. The collembolans were fed with cheese mite (*Tyrophagus putrescentiae) ad libitum* at test start and on day 2, 5, 7, 9 and 12. The assessments of adult mortality, morphological differences and reproduction were performed after 14 d.
The artificial soil contained 74.8 % fine quartz sand, 20 % kaolin clay, 5 % sphagnum peat, air dried and finely ground, and 0.2 % $CaCO_3$ for the adjustment to pH to 6.0 ± 0.5 according to OECD 226; the pH was 5.7 to 5.8 at experimental start and 5.8 to 5.9 at experimental end; the water content at experimental start was 21.2% to 21.7% (55.8% to 57.1% of the maximum water holding capacity) and at experimental end 20.3% to 21.8% (53.5% to 57.5% 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: (Dimethoate (BAS 152 I), 400.0 g/L (nominal), 411.7 g/L (nanlysed)): 1.0 – 1.7 – 2.7 – 4.3 – 6.8 mg a.s./kg soil dry weight; control: artificial soil moistened with deionized water, solvent control: none.

Dates of experimental work: June 05, 2013 to June 21, 2013

Results:

Table 10.4.2.1-3: Validity criteria

Validity criteria	Recommended	Obtained
Control Mortality (mean mortality of the adult female animals)	≤ 20 %	4 %
Control Reproduction (number of juvenile mites per replicate)	≥ 50	190 - 226
Coefficient of variation of the Control Reproduction	≤ 30 %	5.3 %

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

In a separate GLP conducted study (study code 74661089, performed in May/June 2012) the reference item dimethoate showed statistically significant effects on reproduction at a concentration of 1.7 mg dimethoate/kg soil dry weight and above. The EC_{50} for reproduction was 4.0 mg dimethoate/kg soil dry weight.

Mortality:
Mortality of *Hypoaspis aculeifer* in the test item treated group ranged from 3% to 13%. The values were not significantly different compared to the control where 4% of the soil mites died (Fisher's Exact Test, $\alpha = 0.05$, one-sided greater).
No differences in morphology of the mites between the test item treated groups and the control were observed.

Reproduction:
There were no statistically significant effects on reproduction of *Hypoaspis aculeifer* up to and including the highest test concentration of 370 mg test item/kg soil (Williams t-test, $\alpha = 0.05$, one-sided smaller).
The reference item dimethoate showed statistically significant effects on reproduction at a concentration of 1.7 mg dimethoate/kg soil and above. The EC50 for reproduction was 4.0 mg dimethoate/kg soil.

Table 10.4.2.1-4: Effect of foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) on the Predatory Mite *Hypoaspis aculeifer* in a 14-day reproduction study

Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) [mg/kg soil]	**Control**	**13**	**21**	**34**	**55**	**88**	**142**	**229**	**370**
Mortality (day 14) [%]	4	8	8	8	13	8	8	3	8
Statistical significance[1)]	-	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
No. of juveniles (day 14)	207	213	264	213	233	209	207	223	193
Reproduction in [%] of control (day 14)	100	103	127	103	112	101	100	108	93
Statistical significance [2)]	-	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Endpoints [mg/kg soil]									
NOEC (mortality)	≥370								
LC_{50} (mortality) [3)]	>370								
NOEC (reproduction)	≥370								
LOEC (reproduction)	>370								
EC_{50} (reproduction) [3)]	>370								

n.s. = not significantly different compared to the control - not applicable
[1)] Fisher's Exact Test, $\alpha = 0.05$, one-sided greater [2)] Williams t-test, $\alpha = 0.05$, one-sided smaller
[3)] estimated value

Conclusions:

Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5) G (FSN+IDF OD 45 (22.5+22.5) G) caused no significant effects on mortality and reproduction of *Hypoaspis aculeifer* up to and including the highest test concentration of 370 mg test item/kg soil.

Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be ≥370 mg test item/kg soil. The overall Lowest Observed Effect Concentration (LOEC) and the EC_{50} were estimated to be greater than 370 mg test item/kg soil

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 foramsulfuron on soil non-target micro-organisms is summarised in Table 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 10.5- 1: Effects on soil nitrogen transformation

Test item	Test design	Ecotoxicological endpoint		Reference
N-transformation				
FSN + IDF OD 45	28 d	no unacceptable effects	≥18.59 L prod./ha ≥23.8 mg prod./mg dws	[redacted], 1999 M-193742-01-1 KCP 10.5/01
Foramsulfuron	28 d	no unacceptable effects	≥0.3 mg a.s./kg dws	[redacted], 1997 M-142972-01-1 KCA 8.5/01
Foramsulfuron + bound residues	28 d	no unacceptable effects	≥0.735 mg a.s./kg dws	[redacted], 2000 M-193916-01-1 KCA 8.5/02
AE F153745	28 d	no unacceptable effects	≥0.240 mg/kg dws	[redacted], 2013 M-453508-01-1 KCA 8.5/07
AE F130619	28 d	no unacceptable effects	≥0.375 mg/kg dws	[redacted], 2013 M-453568-01-1 KCA 8.5/06
AE F092944	28 d	no unacceptable effects	≥0.137 mg/kg dws	[redacted], 2013 M-453511-01-1 KCA 8.5/05

dws = dry weight soil

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. A study testing effects of bound residues of foramsulfuron on nitrogen transformation ([redacted], 2000; M-193916-01-1) measured nitrogen turnover for 28 days starting from the time point when a plateau concentrations of bound residues had been reached in the test soil. No deviations from the control exceeding 25% occurred. It can be concluded that the formation of bound residues does not have a negative impact on the activity of soil microorganisms.

Report:	[redacted]d; [redacted];1999;M-193742-01
Title:	The effects on the respiration and nitrification of soil microflora Code: AE F130360 01 1K05 A304
Report No:	C006355
Document No:	M-193742-01-1
Guidelines:	**BBA: VI, 1-1, 1990;Deviation not specified**
GLP/GEP:	**yes**

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 102000005810, which contains the active substance foramsulfuron (22.5 g/L) and the safener isoxadifen-ethyl (22.5 g/L) solved in an OD-formulation, following OECD testing guidelines 208 and 227, respectively (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 10.6- 1: Survey of non-target plant tests performed with FSN + IDF OD 45

Terrestrial Non-Target Plants			
Number of species tested (species)	**Test method Test substance Application rate**	**Effects**	**Reference**
Dicotyledoneae: 6 (bean, cabbage, radish, tomato, soybean, lettuce) Monocotyledoneae: 4 (rye grass, corn, wheat, onion)	Tier 2 vegetative vigour FSN + IDF OD 45 0 (control), 0.25, 0.74, 2.2, 6.7, 20 and 60 g prod./ha with height and condition observations on Days -1 or 0 (prior to application), 7, 14 and 21, dry weight measurements on Day 21	most sensitive species: radish; **lowest EC50 1.88 g sum of a.s./ha**	[redacted], 1999; B002710 M-238444-01-2 KCP 10.6.2/01
Dicotyledoneae: 4 (cabbage, radish, tomato, lettuce) Monocotyledoneae: 3 (rye grass, wheat, onion)	Tier 2 seedling emergence FSN + IDF OD 45 0 (control), 0.25, 0.74, 2.2, 6.7, 20 and 60 g prod./ha with observations of emergence on Days 10 and 14, with observations of height and condition on Day 14 and measurement of dry weight on Day 14	most sensitive species: lettuce; **lowest EC50 38.8 g sum of a.s./ha**	[redacted], 2000; B002819 M-238550-01-1 KCP 10.6.2/02

Remark: In all studies endpoints are given in g a.i./ha. Descriptions of the experimental design in the two seedling emergence studies (page 9 in each report) indicate that the endpoints are given as g (AE F130360 + AE F122006) per hectare.

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 90^{th} percentile estimates derived by the *BBA (2000)*[5] from the spray-drift predictions of [redacted] *(2000)*[6]. Only a single application was considered as factors such as plant growth will reduce residues per unit area between multiple applications. For a single application to maize, 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 foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L) is 2.7 L product/ha (corresponding to 120 g foramsulfuron + isoxadifen a.i./ha), giving a maximum off-field predicted environmental rate ($PER_{off-field}$) of 3.324 g sum of a.i./ha.

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

Deterministic Risk assessment

According to the Terrestrial Guidance Document[7], the risk to non-target plants is evaluated by comparing the lowest ER50 observed in the laboratory studies with the drift rates ($PER_{off-field}$) inclosing a safety factor of 5. In addition, the usage of drift reducing nozzles is considered.

Table 10.6-2: Deterministic risk assessment for foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L) based on effects on seedling emergence

arable field crops, one application, 120.0 g sum of a.i./ha; lowest ER_{50} = 38.8 g sum of a.i./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	3.324	**11.67**	**23.35**	**46.69**	**116.73**
5	0.57	0.684	**56.73**	**113.45**	**226.90**	**567.25**
10	0.29	0.348	**111.49**	**222.99**	**445.98**	**1114.94**

Table 10.6-3: Deterministic risk assessment for foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L) based on effects on vegetative vigour

arable field crops, one application, 120.0 g sum of a.i./ha; lowest ER50 = 1.880 g sum of a.i./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	3.324	0.57	1.13	2.26	**5.66**
5	0.57	0.684	2.75	**5.50**	**10.99**	**27.49**
10	0.29	0.348	**5.40**	**10.80**	**21.61**	**54.02**

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

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

$HC_5 = 10 \exp(avg\text{-}ks*std)$

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

From the data sets of ER_{50}-levels obtained from the tests with foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L) only the vegetative vigour data are applicable for an HC_5-calculation. The seedling emergence data contain too many greater-than figures.

Table 10.6-4: HC_5-figures for seedling-emergence and vegetative vigour with foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L).

HC_5	Seedling emergence	Vegetative vigour
HC_5 based on lowest endpoint from all species	n.a.	0.625 g sum of a.i./ha

Table 10.6-5 Probabilistic risk assessment for foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 g/L) based on effects on vegetative vigour

arable field crops, one application, 120.0 g sum of a.i./ha; HC_5 = 0.6250 g sum of a.i./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	3.324	0.19	0.38	0.75	**1.88**
5	0.57	0.684	0.91	**1.83**	**3.65**	**9.14**
10	0.29	0.348	**1.80**	**3.59**	**7.18**	**17.96**

Since foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 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 10.8.1-3 and -5 it becomes obvious, that a 10-m buffer zone is sufficient to protect terrestrial non-target plants if conventional spraying equipment is used. With the use of 50% drift reducing nozzles the buffer zone can be reduced to 5 m. With the use of 90% drift reducing nozzles no buffer zone is required.

Foramsulfuron + isoxadifen-ethyl OD 45 (22.5+22.5 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

Screening data are not available.

CP 10.6.2 Testing on non-target plants

Report:	[redacted];[redacted];[redacted];[redacted];1999;M-238444-01
Title:	A Tier II toxicity test to determine the effects of the test substance on vegetative vigor of ten species of plants: AE F130360 + AE F122006, oil flowable, 22.5+22.5 g/L
Report No:	B002710
Document No(s):	Report includes Trial Nos.: 312-122 M-238444-01-2
Guidelines:	**MAFF: 3850; OECD: (98)17; USEPA (=EPA): 850.4250;Deviation not specified**
GLP/GEP:	**yes**

Report:	[redacted];[redacted];[redacted];[redacted];2000;M-238550-01
Title:	A tier II toxicity test to determine the effects of the test substance on seedling emergence of seven species of plants: AE F130360 + AE F122006 oil flowable 22.5 + 22.5 g/L: AE F130360.01 1K05 A304
Report No:	B002819
Document No(s):	Report includes Trial Nos.: 312-123 CF001382 M-238550-01-1
Guidelines:	**MAFF: 59 NohSan Notification No. 3850; OECD: ENV/MC/CHEM(98)17; USEPA: EPA: 160;Deviation not specified**
GLP/GEP:	**yes**

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 foramsulfuron are not available.