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Document Title

Summary of the ecotoxicological studies Flurtamone + Diflufenican SC 350

Data Requirements

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

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

Date

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[redacted]

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Version history

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

[1] Note how the amendments or additions are represented (italics/colour etc)

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CP Section 10 - ECOTOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCT

Introduction

A risk assessment for Non-Target Organisms is presented for flurtamone in the formulation flurtamone and diflufenican (FLT + DFF SC 350), for the use as herbicide in winter and spring cereals. Ecotoxicity data used in the following risk assessment were derived from studies with the formulated product and the active substance flurtamone. The focus of this risk assessment is flurtamone, there is currently no straight formulation of flurtamone commercially supported in Europe, hence the representative formulation is a mixture product. End points are provided for the mixture partner diflufenican and where the product is tested for ecotoxicity these values are used in the risk assessments. For some studies a straight formulation of flurtamone has been specifically prepared to ensure that the end points are clearly related to flurtamone. In this case the risk assesments are conducted with flurtamone since it is renewal of flurtamone at EU level that is the objective of this submission.

Intended application pattern

The use pattern for this formulation is summarised in Table 10-1.

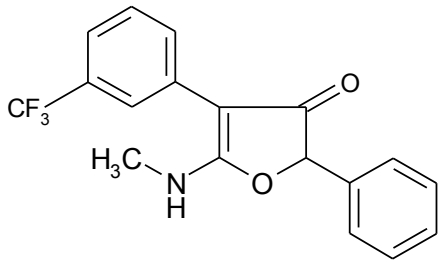
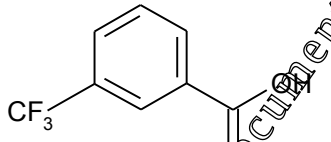
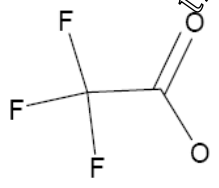
Table10- 1: Intended application pattern

Crop	Timing of application	Number of applications	Maximum label rate	Maximum application rate, individual treatment [g a.s./ha]	
	BBCH		L/ha	FLT	DFF
Winter and spring cereals	00 - 29	1	0.5	125	50

General remarks concerning metabolites

In addition to the active substance flurtamone, the following metabolites were addressed in this document as they were considered important due to the amounts in which they were found during the course of environmental fate studies, or due to their specific properties. Study authors sometimes have used different names or short codes for the active substances and degradation products. In this summary, a single name for each substance is always used.

Table 10- 1: Flurtamone and its metabolites (including Aventis and/or BCS [a], Chevron [b] and Rhone-Poulenc [c] codes)

No.	Name, Structure IUPAC name CAS name, CAS number (if known)	Molecular formula molar mass Other names / codes	Occurrence Major/Minor Compartment(s)
AS	FLURTAMONE  Name IUPAC: 5-Methylamino-2-phenyl-4-(3-trifluoromethylphenyl)-3(2H)-furanone Name CAS: 3(2H)-Furanone, 5-(methylamino)-2-phenyl-4-[3-(trifluoromethyl)phenyl]-, (±)- CAS No.: 96525-23-4	$C_{18}H_{14}F_3NO_2$ 333.3 g mol-1 [a] AE B107137 [a] BCS-AL26195 [b] RE 40885 [c] RPA 590515 (also 201918 and 304563) Report name: Flurtamone	Active substance
M04	SM4/PM11/AM30  Name IUPAC: 3-Trifluoromethylbenzoic acid Name CAS: Benzoic acid, 3-(trifluoromethyl)- CAS No.: 454-92-2 Sodium salt: Name IUPAC: sodium 3-(trifluoromethyl)benzoate CAS No.: 69226-41-1	C8H5F3O2 190.1 g mol-1 [a] AE C518919 [a] BCS-AA52670 [a] BCS-CX97256 (sodium salt) [b] RE 54488 [c] RPA 025905 Common abbreviation: TFMBA Report name: Flurtamone-TFMBA	Major in soil Aerobic soil – max. 24.7% Soil photolysis – max. 3.8% Water/sediment total – max. 4.1% Cereals, Sunflower Rat, Hen, Goat
M05	SM5/PM12  Name IUPAC: Trifluoroacetic acid Sodium trifluoroacetate Name CAS: Trifluoroacetic acid Sodium trifluoroacetate CAS No.: 76-05-1 (acid) 2923-18-4 (sodium salt)	C2HF3O2 114.0 g mol-1 [a] AE C502988 (acid) [a] BCS-AL85845 (acid) [b] none given [c] RPA 017503 (acid) [a] AE1046319 (sodium salt) [a] BCS-AZ56567 (sodium salt) Common abbreviation: TFA (or TFAA) Report name: Trifluoroacetic acid or trifluoroacetate	Major in soil Aerobic soil – max. 9.8% Confined rotational crops

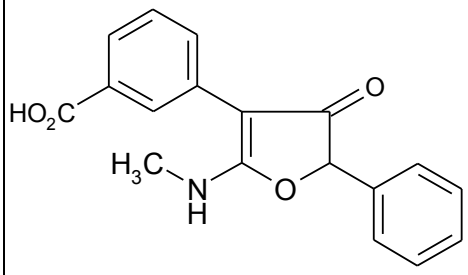
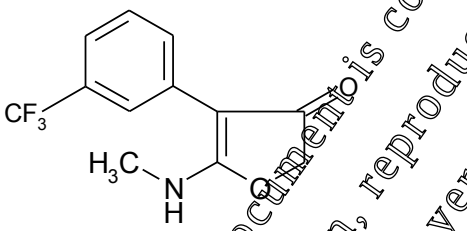
No.	Name, Structure IUPAC name CAS name, CAS number (if known)	Molecular formula molar mass Other names / codes	Occurrence Major/Minor Compartment(s)
M07	AQM1  Name IUPAC: 3-(2-Methylamino-4-oxo-5-phenyl-4,5-dihydrofuran-3-yl)benzoic acid Name CAS: Benzoic acid, 3-[4,5-dihydro-2-(methylamino)-4-oxo-5-phenyl-3-furanyl]- CAS No.: 148681-60-1	C18H15NO4 309.3 g mol-1 [a] AE 1083976 [a] BCS-BA29451 [b] none given [c] RPA 203597 Report name: Flurtamone-carboxylic acid	Major in Aqueous photolysis – max. 33.5%
M08	AQM2  Name IUPAC: 5-methylamino-4-(3-trifluoromethylphenyl)-3(2H)-furanone Name CAS: 3(2H)-Furanone, 5-(methylamino)-4-[3-(trifluoromethyl)phenyl]- CAS No.: 96525-53-0	C12H10F3NO2 257.2 g mol-1 [a] AE 2093305 [a] BCS-BT61400 [b] none given [c] RPA 591120 Report name: Flurtamone-desphenyl	Major in Aquatic Water – max. 7.8% Sediment – max.3.6% Total max. 10.7%

Table 10- 2: Definition of the residue for risk assessment*

Compartment	Compound /Code
Soil	Flurtamone, M04 TFMBA and M05 TFA
Groundwater	Flurtamone and M05 TFA
Surface water	Flurtamone, M07 flurtamone-carboxylic acid and M08 flurtamone-desphenyl.
Plant material	Flurtamone and M05 TFA

*Justification for the residue definition for risk assessment is provided in MCA Sec.7, Point CA 7.4.1 and MCA Sec. 6, Point CA 6.7.1. The soil photolysis metabolite M06 benzoic acid has been considered as non-relevant for risk assessment as outlined in the position paper under KCP-9.1 /01; Lowden P. 2013.

CP 10.1 - Effects on birds and other terrestrial vertebrates

In addition to the parent compound flurtamone, a risk assessment is performed for one metabolite, namely trifluoroacetic acid (M05 TFA). TFA has been identified as an environmental metabolite of different chemicals including pesticide active substances as e.g. flurtamone. As residues of M05 TFA may occur in plant food items of birds and wild mammals, it was considered necessary to establish appropriate ecotoxicological endpoints to be used for risk assessment purposes. However, toxicity endpoints are only available for mammals. As birds are not expected to be more susceptible to M05 TFA than mammals, these endpoints were also used for the screening assessment of omnivorous and herbivorous birds.

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

The summary of the toxicity profile of the active substances flurtamone and diflufenican to birds is provided in the following tables.

Table 10.1.1- 1: Avian toxicity data of flurtamone

Test species	Study	Ecotoxicological endpoint		Reference
Bobwhite quail	acute oral	LD_{50} > **2530**[1) 2)] LD_{50} = **4777**[3)]	mg/kg bw	[redacted] & [redacted] 1988, M-160680-01-1
Bobwhite quail	*5-day dietary*	*LC_{50} > 6000*[1) 2)] *≙ LDD_{50} > 1535*[4)]	*ppm* *mg/kg bw/day*	[redacted] & [redacted] *1989, M-160689-01-1*
Mallard duck		*LC_{50} = 2000*[2)] *≙ LDD_{50} = 545*	*ppm* *mg/kg bw/day*	[redacted] & [redacted] *1989, M-160687-01-1* [redacted] *2005, M-347726-01-1* [5)]
Bobwhite quail	1-generation reproduction (21-weeks feeding)	NOAEL = 80[2)] ≙ NOAEL = **7.5**	ppm mg/kg bw/day	[redacted] *et al.* 1990, M-203211-01-1
Mallard duck	1-generation reproduction (22-weeks feeding)	NOAEL = 200[2)] ≙ NOAEL = 28	ppm mg/kg bw/day	[redacted] *et al.* 1990, M-203217-01-1
"Bird" acute/10		*LD_{50}/10 = 477.7*	*mg/kg bw*	*Calculated "acute/10"- endpoint is higher than reproductive endpoint*

Underlined bold values: Endpoints used for Tier 1 TER calculation
Bold values: Endpoints used for refined TER calculation
Italics: Studies and endpoints not used in risk assessment (not required or not adequate, e.g. if bird acute/10 is higher than reproductive endpoint
1) 10 birds per group; no mortality occurred during study
2) Endpoint listed in EFSA review report for the active substance Flurtamone (2003)
3) LD_{50} extrapolated according EFSA GD birds & mammals (2009)
4) Parameters over 5-day exposure period (6000 ppm group): mean feed consumption: 8.7 g/bird /day; mean bodyweight: 34g
5) Calculation of daily dietary dose in amendment

Table 10.1.1- 2: Avian toxicity data of mixing partner diflufenican

Test substance	Test species	EU agreed endpoints acc. to EFSA Scientific Report (2007) 122, 1-84	
Diflufenican	"Bird", acute, oral	NOLED[1] LD_{50}	≥ 2150 mg as/kg bw 5537 mg as/kg bw [2)]
	Bobwhite quail, reproduction	NO(A)EL	91.84 mg as/kg bw/d

[1)] NOLED = no observed lethal effect dose
[2)] geometric mean of extrapolated LD_{50} values according to EFSA GD 2009

Toxicity of the formulation

No study was performed with the formulation on birds due to animal welfare reasons.
Thus the risk assessment will be based on the individual active substances.

Selection of endpoints for the risk assessment

(According to the Guidance Document on Risk Assessment for Birds & Mammals, EFSA 2009[1], abbreviated subsequently EFSA GD B&M 2009)

Data are available for more than one species and/or from more than one study

Data on more than one species will cause an increasingly conservative risk assessment if the same fixed assessment factors are applied to the most sensitive species' toxicity value. In the EFSA Guidance Document methods are described that allow maintaining the level of protection when more than the required number of species has been tested. For that reason the endpoints for risk assessment depicted in the table above have been established in accordance with the following criteria:

- If acute tests for more than one species are available the geometric mean should be used for the refined assessment, except when the endpoint for the most sensitive species is more than a factor 10 below the geometric mean of all the tested species. Where this is the case, the most sensitive species will be used for the risk assessment but generally without any assessment factor.
- For reproductive studies, the endpoint from the most sensitive tested species should be used.

- If separate values for males and females are measured, it is proposed that the geometric mean be used unless there is a clear indication of a difference in sensitivity between the sexes (e.g. > 25%).

Short-term endpoints

A short-term risk assessment is not required. However, the endpoint from short-term dietary studies, e.g. 5-day dietary study in birds (OECD 205) should be used in an acute risk assessment when indicating a higher toxicity via the dietary exposure rout (lower LDD_{50}).
But there is no indication that 5-day exposure via dietary rout might provoke higher toxicity than one application via gavage in acute study.
Therefore, in the acute risk assessment the acute endpoints will be used.

Reproductive endpoints

The LD50/10 is used to take account of the possibility of reproductive impairment due to sublethal/short-term effects on pair formation and breeding site selection, incubation, parental care of nestlings, and survival of fledging birds. This value is based on a review of acute studies showing that severe signs of toxicity likely to lead to reproductive deficits tend to be recorded at dosing levels greater than 1/10 of the LD50.
The lower endpoint from the reproduction study will be used in avian reproductive risk assessment.

Flurtamone

An acute oral study on bobwhite quail was performed. No mortality occurred.

[1] EFSA (2009): Guidance Document on Risk Assessment for Birds & Mammals on request from EFSA. The EFSA Journal (2009), 7(12):1438.

According to EFSA GD B&M 2009, a factor of 1.888 has been applied to the top dose in case 10 animals have been tested and no mortality occurred to calculate the LD_{50}. This procedure reveals an acute endpoint for potential refinement of 4777 mg a.s./kg bw/d for the bobwhite quail.
Considering the results of the 5-day short-term study there is no indication that exposure via dietary route might provoke higher toxicity than one application via gavage in acute study.

Risk assessment for birds

The risk assessment procedure follows the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009).
The risk is considered acceptable, if the 'Toxicity Exposure Ratio' (TER) value pass the trigger values of ≥ 10 for acute and ≥ 5 for chronic exposure.
If the TER values are below the trigger values in certain areas, a refined risk assessment based on more relevant and realistic conditions is performed for those particular areas.

Calculation of Toxicity Exposure Ratio (TER)

The calculation of acute and long-term Toxicity to Exposure Ratio (TER) is defined as follows:

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

Long-term risk: TER_{LT} = NO(A)EL [mg as/kg bw/d] / DDD_{LT} or
LD50/10 [mg as/kg bw] / DDD_{LT}

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

Calculation of Daily Dietary Dose (DDD)

Acute exposure (DDD_A):

The daily dietary dose is given by the following equation:

DDD_A= application rate [kg/ha] × shortcut value (SV_{90}) x MAF_{90}

Long-term exposure (DDD_{LT}):

The daily dietary dose is given by the following equation:

DDD_{LT}= application rate [kg/ha] × shortcut value (SV_m) × f_{TWA} x MAF_m

Where:

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

For potential higher tier risk assessments, MAF and ftwa, which are based on the default DT_{50} of 10 days in Tier 1, can be refined with a lower DT_{50}. For this purpose, a kinetic evaluation of flurtamone residue decline in monocotyledonous plants is summarised under KCP 10.1.1.2/01 ([redacted], 2014, M-475193-01-1), revealing a geomean DT_{50} of 3.1 days.

Standard exposure scenario for Tier 1 risk assessment

The main potential exposure route for birds is expected to be consumption of contaminated feed. Default ("shortcut"-) values for the exposure estimate will be used as provided in Appendix A of the EFSA GD B&M 2009 representing a worst case assessment.

It is assumed that

- animals satisfy their entire food demand in the treated area (PT = 1),
- over an acute time frame (hours) the animals feed on items containing maximum residues (90th percentile), whereas they would ingest food containing mean residues over a long-term period (days to weeks),
- the multiple application factor (MAF) for the acute or long-term exposure is based on default values based on a generic DT_{50} value of 10 days, considering the actual (maximum) number of applications and the interval between them,
- long-term predicted environmental concentrations to be compared with chronic endpoints can be calculated as the time-weighted average concentration. Default assumptions are a time window of 21 days and a DT_{50} of 10 days leading to a time weighted average factor (= f_{twa}) of 0.53.

Avian generic focal species for Tier 1 risk assessment

The product is intended to be used in winter and spring cereals at 0.5 L prod/ha, corresponding to 0.125 kg flurtamone (FLT) and 0.05 kg diflufenican (DFF) at BBCH 00 - 29. The following generic focal species have to be addressed in Tier 1 risk assessment**.**

Table 10.1.1- 3: Relevant generic avian focal species for Tier 1 risk assessment

Crop	Growth stage (BBCH)	Generic focal species	Representative species	Shortcut value	
				For long-term RA based on RUD_m	For acute RA based on RUD_{90}
Bare soils	< 10	Small granivorous bird "finch"	Linnet (*Carduelis cannabina*)	11.4	24
Bare soils	< 10	Small omnivorous bird "lark"	Woodlark (*Lullula arborea*)	8.2	17.4
Bare soils	< 10	Small omnivorous bird "wagtail"	Yellow wagtail (*Motacilla flava*)	5.9	10.9
Cereals	Early (shoots) autumn-winter 10 - 29	Large herbivorous bird "goose"	Pink-foot goose (*Anser brachyrhynchus*)	16.0	30.5
Cereals	10 – 29	Small omnivorous bird "lark"	Woodlark (*Lullula arborea*)	10.9	24.0

CP 10.1.1.1 - Acute oral toxicity

Summary of calculated TER values for birds

Table 10.1.1.1- 1: Summary of acute TER values

Crop (BBCH)	Generic focal species	Active substance	SV_{90}	TER_A	Assessment level
Bare soil BBCH < 10	Small granivorous bird "finch" <Linnet>	Flurtamone	24.7	819	Tier 1
	Small omnivorous bird "lark" <Woodlark>		17.4	1163	Tier 1
	Small insectivorous bird "wagtail" <Yellow wagtail>		10.9	1857	Tier 1
Early cereal shoots, autumn-winter BBCH 10-29	Large herbivorous bird "goose" <Pink-foot goose>		30.5	664	Tier 1
Cereals, BBCH 10 - 29	Small omnivorous bird "lark" <Woodlark>		24.0	843	Tier 1

Tier 1 acute toxicity exposure ratio for birds

Table 10.1.1.1- 2: Tier 1 acute DDD and TER calculation for birds

Crop	Generic focal species	LD_{50} [mg/kg bw]	DDD			DDD	TER_A	Trigger
			Appl. rate [kg/ha]	SV_{90}	MAF_{90}			
Flurtamone								
Bare soil	Small granivorous bird "finch" <Linnet>	≥ 2530	0.125	24.5	1	3.063	849	10
	Small omnivorous bird "lark" <Woodlark>			47.4		2.175	1163	
	Small insectivorous bird "wagtail" < Yellow wagtail>			10.9		1.563	1617	
Cereals	Large herbivorous bird "goose" <Pink-foot goose>			30.5		3.813	664	
	Small omnivorous bird "lark" <Woodlark>			24.0		3	843	

All TER values are above the trigger of 10 for acute exposure. Accordingly, safe use of the product in cereals can be concluded.

Acute risk assessment for birds drinking contaminated water

An assessment of the risk potentially posed by consumption of contaminated drinking water is required. For details see point 10.1.1.2 of this document.

As the product is applied in cereals, no pools in leaf axils where an acute exposure possibly might occur are to be expected.

The acute risk from water in puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil is covered by the long-term risk assessment under Point 10.1.1.2 of this document.

CP 10.1.1.2 - Higher tier data on birds

Table 10.1.1.2- 1: Summary of reproductive (long-term) TER values

Crop (BBCH)	Generic focal species	Active substance	SV_m	TER_{LT}	Assessment level
Bare soil BBCH < 10	Small granivorous bird "finch" <Linnet>	Flurtamone	11.4	9.7	Tier 1
	Small omnivorous bird "lark" <Woodlark>		8.2	13.4	Tier 1
	Small insectivorous bird "wagtail" < Yellow wagtail>		5.9	18.7	Tier 1
Early cereal shoots, autumn-winter BBCH 10-29	Large herbivorous bird "goose" <Pink-foot goose>		16.2	6.8	Tier 1
Cereals, BBCH 10 - 29	Small omnivorous bird "lark" <Woodlark>		10.9	10.1	Tier 1

Tier 1 long-term/reproductive toxicity exposure ratio for birds

Table 10.1.1.2- 2: Long-term/reproductive DDD and TER calculation for birds

Crop	Generic focal species	NOAEL [mg/kg bw/d]	DDD				DDD	TER_{LT}	Trigger
			Appl. rate [kg/ha]	SV_m	MAF_m	f_{twa}			
Flurtamone									
Bare soil	Small granivorous bird "finch" <Linnet>	7.3	0.125	11.4	1	0.53	0.755	9.7	5
	Small omnivorous bird "lark" <Woodlark>			8.2			0.543	13.4	
	Small insectivorous bird "wagtail" < Yellow wagtail>			5.9			0.391	18.7	
Cereals	Large herbivorous bird "goose" <Pink-foot goose>			16.2			1.073	6.8	
	Small omnivorous bird "lark" <Woodlark>			10.9			0.722	10.1	

All TER values are above the trigger of 5 for long-term exposure. Accordingly, safe use of the product in cereals can be concluded.

Long-term risk assessment for birds drinking contaminated water

An assessment of the risk potentially posed by consumption of contaminated drinking water is required.

Due to the incidental nature of occurrence of drinking water reservoirs on agricultural fields (as compared to the contamination of food items growing or dwelling on those fields), a separate assessment of this exposure route is considered appropriate at least on the first-tier level.

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 product is applied in cereals, no pools in leaf axils where an acute exposure possibly might occur are to be expected.
- Puddle scenario. Birds and mammals taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. This scenario is only relevant for acute and long-term exposure.

An "escape clause" recommended in the EFSA Guidance Document (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 5000 in the case of more sorptive substances (Koc ≥ 500 L/kg)."* [2].

Table 10.1.1.2- 3: Evaluation of potential concern for exposure of birds to drinking water (escape clause)

Compound	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
Flurtamone	257	125	7.3	17.12	≤ 50	No concern

This evaluation confirms that the risk for birds from drinking water that may contain residues from the use of the product in cereals is acceptable.

Effects of secondary poisoning on birds

Substances with a high bioaccumulation potential could theoretically bear a risk of secondary poisoning for birds if feeding on contaminated prey like fish or earthworms. For organic chemicals, a log P_{OW} > 3 is used to trigger an in-depth evaluation of the potential for bioaccumulation. The log P_{ow} of flurtamone is 2.8 by HPLC and 3.2 by the shake flask method. The metabolites, M04, M05, M08 and M07 all have log P_{ow} values less than 3.0.

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

Flurtamone is therefore considered for an assessment of secondary poisoning.

Table 10.1.1.2- 4: Log P_{OW} values of flurtamone and metabolites

Compound	Log P_{OW}	Reference
Flurtamone	**3.2**	M-161509-02-1
M04 TFMBA AE C518919 (RE-54488)	1.7 (pH 5) -0.25 (pH 7) -1.2 (pH 9)	M-449697-01-1
M05 TFA AE C502988 (MB 11712)	-2.5 (pH 5) -2.6 (pH 7) -2.8 (pH 9)	M-420136-01-1
M08 AE 2093305 (RPA 591120)	1.9 (pH 5) 1.9 (pH 7) 1.9 (pH 9)	M-449697-01-1
M07 AE 1083976 (RPA 203597)	1.20 (pH 5) -0.74 (pH 7) -1.70 (pH 9)	M-444938-01-1

Risk assessment for bioaccumulation and food chain behaviour for birds

The risk is considered acceptable, if the 'Long-term Toxicity Exposure Ratio' (TER_{LT}) value pass the trigger values of ≥ 5 for long-term exposure.
If the TER values are below the trigger values, a refined risk assessment based on more relevant and realistic conditions is performed for those particular areas.

Calculation of Toxicity Exposure Ratio (TER)

The calculation of the long-term Toxicity to Exposure Ratio (TER) depends on the selection of the suitable endpoint and is defined as follows:

Long-term risk: TER_{LT} = NO(A)EL [mg a.s./kg bw/d] / DDD_{LT}

Calculation of Daily Dietary Dose (DDD) for earthworm-eating birds

$$DDD_{earthworm} = PEC_{worm} \times FIR / bw$$

Residues in earthworms are calculated according to the following equation:

$$PEC_{worm} = PEC_{soil} \times BCF$$

The bioconcentration factor ($BCF = C_{worm}/C_{soil}$) is calculated according to the following equation:

$$BCF = (0.84 + 0.012\ K_{ow}) / f_{oc} \times K_{oc}$$

Where:

K_{OC} = Organic carbon adsorption coefficient
f_{OC} = Organic carbon content of soil (take 0.02 as a default value)

Calculation of Daily Dietary Dose (DDD) for fish-eating birds

$$DDD_{fish} = PEC_{fish} \times FIR / bw$$

Residues in earthworms are calculated according to the following equation:

$$PEC_{fish} = PEC_{sw} \times BCF_{fish}$$

Where:

BCF_{fish}
sw = surface water

The time window used for PEC_{sw} is 21 days.

Avian generic focal species for Tier 1 risk assessment

The following generic focal species have to be addressed in the Tier 1 risk assessment.

Table 10.1.1.2- 5: Avian generic focal species for the Tier 1 risk assessment of secondary poisoning

Generic avian indicator species	Body weight [g]	Example	FIR/bw
Earthworm eater	100	Blackbird	1.05
Fish eater	1000	Heron	0.159

Long-term DDD and TER calculation for earthworm-eating birds

Table 10.1.1.2- 6: Evaluation of risks to birds due to secondary poisoning via earthworms

Compound	Flurtamone	Origin of values
BCF_{worm} calculation:		
P_{OW}	1744	
K_{OC} [mL/g]	257	MCP, 9.1.2
f_{OC}	0.02	Default
BCF_{worm}	3.308	
PEC_{worm} calculation:		
PEC_{soil} (twa, 21 d) [mg/kg] [1]	0.154	MCP, 9.1.3
PEC_{worm} [mg/kg]	0.509	
DDD calculation:		
FIR/bw	1.05	Default
DDD [mg/kg bw/d]	0.536	
TER_{LT} calculation:		
NO(A)EL [mg/kg bw/d]	7.3	MCP, 10.1.1
TER_{LT}	13.6	
Trigger	5	EC 1107/2009
Refined risk assessment required?	no	

[1] Worst-case PEC_{soil} value resulting from 1 x 125 g/ha, 0% interception

The TER values are above the trigger of 5. Accordingly, the risk to earthworm-eating birds following the use of the product on cereals is acceptable.

Long-term DDD and TER calculation for fish-eating birds

Table 10.1.1.2- 7: Evaluation of risks to birds due to secondary poisoning via fish

Compound	Flurtamone	Origin of values
PEC_{fish} calculation		
BCF_{fish}	27	
PEC_{SW} (max) [mg/L] [1]	0.0141	MCP, 9.2.5
PEC_{fish} [mg/kg]	0.381	
DDD calculation:		
FIR/bw	0.159	Default
DDD [mg/kg bw/d]	0.061	
TER calculation:		
NO(A)EL [mg/kg bw/d]	7.3	MCP, 10.1.1
TER_{LT}	120	
Trigger	5	EC 1107/2009
Refined risk assessment required?	no	

[1] Worst-case max PEC_{sw} value resulting from 1 x 125 g/ha, in winter cereals, N-EU FOCUS Step 2

The TER value is above the trigger of 5. Accordingly, the risk to fish-eating birds following the use of the product in cereals is considered acceptable.

Study summaries for higher tier terrestrial vertebrate risk assessments

Report:	**KCP 10.1.1/01 [redacted].; 2014**
Title:	Statement on residue dissipation of flurtamone in treated foliage of cereal plants: kinetic evaluation
Document No.:	M-475193-01-1
Guidelines:	Not applicable
GLP	no

Objective:

This statement provides kinetic evaluations of the residues of flurtamone in green parts of monocotyledonous plants (wheat, barley and rye) that may represent food items for leaf-eating herbivorous birds or mammals.

Material and methods:

The residue decline data are available from regulatory plant residue studies. The determinations of the kinetic values followed the recommendations of FOCUS rules. These were aimed at deriving DT_{50} values for use as model input according to the FOCUS guidance document on degradation kinetics (FOCUS, 2006). The kinetic evaluations and the statistical calculations were conducted with KinGUI (v2.0) (Meyer, 2011) and data was subjected to a single-first-order (SFO) kinetic. The model fits were evaluated using a chi-square (χ^2) error statistic and visual inspection of residual plots. FOCUS Kinetics guidance (FOCUS, 2006) indicates that a min Chi^2 error value of <15% is acceptable for laboratory data. Higher min Chi^2 error values may be acceptable due to higher inherent variability of the data, but expert judgement must be applied based on the visual fit to the data.

Results

The single-first-order (SFO) half-lives for flurtamone residues derived in this evaluation are summarised as follows. All fitted DT_{50} values are evaluated as valid and visually acceptable, describing the the dissipation properties of flurtamone residues in wheat, barley and rye. Statistical evaluation of the results leads to the same conclusion.

Table **Summary of DT_{50} values for flurtamone residues in the cereal trials evaluated calculated with SFO**

Code	Trial		Location	DT_{50} (days)	Chi^2 (%)	t-test (-)	Visual
CE01	11-2094-01	DE	EU-N	3.9	19.9	0.09276	Acceptable
CE02	11-2094-02	UK	EU-N	1.8	21.2	0.02042	Good
CE03	11-2094-03	FR	EU-S	3.7	9.5	0.005736	Very good
CE04	11-2094-04	IT	EU-S	4.3	7.3	0.002932	Good
CE05	11-2095-01	DE	EU-N	3.9	4.1	0.000572	Very good
CE06	11-2095-02	NL	EU-N	3.5	6.0	0.00155	Good
CE07	11-2095-03	FR	EU-S	3.3	5.2	0.000844	Very good
CE08	11-2095-04	SP	EU-S	2.3	22.4	0.03160	Acceptable
CE09	24 95 04 01	DK	EU-N	1.7	4.7	0.000180	Very good
CE10	24 95 04 02	DK	EU-N	2.3	14.1	0.00366	Very good
CE11	24 95 06 01	DK	EU-N	3.6	9.1	3.89E-07	Very good
CE12	24 95 06 02	DK	EU-N	2.3	7.0	0.00190	Very good
CE13	24 95 05 01	DK	EU-N	3.4	5.4	0.000146	Very good
CE14	24 95 05 02	DK	EU-N	15.2	13.7	0.032403	Acceptable
	Geometric mean			**3.1**			

Conclusion
A geometric mean DT_{50} of 3.1 days was derived from residue decline studies with flurtamone on cereals.

Metabolites of flurtamone

The metabolism of flurtamone has been investigated in cereals and sunflower. Parent compound and some metabolites could be identified, however the residue quantities were very low. Therefore, metabolites were not considered for risk assessment for birds. Uptake from the soil of M05 TFA into rotated crops has been shown to occur. The potential dietary exposure of birds and mammals to the metabolite TFA has been addressed in a statement ([redacted], 2013, M-465860-01-1, KCP 10.1.1/02) presented below.

Report: **KCP 10.1.1/02 [redacted], L.; 2013**
Title: Residues of trifluoroacetic acid (TFA) in plants: risk assessment for birds and mammals
Document No.: M-465860-01-1
Guidelines: Not applicable
GLP No

Summary

In plant metabolism studies on wheat, lettuce and radish as rotational crops, only moderate M05 TFA residues were found. Highest concentrations occurred after pre-emergence application in the leafy parts of the plant (0.454 mg/kg in straw); the concentration in grain was lower (0.137 mg/kg). M05 TFA residues were even lower after post-emergence application and in rotational crops indicating that flurtamone degradation in soil and uptake into the plant is a minor pathway.

For M05 TFA a limited package of toxicological studies is available in mammalian species, but no studies have been performed in birds. It can be assumed that birds are not more susceptible than mammalian species so that the mammalian endpoints can be used for the bird risk assessment.

Assuming a M05 TFA concentration of 1 mg/kg in plant material, a risk assessment for birds and mammals is performed with the following mammalian endpoints: acute LD_{50} >2000 mg/kg bw (rats) and reproductive $NOAEL_{ecotox}$: 98 mg/kg bw/day (rats).

Table 10.1.1- 4: Toxicity exposure ratio (TER) for herbivorous birds and mammals feeding on plants containing M05 TFA (1 mg/kg)

Species	bw [g]	FIR/bw	DDD [mg/kg bw/day]	**TER to rat LD_{50}** (>2000 mg/kg bw)	**TER to long-term NOAEL** (98 mg/kg bw/day)
woodlark	28.5	2.26	2.26	>885	43.4
goose	2645	0.3	0.3	>6666	326.7
wood mouse	21.7	1.68	1.68	>1190	58.3
rabbit	1543	0.50	0.50	>4000	196.0
hare	3800	0.32	0.32	>6250	306.3

No acute or long-term/reproduction risk is discernible for herbivorous birds and mammals from the uptake of M05 TFA via residues in plant material. The TER values significantly exceed the trigger values of 10 for acute exposure and 5 for the long-term scenario.

CP 10.1.2 - Effects on terrestrial vertebrates other than birds

The summary of the toxicity profile of the active substances flurtamone and diflufenican to mammals is provided in the following tables.

Table 10.1.2- 1: Toxicity of flurtamone and M05 TFA to mammals

Test species	Study	Ecotoxicological endpoint		Reference
Flurtamone				
Rat	acute oral	LD_{50} > **5000**[1) 2)]	mg/kg bw	[redacted] 1989, M-160698-01-1
Rabbit	developmental toxicity	NOAEL = **20**[2)]	mg/kg bw/day	[redacted] 1989, M-160656-01-1
Rat	2-generation reproduction	NOAEL = 500 NOAEL = 25	ppm mg/kg a.s./bw/day	[redacted] 1992, M-203254-01-1
M05 TFA				
Rat	acute, oral	LD_{50} > **2000**	mg p.m./kg bw	[redacted] (2013) M-444479-01-1 KCA 5.8.1
Rat	28 days dietary	NOEL ♂ 1315 ♀ 1344 1329 [4)]	mg p.m./kg bw/d	[redacted] (2005) M-259106-01-1 KCA 5.8.1
Rat	90 days dietary	NOEL ♂ **98**[3)] ♀ 123 110 [4)]	mg p.m./kg bw/d	[redacted] (2007) M-283994-01-1 KCA 5.8.1

Bold values: Endpoint used for risk assessment
[1)] 10 rats per group; no mortality occurred during study
[2)] Endpoints listed in EFSA Review Report for the active substance Flurtamone (2003)
[3)] ecotoxicological relevant NOEL derived from administered dose of 1600 ppm (evaluated by [redacted] 2014, M-477154-01-1, KCA 8.1.2.2/01)
[4)] geometric mean of male and females

The potential dietary exposure of birds and mammals to the metabolite M05 TFA has been addressed in a statement ([redacted], 2013, M-465860-01-1, KCP 10.1.1/02). No acute or long-term/reproduction risk is discernible for herbivorous birds and mammals from the uptake of M05 TFA via residues in plant material. The TER values significantly exceed the trigger values for the acute and long-term/reproduction scenario.

Table 10.1.2- 2 Toxicity of mixing partner diflufenican to mammals

Test substance	Test species	EU agreed endpoints acc. to EFSA Scientific Report (2007) 122, 1-84	
Diflufenican	Rat acute, oral	NOLED[1]	> 5000 mg as/kg bw
	Rat reproduction	NO(A)EL	35.5 mg as/kg bw/d

[1)] NOLED = no observed lethal effect dose

Toxicity of the formulated product

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

Table 10.1.2- 3: Toxicity of the formulated product FLT +DFF SC 350 to mammals

Test species	Test design	Ecotoxicological endpoint	Reference
Rat	acute, oral	LD_{50} > 2000 mg/kg bw	[redacted]1092, M-461287-01-2

Selection of endpoints for risk assessment

The selection of mammalian endpoints for risk assessment follows the same principles as described in detail under point 10.1 for birds.

Risk Assessment for mammals

The risk assessment procedure for wild mammals follows the same principles as described in detail under point 10.1 for birds, i.e. EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009).

Mammalian indicator species for Tier 1 risk assessment

The intended use of the product is pre and post emergence (up to BBCH 29) in spring and winter cereals based on the proposed use pattern. The following generic focal species have to be addressed in the risk assessment.

Table 10.1.2- 4: Relevant mammalian generic species for risk assessment Tier 1 risk assessment

Crop	Growth stage (BBCH)	Generic focal species	Representative species	Shortcut value	
				For long-term RA based on RUD_m	For acute RA based on RUD_{90}
Bare soils	< 10	Small omnivorous mammal "mouse"	Wood mouse (*Apodemus sylvaticus*)	5.7	14.3
Cereals	10-19	Small insectivorous mammal "shrew"	Common shrew (*Sorex araneus*)	4.2	7.6
Cereals	≥ 20	Small insectivorous mammal "shrew"	Common shrew (*Sorex araneus*)	1.9	5.4
Cereals	Early (shoots)	Large herbivorous mammal "lagomorph"	Rabbit (*Oryctolagus cuniculus*)	22.3	42.1
Cereals	10-29	Small omnivorous mammal "mouse"	Wood mouse (*Apodemus sylvaticus*)	7.8	17.2

CP 10.1.2.1 - Acute oral toxicity to mammals

Summary of calculated acute TER values for mammals

Table 10.1.2.1- 1: Summary of acute TER values

Crop (BBCH)	Generic focal species	Active substance	SV_{90}	TER_A	Assessment level
Bare soil (< 10)	Small omnivorous mammal "mouse"	Flurtamone	14.3	2797	Tier 1
Cereals (10-19)	Small insectivorous mammal "shrew" <Common shrew>		7.6	5263	Tier 1
Cereals (≥ 20)			5.4	7407	Tier 1
Cereals (Early (shoots))	Large herbivorous mammal "lagomorph" <Rabbit>		42.1	950	Tier 1
Cereals (10-29)	Small omnivorous mammal "mouse" <Wood mouse>		17.2	2326	Tier 1

Tier 1 acute toxicity exposure ratio for mammals

Table 10.1.2.1- 2: Tier 1 acute DDD and TER calculation for mammals

Crop	Generic focal species	LD50 [mg/kg bw]	Appl. rate [kg/ha]	DDD SV_{90}	DDD MAF_{90}	DDD	TER_A	Trigger
Flurtamone								
Bare soil	Small omnivorous mammal "mouse"	5000	0.125	14.3	1	1.7875	2797	10
Cereals	Small insectivorous mammal "shrew" <Common shrew>			7.6		0.95	5263	
				5.4		0.675	7407	
	Large herbivorous mammal "lagomorph" <Rabbit>			42.1		5.2625	950	
	Small omnivorous mammal "mouse" <Wood mouse>			17.2		2.15	2326	

All TER values pass the trigger of 10 for acute exposure. Accordingly, an acceptable acute risk to mammals from the use of the product can be expected.

Acute risk assessment for mammals drinking contaminated water

For further details, reference is made to point 10.1.1.1 of this document. However, unlike for birds the scenario of pools formed in leaf axils is not relevant for mammals. Therefore the risk assessment for mammals is limited to the scenario of puddles formed on the ground after application.

The acute risk from water in puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil is covered by the long-term risk assessment under point 10.1.1.2 of this document.

CP 10.1.2.2 - Higher tier data on mammals

Summary of calculated long-term TER values

Table 10.1.2.2- 1:Summary of reproductive (long-term) TER values

Crop (BBCH)	Generic focal species	Active substance	SV_m	TER_{LT}	Assessment level
Bare soil (< 10)	Small omnivorous mammal "mouse"	Flurtamone	7.7	53	Tier 1
Cereals (10-19)	Small insectivorous mammal "shrew" <Common shrew>		4.2	72	Tier 1
Cereals (≥ 20)			1.9	159	Tier 1
Cereals (Early (shoots))	Large herbivorous mammal "lagomorph" <Rabbit>		22.3	14	Tier 1
Cereals (10-29)	Small omnivorous mammal "mouse" <Wood mouse>		7.8	39	Tier 1

Tier 1 long-term/reproductive toxicity exposure ratio for mammals

Table 10.1.2.2- 2: Tier 1 long-term/reproductive DDD and TER calculation for mammals

Crop	Generic focal species	NO(A)EL [mg/kg bw/d]	DDD Appl. rate [kg/ha]	SV_m	MAF_m	f_{twa}	DDD	TER_{LT}	Trigger
Flurtamone									
Bare Soil	Small omnivorous mammal "mouse"	20	0.125	5	1	0.53	0.378	53	5
Cereals	Small insectivorous mammal "shrew" <Common shrew>			4.2			0.278	72	
				1.9			0.126	159	
	Large herbivorous mammal "lagomorph" <Rabbit>			22.3			1.477	14	
	Small omnivorous mammal "mouse" <Wood mouse>			7.8			0.517	39	

All TER values are above the trigger of 5 for long-term exposure, indicating safe use of the product on cereals.

Long-term risk assessment for mammals drinking contaminated water

For further details, reference is made to Point 10.1.1.2.

Table 10.1.2.2- 3: Evaluation of potential concern for exposure via drinking water of mammals (escape clause)

Compound	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
Flurtamone	257	125	20	6.25	≤ 50	No concern

This evaluation confirms that the risk for mammals from drinking water that may contain residues from the use of the product is acceptable.

Effects of secondary poisoning to mammals

The risk assessment procedure for wild mammals follows the same principles as described in detail under Point 10.1.1.2 for birds).

Mammalian generic focal species for Tier 1 risk assessment

The following generic focal species have to be addressed in the Tier 1 risk assessment.

Table 10.1.2.2- 4: Mammalian generic focal species for the Tier 1 risk assessment of secondary poisoning

Generic focal species	Body weight [g]	Example	FIR/bw
Earthworm eater	10	Common shrew	1.28
Fish eater	3000	Otter	0.142

Long-term DDD and TER calculation for earthworm-eating mammals

Table 10.1.2.2- 5: Tier 1 long-term DDD and TER calculation for earthworm-eating mammals

Compound	Flurtamone	Origin of values
PEC_{worm} [mg/kg]	0.509	see 10.1.1.2
DDD calculation:		
FIR/bw	1.28	Default
DDD [mg/kg bw/d]	0.652	
TER calculation:		
NO(A)EL [mg/kg bw/d]	20.0	MCP 10.1.2
TER_{LT}	30.7	
Trigger	5	EC1107/2009
Refined risk assessment	no	

The TER values are above the trigger of 5. Accordingly the risk to earthworm-eating mammals from the use of the product in cereals is acceptable.

Long-term DDD and TER calculation for fish-eating mammals

Table 10.1.2.2- 6: Tier 1 long-term DDD and TER calculation for fish-eating mammals

Compound	Flurtamone	Origin of values
PEC_{fish} [mg/kg]	0.381	see 10.1.1.2
DDD calculation:		
FIR/bw	0.142	Default
DDD [mg/kg bw/d]	0.054	
TER calculation:		
NO(A)EL [mg/kg bw/d]	20.0	MCP 10.1.2
TER_{LT}	370	
Trigger	5	EC1107/2009
Refined risk assessment	no	

The TER values are above the trigger of 5. Accordingly the risk to fish-eating mammals from the use of the product in cereals is acceptable.

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

No studies were conducted on reptiles or amphibians with the formulation.

CP 10.2 - Effects on aquatic organisms

The summary of the toxicity profile of the active substances flurtamone and diflufenican to aquatic organisms is provided in the following tables. For diflufenican reference is made to the EU agreed endpoints according to the EFSA Scientific Report (2007) 122.

Toxicity of the formulation

Table 10.2- 1: Acute toxicity of the formulation to aquatic organisms

Test organism	Test system	Test duration	Endpoint [mg prod/L]		Reference
FLT + DFF SC 350					
Oncorhynchus mykiss (rainbow trout)	acute, static, renewal	96 h	LC_{50} NOEC	**56** 18	[redacted] et al., 1994; M-162501-01-1 KCP 10.2.1/01
Daphnia magna (water flea)	acute, static	48 h	EC_{50} NOEC	**28** 10	[redacted] et al., 1995; M-170697-01-1 KCP 10.2.1/02
Desmodesmus subspicatus (green alga)	acute, static	96 h	48h-E_rC_{50} 96h-E_bC_{50} NOEC	0.016 **0.018** 0.010	[redacted] et al., 1994; M-162497-01-1 KCP 10.2.1/03
Lemna gibba (duck weed)	acute, static, renewal	7 d	E_rC_{50}	**0.0398**	[redacted] et al., 2005; M-247297-01-1 KCP 10.2.1/04

Bold figures are used for risk assessments
[1] for diflufenican, only the E_bC_{50} for algae is available

Toxicity of flurtamone to aquatic organisms

The acute and chronic toxicity of technical flurtamone and its metabolites on a range of aquatic species in accordance with established test guidelines has been extensively tested and summarized in the table below.

Table 10.2- 2: Toxicity of flurtamone to aquatic organisms

Test species	Test system	Duration of exposure	Toxicity [mg/L]	Reference
Pimephales promelas (Fathead minnow)	acute, semi-static	96 h	LC_{50} > 6.64 * NOEC 6.64 *	[redacted], 2012a; M-424825-01-1 KCA 8.2.1/01
	ELS, flow-through	35 d	NOEC 0.188	[redacted], 2012b; M-443501-01-1 KCA 8.2.2.1/01
Oncorhynchus mykiss (Rainbow trout)	acute, static	96 h	LC_{50} 7.0	[redacted], 1989; M-160659-01-1
	chronic, juvenile growth, flow through	28 d	NOEC 0.63	[redacted] et al., 1994; M-162489-01-1
Lepomis macrochirus (Bluegill sunfish)	acute, static	96 h	LC_{50} 11	[redacted], 1989; M-160664-01-1
	bioaccumulation	28 d	BCF = 27	[redacted], 1994 M-162223-01-1
Xenopus laevis (amphibian)	acute, static	48 h	LC_{50} > 20	[redacted] & [redacted], 2013 M-475146-01-1 KCA 8.2.8/01
Daphnia magna (Waterflea)	acute, static	48 h	EC_{50} 13.0	[redacted], 1989; M-160662-01-1
	acute, static	48 h	EC_{50} 5.1	[redacted], 2011 M-420504-01-1 KCA 8.2.4.1/01
	chronic, flow through	21 d	NOEC 0.071	[redacted] & [redacted], 1992; M-203224-01-1
Chironomus riparius (Chironomid)	chronic, static, spiked water	22 d	NOEC 0.1	[redacted], 1997; M-247873-01-1
Pseudokirchneriella subcapitata (Green algae)	chronic (growth inhibition test), static	96 h	E_bC_{50} 0.020	[redacted] et al, 1992; M-203220-01-1
		72 h	recalculation based on new OECD 201: E_rC_{50} 0.038	[redacted], 2005; M-247782-01-1 KCA 8.2.6.1/01
		72 h	E_rC_{50} 0.053 NOE_rC 0.010	[redacted], 2013; M-473178-01-1 KCA 8.2.6.1/02
	chronic, flow-through, variable exposure	one pulse at 0.04 mg/L day 7: one pulse at 0.02 mg/L day 14: one pulse at 0.035 mg/L	$EC_{50(population)}$ >0.04	[redacted], 2014; M-474520-01-1 KCA 8.2.6.1/03
Navicula pelliculosa (Diatom)	chronic (growth inhibition test), static	72 h	E_bC_{50} 0.011 E_rC_{50} 0.024	[redacted], 1997; M-242493-01-1
Lemna gibba (Duck weed)	chronic (growth inhibition test), static renewal	14 d	E_rC_{50} 0.0140 (frond density) E_bC_{50} 0.0099	[redacted], 1997; M-244591-01-1
			recalculation based on new OECD 221:	[redacted], 2005; M-258189-01-1

Test species	Test system	Duration of exposure	Toxicity [mg/L]	Reference
			E_rC_{50} 0.0445 (frond no.) E_rC_{50} 0.0429 (dry weight)	KCA 8.2.7/01
	chronic, static	7 d	E_rC_{50} 0.0198 (frond number) E_rC_{50} 0.0411 (frond area) NOE_rC 0.000916	[redacted], 2013 M-470528-01-1 KCA 8.2.7/02
Myriophyllum spicatum (higher aquatic plant)	acute,static	14 d	E_yC_{50} > 0.123 mm NOEC 0.0071 mm LOEC 0.015 mm	[redacted] & [redacted], 2012 M-461579-01-1 KCA 8.2.7/04
Mesocosm Lentic freshwater community	chronic, static	68 d	No Observed Ecologically Adverse Effect Concentration NOEAEC 0.003	[redacted], 2010 M-449526-01-1 KCA 8.2.7/05
Outdoor potted plant *Potamogeton crispus* *Elodea canadensis*	chronic static	42 d	*Potamogeton*: 42-day-NOEC: 0.003 *Elodea*: 42-day-NOEC: 0.001	[redacted] & [redacted], 2013 M-469643-01-1 KCA 8.2.7/06
Lemna gibba (Duck weed)	peak exposure	one 48h peak and two 48h peaks; total test duration 14 days	day 0-7 **after single peak**: E_rC_{50} 0.124 (frond number) E_rC_{50} 0.0618 (frond area) NOE_rC <0.01 day7-14 **after two peaks at 7-day-intervall**: E_rC_{50} 0.0719 (frond number) E_rC_{50} 0.0608 (frond area) NOE_rC <0.01	[redacted], 2014 M-475376-01-1 KCA 8.2.7/03
Myriophyllum spicatum *Elodea canadensis*	peak exposure	one 48h peak and two 48h peaks; total test duration 56 days	***Elodea***: **one peak:** 56-day-EC50 >0.036 14-day-$NOEC_{population}$ 0.004 56-day-$NOEC_{population}$ 0.036 **two peaks:** 56-day-EC50 >0.036	[redacted], 2013 M-470995-01-1 KCA 8.2.7/07

Test species	Test system	Duration of exposure	Toxicity [mg/L]	Reference
			$NOEC_{population}$ 0.004 ***Myriophyllum***: 56-day-$NOEC_{population}$ > 0.036	

* geometric mean of measured concentrations
mm = mean measured

Metabolites of flurtamone

The two soil metabolites M04 TFMBA have the potential to reach the aquatic environment by run-off and drainage. The degradation product AE 1883976 (M07) was formed in aqueous medium by photolytic degradation of flurtamone and was found at a concentration of 33.5 %. AE 2093305 (M08) was found at maximum concentrations of 7.8 % in water and 3.6 % sediment (total 10.7 %).
Therefore, a risk assessment for aquatic organisms with these metabolites was conducted.

Table 10.2- 3: Toxicity of flurtamone metabolites to aquatic organisms

Test species	Test system	Duration of exposure	Toxicity [mg/L]	Reference
M04 TFMBA (AE C518919)				
Oncorhynchus mykiss (Rainbow trout)	acute, static	96 h	LC_{50} > 76.3	[redacted], 1999; M-243657-01-1
Daphnia magna (Water flea)	acute, static	48 h	EC_{50} > 95.0	[redacted], 1999; M-247910-01-1
Pseudokirchneriella subcapitata (Green alga)	chronic (growth inhibition test), static	72 h	$E_{b/r}C_{50}$ > 104.8	[redacted], 1999; M-243659-01-1
Lemna gibba (Duck weed)	chronic, static	7 d	E_rC_{50} 9.2	[redacted], 2005; M-253816-01-1 KCA 8.2.7/08
M05 TFA (AE C502988)				
Brachydanio rerio (Zebra fish)	acute, static	96 h	LC_{50} > 1200	[redacted] et al., 1992; M-247889-01-1 KCA 8.2.1/02
Brachydanio rerio (Zebra fish)	ELS	144 h	LC_{50} 3000 EC_{50} 700 NOEC 3000 (heart rate) NOEC 300 (hatching time)	Ulhaq et al. 2013; M-462660-01-1 KCA 8.2.2.1/02
Daphnia magna (Water flea)	acute, static	48 h	EC_{50} > 1200	[redacted] et al., 1992; M-247890-01-1 KCA 8.2.4.1/03
Pseudokirchneriella subcapitata (Green alga)	chronic (growth inhibition test), static	72 h	E_rC_{50} 160 E_bC_{50} 4.8	[redacted] et al., 1992; M-247820-01-1
Pseudokirchneriella subcapitata (Green alga)	chronic (growth inhibition test), static	72 h	E_rC_{50} > 1.2 [1]	[redacted], 1993 M-247818-02-1 KCA 8.2.6.1/04
Green algae (various species)	chronic (growth inhibition test), static	72 h	E_rC_{50} >112 to > 2400 [1]	[redacted], 1996 M-247822-01-1 KCA 8.2.6.2/01
Desmodesmus subspicatus (green algae)	chronic (growth inhibition test), static	72 h	E_rC_{50} 120 [1]	[redacted] et al, 1995 M-247825-01-1 KCA 8.2.6.1/05
Lemna gibba (Duck weed)	chronic, static	7 d	$EC_{50, \text{frond increase}}$ 1100	[redacted] et al., 1993; M-247900-01-1
Lemna gibba *Myriophyllum spicatum* *Myriophyllum sibiricum*	chronic	7 d 14 d 14 d	EC_{50} 618.3 (wet mass) EC_{50} 312.9 (wet mass) EC_{50} 357 (wet mass)	Hanson & Solomon, 2004 M-455787-01-1 KCA 8.2.7/10
M07 (AE 1083976)				
Cyprinus carpio (Common carp)	acute, static (screening)	96 h	LC_{50} ≥ 36	[redacted], 1997 M-242462-01-1 KCA 8.2.1/03
Daphnia magna (Water flea)	acute, static (screening)	48 h	EC_{50} > 36	[redacted], 1997 M-242461-01-1 KCA 8.2.4.1/02

Pseudokirchneriella subcapitata (Green alga)	chronic (growth inhibition test), static (screening)	72 h	EC_{50} > 0.1	[redacted], 1997 M-242463-01-1 KCA 8.2.6.1/06
Pseudokirchneriella subcapitata (Green algae)	chronic (growth inhibition), static	72 h	ErC_{50} > 100 NOEC 100	[redacted], 2005, M-255213-01-1 KCA 8.2.6.1/07
Lemna gibba (Duck weed)	chronic, static	7 d	E_rC_{50} > 100	[redacted], 2005, M-255205-01-1 KCA 8.2.7/11
M08 (AE 2093305)				
Pseudokirchneriella subcapitata (Green algae)	chronic (growth inhibition test), static	72 h	E_rC_{50} 0.306 NOE$_r$C 0.0307	[redacted], 2013, M-470662-01-1 KCA 8.2.6.1/08
Lemna gibba (Duck weed)	chronic, static	7 d	E_rC_{50} >0.38	[redacted], 2005; M-255526-01-1 KCA 8.2.7/12
Lemna gibba (Duck weed)	chronic, static	7 d	E_rC_{50} 0.22 NOE$_r$C 0.0763	[redacted], 2013 M-470493-01-1 KCA 8.2.7/13

[1] test with TFA Na-salt

Table 10.2- 4: Toxicity of mixing partner diflufenican and its metabolites to aquatic organisms

Test substance	Test species	EU agreed endpoints acc. to EFSA Scientific Report (2007) 122, 1-84	
Diflufenican	Fish, acute *Cyprinus carpio*	LC_{50}	> 0.0985 mg as/L
	Fish, chronic *Pimephales promelas*	NOEC	0.015 mg as/L
	Invertebrate, acute *Daphnia magna*	EC_{50}	> 0.240 mg as/L
	Invertebrate, chronic *Daphnia magna*	NOEC	0.052 mg as/L
	Sediment dweller, chronic *Chironomus riparius* (spiked water)	NOEC	0.100 mg as/L
	Sediment dweller, chronic *Chironomus riparius* (spiked sediment)	NOEC	2.0 mg as/kg
	Algae *Desmodesmus subspicatus*	EC_{50}	0.00025 mg as/L
	Algae *Desmodesmus subspicatus (with recovery)*	Maximum concentration from which recovery is possible[1] overall NOEC[3]	0.0042 mg as/L 0.0001 mg as/L
	Aquatic plant *Lemna gibba*	E_rC_{50}	0.039 mg as/L
AE B107137	Fish, acute *Oncorhynchus mykiss*	LC_{50}	> 17.3 mg/L [2)]
	Invertebrate, acute *Daphnia magna*	EC_{50}	> 20.4* mg/L [2)]
	Algae *Desmodesmus subspicatus*	EC_{50}	> 20.4* mg/L [2)]
AE 0542291	Invertebrate, acute	EC_{50}	> 10 mg/L [2)]

Test substance	Test species	EU agreed endpoints acc. to EFSA Scientific Report (2007) 122, 1-84	
	Daphnia magna		
	Algae *Desmodesmus subspicatus*	EC_{50}	36 mg/L

[1)] *EFSA Scientific Report* (2007) 122, 1-84: "In order to cover effects on less sensitive but slower reproducing algal species the safety factor of 10 was maintained in the risk assessment. The exposure pattern of the FOCUS scenarios were analysed and the risk was considered acceptable provided that the peak exposure is below 0.47 µg diflufenican/L and that this exposure does not last longer than 3 days. In order to cover the overall NOEC of 0.1 µg diflufenican/L no other peak exposure should exceed the NOEC of 0.1 µg diflufenican/L.
[2)] above the limit of aqueous solubility
*above the limit of aqueous solubility

Selection of algae and macrophyte endpoints for risk assessment

According to the new guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters (EFSA 2013[1], p. 80ff.), the preferred endpoint to be used for macrophytes and algae risk assessment should be based on growth rate. Thus, the toxicity-exposure-ratios in the risk assessment for algae and macrophytes are calculated based on E_rC_{50}-values.

Risk assessment for flurtamone

Algae

The algae risk assessment is based on the lowest available **E_rC_{50}** for the freshwater diatom *Navicula pelliculosa* of **24 µg a.s./L**, resulting in an Regulatory Acceptable Concentration (RAC) of 2.4 µg a.s./L. The growth related endpoint is used as it is the most suitable value for risk assessments. The use of growth rates instead of biomass related endpoints represents the current state of the art. This is demonstrated by the already published new aquatic guidance document (Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters, August 5, 2013), but not yet noted by SCFCAH, where it is stated that risk assessments should be based on growth rates where available.

In addition to the existing standard algae studies a mesocosm study exists ([redacted] et al. 2010, M-389526-01-1, KCA 8.2.7.05) which delivers as well information on phytoplankton. The phytoplankton results observed within the mesocosm study did not reveal any consistent treatment related effect up to 100 µg/L. For some species an increase in abundance was observed. The overall NOEC covering all phytoplankton species was 3 µg a.s./L. The corresponding LOEC in this study was 10 µg/L. In most cases where a difference to the control was statistically observed only an increase in abundance was observed at the LOEC which can be interpreted as an indirect effect due to direct effects on macropyhtes. At concentrations where an effect on macrophytes occurs this has an impact on the related nutritional situation in the water body. More nutrients result in more algae.

Only for the Pseudoanabaenaceae (Cynophyte, Oscillatoriales) and for Pennales a significant lower abundance was observed compared to the controls. In both cases the observed idfferences were minor

[1] 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

and it is questionable whether they really are flurtamone related. For both groups there is no clear treatment related effect up to 100 µg/L.

Within the mesocosm study flurtamone dissipated slowly. At the end of the study (day 68) 5 % of the applied test item were still detectable. The dissipation half-life of flurtamone within the mesocosm study was about 14 days.

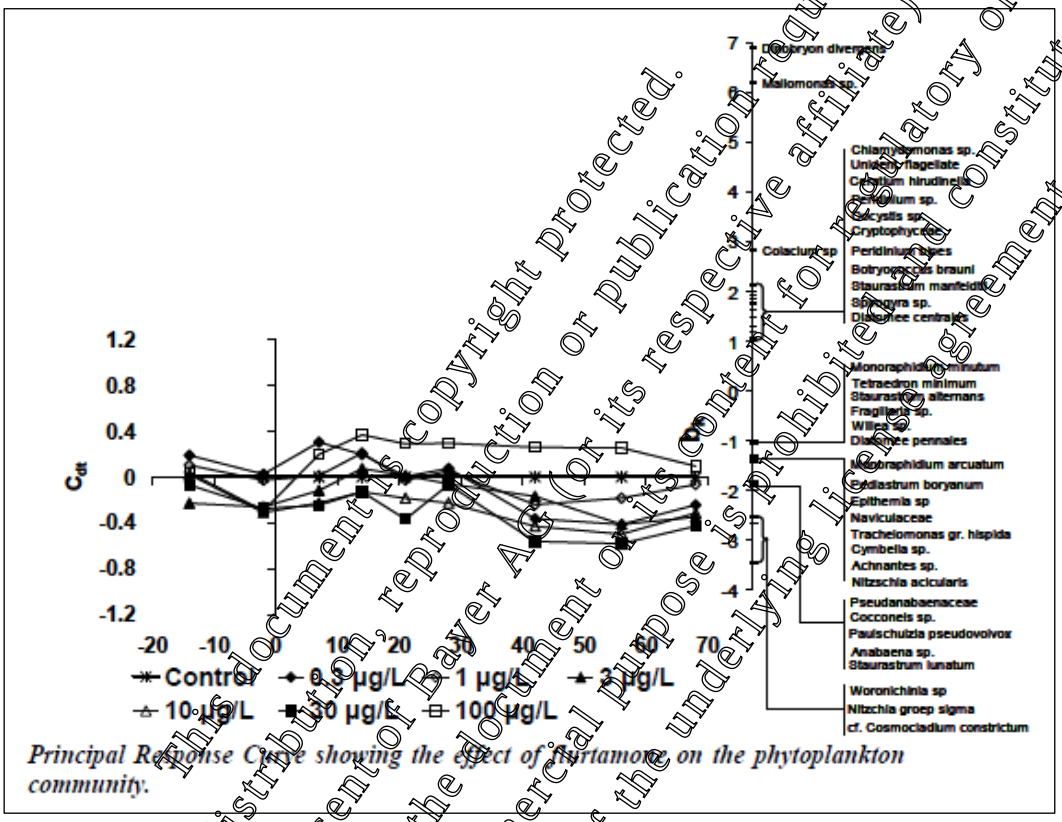


Figure 10.2- 1: Principle response curve for the effect of flurtamone on the phytoplankton community (from mesocosm study [redacted] et al, 2010, M-389526-01-1)

The results of the mesocosm study are well in line and support the use of the regulatory acceptable concentration **(RAC)** of **2.4 µg a.s./L** found for *Navicula pelliculosa*. No effects on phytoplankton were detected at that concentration range.

Macrophyte-endpoints

Studies where macrophytes received a long-term constant exposure were conducted in the laboratory with *Lemna gibba* and *Myriophyllum spicatum*. In addition, outdoor studies were conducted with *Elodea canadensis* and *Potamogeton crispus*. Additionally, within the mesocosm study ([redacted] 2010; M-389526-01-1) another four species (*Salvinia natans, Potamogeon natans, Sagitaria sagittifolia* and *Eleocharis palustris*) were studied. In total, effect data on eight macrophyte species are available for Flurtamone.

The comparison of the results from these studies allows the identification of the **most sensitive species**. EC_{50}-figures were obtained from the laboratory studies only and revealed that *Lemna gibba* is clearly more sensitive than *Myriophyllum spicatum*. From the outdoor study 42-day-NOECs of 1.0 and

3.0 µg/L were obtained for *Elodea canadensis* and *Potamogeton crispus*, respectively. The NOEC of 1.0 µg/L for *Elodea* is very close to the NOEC of 0.916 µg/L obtained from the standard *Lemna*-study, indicating that *Lemna gibba* and *Elodea canadensis* are of almost equal sensitivity. Moreover, it should be emphasized that the No Observed Ecologically Adverse Effect Concentration (NOEAEC) of 3.0 µg/L, as derived from the mesocosm study ([redacted] & [redacted], 2013; M-469643-01-1) is in line with these results, although the NOEAEC with not be used in course of a refined risk assessment.

From this comparison it can be concluded, that …

1. *Lemna gibba* represents a species being highly sensitive to flurtamone.
2. the endpoints obtained from the 7-day *Lemna* study are applicable for a tier-1 risk assessment.

The EU previously agreed endpoint of 9.9 µg a.s./L derived from the study by [redacted] (1997; M-244591-01-1) has to be replaced by **14.1 µg a.s./L** from the recent study conducted by [redacted] (2013; M-470528-01-1) for the following reasons:

1. The former study has not been conducted according to recent guidelines. Frond number (called density in the report) and frond dry weight was determined, but endpoints were derived from numerical comparisons with the control. The study duration was 14 days. The 7-day endpoint is the data requirement.
2. The recent aquatic guidance document (EFSA 2013[3]) recommends the use of endpoints based on growth rates. The endpoints presented in the new *Lemna* study are based on growth rates and therefore the study is suitable for risk assessment. The recalculation of frond numbers and dry weight figures from the old study resulted in 7-day E_rC_{50}-figures of 44.5 and 42.9 µg a.s./L for frond number and frond dry weight, respectively ([redacted] 2005; M-258189-01-1). However, the new and lower figure of 14.1 µg a.s./L will be used for tier-1 risk assessments.

In order to address short-term peak exposures in streams in risk assessments (see below) the effects of one or two 48-h-peaks of flurtamone to macrophytes were observed in **peak-exposure studies**. Such studies were conducted in the laboratory with *Lemna gibba* and in outdoor ponds with *Elodea canadensis* and *Myriophyllum spicatum*. While the *Lemna*-peak study was conducted with five concentrations ranging from 10 to 160 µg/L, the macrophytes in the ponds were treated with peaks of 4, 12 and 36 µg/L. Consequently, NOEC-figures derived from the results of these studies are not directly comparable. The summary table of the outdoor peak study shows figures with >50% decrease only after 14 and 28 days and only for *Elodea* exposed to two peaks. At study termination after 56 days no % decrease above 50% was observed. For *Elodea* and *Myriophyllum* a **peak EC_{50} > 36 µg/L** can be derived. This endpoint covers the peak-E_rC_{50}-figures obtained for *Lemna gibba*, and therefore is suitable for risk assessment.

Toxicity exposure ratios

Aquatic organisms may be exposed to a plant protection product to some extent by spray drift, run-off or drainage from treated fields. The provided studies and data permit a risk assessment following exposure to the product under practical conditions.

[3] 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.

Predicted Environmental Concentrations in surface water bodies

Predicted environmental concentrations for the active substances and relevant metabolites were calculated in surface water (PEC_{SW}) and in sediment (PEC_{sed}) according to FOCUS surface water scenarios as described in detail in CP Point 9.2.5.

Concentrations in groundwater are also considered, as groundwater might become surface water, leading to exposure of aquatic organisms. However, the PEC values for flurtamone and its metabolites are <0.1 µg/L in groundwater for all relevant FOCUS scenarios and application rates(for details see Point 9.2.4.1), except for M05 TFA where values up to 7 µg/L may occur. Given that dilution will occur it is considered that the PECsw values will cover the risk assessment for the PECgw values for the metabolite M05 TFA by dividing by 10 as recommended in the current aquatic guidance document, thus 0.7 µg/L is covered by the PECsw values.

The relevant PECsw values considered for TER calculations are summarised in the tables below.

Table 10.2- 5: Maximum aquatic PEC values of flurtamone and metabolites resulting from FOCUS Step 2 calculations, following application in winter and spring cereals

	PECsw [µg/L] at 1 x 125 g a.s./ha			
	Step 2 N-EU		Step 2 S-EU	
Compound	Winter cereals	Spring cereals	Winter cereals	Spring cereals
Flurtamone	**14.10**	6.18	11.46	11.46
TFMBA (M04)	**2.23**	0.90	1.79	1.79
TFA (M05)	**4.18**	1.67	3.35	3.35
AE 1083976 (M07)	**0.36**	0.36	0.36	0.36
AE 2093305 (M08)	**0.10**	0.10	0.10	0.10

Bold values used for risk assessment.

Table 10.2- 6: Maximum and time weighted average (TWA_{7d}) aquatic PEC values of flurtamone resulting from FOCUS Step 3 calculations, following application in winter and spring cereals

Step 3		Flurtamone 1 x 125 g/ha		
		PECsw,max [µg/L]		
FOCUS scenario	Mitigation	Winter cereals autumn application	Winter cereals spring application	Spring cereals
D1 (ditch)	-	2.414	0.860	0.857
D1 (stream)	-	1.507	0.712	0.693
D2 (ditch)	-	2.169	0.807	-
D2 (stream)	-	1.356	0.717	-
D3 (ditch)	-	0.789	0.792	0.791
D4 (pond)	-	0.274	0.028	0.028
D4 (stream)	-	0.685	0.628	0.616
D5 (pond)	-	0.432	0.028	0.028
D5 (stream)	-	0.739	0.625	0.612
D6 (ditch)	-	2.448	0.792	-
R1 (pond)	-	0.070	0.064	-
R1 (stream)	-	2.645	1.843	-
R3 (stream)	-	3.408	2.368	-
R4 (stream)	-	1.277	0.522	0.521
		PECsw,7 d-twa [µg/L]		
D1 (ditch)	-	2.354	-	-
D1 (stream)	-	1.447	-	-
D2 (ditch)	-	1.058	-	-
D6 (ditch)	-	1.138	-	-

Risk assessment

The risk assessment is based on

- Guidance Document on Aquatic Ecotoxicology, SANCO/3268/2001, rev 4 final, 17 October 2002.
- new Guidance Document on Aquatic Ecotoxicology[4], (EFSA 2013).

Toxicity exposure ratios (TER values) are calculated based on the most sensitive species and worst-case PEC_{SW} values.
The TER-values have been calculated based on the following equations:

$TER_A = LC_{50}$ or EC_{50} / $PEC_{SW,max}$
$TER_{LT} = NOEC$ or E_rC_{50} / $PEC_{SW,max\ or\ twa}$

The risk is considered acceptable if the TER_A values are ≥ 100, and the TER_{LT} values ≥ 10.

[4] 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

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

Table 10.2.1- 1: TER_A calculations for aquatic organisms Fish and Daphnia exposed to flurtamone and metabolites following application in winter and spring cereals (FOCUS Step 2)

Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_A	Trigger
Winter and spring cereals						
Flurtamone	*P. promelas*	LC_{50}	6640	14.10	471	100
	D. magna	EC_{50}	25 100	14.10	1780	
TFMBA (M04)	*O. mykiss*	LC_{50}	>76300	2.23	>34215	
	D. magna	EC_{50}	95000	2.23	>42601	
TFA (M05)	*B. rerio*	LC_{50}	>1200000	4.18	>287081	
	D. magna	EC_{50}	>1200000	4.18	>287081	
AE 1083976 (M07)	*C. carpio*	LC_{50}	> 36000	0.36	≥100000	
	D. magna	EC_{50}	>36000	0.36	>100000	

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

Table 10.2.2- 1: TER_{LT} calculations for aquatic organisms exposed to flurtamone and metabolites following application in winter and spring cereals (FOCUS Step 2)

Compound	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	TER_{LT}	Trigger
Winter and spring cereals						
Flurtamone	*P. promelas*	NOEC	188	14.10	13.3	10
	D. magna	NOEC	71	14.10	**5.0**	
	C. riparius (spiked water)	NOEC	100	14.10	**7.1**	
	N. pellicuosa	E_rC_{50}	24	14.10	**1.7**	
	L. gibba	E_rC_{50}	14.1	14.10	**1.0**	
	M. spicatum	E_yC_{50}	> 123	14.10	**>8.7**	
TFMBA (M04)	*P. subcapitata*	E_rC_{50}	>104800	2.23	>46996	
	L. gibba	E_rC_{50}	9200	2.23	4126	
TFA (M05)	*B. rerio*	NOEC	300 000	4.18	71 770	
	P. subcapitata	E_rC_{50}	>1200	4.18	>287	
	L. gibba	EC_{50}	1100000	4.18	263158	
	M. spicatum	EC_{50}	312900	4.18	74856	
AE 1083976 (M07)	*P. subcapitata*	E_rC_{50}	>100	0.36	>278	
	L. gibba	E_rC_{50}	>100000	0.36	>277778	
AE 2093305 (M08)	*P. subcapitata*	E_rC_{50}	306	0.10	3060	
	L. gibba	E_rC_{50}	722	0.10	7220	

Table 10.2.2- 2: TER_{LT} calculations for aquatic organisms exposed to flurtamone following application in winter and spring cereals (FOCUS Step 3)

Crop	Species	Endpoint [µg/L]		$PEC_{sw,max}$ [µg/L]	Scenario	TER_{LT}	Trigger
Flurtamone							
Winter and spring cereals	*D. magna*	NOEC	71	3.408	R3 (stream)	21	10
	C. riparius (spiked water)	NOEC	100	3.408	R3 (stream)	29	
	M. spicatum	E_yC_{50}	> 123	3.408	R3 (stream)	36	
Winter cereals (autumn application)	*N. pelliculosa*	E_rC_{50}	24	3.414	D1 (ditch)	**9.9**	10
				1.507	D1 (stream)	15.9	
				2.169	D2 (ditch)	11.1	
				1.356	D2 (stream)	17.7	
				0.789	D3 (ditch)	30.4	
				0.274	D4 (pond)	87.6	
				0.685	D4 (stream)	35.0	
				0.432	D5 (pond)	55.6	
				0.739	D5 (stream)	32.5	
				2.448	D6 (ditch)	**9.8**	
				0.070	R1 (pond)	342.9	
				2.645	R1 (stream)	**9.1**	
				3.408	R3 (stream)	**7.0**	
				1.277	R4 (stream)	18.8	
Winter cereals (spring application)	*N. pelliculosa*	E_rC_{50}	24	0.860	D1 (ditch)	27.9	10
				0.712	D1 (stream)	33.7	
				0.807	D2 (ditch)	29.7	
				0.717	D2 (stream)	33.5	
				0.792	D3 (ditch)	30.3	
				0.028	D4 (pond)	857.1	
				0.628	D4 (stream)	38.2	
				0.028	D5 (pond)	857.1	
				0.623	D5 (stream)	38.5	
				0.792	D6 (ditch)	30.3	
				0.064	R1 (pond)	375.0	
				1.843	R1 (stream)	13.0	
				2.368	R3 (stream)	10.1	
				0.522	R4 (stream)	46.0	
Spring cereals	*N. pelliculosa*	E_rC_{50}	24	0.857	D1 (ditch)	28.0	10
				0.693	D1 (stream)	34.6	
				0.791	D3 (ditch)	30.3	
				0.028	D4 (pond)	857.1	
				0.616	D4 (stream)	39.0	
				0.028	D5 (pond)	857.1	
				0.612	D5 (stream)	39.2	
				0.521	R4 (stream)	46.1	

Winter cereals (autumn application)	*L. gibba*	E_rC_{50}	14.1	2.414	D1 (ditch)	**5.84**	10
				1.507	D1 (stream)	**9.36**	
				2.169	D2 (ditch)	**6.50**	
				1.356	D2 (stream)	10.40	
				0.789	D3 (ditch)	17.87	
				0.274	D4 (pond)	51.46	
				0.685	D4 (stream)	20.58	
				0.492	D5 (pond)	32.64	
				0.739	D5 (stream)	19.08	
				2.448	D6 (ditch)	**5.76**	
				0.970	R1 (pond)	204.43	
				2.645	R1 (stream)	**4.33**	
				3.408	R3 (stream)	**4.14**	
				1.277	R4 (stream)	11.04	
Winter cereals (spring application)	*L. gibba*	E_rC_{50}	14.1	0.860	D1 (ditch)	16.40	10
				1.712	D1 (stream)	9.80	
				0.807	D2 (ditch)	17.47	
				0.717	D2 (stream)	19.67	
				0.792	D3 (ditch)	17.80	
				0.028	D4 (pond)	503.57	
				0.628	D4 (stream)	22.45	
				0.028	D5 (pond)	503.57	
				0.623	D5 (stream)	22.63	
				0.792	D6 (ditch)	17.80	
				0.064	R1 (pond)	220.31	
				1.843	R1 (stream)	**7.65**	
				2.368	R3 (stream)	**5.95**	
				0.522	R4 (stream)	27.01	
Spring cereals	*L. gibba*	E_rC_{50}	14.1	0.857	D1 (ditch)	16.45	10
				0.693	D1 (stream)	20.35	
				0.791	D3 (ditch)	17.83	
				0.028	D4 (pond)	503.57	
				0.616	D4 (stream)	22.89	
				0.028	D5 (pond)	503.57	
				0.612	D5 (stream)	23.04	
				0.521	R4 (stream)	27.06	

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

For the application in spring cereals all TER_{LT} values at FOCUS Step 3 meet the trigger of 10. As regards to algae and *Lemna* some scenarios do not pass the trigger for application in winter cereals (autumn and spring).

Refinement for algae and aquatic macrophytes

Algae

Based on the E_rC_{50} of 24 µg a.s./L, the TER of 10 is not passed in FOCUS Step 3 for the four scenarios D1 (ditch), D6 (ditch), R1(stream) and R3 (stream). The exposure patterns of the four scenarios are presented in the following figures:

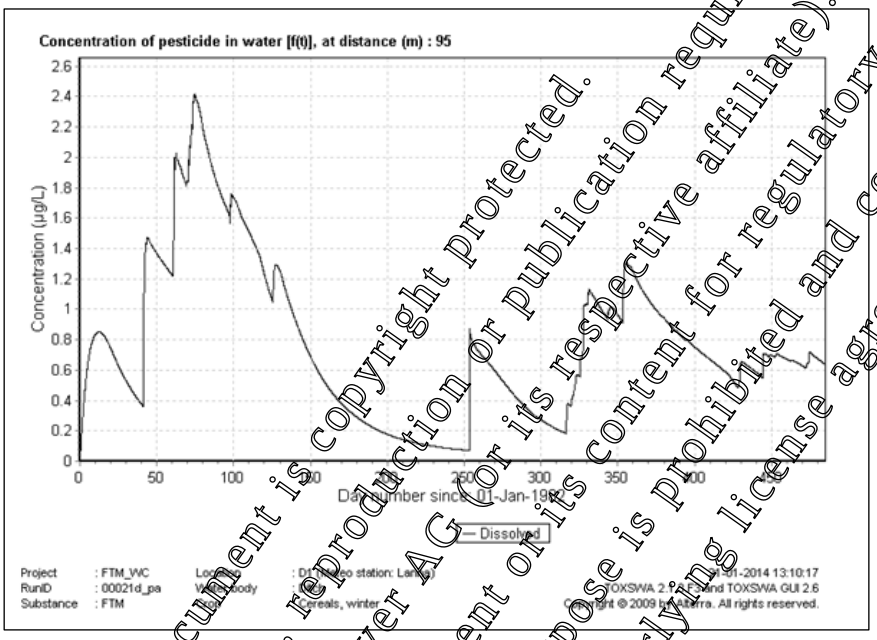


Figure 10.2.2- 1: Predicted concentration of flurtamone in surface water following application of 125 g a.s./ha in autumn in winter cereals at location D1 (ditch)

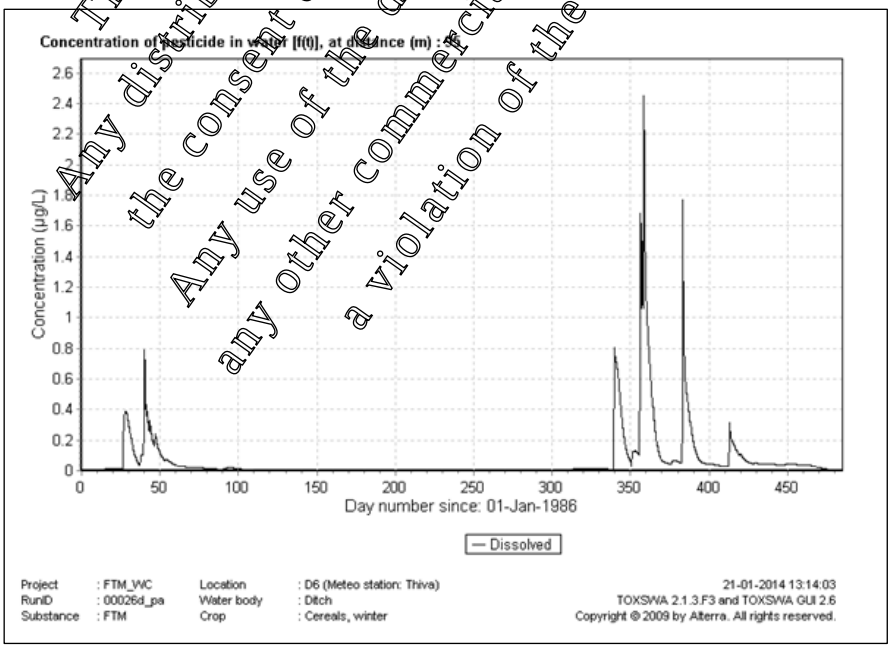


Figure 10.2.2- 2: Predicted concentration of flurtamone in surface water following application of 125 g a.s./ha in autumn in winter cereals at location D6 (ditch)

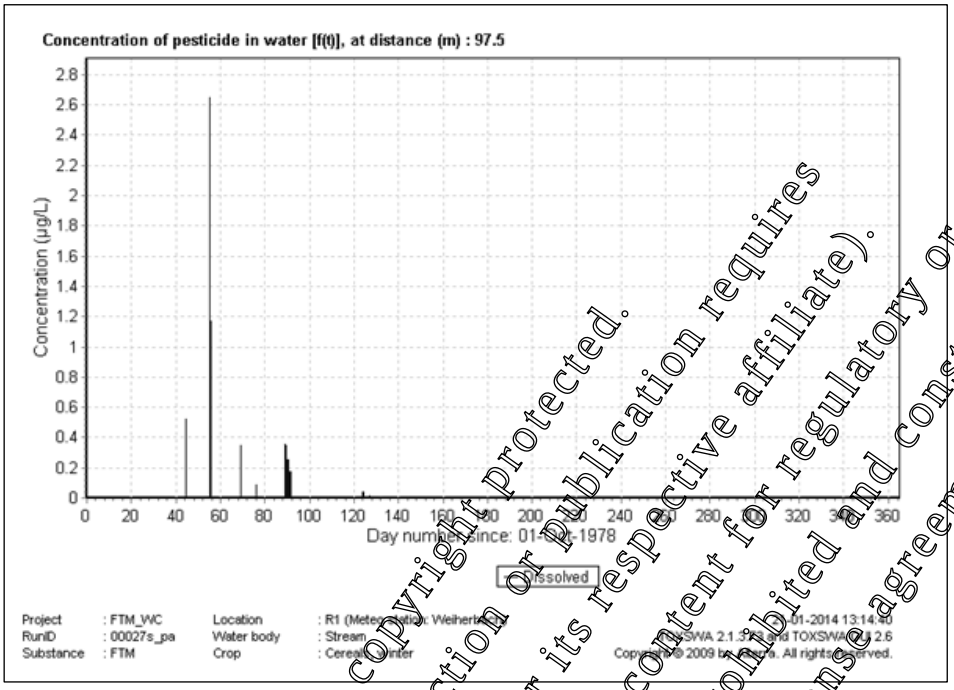


Figure 10.2.2- 3: Predicted concentration of flurtamone in surface water following application of 125 g a.s./ha in autumn in winter cereals at location R1 (stream)

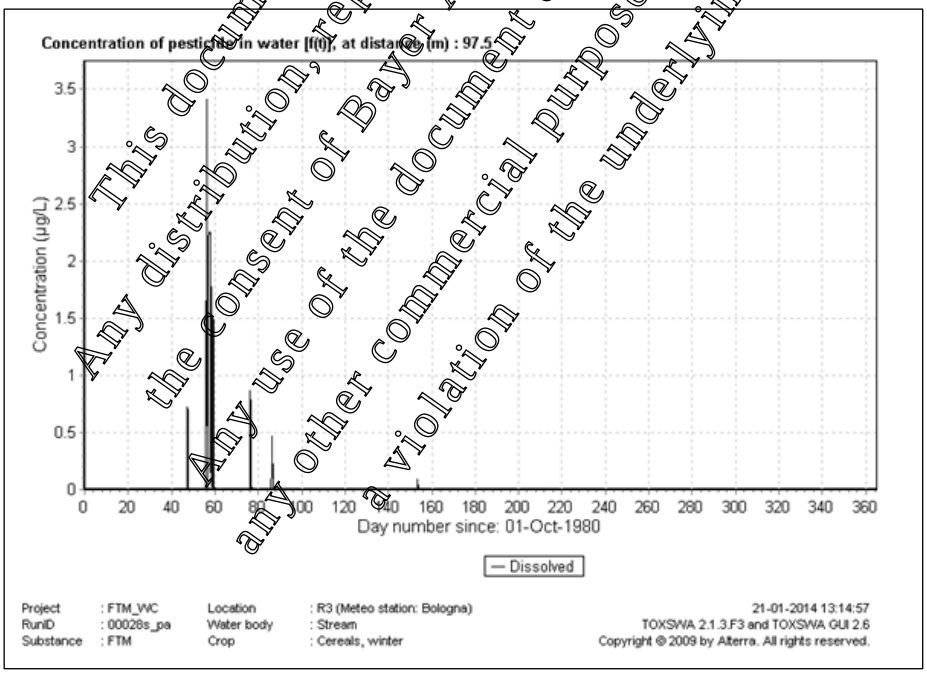
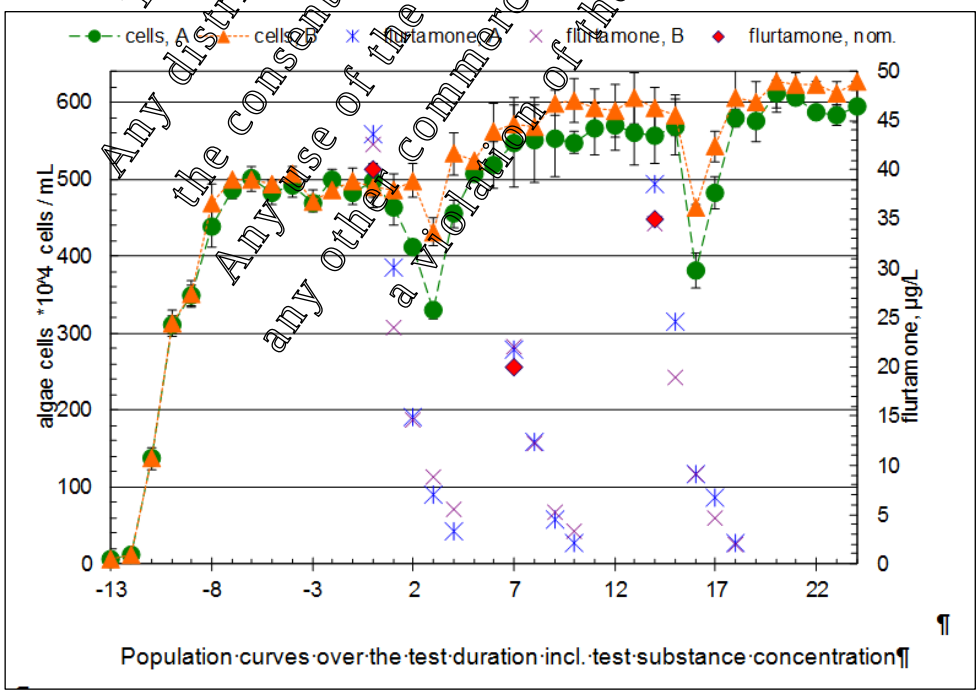


Figure 10.2.2- 4: Predicted concentration of flurtamone in surface water following application of 125 g a.s./ha in autumn in winter cereals at location R3 (stream)

In all four scenarios (D1, D6, R1 and R3), the exceedance of the **RAC of 2.4 µg a.s./L** only occurrs for very short time periods as demonstrated by the above presented exposure profiles.
In addition it should be considered that for the scenarios which are not passed with the standard risk assessment the exceedance of the regulatory acceptable concentration of 2.4 µg a.s./L occurs only in

winter. The concentration of 2.4 µg a.s./L is exceeded for a very short time period in March for D1 (ditch), in January for D6 (ditch), in November for R1 (stream) and in December for R3 (stream).
In the respective time of the year algae growth does not occur in northern or central Europe. As the effect of flurtamone on the algae is algistatic and not algicidal, no long term effect after winter exposure has to be expected.
Nevertheless a flow-through study with the green algae *Pseudokirchneriella subcapitata* has been performed to address short term exposure. The flow-through experiment under variable exposure with flurtamone ([redacted] 2014, M-474520-01-1, KCA 8.2.6.1/03) was performed with *Pseudokirchneriella subcapitata* as the experimental test design is not suitable for *Navicula pelliculosa*. The use of the green algae is justified as the two species differ only slightly with respect to their sensitivity towards flurtamone. For the freshwater diatom the E_rC_{50} is 24 µg a.s./L. This is comparable to the E_rC_{50} values for *Pseudokirchneriella subcapitata* of 38 µg a.s./L and 53 µg a.s./L respectively ([redacted], 2005, M-247782-01-1, KCA 8.2.6.1/01 and [redacted] 2013, M-473178-01-1, KCA 8.2.6.1/02).

The exposure pattern of the algae flow-through study was based on existing exposure profiles (Figure 10.2.2- 1 to Figure 10.2.2- 4) and represents a worst-case exposure situation. The algae flow-through study is based on ideas and guidance as given by the SETAC Europe workshop LINK (Brock TCM, Alix A, Brown CD, Capri E, Gottesbüren BFE, Heimbach F, Lythgo CM, Schulz R and Streloke M (Eds), 2010. Linking aquatic exposure and effects: risk assessment of pesticides. SETAC Press & CRC Press, Taylor & Francis Group, Boca Raton, FL, USA, 398 pp.) which was related to the linking of effect and exposure within the risk assessment of plant protection products. In the algae flow-through study, three short-term pulses of up to 40 µg a.s./L were investigated. At 40 µg a.s./L the effect on the population was clearly lower than 50%. Therefore the result of this flow-through study simulating three pulses of short-term exposure is that the $EC_{50\ population}$ is greater than 40 µg a.s./L.



Within this study the algae received three pulses of flurtamone. The first peak was applied after the cell density reached a steady state. After the first peak of nominally 40 µg a.s./L (measured 43.1 µg a.s./L) the cell density decreased slightly on the two next days. On day 3 the density scaled down to 76.9 % for one day. The next two days the cell number ranged between 99.9 and 104 % of the steady state . The second peak of nominally 20 µg a.s./L (measured 22.0 µg a.s./L) was applied on day 7. This peak had no influence on the cell number. The cell number ranged within the following three days after application between 100 and 103 % of the steady state. The last peak of nominally 35 µg a.s./L (measured 36.6 µg a.s./L) was applied on day 14 resulting in a cell density reduction after one day of about 27.1 % followed by a fast recovery of cell density one day later. The study demonstrated fast recovery of the algae population even after repeated short term pulses with flurtamone.
After the application of the highest peak concentration of nominally 40 µg a.s./L, the cell density was reduced by 23.9%. Therefore it can be stated that the **$EC_{50\ population}$** under the respective exposure conditions was clearly above **40 µg a.s./L**. If the 40 µg a.s./L are used to generate a regulatory acceptable concentration using a TER of 10 this results in a regulatory acceptable concentration (RAC) of 4 µg a.s./L which can be used to address short term exposures. As the critical scenarios are all representing short term exceedances of the original RAC of 2.4 µg/L the use of this new RAC is justified. With this new RAC all scenarios are passed. The resulting TER values are presented below:

Table 10.2.2- 3: Refined TER_{LT} calculations for aquatic organisms exposed to flurtamone following application in winter cereals in autumn (FOCUS Step 3) based on RAC 4 µg a.s./L

Crop	Species	Endpoint [µg/L]	$PEC_{sw\ max}$ [µg/L]	Scenario	TER_{LT}	Trigger
Flurtamone						
Winter cereals (autumn application)	*P. subcapitiata*	EC_{50} (population) >40	2.414	D1 (ditch)	18.4	10
			2.448	D6 (ditch)	16.3	
			2.645	D2 (ditch)	15.1	
			3.408	R3 (ditch)	11.7	

Conclusion: For all four scenarios TERs are above the trigger of 10. Based on the available information generated in short-term algae studies, a mesocosm study and a higher tier study investigating effects of pulsed exposures, it can be stated that effects on algae are not to be expected.

Macrophytes

The ELINK-Workshop identified five situations where a TWA-approach is NOT appropriate (http://elink-info.unicatt.it/ELINK_Executive_Summary.pdf).

The TWA-approach is not appropriate if the risk assessment is based on endpoints from studies where the exposure is not maintained and loss of the active substance in the test system other than uptake by the test organism is fast. The analytical measurements resulted in a recovery of 101 to 111% and 102 to 110 % at day 0 and 7, respectively ([redacted], 2013; M-470528-01-1). Thus, Lemna were constantly exposed during the test. Consequently it is justified to use the 7-day-time weighted average PEC-figures from FOCUS-scenarios with long-term exposure.

Points 2 to 4 identified by ELINK refer to sensitive stages within the life cycle, endocrine effects and mortality. These points do not apply to a *Lemna* growth inhibition test.

Moreover, the TWA-approach is not appropriate if latency of effects has been demonstrated, or might be expected due to mode of action of the pesticide or by appropriate other data. In course of the 7-day *Lemna*-study frond numbers and frond area were assessed on day 3, 5 and 7 ([redacted], 2013; M-470528-01-1). Latency of effects occur only at the two highest treatment levels of 9.38 and 30.0 µg/L which are far above the PEC-figures used in the risk assessment (see Table 10.2.2- 4 below). In addition, the endpoints derived from the *Lemna* peak exposure study ([redacted], 2013; M-475376-01-1) are very similar when effects after one peak is compared to the effects after two peaks. This also indicates that no retarded onset of effects is expected after a previous exposure to Flurtamone.

As summarized in Table 10.2- 2 four macrophyte species have been tested with Flurtamone. *Lemna gibba* und *Elodea canadensis* turned out to be highly sensitive, while *Potamogeton crispus* was of medium and *Myriophyllum spicatum* and the other four species from the mesocosm study are of low sensitivity. Thus, it is justified to reduce the assessment factor from 10 to 5.

The refined risk assessment considers only those scenarios for which a TER < 10 was calculated.

Table 10.2.2- 4 *Lemna*-risk assessment using 7-day time-weighted average for scenarios with long-term exposure of flurtamone

Crop	Species	Endpoint [µg/L]	$PEC_{sw,twa}$ [µg/L]	Scenario	TER_{LT}	Trigger
Winter cereals (autumn application)	*L. gibba*	E_rC_{50} 141	2.324	D1 (ditch)	6.07	5
			1.447	D1 (stream)	9.74	
			1.058	D2 (ditch)	13.33	
			1.138	D6 (ditch)	12.39	

After run-off events the concentrations in streams are peaking for a few hours only. The comparison with the endpoints from a standard 7-day *Lemna*-study leads to a overconservative risk assessment.

On the other hand, it is not justified to use a 7-day time weighted average PEC while the exposure in the stream lasts for less than one day.

Figure 10.2.2- 3 and Figure 10.2.2- 4 show the concentrations in streams after run-off events. In comparison to the drainiage scenarios (Figure 10.2.2- 1 and Figure 10.2.2- 2) it is obvious that such short-term peaks which last for about one day, are not comparable to a constant 7-day exposure like in the standard *Lemna*-study. In order to address peak exposure scenarios in the risk assessment the effects of short-term concentrations of flurtamone to aquatic plants were tested in peak-exposure studies. Therefore, instead of the standard *Lemna* E_rC_{50} the peak E_rC_{50} > 36 µg/L is used for the risk assessment.

Table 10.2.2- 5 Aquatic macrophyte risk assessment using the peak EC_{50} for scenarios with short-term peak exposures of flurtamone

Crop	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	Scenario	TER_{LT}	Trigger
Winter cereals (autumn application)	macrophytes *(Lemna gibba*, *Elodea canadensis* and *Potamogeton crispus)*	peak E_rC_{50} >36	2.645	R1 (stream)	>13.61	10
			3.408	R3 (stream)	>10.56	
Winter cereals (spring application)			1.843	R1 (stream)	>19.52	10
			2.368	R3 (stream)	>15.20	

Overall, it can be concluded, that the application of flurtamone to cereals at the rate of 1.25 g a.s./ha as recommended according to good agricultural practice does not cause any unacceptable effects to aquatic macrophytes.

Study summaries

Report: **KCP 10.2.1/01 [redacted], J.W., [redacted], D., [redacted], A.J.; 1994**
Title: The Acute Toxicity of EXP30930 (RPA309301H) to rainbow trout (*Oncorhynchus mykiss*)
Document No.: M-162501-01-1
Guidelines: OECD 203 (1992), EC Directive 92/69, method C1 (1992)
GLP Yes (certified laboratory)

Objective
The primary objective of this study was to estimate the fifty percent lethal concentration (LC_{50}) for the formulation flurtamone + diflufenican SC 350 to *Oncorhynchus mykiss* under static renewal conditions.

Material and methods:
Test item: EXP 30930 (RPA 309301H), content: 91.7 g/L diflufenican and 250 g/L flurtamone, batch no. OP930604.
Rainbow trout (*Oncorhynchus mykiss*), mean body length 4.3 cm, mean body weight 0.98 g.
Ten fish per treatment level (loading: 0.49 g bodyweight/L) were exposed for 96 h under static-renewal test conditions to nominal concentrations of 18, 32, 56, 100 and 180 mg formulation/L against a water control. Dissolved oxygen (DO) concentration was 9.9-10.0 O_2/L, the pH values ranged from 7.4 to 7.6 and the water temperature was 14°C in all aquaria over the whole period of testing under 16 h light and 8 h dark conditions. Analytical verification of test concentrations showed that actual concentrations of flurtamone (mean of 105.9% at test initiation, 112.1% at test termination) and diflufenican (102.3%, 108.7%) were near nominal over the 96 hour study period. All results of the study were therefore expressed based on nominal values.

Findings:
There were neither any visible abnormalities nor any mortality in the control group.

Table 1: Cumulative mortality was observed as follows (with a total number of 10 fish tested in each test level):

Nominal concentration (mg/L)	Exposure time				
	6 h	24 h	48 h	72 h	96 h
Control	0	0	0	0	0
18	0	0	0	0	0
32	0	0	0	1	1
56	0	2	4	4	4
100	0	5	10	10	10
180	0	0	10	10	10

Table 2: Chronological record of observations:

Nominal concentration (mg/L)	Abnormality	Exposure time					
		3 h	6 h	24 h	48 h	72 h	96 h
Control	None						
18	None						
32	IP		10/10	10/10	7/10	5/9	5/9
	LoE			8/10	7/10	5/9	5/9
	M				3/10	4/9	4/9
56	IP	10/10	10/10	3/8			
	LoE	2/10	5/10	3/8			
	M			5/8	6/6	6/6	6/6
100	IP	3/10		A/D			
	M	7/10	10/10	5/5			
180	IP	1/10		A/D			
	M	9/10	10/10				

IP Increased pigmentation, LoE Loss of equilibrium, M Moribund, A/D All fish dead

Conclusion:

The 96h-LC_{50} of EXP 30930 to Rainbow trout (*Oncorhynchus mykiss*) under static-renewal test conditions was calculated to be 56 mg formulation/L with 95% confidence intervals ranging from 45 to 70 mg formulation/L. LC_{50} values at 24 and 48 hours were 90 and 60 mg formulation/L respectively. The 96 hour NOEC in this study was determined to be 18 mg formulation/L based on the lack of mortality or sub-lethal effects at this concentration.

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Report:	**KCP 10.2.1/02, [redacted] I.G., [redacted] J., [redacted] A.J., 1995**
Title:	EXP 30930 (RPA 30930H): Acute Toxicity to *Daphnia magna*
Document No	M-170697-01-1
Guidelines:	OECD No. 202, (1984)
	EEC Directive 92/69/EWG, part C.2.
GLP	Yes (certified laboratory)

Objective:

The primary objective of this study was to estimate the fifty percent effective concentration (EC_{50}) for the formulation flurtamone + diflufenican SC 350 to *Daphnia magna* under static conditions.

Material and methods:

Test item: EXP 30930 (RPA 30930H), content: 99.1 g/L diflufenican and 252 g/L flurtamone, batch no. OP930730.

Two replicates with 10 *Daphnia magna* (neonates, <24 h old) per test concentration and the control were exposed in a static test system for 48 hours to nominal concentrations of 0 (water-control), 1.0, 1.8, 3.2, 5.6, 10, 18, 32, 56 and 100 mg a.s./L. Daphnids were observed for immobilisation and behavioural abnormalities at 24 and 48 hours after exposure. The test vessels were maintained at 21°C with a photoperiod of 16 hours light and 8 hours dark.

Water samples were taken from the control and the 1.0, 3.2, 10, 32 and 100 mg/L test groups (replicates pooled) at 0 hours and from the control and all test groups at 48 hours for quantitative analysis. Chemical analysis of the test preparations showed that mean measured concentrations over the 48 hour test period to be near nominal for flurtamone except for the highest test level. Measured concentrations of diflufenican were below nominal values likely due to the limited solubility of the compound. Particles were seen in all concentrations above 5.6 mg formulation/L. Based on the findings for flurtamone, all results were expressed based on nominal values. Recovery and stability analysis confirmed that the method of analysis was satisfactory. The active ingredient diflufenican was shown to be physically unstable during the study and flurtamone was shown to be physically unstable at the higher test concentrations employed in the study.

Findings:

There were no adverse reactions to exposure. No immobilisation or intoxication symptoms of the test animals occurred in the untreated control.

Nominal concentration	Immobilisation (%)	
mg/L	24 h	48 h
Control	0	0
1.0	0	0
1.8	0	0
3.2	0	0
5.6	0	0
10	0	0
18	0	35
32	1	55
56	7	80
100	15	100
NOEC	18 mg/L	10 mg/L

Conclusion:

In a static-acute toxicity test to determine the effects of EXP 30930 (RPA 30930H) to Daphnia magna (water flea), the concentration calculated to immobilise 50% of the test animals (EC_{50}) after 48 hours test duration was 28 mg formulation/L (95% confidence limits of 23 – 35 mg/L).

The concentration without any observed effects (NOEC) after 24 and 48 hours test duration was 18 and 10 mg formulation/L, respectively.

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Report:	**KCP 10.2.1/03, [redacted] J.W., [redacted] C., [redacted] A.J., 1994**
Title:	EXP 30930 (RPA 30930 H): Algal Inhibition Test
Document No	M-162497-01-1
Guidelines:	OECD guideline no. 201 (1984)
	EU directive 92/69/EEC Annex Part C: C.3
GLP	Yes (certified laboratory)

Objective:
The primary objective of this study was to estimate the fifty percent effective concentration ($E_{b/r}C_{50}$) for the formulation flurtamone + diflufenican SC 350 to *Desmodesmus subspicatus* (syn. *Scenedesmus subspicatus)* under static conditions.

Material and methods:
Test item: EXP 30930 (RPA 30930 H), content: 91.7 g/L diflufenican and 250 g/L flurtamone, batch no. OP930604.
Scenedesmus subspicatus were exposed under static conditions for 96 hours to the following nominal concentrations: Control, 0.010, 0.020, 0.040, 0.080 and 0.16 mg formulation/L. The measured test concentrations of both active ingredients at 0 hours and 96 hours were in excess of 80% of nominal.
All reported toxicity values were calculated based on the nominal concentrations of the formulation.
Three replicate vessels were prepared for each concentration. The pH values ranged from 7.8-7.9 (test initiation) to pH 7.9-10.5 (test termination) in the controls and the incubation temperature was 24 +/- 2°C over the whole period of testing at a continuous illumination of approximately 7000 lux.
Mean cell density of control at 0 hours was 3.39 x 10^4 cells/ml. Each day, algal density was determined. All test and control cultures were inspected microscopically at 96 hours.

Findings:
The cell concentration of the control cultures increased at a factor of 24 during the test. Therefore, the validity criteria were fulfilled. There were no abnormalities detected in any of the control or test cultures at 0.01, 0.02 and 0.04 mg/L. At the test concentrations of 0.08 and 0.16 mg/L, the algal cells were observed to be colourless and smaller.

Growth inhibition

Nominal concentration (mg /L)	Area under curve (72 h)	Percent (%) inhibition	Area under curve (96 h)	Percent (%) inhibition	Growth rate (24-48 h)	Percent (%) inhibition
Control	1.97×10^7	-	4.38×10^7	-	0.039	-
0.010	1.91×10^7	3	4.35×10^7	1	0.040	(3)
0.020	9.71×10^6	51	1.92×10^7	56	0.010	73
0.040	5.82×10^6	70	1.12×10^7	74	0.007	83
0.080	1.96×10^6	90	3.33×10^6	92	0.004	90
0.16	-2.21×10^5	101	-3.69×10^{-5}	101	-0.013	133

( ) increase in growth as compared to control

Conclusion:
The 48 hour growth rate E_rC_{50} value for EXP 30930 formulation to *Scenedesmus subspicatus* was 0.016 mg formulation/L. The 96 hour E_bC_{50} for growth inhibition based on the area under the growth curve, was calculated to be 0.018 mg formulation/L. The 96 hour NOEC was determined to be 0.01 mg formulation/L (based on nominal concentration of the formulation).

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Report:	**KCP 10.2.1/04, [redacted] M.E., [redacted] C.S., [redacted] C.V.; 2005**
Title:	Toxicity of AE F088657 01 SC31 A202 to Duckweed (*Lemna gibba* G3) Under Static Renewal Conditions
Document No.:	M-243297-01-1
Guidelines:	OECD 221 (draft, April 2004); OPPTS No. 850.4400
GLP	Yes (certified laboratory)

Objective
The primary objective of this growth study was to estimate the fifty percent effective concentration (EC_{50}) for AE F088657 01 SC31 A202 to *Lemna gibba* under static renewal conditions.

Material and methods
Test item: A formulation of Diflufenican 100 + Flurtamone 250 (code: AE F088657 01 SC31 A202); Batch No. V355010344, 9.18% a.s. diflufenican and 23.2% a.s flurtamone.

A total of 3 x 12 fronds of the freshwater duckweed, *Lemna gibba* G3, per test concentration were exposed in a chronic multi-generation test for 7 days under static-renewal (Day 4 renewal) conditions to the nominal concentrations of 1.56, 3.13, 6.25, 12.5, 25 and 50 µg formulation/L in comparison to control. The pH values ranged from 7.7 to 9.0 in the control and the temperature in the incubation ranged from 24.4 to 25.9°C at a continuous illumination of 5.2 klux.
Recoveries of flurtamone in test solutions ranged from 80 to 116% of nominal for freshly prepared solutions (Day 0), and from 71 to 101% of nominal in old test solutions (Day 4 and 7). The results of this study are reported in terms of nominal concentrations of the formulation.

Findings:
Test conditions met the validity criteria as the frond number doubling time was 1.69 days.

Growth was determined by frond counts on days 0, 3, 5, and 7.

The static-renewal 7 days exposure of *Lemna gibba* provided the following results:

Nominal test levels (µg form./L)	Inhibition [%]				
	Frond counts	Biomass	Growth rate	Frond weight	Growth rate for weight
Control	--	--	--	--	--
1.56	2	3	1	-1	-1
3.13	4	9	1	2	1
6.25	-5	-2	-2	-19	0
12.5	5	3	2	25	10*
25	41*	25	19	61	33*
50	68*	51	39	81	57*

At test initiation: 12 fronds corresponding to 108 mm^2 total frond area of plants

A portion of the fronds in the highest test concentration (50.0 µg formulation/L) appeared pale, white and were curled. A majority of the fronds in the 25.0 µg formulation/L appeared pale. A few fronds (<4%) appeared pale in the 12.5 µg formulation/L. This low incidence of paleness is within the historical frequency within controls and healthy cultures. Fronds in the 1.56, 3.13 and 6.25 µg formulation/L levels were all normal as compared to the control.

Conclusion:
The E_rC_{50} for growth rate for frond numbers was > 50 µg formulation/L which was the highest concentration tested. The E_rC_{50} for growth rate for frond dry weight was 39.8 µg formulation/L.

CP 10.2.3 - Further testing on aquatic organisms

The following higher tier studies were done with the formulation Flurtamone SC 600 and summaries are provided in the MCA:

Report: **KCA 8.2.7/05; [redacted]; 2010**
Title: Ecological effects of the herbicide flurtamone in outdoor freshwater microcosms
Document No: M-389526-01-1
Guidelines: OECD 221 (2006)
GLP: Yes (certified laboratory)

Report: **KCA 8.2.7/06; [redacted] I., [redacted] D.; 2013**
Title: Outdoor potted plant study to the effect of the herbicide Flurtamone on aquatic macrophytes *Elodea canadensis* and *Potamogeton crispus.*
Document No: M-469643-01-1
Guidelines: HARAP (Campbell, Arnold et al. 199)
CLASSIC guidance document (Giddings, Brock et a. 2002)
SANCO (SANCO/3268/2001_rev4 (final) 2002)
GLP: Yes (certified laboratory)

CP 10.3 - Effects on arthropods

CP 10.3.1 - Effects on bees

A summary of the toxicity profile of the active substances flurtamone and diflufenican and the representative formulation Flurtamone + Diflufenican SC 350G to bees is given in the following tables.

Table 10.3.1- 1 Honey bee toxicity data generated with technical flurtamone

Test substance	Ecotoxicological endpoint		Reference
Acute oral and contact toxicity (laboratory) in honey bees			
Flurtamone, tech.	LD_{50}-oral 48 h	> 304 µg a.s./bee	[redacted], 1995; M-170680-01-1
Flurtamone, tech.	LD_{50}-contact 48 h	> 100 µg a.s./bee	[redacted], 1989; M-160868-01-1
Flurtamone, tech.	LD50-oral, 48 h LD50-contact, 48 h	**> 105.1 µg a.s./bee** **> 100 µg a.s./bee**	[redacted], 2011; M-421682-01-1 KCA 8.3.1.1/01
Acute contact toxicity (laboratory) in bumble bees			
Flurtamone, tech.	LD_{50}-contact, 48 h	LD_{50} > 100 µg a.s./bee	[redacted], 2014; M-478122-01-1 KCA 8.3.1.1.2/01

Bold values: Endpoints considered relevant for HQ calculation

Table 10.3.1- 2 Endpoints of the mixing partner diflufenican

Test substance	Test species	EU agreed endpoints acc. to EFSA Scientific Report (2007) 122, 1-84	
Diflufenican, tech.	Honey bee (oral 48 h)	$LD_{50 (oral)}$	> 112.3 µg a.s./bee
	Honey bee (contact 48 h)	$LD_{50 (contact)}$	> 100 µg a.s./bee

For the second active substance in the representative formulation, diflufenican, references is made to the EU agreed endpoints according to the EFSA Scientific Report (2007) 122.

Table 10.3.1- 1 Honey bee toxicity data generated with formulated flurtamone

Test substance	Ecotoxicological endpoint		Reference
Acute oral and contact toxicity (laboratory) in honey bees			
Diflufenican + Flurtamone SC 350 (100+250)	48 h-LD_{50}-oral 48 h-LD_{50}-contact	> 200 µg total a.s./bee > 500 µg total a.s./bee	[redacted], 1995; M-170745-01-1
Diflufenican + Flurtamone SC 350 (100+250)	48 h-LD_{50}-oral 48 h-LD_{50}-contact	**> 213.2 µg product/bee** **> 200 µg product/bee**	[redacted], 2012 M-442119-01-1 KCP 10.3.1.1.1/01

Chronic toxicity in adult honey bees (laboratory)			
Flurtamone SC 350	10 d chronic adult feeding study	LC_{50} > 120 mg a.s./kg NOEC ≥ 120 mg a.s./kg	[redacted], 2014; M-477293-01-1 KCA 8.3.1.2/01
Bee brood feeding test			
Flurtamone SC 350	Honey bee brood feeding (Oomen *et al*., 1992)	No adverse effects on mortality, bee brood development (eggs, young larvae, old larvae, pupae) and colony development by feeding honey bee colonies sugar syrup at a concentration typically present in the spray tank (≤13 ppm).	[redacted], 2013 M-462016-01-1 KCA 8.3.1.3/01

Bold values: Endpoints considered relevant for HQ calculation

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 Diflufenican + Flurtamone SC 350 (100+250) G is 0.5 L (500 mL) product/ha in cereals (BBCH 00 - 29). With the content of diflufenican and flurtamone within the formulation being 100 g diflufenican/L and 250 g flurtamone/L, respectively, this accounts to a maximum application rate of 125 g flurtamone a.s./ha. Considering a realistic worst case density of Diflufenican + Flurtamone SC 350 (100+250) of 1.13 g/mL, 500 mL product/ha corresponds to 565 g product/ha.

Table 10.3.1- 2 Hazard quotients for bees – oral exposure

Test item	Oral LD_{50} [µg a.s./bee] / *[µg product/bee]*	Max. application rate [g a.s./ha] / *[g product/ha]*	Hazard quotient Q_{HO}	Trigger	*A-priori* acceptable risk for adult bees
Max. application rate = 125 g flurtamone a.s. / ha via 0.5 L Diflufenican + Flurtamone SC 350 / ha, which corresponds to 565 g Diflufenican + Flurtamone SC 350 / ha					
Flurtamone, tech.	> 105.1	125	1.2	50	yes
Diflufenican + Flurtamone SC 350 (100+250)	*>213.2*	*565*	*<2.6*	50	yes

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

Table 10.3.1- 3 Hazard quotients for bees – contact exposure

Test item	Oral LD_{50} [µg a.s./bee] / *[µg product/bee]*	Max. application rate [g a.s./ha] / *[g product/ha]*	Hazard quotient Q_{HO}	Trigger	*A-priori* acceptable risk for adult bees
Max. application rate = 125 g flurtamone a.s. / ha via 0.5 L Diflufenican + Flurtamone SC 350 / ha, which corresponds to 565 g Diflufenican + Flurtamone SC 350 / ha					
Flurtamone, tech.	100	125	1.3	50	yes
Diflufenican + Flurtamone SC 350 (100+250)	*200*	*565*	*<2.8*	50	yes

The hazard quotient for contact exposure is well 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, flurtamone was further subjected to topical acute bumble bee testing. The study did not reveal sensitivity differences between honey bee and bumble bee foragers.

Moreover, flurtamone 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 flurtamone a.s./kg in aqueous sugar solution. As flurtamone is only slightly soluble in water (10.5 - 10.7 mg/L at 20 °C at pH 5 - 9), the test was conducted by using formulated flurtamone via straight Flurtamone SC 350, in order to increase the solubility of flurtamone in the honey bee feeding solutions. The nominal test concentration as such equals about 10× the water solubility of flurtamone. 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 flurtamone (nominal).

In order to reveal whether flurtamone poses a risk to immature honey bee life stages, a bee brood feeding study has been conducted by following the provisions/method of Oomen P.A., de Ruijter, A.

& van der Steen, J. (OEPP/EPPO Bulletin 22:613-616 (1992)), which require, amongst other parameters to "*…use formulated products only… products are fed at a concentration recommended for high-volume use…"*. The honey bee brood feeding test is a worst-case screening test, by feeding the honey bees directly in the hive with a treated sugar solution which contains the test substance at a concentration typically present in the spray tank (and as such at a very high concentration) and by investigating the development of eggs, young and old larvae by employing digital photo imaging technology.

This particular study was conducted by mixing formulated flurtamone via straight Flurtamone SC 350 into 1 litre of aqueous sugar solution, and the tested concentration corresponded to a typical concentration of flurtamone via Diflufenican + Flurtamone SC 350 (100+250) present in the spray tank. The actual test concentration of flurtamone was 313 mg/L. The administration of 1 litre sugar solution per colony, containing 313 ppm flurtamone has not resulted in adverse effects. There were neither adverse acute or chronic effects on adult honey bees nor adverse effects on immature honey bee life stages (eggs, young larvae, old larvae, pupae) or on the colony itself. Neither mortality of worker bees and larvae/pupae (as assessed via dead bee traps) for the termination rate of eggs, young larvae and old larvae (as assessed via digital imaging of individual marked cells) was statistically significantly different from the untreated control.

Conclusions

Flurtamone has a low acute toxicity to honey bees, with LD_{50} (oral and contact) values always above the highest tested dose levels (oral: LD_{50} > 105.1 µg a.s./bee, contact: LD_{50} > 100 µg a.s./bee).

The calculated Hazard Quotients for both, flurtamone and Diflufenican + Flurtamone SC 350 (100+250) are well below the validated trigger value which would indicate the need for a refined risk assessment; no adverse effects on honey bee mortality are to be expected. This conclusion is confirmed by the results of the bee brood feeding study.

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

Regarding potential side effects of flurtamone on immature honey bee life stages as well as on colony development, 313 ppm flurtamone, a concentration which corresponds to a typical concentration of flurtamone via Diflufenican + Flurtamone SC 350 (100+250) present in the spray tank, has not resulted in adverse/statistical significant effects on mortality of worker bees and pupae nor in adverse/statistically significant effects on the termination rate of eggs, young larvae and old larvae (as assessed via digital imaging of individually marked cells) in the bee brood feeding study on colony level. Even at this very high concentration under the worst case conditions of the honey bee brood feeding test, no adverse effects on immature honey bee life stages were found; the findings in this study regarding the absence of chronic/delayed effects on adults honey bees are in line with the absence of adverse chronic effects on adult bees in the chronic 10 day laboratory feeding test with adult honey bees under laboratory conditions (at 120 ppm).

Overall, it can be concluded that flurtamone, when applied at the maximum application rate of 125 g a.s./ha in cereals, 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 10.3.1.1.1 - Acute oral toxicity to bees

Report:	**KCP 10.3.1.1.1/02; [redacted] S.; 2012**
Title:	Effects of diflufenican + flurtamone SC 350 (100+250) G (Acute Contact and Oral) on Honey Bees (*Apis mellifera* L.) in the Laboratory
Document No:	M-442119-01-1
Guidelines:	OECD Guideline No. 213 and 214 (1998)
GLP:	Yes (certified laboratory)

Objective:

The aim of this study was to investigate the acute contact and oral toxicity of diflufenican + flurtamone SC 350 (100+250) G to the honey bee (*Apis mellifera* L.) according to OECD Guideline No. 213 and 214 (1998). As test endpoint was determined mortality 4 h, 24 h and 48 h after application. Other biological effects and any abnormal responses of the bees were also assessed.

Materials and Methods:

Test item: Diflufenican + flurtamone SC 350 (100+250) G, Batch-ID: EV06003440, Sample Description: FAR01581-00, Material No.: 05945828, Specification No.: 102000003844 – 03 Diflufenican (AE F088657) purity: 8.97% w/w, Flurtamone (AE B107587) purity: 22.4% w/w. As a toxic reference Perfektion EC (BAS 142 11 I) (Batch-ID: 0001017531, dimethoate: 400 g/L nominal) was used.

Contact limit test

Under laboratory conditions 50 worker bees of *Apis mellifera* were exposed for 48 h to a single dose of 200.0 µg product per bee by topical application. The test item was applied as one 5 µL droplet of diflufenican + flurtamone SC 350 (100+250) G, dissolved in tap water with 0.5% Adhäsit, placed on the dorsal bee thorax using a Burkard – Applicator.

The reference was applied as one 5 µL droplet of dimethoate, dissolved in tap water with 0.5% Adhäsit. For the control, one 5 µL droplet of tap water containing 0.5% Adhäsit was used. The number of dead bees and behavioural abnormities were assessed 4 h, 24 h and 48 h after application.

Oral limit test

Additionally, 50 worker bees were fed with sugar syrup (Apiinvert, Südzucker, D-97195 Ochsenfurt; composition of the sugar component: 30 % sucrose, 31 % glucose, 39 % fructose) containing a single nominal dose of 200 µg product per bee (50 % w/w). The treated food was offered in syringes, which were weighed before and after introduction into the cages (duration of uptake was 40 minutes for the test item treatments). After a maximum of 40 minutes, the uptake was complete and the syringes containing the treated food were removed, weighed and replaced by ones containing fresh, untreated food.

The reference was also mixed with the same type of sugar syrup and the final concentration contained 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 number of dead bees and behavioural abnormities were assessed 4 h, 24 h and 48 h after application.

Results:

Validity criteria:

Validity Criteria		Recommended	Obtained
Control Mortality	**Contact Test**		
	CO_2/water control	< 10%	0.0%
	Oral Test		
	water/sugar control	< 10%	0.0%
LD_{50} of Reference Item (24 h)	**Contact Test**		
		0.10 - 0.30 µg/bee	0.23 µg/bee
	Oral Test		
		0.10 - 0.30 µg/bee	0.18 µg/bee

All validity criteria for the study were met

Reference test:

The contact and oral LD_{50} (24 h) values of the reference item (dimethoate) were calculated to be 0.23 µg a.s./bee and 0.18 µg a.s./bee, respectively.

Biological results:

Contact test

At the end of the contact toxicity test (48 h after application), there was no mortality at 200.0 µg product/bee. Also no mortality occurred in the control group (water + 0.5 % Adhäsit). There were no behavioural abnormalities of the bees during the entire trial at 200.0 µg product/bee.

Oral test

In the oral toxicity test, the maximum nominal test level of diflufenican + flurtamone SC 350 (100+250) G (*i.e.* 200 µg product/bee) corresponded to an actual intake of 213.2 µg product/bee. This dose level led to no mortality after 48 h. No mortality occurred in the control group (50 % sugar syrup solution). There were no behavioural abnormalities of the bees during the entire trial at 213.2 µg product/bee.

Effects of diflufenican + flurtamone SC 350 (100+250) G on honey bees (*Apis mellifera*) (contact, oral)

Test Item	diflufenican + flurtamone SC 350 (100+250)	
Test Object	*Apis mellifera*	
Exposure	contact (solution in Adhäsit (0.5 %)/water)	oral (sugar syrup solution)
Application rate µg product/bee	200.0	213.2
LD_{50} µg product/bee	> 200.0	> 213.2
LD_{20} µg product/bee	> 200.0	> 213.2
LD_{10} µg product/bee	> 200.0	> 213.2
NOED µg product/bee*	≥ 200.0	≥ 213.2

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

Conclusion:

For the formulation the contact LD_{50} (48 h) was > 200.0 µg product/bee and the oral LD_{50} (48 h) was > 213.2 µg product/bee.

CP 10.3.1.1.2 - Acute contact toxicity to bees

Refer to Point 10.3.1.

CP 10.3.1.2 - Chronic toxicity to bees

Refer to Point 10.3.1.

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

Refer to Point 10.3.1.

CP 10.3.1.4 - Sub-lethal effects

These studies are not considered necessary.

CP 10.3.1.5 - Cage and tunnel tests

These studies are not considered necessary.

CP 10.3.1.6 - Field tests with honeybees

These studies are not considered necessary.

CP 10.3.2 - Effects on non-target arthropods other than bees

Toxicity tests on non-target arthropods were conducted with FLT + DFF SC 350 on the sensitive standard species *Typhlodromus pyri*, *Aphidius rhopalosiphi* and two additional species. A summary of the results is provided in Table 10.3.2- 1.

Table 10.3.2- 1: FLT + DFF SC 350: Effects on non-target terrestrial arthropods (see KCA 8.3.2 for details)

Test species, Reference	Tested Formulation, study type, Duration, exposure	Ecotoxicological Endpoint
FLT + DFF SC 350		
Aphidius rhopalosiphi M-170701-01-1 Rep.Nr R005248 [redacted], M. P (1995)	SC (100 + 250) Lab. Glass plates, 24h 1 L product/ha	Corr. Mortality[%] 13.3 Effect on Reproduction[%] 43 %
Typhlodromus pyri M-170715-01-1 Rep.Nr R005248 [redacted], M. P (1995)	SC (100 + 250) Lab. Glass plates, 14d 1L product/ha	Corr.Mortality[%] 0 Effect on Reproduction [%] 8.2%
Poecilus cupreus M-170719-01-1 Rep.Nr R005252 [redacted], M. P.; [redacted], P (1995)	SC (100 + 250) Laboratory, spray deposits on sand, exposure (15d). 1L product/ha	Corr. Mortality [%] 0 Effect on Feeding Rate [%] 26.1
Pardosa sp M-170885-01-1 Rep.Nr: R005402 [redacted], M. P.; [redacted], M. D. (1995)	SC (100 + 250) Laboratory, spray deposits on quartz sand, exposure (14d). 1L product/ha	ER50 [g as/ha] value Corr. Mortality [%] 0 Effect on Feeding Rate [%] 4
Aphidius rhopalosiphi M-248106-01-1 Rep.Nr CW04/051 [redacted], A (2005a) KCA 8.3.2.1/01	SC (100 + 250) Lab. glass plates 48h 0.100 L product/ha 0.125 L product/ha 0.464 L product/ha 1 L product/ha	LD_{50} > 1 L product/ha Corr. Mortality [%] -5.6 [B] -3 [B] -9.1 [B] -9.1 [B] Effect on Reprod. [%] not detected -27.2 [A] - 0.6 [A] 11.4
Typhlodromus pyri M-248338-01-1 Rep.Nr CW04/054 [redacted], A (2005b) KCA 8.3.2.2/01	SC (100 + 250) Lab. Glass plates, 14d 0.100 L product/ha 0.125 L product/ha 0.464 L product/ha 1 L product/ha	LR_{50}> 1 L product/ha Corr. Mortality [%] 0 6.1 0 5.1 Effect on Reproduction [%] -39.0 [A] -23 [A] -33.0 [A] -2.4 [A]

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

Risk assessment procedures

The risk assessment was performed according to Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002) and to the Guidance Document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods (ESCORT 2, [redacted] et al. 2000[5]).

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

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

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

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

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

The product is intended to be applied once with an application rate of 500 mL/ha. Therefore, the multiple application factor (MAF) was set 1. Resulting HQ values are presented in Table 10.3.2- 2.

Table 10.3.2- 2: Exposure of terrestrial non-target arthropods for the in-field scenario, based on laboratory studies

Crop	Species	Appl. rate [mL/ha]	MAF	LR_{50} / ER_{50} [mL/ha]	HQ	Trigger
Cereals	*T. pyri*	500	1	>1000	< 0.5	2
	A. rhopalosiphi	500	1	>1000	< 0.5	2

The in-field trigger of concern is met for the intended use and a refined risk assessment is not needed.

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

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

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

MAF = multiple application factor
Drift factor = i.e 0.0277, 90th percentile for one application according to Ganzelmeier)
VDF = vegetation distribution factor
Vegetation distribution factor = 10
Correction factor = 10 (tier 1 tests, *Aphidius* - *Typhlodromus*)

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

Table 10.3.2- 3: Exposure of terrestrial non-target arthropods for the off-field scenario

Crop	Species	Appl. rate [mL/ha]	MAF	Drift [%]	VDF	Correction factor	LR_{50} / ER_{50} [mL/ha]	HQ	Trigger
Cereals	*T. pyri*	500	1	2.77	10	10	> 1000	< 0.01	2
	A. rhopalosiphi	500	1	2.77	10	10	> 1000	< 0.01	2

Conclusion: The estimated HQ is below the trigger of concern, indicating no unacceptable risk for non-target arthropods. Additionally, the results of the laboratory studies conducted on the species *Poecilus cupreus* and *Pardosa* sp. confirm the conclusion since no effects were detected on mortality or food consumption of these species.

CP 10.3.2.1 - Standard laboratory testing for non-target arthropods

New laboratory tests with the formulation are summarized in the MCA document for flurtamone:

Report:	**KCA 8.3.2.1 /01; [redacted] A.; 2005a**
Title:	Toxicity to the parasitoid wasp *Aphidius rhopalosiphi* (DeStephani-Perez) (Hymenoptera: Braconidae) in the laboratory; Flurtamone + Diflufenican Suspension concentrate 250 + 100g/l
Document No:	M-248106-01-1
Guidelines:	IOBC (Mead-Briggs et al. 2000)
GLP:	Yes (certified laboratory)

Report:	**KCA 8.3.2.2/01; [redacted], A.; 2005b**
Title:	Toxicity to the predatory mite *Typhlodromus pyri* SCHEUTEN (Acari, Phytoseiidae) in the laboratory Flurtamone & Diflufenican Suspension concentrate 250 + 100 g/L
Document No:	M-248338-01-1
Guidelines:	IOBC (Blümel et al. 2000)
GLP:	Yes (certified laboratory)

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

These studies are not considered necessary.

10.3.2.3 - Semi-field studies with non-target arthropods

These studies are not considered necessary.

10.3.2.4 - Field studies with non-target arthropods

These studies are not considered necessary.

10.3.2.5 - Other routes of exposure for non-target arthropods

These studies are not considered necessary.

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

Table 10.4- 1: Effects of the representative formulation on soil macro-organisms – earthworms

Test species	Test substance	Test design	Ecotoxicological endpoint	Reference
Eisenia fetida	FLT + DFF SC 350	acute, 14 d (10% peat in test soil)	LC_{50} > 1000 mg/kg dws LC_{50} > 500*	[redacted] 1996 M-264050-01-1 KCP 10.4.1/01
Eisenia fetida	FLT + DFF SC 350	chronic, 56 d (5% peat in test soil)	NOEC 118.4 mg/kg dws NOEC 59.2*	[redacted] 2004 M-215630-01-1 KCP 10.4.1/01

* endpoint corrected to account for logPow > 2

Table 10.4- 2: Effects of flurtamone on soil macro-organisms – earthworms

Test species	Test substance	Test design	Ecotoxicological endpoint	Reference
Eisenia fetida	Flurtamone	acute, 14 d (10% peat in test soil)	LC_{50} > 900* mg as/kg dws	[redacted], 1992; M-203222-01-1
Eisenia fetida	Flurtamone	chronic, 56 d (5% peat in test soil)	NOEC 47.5* mg as/kg dws	[redacted], 2011 M-415904-01-1 KCA 8.4.1/01
Eisenia fetida	M04 TFMBA	acute, 14 d (10% peat in test soil)	LC_{50} 123.2 mg pm/kg dws	[redacted], 2005; M-252227-01-1 KCA 8.4/01
		chronic, 56 d (10% peat in test soil)	NOEC ≥ 100 mg pm/kg dws	[redacted], 2013 M-444573-01-1 KCA 8.4.1/02
Eisenia fetida	M05 TFA	chronic, 56 d (10% peat in test soil)	NOEC 320 mg pm/kg dws	[redacted], 2005; M-251328-01-1 KCA 8.4.1/03

* endpoints corrected to account for logPow > 2
dws = dry weight soil, pm = pure metabolite
[1)] NOEC reduced to 320 mg/kg based on effects on the body weight in the concentration 1000 mg/kg

Table 10.4- 3: Effects of mixing partner diflufenican on soil macro-organisms – earthworms

Test substance	Test species	EU agreed endpoints acc. to EFSA Scientific Report (2007) 122, 1-84	
Diflufenican	Earthworm, reproduction (10% peat in test soil)	NOEC	500 mg as/kg dws*

* endpoints corrected to allow for log P_{ow} > 2

CP 10.4.1 – Earthworms

Exposure in soil

Predicted environmental concentrations in soil (PEC_{soil}) values were calculated for flurtamone and its metabolites as described in detail in Point 9.1.3 of this document.

The PEC_{soil} for the formulation was calculated based on a maximum application rate of 0.5 L product/ha, no interception, standard soil conditions and a density of 1.11g/mL for the formulation in order to conduct risk assessments.

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

Table 10.4.1- 1: Maximum PEC_{soil} values

Compound	$PEC_{soil, max}$ [mg/kg]
FLT + DFF SC 350	0.740
Flurtamone	0.167
M04 TFMBA	0.024
M05 TFA	0.034

Risk asssessment

The risk assessment procedure follows current regulatory requirements and the Guidance Document on Terrestrial Ecotoxicology.

Based on most sensitive endpoints the TER values are calculated using the following equations:

$TER_A = LC_{50} / PEC_{soil}$
$TER_{LT} = NOEC / PEC_{soil}$

The risk is considered acceptable if the TER_A is >10 and the TER_{LT} is >5.

For lipophilic substances (log P_{OW} > 2) all results from the laboratory studies have to be corrected by a factor 2 when the organic matter is higher or equal to 5 % (PRAPER decision, April 2012).
This was applied to flurtamone (log P_{OW} = 3.2).

Table 10.4.1- 2: TER calculations for earthworms

Compound test design	Endpoint	[mg/kg soil]	PEC_{max} [mg/kg soil]	TER_A / TER_{LT}	Trigger	Refined risk assessment needed?
FLT + DFF SC 350 acute	LC_{50}	> 500	0.740	676	10	no
FLT + DFF SC 350 chronic	NOEC	59.2	0.740	80	10	no
Flurtamone acute	LC_{50}	> 900	0.167	> 5389	10	no
Flurtamone chronic	NOEC	47.5	0.167	284	10	no
M04 TFMBA acute	LC_{50}	123.2	0.024	5133	10	no
M04 TFMBA chronic	NOEC	≥ 100	0.024	4167	10	no
M05 TFA chronic	NOEC	320	0.034	9412	10	no

Conclusion: The TER values are above the trigger of concern, indicating no unacceptable risk for earthworms and soil non-target macro-organisms.

CP 10.4.1.1 - Earthworms - sub-lethal effects

Report: **KCP 10.4.1.1/01; [redacted], U.; 2004**
Title: Effects of AE F088657 01 SC31 A202 on reproduction and growth of earthworm *Eisenia fetida* in artificial soil with 5 % peat
Document No. M-235630-01-1
Guidelines: BBA VI, No. 2-2 Kula, 1994; ISO 11268-2 (1998)
GLP Yes (certified laboratory)

Objective
The purpose of this study was to investigate the effects of AE F088657 01 SCSI A202 on the mortality, body weight, feeding activity and reproduction of adult *Eisenia fetida* at 5 different application rates. The content of peat was 5% because the log Pow of the active substances is >2.

Material and methods:
Test item: AE F088657 01 SC31 A202 (Diflufenican + Flurtamone SC 350), Batch No.: V355010344, Content of a.i: AE B107587 (flurtamone): 23.2% w/w, AE F088657 (diflufenican): 9.18% w/w; toxic standard: Derosal SC 360 (active ingredient carbendazim) is tested at least once a year in a dose response study; control: untreated.

AE F088657 01 SC31 A202 was sprayed onto the soil surface at rates resulting in soil concentrations of 7.4, 14.8, 29.6, 59.2 and 118.4 mg/kg artificial soil (dry weight) to which earthworms *Eisenia fetida* (40 worms per treatment group) were exposed at 19 - 22 °C, light 460 - 700 lux, 16 h light : 8 h dark, fed weekly with dried cattle manure, initial soil water content 22.7 to 22.9% (52.8 - 53.3% of the max.

water holding capacity), water content at experimental termination 27.8% - 30.3% (64.7 - 70.5% of the max. water holding capacity), initial pH 5.5, pH 5.6 - 6.0 at experimental termination.

Endpoints were mortality, body weight change, feeding activity and reproduction.

Findings:

Test item	AE F088657 01 SC31 A202					
Test species	*Eisenia fetida*					
Exposure	Test item sprayed onto soil					
Test duration	56 days					
	control	AE F088657 01 SC31 A202 [mg/kg]				
		7.4	14.8	29.6	59.2	118.4
Mortality [%]	0	0	0	0	0	0
Body weight change [%]	40.9 ± 3.1	29.1 ± 10.9 n.s.	36.5 ± 4.1 n.s.	28.0 ± 7.9 n.s.	38.4 ± 7.6 n.s.	36.9 ± 9.9 n.s.
Reproduction of juveniles *	291 ± 30	270 ± 45 n.s.	303 ± 40 n.s.	249 ± 24 n.s.	251 ± 14 n.s.	252 ± 12 n.s.
% of control	-	92.8	104.0	85.5	86.3	86.6
Amount of food added [g]	25.0	25.0	25.0	25.0	25.0	25.0

* mean ± standard deviation of 4 replicates, rounded
n.s. not significantly different as compared to control; Dunnett Test, α=0.05 (two-sided for weight changes, one-sided smaller for reproduction)

Conclusion:
AE F088657 01 SCSI A202 did not show effects on mortality, growth, reproduction and feeding activity of the earthworm *Eisenia fetida* when sprayed onto the soil surface to result in a concentration of 118.4 mg/kg dry artificial soil.
The Lowest Observed Effect Concentration (LOEC) found in this study was greater than 118.4 mg/kg dry artificial soil. The overall No Observed Effect Concentration (NOEC) found in this study was 118.4 mg AE F088657 01 SC31 A202/kg dry artificial soil, i.e. the highest concentration tested.

CP 10.4.1.2 - Earthworms - field studies

No studies are necessary.

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

Table 10.4.2- 1: Effects of FLT + DFF SC 350 on other soil non-target macro-organisms

Test species	Test design	Ecotoxicological endpoint			Reference
FLT + DFF SC 350					
Folsomia candida	chronic 28 d (5% peat in test soil)	NOEC NOEC	562 281*	mg prod/kg dws mg prod/kg dws	[redacted], 2013; M-444290-01-1 KCP 10.4.2.1/01
Hypoaspis aculeifer	chronic 14 d (5% peat in test soil)	NOEC NOEC	≥ 1000 ≥ 500*	mg prod/kg dws mg prod/kg dws	[redacted], 2012; M-443179-01-1 KCP 10.4.2.1/02

* adjusted by a factor of 2 to address the log P_{ow}

Table 10.4.2- 2: Effects of flurtamone and its metabolites on other soil non-target macro-organisms

Test species	Test design	Ecotoxicological endpoint			Reference
Flurtamone					
Folsomia candida	chronic 28 d (5% peat in test soil)	NOEC NOEC	≥ 1000 ≥ 500*	mg as/kg dws mg as/kg dws	[redacted], 2012; M-438621-01-1
Hypoaspis aculeifer	chronic 14 d (5% peat in test soil)	NOEC	≥ 178 ≥ 89*	mg as/kg dws mg as/kg dws	[redacted], 2012; M-439623-01-1
M04 TFMBA					
Folsomia candida	chronic 14 d (5% peat in test soil)	NOEC	52	mg pm/kg dws	[redacted], 2013; M-444231-01-1
Hypoaspis aculeifer	chronic 14 d (5% peat in test soil)	NOEC	≥ 100	mg pm/kg dws	[redacted], 2012; M-443198-01-1
M05 Trifluoroacetic acid Na-salt					
Folsomia candida	chronic 28 d (10% peat in test soil)	NOEC	≥ 100	mg pm/kg dws	[redacted], 2012; M-436127-01-1
Hypoaspis aculeifer	chronic 14 d (5% peat in test soil)	NOEC	≥ 100	mg pm/kg dws	[redacted], 2012 ; M-436326-01-1

* adjusted by a factor of 2 to address the log P_{ow}

Table 10.4.2- 3 Endpoints for the mixing partner diflufenican

Test substance	Test species	EU agreed endpoints acc. to EFSA Scientific Report (2007) 122, 1-84	
Diflufenican	*Folsomia candida*	NOEC	≥ 438 mg as/kg dws

Chronic toxicity exposure ratios for soil non-target macro-organisms

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

$TER = NOEC / PEC_{soil}$

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

Table 10.4.2- 4: TER calculations for soil macro-organisms

Compound	Endpoint	[mg/kg soil]	PEC_{max} [mg/kg soil]	TER	Trigger	Refined risk assessment needed?
Folsomia candida						
FLT+DFF SC 350	NOEC	281	0.740	380	5	no
Flurtamone	NOEC	≥ 500	0.167	≥ 2994		
M04 TFMBA	NOEC	52	0.024	2167	5	
M05 TFA	NOEC	≥ 100	0.034	≥ 2941	5	
Hypoaspis aculeifer						
Flurtamone	NOEC	≥ 89	0.167	≥ 533	5	no
M04 TFMBA	NOEC	≥ 100	0.024	≥ 4167	5	
M05 TFA	NOEC	≥ 100	0.034	≥ 2941	5	
FLT+DFF SC 350	NOEC	≥ 500	0.740	≥ 676	5	

Conclusion: The TER value is above the trigger of concern, indicating no unacceptable risk for soil non-target macro-organisms, i.e. collembolan and soil mites.

CP 10.4.2.1 - Species level testing

Report: **KCP 10.4.2.1/01 [redacted], S.; 2013**
Title: Diflufenican + flurtamone SC 350 (100+250) G: Effects on the reproduction of the collembolan *Folsomia candida*
Document No: M-444296-01-1
Guidelines: OECD 232 (2009), ISO 11267 (1999)
GLP Yes (certified laboratory)

Objective

The purpose of this study was to investigate the effect of diflufenican + flurtamone SC 350 (100+250) G on survival and reproduction of the collembolan species *Folsomia candida* during an exposure of 28 days in an artificial soil comparing control and treatment. The test was performed in accordance with the OECD Guideline 232 (2009) and the International Standard ISO 11267 (1999).

Material & Methods

Test item: Diflufenican + flurtamone SC 350 (100+250) G [short name: DFF+FLT SC 350 (100+250) G], Sample description: FAR01581-00, Specification No.: 102000003844 - 03, Batch ID: EV56003440, Material No.: 05945828, analytical findings: 99.93 g diflufenican/L, 249.5 g flurtamone/L, Density (20 °C): 1.114 g/mL, water solubility: dispersible.

Ten *Collembola* (9-12 days old) were exposed to 100, 178, 316, 562 and 1000 mg test item/kg soil dry weight (d.w.) containing 74.7% quartz sand, 20% kaolin clay, 5% sphagnum peat and 0.3% $CaCO_3$, at 18.0 – 20.8 °C and a photoperiod: light : dark = 16 h : 8 h (640 lx) and were fed weekly with granulated dry yeast. Mortality and reproduction were determined after 28 days. For each concentration, 4 replicates were conducted.

To verify the sensitivity of the test system the reference item boric acid is routinely tested at concentrations of 44, 67, 100, 150 and 225 mg a.s./kg soil d.w. Deionised water only was used as control (8 replicates).

Results

Validity Criteria

Validity Criteria	Recommended	Obtained
Mean adult mortality	≤ 20%	3.8%
Mean number of juveniles per test vessel	≥ 100	average of 709/vessel
Coefficient of variation for the mean	< 30%	10.1%
Precision of counting method	Error < 10%	Error 4.3%

Reference test

In the most recent study (BioChem project No. R 12 10 48 002 S, dated May 24, 2013) the EC_{50} was determined to be 104 mg/kg soil dry weight. The LC_{50} was determined to be 199 mg/kg soil dry weight. The NOEC for mortality and for reproduction was determined to be 100 and 44 mg/kg soil dry weight, respectively.

Biological results:

Effects on mortality

No statistically significant differences were observed for mortality (Fisher's Exact Binomial Test with Bonferroni Correction, $\alpha = 0.05$, one-sided greater).

Effects on reproduction

Only the concentration 1000 mg test item/kg soil d.w. indicated a statistically significant difference compared to the control (Williams t-test for reproduction, $\alpha = 0.05$, one-sided smaller). The other concentrations showed no statistically significant effect.

Effects of diflufenican + flurtamone SC 350 (100 + 250) G on *Folsomia candida* (concentrations of the test item [mg/kg soil d.w.])

Test item Test object Exposure	Diflufenican + flurtamone SC 350 (100 + 250 G) *Folsomia candida* Artificial soil		
mg test item/kg soil d.w.	Mean mortality of parental collembolans after 4 weeks (%)	Mean number of juveniles after 4 weeks	Reduction of reproduction compared to control (%)
Control	3.8	709	-
100	0.0	704	99
178	2.5	705	99
316	0.0	758	107
562	2.5	680	96
1000	5.0	584*	82
	Adult mortality	Reproduction	
	mg test item/kg soil d.w.		

NOEC	≥ 1000	562
LOEC	> 1000	1000

* statistically significantly different from control (Williams t-test for reproduction; $\alpha = 0.05$, one-sided smaller)

Conclusion

The test item diflufenican + flurtamone SC 350 (100+250) G showed no statistically significantly adverse effects on adult mortality of the collembolan *Folsomia candida* in artificial soil up to and including 1000 mg test item/kg soil d.w..

The test item caused a significant reduction of reproduction of the collembolan *Folsomia candida* in artificial soil at 1000 mg test item/kg soil dry weight. Therefore, the overall No-Observed-Effect-Concentration (NOEC) was determined to be 562 mg test item/kg soil d.w., and the overall Lowest-Observed-Effect-Concentration (LOEC) was determined to be 1000 mg test item/kg soil d.w. The EC_{50} for reproduction could not be determined, but it can be concluded that the EC_{50} is higher than 1000 mg test item/kg soil dry weight.

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Report: **KCP 10.4.2.1/02 [redacted], L.; 2012**

Title: Diflufenican + flurtamone SC 350 (100+250) G: Effects on the reproduction of the predatory mite *Hypoaspis aculeifer*

Document No: M-443179-01-1

Guidelines: OECD 226 (2008)

GLP Yes (certified laboratory)

Objective

The purpose of this study was to determine potential effects of the test item on the mortality and the reproductive output of the soil mite species *Hypoaspis aculeifer* as a representative of soil micro-arthropods during a test period of 14 days. A NOEC and a LOEC were determined. The test was performed according to the OECD guideline 226 (2008).

Material & Methods

Test item: Diflufenican + flurtamone SC 350 (100+250) G [short name: DFF+FLT SC 350 (100+250) G], Sample description: FAR01581-00, Specification No.: 102000003844 - 03, Batch ID: EV56003440, Material No.: 05945828, analytical findings: 99.93 g diflufenican/L, 249.5 g flurtamone/L, Density (20 °C): 1.114 g/mL, water solubility: dispersible.

Ten adult soil mites (females) were exposed to 100, 178, 316, 562 and 1000 mg test item/kg dry weight (d.w.) of soil containing 74.7% quartz sand, 20% kaolin clay, 5% sphagnum peat and 0.3% $CaCO_3$, at 18.2 - 21.6°C and a photoperiod: light : dark = 16 h : 8 h (611 lx) and were fed every 2 days with *Tyrophagus putrescentiae* (SCHRANK). Mortality and reproduction were determined after 14 days of exposure.

The reference item dimethoate EC 400 (trade product Perfekthion, active ingredient: Dimethoate, nominal content: 400 g/L) was tested in a separate study to verify the sensitivity of the test system (concentrations: 4.10, 5.12, 6.40, 8.00 and 10.00 mg a.s./kg soil d.w.). The control substrate was left untreated, i.e. was prepared with deionised water only.

Results

Validity *Criteria*

Validity Criteria	Recommended	obtained
Mean mortality of adult females	≤ 20%	3.8
Mean number of juvenile per replicate	≥ 50%	262.3
Coefficient of variation (mean number of juveniles per replicate)	≤ 30%	13.2

Reference test

In a separate study (BioChem project No. R 12 10 48 002 S, dated March 05, 2012), the EC_{50} (reproduction) of the reference item Dimethoate EC 400 was calculated to be 6.87 mg a.s./ kg soil d.w. The results of the reference test demonstrate the sensitivity of the test system.

Biological results:

Effects on mortality

There was no statistically significant difference compared to the control (Fisher´s Exact Binominal Test, α = 0.05, one-sided greater).

Effects on reproduction

The treated groups showed no statistically significant difference compared to the control (Williams t-test, α = 0.05, one sided smaller).

Effects of diflufenican + flurtamone SC 350 (100+250) G on *Hypoaspis aculeifer* (concentrations of the test item [mg test item/ kg soil d.w.])

Test item Test object Exposure	**Diflufenican + flurtamone SC 350 (100+250) G** *Hypoaspis aculeifer* Artificial soil		
	Mean Mortality of soil mites after 14 days (%)	Mean number of juveniles after 14 days	Reproduction (% to control)
Control	3.8	262.3	100
100	2.5	251.8	96
178	5.0	249.5	95
316	5.0	276.5	105
562	2.5	275.8	105
1000	0.0	249.5	95

	Adult mortality	Reproduction
	mg test item/kg soil d.w.	
NOEC	≥ 1000	≥ 1000
LOEC	> 1000	> 1000

Conclusion

The test item diflufenican + flurtamone SC 350 (100+250) G showed no statistically significantly adverse effects on adult mortality and reproduction of the predatory mite *Hypoaspis aculeifer* in artificial soil at all tested concentrations.

Therefore, the overall No-Observed-Effect-Concentration (NOEC) for mortality and reproduction was determined to be ≥ 1000 mg test item/kg soil d.w.

The Lowest-Observed-Effect-Concentration (LOEC) for mortality and reproduction was determined to be > 1000 mg test item/kg soil d.w.

CP 10.4.2.2 - Higher tier testing

No studies on higher tier testing for flurtamone were needed.

CP 10.5 - Effects on soil nitrogen transformation

The influence of the formulation FLT + DFF SC 350, flurtamone and metabolites on carbon transformation and nitrogen transformation in soil has been studied in the laboratory and effects on soil non-target micro-organisms are summarised in the following table.

Table 10.5- 1: Effects of the formulation on soil non-target micro-organisms

Test	Test item	Test design	Ecotoxicological endpoint		Reference
N-cycle	FLT+DFF SC 350	60 d	no influence	2.235 mg prod/kg dws 11.175 mg/kg dws	[redacted], 1995; M-209125-01-1
N-cycle	FLT+DFF SC 350	28 d	no influence	1.487 mg prod/kg dws 7.43 mg prod/kg dws	[redacted], 1998; M-243646-01-1

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

Test	Test item	Test design	Ecotoxicological endpoint		Reference
N-cycle	Flurtamone	28 d	no influence	0.625 kg as/ha 0.83 mg as/kg dws	[redacted], 2012; M-441247-01-1 KCA 8.5/01
N-Cycle	M04 TFMBA	28 d	no influence	0.357 kg pm/ha 0.48 mg pm/kg dws	[redacted], 2013; M-444428-01-1 KCA 8.5/02
N-Cycle	M05 TFA	28 d	no influence	1.20 kg pm/ha 1.60 mg pm/kg dws	[redacted], 2013 M-444423-01-1 KCA 8.5/03

Table 10.5- 3 Endpoints for the mixing partner diflufenican

Test substance	Test	EU agreed endpoints acc. to EFSA Scientific Report (2007) 122, 1-84	
Diflufenican	N-cycle	no influence	test rate not mentioned
AE B107137	N-cycle	no influence	test rate not mentioned
AE 0542291	N-cycle	no influence	test rate not mentioned

Risk assessment

The risk is acceptable, if the effect of the recommended application rate on nitrogen or carbon mineralisation is < 25% after 100 days.

In no case, deviations from the control exceeded ±25% after 28 days, indicating low risk to soil micro-organisms.

For FLT+DFF SC 350, flurtamone and its metabolites no influence on the N-cycle could be detected at concentrations even higher than the respective PEC-values.

CP 10.6 - Effects on terrestrial non-target higher plants

For herbicides and plant growth regulators, it is considered not necessary 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. Therefore Tier 2 studies have been conducted directly.

Ecotoxicological endpoints

The effects of the formulation FLT + DFF SC 350 on seedling emergence and vegetative vigour and phytotoxicity of a range of terrestrial non-target plants was assessed in two laboratory studies:

Table 10.6- 1: Effects of FLT + DFF SC 350 on non-target plant tests

Test organism	study type	test duration	lowest EC_{50} (mL prod/ha)	most sensitive species	References
Terrestrial non-target plants; 10 species	vegetative vigour; Tier 2 dose response	21 days	192.6 (shoot dry weight)	sugar beet	[redacted] & [redacted], 2005; M-251319-01-1 KCA 8.6.2/01
Terrestrial non-target plants; 10 species	seedling emergence; Tier 2 dose response	14 days after 25% emergence in the controls	25.2 (survival) 36.3 (shoot dry weight)	sugar beet	[redacted] & [redacted], 2005; M-251318-01-1 KCA 8.6.2/02

Risk assessment

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 off -crop plants located outside the treated area. Spray drift from the treated areas may lead to residues of a product in off-crop areas.

Exposure

Effects on non-target plants are of concern in the off-field environment, where they may be exposed to spray drift. The amount of spray drift reaching off-crop habitats is calculated using the 90th percentile

estimates derived by the *BBA (2000)*[6] from the spray-drift predictions of *Ganzelmeier & Rautmann (2000)*[7]. Only a single application was considered as factors such as plant growth will reduce residues per unit area between multiple applications.

The off-field exposure for non-target terrestrial plants is based on drift values as given in the Terrestrial Guidance Document[8] including the use of drift reducing spray nozzles. The drift factors for arable crops according to SANCO/10329/2002 are 2.77% without any buffer zone to the adjacent field edge or 0.57% considering a buffer zone of 5 m or 0.29% considering a buffer zone of 10 m.

Table 10.6- 2: Off-crop exposure for non-target terrestrial plants

Max. application rate [mL product/ha]	Distance [m]	Drift* (%)	PEC [mL /ha]	PEC 50% drift reduction or 50% interception [mL /ha]	PEC 75% drift reduction [mL /ha]	PEC 90% drift reduction [mL /ha]
500	1	2.77	13.85	6.925	3.463	1.385
	5	0.57	2.85	1.425	0.715	0.285

* drift value (1 application, field crops)

Deterministic risk assessment for non-target terrestrial plants

TER values are calculated based on the lowest ER_{50} values of the plant tests, seedling emergence and vegetative vigour. A TER of ≥ is considered acceptable when 6 plant species have been tested (deterministic approach).

The deterministic risk assessment is based on the most sensitive endpoint, i.e. ER_{50} of 25.2 mL product/ha for sugar beet in the seedling emergence test, and ER_{50} of 192.6 mL product/ha for sugar beet in the vegetative vigour test.

Table 10.6- 3: Deterministic off-crop risk assessment for non-target terrestrial plants: seedling emergence

cereals, one application, lowest ER_{50} = 25.2 mL/ha (sugar beet)						
Distance+ [m]	Drift* (%)	PEC no drift reduction [mL/ha]	TER [a]			
			No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
1	2.77	13.85	**1.8**	**3.6**	7.3	18.2
5	0.57	2.85	8.8	17.7	35.4	88.4

\+ 1 m distance is defined as "no in-crop buffer zone"

* BBA drift values (1 application, field crops), see Terr. Guidance Doc. SANCO/10329/2002 rev 2 final

[a] TER values not meeting the trigger are marked in bold

[6] 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.

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

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

Table 10.6- 4: Deterministic off-crop risk assessment for non-target terrestrial plants: vegetative vigour

cereals, one applications, lowest ER_{50} = 192.6 mL/ha (sugar beet)						
Distance+ [m]	Drift* (%)	PEC no drift reduction [mL/ha]	TER			
			No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
1	2.77	13.85	13.9	27.8	55.6	139.1
5	0.57	2.85	67.6	135.2	270.3	675.8

\+ 1 m distance is defined as "no in-crop buffer zone"

* BBA drift values (1 application, field crops), see Terr. Guidance Doc. SANCO/10329/2002 rev. 2 final

Based on these deterministic risk assessments, according to EU requirements the risk for non-target terrestrial plants is considered acceptable. Based on seedling emergence exposure a 5 m buffer zone is required or 75% drift reducing nozzles are needed in order to guarantee safe use to non-target plants when the product is applied at the application rates recommended according to good agricultural practice.

Probabilistic approach for non-target terrestrial plants

Taking into account that fact that ten species have been tested, a deterministic risk assessment based on the lowest endpoint is highly over-conservative. The probabilistic risk assessment considers the species sensitivity distribution based on the results of all ten species tested.

SANCO/10329/2002 states "If the EC_x 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, a TER of 1 is sufficient to prove safe use.

The HC_5 (the concentration below which less than 5% of species will be harmed above the 50%-level) was calculated from the datasets of EC_{50}-growth inhibition-levels.

The HC_5 is calculated according to the following equation (Aldenberg, T. & Jaworska, J.S.; 2000[9]):

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

with

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

Although there is no common agreement whether to exclude "greater-than"- figures from the HC5-calculation or to include them as "equal to"-figures, the exclusion of "greater than"-figures can be regarded as a very conservative approach. Moreover, it has to be decided, whether the HC5 is calculated with ER50 for dry weight only (the lowest endpoint in most species) or with the lowest ER50.

[9] [redacted], J.S.; 2000: Uncertainty of the hazardous concentration and fraction affected for normal species sensitivity distributions. Ecotoxicology and Environmental Safety 46: 1-18 (M-047079-01-1)

Table 10.6-5 HC5-figures obtained from different calculation modes for seedling-emergence and vegetative vigour. Lowest figures are printed in bold

HC5	Seedling emergence	Vegetative vigour
HC5 based on dry weight data from all species	22.802	295.4
HC5 based on dry weight data after exclusion of greater-than-figures	21.985	167.0
HC5 based on lowest endpoint from all species	19.799	295.4 *
HC5 based on lowest endpoint from all species after exclusion of greater-than-figures	**18.041**	167.0 *

* figures same as for dry weight, since the dryweight-ER50 was the lowest endpoint for all species

Based the calculations presented in Table 10.6.-5 the lowest HC5 levels were taken as a most conservative approach. The following probabilistic risk assessment has been conducted with the seedling-emergence data only, since the HC5 is considerably lower than for vegetative vigour.
The TER calculation is summarised in the following table.

Table 10.6- 6: Probabilistic off-crop risk assessment for non-target terrestrial plants: seedling emergence

cereals, one application, 500 mL product/ha; mean HC_5 = 18.041 mL/ha						
Distance + [m]	Drift * (%)	PEC no drift reduction [mL/ha]	TER [a]			
			No drift reduction	50% drift reduction	75% drift reduction	90% drift reduction
1	2.77	13.85	1.30	2.61	5.21	13.03
5	0.57	2.85	6.33	12.66	25.32	63.30

\+ 1 m distance is defined as "no buffer zone"
* BBA drift values 1 application, field crops, see Terr. Guidance Doc. SANCO/10329/2002 rev 2 final
[a] TER values not meeting the trigger are marked in bold, a trigger 1 is used for HC_5

Based on the probabilistic risk assessment, according to EU requirements the risk for non-target terrestrial plants is considered acceptable with no buffer zone or drift reducing spraying equipment.

CP 10.6.1 - Summary of screening data

No new studies are necessary.

CP 10.6.2 - Testing on non-target plants

Vegetative vigour and seedling emergence studies have been conducted and are summarized in the MCA:

Report: **KCA 8.6.2/01; [redacted] K. & [redacted] H.; 2005**
Title: Diflufenican and flurtamone (AE F088657 01 SC31 A202)
Effects on ten species of non-target terrestrial plants: vegetative vigour test (Tier 2)
Document No: M-251319-01-1
Guidelines: OECD 208 B (July 2000, draft)
GLP: Yes (certified laboratory)

Report: **KCA 8.6.2/02; [redacted] K. & [redacted] H.; 2005**

Title: Diflufenican and flurtamone (AE F088657 01 SC31 A202) Effects on ten species of non-target terrestrial plants: seedling emergence and growth test (Tier 2)
Document No: M-251318-01-1
Guidelines: OECD 208 a (July 2000, draft)
GLP: Yes (certified laboratory)

CP 10.6.3 - Extended laboratory studies on non-target plants

These studies are not considered necessary.

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

These studies are not considered necessary.

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

These studies are not considered necessary.

10.8 - Monitoring data

There is no need for any ecotoxicological monitoring studies for this formulation.