Document Title

Summary of the ecotoxicological studies for Fosetyl-aluminium + Fluopicolide WG 71.11 (666.7 + 44.4 g/kg)

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

2016-11-14

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Bayer CropScience

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Version history

Date (yyyy-mm-dd)	Data points containing amendments or additions[1] and brief description	Document identifier and version number
2015-10-05	Original Document MCP – Section 10 of Supplementary Dossier	M-534861-02-1
2016-07-20	Dossier update according to "Request for additional information on the supplementary dossier submitted by Bayer CropScience for the approval renewal of the active substance Fosetyl (2015-5865)" by RMS France on 2016-04-04 and its follow up on 2016-06-02: - BCS responses to RMS requests have been added throughout Section 10. - All relevant BBCH stages for the Tier 1 risk assessments for birds have been added to Table 10.1.1- 4 and Table 10.1.1- 6. - The LC_{50} value for the formulation FEA + FLC WG 71.11 for *Daphnia magna* has been corrected in Table 10.2- 1 from > 25 mg product/L to > 100 mg product/L. - Endpoints from study [redacted] U.S.; 1988; M-163531-01-1, KCA 8.2.6.2/01, added to Table 10.2- 1.	M-534861-03-1
2016-09-01	Dossier update according to "Request for additional information on the supplementary dossier submitted by Bayer CropScience for the approval renewal of the active substance Fosetyl (2015-5865)" by RMS France on 2016-07-27: - New risk assessments for aquatic organisms have been added to chapter CP 10.2.	M-534861-04-1
2016-11-14	Dossier update according to "Request for additional information on the supplementary dossier submitted by Bayer CropScience for the approval renewal of the active substance Fosetyl (2015-5865)" by RMS France on 2016-11-14: - Addition of new earthworm reproduction study [redacted]=; 2016; M-566335-01-1 (formulation mixed into soil) to chapter CP 10.4.1.4 as well as to Table 10.4.1- 1 and Table 10.4.1- 2.	M-534861-05-1

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

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CP 10 ECOTOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCT

Fosetyl was included in Annex I to Directive 91/414/EEC in 2006 (Directive 2006/64/CE of 18 July 2006, Entry into Force on 1 May 2007). This Supplementary Dossier contains only data which were not submitted at the time of the Annex I inclusion of fosetyl under Directive 91/414/EEC and which were therefore not evaluated during the first EU review. All data which were already submitted by Bayer CropScience (BCS) for the Annex I inclusion under Directive 91/414/EEC are contained in the DAR, its Addenda and are included in the Baseline Dossier provided by BCS. These data are only mentioned in the Supplementary Dossier for the sake of completeness and only general information (e.g. author, reference etc.) is available for these data. In order to facilitate discrimination between new data and data submitted during the Annex I inclusion process under Directive 91/414/EEC, the old data are written in grey typeface. For all new studies, detailed summaries are provided within this Supplementary Dossier. However, for a better understanding of the ecotoxicological behaviour of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11), short summaries including the results of all studies are given at the beginning of the relevant sections. Additional information requested by the RMS France on 2016-04-04 and its follow up on 2016-06-02 during the evaluation of the Supplementary Dossier is highlighted in yellow. Additional information requested by the RMS France on 2016-07-27 as follow up of the requests of 2016-04-04 and 2016-06-02 during the evaluation of the Supplementary Dossier is highlighted in green. Additional information requested by the RMS France on 2016-11-14 during the evaluation of the Supplementary Dossier is highlighted in grey.

Fosetyl is the ISO common name for ethyl hydrogen phosphonate (IUPAC) but the aluminium salt fosetyl-aluminium (fosetyl-Al), a variant of fosetyl, is used in the formulated product.

In original reports study authors may have used different names or codes for metabolites of fosetyl-Al. In this summary, a single name or a single code is used for each metabolite. A full list containing structural formula, various names, short forms, codes and occurrences of metabolites is provided as Document N3.

As some pragmatic approach "phosphonic acid" formed as a major metabolite is reported in this Supplementary Dossier as the free acid for the sake of clarity and unequivocal handling. After application, aluminium tris-O-ethyl phosphonate (i.e. fosetyl-Al) dissociates into the O-ethyl phosphonate and aluminium ions. Any phosphonate formed from O-ethyl phosphonate in the following would never be present in the form of the free acid (i.e. phosphonic acid) under the conditions of the environment (pH 4 to 9). This conclusion is supported by the molecular structure and by the dissociation constant observed (dissociation constant for the first step of deprotonation: pKa = 2.0). Consequently phosphonates in their fully protonated form are strong acids that spontaneously form salts in contact with soil or natural water with any suitable counter ion present (i.e. sodium, potassium, magnesium, calcium). With the ability to readily form salts in the environment phosphonates are, in terms of their acidic or alkaline character, similar to the salts of phosphoric acid (i.e. phosphates) in their environmental behaviour.

The formulation FEA + FLC WG 71.11 is a water dispersible granule (WG) formulation containing 666.7 g/kg of fosetyl-Al and 44.4 g/kg of fluopicolide. This formulation is registered throughout Europe under trade names such as Profiler. FEA + FLC WG 71.11 was not a representative formulation for the Annex I inclusion of fosetyl under Directive 91/414/EEC but has been evaluated as the representative formulation for the Annex I inclusion of fluopicolide under Directive 91/414/EEC. As FEA + FLC WG 71.11 is a representative formulation for the approval renewal of fosetyl, only the ecotoxicological risk assessment for this active substance will be described.

Use pattern considered in this risk assessment

Table 10- 1: Intended application pattern

Crop	Timing of application (range)	Number of applications	Application interval [days]	Maximum label rate [kg prod./ha]	Maximum application rate, individual treatment (ranges) [kg a.s./ha]	
					Fluopicolide	Fosetyl-Al
Grapes	BBCH 15-81	1-3	10-14	3.0	0.133	2.0

Definition of the residue for risk assessment

Justification for the residue definition for risk assessment is provided in Document MCA, Section 7.4.1.

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

Compartment	Residue Definition
Soil	Fosetyl-Al, phosphonic acid
Surface water	Fosetyl-Al, phosphonic acid
Sediment	Phosphonic acid
Groundwater	Fosetyl-Al, phosphonic acid
Air	Fosetyl-Al

CP 10.1 Effects on birds and other terrestrial vertebrates

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

CP 10.1.1 Effects on birds

Table 10.1.1- 1: Endpoints used in risk assessment

Test substance	Test design	Test species	Endpoint		Reference
Fosetyl-Al	acute toxicity	Bobwhite quail	LD_{50}	> 8000 mg a.s./kg bw [a)]	[redacted], N. L.; [redacted], C. N. K.; 1981; M-159690-01-1 KCA 8.1.1.1/01
	acute toxicity	Japanese quail	LD_{50}	4997 mg a.s./kg bw	[redacted], D. B.; [redacted], D. M.; [redacted], N. L.; 1977; M-158803-01-1 KCA 8.1.1.1/02
	acute toxicity	Bobwhite quail	LD_{50}	> 2000 mg a.s./kg bw ≡ 3228 mg a.s./kg bw [b)]	[redacted], T. L.; [redacted], M. T.; 2012; M-444760-01-1 KCA 8.1.1.1/04
	geomean LD_{50}	**Bobwhite quail**	**8000 mg a.s./kg bw**	**5082 mg a.s./kg bw**	**5039 mg a.s./kg bw**
			3228 mg a.s./kg bw		
		Japanese quail	**4997 mg a.s./kg bw**	**4997 mg a.s./kg bw**	
	dietary toxicity (short-term)	Bobwhite quail	LC_{50} LDD_{50}	> 20000 mg a.s./kg diet > 3122 mg a.s./kg bw/d	[redacted], N. L.; [redacted], C. N. K.; [redacted], R. H.; 1982; M-159687-01-1 KCA 8.1.1.2/01
	dietary toxicity (short-term)	Mallard duck	LC_{50} LDD_{50}	> 20000 mg a.s./kg diet > 4616 mg a.s./kg bw/d	[redacted], N. L.; [redacted], C. N. K.; [redacted], R. H.; 1981; M-159685-01-1 KCA 8.1.1.2/02
	6-weeks feeding chronic, reproduction	Japanese quail	NOEC NOEL	1500 mg a.s./kg diet 216 mg a.s./kg bw/d	[redacted], S. P.; [redacted], M.; [redacted], J. B.; 1999; M-189216-01-1 KCA 8.1.1.3/01
	7-weeks feeding chronic, reproduction	Japanese quail	NOEC **NOEL**	≥ 3000 mg a.s./kg diet **≥ 331 mg a.s./kg bw/d**	[redacted], R.; 2008; M-298080-01-1 KCA 8.1.1.3/02
	LD_{50} / 10	geomean LD_{50}	5039 / 10 = 503.9 mg a.s./kg bw		

Test substance	Test design	Test species	Endpoint		Reference
Phosphonic acid	acute toxicity	Bobwhite quail	LD_{50} LD_{50}	> 2250 mg test item/kg bw > 675 mg pm/kg bw	[redacted], S. M.; [redacted], J. B.; 1995; M-200039-01-1 KCA 8.1.1/03
	dietary toxicity (short-term)	Bobwhite quail	LC_{50} LC_{50} LDD_{50}	> 5620 mg test item/kg diet > 1692 mg pm/kg diet [c)] > 508 mg pm/kg bw/d	[redacted], S. J.; [redacted], S. M.; [redacted], J. B.; 1995; M-200041-01-1 KCA 8.1.2/03

Bold: endpoints used in risk assessment
pm = pure metabolite

a) 3 mortalities from 10 birds tested at 8000 mg/kg bw, therefore extrapolation factors (EFSA GD 2009; Table 1) not applicable. Included as LD_{50} = 8000 mg/kg bw into the calculation of geomean LD_{50} values.

b) no mortalities among the 5 birds tested at 2000 mg/kg bw, therefore extrapolation factor of 1.614 (EFSA GD 2009; Table 1) applicable: 2000 x 1.614 = 3228 mg/kg bw

c) Values were corrected for a purity of 41% phosphonic acid weight by volume which is equal to 30.1% weight by weight. Test substance potassium salts of phosphonic acid has a density of 1.36. Therefore, one L of test substance weighs 1360 g and contains 410 g phosphonic acid (410/1360 = 0.301) with a weight/weight purity of 30.1%.

Request from the RMS:

The calculation of an extrapolate LD_{50} value and the calculation of an LD_{50} based on the geometrical mean of the endpoints from several species are two methods indicated in the guidance document EFSA/2009/1438 for the determination of the relevant toxicity value for the acute TER estimation. However, the guidance document does not indicate if both methods could be combined. It is the RMS opinion that both methods should not be combined as the combination of these extrapolations would induce too much uncertainty in the obtained endpoint. The reliable toxicity value for acute is the LD_{50} of 4997 mg a.s./kg b.w.

Response from BCS:

According to the EFSA Guidance document, the geometric mean LD_{50} is a fully valid approach to assess the acute toxicity endpoint, appropriately maintaining the level of protection. In order to correctly calculate statistics like the geometric mean, unbound values should be avoided. Therefore it is necessary and appropriate to apply the very conservative extrapolation factor recommended in the EFSA GD to "LD_{50} > x" values before inclusion into the geomean. In the view of the notifier, it is therefore not to be expected that the combination of the two methods would unduly increase the uncertainty of the acute risk assessment estimate.

Request from the RMS:

In accordance with the guidance document EFSA (2009), a justification that no mortality or no clinical signs were observed during the test should be provided to exclude the dietary endpoint from the acute TER calculations. Please provide such justification.

Response from BCS:

In the Mallard duck short term dietary study with fosetyl-aluminium (fosetyl-Al), no mortalities or clinical signs were reported for the birds treated with fosetyl-Al. In the Bobwhite quail short term dietary study, no clinical signs were observed and a single mortality was observed among the birds receiving 20000 ppm of fosetyl-Al. However, this single mortality occurred on day 6 of testing, and at the same time one mortality also occurred in the untreated controls. Therefore it is questionable whether this single mortality at 20000 ppm is actually a treatment related effect, and with regard to the time course certainly not appropriate for the use in an acute risk assessment which addresses a single

day of exposure.

Request from the RMS:

A justification that no risk assessment is required for the metabolite phosphonic acid would be suitable.

Response from BCS:

The toxicity of phosphonic acid, the major metabolite of fosetyl-Al, has been evaluated in birds. Due to the absence of notable toxicity of phosphonic acid (no mortalities or treatment related effects have been found up to the highest doses tested), a quantitative risk assessment is not considered necessary.

Table 10.1.1- 2: Toxicity data of the formulated product FEA + FLC WG 71.11

Test species	Test design	Endpoint	Reference
Bobwhite quail	acute, oral	LD_{50} > 2000 mg product/kg bw	[redacted]E; [redacted], 2014; M-479470-01-1 KCP 10.1.1.1/01

Table 10.1.1- 3: Relevant generic avian focal species for risk assessment on Tier 1 level according to EFSA GD (2009)

Crop scenario	Most critical window of relevance for generic focal species scenario	Generic focal species	Representative species	Short cut values for reproductive RA based on RUD_{90}	Short cut values for reproductive RA based on RUD_m
Grapes 3 × 2.0 kg/ha BBCH 15-81 10d interval	BBCH 10-19	Small insectivorous species "redstart"	Black Redstart	**27.4**	**11.5**
	BBCH ≥ 20	Small insectivorous species "redstart"	Black Redstart	25.7	9.9
	BBCH 10-19	Small granivorous bird "finch"	Linnet	**14.8**	**6.9**
	BBCH 20-39	Small granivorous bird "finch"	Linnet	12.4	5.7
	BBCH ≥ 40	Small granivorous bird "finch"	Linnet	7.4	3.4
	Ripening	Frugivorous bird "thrush/starling"	Song Thrush	**28.9**	**14.4**
	BBCH 10-19	Small omnivorous bird "lark"	Wood Lark	**14.4**	**6.5**
	BBCH 20-39	Small omnivorous bird "lark"	Wood Lark	12	5.4
	BBCH ≥ 40	Small omnivorous bird "lark"	Wood Lark	7.2	3.3

Bold values: worst case shortcut values used in risk assessment

ACUTE DIETARY RISK ASSESSMENT

Request from the RMS:
All the relevant scenario covering all the application period (BBCH 15-81) should be presented for the Tier 1 risk assessment.

Table 10.1.1- 4: Tier 1 acute risk assessment for birds

Crop scenario	Generic focal species	DDD			DDD	LD_{50} [mg a.s./kg bw]	TER_A	Trigger
		Appl. rate [kg a.s./ha]	SV_{90}	MAF_{90}				
Fosetyl-Al								
Grapes BBCH 10-19	Small insectivorous species "redstart"	2.0	27.4	1.5	82.2	5039	61	10
Grapes BBCH ≥ 20	Small insectivorous species "redstart"		25.7		77.1		65	
Grapes BBCH 10-19	Small granivorous bird "finch"		14.8		44.4		113	
Grapes BBCH 20-39	Small granivorous bird "finch"		12.4		37.2		136	
Grapes BBCH ≥ 40	Small granivorous bird "finch"		7.4		22.2		227	
Grapes Ripening	Frugivorous bird "thrush/starling"		28.9		86.7		58	
Grapes BBCH 10-19	Small omnivorous bird "lark"		14.4		43.2		117	
Grapes BBCH 20-39	Small omnivorous bird "lark"		12.0		36.0		140	
Grapes BBCH ≥ 40	Small omnivorous bird "lark"		7.2		21.6		223	

The TER_A values calculated in the acute risk assessment on Tier 1 level exceed the a-priori-acceptability trigger of 10 for all evaluated scenarios. Thus, the acute risk to birds can be considered as low and acceptable without need for further, more realistic risk assessment.

Acute risk assessment for birds drinking contaminated water from pools in leaf whorls
In the EFSA GD (2009), section 5.5, step 1 the following guidance is given on the selection of relevant scenarios for assessing the risk of pesticides via drinking water to birds and mammals:

- Leaf scenario: Birds taking water that is collected in leaf whorls after application of a pesticide to a crop and subsequent rainfall or irrigation.
- 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.

For the crops under assessment in this evaluation (grapes) the leaf scenario is not considered relevant. The risk for birds from drinking water in puddles is addressed in Table 10.1.1- 5.

Acute risk assessment for birds drinking contaminated water in puddles

Table 10.1.1- 5: Evaluation of potential concern for exposure of birds drinking water

Crop	K_{oc} [L/kg]	Application rate × MAF_m [g a.s./ha]	LD_{50} [mg a.s./ kg bw/d]	Ratio (Application rate × MAF) / LD_{50}	"Escape clause" No concern if ratio	Conclusion
Fosetyl-Al						
Grapes	0.1	2000 × 1.0 = 2000	5039	0.4	**≤ 50**	No concern

LONG-TERM REPRODUCTIVE ASSESSMENT

Request from the RMS:
All the relevant scenario covering all the application period (BBCH 15-81) should be presented for the Tier 1 risk assessment.

Table 10.1.1- 6: Tier 1 reproductive risk assessment for birds

Crop	Generic focal species	DDD Appl. rate [kg a.s./ha]	DDD SV_m	DDD MAF_m	DDD f_{TWA}	DDD	NOAEL [mg a.s./ kg bw/d]	TER_{LT}	Trigger
Fosetyl-Al									
Grapes BBCH 10-19	Small insectivorous species "redstart"	2.0	11.5	1.8	0.53	21.9	≥ 331	≥ 15.1	5
Grapes BBCH ≥ 20	Small insectivorous species "redstart"		9.9			18.9		≥ 17.5	
Grapes BBCH 10-19	Small granivorous bird "finch"		6.9			13.2		≥ 25.1	
Grapes BBCH 20-39	Small granivorous bird "finch"		5.7			10.9		≥ 30.4	
Grapes BBCH ≥ 40	Small granivorous bird "finch"		3.4			6.5		≥ 51.0	
Grapes Ripening	Frugivorous bird "thrush/starling"		14.4			27.5		≥ 12.0	
Grapes BBCH 10-19	Small omnivorous bird "lark"		6.4			12.4		≥ 26.7	
Grapes BBCH 20-39	Small omnivorous bird "lark"		5.4			10.3		≥ 32.1	
Grapes BBCH ≥ 40	Small omnivorous bird "lark"		3.3			6.3		≥ 52.6	

The TER_{LT} values calculated in the reproductive risk assessment on Tier 1 level exceed the a-priori-acceptability trigger of 5 for all evaluated scenarios. Thus, the reproductive risk to birds can be considered as low and acceptable without need for further, more realistic risk assessment.

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

Table 10.1.1- 7: Evaluation of potential concern for exposure of birds drinking water

Crop	K_{oc} [L/kg]	Application rate × MAF_m [g a.s./ha]	NO(A)EL [mg a.s./ kg bw/d]	Ratio (Application rate × MAF) / NO(A)EL	"Escape clause" No concern if ratio	Conclusion
Fosetyl-Al						
Grapes	0.1	2000 × 1.0 = 2000	≥ 331	≤ 6.0	**≤ 50**	No concern

RISK ASSESSMENT OF SECONDARY POISONING

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

Table 10.1.1- 8: Log P_{ow} values of fosetyl-Al and its metabolite

Substance	log P_{ow}	Reference
Fosetyl-Al	- 2.1 (pH 6)	Document MCA, Section 2.7 EFSA Scientific Report 54 (2005)
Phosphonic acid - H_3PO_3	- 4.96 (pH 5)	Document MCA, Section 2.7

The log P_{ow} values of fosetyl-Al and phosphonic acid are below the trigger value of 3, indicating a very low risk of secondary poisoning.

CP 10.1.1.1 Acute oral toxicity

Report: KCP 10.1.1.1/01; [redacted]E.; [redacted]; 2014; M-479470-01-1
Title: Toxicity of fluopicolide + fosetyl-Al WG 2.22+33.34 percent w/w during an acute oral LD50 with the northern bobwhite quail (Colinus virginianus)
Report No.: 7SRLS14C6
Document No.: M-479470-01-1
Guideline(s): EU Directive 91/414/EEC
Regulation (EC) No. 1107/2009
OECD 223, OCSPP 850.2100
Guideline deviation(s): none
GLP/GEP: **yes**

Objective:
An acute oral toxicity test was conducted to estimate the LD_{50} of Fosetyl-aluminium + Fluopicolide WG 33.34 + 2.22% w/w (FEA + FLC WG 71.11) to the Northern Bobwhite Quail (*Colinus virginianus*).

Material and Methods:
Test item: FEA + FLC WG 71.11 (Fosetyl-aluminium + Fluopicolide WG 33.34 + 2.22% w/w; Batch ID: EV36002902; Sample Description: TOX09816-00; Material No.: 79975694; Purity: 67.7% w/w (fosetyl-al); 4.30% w/w (fluopicolide); Specification No.: 102000024700 – 01).

Northern Bobwhite quail (22-week-old adults) were orally dosed with FEA + FLC WG 71.11 based on body weight at a limit dose level of 2000 mg product/kg body weight. A control group was run in parallel. Five birds per treatment level (two males and three females) were randomized by body weight into the treatment level and control group on experimental Day -1. Birds were dosed with gelatin capsules on Day 0 following 15 hours of starvation and monitored for 14 days post-dosing. All feed and water was provided ad libitum. Adult body weights were taken on experimental Day -1, Day 3, Day 7, and Day 14. Individual feed consumption was recorded for the first three days of the study and then for the Day 7 to 14 interval. Clinical observations occurred at least daily. Post-mortem examinations were conducted on all birds sacrificed at study termination.

Dates of experimental work: February 04, 2014 – February 18, 2014

Results:

Mortality & Clinical Observations

No mortality occurred in the control or the 2000 mg product/kg body weight treatment group. There were no observed effects in the control or 2000 mg product/kg body weight treatment groups during the study.

Body Weight & Feed Consumption

Body weight measurements (Day 0, Day 3, Day 7, and Day 14) and changes in body were evaluated for each treatment group. Body weight measurements and changes in body weight between the time points listed above for the 2000 mg/kg treatment group was not significantly different from the control group.

No significant differences were observed in daily food consumption between the control and 2000 mg/kg treatment groups.

Conclusion:

The acute oral LD_{50} for FEA + FLC WG 71.11 in the northern bobwhite quail was >2000 mg product/kg body weight. The Lowest Lethal Dose was >2000 mg product/kg body weight.

CP 10.1.1.2 Higher tier data on birds

In view of the results presented in Section CP 10.1.1.1, no further studies were necessary.

CP 10.1.2 Effects on terrestrial vertebrates other than birds

Table 10.1.2- 1: Endpoints used in risk assessment

Test substance	Exposure	Species	Endpoint		Reference
Fosetyl-Al	Acute risk assessment	Rat	LD_{50}	>7080 mg a.s./kg bw	[redacted], I.; 1997; M-179086-01-1 KCA 5.2.1/01
	Long-term risk assessment	Rat	NOAEL	6000 ppm ≡ 439 mg a.s./kg bw/d	[redacted] A.K.; [redacted] A.M.; [redacted] S.J.; [redacted], R.; [redacted] J.M.; [redacted] A.J.; [redacted] R.N.; [redacted] A.E.; 1981; M-203019-01-1 KCA 5.6.1/01
			NOAEL	6000 ppm ≡ 720 mg/kg bw/d [a]	

[a] please refer to Document MCA, Section 8.1.2.2

Request from the RMS:
A justification that no risk assessment is required for the metabolite phosphonic acid would be suitable.

Response from BCS:
Phosphonic acid is a confirmed mammalian metabolite of fosetyl-aluminium (fosetyl-Al) and its toxicity was accounted for in the acute and long term studies with fosetyl-Al in mammals. Therefore, the mammalian risk assessment for fosetyl-Al also adequately addresses the risk for the phosphonic acid.

Table 10.1.2- 2: Relevant generic focal species for risk assessment on Tier 1 level acc. to EFSA GD (2009)

Crop scenario	Most critical window of relevance for generic focal species scenario	Generic focal species	Representative species	Short cut values for reproductive RA based on RUD_{90} / RUD_{m}	
Grapes 3 × 2.0 kg/ha BBCH 15-81 10d interval	BBCH 10-19	Large herbivorous mammal "lagomorph"	Brown hare	**16.3**	**6.7**
	BBCH 20-39	Large herbivorous mammal "lagomorph"	Brown hare	13.6	5.5
	BBCH ≥ 40	Large herbivorous mammal "lagomorph"	Brown hare	8.1	3.3
	BBCH 10-19	Small insectivorous mammal "shrew"	Common shrew	**7.6**	**4.2**
	BBCH ≥ 20	Small insectivorous mammal "shrew"	Common shrew	5.4	1.9
	Application crop directed BBCH 10-19	Small herbivorous mammal "vole"	Common vole	**81.9**	**43.4**
	Application crop directed BBCH 20-39	Small herbivorous mammal "vole"	Common vole	68.2	36.1
	Application crop directed BBCH ≥ 40	Small herbivorous mammal "vole"	Common vole	40.9	21.7
	Application crop directed BBCH 10-19	Small omnivorous mammal "mouse"	Wood mouse	**10.3**	**4.7**
	Application crop directed BBCH 20-39	Small omnivorous mammal "mouse"	Wood mouse	8.6	3.9
	Application crop directed BBCH ≥ 40	Small omnivorous mammal "mouse"	Wood mouse	5.2	2.3

ACUTE DIETARY RISK ASSESSMENT

Table 10.1.2- 3: Tier 1 acute risk assessment for wild mammals

Crop	Generic focal species	DDD			DDD	LD_{50} [mg a.s./kg bw]	TER_A	Trigger
		Appl. rate [kg a.s./ha]	SV_{90}	MAF_{90}				
Fosetyl-Al								
Grapes BBCH 10-19	Large herbivorous mammal "lagomorph"	2.0	16.3	1.5	48.9	> 7080	> 145	10
Grapes BBCH 10-19	Small insectivorous mammal "shrew"		7.6		22.8		> 311	
Grapes crop directed BBCH 10-19	Small herbivorous mammal "vole"		81.9		245.7		> 246	
Grapes crop directed BBCH 10-19	Small omnivorous mammal "mouse"		10.3		30.9		> 31	

The TER_A values calculated in the acute risk assessment on Tier 1 level for wild mammals exceed the a-priori-acceptability trigger of 10 for all evaluated scenarios. Thus, the acute risk to wild mammals can be considered as low and acceptable without need for further, more realistic risk assessment.

Acute risk assessment for mammals drinking contaminated water

The puddle scenario is relevant for the acute risk assessment.

Table 10.1.2- 4: Evaluation of potential concern for exposure of mammals drinking water

Crop	K_{oc} [L/kg]	Application rate * MAF [g a.s./ha]	LD_{50} [mg a.s./ kg bw/d]	Ratio (Application rate * MAF) / LD_{50})	"Escape clause" No concern if ratio	Conclusion
Fosetyl-Al						
Grapes	0-1	2000 × 1.0 = 2000	7080	< 0.3	**≤ 50**	No concern

LONG-TERM REPRODUCTIVE ASSESSMENT

Table 10.1.2- 5: Tier 1 reproductive risk assessment for wild mammals

Crop	Generic focal species	DDD				DDD	NOAEL [mg a.s./kg bw/d]	TER_{LT}	Trigger
		Appl. rate [kg a.s./ha]	SV_m	MAF_m	f_{TWA}				
Fosetyl-Al									
Grapes BBCH 10-19	Large herbivorous mammal "lagomorph"	2.0	6.7	1.8	0.53	12.8	720	56	5
Grapes BBCH 10-19	Small insectivorous mammal "shrew"		4.2			8.0		90	
Grapes crop directed BBCH 10-19	Small herbivorous mammal "vole"		43.4			82.8		8.7	
Grapes crop directed BBCH 10-19	Small omnivorous mammal "mouse"		4.7			9.0		80	

The TER_{LT} values calculated in the reproductive risk assessment on Tier 1 level for wild mammals exceed the a-priori-acceptability trigger of 5 for all evaluated scenarios. Thus, the long-term risk to wild mammals can be considered as low and acceptable without need for further, more realistic risk assessment.

Long-term risk assessment for mammals drinking contaminated water
The puddle scenario is relevant for the long-term risk assessment.

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

Crop	K_{oc} [L/kg]	Application rate * MAF [g a.s./ha]	NO(A)EL [mg a.s./ kg bw/d]	Ratio (Application rate * MAF) / NO(A)EL)	"Escape clause" No concern if ratio	Conclusion
Fosetyl-Al						
Grapes	0.1	2000 × 1.0 = 2000	720	2.8	**≤ 50**	No concern

RISK ASSESSMENT OF SECONDARY POISONING

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

As presented in Table 10.1.1- 8, log P_{ow} values are below the trigger value indicating a very low risk of secondary poisoning.

CP 10.1.2.1 Acute oral toxicity to mammals

Reference is made to the respective Document MCP, Section 7.1.1.

Table 10.1.2.1- 1: Mammalian toxicity data of the formulated product FEA + FLC WG 71.11

Test species	Test design	Endpoint			Reference
Rat	acute, oral	LD_{50}	> 2000	mg product/kg bw	[redacted]P; 2003; M-220866-01-1 KCP 7.1.1/01

CP 10.1.2.2 Higher tier data on mammals

In view of the results presented above, no further studies were necessary.

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

Information on effects of fosetyl-Al on reptiles or amphibians is not available. No guidelines for studies with terrestrial amphibian life stages and reptiles are available and no risk assessment schemes are established so far. Therefore no further studies can be suggested for these groups of organisms.

CP 10.2 Effects on aquatic organisms

The risk assessment is based on the current guidance: 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.

Risk assessment for aquatic organisms

Ecotoxicological endpoints used in risk assessment

Table 10.2- 1: Endpoints used in risk assessment and additional studies for fosetyl-Al, its metabolite and FEA + FLC WG 71.11

Test substance	Test species	Endpoint		Reference
FEA + FLC WG 71.11	Fish, acute, *Oncorhynchus mykiss*	LC_{50}	8.54 mg product/L (nom)	[redacted],; 2003; M-225113-01-1 KCP 10.2.1/04
	Invertebrate, acute *Daphnia magna*	LC_{50}	> 100 mg product/L (nom)	[redacted],; 2003; M-227282-01-1 KCP 10.2.1/01
	Algae, growth inhibition *Pseudokirchneriella subcapitata*	E_bC_{50} E_rC_{50}	3.9 mg product/L (nom) 12.5 mg product/L (nom)	[redacted]Z; 2003; M-227291-01-1 KCP 10.2.1/03
	Navicula pelliculosa (diatom), growth inhibition test	E_bC_{50} E_rC_{50}	0.58 mg product/L (nom) 0.91 mg product/L (nom)	[redacted],; 2003; M-227285-01-1, KCP 10.2.1/02

Test substance	Test species	Endpoint		Reference
Fosetyl-Al	Fish, acute *Lepomis macrochirus*	**LC_{50}**	**> 60 mg a.s./L (mm)**	[redacted], P. M.; 1997; M-184477-01-1 KCA 8.2.1/02
	Fish, acute *Oncorhynchus mykiss*	LC_{50}	> 122 mg a.s./L (mm)	[redacted], G.; 1999; M-189219-01-1 KCA 8.2.1/01
	Fish, acute *Cyprinus carpio*	LC_{50}	> 100 mg a.s./L (nom)	[redacted], E.; 2013; M-449083-01-1 KCA 8.2.1/05
	Fish, chronic *Oncorhynchus mykiss*	NOEC	≥ 100 mg a.s./L (nom)	[redacted], P. M.; 1997; M-184572-01-1 KCA 8.2.2.2/01
	Fish, chronic *Pimephales promelas*	**NOEC**	**0.213 mg a.s./L (nom)**	[redacted], D.; [redacted], K.; 2015; M-531353-01-1 KCA 8.2.2.1/01
	Invertebrate, acute *Daphnia magna*	**EC_{50}**	**> 100 mg a.s./L (nom)**	[redacted], I. G.; 1996; M-170914-01-1 KCA 8.2.4.1/01
	Invertebrate, chronic *Daphnia magna*	**NOEC**	**17 mg a.s./L (mm)**	[redacted], I. G.; 1996; M-189214-01-1 KCA 8.2.5.1/01
	Algae *Desmodesmus subspicatus* (*Scenedesmus subspicatus*, green algae)	E_bC_{50} E_rC_{50}	5.9 mg a.s./L (mm) > 16 mg a.s./L (mm)	[redacted], G.; 1999; M-189220-01-1 KCA 8.2.6.1/01
	Algae *Pseudokirchneriella subcapitata* (*Selenastrum capricornutum*, green algae)	7d-E_dC_{50} **72h-E_rC_{50}**	4.99 mg a.s./L (mm) recalculation **9.54 mg a.s./L (mm)**	[redacted], J. S.; 1989; M-163526-01-1 KCA 8.2.6.1/03 [redacted], M.; 2005; M-253825-01-1 KCA 8.2.6.1/04
	Algae *Desmodesmus subspicatus* (*Scenedesmus subspicatus*, green algae)	E_bC_{50} E_rC_{50}	24.9 mg a.s./L (nom) 43.3 mg a.s./L (nom)	[redacted], M.; 2007; M-289324-01-1 KCA 8.2.6.1/05
	Algae *Navicula pelliculosa* (diatom)	7d-E_dC_{50} 72h-E_rC_{50}	8.93 mg a.s./L (mm) recalculation 18.11 mg a.s./L (mm)	[redacted], J.S.; 1988; M-163531-01-1 KCA 8.2.6.2/01
	Aquatic plant *Lemna gibba*	14d-E_yC_{50} **7d-E_rC_{50}**	79.67 mg a.s./L (mm) recalculation: **166.6 mg a.s./L (mm)**	[redacted], J. S.; 1989; M-163537-02-1 KCA 8.2.7/01 [redacted], C.; 2015; M-525565-01-1 KCA 8.2.7/02

Test substance	Test species	Endpoint		Reference
Phosphonic acid	Fish, acute, *Oncorhynchus mykiss*	LC_{50}	> 28.6 mg pm/L (mm) a)	[redacted], J. W.; [redacted], H. J.; 1994; M-179069-01-1 KCA 8.2.1/03
	Fish, acute, *Oncorhynchus mykiss*	**LC_{50}**	**> 400 mg pm/L (nom)**	[redacted], M.; 2008; M-310496-01-1 KCA 8.2.1/06
	Fish, acute *Lepomis macrochirus*	LC_{50}	> 35.7 mg pm/L (nom) b)	[redacted], M.; 1999; M-171840-01-1 KCA 8.2.1/04
	Invertebrate, acute *Daphnia magna*	EC_{50}	> 29.7 mg pm/L (mm) a)	[redacted], J. W.; [redacted], H. J.; 1994; M-179068-01-1 KCA 8.2.4.1/02
	Invertebrate, acute *Daphnia magna*	**EC_{50}**	**> 400 mg pm/L (nom)**	[redacted], M.; 2008; M-310318-01-1 KCA 8.2.4.1/03
	Sediment dweller *Chironomus riparius*	**NOEC**	**> 100.2 mg pm/L (nom)** b)	[redacted]-[redacted], M.; 1999; M-171912-01-1 KCA 8.2.5.4/01
	Algae *Pseudokirchneriella subcapitata* (*Selenastrum capricornutum*, green algae)	E_bC_{50} **E_rC_{50}**	8.6 mg pm/L (nom) b) **29.4 mg pm/L (nom)** b)	[redacted], M. J.; [redacted], M.; [redacted], D.; 1999; M-171844-01-1 KCA 8.2.6.1/02

Bold: endpoints used in risk assessment
a.s. = active substance, pm = pure metabolite
mm = mean measured; nom = nominal

a) Values were corrected for a purity of 41% phosphonic acid weight by volume which is equal to 29.7% weight by weight. Test substance potassium salts of phosphonic acid has a density of 1.38. Therefore, one L of test substance weighs 1380 g and contains 410 g phosphonic acid (410/1380 = 0.297) with a weight/weight purity of 29.7%.

b) Values were corrected for a purity of 40.9% phosphonic acid weight by volume which is equal to 29.7% weight by weight. Test substance potassium salts of phosphonic acid has a density of 1.376. Therefore, one L of test substance weighs 1376 g and contains 409 g phosphonic acid (409/1376 = 0.297) with a weight/weight purity of 29.7%.

Selection of algae and macrophytes endpoints for risk assessment

Processes in ecosystems are dominantly rate driven and therefore, the unit development per time (growth rate) is more suitable to measure effects in algae and macrophytes. Also, growth rates and their inhibition can easily be compared between species, test durations and test conditions, which is not the case for yield or biomass based endpoints. Following current state of science, the test guidelines, OECD TG 201 and 221, the EU-Method C3, the EC regulation for Classification and Labeling (EC regulation 1272/2008), the PPR Opinion (EFSA Journal 461, 1-44; 2007) and also the EFSA Aquatic Guidance Document (AGD, 2013, noted by SCFCAH on July 10-11th, 2014), list growth rate as the relevant endpoint of the algae and the *Lemna* growth inhibition test. The previous Guidance Document on Aquatic Toxicology (SANCO/3268/2001 rev. 4) still stated that "As there is no clear evidence available to indicate which is the most relevant endpoint for the field situation, the lower figure should be used in the risk assessment". As this statement is clearly superseded by recent scientific and regulatory developments toxicity-exposure-ratios in this assessment were based on the E_rC_{50}, when available.

Request from the RMS:
The preparation seems to be more toxic than fosetyl-Al. The toxicity data of the preparation should also be used in the risk assessment (TER estimation for the preparation based on PECsw estimated for the drift of a single application is required).

Response from BCS:
The RMS is right: the formulated product is more toxic than fosetyl-aluminium (fosetyl-Al) active substance. However, this is not due to the intrinsic toxicity of fosetyl-Al but to that of fluopicolide, as shown in the table below.

Comparative acute toxicity of fosetyl-Al (a.s.), fluopicolide (a.s.) and the formulation Fosetyl-Al + Fluopicolide WG 71.11

Test species	Endpoint	Fosetyl-Al (FEA; a.s.)	Fluopicolide (FLC; a.s.)*	FEA 666.7 + FLC 44.4 WG 71.11	Finney´s calculation output
Fish, acute *Oncorhynchus mykiss*	LC_{50}	> 122 mg a.s./L	0.36 mg a.s./L	8.54 mg prod./L (5.694 mg FEA a.s./L; 0.379 mg FLC a.s./L)	- Expected value: 7.76 mg prod./L - Ratio expected to actual: 0.91
Invertebrate, acute *Daphnia magna*	EC_{50}	> 100 mg a.s./L	> 1.8 mg a.s./L	> 100 mg prod./L (> 66.67 mg FEA a.s./L; > 4.44 mg FLC a.s./L)	Not relevant with endpoints "superior to"
Non-green algae growth inhibition test *Navicula pelliculosa* (diatom)	E_rC_{50}	18.11 mg a.s./L**	0.069 mg a.s./L	0.91 mg prod./L (0.607 mg FEA a.s./L; $4.04 \cdot 10^{-5}$ mg FLC a.s./L)	- Expected value: 1.47 mg prod./L - Ratio expected to actual: 1.62

*Endpoints taken from the EFSA Conclusion on the peer review of the pesticide risk assessment of the active substance fluopicolide (EFSA Scientific Report, 2009; 299, 1-158).

**Recalculated over the first 72 hours from [redacted], J. S.; 1988; M-163531-01-1 (please refer to Document MCA, Section CA 8.2.6.2, KCA 8.2.6.2/01) using ToxRatPro Version 2.10@.

When comparisons can be made, it clearly appears that fluopicolide drives the toxicity of the formulation, and this is supported by Finney´s calculations. Therefore, the use of the toxicity data for the formulation is not relevant for the risk assessment of fosetyl-Al, and there is no need to estimate TER for fosetyl-Al for the intended uses of the formulation.

Predicted environmental concentrations used in risk assessment

Table 10.2- 2: Initial max PECsw values – FOCUS Steps 1 and 2

Compound	FOCUS Scenario	Grapes [B] 3 × 2.0 kg a.s./ha, 10 d int., BBCH 15-81	new PEC_{sw} according to RMS request: Grapes [B] 3 × 2.0 kg a.s./ha, 10 days int., BBCH 15-81
		$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]
Fosetyl-Al	STEP 1	720.1	720.1
	STEP 2 – North [A]	53.52	53.52
	STEP 2 - South [A]	53.52	53.52
Phosphonic acid	STEP 1	1472.0	2062.8
	STEP 2 – North [A]	124.4	183.0
	STEP 2 - South [A]	197.2	291.9

[A] Worst case values for single or multiple application
[B] Worst case values for early application

Table 10.2- 3: Initial max PECsw values – FOCUS Step 3

Compound	FOCUS Scenario	Grapes [A] 3 × 2.0 kg a.s./ha, 10 d int., BBCH 15-81
		$PEC_{sw, max}$ [B] [µg/L]
Fosetyl-Al	D6 (ditch, 1st)	34.330
	R1 (pond, 1st)	1.222
	R1 (stream, 1st)	25.100
	R2 (stream, 1st)	33.750
	R3 (stream, 1st)	35.490
	R4 (stream, 1st)	26.180

[A] Worst case for late application
[B] Worst case values for single or multiple application

Table 10.2- 4: Summary of FOCUS Step 4 PEC_{sw} values of fosetyl-Al (3×2.0 kg fosetyl-Al/ha, 10d int.). Entries marked with * result from single applications.

Fosetyl-Al PEC_{sw} [µg/L]													
Buffer Width & Type	**Scenario**	**Nozzle Reduction**											
		0%			**50%**			**75%**			**90%**		
5m Spray drift	D6 (Ditch)	S	20.760	*	S	10.380	*	S	5.1890	*	S	2.0760	*
	R1 (Pond)	S	1.4190	*	S	0.7095	*	S	0.3730		S	0.1742	
	R1 (Stream)	S	18.290	*	S	9.1450	*	S	4.5720	*	S	1.8290	*
	R2 (Stream)	S	24.590	*	S	12.290	*	S	6.1470	*	S	2.4590	*
	R3 (Stream)	S	25.860	*	S	12.930	*	S	6.4640	*	S	2.5860	*
	R4 (Stream)	S	18.340	*	S	9.1710	*	S	4.5850	*	S	1.8340	*
10m Spray drift & Runoff	D6 (Ditch)	S	7.5180	*	S	3.7590	*	S	1.8800	*	S	0.7518	*
	R1 (Pond)	S	0.7813	*	S	0.3906	*	S	0.1976		S	0.0891	
	R1 (Stream)	S	6.6250	*	S	3.3120	*	S	1.6560	*	S	0.6625	*
	R2 (Stream)	S	8.9060	*	S	4.4530	*	S	2.2270	*	S	0.8906	*
	R3 (Stream)	S	9.3660	*	S	4.6830	*	S	2.3410	*	S	0.9366	*
	R4 (Stream)	S	6.6440	*	S	3.3220	*	S	1.6610	*	S	0.6644	*
15m Spray drift & Runoff	D6 (Ditch)	S	4.0850	*	S	2.0420	*	S	1.0210	*	S	0.4085	*
	R1 (Pond)	S	0.5291	*	S	0.2646	*	S	0.1385		S	0.0654	
	R1 (Stream)	S	3.5990	*	S	1.8000	*	S	0.8998	*	R	0.3854	
	R2 (Stream)	S	4.8390	*	S	2.4200	*	S	1.2100	*	S	0.4839	*
	R3 (Stream)	S	5.0890	*	S	2.5440	*	S	1.2720	*	S	0.5089	*
	R4 (Stream)	S	3.6100	*	S	1.8050	*	S	0.9024	*	S	0.3610	*
20m Spray drift & Runoff	D6 (Ditch)	S	2.6370	*	S	1.3180	*	S	0.6593	*	S	0.2637	*
	R1 (Pond)	S	0.3931	*	S	0.1965	*	S	0.0985		S	0.0444	
	R1 (Stream)	S	2.3230	*	S	1.1620	*	S	0.5808	*	S	0.2323	*
	R2 (Stream)	S	3.1240	*	S	1.5620	*	S	0.7809	*	S	0.3124	*
	R3 (Stream)	S	3.2850	*	S	1.6420	*	S	0.8212	*	S	0.3285	*
	R4 (Stream)	S	2.3300	*	S	1.1650	*	S	0.5825	*	S	0.2330	*

S, R and D denote main entry route via spray drift, runoff or drainage, respectively

Risk assessment for aquatic organisms

ACUTE RISK ASSESSMENT FOR AQUATIC ORGANISMS

Table 10.2- 5: TER_A calculations based on FOCUS Step 2

Compound	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_A	Trigger
Grapes					
Fosetyl-Al	Fish, acute	LC_{50} > 60000	53.52	> 1121	100
	Invertebrate, acute	EC_{50} > 100000		> 1869	
Phosphonic acid	Fish, acute	LC_{50} > 400000	197.2	> 2028	
	Invertebrate, acute	EC_{50} > 400000		> 2028	

As requested by the RMS France, new PEC_{sw} calculations were performed using the input parameters as provided by ANSES. As the PEC_{sw} values for fosetyl-Al did not change due to the new calculations the risk assessment for fosetyl-Al remains unchanged. In the following an updated risk assessment is presented for the metabolite phosphonic acid, based on new maximum FOCUS Step 2 PEC_{sw} values for grapes.

Table 10.2- 5a: TER_A calculations based on FOCUS Step 2

Compound	Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_A	Trigger
Grapes					
Phosphonic acid	Fish, acute	LC_{50} > 400000	391.9	> 1370	100
	Invertebrate, acute	EC_{50} > 400000		> 1370	

CHRONIC RISK ASSESSMENT FOR AQUATIC ORGANISMS

Table 10.2- 6: TER$_{LT}$ calculations based on FOCUS Step 2

Compound	**Species**	**Endpoint [µg/L]**		**PEC$_{sw.max}$ [µg/L]**	**TER$_{LT}$**	**Trigger**
Grapes						
Fosetyl-Al	Fish, chronic	NOEC	213	53.52	**4.0**	10
	Invertebrate, chronic	NOEC	17000		318	
	Green algae, chronic	E_rC_{50}	9540		178	
	Aquatic plants, chronic	E_rC_{50}	166600		3113	
Phosphonic acid	Sediment dweller, chronic	NOEC	> 100200	197.2	> 508	
	Green algae, chronic	E_rC_{50}	29400		149	

Bold values do not pass the risk assessment

As requested by the RMS France, new PEC$_{sw}$ calculations were performed using the input parameters as provided by ANSES. As the PEC$_{sw}$ values for fosetyl-Al did not change due to the new calculations the risk assessment for fosetyl-Al remains unchanged. In the following an updated risk assessment is presented for the metabolite phosphonic acid, based on new maximum FOCUS Step 2 PEC$_{sw}$ values for grapes.

Table 10.2- 6a: TER$_{LT}$ calculations based on FOCUS Step 2

Compound	**Species**	**Endpoint [µg/L]**		**PEC$_{sw.max}$ [µg/L]**	**TER$_{LT}$**	**Trigger**
Grapes						
Phosphonic acid	Sediment dweller, chronic	NOEC	> 100200	291.9	> 343	10
	Green algae, chronic	E_rC_{50}	29400		101	

Request from the RMS:
The chronic risk assessment for *Chironomus riparius* (phosphonic acid) should be done with the toxicity endpoint and the PECsed expressed in mg a.s./kg sediment as phosphonic acid has a potential of accumulation in the sediment.

Response from BCS:
The chronic toxicity endpoint of phosphonic acid to the sediment dweller *Chironomus riparius* is derived from the study by [redacted], M.; 1999; M-171912-01-1 (please refer to Document MCA, Section 8.2.5.4, KCA 8.2.5.4/01), which provided a NOEC > 100.2 mg/L. In this study, phosphonic acid concentrations were measured only in the overlying water after 1 hour, 7 days and 21 days. The analytical results (see Table 2 in the study report) show that the recovery of phosphonic acid was close to 100%, without decrease with time, for the three highest concentrations tested (*i.e.*, 25, 50.1 and 100.2 mg/L). This indicates that, over the experimental period, phosphonic acid remained in the water phase, and did not accumulate in the sediment. Results were therefore expressed with respect to the matrix where phosphonic acid was present (*i.e.*, the overlying water), thus as mg/L.

All TER values for the uses in grapes meet the trigger value based on FOCUS Step 2 PEC_{sw} values, except for the long-term exposure to fish. Therefore TER calculations for fish based on FOCUS Step 3 values are presented below.

Table 10.2- 7: Refined TER calculations for fosetyl-Al based on FOCUS Step 3

Compound	Species	Endpoint [µg/L]	FOCUS scenario	$PEC_{sw,max}$ [µg/L]	TER	Trigger
Grapes						
Fosetyl-Al	Fish, chronic	NOEC 213	D6 (ditch)	34.33	**6.2**	10
			R1 (pond, 1st)	1.222	174.3	
			R1 (stream, 1st)	25.10	**8.5**	
			R2 (stream, 1st)	33.75	**6.3**	
			R3 (stream, 1st)	35.49	**6.0**	
			R4 (stream, 1st)	25.18	**8.5**	

Bold values do not pass the risk assessment

The FOCUS pond scenario meets the required trigger. Nevertheless, further refinement using FOCUS Step 4 values is necessary for all stream and ditch scenarios and is presented below.

Table 10.2- 8: Refined TER calculations for fosetyl-Al based on FOCUS Step 4 including mitigation measures

Species	Endpoint [µg/L]	Mitigation	FOCUS scenario	$PEC_{sw,max}$ [µg/L]	TER	Trigger
Grapes						
Fish, chronic	NOEC 213	10 m vegetated buffer strip	D6 (ditch)	7.518	28.3	10
			R1 (stream)	6.625	32.2	
			R2 (stream)	8.906	23.9	
			R3 (stream)	9.366	22.7	
			R4 (stream)	6.644	32.1	
Fish, chronic	NOEC 213	5 m non-spray buffer zone + 50% reducing nozzles	D6 (ditch)	10.38	20.5	10
			R1 (stream)	9.145	23.3	
			R2 (stream)	12.29	17.3	
			R3 (stream)	12.93	16.5	
			R4 (stream)	9.171	23.2	

According to the presented risk assessment based on FOCUS Step 4 calculations, the risk to aquatic organisms from the use of the product in grapes is unlikely if
- 5 m non-spray buffer zone and 50% drift reduction, or
- 10 m vegetated buffer strip

are maintained during application of the product.

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

Formulation studies on aquatic organisms were carried out with Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11 = EXP 11074B) and reviewed by the RMS for the Annex I inclusion of fluopicolide under Directive 91/414/EEC. The studies have been considered acceptable (EFSA Scientific Report 299 (2009)). Summaries of these studies are given below.

Report:	KCP 10.2.1/01 [redacted]; 2003; M-227282-01-1
Title:	AE F05361606 WG71 A1: Acute immobilisation test with daphnids (Daphnia magna) under static conditions
Report No.:	C039855
Document No.:	M-227282-01-1
Guideline(s):	OECD: 202-1 (1984)
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The purpose of this study was to estimate the acute toxicity (EC_{50}) of the test item to *Daphnia magna* under static test conditions. The test species were exposed for 48 hours to a series of geometrical concentrations of the test item.

Material and Methods:
The toxicity of FEA + FLC WG 71.11 (AE F05361606 WG71 A1 (batch OP230059, a light beige granular, containing 671 g fosetyl-Al/kg and 45.1 g AE C638206/kg)) to the water flea, *Daphnia magna*, was determined under static conditions over an exposure period of 48 hours.
Five daphnids per replicate, 4 replicates per concentrations, were exposed to a dilution water control and nominal test concentrations of FEA + FLC WG 71.11 equal to 6.25, 12.5, 25, 50 and 100 mg/L for 48 hours.
The test solutions were sampled and analyzed at the beginning and the end of the test period.
Immobilization and adverse reactions were recorded at 24 and 48 hours after the start of exposure.

Findings:
Test conditions during the exposure period were:

Dissolved oxygen:	6.9 – 8.3 mg/L
pH:	ranged from 6.5 - 7.8
Temperature:	20 – 20.8 °C

The recoveries of AE C638206 concentrations (compared to nominal values) from the freshly prepared and aged test solutions ranged from 84.5 to 110%, except for the 100 mg FEA + FLC WG 71.11/L treatment level where 77.4% recovery was found at hour 0. The 48 hour analysis confirmed correct dosage (110%). There was no AE C638206 residue found in the dilution water or control samples greater that the limit of quantification. Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, EC_{50} values and biological data are based on nominal concentrations.
Undissolved product was observed at the test levels of 25, 50 and 100 mg/L.

At hour 48, immobilization of 0, 5, 0, 20, 26 and 5% of the exposed daphnids was observed in the control and concentrations of 6.25, 12.5, 25, 50 and 100 mg product/L. Lethargic daphnids were observed at the 25, 50 and 100 mg/L treatment levels.

Cumulative immobilization data are shown in the table below.

Nominal concentration (mg/L)	**Definitive test**			
	Cumulative immobilized Daphnids (initial population = 40 per replicate*)			
	24 hours		**48 hours**	
	Total	**%**	**Total**	**%**
Control	0	0%	0	**0%**
6.25	0	0%	1	**5%**
12.5	0	0%	0	**0%**
25.0	0	0%	4	**20%**
50*	0	0%	5	**26%**
100	0	0%	1	**5%**

*only 19 daphnids were exposed to the level of 50 mg/L

Conclusions:
Under the conditions of the test and based on nominal concentrations, the acute toxicity of FEA + FLC WG 71.11 to daphnids (*Daphnia magna*) in a static test system is defined as follows;

48-hour EC_{50}	**>100 mg/L**
NOEC (48 hours)	**12.5 mg/L**

Report:	KCP 10.2.1/02 [redacted] E; 2003; M-227285-01-1
Title:	Alga, growth inhibition test with Navicula pelliculosa AE F05361606 WG71 A1
Report No.:	C039858
Document No.:	M-227285-01-1
Guideline(s):	OECD: 201
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The purpose of this study was to estimate the toxicity of the test item on the freshwater diatom *Navicula pelliculosa*. The test species was exposed to a series of concentrations in order to determine the NOEC as well as the EC_{50} with corresponding 95% confidence intervals.

Material and Methods:
The effect of FEA + FLC WG 71.11 (AE F05361606 WG71 A1 (batch OP230059, a light beige granular, containing 671 g fosetyl-Al/kg and 45.1 g fluopicolide/kg)) on growth of the freshwater diatom, *Navicula pelliculosa*, was determined under static conditions over an exposure period of 72 hours.
Cultures of alga were exposed to a dilution water control and to nominal test concentrations of the test formulated product (3 replicates for the control, 3 replications of each product concentration) equal to 0.1, 0.32, 1.0, 3.2 and 10 mg/L.
Measurements of culture density were made at test initiation (0 hours), at 24 and 48 hours and at test termination (72 hours).
The test solutions were sampled and analyzed at the beginning and the end of the test period.

Findings:
Test conditions during the exposure period were:

pH:	7.73 – 8.45
Temperature:	21.3 – 24.0 °C
Light intensity	7700 – 8200 Lux

The analysis of the 0 hour test preparations for AE C638206 showed the measured concentrations to range between 84.6% and 103% of the nominal test concentrations. Analysis of the test solutions at 72 hours showed the measured concentrations of AE C638206 to range from 96.1 to 109% nominal. There was no AE C638206 residue found in the dilution water or control samples greater that the limit of quantification. Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, EC_{50} values and biological data are based on nominal concentrations.

Within the 72 hour exposure period, the cell density in the control cultures increased by a factor of 91.9 and thus, more than the minimum factor of 16 as prescribed in the Guidelines (OECD 1984, EC 1992), which renders this test valid.
The mean algal cell densities over the exposure period were as follows:

Nominal concentrations (mg/L)	Definitive test Mean cell densities* (x 10^4 cells/ml)		
	24 hours	48 hours	72 hours
0 (control)	3.6	6.4	91.9
0.1	2.4	7.6	83.4
0.32	2.3	5.2	75.5
1.0	1.6	2.8	47.8
3.2	0.4	0.8	0.8
10	0.6	0.9	0.1

The following table shows the inhibition of growth rate and biomass:

Nominal concentration (mg/L)	Area under curve at 72 h (10^4cells x days/mL)	% inhibition	Growth rate (0 - 72 h)	% inhibition
0 (control)	53.7	**0**	1.49	**0**
0.1	49.2	**8.3**	1.46	**2.1**
0.32	42.9*	**20.0**	1.41	**4.8**
1.0	10.8*	**79.8**	0.95*	**36.4**
3.2	-0.8*	**101.6**	-0.08*	**105.1**
10	-1.0*	**101.8**	NA	**NA**

* Statistically significant difference compared to the control

Conclusions:
Under the conditions of the test and based on nominal concentrations, the toxicity of FEA + FLC WG 71.11 to the freshwater diatom (*Navicula pelliculosa*) is defined as follows:

Exposure interval	72 hours
E_bC_{50} (mg/L)	0.58 (NOEC = 0.1)
E_rC_{50} (mg/L)	0.91 (NOEC = 0.32)

Request from the RMS:
Further explanations are required to justify that the study of the effects of the preparation on *Navicula pelliculosa* ([redacted]; 2003; M-227285-01-1) are still reliable for the risk assessment as the coefficient of variation is estimated to be 71% for the control.

Response from BCS:
The study does not meet the validity criteria according to the OECD TG 201. BCS´s calculations resulted in the value of 71.2% for the mean coefficient of variation for section-by-section specific growth rates of controls.
However, this study was provided because *Navicula pelliculosa* has been identified as the most sensitive taxa to the formulation. This is in line with the data requirement of EFSA Aquatic Guidance Document for formulated products (EFSA Journal 2013; 11(7):3290, p. 82). In fact, this study is not relevant for the risk assessment of fosetyl-Al, but allows comparison between the endpoints of each active substance (fosetyl-Al and fluopicolide) and those of the formulated product.

Report:	KCP 10.2.1/03[redacted]; 2003; M-227291-01-1
Title:	AE F05361606 WG71 A1; Alga, growth inhibition test with Pseudokirchneriella subcapitata (syn Selenastrum capricornutum)
Report No.:	C039864
Document No.:	M-227291-01-1
Guideline(s):	OECD: 201 (1984)
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The purpose of this study was to estimate the toxicity of the test item on the freshwater green alga *Pseudokirchneriella subcapitata*, previously called *Selenastrum capricornutum*. The test species was exposed to a series of concentrations in order to determine the NOEC as well as the EC_{50} with corresponding 95% confidence intervals.

Material and Methods:
The effect of FEA + FLC WG 71.11 (AE F05361606 WG71 A1 (batch OP230059, a light beige granular, containing 671 g fosetyl-Al/kg and 45.1 g fluopicolide/kg)) on growth of the freshwater green alga, *Pseudokirchneriella subcapitata*, (syn. *Selenastrum capricornutum*), was determined under static conditions over an exposure period of 72 hours.
Cultures of alga were exposed to a dilution water control and to nominal test concentrations of the test formulated product (12 replicates for the control, 3 replications of each product concentration) equal to 1.0, 2.1, 4.7, 10, 22 and 50 mg/L.
Measurements of culture density were made at test initiation (0 hours), at 24 and 48 hours and at test termination (72 hours).
The test solutions were sampled and analyzed at the beginning and the end of the test period.

Findings:
Test conditions during the exposure period were:

pH:	6.9 – 10.1
Temperature:	23.7 – 25.2 °C
Light intensity	7300 – 8650 Lux

The analysis of the 0 hour test preparations for AE C638206 showed the measured concentrations to range between 99.8% and 121% of the nominal test concentrations. Analysis of the test solutions at 72 hours showed the measured concentrations of AE C638206 to range from 98.1 to 123% nominal. There was no AE C638206 residue found in the dilution water or control samples greater that the limit of quantification. Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, EC_{50} values and biological data are based on nominal concentrations.
Due to a high variability in the results of the growth of the control vessels, the controls of a second test which had run in parallel to this test and under the same environmental conditions are included.

Within the 72 hour exposure period, the cell density in the control cultures increased by a factor of 95.6 and thus, more than the minimum factor of 16 as prescribed in the Guidelines (OECD 1984, EC 1992), which renders this test valid.
The mean algal cell densities over the exposure period were as follows:

Nominal concentrations (mg/L)	**Definitive test Mean cell densities* (x 10^4cells/ml)**		
	24 hours	**48 hours**	**72 hours**
0 (control)	6.2	25.5	95.6
1.0	4.3	21.5	93.4
2.1	2.3	17.2	67.3
4.7	2.3	13.3	66.3
10	0.2	5.0	20.5
22	0.3	1.6	6.3
50	0.4	0.2	0.5

The following table shows the inhibition of growth rate and biomass:

Nominal concentration (mg/L)	**Area under curve at 72 h (10^4cells x days/mL)**	**% inhibition**	**Growth rate (0 - 72 h)**	**% inhibition**
0 (control)	79.8	**0**	1.48	**0**
1.0	71.8	**10**	1.50	**-1.1**
2.1	52.0	**34.9**	1.39	**6.2**
4.7	47.4*	**40.6**	1.38	**6.6**
10	13.3*	**83.3**	1.00*	**32.7**
22	2.6*	**96.7**	0.59*	**60.3**
50	1.7*	**102.1**	-0.26*	**117.6**

*Statistically significant difference compared to the control

Conclusions:
Under the conditions of the test and based on nominal concentrations, the toxicity of FEA+FLC WG 71.11 to the freshwater green alga (*Pseudokirchneriella subcapitata*) is defined as follows:

Exposure interval	**72 hours**
E_bC_{50} (mg/L)	3.9 (NOEC = 2.1)
E_rC_{50} (mg/L)	12.5 (NOEC = 4.7)

Request from the RMS:
Further explanations are required to justify that the study of the effects of the preparation on *Pseudokirchneriella subcapitata* (syn. *Selenastrum capricornutum*) ([redacted].; 2003; M-227291-01-1) are still reliable for the risk assessment due to the high variability of the results in the control and since the coefficient of variation is estimated to be 39% for the control.

Response from BCS:
The study failed to meet the criterion related to the coefficient of variation for section-by-section specific growth rates of controls. BCS´s calculations result in a value of 39.7%. However, a close look to the data clearly shows that this is due to the outlier value of -0.405, resulting in a CV of 119.6%, for the growth rate in one replicate between 24 and 48 hours. This replicate also had the highest growth rate over the 0 to 24 hours period.

	Growth Rates		0-72h			
0-24h	24-48h	48-72h	mean	SD	% CV	% CV
1,872	1,255	1,466	1,531	0,313	20,5	20,5
1,841	1,737	1,210	1,596	0,338	21,2	21,2
1,758	1,943	1,076	1,592	0,457	28,7	28,7
1,194	2,370	1,132	1,565	0,698	44,6	44,6
2,380	1,346	0,988	1,571	0,722	46,0	46,0
1,988	1,773	1,134	1,632	0,444	27,2	27,2
2,890	-0,405	1,702	1,396	1,669	119,6	
1,705	0,693	1,504	1,301	0,536	41,2	41,2
1,099	1,969	1,545	1,538	0,435	28,3	28,3
1,194	1,685	1,709	1,529	0,291	19,0	19,0
0,833	2,000	1,514	1,449	0,586	40,5	40,5
1,030	1,110	2,019	1,386	0,549	39,6	39,6
		mean	1,507	0,587	**39,7**	**32,4**

So, obviously, something went wrong with this very replicate. When this outlier is removed from the dataset, the mean CV value drops to 32.4%. In this particular case, because the number of control replicates is high (12), we believe that removing the outlier replicate is a reasonable option. By doing so, the study fulfills the validity criteria according to the OECD TG 201 (ToxRat re-calculated control values for the biomass increase, coefficient of variation of average specific growth rates in replicates over 72 hours, and coefficient of variation for section-by-section specific growth rates over 72 hours are 98.4, 6.6 and 32.4%).

Endpoints were recalculated accordingly, delivering the following values:
72-h E_bC_{50} = 5.07 mg/L; 72-h E_bC_{10} = 1.30 mg/L
72-h E_rC_{50} = 15.2 mg/L; 72-h E_rC_{10} = 5.11 mg/L

Report:	KCP 10.2.1/04[redacted]L; 2003; M-225113-01-1
Title:	AE F05361606 WG71 A1: Acute toxicity test with rainbow trout (Oncorhynchus mykiss) under static conditions
Report No.:	C038495
Document No.:	M-225113-01-1
Guideline(s):	OECD: 203, (1992)
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The purpose of this study was to determine the acute toxicity (LC_{50}) of AE F05361606 WG71 A1 on rainbow trout (*Oncorhynchus mykiss*) under static conditions.

Material and Methods:
The toxicity of FEA + FLC WG 71.11 (AE F05361606 WG71 A1 /batch OP230059, a light beige granular, containing 671 g fosetyl-Al/kg and 45.1 g AE C638206/kg)) to the rainbow trout, *Oncorhynchus mykiss*, was determined under static conditions over an exposure period of 96 hours. Juvenile trouts had a weight ranging from 0.77 to 2.12 g and a length ranging from 4.4 to 6.0 cm.
A total of 60 fish (10 fish per treatment, 5 concentrations + 1 negative control), were exposed to FEA+FLC WG 71.11 nominal test concentrations of 0 (dilution water control), 0.625, 1.25, 2.50, 5.0 and 10 mg/L. Test concentrations were not renewed and analytical verifications were performed at 0 and 96 hours for concentrations of AE C638206.
No solvent was used and fish were not fed during the test.

Findings:
Test conditions during the exposure period were:

Dissolved oxygen:	Test solutions were aerated in order to avoid oxygen depletion below 80% of the air saturation value.
pH: :	7.07 – 7.72 pH units
Temperature:	13.6 – 14.3 °C
Conductivity:	380 – 395 µS/cm
Hardness:	152 – 156 mg $CaCO_3$/L

The recoveries of AE C638206 concentrations (compared to nominal values) from the freshly prepared and aged test solutions ranged from 93.3 to 109%, except for the 1.25 mg FEA + FLC WG 71.11/L treatment level where 72.2% recovery was found at hour 0. The 96 hour analysis verified correct dosage (108%). There was no AE C638206 residue found in the dilution water or control samples greater that the limit of quantification. Given that the toxicity of the product cannot be attributed to any one of the active ingredients but to the product formulation as a whole, LC_{50} values and biological data are based on nominal concentrations.
The quality criteria for the validity of the test were fulfilled since no mortality was observed in the control group, the oxygen concentration was higher than 60% of the air-saturation value and the pH varied by not more than 1 unit.
During the 96 hour observation period, neither mortality nor sublethal effects were observed among trout exposed to the test solutions with 0.625, 1.25, 2.50 and 5.0 mg product/L. After 24, 48, 72 and 96 hours of exposure, 10, 40, 40 and 70% mortality was observed in the test solution with 10 mg FEA + FLC WG 71.11/L respectively.

Nominal Concentrations (mg/L)	Definitive test – FEA + FLC WG 71.11				
	Cumulative mortality (%)				
	0-6-hour	24-hour	48-hour	72-hour	96-hour
(Control) < LOQ	0	0	0	0	0
0.625	0	0	0	0	0
1.25	0	0	0	0	0
2.50	0	0	0	0	0
5.0	0	0	0	0	0
10.0	0	10	40	40	40

LOQ= Limit of Quantification (0.006 mg AE C638206/L)

Conclusion:
Under the conditions of the test and based on nominal concentrations, the acute toxicity of FEA + FLC WG 71.11 to the rainbow trout, *Oncorhynchus mykiss*, in a static test system is defined as follows:
96-hour LC_{50}: 8.5 mg/L
NOEC (96 hour): 5.0 mg/L

Request from the RMS:
For the study of the acute effects of the preparation to fish ([redacted] Z, 2003, M-225113-01-1), further explanations on the reliability of the estimated LC_{50} are considered necessary. Indeed, the LC_{50} is based on the 2 highest concentrations, one producing 0% mortality and the other 70%.

Response from BCS:
The study did not provide an ideal concentration-response relationship. However, if the two highest concentrations revealed 0 and 70% lethality, it is scientifically justified to assume that the LC_{50} lies between these two concentrations. Thus, based on the calculation method used in the study, an LC_{50} value of 8.5 mg/L was derived.
Another option would be to calculate the geometric mean concentration using the two highest concentrations. In this case, the geomean LC_{50} value is 7.07 mg/L.

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

No new studies were necessary based on the current data requirements. Please refer to Document MCA, Section 8.2.

CP 10.2.3 Further testing on aquatic organisms

No studies were necessary based on the current data requirements. Please refer to Document MCA, Section 8.2.

CP 10.3 Effects on arthropods

CP 10.3.1 Effects on bees

The risk assessment has been performed according to the existing guidance in force at the time of the preparation and submission of this dossier namely the EU Guidance Document on Terrestrial Ecotoxicology (SANCO/ 10329/2002 rev 2) and EPPO Standard PP 3/10 (3) Environmental Risk Assessment Scheme for Plant Protection Products - Chapter 10: honey bees.

Commission Regulations (EU) 283/2013 and 284/2013 require, where bees are likely to be exposed, testing by both acute (oral and contact) and chronic toxicity, including sub-lethal effects, to be conducted. Consequently in addition to the standard toxicity studies performed with adult bees (OECD 213 and 214) the following additional studies are also provided:

- Chronic 10 day toxicity to adult bees under laboratory conditions,
- Acute contact toxicity to bumble bees under laboratory conditions,
- A colony feeding study following Oomen *et al.* 1992 (using a realistic worse case spray solution concentration and covering exposure for effects on brood (eggs, young and old larvae) and their development, nurse bee on-going behaviour in brood care and colony strength),
- Semi-field brood feeding studies following OECD Guidance Document No. 75 (using a more realistic spray scenario onto flowering *Phacelia* at the maximum application rate for the approval renewal of fosetyl and covering exposure for effects on brood (eggs) and their development and colony parameters),

Details of the bee testing with fosetyl-Al and ecotoxicological endpoints are presented in Document MCA, Section 8.3.1, Document MCP, Section 10.3.1, as well as within the existing EFSA Scientific Report (2005) 54, 1-79.

Table 10.3.1- 1: Honey bee toxicity data generated with FEA + FLC WG 71.11

Test substance	Test species/study design	Endpoint	Reference
FEA + FLC WG 71.11	Honey bee, 48 h	LD_{50} – oral > 169 µg prod./bee	[redacted];; 2002; M-213718-01-1 KCP 10.3.1.1.1/01
	Honey bee, 48 h	LD_{50} – contact > 70 µg prod./bee	[redacted];; 2002; M-213109-01-1 KCP 10.3.1.1.2/01
	Honey bee, 48 h	**LD_{50} – oral > 219 µg prod./bee** **LD_{50} – contact > 200 µg prod./bee**	KCP 10.3.1.1.1/02 [redacted]E; 2015; M-528130-01-1 KCP 10.3.1.1.1/02 KCP 10.3.1.1.2/02

prod.: product
Bold: endpoint used for risk assessment

Table 10.3.1- 2: Honey bee toxicity data generated with fosetyl-Al, phosphonic acid and Fosetyl-Al WG 80

Test substance	Test species/ study type	Endpoint	References
Fosetyl-Al	Honey bee, 48 h	LD_{50} – oral > 140 µg a.s./bee LD_{50} – contact > 100 µg a.s./bee	[redacted], H.; 1997; M-184568-01-1 KCA 8.3.1.1.1/01 KCA 8.3.1.1.2/01
	Honey bee, 48 h	LD_{50} – oral 462 µg a.s./bee [a)] LD_{50} – contact > 1000 µg a.s./bee	[redacted], S.; [redacted], N.; 1999; M-185217-01-1 KCA 8.3.1.1.1/02 KCA 8.3.1.1.2/02
	Honey bee, 48 h	**LD_{50} – oral > 108.5 µg a.s./bee** **LD_{50} – contact > 100 µg a.s./bee**	[redacted], S.; 2012; M-440802-01-1 KCA 8.3.1.1.1/04 KCA 8.3.1.1.2/04
Phosphonic acid	Honey bee, 48 h	LD_{50} – oral > 212 µg p.m./bee	[redacted], S.; 2000; M-238701-01-1 KCA 8.3.1.1.1/03
	Honey bee, 48 h	LD_{50} – contact 29.7 µg p.m./bee [b)]	[redacted], S. J.; [redacted], J. B.; 1995; M-179067-01-1 KCA 8.3.1.1.2/03
	Honey bee, 48 h	LD_{50} – oral **> 848 µg p.m./bee** LD_{50} – contact **> 1050 µg p.m./bee**	[redacted], T.; 2010; M-389965-01-1 KCA 8.3.1.1.1/05 KCA 8.3.1.1.2/05

Test substance	Test species/ study type	Endpoint	References
Fosetyl-Al WG 80	Honey bee, 10 d chronic adult feeding study	NOEC 750 mg a.s./kg LC_{50} > 750 mg a.s./kg NOEDD 37.3 µg a.s./bee/day LDD_{50} > 37.3 µg a.s./bee/day	[redacted], A.; 2015; M-527665-01-1 KCA 8.3.1.2/01
	Honey bee brood feeding (Oomen *et al.*, 1992)	Slightly increased termination rate of eggs, young and old larvae; comparable brood nest development as in control; brood index and brood compensation index displayed continuous increase, indicating a successful development of the brood. No effects on the survival of adult bees and pupae, colony strength and overall colony conditions by feeding honey bee colonies sugar syrup at a fosetyl-Al concentration of 2.4 g a.s./L (2.97 g test item/L).	[redacted], C.; 2015; M-508986-01-2 KCA 8.3.1.3/01
	Semi-field honey bee brood study (according to OECD 75; forced exposure conditions) in *Phacelia*; application during full-bloom and bees actively foraging	No adverse effects on mortality, flight intensity, brood development (brood termination rate, brood index, compensation index) as well as on colony strength and brood and food abundance at 3600 g a.s./ha. No adverse effects on mortality, flight intensity, colony strength and brood and food abundance at 570 g a.s./ha.	[redacted], B.; 2015; M-526896-01-1 KCA 8.3.1.3/02
	Semi-field honey bee brood study (according to OECD 75; forced exposure conditions) in *Phacelia*; application during full-bloom and bees actively foraging	No adverse effects on mortality, flight intensity, behaviour, brood development (brood termination rate, brood index, compensation index) as well as on colony strength and brood and food abundance at 570 g a.s./ha.	[redacted], B.; 2015; M-528899-01-1 KCA 8.3.1.3/03
	EPPO guideline No. 170 (1992)	Application of 100 kg product/ha at approx. 30% flowering of *Phacelia*, 28 h before the introduction of bees in the tents (7 d-exposure) did not cause adverse effects to honeybees	[redacted], A.; 2008; M-238790-01-2 KCP 10.3.1.5/01
Fosetyl-Al	Bumble bee, 48 h	LD_{50} contact > 250 µg a.s./bumble bee	[redacted], S.; 2015; M-525339-01-1 KCA 8.3.1.1.2/06

- Studies written in grey typeface are referring either to studies in the corresponding Baseline Dossier for the active substance or the old representative formulation for Annex I inclusion of fosetyl under Directive 91/414/EEC (which is provided for approval renewal as well); whereas studies in black typeface are studies of the Supplementary Dossier for the active substance or the representative formulation Fosetyl-Al WG 80.

p.m. = pure metabolite

[a] 96h-endpoint

[b] Values were corrected for a purity of 41% phosphonic acid weight by volume which is equal to 29.7% weight by weight. Test substance potassium salts of phosphonic acid has a density of 1.38. Therefore, one L of test substance weighs 1380 g and contains 410 g phosphonic acid (410/1380 = 0.297) with a weight/weight purity of 29.7%.

Bold: endpoint used for risk assessment

Risk assessment for bees

The risk assessment for bees is based on the application rate of fosetyl-aluminium (fosetyl-Al) with 2000 g a.s./ha for applications in grapes using the endpoints (LD_{50} values) for fosetyl-Al and its metabolite phosphonic acid.

Hazard Quotients

The risk assessment is based on Hazard Quotient approach (Q_H) by calculating the ratio between the application rate (expressed in g a.s./ha or in g total substance/ha) and the laboratory contact and oral LD_{50} (expressed in µg a.s./bee or in µg total substance/bee).

Q_H values are 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: $$Q_{HO} = \frac{\text{maximum application rate}}{LD_{50}\ \text{oral}} = \frac{[\text{g a.s./ha or g total substance/ha}]}{[\mu\text{g a.s./bee or }\mu\text{g total substance/bee}]}$$

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

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

Compound	**Oral LD_{50} [µg a.s./bee]**	**Max. application rate [g a.s./ha]**	**Hazard quotient Q_{HO}**	**Trigger**	***A-priori* acceptable risk for adult bees**
FEA + FLC WG 71.11	>219.0 [µg product/ha]	3000 [g product/ha]	<13.7	50	yes
Fosetyl-Al	>108.5	2000	<18.4	50	yes
Phosphonic acid	>848.0	1389 *	<1.6	50	yes

* assuming a quantitative conversion of the parent to the metabolite, 2.0 kg fosetyl-Al corresponds to 1.389 kg H_3PO_3, based on a molar mass of 354.1 g/mol for fosetyl-Al and 82.0 g/mol for H_3PO_3 and assuming that 1 mol fosetyl-Al degrades to 3 mol H_3PO_3

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

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

Compound	**Contact LD_{50} [µg a.s./bee]**	**Max. application rate [g a.s./ha]**	**Hazard quotient Q_{HC}**	**Trigger**	***A-priori* acceptable risk for adult bees**
FEA + FLC WG 71.11	>200.0 [µg product/ha]	3000 [g product/ha]	<15.0	50	yes
Fosetyl-Al	>100.0	2000	<20	50	yes
Phosphonic acid	>1050.0	1389 *	<1.3	50	yes

* assuming a quantitative conversion of the parent to the metabolite, 2.0 kg fosetyl-Al corresponds to 1.389 kg H_3PO_3, based on a molar mass of 354.1 g/mol for fosetyl-Al and 82.00 g/mol for H_3PO_3 and assuming that 1 mol fosetyl-Al degrades to 3 mol H_3PO_3

The hazard quotients for contact exposure are 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, fosetyl-aluminium (fosetyl-Al) was further subjected to topical acute bumble bee testing (KCA 8.3.1.1.2/06; [redacted]; 2015; M-525339-01-1). The study resulted in an LD_{50} of > 250 µg a.s./bumbe bee and did not reveal sensitivity differences between honey bee and bumble bee foragers.

Moreover, fosetyl-Al was further subjected to chronic laboratory testing with adult honey bees (KCA 8.3.1.2/01; [redacted], A.; 2015; M-527665-01-1).
This chronic study was designed as a dose-response test by exposing adult honey bees for 10 consecutive days to nominal concentrations of 46.88, 93.75, 187.5, 375 and 750 mg fosetyl-Al/kg feeding solution. The actual test was conducted by using the formulated product Fosetyl-aluminium WG 80 (Fosetyl-Al WG 80). After exposing honey bees for ten consecutive days exclusively to sugar solution containing fosetyl-Al at the respective treatment levels, the 10 day LC_{50} (Lethal Concentration) was determined to be > 750 mg fosetyl-Al/kg, which corresponds to a LDD_{50} (Lethal Dietary Dose) of > 37.3 µg a.s./bee/day. The respective NOEC (No Observed Effect Concentration) for mortality was determined to be 750 mg fosetyl-Al/kg, which corresponds to the NOEDD (No Observed Effect Dietary Dose) of > 37.3 µg a.s./bee/day.

In order to reveal whether fosetyl-Al poses a risk to immature honey bee life stages, a bee brood feeding study (KCA 8.3.1.3/01; [redacted]; 2015; M-508986-01-2) 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 with Fosetyl-Al WG 80 and the actual test concentration of fosetyl-Al was 2.4 g a.s./L (2.97 g Fosetyl-Al WG 80/L). The administration of Fosetyl-Al WG 80 at a concentration of ~2400 ppm fosetyl-Al to honeybee colonies via feeding of 1 litre spiked sucrose solution has neither resulted in adverse effects on worker or pupal mortality, nor in behavioural abnormalities as compared to the control. Regarding brood development, the Brood Termination Rates of the test item treatment were overall on a low to moderate level with 27.3, 11.3 and 11.0% for eggs, young larvae and old larvae, respectively. Yet, as compared to the Brood Termination Rates in the control (13.3, 3.7 and 1.7% for eggs, young larvae and old larvae respectively), a slight but statistically significant increase was detected for the test item at the end of the brood observation period. However, neither Brood Indices nor Brood Compensation Indices were significantly increased in the test item as compared to the control for any brood stage, indicating that these indices performed comparable to the control, including compensations of previous brood losses.

All in all, it can be concluded from the acute and chronic laboratory studies in adult honey bees as well as from the bee brood feeding study (Oomen *et al.*, 1992) investigating side-effects on immature honey bee life stages, that fosetyl-Al is of moderate, general intrinsic toxicity to honey bees.

In order to clarify whether the moderate, general intrinsic bee toxicity of fosetyl-Al poses a risk to honey bee brood and colony development in particular as well as on honey bees in general under realistic worst-case conditions, a higher tier semi-field honey bee brood study (according to the provisions of the OECD Guidance Document 75) was conducted in 2014 under forced/confined exposure conditions, by application of 3600 g a.s./ha as well as a rate of 570 g a.s./ha (spray drift rate) under tunnel conditions to the full flowering and highly bee attractive surrogate crop *Phacelia tanacetifolia* (KCA 8.3.1.3/02; [redacted], B.; 2015; M-526896-01-1). Considering that the higher test rate exceeds the envisaged application rate of 2000 g fosetyl-Al/ha in 3 L FEA + FLC WG 71.11 per hectare in grapes and that the application is performed in a crop not attractive to bees, this study is seen to present a worst case scenario.
The study included four treatment groups: Control (tap water), Test item 1 (3600 g a.s./ha), Test item 2 (570 g a.s./ha) and Reference item (300 g fenoxycarb/ha) with all applications being carried out with a spray volume of 400 L water/ha. For all treatment groups, four replicates (tunnels) were set up. The application of all treatments was conducted during daily bee flight activity at the time of full flowering of the crop. Thereafter, the bees were kept for 7 days within the tunnels (confined exposure phase) and in the evening of the 7th day after application (after bee flight activity) the colonies were relocated out of the tunnels and transferred to a monitoring site without flowering crops and intensive agricultural area for further monitoring (day 8 to day 27 after treatment). Daily, throughout the confined exposure phase, mortality of worker bees, larvae and pupae was assessed along with assessments of foraging activity and behaviour. Daily mortality assessments were continued along with behaviour around the hive during the post-exposure observation period (day 8 to day 27 after treatment). Colony assessments (food stores, brood areas, colony strength) were made before confinement, after confinement and at the end of the study. Detailed brood assessments (brood termination rate, brood index and brood compensation index) by employing digital photo imaging technology, investigating the fate of more than 200 individually marked cells was performed on 5 occasions throughout the study, covering an entire brood cycle of honey bees.
The application of fosetyl-Al at the rate of 3600 g a.s./ha under tunnel conditions to the full flowering and highly bee attractive surrogate crop *Phacelia tanacetifolia* did not cause any adverse effects on mortality, flight intensity, brood development (brood termination rate: 36.5%, brood index: 3.2, compensation index: 3.8 in test item compared to the control with brood termination rate: 41.2%, brood index: 2.9, compensation index: 3.5), as well as on colony strength and brood and food abundance. The application of fosetyl-Al at the rate of 570 g a.s./ha did not cause adverse effect on mortality, flight intensity, colony strength and brood and food abundance but resulted in unclear findings on brood development (brood termination rate: 79.9%, brood index: 1.0, compensation index: 2.1). Since effects were only seen at the lower test rate of 570 g a.s./ha tested in this study but not at all in the higher application rate of 3600 g a.s./ha, the investigation of the lower test rate was repeated in a second study conducted in 2015.

The study conducted in 2015 (KCA 8.3.1.3/03; [redacted], B.; 2015; M-528899-01-1) was performed following the same study design as in 2014. In the repeat study for the lower rate of 570 g a.s./ha no adverse effects on mortality, flight intensity, behaviour, brood development (brood termination rate: 36.1%, brood index: 3.2, compensation index: 3.7 in test item compared to the control with brood termination rate: 29.6%, brood index: 3.5, compensation index: 4.1) as well as on colony strength and brood and food abundance were determined. Thus, this study confirms that fosetyl-Al has no overall adverse effect on brood development at the rate of 570 g a.s./ha.

Synopsis

Fosetyl-Al and Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) are of low acute toxicity to honey bees, with LD50 (oral and contact) above the highest tested dose levels (oral: LD_{50}> 108.5 µg a.s./bee and >219.0 µg prod/bee, contact: LD_{50}> 100 µg a.s./bee and >200.0 µg prod/bee).

The calculated Hazard Quotients for fosetyl-Al are 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 at the maximum envisaged fosetyl-Al application rate. This conclusion is confirmed by the results of the bee brood feeding study as well as by the results of the semi-field studies, which covered an application rate of 2000 g a.s./ha.

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

It can be concluded from the acute and chronic laboratory studies in adult honey bees as well as from the bee brood feeding study (Oomen *et al.*, 1992), investigating side-effects on immature honey bee life stages that fosetyl-Al is of a moderate general intrinsic toxicity to honey bees.

Regarding potential side effects of fosetyl-Al on immature honey bee life stages, the conducted bee brood feeding study (Oomen *et al.*, 1992) found slightly to moderately, but statistically significantly increased termination rates of eggs, young and old larvae. Despite of this observation, the brood index and brood compensation indices displayed a continuous increase without any statistical significant difference to the control, indicating a successful development of the brood. Overall the study revealed no ecologically adverse effects on the survival of adult bees and pupae, behaviour, colony strength and overall colony conditions. Thus, when considering the severity of the exposure situation in this worst-case screening test in combination with the absence of effects on both, colony level parameters and also on the overall development of bee brood, it can be concluded even on the basis of this worst-case screening study that the use of fosetyl-Al does not pose an unacceptable risk for adult honey bees, immature honey bee life stages and honey bee colonies.

In order to clarify whether the conclusions on the basis of lower tiered honey bee studies are correct, fosetyl-Al was subjected to confined semi-field testing (according to the provisions of OECD Guidance Document No. 75), by applying the two rates of 3600 and 570 g a.s./ha for Fosetyl-Al WG 80 to full-flowering *Phacelia* during honey bees actively foraging on the crop. This study design is from an apidological and apicultural point of view more realistic than an in-hive feeding of the test compound via a treated sugar solution, which contains the test substance at a concentration typically present in the spray tank (and as such at a very high concentration). The results of this first higher tier semi-field study confirmed the conclusions made above on the basis of the outcome of the lower-tiered studies, as no adverse direct or delayed effects on mortality of worker bees or pupae, foraging activity, behaviour, nectar- and pollen storage, colony strength, colony development as well as the development of bee brood were observed for the higher test rate of 3600 g a.s./ha, even under aggravated, forced exposure conditions and by digitally following-up in a very detailed manner the fate of individually marked brood cells (digital photographic assessment) from egg stage until emergence. In the same study the application of fosetyl-Al at the rate of 570 g a.s./ha did not cause adverse effect on mortality, flight intensity, colony strength and brood and food abundance. However, unclear findings were determined on brood development. In a repeated test following the same study design the absence of adverse effects on these assessment parameters together with the absence of adverse effects on the development of brood for the rate of 570 g a.s./ha was confirmed. Thus, this study confirms that fosetyl-Al has no overall adverse effect on brood development at the rate of 570 g a.s./ha.

Conclusion

The use of FEA + FLC WG 71.11 is intended on grapes at BBCH 15-81, that are not attractive to bees and at a rate of 3000 g product/ha, corresponding to 133 g fluopicolide/ha + 2000 g fosetyl-Al/ha. Overall, it can be concluded that fosetyl-Al, when applied at the maximum application rate of 2000 g a.s./ha does not pose an unacceptable risk to honey bees and honey bee colonies.

CP 10.3.1.1 Acute toxicity to bees

CP 10.3.1.1.1 Acute oral toxicity to bees

A formulation study on bees was carried out with Fosetyl-aluminium + Fluopicolide WG 71.11 ((FEA + FLC WG 71.11 = EXP 11074B) and reviewed by the RMS for the Annex I inclusion of fluopicolide under Directive 91/414/EEC. The study has been considered acceptable (EFSA Scientific Report 299 (2009)). A summary of this study is given below.
A new study was conducted based on recent guidelines and is presented under [redacted] ; [redacted]; 2015; M-528130-01-1.

Report:	KCP 10.3.1.1.1/01 [redacted]D; 2002; M-213718-01-1
Title:	Oral toxicity (LD50) to honey bees (*Apis mellifera* L.) Fosetyl-aluminium + AE C638206 water dispersible granule 667 + 44.4 g/kg Code: AE F053616 06 WG71 A101
Report No.:	C027638 (CW02/071)
Document No.:	M-213718-01-1
Guideline(s):	EPPO 170 (1992); OECD 213 (1998)
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The objective of this study was to investigate the effects of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) as a stomach poison (LD_{50}) on adult honey bees by oral application of the test substance.

Material and Methods:
Test item: FEA + FLC WG 71.11 (AE F053616 06 WG71 A1), Batch No.: OP210313, a fungicide WG type product containing fosetyl-Al + AE C638206 (measured concentrations 670 + 47.3 g/kg, respectively) as active ingredients.
Groups of 50 (10 x 5 replicates) honey bees (*Apis mellifera* L.) were exposed to 3 concentrations of the test substance, one control (food without any test substance) and 3 concentrations of a positive control (triazophos 40.9% w/w) in a sucrose diet paste for 5 hours. The concentrations of the test substance in the diet were 0.0139, 0.139 and 1.39% w/w. Actual food consumption was measured after 5 hours and then, the numbers of dead bees in each cage were assessed after 24, 48 and 72 hours.

Reference item (nominal dose): 0.0006, 0.0012 and 0.0047% triazophos: (oral test); control: 50% sucrose solution (oral test).

Dates of experimental work: July 18, 2002 – July 21, 2002

Results:

Validity criteria:

Validity Criteria	Recommended	Obtained
Control Mortality - Oral Test	≤ 10%	0.0%

The oral LD_{50} for the reference substance was 0.196 µg product per bee after 72 hr, which is within the expected range and so it can be concluded that the test system fulfilled the necessary requirements and the values for the test substance should be considered as valid.

The results of mortality among treated and control groups are presented in the table below:

Oral Toxicity Test			
Dose Level (µg product/bee)	**Mortality (%)**		
	24 hour	**48 hour**	**72 hour**
0 (Control)	0	0	0
FEA+FLC WG 71.11			
1.49	0	0	0
10.64	0	0	0
168.76	0	0	0
Toxic reference			
0.096	9	9	9
0.171	13	17	17
0.823	50	50	50

Observations:
Based on the quantity of food actually consumed during the 5 hour feeding period, the mean measured dose rates to which the bees were exposed were equivalent to 1.49, 10.64 and 168.76 µg product/bee. There were no mortality in the controls and the test substance treatments over the 72 hour duration of the study.

Conclusion:
Under the conditions of the test, FEA + FLC WG 71.11 the acute oral LD_{50} in honeybees is > 168.8 µg product/bee (72 hour).

Report:	[redacted]; 2015; M-528130-01-1
Title:	Fluopicolide + fosetyl-aluminium WG 71.14 (4.44+66.7) W: Effects (Acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory
Report No.:	99571035
Document No.:	M-528130-01-1
Guideline(s):	OECD 213 and 214 (1998)
Guideline deviation(s):	none
GLP/GEP:	**yes**

Objective:
The purpose of this study was to determine the acute contact and oral toxicity of Fosetyl-aluminium + Fluopicolide WG 71.14 (66.7 + 4.44) to the honey bee (*A. mellifera* L.).
Mortality of the bees was used as the toxic endpoint. Sublethal effects, such as changes in behaviour, were also assessed.

Material and Methods:
Test item: FEA + FLC WG 71.11 (Fosetyl-aluminium + Fluopicolide WG 71.14 (66.7 + 4.44)): fosetyl-aluminium (LS 74783): 67.2% w/w, fluopicolide (AE C638206): 4.47% w/w (all values analysed); Specification No.: 102000024700, Batch No.: EV39000244; TOX10794-00.
Under laboratory conditions *Apis mellifera* 50 worker bees were exposed for 48 hours to a single dose of 200.0 µg product per bee by topical application (contact limit test) and 30 worker bees per treatment level were exposed for 48 hours to doses of 219.0, 111.5, 55.5, 27.7 and 13.9 µg product per bee by feeding (oral dose response test, value based on the actual intake of the test item). It was not necessary to prolong the contact or the oral test, respectively.

Reference item (nominal dose): 0.30, 0.20, 0.15 and 0.10 µg dimethoate/bee (contact test); 0.30, 0.15, 0.08 and 0.05 µg dimethoate/bee (oral test); control: tap water with 0.5 % Adhäsit (contact test); 50% w/v sucrose solution (oral test).

Dates of experimental work: April 13, 2015 – May 28, 2015

Results:

Validity criteria:

Validity Criteria	**Recommended**	**Obtained**
Control Mortality - Contact Test	≤ 10%	6.0%
Control Mortality - Oral Test	≤ 10%	0.0%
LD_{50} of Reference Item (24 hours) - Contact Test	0.10 – 0.30 µg a.s./bee	0.23 µg a.s./bee
LD_{50} of Reference Item (24 hours) - Oral Test	0.10 – 0.35 µg a.s./bee	0.10 µg a.s./bee

The contact and oral tests are considered valid as the control mortality in each case was < 10% and the LD_{50} values obtained with the reference item (dimethoate), were within the required ranges.
The contact and oral LD_{50} (24 h) values of the reference item (dimethoate) were calculated to be 0.23 and 0.10 µg a.s./bee, respectively.

Toxicity to Honey Bees; laboratory tests

Test Item	FEA – FLC WG 71.11	
Test Species	*Apis mellifera*	
Exposure	contact (solution in Adhäsit (0.5 %)/water)	oral (sugar solution)
Application rate µg product/bee	200.0	219.0, 111.5, 55.5, 27.7 and 13.9
LD_{50} µg product/bee	> 200.0	> 219.0
LD_{20} µg product/bee	> 200.0	> 219.0
LD_{10} µg product/bee	> 200.0	> 219.0
NOED µg product/bee *	≥ 200.0	≥ 219.0

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

Mortality and behavioural abnormalities of the bees in the contact toxicity test

Dosage [µg product/bee]	**After 4 hours**		**After 24 hours**		**After 48 hours**	
	Mortality	**Behavioural abnormalities**	**Mortality**	**Behavioural abnormalities**	**Mortality**	**Behavioural abnormalities**
	Mean %	**Mean %**	**Mean %**	**Mean %**	**Mean %**	**Mean %**
Test item						
200.0	0.0	0.0	0.0	0.0	2.0	0.0
water	0.0	0.0	0.0	0.0	6.0	0.0
Reference item						
0.30	22.0	6.0	74.0	2.0	78.0	2.0
0.20	6.0	0.0	36.0	4.0	48.0	6.0
0.15	2.0	0.0	20.0	2.0	30.0	6.0
0.10	0.0	0.0	8.0	0.0	8.0	0.0

results are averages from three replicates (ten bees each) per dosage / control
water = CO_2/water-treated control

Mortality and behavioural abnormalities of the bees in the oral toxicity test

Ingested [µg product/bee]	After 4 hours		After 24 hours		After 48 hours	
	Mortality	behavioural abnormalities	Mortality	Behavioural abnormalities	Mortality	Behavioural abnormalities
	Mean %	Mean %	Mean %	Mean %	Mean %	Mean %
Test item						
219.0	0.0	0.0	0.0	0.0	3.3	0.0
111.5	0.0	0.0	0.0	0.0	6.7	0.0
55.5	0.0	0.0	0.0	0.0	0.0	0.0
27.7	0.0	0.0	0.0	0.0	3.3	0.0
13.9	0.0	0.0	0.0	0.0	3.3	0.0
water	0.0	0.0	0.0	0.0	0.0	0.0
Reference item						
0.31	16.7	83.3	100.0	0.0	100.0	0.0
0.16	0.0	93.3	96.7	3.3	96.7	0.0
0.08	0.0	23.3	13.3	3.3	26.7	0.0
0.05	0.0	0.0	0.0	0.0	0.0	0.0

results are averages from three replicates (ten bees each) per dosage / control
water = water/sugar treated control

Observations:

Contact Test:
At the end of the contact toxicity test (48 hours after application), there was 2.0% mortality at 200.0 µg product/bee. There was 6.0% mortality 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:
Actual oral doses of 219.0, 111.5, 55.5, 27.7 and 13.9 µg product per bee resulted in mortality ranging from 6.7 to 3.3% at the end of the test (after 48 hours). No mortality occurred in the 55.5 µg product/bee treatment as well as in the water control group. No test item induced behavioural abnormalities occurred after 48 hours.

Conclusions:
The toxicity of FEA + FLC WG 71.11 was tested in both, an acute contact (limit test) and an acute oral (dose response test) toxicity test on honey bees.
The contact LD_{50} (48 h) was > 200.0 µg product/bee. The oral LD_{50} (48 h) was > 219.0 µg product/bee.

CP 10.3.1.1.2 Acute contact toxicity to bees

Please refer also to Section CP 10.3.1.1.1.

Report:	KCP 10.3.1.1.2/01 [redacted]; 2002; M-213109-01-1
Title:	Contact toxicity (LD50) to honey bees (Apis mellifera L.) Fosetyl-aluminium + AE C638206 water dispersible granule 667 + 44.4 g/kg Code: AE F053616 06 WG71 A101
Report No.:	C027326
Document No.:	M-213109-01-1
Guideline(s):	EPPO: 170; OECD: 214
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The objective of this study was to investigate the effects of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) as a contact poison (LD_{50}) on adult honey bees by topical application of the test substance.

Material and Methods:
Test item: FEA + FLC WG 71.11 (AE F053616 06 WG71 A1), Batch No. OP210313, a fungicide WG type product containing fosetyl-Al + AE C638206 (measured concentrations 670 + 47.3 g/kg, respectively) as active ingredients.
Groups of 50 (10 x 5 replicates) honey bees (*Apis mellifera* L.) were tested in one control group, 5 test substance groups and 3 toxic reference groups.
Exposure of the bees was conducted by topical application of a single dose of 1.0 µl of the substance to the ventral thorax. The five dose rates of the test substance were 13.9, 34.9, 69.7, 104.6 and 139.5 µg product/bee. Before application, the bees were slightly anaesthetized with CO_2.
The numbers of dead bees in each cage were assessed after 24, 48 and 72 hours.

The positive control (triazophos 40.9%w/w) prepared in water was tested in 3 dose rates of 0.2, 0.3 and 0.4 µg product/bee.

Dates of experimental work: July 05, 2002 – July 08, 2002

Results:

Validity criteria:

Validity Criteria	Recommended	Obtained
Control Mortality - Contact Test	≤ 10%	0.0%

The contact LD_{50} for the reference substance was 0.254 µg product per bee after 24; 48 and 72h, which is within the expected range and so it can be concluded that the test system fulfilled the necessary requirements and the values for the test substance should be considered as valid.

The results of mortality among treated and control groups are presented in the table below:

Contact Toxicity Test			
Dose rate (µg product/bee)	**Total number of dead bees**		
	24 hour	**48 hour**	**72 hour**
0 (Control)	0	0	0
FEA+FLC WG 71.11			
13.9	1	1	1
34.9	2	2	2
69.7	0	0	0
104.6*	0	0	0
139.5*	0	0	0
Toxic reference			
0.2	6	6	6
0.3	45	45	45
0.4	44	44	44

*Application was not insured since there was sedimentation during the application

Observations:
The application of the two highest rates of the test substance was not insured since there was sedimentation during the application.

Conclusion:
Under the conditions of the test, FEA + FLC WG 71.11 the acute contact LD_{50} on honeybees is > 69.7 µg product/bee (72 hour).

CP 10.3.1.2 Chronic toxicity to bees

A 10 day chronic oral toxicity study was conducted with Fosetyl-Aluminium WG 80; the corresponding summary is provided in Document MCA, Section 8.3.1.2 (KCA 8.3.1.2/01, [redacted], A.; 2015; M-527663-01-1).

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

A honey bee brood feeding study according to the method of Oomen *et al.* 1998 (KCA 8.3.1.3/01, [redacted]; 2015; M-508986-01-2) has been conducted with Fosetyl-Aluminium WG 80 (Fosetyl-Al WG 80) and is included in Document MCA, Section 8.3.1.3.
Two semi-field honey bee brood studies (according to OECD 75) (KCA 8.3.1.3/02, [redacted], B.; 2015; M-526896-01-1, and KCA 8.3.1.3/03, [redacted], B.; 2015; M-528899-01-1) have been conducted with the Fosetyl-Al WG 80 and are included in the Document MCA, Section 8.3.1.3.

CP 10.3.1.4 Sub-lethal effects

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

CP 10.3.1.5 Cage and tunnel tests

Additional testing was not necessary when considering the outcome of the risk assessment and the results of the lower-tier studies.

CP 10.3.1.6 Field tests with honeybees

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

CP 10.3.2 Effects on non-target arthropods other than bees

The risk assessment was performed according to Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002) and to the Guidance Document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods (ESCORT 2, Candolfi *et al.*. 2000[1]).

Table 10.3.2- 1: FEA + FLC WG 71.11: Ecotoxicological endpoints for arthropods other than bees (current representative formulation)

Test species, Dossier-file-No., reference	Tested Formulation, study type, exposure	Ecotoxicological Endpoint
Aphidius rhopalosiphi [redacted].; 2003; M-230334-01-1 Rep.No: CW02/077 KCP 10.3.2.1/03	FEA + FLC WG 71.11; Laboratory, glass plates	Corr. Mortality [%] / Effect on Reproduction [%]
	200 g prod/ha	1.9 [A] / 19.7
	400 g prod/ha	-1.8 [A] / 16.9
Aphidius rhopalosiphi [redacted].; 2003; M-218198-01-1 Rep.No: C035091 KCP 10.3.2.1/01	FEA + FLC WG 71.11	LR_{50}: 8.22 kg prod/ha; ER_{50}: > 4.6 kg prod/ha
	Laboratory, glass plates	Corr. Mortality [%] / Effect on Reproduction [%]
	2.04 kg prod/ha	0.0 / -9.8 [B]
	3.07 kg prod/ha	3.3 / -4.2 [B]
	4.6 kg prod/ha	0.0 / 44.1
	6.9 kg prod/ha	6.7 / 66.4
	10.35 kg prod/ha	100 / n.a.
Typhlodromus pyri [redacted].; 2003; M-218199-01-1 Rep.No: C035092 KCP 10.3.2.1/02	FEA + FLC WG 71.11	LR_{50}: 7.13 kg prod/ha; ER_{50}: > 6.9 kg prod/ha
	Laboratory, glass plates.	Corr. Mortality [%] / Effect on Reproduction [%]
	2.04 kg prod/ha	3 / -4.4 [B]
	3.07 kg prod/ha	3 / 2.4
	4.6 kg prod/ha	14 / 23.9
	6.9 kg prod/ha	32 / 19.9
	10.35 kg prod/ha	97 / n.a.

[A]: A negative value indicates a higher mortality rate in the control than in the treatment.
[B]: A negative value indicates a higher reproduction rate in the treatment than in the control.
n.a.: not assessed

[1] 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

Tier 1 in-field risk assessment for other non-target arthropods

Table 10.3.2- 2: Tier 1 in-field risk assessment for non-target arthropods

Crop	Species	Appl. rate [kg prod./ha]	MAF	LR_{50} [kg prod./ha]	HQ	Trigger
Grapes	*T. pyri*	3.0	2.3	7.13	0.97	2
	A. rhopalosiphi	3.0	2.3	8.23	0.84	2

Tier 1 off-field risk assessment for other non-target arthropods

Table 10.3.2- 3: Tier 1 off-field risk assessment for non-target arthropods

Crop	Species	Appl. rate [kg prod./ha]	MAF	Drift [%]	VDF	Correction factor	LR_{50} [kg prod./ ha]	HQ	Trigger
Grapes	*T. pyri*	3.0	2.3	6.90	10	10	7.13	0.061	2
	A. rhopalosiphi	3.0	2.3	6.90	10	10	8.23	0.058	2

Conclusions
The calculated HQ values for the in-field and off-field scenario are below the trigger of concern indicating acceptable risk for non-target arthropods.

CP 10.3.2.1 Standard laboratory testing for non-target arthropods

Formulation studies on non-target arthropods were carried out with Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11 = EXP 11074B) and reviewed by the RMS during the European review of fluopicolide and the studies have been considered acceptable (EFSA Scientific Report 299 (2009)). Summaries of these studies are given below.

Report: KCP 10.3.2.1/01 [redacted]; 2003; M-218198-01-1
Title: Acute dose-response toxicity (LR50) of AE F053616 06 WG71 A1 to the cereal aphid parasitoid Aphidius rhopalosiphi (Destefani-Perez) under laboratory conditions
Report No.: C035091
Document No.: M-218198-01-1
Guideline(s): IOBC; Mead Briggs et all 2000
Guideline deviation(s): not specified
GLP/GEP: **yes**

Objective:
The purpose of this study was to determine the acute dose-response toxicity for the cereal aphid parasitoid *Aphidius rhopalosiphi* (DESTEFANI-PEREZ) exposed to different application rates of the test item and the fecundity of the surviving wasps affected by the test item in a laboratory test after residual contact exposure to fresh spray deposits on glass plates. Survival and fecundity of the parasitoid wasps were used as the test endpoints.

Material and Methods:

Test item: FEA + FLC WG 71.11 (AE F053616 06 WG71 A1), batch OP230059, a fungicide WG type product containing fosetyl-Al + fluopicolide (measured concentrations 671 + 45.1 g/kg, respectively) as active ingredients.

The fungicide product was tested under laboratory conditions after residual contact exposure of adults of the cereal parasitoid *Aphidius rhopalosiphi* to spray residues with rates of 2.04, 3.07, 4.6, 6.9 and 10.35 kg product/ha in 200 L deionized water/ha applied onto glass plates. The control was treated with deionized water (200 L/ha). Dimethoate EC 400 (0.3 mL product/ha in 200 L/ha of water) was used as a toxic reference treatment.

Adults of *Aphidius rhopalosiphi* were exposed in 3 replicates of 7 females and 3 males wasps (per treatment group) to the residues of the test item, reference item (only 1 replicate) and control, respectively. During the mortality test, the wasps were fed with aqueous fructose solution (25% w/v). The number of surviving wasps and the number of parasitised aphids (mummies) were recorded over a period of 2 days (mortality) + 12 days (reproduction). From these data the endpoints mortality and fecundity were calculated.

Findings:

Validity criteria were met during the test: only <13% mortality in the control (actual 0%), 50 to 100% corrected mortality with the reference substance (actual 100%), mean reproduction of ≥5 in the negative control (actual 14.3).

Only in the 10.35 kg product/ha test item group, 100% corrected mortality was observed, i.e. there was significant difference in mortality compared to the control group. No significant mortality was observed among parasitoids exposed to any other rates of FEA + FLC WG 71.11 compared to the control group.

Test item	**FEA + FLC WG 71.11**			
Test object	***Aphidius rhopalosiphi* (DESTEFANI-PEREZ)**			
Exposure	**Dried spray deposits onto glass plates**			
Treatment	**Mortality after 48 hours [%]**	**Reproduction**		
		mean number of mummies/ female	**Relative to control [%]**	**Reduction relative to control [%]**
Control	0	14.3	-	-
Application rate [kg product/ha]	Corrected mortality [%]			
2.04	0	15.7	109.8	0 (+ 9.8)
3.07	3.3	14.9	104.2	0 (+ 4.2)
4.6	0	8.0	55.9	44.1
6.9	6.7	4.8*	33.6	66.4
10.35	100*	not assessed	-	-
LR_{50} [CL 95 %]	**8.23 kg/ha (7.81 – 8.67)**			
Reference item Dimethoate 0.12 g a.i./ha	100	not assessed	-	-

*statistic difference from the control

The LR_{50} of was calculated as 8.23 kg product/ha with 95% confidence limits ranging from 7.81 to 8.67 kg/ha.

A statistically significant difference in reproduction (mean number of mummies/female) was observed in the highest dosed test item group (6.9 kg/ha) which was tested, where 66.4% reduction in reproduction was calculated when compared to the control group.

Conclusion:
The LR_{50} (median lethal rate) of FEA + FLC WG 71.11 to the cereal aphid parasitoid *Aphidius rhopalosiphi* was 8.23 kg product/ha. Less than 50% effects on reproduction were observed up to the rate of 4.6 kg product/ha (ER_{50} > 4.6 kg product/ha).

Report:	KCP 10.3.2.1/02[redacted]X; 2003; M-218199-01-1
Title:	Acute dose-response toxicity (LR50) of AE F053616 06 WG71 A1 to predatory mite Typhlodromus pyri (Scheuten) under laboratory conditions
Report No.:	C035092
Document No.:	M-218199-01-1
Guideline(s):	IOBC: Bluemel et al 2000
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The purpose of this study was to determine the acute dose-response toxicity for the predatory mite *Typhlodromus pyri* (SCHEUTEN) exposed to different application rates of the test item and the fecundity of the surviving mites in a laboratory test after residual contact exposure to fresh spray deposits on glass plates. Mortality and the effect on reproduction were used as the test endpoints.

Material and Methods:
Test item: FEA + FLC WG 71.11 (AE F053616 06 WG71 A1), batch OP230059, a fungicide WG type product containing fosetyl-Al + fluopicolide (measured concentrations 671 + 45.1 g/kg, respectively) as active ingredients.
FEA + FLC WG 71.11 was tested under laboratory conditions on protonymphs of the predatory mite *T. pyri* (SCHEUTEN) with rates of 2.04, 3.07, 4.6, 6.9 and 10.35 kg product/ha in 200 L deionized water/ha applied onto glass plates. The control was treated with deionized water (200 L/ha). Dimethoate EC 400 (10 mL product/ha in 200 L/ha of water) was used as a toxic reference treatment.
Protonymphs of *T. pyri* were exposed in 5 replicates of 20 mites (per treatment group) to the spray residues of the test item, reference item and control, respectively. During the assessments the predatory mites were fed with pollen (*Pinus negra* and *Betula pendula*). The number of surviving, dead and escaped predatory mites and the number of eggs laid per viable female per evaluation period were recorded over a period of 14 days. From these data the endpoints mortality and effect on reproduction were calculated.
The dose-response relationship in regard to mortality (LR_{50}) was determined.
The toxic reference treatment resulted in 100 % corrected mortality within 7 days.

Findings:
7 days after testing was started, 0 out of 100 predatory mites were recorded as dead in the control replicates (= 0%). By the end of the fecundity phase (day 14) the mean oviposition in the control was 5.93 eggs/female. After 7 days of exposure, 100 % of the mites were dead in the reference group (corrected mortality compared to control group: 100 %). Thus, the test accomplished the validity criteria (control group: < 20% mortality, > 4 eggs/female; reference group: 50 to 100% corrected mortality).
There were statistically significant differences in mortality in the 4.6, 6.9 and 10.35 kg product/ha test item treatment groups compared to control group.
With regard to reproduction statistically significant differences compared to control group were found in the test item treatment groups of 4.6 and 6.9 kg/ha, compared to the control group although less than 50% reduction of reproduction relative to the control was observed.
The LR_{50} (median lethal dose) of FEA + FLC WG 71.11 to *Typhlodromus pyri* was 7.13 kg product/ha with 95% confidence limits ranging from 6.62 to 7.67 kg product/ha.

Test item	**FEA + FLC WG 71.11**			
Test object	***Typhlodromus pyri*** **(SCHEUTEN)**			
Exposure	**Dried spray deposits on glass plates**			
Treatment	**Mortality after 7 days [%]**	**Reproduction**		
		mean number of eggs/female	**Relative to control [%]**	**Reduction relative to control [%]**
Control	0	5.93	-	-
Application rate [kg product/ha]	Corrected mortality [%]			
2.04	3	6.19	104.4	0 (-4.4)
3.07	3	5.79	97.6	2.4
4.6	14*	4.51*	76.1	23.9
6.9	32*	4.75*	80.1	19.9
10.35	97*	not assessed**	-	-
LR_{50} [CL 95 %]	**7.13 kg product/ha** (lower CL: 6.62) (upper CL: 7.67)			
Reference item Dimethoate EC 400 10 ml product/ha	100	not assessed	-	-

* statistically significantly different from the control ($p < 0.05$)

** Reproduction was not assessed because the corrected mortality was not ≤ 50%

Conclusion:
The LR_{50} (median lethal dose) of FEA+FLC WG 71.11 to *Typhlodromus pyri* was 7.13 kg product/ha with 95% confidence limits ranging from 6.62 to 7.67 kg product/ha. Effects on reproduction were at all test rates less than 50% (ER_{50} >10.35 kg product/ha).

Report:	KCP 10.3.2.1/03 [redacted], 2003; M-230334-01-1
Title:	Toxicity to the parasitoid wasp Aphidius rhopalosiphi (DeStephani-Perez) (Hymenoptera: Braconidae) in the laboratory Fosetyl-aluminium + AE C638206 water dispersible granule 667 + 44.4 g/kg Code: AE F053616 06 WG71 A101
Report No.:	C031825
Document No.:	M-230334-01-1
Guideline(s):	ESCORT: 2000; IOBC: 2000
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The objective of this laboratory study was to investigate the lethal and sublethal effects of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) on the parasitoid wasp *Aphidius rhopalosiphi* when exposed on a glass surface.

Material and Methods:
Test item: FEA + FLC WG 71.11 (AE F053616 06 WG71 A101), batch OP210313, a fungicide WG type product containing fosetyl-Al + fluopicolide (measured concentrations 670 + 47.3 g/kg, respectively) as active ingredients.
In this laboratory study the toxicity of freshly dried residues of the product FEA + FLC WG 71.11 applied onto glass plates, to the parasitoid wasp *Aphidius rhopalosiphi* was examined in compliance with the Principles of Good Laboratory Practice.
The test substance was applied at rates of 200 and 400 g product/ha and the effects were compared to a toxic reference (a.i.: dimethoate) applied at 0.12 g a.i./ha, and a water treated control.

Mortality of the adults was assessed 24 and 48 hours after exposure. From the water control and both test rates of FEA + FLC WG 71.11 impartially chosen females per treatment were each transferred to a cylinder containing untreated cereal plants infested with *Rhopalosiphum padi* for a period of 24 hours. This parasitation period provided a measure of reproductive success. The number of mummies was assessed 14 days later.

Findings:
Validity criteria were met during the test: only <13% mortality in the control (actual 3%), 50 to 100% corrected mortality with the reference substance (actual 100%), mean reproduction of >5 in the negative control (actual 26.8).
Mortality in the toxic reference substance was 100% at 0.12 g a.i. dimethoate/ha.

	Control	FEA + FLC WG 71.11 g product/ha		Reference substance (Dimethoate)
		200	400	
Correct, mortality (%) 48 hrs after application		- 1.9	- 1.8	100
Reproduction (after 1 day; average no. of mummies/ female)	26.8	21.5	22.3	n.d.
% Reduction of reproduction (relative to the control)	-	19.7	16.9	n.d.

Conclusion:
In both dose rates there was no treatment related mortality. The reduction in reproductive success relative to the control was <20%.

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

In view of the results presented in CP 10.3.2.1, no extended laboratory or aged residue studies were deemed necessary.

CP 10.3.2.3 Semi-field studies with non-target arthropods

In view of the results presented in Sections CP 10.3.2.1 and CP 10.3.2.2, no semi-field studies were deemed necessary.

CP 10.3.2.4 Field studies with non-target arthropods

In view of the results presented in Sections CP 10.3.2.1 to CP 10.3.2.3, no additional field studies were deemed necessary.

CP 10.3.2.5 Other routes of exposure for non-target arthropods

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

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

The risk assessment procedure follows the requirements as given in the Council Directive 91/414/EEC (Annex III), Council Directive 97/57/EC (Annex VI) and the Guidance Document on Terrestrial Ecotoxicology.

Predicted environmental concentrations used in risk assessment

The PEC_{soil} values below are taken from Document MCP, Section 9.1.3.

Table 10.4- 1: Initial max PEC_{soil} values (bold values were used in the tier 1 risk assessment)

Compound	Grapes
	$PEC_{soil, max}$
FEA + FLC WG 71.11 [a)]	**4.8 mg prod./kg dws**
Fosetyl-Al	**1.067 mg a.s./kg dws**
Phosphonic acid	2.167 mg pm/kg dws

a) calculated for a soil depth of 5 cm, a soil density of 1.5 g/mL and the use pattern for vines: 3 × 5.0 kg product/ha 60% interception for all applications

Table 10.4- 2: $PEC_{soil\ accu}$ values (mixing depth of 5 cm for plateau calculation; bold values were used in the tier 1 risk assessment)

Compound	Grapes	
	$PEC_{soil, plateau}$	$PEC_{soil, accu}$ [a]
Phosphonic acid	1.396 mg pm/kg dws	**3.563 mg pm/kg dws**

[a] $PEC_{soil, accu}$ means the sum of $PEC_{soil, max}$ and $PEC_{soil, plateau}$

CP 10.4.1 Earthworms

Table 10.4.1- 1: Endpoints used in risk assessment

Test item	Test species, test design	Ecotoxicological endpoint		Reference
FEA + FLC WG 71.11	*Eisenia fetida* reproduction 56 d, sprayed onto soil	NOEC	≥40500 g prod./ha (≥153.7 mg prod./kg dws)	[redacted],; 2003; M-219213-02-1 KCP 10.4.1.1/01
FEA + FLC WG 71.11	*Eisenia fetida* reproduction 56 d, mixed into soil	**NOEC**	**178 mg prod./kg dws**	[redacted],; 2016; M-566355-01-1 KCP 10.4.1.1/02
Fosetyl-Al WG 80	*Eisenia fetida* reproduction 56 d, mixed	**NOEC**	316 mg prod./kg dws **254.4 mg a.s./kg dws**	[redacted], S.; 2015; M-531997-01-1 KCA 8.4.1/02
Phosphonic acid	*Eisenia fetida* reproduction 56 d, mixed	NOEC	**≥498.79 mg pm/kg dws** [a)]	[redacted], U.; 1999; M-189218-01-1 KCA 8.4.1/01
	Eisenia fetida reproduction, 56 d, mixed	NOEC	<693 mg pm/kg dws	[redacted], T.; 2009; M-327177-01-1 KCA 8.4.1/03

dws = dry weight soil, a.s. = active substance; prod. = product; pm = pure metabolite
grey typeface = study is part of the Baseline Dossier

a) Values were corrected for a purity of 41.8% phosphonic acid weight by volume which is equal to 29.9% weight by weight. Test substance potassium salts of phosphonic acid has a density of 1.397. Therefore, one L of test substance weighs 1397 g and contains 418 g phosphonic acid (418/1397 = 0.299) with a weight/weight purity of 29.9%.

Bold values: endpoints used for risk assessment

Risk assessment for earthworms

Table 10.4.1- 2: TER calculations for earthworms

Compound	Species, study type	Endpoint		worst case $PEC_{soil,max}$	TER_{LT}	Trigger
FEA + FLC WG 71.11	Earthworm, reproduction	NOEC	≥153.7 mg prod./kg dws [b)]	4.8 mg prod./kg dws [a)]	≥32.0	5
FEA + FLC WG 71.11	Earthworm, reproduction	NOEC	178 mg prod./kg dws	4.8 mg prod./kg dws [a)]	37.1	5
Fosetyl-Al WG 80	Earthworm, reproduction	NOEC	254.4 mg a.s./ kg dws	1.067 mg a.s./ kg dws	238.4	5
Phosphonic acid	Earthworm, reproduction	NOEC	≥498.79 mg pm/ kg dws	3.563 mg pm/ kg dws	≥140.0	5

a) calculated for a soil depth of 5 cm, a soil density of 1.5 g/mL and the use pattern for vines: 3 × 3.0 kg product/ha 60% interception for all applications

b) NOER of ≥ 40.5 kg prod./ha from the sprayed study was recalculated to a NOEC ≥153.7 mg prod./kg dws, based on a surface of the test vessel of 189.75 cm² and 500 g dws per test vessel

All TER values calculated with the worst case $PEC_{soil,\ max}$ values clearly exceed the trigger value of 5 indicating that no unacceptable adverse effects on earthworms are to be expected from the intended uses of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11).

CP 10.4.1.1 Earthworms sub-lethal effects

A formulation study on earthworms was carried out with Fosetyl-aluminium + Fluopicolide (FEA + FLC WG 71.11 = EXP 11074B) and was reviewed by the RMS for the Annex I inclusion of fluopicolide under Directive 91/414/EEC. The study has been considered acceptable (EFSA Scientific Report 299 (2009)). A summary of this study is given below.

Report: KCP 10.4.1.1/01; [redacted] A; 2003; M-219213-02-1
Title: Effects of AE F053616 06 WG71 A1 on reproduction and growth of earhworms Eisenia fetida in artificial soil with 5% peat in the test substrate
Report No.: C035801
Document No.: M-219213-02-1
Guideline(s): BBA: VI 2-2; 1994; ISO: 11268 part 2 (1998)
Guideline deviation(s): not specified
GLP/GEP: **yes**

Objective:
The purpose of this study was to assess the sublethal effects of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) on reproduction, mortality and growth of the earthworm *Eisenia fetida* during an exposure in an artificial soil with 5 different test concentrations.

Material and Methods:
Test item: FEA + FLC WG 71.11 (AE F053616 06 WG71 A1), batch OP230059, a fungicide WG type product containing fosetyl-Al + fluopicolide (measured concentrations 671 + 45.1 g/kg, respectively) as active ingredients.
240 adult earthworms *Eisenia foetida* (approximately 11 to 12 months old, 4 x 10 animals per test group) were exposed in an artificial soil to the spraying rates of 2430, 8100, 12150, 16200 and 40500 g product/ha.
After 28 days, the number of surviving animals and their weight change were determined. They were then removed from the artificial soil.

After further 28 days, the number of offspring was determined.
The most recent reference test with Carbendazim (360 g a.s./L; trade name "Derosal SC360") was performed from August to October 2002. The test ensured that the laboratory test conditions were adequate and verified that the response of the test organisms did not change significantly over time.

Findings:
During the 4 weeks of exposure, one adult worm died at the treatment groups of 8100 and 16200 mg/ha and two worms died in the control group and in the 250 mg/ha group. No dead adult earthworms were observed in any other test groups.
The body weights of adult worms in the treatment groups increased by 32.9 to 41.9% compared to 28.5% in the control. None of the weight changes was significantly different compared to the control group (Dunnett-test, $\alpha = 0.05$).
The reproduction ranged from 292 to 377 juvenile worms in the groups treated with test item. The reproduction was not significantly different compared to the control group, where 291 juvenile worms were found (Dunnett-test test, $\alpha = 0.05$).
The quantity of food added (which roughly reflects the amount of food eaten) was 25.0 g in all the control and treatment groups.

Observations:
Effects on mortality and changes in body weight of the adults after an exposure period of 28 days and the number of offspring after 56 days.

	Eisenia foetida					
Test substance	**Control**	**FEA + FLC WG 71.11**				
Application rates (g product/ha)	**--**	**2430**	**8100**	**12150**	**16200**	**40500**
Mortality of adults after 28 days (%)	5.0	0	2.5	5.0	2.5	0
Mean change of adult body weights (%)	+ 28.5	+ 36.3	+ 32.9	+ 37.7	+ 36.7	+ 41.9
Standard deviation	± 11.3	± 8.3	± 14.4	± 8.0	± 4.8	± 1.9
Statistical comparison to the control*	--	n.s.	n.s.	n.s.	n.s.	n.s.
Number of offspring per group (56 days)	291	363	377	292	311	345
Standard deviation	± 46	± 60	± 44	± 69	± 45	± 38
Statistical comparison to the control*	--	n.s.	n.s.	n.s.	n.s.	n.s.

* Result of a Dunnett's multiple t-test, one sided smaller, $\alpha = 0.05$
n.s.: mean value not statistically significantly different compared to the control ($p \geq 0.05$)

Validity Criteria	**Recommended**	**Obtained**
Adult mortality	≤ 10%	5%
Number of juveniles per replicate	≥ 30	mean of four replicates was 291 worms
Coefficient of variation of reproduction	≤ 30%	15.9%

All validity criteria for the study were met.

Results of the most recent test with the reference substance (Carbendazim 360 g a.s./L): The EC_{50} for reproduction was calculated as 1.9 mg carbendazim/kg dry soil. The reproduction rate was significantly reduced at the application rates of 1.6 mg a.s./kg dry substrate.

Conclusion:
Under the conditions of the test, the chronic toxicity of FEA + FLC WG 71.11 to the earthworm *Eisenia foetida*, is defined as follows:
28 day NOEL related to growth of adults: 40500 g/ha
56 day NOEL related to parent mortality and reproduction: 40500 g/ha

EC_{10} cannot be calculated, since the exposure to test item did not result in an adverse effect on reproduction. The data meet the guideline requirements (coefficient of variation of the control reproduction < 30%). The NOEC is therefore considered reliable.

Report:	KCP 10.4.1.1/02[redacted]; 2016; M-566355-01-1
Title:	Fluopicolide + fosetyl-Al WG 71.1 (4.44+66.66) W: Effects on survival, growth and reproduction of the earthworm Eisenia andrei tested in artificial soil
Report No.:	16 10 48 204 S
Document No.:	M-566355-01-1
Guideline(s):	EU Directive 91/414/EEC Regulation (EC) No. 1107/2009 (2009) US EPA OCSPP Not Applicable
Guideline deviation(s):	none
GLP/GEP:	**yes**

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

Materials and Methods:
Test item: Fluopicolide + Fosetyl-Al WG 71.1 (4.44+66.66) W, Short name: FLC + FEA WG 71.1 (4.44 + 66.66) W, Supplier batch No.: EV39000244, Sample description: TOX10794-00, Specification No.: 102000024700, active ingredients (analysed content): 4.47% w/w fluopicolide (AE C638206), 67.2% w/w fosetyl-aluminium (LS 74783), water solubility: dispersible.

Adult earthworms (*Eisenia andrei*, about 3 months old) were exposed to 18, 32, 56, 100, 178, 316, 562 and 1000 mg test item/kg dry weight (dw) mixed into artificial soil containing 69.5% quartz sand, 20% kaolin clay, 10% sphagnum peat and 0.5% $CaCO_3$, at 18.1 to 21.9 °C and a photoperiod: light : dark = 16 h : 8 h (580 lux) and were fed with horse manure. Mortality and biomass change were determined after 4 weeks and reproduction was determined after 8 weeks.

Toxic standard: 5 and 10 mg Maypon Flow/kg soil dw; control: untreated, solvent control: none.

Dates of experimental work: June 02, 2016 - July 28, 2016

Findings:

Validity criteria:

Validity Criteria (OECD 222)	Recommended	Obtained
Adult mortality after 4 weeks	≤ 10%	≤ 1.3%
Number of juveniles per replicate	≥ 30	143, 161, 129, 187, 104, 165, 113 and 146
Coefficient of variation of reproduction:	≤ 30%	19.3%

Effects on mortality, growth and reproduction of the earthworms

Test item **Test object** **Exposure**	**Fluopicolide + Fosetyl-Al WG 71.1 (4.44+66.66)** ***Eisenia andrei*** **Artificial soil**		
	Mortality	**Biomass change**	**Reproduction**
	[mg test item/kg dw]		
NOEC	≥ 1000	≥ 1000	178
LOEC	> 1000	> 1000	316
EC_{10} [1)]	-	-	133
(95% confidence limits)			(99 – 179)
EC_{20} [1)]	-	-	223
(95% confidence limits)			(182 – 274)

[1)] based on Logit analysis

Observations:

Fluopicolide + Fosetyl-Al WG 71.1 (4.44+66.66) **[mg test item/kg d.w.]**									
	Control	**18**	**32**	**56**	**100**	**178**	**316**	**562**	**1000**
Mortality of adult worms after 4 weeks									
Mortality (%)	1.3	2.5	2.5	0.0	2.5	5.0	2.5	5.0	2.5
Biomass change (change in fresh weight after 4 weeks relative to initial fresh weight)									
Mean (mg)	102.9	105.8	96.6	100.3	103.5	99.4	104.7	110.0	102.4
Mean (%)	31.3	32.4	29.4	30.6	31.3	30.0	31.4	32.5	31.9
Number of juveniles per surviving adult worm after 8 weeks									
Mean	14.5	14.8	13.5	13.8	14.2	12.6	10.2	7.64	3.72
Number of juveniles per replicate after 8 weeks									
Mean	143.5	144.5	132.3	137.8	138.5	119.5	100.3*	72.5*	36.8*
Reproduction compared to control (%)									
% to control	100	100.7	92.2	96.0	96.5	83.3	69.9	50.5	25.6

No statistically significant differences between control and test item were calculated for mortality (Multiple Sequentially-rejective Fisher Test After Bonferroni-Holm, α = 0.05, one-sided greater and for biomass Williams-t-test, α = 0.05, two-sided)

* statistically significant different compared to control (Williams-t-test for reproduction, α = 0.05, one-sided smaller)

In a reference test, the number of juveniles was reduced by 39 and 96% by the toxic standard Maypon Flow (Carbendazim, SC 500) at concentrations of 5 and 10 mg product/kg dw in comparison to the control. Therefore, the observed effects assure a high sensitivity of the test system.

Conclusion:

Fluopicolide + Fosetyl-Al WG 71.1 (4.44+66.66) showed no statistically significantly adverse effects on survival and growth of the earthworm *Eisenia andrei* in artificial soil up to and including 1000 mg test item/kg soil dw, i.e. the highest concentration tested. The test item showed statistically significant adverse effects on reproduction at 316, 562 and 1000 mg test item/kg dw. Therefore, the No Observed Effect Concentration (NOEC) for reproduction was determined to be 178 mg test item/kg dw, and the Lowest Observed Effect Concentration (LOEC) for reproduction was determined to be 316 mg test item/kg dw.

CP 10.4.1.2 Earthworms field studies

In view of the results presented in Section CP 10.4.1.1, no additional field studies were deemed necessary.

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

Table 10.4.2- 1: Endpoints used in risk assessment

Test item	Test species, test design	Ecotoxicological endpoint	Reference
Collembola, reproduction			
FEA + FLC WG 71.11	*Folsomia candida* reproduction 28 d, mixed	**NOEC ≥ 1000 mg prod./kg dws**	[redacted]; 2015; M-530597-01-1 KCP 10.4.2.1/01
Fosetyl-Al WG 80	*Folsomia candida* reproduction 28 d, mixed	**NOEC** 562 mg prod./kg dws **452.4 mg a.s./kg dws**	[redacted], S.; 2015; M-529932-01-1 KCA 8.4.2.1/01
Phosphonic acid	*Folsomia candida* reproduction 28 d, mixed	**NOEC ≥ 1000 mg pm/kg dws**	[redacted], S.; 2015; M-529267-01-1 KCA 8.4.2.1/03
Soil mites, reproduction			
FEA + FLC WG 71.11	*Hypoaspis aculeifer* reproduction 14 d, mixed	**NOEC ≥ 1000 mg prod./kg dws**	[redacted]T; 2015; M-533325-01-1 KCP 10.4.2.1/02
Fosetyl-Al WG 80	*Hypoaspis aculeifer* reproduction 14 d, mixed	**NOEC** ≥ 1000 mg prod./kg dws **≥ 805 mg a.s./kg dws**	[redacted], L.; 2015; M-531417-01-1 KCA 8.4.2.1/02
Phosphonic acid	*Hypoaspis aculeifer* reproduction 14 d, mixed	**NOEC ≥ 1000 mg pm/kg dws**	[redacted], M. I.; 2015; M-532897-01-1 KCA 8.4.2.1/04

dws = dry weight soil; a.s. = active substance; pm = pure metabolite; prod.: product

Bold values: endpoints used for risk assessment

Risk assessment for other non-target soil meso- and macrofauna (other than earthworms)

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

Compound	Species	Endpoint	$PEC_{soil,max}$	TER_{LT}	Trigger
FEA + FLC WG 71.11	*Folsomia candida*	NOEC ≥ 1000 mg prod./ kg dws	4.8 mg prod./ kg dws	≥ 208.3	5
	Hypoaspis aculeifer	NOEC ≥ 1000 mg prod./ kg dws		208.3	
Fosetyl-Al WG 80	*Folsomia candida*	NOEC 452.4 mg a.s./ kg dws	1.067 mg a.s./ kg dws	424.0	
	Hypoaspis aculeifer	NOEC ≥ 805 mg a.s./ kg dws		≥ 754.3	
Phosphonic acid	*Folsomia candida*	NOEC ≥ 1000 mg pm/ kg dws	3.563 mg pm/ kg dws	≥ 280.7	
	Hypoaspis aculeifer	NOEC ≥ 1000 mg pm/ kg dws		≥ 280.7	

All TER values calculated with the worst case $PEC_{soil, max}$ values clearly exceed the trigger value of 5 indicating that no unacceptable adverse effects on soil macro-organisms are to be expected from the intended use of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11).

CP 10.4.2.1 Species level testing

Folsomia candida

Report: KCP 10.4.2.1/01 [redacted]; 2015; M-530597-01-1
Title: Fluopicolide + fosetyl-Al WG 71.14 (4.44+66.7) W - Effects on the reproduction of the collembolan *Folsomia candida*
Report No.: 15 10 48 144 S
Document No.: M-530597-01-1
Guideline(s): OECD 232 (2009): OECD Guideline for testing of chemicals No. 232 (adopted 7 September 2009): Collembolan reproduction test in soil ISO 11267 (1999): Soil quality - Inhibition of reproduction of *Collembola* (*Folsomia candida*) by soil pollutants
Guideline deviation(s): not specified
GLP/GEP: **yes**

Objective
The purpose of this study is to determine potential effects of different concentrations of the test item on the reproductive output of the collembolan *Folsomia candida* as a representative of soil micro-arthropods during a test period of 28 days. After 4 weeks the number of offspring (juveniles) and surviving parental collembolans were counted.

Material and methods:
Test item: Fosetyl-Al + Fluopicolide WG 71.14 (66.7 + 4.44), Short name: FEA + FEA WG 71.14 (66.7 + 4.44), Supplier batch No.: EV39000244, Sample description: TOX10794-00, Specification No.: 102000024700, active ingredients (analysed content): 67.2% w/w fosetyl-aluminium (LS 74783), 4.47% w/w fluopicolide (AE C638206), water solubility: dispersible.

10 *Collembola* (9-12 days old) were exposed to 100, 178, 316, 562 and 1000 mg test item/kg dry weight of soil containing 74.7% quartz sand, 20% kaolin clay, 5% sphagnum peat and 0.3% $CaCO_3$, at 19.8 – 21.7 °C and a photoperiod: light : dark = 16 h : 8 h (540 lux) and were fed weekly with granulated dry yeast. Mortality and reproduction were determined after 28 days.

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

Findings:

Mortality:
Mortality rates of 0 to 2.5% were recorded in the test item treatment groups. 2.5% parental mortality was observed in the control. No statistically significant effect (Multiple Sequentially-rejective Fisher Test After Bonferroni-Holm, α = 0.05, one-sided greater) on parental mortality was found for any concentration tested. No effects on behaviour of the collembolans were observed during the test.

Reproduction:
The mean number of juvenile collembolans counted four weeks after introduction of the parental collembolans into the test vessels was 797 in the control and 778, 799, 777, 805 and 788 at concentrations of 100, 178, 316, 562 and 1000 mg test item/kg soil d.w., respectively. No statistically significant effects (Williams-t-test, α = 0.05, one-sided smaller) on the number of juveniles were found for any concentration tested.

Test item **Test object** **Exposure**	**Fosetyl-Al + Fluopicolide WG 71.14 (66.7 + 4.44)** ***Folsomia candida*** **Artificial soil**			
mg test item/kg soil dry weight nominal concentration	**Adult mortality (%)**	**Mean number of juveniles per test vessel ± standard deviation**	**Reproduction (% of control)**	**Significance (*)**
Control	2.5	797 ± 104	-	
100	0.0	778 ± 74	98	-
178	2.5	799 ± 53	100	-
316	2.5	777 ± 76	97	-
562	0.0	805 ± 115	101	-
1000	2.5	788 ± 44	99	-
			Reproduction	
$NOEC_{reproduction}$ (mg pure substance/kg soil dry weight) $LOEC_{reproduction}$ (mg pure substance/kg soil dry weight)			≥ 1000 > 1000	

The calculations were performed with unrounded values
(*) = (Williams-t-test one-sided-smaller, α = 0.05, + = significant, - = not significant)
Percent reproduction: $(R_t / R_c) * 100$ %
R_t = mean number of juveniles observed in the treated groups
R_c = mean number of juveniles observed in the control group

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

Validity criteria	Recommended by the guideline	Obtained in this study
Mean adult mortality	≤ 20 %	2.5 %
Mean number of juveniles per replicate (with 10 collembolans introduced)	≥ 100	797
Coefficient of variation calculated for the number of juveniles per replicate	≤ 30 %	13.0 %

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

In a separate study (BioChem project No. R 14 10 48 003 S, dated July 30, 2014), the EC_{50} (reproduction) of the reference item boric acid was calculated to be 104 mg/kg soil dry weight. The results of the reference test demonstrate the sensitivity of the test system.

Conclusion:
The test item Fosetyl-Al + Fluopicolide WG 71.14 (66.7 + 4.44) showed no statistically significantly adverse effects on adult mortality and reproduction of the collembolan *Folsomia candida* in artificial soil up to and including 1000 mg test item/kg d.w.
Therefore, the overall No-Observed-Effect-Concentration (NOEC) was determined to be ≥ 1000 mg test item/kg d.w., and the Lowest-Observed-Effect-Concentration (LOEC) was determined to be > 1000 mg test item/kg d.w.

EC_{10} cannot be calculated, since the exposure to test item did not result in an adverse effect on reproduction. The maximum deviation from the control was < 10%. The data meet the guideline requirements (coefficient of variation of the control reproduction < 30%). The NOEC is therefore considered reliable.

Hypoaspis aculeifer

Report:	KCP 10.4.2.1/02 [redacted], 2015; M-533325-01-1
Title:	Fluopicolide + fosetyl-Al WG 71.110 (44.440+666.660) W: Effects on the reproduction of the predatory mite Hypoaspis aculeifer
Report No.:	15 10 48 145 S
Document No.:	M-533325-01-1
Guideline(s):	OECD 226 (2008)
Guideline deviation(s):	not specified
GLP/GEP:	yes

Objective
The purpose of this study was to determine potential effects of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) on the mortality and the reproductive output of the soil mite species *Hypoaspis aculeifer* (Canestrini) as a representative of soil micro-arthropods during a test period of 14 days.

Material and methods:
Test item: Fosetyl-Al + Fluopicolide WG 71.110 (666.660 + 44.440) [short name: FEA + FLC WG 71.110 (666.660 + 44.440)], Supplier batch No.: EV39000244, Sample description: TOX10794-00, Specification No.: 102000024700, analytical findings: 67.2% w/w fosetyl-aluminium (LS 74783); 4.47% w/w fluopicolide (AE C638206).

Ten adult, female *Hypoaspis aculeifer* per replicate (8 control replicates and 4 replicates for each test item concentration) were exposed to control (water treated) and treatments. Concentrations of 100, 178, 316, 562 and 1000 mg test item/kg dry weight soil were tested. In each test vessel 20 g dry weight artificial soil were weighed in. The *Hypoaspis aculeifer* were of a uniform age not differing more than two days (35 days after start of egg laying). During the test, they were fed every 2 - 3 days with *Tyrophagus putrescentiae* (Schrank).
During the study a temperature of 19.7 to 21.9 °C and light regime of 509 Lux, 16 h light : 8 h dark was applied. The artificial soil was prepared according to the guideline with the following constituents (percentage distribution on dry weight basis): 74.8% fine quartz sand, 5% sphagnum peat, 0.2 % $CaCO_3$ and 20% kaolin clay.
After a period of 14 days, the surviving adults and the living juveniles were extracted by applying a temperature gradient using a MacFadyen-apparatus. Extracted mites were collected in a fixing liquid.
All *Hypoaspis aculeifer* were counted.

Reference item (Dimethoate): 1.00, 1.60, 2.56, 4.10, 6.55 and 10.5 mg/kg soil d.w., control: untreated, solvent control: none.

Findings:

Validity Criteria	Recommended	Obtained
Mean mortality of adult females	≤ 20%	5.0%
Mean number of juveniles per replicate	> 30	255.5
Coefficient of variation (mean number of juveniles per replicate)	≤ 30%	13.4%

All validity criteria for the study were met.

Effects on mortality and reproduction of *Hypoaspis aculeifer*

Test item **Test object** **Exposure**	**FEA + FLC WG 71.110 (666.660 + 44.440)** ***Hypoaspis aculeifer*** **Artificial soil**	
	Adult mortality	**Reproduction**
	(mg test item/kg soil d.w.)	
NOEC	≥ 1000	≥ 1000
LOEC	> 1000	> 1000
EC_{10}	> 1000	> 1000
EC_{20}	> 1000	> 1000

Reference test:
In a separate study (Biochem project No. B 14 10 48 001 S, dated June 10, 2014), the EC_{50} (reproduction) of the reference item Dimethoate was calculated to be 6.2 mg/kg soil d.w.
The results of the reference test demonstrate the sensitivity of the test system.

Observations:

Endpoint	Control	Treatment group (mg test item/kg soil d.w.)				
		100	178	316	562	1000
Mortality of soil mites after 14 days (%)	5.0	0.0	0.0	0.0	2.5	0.0
Mean number of juveniles after 14 days	255.5	253.8	252.3	248.5	269.5	253.8
CV (%)	13.4	19.7	10.7	6.7	7.3	7.9
Reproduction (% of control)	**100**	**99**	**99**	**97**	**105**	**99**

Not statistically significantly different compared to the control (Chi^2 2x2 Table Test with Bonferroni Correction for mortality, α = 0.05, one-sided greater; Welch-t-test for Inhomogeneous Variances with Bonferroni-Holm Adjustment for reproduction, α = 0.05, one-sided smaller)
Calculations were done using unrounded values
Percent reproduction: (R_t / R_c) * 100 %
R_t = mean number of juvenile mites in the treated group(s)
R_c = mean number of juvenile mites in the control group
CV (%) = Coefficient of variation

Mortality:
In the control group a parental mortality of 5.0% could be observed. The mortality in the test item treatment groups ranged between 0.0 and 2.5%.

Reproduction:
Fourteen days after introduction of the parental mites into the test vessels, the mean number of juveniles was 255.5 in the control and 253.8, 252.3, 248.5, 269.5 and 253.8 at concentrations of 100, 178, 316, 562 and 1000 mg test item/kg soil d.w., respectively.

Conclusion:
The test item FEA + FLC WG 71.11 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 No-Observed-Effect-Concentration (NOEC) and Lowest-Observed-Effect-Concentration (LOEC) for mortality and for reproduction were determined to be ≥ 1000 and > 1000 mg test item/kg soil d.w., respectively.

EC_{10} cannot be calculated, since the exposure to test item did not result in an adverse effect on reproduction. The maximum deviation from the control was < 10%. The data meet the guideline requirements (coefficient of variation of the control reproduction < 30%). The NOEC is therefore considered reliable.

CP 10.4.2.2 Higher tier testing

In view of the results presented in Section CP 10.4.2.1, no further testing is necessary.

CP 10.5 Effects on soil nitrogen transformation

Table 10.5- 1: Endpoints used in risk assessment

Test item	Test design	Endpoint	Reference
N-transformation			
FEA + FLC WG 71.11	Study duration 28 d	no unacceptable effects 30.6 kg prod./ha **40.8 mg prod./kg dws**	[redacted],; 2003; M-218266-01-1 KCP 10.5/01
Fosetyl-Al	Study duration 28 d	no unacceptable effects 20.0 kg a.s./ha **26.6 mg a.s./kg dws**	[redacted], J.; 1998; M-184321-01-1 KCA 8.5/01
Fosetyl-Al WG 80	Study duration 42 d	no unacceptable effects 978 kg prod./ha 1304 mg prod./kg dws **1067 mg a.s./kg dws**	[redacted], T.; 2008; M-307736-01-1 KCA 8.5/02
Phosphonic acid	Study duration 42 d	no unacceptable effects 48.98 kg pm/ha **65.31 mg pm/kg dws**	[redacted], L.; 2015; M-528580-01-1 KCA 8.5/03

Bold values are used in the risk assessment
dws = dry weight soil; a.s. = active substance; pm = pure metabolite; prod.: product

Risk assessment for Soil Nitrogen Transformation

Table 10.5- 2: Risk Assessment for soil micro-organisms

Compound	Species	Endpoint [mg/kg]	$PEC_{soil,max}$ [mg/kg]	Refinement required
FEA + FLC WG 71.11	Soil micro-organisms	40.80 kg prod./ha	4.8 kg prod./ha	No
Fosetyl-Al	Soil micro-organisms	26.60 mg a.s./kg dws	1.067 mg a.s./kg dws	No
Fosetyl-Al WG 80	Soil micro-organisms	1067 mg a.s./kg dws	1.067 mg a.s./kg dws	No
Phosphonic acid	Soil micro-organisms	65.31 mg pm/kg dws	3.563 mg pm/kg dws	No

According to regulatory requirements the risk is acceptable, if the effect on nitrogen transformation at the maximum PEC_{soil} values is <25% after 100 days. In no case, deviations from the control exceeded 25% after 28 up to 42 days, indicating low risk to soil micro-organisms.

A formulation study on soil nitrogen transformation was carried out with Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11 = EXP 11074B) and reviewed by the RMS for the Annex I inclusion of fluopicolide under Directive 91/414/EEC. The study has been considered acceptable (EFSA Scientific Report 299 (2009)). A summary of this study is given below.

Report:	KCP 10.5/01 [redacted],; 2003; M-218266-01-1
Title:	AE C638206 & fosethyl Al WG71: Determination of effects on nitrogen transformation in soil
Report No.:	C035159
Document No.:	M-218266-01-1
Guideline(s):	OECD: 216
Guideline deviation(s):	not specified
GLP/GEP:	**yes**

Objective:
The objective of the experiment was to determine the influence of 4.08 and 40.80 mg of FEA + FLC WG 71.11/kg dry weight soil on nitrogen transformation in an agricultural soil.

Material and Methods:
Test item: FEA + FLC WG 71.11 (AE F053616 06 WG71 A1, batch OP220226, a fungicide WG type product containing fosetyl-Al + fluopicolide (measured concentrations 687 + 43.5 g/kg, respectively) as active ingredients).
A silty sand soil was exposed for 28 days to concentrations of 4.08 and 40.8 mg FEA + FLC WG 71.11/kg dry weight soil (application rates were equivalent to 3.06 and 30.60 kg FEA + FLC WG 71.11/ha, which is equivalent to 1x and 10x maximum field rate, respectively).
Lucerne-grass-green meal (5 g/kg dry weight soil) was added to soil samples to stimulate nitrogen transformation.

Findings:

Validity Criteria of the Study
In this study, the highest coefficient of variation (CV) between nitrate-N concentration in replicate control samples was 6% (7 and 14 days after treatment) and thus did not exceed the required limit <15%.

Effects on non-target soil micro-organisms

Test substance	FEA + FLC WG 71.11	
Test object	soil micro-organisms Nitrogen transformation (silty sand soil)	
Exposure	28 days	
mg/kg dry weight soil	4.08	40.80
kg/ha (equivalent)	3.06 (recommended field rate)	30.60 (10x recommended field rate)
Final result after 28 days	Difference to control: 0% (<25%)	Difference to control: +11% (<25%)

Conclusion:
During the 28-day experiment, the maximum field rate of FEA + FLC WG 71.11 (3 kg/ha) and 10-fold this field rate of FEA + FLC WG 71.11 had no influence on the microbial mineralization of nitrogen to a silty sand amended with lucerne-grass-green meal.

CP 10.6 Effects on terrestrial non-target higher plants

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

Tier 1 limit tests have been conducted with the formulation Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) according to OECD testing guideline 208A and 208B. These studies have been reviewed by the RMS for the Annex I inclusion of fluopicolide under Directive 91/414/EEC. The studies have been considered acceptable (EFSA Scientific Report 299 (2009)). The findings of these studies are provided in the following table and summaries can be found in Section CP 10.6.2.

Table 10.6- 1: Endpoints used in risk assessment (FEA + FLC WG 71.11)

Test organism	Study type	Max. effects	Test species	References
Maximum application rate: 3.0 kg product/ha				
Terrestrial non-target plants; 6 species	Vegetative vigour; Tier 1 single dose 21 days	no adverse effect	Lettuce	[redacted]; [redacted]; 2003; M-235777-01-1 KCP 10.6.2/01
		5% reduction of shoot fresh weight	Oilseed rape	
		no adverse effect	Cucumber	
		no adverse effect	Soybean	
		no adverse effect	Oats	
		no adverse effect	Onion	
Maximum application rate: 3.0 kg product/ha				
Terrestrial non-target plants; 6 species	Seedling emergence; Tier 1 single dose 21 days	11% reduction of germination	Lettuce	[redacted]A; [redacted]; 2003; M-115892-01-1 KCP 10.6.2/02
		no adverse effect	Oilseed rape	
		16% reduction of germination	Cucumber	
		no adverse effect	Soybean	
		no adverse effect	Oats	
		no adverse effect	Onion	

In the case of FEA + FLC WG 71.11, neither the tier 1 seedling emergence nor the vegetative vigour study showed phytotoxic effects >50% at the tested rate of 3.0 kg prod./ha.

Risk assessment for Terrestrial Non-Target Higher Plants

Effects on non-target plants are of concern in the off-field environment, where they may be exposed to spray drift. To demonstrate the low risk of the formulation to terrestrial non-target plants, TER calculations have been performed for the representative use in grapes. The test rate of 3.0 kg prod./ha was used as a most conservative endpoint estimate (i.e., ER_{50} > 3.0 kg prod./ha). For three applications to grapes up to 6.9% of the full application rate of 3.0 kg prod./ha are assumed to reach areas at 3m from the edge of the crop. The amount of spray drift from three applications reaching off-crop habitats is calculated using the 77th percentile estimates derived by the BBA (2000)[2] from spray-drift predictions of Ganzelmeier & Rautmann (2000)[3]. According to Table 13 in the Guidance document for Risk Assessment on Birds and Mammals (EFSA, 2009[4]) a multiple application factor of 1.8 (MAF_{7mean}) has to be applied for three applications in grapes with a minimum interval of 10 days. It should be pointed out that the use of MAF_{mean} for residues on plant surfaces is also supported by the new ESCORT 3 document (cf. [redacted], 2012[5]).

A deterministic risk assessment is provided in the following.

Table 10.6- 2: Deterministic risk assessment based on the ER_{50} > 3.0 kg prod./ha

Crop	Use pattern	Distance from field edge [m]	Drift [%]	MAF_m	PER [kg prod./ha]	TER (Trigger = 5)
Grapes	3 x 3.0 kg prod./ha (10 days interval)	3	6.90	1.8	0.373	> 8.1

From the calculation above, it is concluded that effects of the product on non-target terrestrial plants are not to be expected.

CP 10.6.1 Summary of screening data

Not necessary as guideline GLP studies for terrestrial non-target plants are available (see Section CP 10.6.2).

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

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

[4] European Food Safety Authority; Guidance Document on Risk Assessment for Birds & Mammals on request from EFSA. EFSA Journal 2009; 7(12):1438. [139 pp.].

[5] [redacted], P. (2012): Rationale for harmonization of the multiple application factor (MAF) approach in ecotoxicological risk assessment. In: Alix, A., Bakker, F., Barrett, K., Brühl, C.A., Coulson, M., Hoy, S., Jansen, J.-P., Jepson, P., Lewis, G., [redacted], P., Süßenbach, D., van Vliet, P. (eds.): ESCORT 3: Linking Non-Target Arthropod Testing and Risk Assessment with Protection Goals. pp. 90-94. SETAC Press

CP 10.6.2 Testing on non-target plants

<u>Vegetative vigour</u>

Report:	KCP 10.6.2/01 [redacted]力; [redacted]; 2003; M-235777-01-1
Title:	Non-target terrestrial plants: An evaluation of the effects of AE F053616 06 WG71 A1 in the vegetative vigour test (Tier 1)
Report No.:	C034924
Document No.:	M-235777-01-1
Guideline(s):	OECD 208 B (July 2000, draft)
Guideline deviation(s):	not specified
GLP/GEP:	**no**

Objective:
The purpose of the study was to evaluate the phytotoxic effects of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) on six species representing non-target terrestrial plant species during the seedling emergence and growth following a pre-emergence application of the product.

Material and methods:
Test item was FEA + FLC WG 71.11 (AE F053616 06 WG71 A1; other Code No.: EXP11074); Lot No.: OP230059; active ingredient: fosetyl-Al (AE F053616) 671 g/kg and fluopicolide (AE C638206) 45.1 g/kg.
Six species of terrestrial non-target plants (2 monocots and 4 dicots) were treated with the highest nominal product application rate of 3 kg/ha.
The species tested were cucumber (*Cucumis sativus*), lettuce (*Lactuca sativa*), oat (*Avena sativa*), oil seed rape (*Brassica napus*) onion (*Allium cepa*) and soybean (*Glycine max*). Plants were treated at the 2-4-leaf stage with foliar spray application.
Spray treatments were applied once, at test initiation, with a sprayer set at the nominal spray volume of 400 L/ha. Control pots were sprayed with deionized water. Four replicates with five seeds per pot for each species were tested. All pots were individually contained in saucers and retained on benches within a greenhouse. Plants were assessed for emergence, survival and rated for phytotoxicity on days 7, 14 and 21 days. At study termination, biomass endpoint determinations were performed for plant fresh weights.

Findings:
A summary of all the assessments for the day 21 vegetative vigor test (Tier 1) for the effects of FEA + FLC WG 71.11 are shown in the table below:

	Lettuce	Oilseed rape	Cucumber	Soybean	Oats	Onion
Mortality * (% of control)	0	0	0	0	0	0
Phytotoxicity (% of control)	0	0	0	0	0	0
Fresh Weight (% growth inhibition)	+21	-5	+9	+1	+1	+25

"+" means an increase of the evaluated endpoint; "-" means a decrease
* Mortality is a measure of the survival of those plants that germinated and effect of the treatment is presented as a percentage of the survival in the control.

There was no effect of FEA + FLC WG 71.11 on the emergence and mortality of the six species tested.
No phytotoxicity was observed in the six species tested.
The only adverse effect on biomass was a 5% reduction of fresh weight for oilseed rape.
No statistically significant effect for any measurement parameter was detected for any species tested.

Conclusion:
This study shows that the highest nominal product application rate for FEA+FLC WG 71.11 of 3 kg/ha shows no adverse effect >50% to representative non-target crops in the vegetative vigor test.

Seedling emergence

Report:	KCP 10.6.2/02[redacted]; [redacted], 2003, M-115892-01-1
Title:	Non-target terrestrial plants: An evaluation of the effects of AE F053616 WG71 A1 in the seedling emergence and growth test (Tier 1)
Report No.:	SE03/07
Document No.:	M-115892-01-1
Guideline(s):	OECD: 208 A
Guideline deviation(s):	not specified
GLP/GEP:	**no**

Objective:
The purpose of the study was to evaluate the phytotoxic effects of Fosetyl-aluminium + Fluopicolide WG 71.11 (FEA + FLC WG 71.11) on six species representing non-target terrestrial plant species during the seedling emergence and growth following a pre-emergence application of the product.

Material and methods:
Test item was FEA + FLC WG 71.11 (AE F053616 00 WG71 A1; other Code No.: EXP11074); Lot No.: OP230059; active ingredient: fosetyl-Al (AE F053616) 671 g/kg and fluopicolide (AE C638206) 45.1 g/kg.
Six species of terrestrial non-target plants (2 monocots and 4 dicots) were treated with the highest nominal product application rate for FEA + FLC WG 71.11 of 3 kg/ha. The species tested were cucumber (*Cucumis sativus*), lettuce (*Lactuca sativa*), oat (*Avena sativa*), oil seed rape (*Brassica napus*) onion (*Allium cepa*) and soybean (*Glycine max*).
All seeds were planted on the day of application and test duration was 21 days following application of the test item.
Spray treatments were applied once at test initiation, with a sprayer set at the nominal spray volume of 400 liters/ha. Control pots were sprayed with deionized water. Four replicates with five seeds per pot for each species were tested. All pots were individually contained in saucers and retained on benches within a greenhouse.
Plants were assessed for emergence, survival and rated for phytotoxicity on days 7, 14 and 21 days. At study termination, biomass endpoint determinations were performed for plant fresh weights.

Findings:
A summary of all the assessments for the day 21 seedling emergence and growth test (Tier 1) for the effects of FEA + FLC WG 71.11 are shown in the table below:

	Lettuce	Oilseed rape	Cucumber	Soybean	Oats	Onion
Germination (% inhibition)	-21	0	-16	+29	0	+13
Mortality * (% of control)	+7	0	-6	+18	0	0
Phytotoxicity (% of control)	0	0	0	0	0	0
Fresh Weight ** (% growth inhibition)	-10	+4	+4	+16	+6	+15

"+" means an increase of the evaluated endpoint; "-" means a decrease

* Mortality is a measure of the survival of those plants that germinated and effect of the treatment is presented as a percentage of the survival in the control.

** on a per plant basis, and statistical analysis using the Williams Test revealed no significant differences between control and treatment for any species at the 5% level.

Reductions in germination of lettuce and cucumber were observed 21 days after application. There were no major adverse effects on mortality.
Similarly there were no major adverse effects on biomass. Only lettuce showed a 10% reduction in biomass, but this was not statistically significant. No statistically significant effect was detected for any species tested.

Conclusion:
This study shows that the highest nominal product application rate for FEA + FLC WG 71.11 of 3 kg/ha shows no adverse effect > 50% to representative non-target crops in the seedling emergence and growth test.

CP 10.6.3 Extended laboratory studies on non-target plants

In view of the results presented in Section CP 10.6.2, no further studies are deemed necessary.

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

In view of the results presented in Sections CP 10.6.2 and CP 10.6.3, no further studies are deemed necessary.

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

No further tests on other terrestrial organism deem to be necessary due to the low to moderate acute and chronic ecotoxicity of Fosetyl-aluminium + Fluopiclide WG 71.11 as presented in Sections CP 10.1 to CP 10.6. Additionally, no public literature reference as evaluated in Document MCA, Section 9, reported on an adverse effect.

CP 10.8 Monitoring data

No monitoring data have been collected by the applicant nor have they been reported in any of the public literature references as evaluated in Document MCA, Section 9. Due to the low to moderate acute and chronic ecotoxicity of Fosetyl-aluminium + Fluopicolide WG 71.11 as presented in Sections CP 10.1 to CP 10.7, no monitoring of non-target organism is deemed to be necessary.