

REGISTRATION REPORT

Part B

Section 9

Ecotoxicology

Detailed summary of the risk assessment

Product code: SAP50SCF

Product name(s): FOLPEC

Chemical active substance:

Folpet, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Selectis Produtos para a Agricultura, S.A.

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August 2024 (final Core Assessment)

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When	What
December 2023	V0 - Initial version submitted by the Selectis Produtos para a Agricultura, S.A. for submission to Poland in the frame of new PPP registration (According Art. 33 of Regulation EC No 1107/2009).
April 2024	V1 - Updated version submitted by the Selectis Produtos para a Agricultura, S.A. with updated PECsw values and the risk assessment for aquatic organism.
May 2024	V2 - Updated version submitted by the Selectis Produtos para a Agricultura, S.A.
May 2024	<p>Initial zRMS assessment</p> <p>The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are struck through and shaded for transparency.</p> <p>Following the evaluation and before sending the document for commenting, all coloured highlighting was removed, from the parts updated by the Applicant, for better legibility.</p>
August 2024	<p>Final report (Core Assessment updated following the commenting period)</p> <p>Additional information/assessments included by the zRMS in the report in response to comments received from the Applicant are highlighted in yellow. Not agreed or not relevant information are struck through and shaded for transparency.</p>

Table of Contents

9	Ecotoxicology (KCP 10).....	6
9.1.1	Overall conclusions.....	8
9.1.1.1	Effects on birds (KCP 10.1.1), Effects on terrestrial vertebrates other than birds (KCP 10.1.2), Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3).....	8
9.1.1.2	Effects on aquatic organisms (KCP 10.2)	8
9.1.1.3	Effects on bees (KCP 10.3.1).....	9
9.1.1.4	Effects on arthropods other than bees (KCP 10.3.2)	9
9.1.1.5	Effects on non-target soil meso- and macrofauna (KCP 10.4), Effects on soil microbial activity (KCP 10.5)	9
9.1.1.6	Effects on non-target terrestrial plants (KCP 10.6)	9
9.1.1.7	Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)	10
9.1.2	Grouping of intended uses for risk assessment.....	10
9.1.3	Consideration of metabolites	10
9.2	Effects on birds (KCP 10.1.1).....	11
9.2.1	Toxicity data	11
9.2.1.1	Justification for new endpoints	12
9.2.2	Risk assessment for spray applications.....	12
9.2.2.1	First-tier assessment (screening/generic focal species)	12
9.2.2.2	Higher-tier risk assessment.....	13
9.2.2.3	Drinking water exposure.....	13
9.2.2.4	Effects of secondary poisoning.....	14
9.2.2.5	Biomagnification in terrestrial food chains.....	15
9.2.3	Risk assessment for baits, pellets, granules, prills or treated seed.....	15
9.2.4	Overall conclusions.....	15
9.3	Effects on terrestrial vertebrates other than birds (KCP 10.1.2).....	16
9.3.1	Toxicity data	16
9.3.1.1	Justification for new endpoints	16
9.3.2	Risk assessment for spray applications.....	16
9.3.2.1	First-tier assessment (screening/generic focal species)	16
9.3.2.2	Higher-tier risk assessment.....	17
9.3.2.3	Drinking water exposure.....	17
9.3.2.4	Effects of secondary poisoning.....	18
9.3.2.5	Biomagnification in terrestrial food chains.....	19
9.3.3	Risk assessment for baits, pellets, granules, prills or treated seed.....	19
9.3.4	Overall conclusions.....	19
9.4	Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)	19
9.5	Effects on aquatic organisms (KCP 10.2).....	20
9.5.1	Toxicity data	20
9.5.1.1	Justification for new endpoints	22
9.5.2	Risk assessment	30
9.5.3	Overall conclusions.....	43
9.6	Effects on bees (KCP 10.3.1).....	44
9.6.1	Toxicity data	44
9.6.1.1	Justification for new endpoints	46

9.6.2	Risk assessment	46
9.6.2.1	Hazard quotients for bees.....	46
9.6.2.2	Higher-tier risk assessment for bees (tunnel test, field studies).....	51
9.6.3	Effects on bumble bees	51
9.6.4	Effects on solitary bees	53
9.6.5	Overall conclusions.....	53
9.7	Effects on arthropods other than bees (KCP 10.3.2)	54
9.7.1	Toxicity data	54
9.7.1.1	Justification for new endpoints	55
9.7.2	Risk assessment	55
9.7.2.1	Risk assessment for in-field exposure.....	55
9.7.2.2	Risk assessment for off-field exposure	56
9.7.2.3	Additional higher-tier risk assessment.....	56
9.7.2.4	Risk mitigation measures	56
9.7.3	Overall conclusions.....	56
9.8	Effects on non-target soil meso- and macrofauna (KCP 10.4)	57
9.8.1	Toxicity data	57
9.8.1.1	Justification for new endpoints	58
9.8.2	Risk assessment	58
9.8.2.1	First-tier risk assessment.....	58
9.8.2.2	Higher-tier risk assessment	59
9.8.3	Overall conclusions.....	59
9.9	Effects on soil microbial activity (KCP 10.5).....	59
9.9.1	Toxicity data	59
9.9.1.1	Justification for new endpoints	60
9.9.2	Risk assessment	60
9.9.3	Overall conclusions.....	61
9.10	Effects on non-target terrestrial plants (KCP 10.6)	61
9.10.1	Toxicity data	61
9.10.1.1	Justification for new endpoints	62
9.10.2	Risk assessment	62
9.10.2.1	Tier-1 risk assessment (based screening data)	62
9.10.2.2	Tier-2 risk assessment (based on dose-response data).....	62
9.10.2.3	Higher-tier risk assessment	62
9.10.2.4	Risk mitigation measures	62
9.10.3	Overall conclusions.....	62
9.11	Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)	63
9.12	Monitoring data (KCP 10.8)	63
9.13	Classification and Labelling	63
Appendix 1	Lists of data considered in support of the evaluation	65
Appendix 2	Detailed evaluation of the new studies	75
A 2.1	KCP 10.1 Effects on birds and other terrestrial vertebrates.....	75
A 2.1.1	KCP 10.1.1 Effects on birds	75
A 2.1.2	KCP 10.1.2 Effects on terrestrial vertebrates other than birds	75
A 2.1.3	KCP 10.1.3 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians).....	75
A 2.2	KCP 10.2 Effects on aquatic organisms	75

A 2.2.1	KCP 10.2.1 Acute toxicity to fish, aquatic invertebrates, or effects on aquatic algae and macrophytes	75
A 2.2.2	KCP 10.2.2 Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms.....	88
A 2.2.3	KCP 10.2.3 Further testing on aquatic organisms	88
A 2.3	KCP 10.3 Effects on arthropods	88
A 2.3.1	KCP 10.3.1 Effects on bees	88
A 2.3.2	KCP 10.3.2 Effects on non-target arthropods other than bees.....	112
A 2.4	KCP 10.4 Effects on non-target soil meso- and macrofauna.....	130
A 2.4.1	KCP 10.4.1 Earthworms	130
A 2.4.2	KCP 10.4.2 Effects on non-target soil meso- and macrofauna (other than earthworms)	144
A 2.5	KCP 10.5 Effects on soil nitrogen transformation.....	144
A 2.5.1	Study 1	144
A 2.5.2	Study 2	146
A 2.6	KCP 10.6 Effects on terrestrial non-target higher plants.....	148
A 2.6.1	KCP 10.6.1 Summary of screening data	148
A 2.6.2	KCP 10.6.2 Testing on non-target plants.....	148
A 2.6.3	KCP 10.6.3 Extended laboratory studies on non-target plants	151
A 2.7	KCP 10.7 Effects on other terrestrial organisms (flora and fauna).....	151
A 2.8	KCP 10.8 Monitoring data.....	151
Appendix 3	Calculations considering the minimum proposed application rate.....	152
Appendix 4	Additional calculations based on soil DT₅₀ of 4.68 days for folpet	165

9 Ecotoxicology (KCP 10)

Critical GAP and overall conclusions

Table 0-1: Table of critical GAPs

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Use-No. *	Member state(s)	Crop and/or situation (crop destination / purpose of crop)	F, Fn, Fpn G, Gn, Gpn or I **	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)	Application				Application rate			PHI (days)	Remarks: e.g. g safener/ synergist per ha	Conclusion						
					Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/season	Min. interval between applications (days)	kg or L product/ha a) max. rate per appl. b) max. total rate per crop/season	g or kg as/ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max			Birds	Mammals	Aquatic organisms	Bees	Non-target arthro-	Soil organisms	Non-target plants
Zonal uses (field or outdoor uses, certain types of protected crops)																				
1	SEU; FR; ES; IT; PT; GR; BG; HR PL	Wheat	F	Septoria	Tractor mounted spray	BBCH 30-59	a) 2 b) 2	14 days	a) 0,9 – 1,2 L/ha b) 1,8 – 2,4 L/ha	a) 450 - 600 g as/ha b) 900 – 1200 g as/ha	150-400	42		A	A	R ¹⁾ (R1)	A	A	A	A
2	SEU; FR; ES; IT; PT; GR; BG; HR PL	Barley	F	Helminstorporium	Tractor mounted spray	BBCH 30-59	a) 2 b) 2	14 days	a) 0,9 – 1,2 L/ha b) 1,8 – 2,4 L/ha	a) 450 - 600 g as/ha b) 900 – 1200 g as/ha	150-400	42		A	A	R ¹⁾ (R1)	A	A	A	A

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

¹⁾ Risk mitigation measures referred to Polnad PECsw scenarios

Explanation for column 15 – 21 “Conclusions”

A	Acceptable, Safe use
R	Further refinement and/or risk mitigation measures required
C	To be confirmed by cMS
N	No safe use

**Remarks
table:**

- (1) Numeration necessary to allow references
- (2) Use official codes/nomenclatures of EU
- (3) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)
- (4) F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application
- (5) Scientific names and EPPO-Codes of target pests/diseases/ weeds or when relevant the common names of the pest groups (*e.g.* biting and sucking insects, soil born insects, foliar fungi, weeds) and the developmental stages of the pests and pest groups at the moment of application must be named
- (6) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench
Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
- (7) Growth stage at first and last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
- (8) The maximum number of application possible under practical conditions of use must be provided
- (9) Minimum interval (in days) between applications of the same product.
- (10) For specific uses other specifications might be possible, *e.g.*: g/m³ in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products
- (11) The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha).
- (12) If water volume range depends on application equipments (*e.g.* ULVA or LVA) it should be mentioned under “application: method/kind”.
- (13) PHI - minimum pre-harvest interval
- (14) Remarks may include: Extent of use/economic importance/restrictions

9.1.1 Overall conclusions

9.1.1.1 Effects on birds (KCP 10.1.1), Effects on terrestrial vertebrates other than birds (KCP 10.1.2), Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)

The risk assessment to birds and mammals was conducted according to the EFSA Guidance Document for the Risk Assessment for Birds and Mammals.

An acceptable risk was obtained for SAP50SCF at the screening phase for acute exposure and at the first-tier for long-term exposure. The risk assessment for drinking water was not triggered. An acceptable risk was also obtained for the secondary poisoning scenarios. Overall, birds present an acceptable risk towards SAP50SCF when used according to the proposed application patterns.

An acceptable risk was obtained for SAP50SCF at the screening phase for both acute and long-term exposure. The risk assessment for drinking water was not triggered. An acceptable risk was also obtained for the secondary poisoning scenarios. Overall, mammals present an acceptable risk towards SAP50SCF when used according to the proposed application patterns.

9.1.1.2 Effects on aquatic organisms (KCP 10.2)

An acceptable risk of SAP50SCF can be concluded when the appropriate mitigation measures are in place:

Dose	Application number	Crop	Mitigation measure
Maximum dose	Single	Winter cereals	None
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	R1 and R3 scenario: 5 meters of vegetated filter strip
		Spring cereals	R4 scenario: 15 meters of vegetated filter strip
Minimum dose (see Appendix 3)	Single	Winter cereals	None
		Spring cereals	R4 scenario: 5 meters of vegetated filter strip
	Multiple	Winter cereals	R3 scenario: 5 meters of vegetated filter strip
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip

Dose	Application number	Crop	Mitigation measure
Maximum dose	Single	Winter cereals	D1 scenario: 10 meters of vegetated filter strip D2 scenario: restriction of application at MSs level
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	D2 scenario: restriction of application at MSs level R1, R3 and R4 scenarios: 20 meters of vegetated filter strip
		Spring cereals	D1, R4 scenario: 20 meters of vegetated filter strip
Minimum dose	Single	Winter cereals	None
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	R1, R3 and R4 scenarios: 10 meters of vegetated filter strip
		Spring cereals	R4 scenario: 20 meters of vegetated filter strip

Based on the risk assessment for relevant scenarios for Poland such as: D3, D4 and R1, the following risk mitigation measures are required for the maximum dose:

- 20-meter vegetative buffer zone (R1 scenario) for multiple application for winter and spring cereals

Based on the risk assessment for relevant scenarios for Poland such as: D3, D4 and R1, the following risk mitigation measures are required for the minimum dose:

- 10-meter vegetative buffer zone (R1 scenario) for multiple application for winter and spring cereals

For remained scenarios included in the Tablow above, which are not relevant for Poland such as (D1, D2, R3 and R4) the risk mitigation measures for aquatic organism are left for decision at MSs.

Please note that additional aquatic risk assessment may be required by the concerned Member States that do not accept simulations performed according to FOCUS recommendations.

For metabolites of active compound, the risk is acceptable with no need for risk mitigation measures.

9.1.1.3 Effects on bees (KCP 10.3.1)

~~The risk assessment for bees was conducted according to SANCO/10329/2002 rev 2 final and according to EFSA Journal 2013;11(7):3295 for illustrative purposes only as the last mentioned guidance document is not yet noted. Acceptable acute and chronic risks were determined towards bees (honey, bumble and solitary ones) after exposure to SAP50SCF in the proposed application patterns.~~

The acute risk assessment for bees and bumble bees was conducted according to SANCO/10329/2002 rev 2 final and according to EFSA Journal 2013;11(7):3295 indicated an acceptable risk.

The chronic adult and larvae risk assessment is not required according to SANCO/10329/2002 rev 2 final. However, based on Tier 1 an unacceptable chronic risk for adult bee and larva bees for scenario weed and next crop (only larvae) based on the EFSA Journal 2013; 11(7):32 (not approved at EU level) is concluded. Further refinement of the chronic risk assessment presented by the Applicant was not verified by zRMS and it is left at MSs level.

9.1.1.4 Effects on arthropods other than bees (KCP 10.3.2)

The risk assessment for non-target arthropods was conducted according to SANCO/10329/2002 rev 2 final. Acceptable in- and off-field risks were determined towards bees after exposure to SAP50SCF in the proposed application patterns.

9.1.1.5 Effects on non-target soil meso- and macrofauna (KCP 10.4), Effects on soil microbial activity (KCP 10.5)

The risk assessment for soil macro- and mesofauna was conducted according to SANCO/10329/2002 rev 2 final. An acceptable risk is proven for earthworms when exposed to the active substance, its metabolites and the formulated product. No data on springtail and mites is submitted since no unacceptable risks were concluded for non-target terrestrial arthropods and earthworms. Therefore, springtail and mites are not expected to be affected at the proposed application rates.

The risk assessment for microorganisms was conducted according to SANCO/10329/2002 rev 2 final. An acceptable risk is proven for microorganisms when exposed to the active substance, its metabolites and the formulated product.

9.1.1.6 Effects on non-target terrestrial plants (KCP 10.6)

The risk assessment for non-target terrestrial plants was conducted according to SANCO/10329/2002 rev 2 final. Since folpet is a fungicide, a tier 1 risk assessment was conducted, and an acceptable risk is proven

when SAP50SCF is applied at the proposed application rates.

9.1.1.7 Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)

No available data and not relevant as an acceptable is proven for all assessed organisms.

9.1.2 Grouping of intended uses for risk assessment

The following table documents the grouping of the intended uses to support application of the risk envelope approach (according to SANCO/11244/2011).

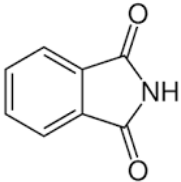
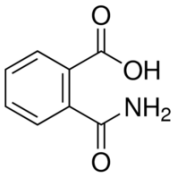
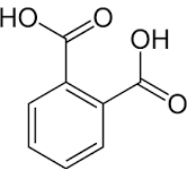
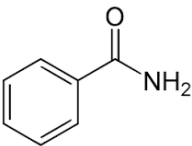
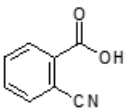
Table 9.1-2: Critical use pattern of SAP50SCF grouped according to application pattern

Grouping according to application pattern			
Group	Intended uses	Relevant use parameters for grouping	Relevant parameter or value for sorting
9.2 and 9.3 Effects on birds and vertebrates other than birds			
Bulbs and onion like crops, cereals , fruiting vegetables, leafy vegetables, legume forage, maize, oilseed rape, potatoes, pulses, root and stem vegetables, strawberries, sugar beet, and sunflower	Wheat Barley	Crop group according to EFSA/2009/1438	2 x 450-600 g a.s./ha, 14 days interval, BBCH 30-59
9.4 Effects on aquatic organisms			
Cereals	Wheat Barley	Grouped according to E-Fate.	2 x 450-600 g a.s./ha, 14 days interval, BBCH 30-59
9.5 Effects on bees			
Field crops	Wheat Barley	Crop group according to application pattern	2 x 450-600 g a.s./ha, 14 days interval, BBCH 30-59
9.6 Effects on non-target arthropods			
Field crops	Wheat Barley	Crop group according to application pattern	2 x 450-600 g a.s./ha, 14 days interval, BBCH 30-59
9.7 and 9.8 Effects on soil macro- and mesofauna and microbial activity			
-	Wheat Barley	Grouped according to E-Fate.	2 x 450-600 g a.s./ha, 14 days interval, BBCH 30-59
9.9 Effects on non-target terrestrial plants			
Field crops	Wheat Barley	Crop group according to application pattern	2 x 450-600 g a.s./ha, 14 days interval, BBCH 30-59

9.1.3 Consideration of metabolites

A list of metabolites found in environmental compartments is provided below. The need for conducting a metabolite-specific risk assessment in the context of the evaluation of SAP50SCF is indicated in the table.

Table 9.1-3 Metabolites of folpet

Metabolite	Chemical structure	Molar mass	Maximum occurrence in compartments	Risk assessment required?
Phthalimide		147.1	Soil: 64.9 %* Water: 26.0 % Sediment: 5.9 %	Yes, soil and aquatic organisms
Phthalamic acid		165.2	Soil: 16.7 %* Water: 13.3 % Sediment: —	Yes, soil and aquatic organisms
Phthalic acid		166.1	Soil: 16.6 %* Water: 37.5 % Sediment: 3.8 %	Yes, soil and aquatic organisms
Benzamide		121.1	Soil: — Water: 10.2 % Sediment: —	Yes, aquatic organisms
2-cyanobenzoic acid		147.1	Soil: — Water: 39.7 % Sediment: —	Yes, aquatic organisms

* Maximum occurrences derived from aerobic soil degradation studies

zRMS comments:

Metabolites relevant for soil and water compartment listed in Table 9.1-3 are the same as indicated in EFSA Scientific Report (2009) 297, 70-80.

The maximum occurrence is relevant for exposure evaluation, for information agreed in this area please refer to the Core Assessment, Part B, Section 8, where all respective data are provided and used in calculation of PEC_{soil} and $PEC_{sw/sed}$ values, considered further in the risk assessment.

As the information on the maximum occurrence was not checked in detail, it was struck through in Table 9.1-3.

9.2 Effects on birds (KCP 10.1.1)

9.2.1 Toxicity data

Avian toxicity studies have been carried out with folpet. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on birds of SAP50SCF were not evaluated as part of the EU assessment of folpet.

However, the provision of further data on the SAP50SCF is not considered essential, because the toxicity of the formulation can reliably be predicted based on the active substance data.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.2-1: Endpoints and effect values relevant for the risk assessment for birds

Species	Substance	Exposure System	Results	Reference
Quail	folpet	Acute	LD₅₀ > 2510 2150 mg/kg bw	EFSA Scientific Report (2009) 297, 70-80
Quail Mallard	folpet	Dietary	LC ₅₀ > 5000 ppm Calculated daily dose: Quail: >1127 mg/kg bw/d Mallard: >746 mg/kg bw/d	EFSA Scientific Report (2009) 297, 70-80
Quail Mallard	folpet	Reproductive toxicity	NOEC = 1000 ppm (highest concentration tested) Calculated daily dose: Quail: 78.3 mg/kg bw/d Mallard: 90.0 mg/kg bw/d	EFSA Scientific Report (2009) 297, 70-80

zRMS comments:

Avian toxicity data for folpet provided in Table 9.2-1 above were verified by zRMS and then confirmed that they are in line with EU agreed endpoints reported in EFSA Journal (2007) 124, 1-84 and EFSA Scientific Report (2007) 106, respectively.

9.2.1.1 Justification for new endpoints

Since the dietary endpoint divided by 10 (74.6 mg/kg bw/d) is lower than the reproductive endpoint (78.3 mg/kg bw/d), the lowest will be used for the long-term risk assessment below.

According to EFSA Scientific Report (2009) 297, 70-80, the risk assessment for the active substance will cover the risk assessment of folpet metabolites.

9.2.2 Risk assessment for spray applications

The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438).

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals covers the risk for birds from all intended uses (see 9.1.2).

9.2.2.1 First-tier assessment (screening/generic focal species)

The results of the acute and reproductive first-tier risk assessments are summarised in the following tables.

Table 9.2-2: Screening step of the acute and long-term/reproductive risk for birds due to the use of SAP50SCF in cereals

Intended use		Cereals				
Active substance/product		folpet				
Application rate (g/ha)		2 x 600				
Acute toxicity (mg/kg bw)		2510 2150				
TER criterion		10				
Crop scenario Growth stage	Indicator/generic focal species	SV ₉₀	MAF ₉₀	DDD ₉₀ (mg/kg bw/d)	TER _a	
-	Small omnivorous bird	158.8	1.2	114.34	21.96	

					18.8
Reprod. toxicity (mg/kg bw/d)	74.6				
TER criterion	5				
Crop scenario Growth stage	Indicator/generic focal species	SV_m	MAF_m × TWA	DDD_m (mg/kg bw/d)	TER_{lt}
-	Small omnivorous bird	64.8	1.4 x 0.53	28.85	2.6

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2-3: First-tier assessment of the long-term/reproductive risk for birds due to the use of SAP50SCF in cereals

Intended use		Cereals			
Active substance/product		folpet			
Application rate (g/ha)		2 x 600			
Reprod. toxicity (mg/kg bw/d)		74.6			
TER criterion		5			
Crop scenario Growth stage	Indicator/generic focal species	SV_m	MAF_m × TWA	DDD_m (mg/kg bw/d)	TER_{lt}
Cereals BBCH ≥ 40	Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods	3.3	1.4 x 0.53	1.46916	50.8
Cereals BBCH 30 -39	Small omnivorous bird “lark” Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods	5.4	1.4 x 0.53	2.40408	31.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

zRMS comments:

The screening step risk assessment for active substance is agreed by zRMS.
TER_A value for the exposure to folpet is above the trigger of 10, indicating acceptable acute risk for birds.
However, TER_{LT} value is below the trigger 5 for long-term exposure, indicating an unacceptable risk for birds.
Therefore, further refinements at Tier-1 level has been provided and an acceptable is concluded as TER_{LT} is above trigger value of 5.

Overall, acceptable acute and long-term risk may be concluded for birds exposed to folpet in SAP50SCF.

9.2.2.2 Higher-tier risk assessment

Not relevant as acceptable risks are observed in the first tier risk assessment.

9.2.2.3 Drinking water exposure

When necessary, the assessment of the risk for birds due to uptake of contaminated drinking water is conducted for a small granivorous bird with a body weight of 15.3 g (*Carduelis cannabina*) and a drinking water uptake rate of 0.46 L/kg bw/d (*cf.* Appendix K of EFSA/2009/1438).

Leaf scenario

Since SAP50SCF is not intended to be applied on leafy vegetables forming heads or crop plants with comparable water collecting structures at principal growth stage 4 or later, the leaf scenario does not have to be considered.

Puddle scenario

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances ($K_{oc} < 500$ L/kg) or 3000 in the case of more sorptive substances ($K_{oc} \geq 500$ L/kg).

With a $K(f)_{oc}$ of 304, folpet belongs to the group of less sorptive substances. To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals covers the risk for birds from all intended uses (see 9.1.2).

Due to the rapid degradation of folpet in water (DT_{50} of 0.018 d), an effective rate of 600 g a.s./ha will be used in the calculations.

Effective application rate (g/ha)	=	600		
Acute toxicity (mg/kg bw)	=	2510	quotient =	0.24
Reprod. toxicity (mg/kg bw/d)	=	78.3	quotient =	7.7

zRMS comments:

The leaf scenario does not have to be considered taking into account the proposed uses (cereals).
The evaluation of the risk resulting from uptake of contaminated water in Puddle scenario was not required since ratio between effective application rate and endpoint relevant for acute risk and long-term assessment is <3000.

9.2.2.4 Effects of secondary poisoning

The $\log P_{ow}$ of folpet amounts to 3.017 and thus exceeds the trigger value of 3. A risk assessment for effects due to secondary poisoning is required.

Risk assessment for earthworm-eating birds via secondary poisoning

According to EFSA/2009/1438, the risk for vermivorous birds is assessed for a bird of 100 g body weight with a daily food consumption of 104.6 g. Bioaccumulation in earthworms is estimated based on predicted concentrations in soil.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals covers the risk for birds from all intended uses (see 9.1.2).

Table 9.2-4: Assessment of the risk for earthworm-eating birds due to exposure to folpet via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

Parameter	folpet	comments
PEC_{soil} (twa = 21 d) (mg/kg soil)	0.193	
$\log P_{ow} / P_{ow}$	3.017/1039.9	
K_{oc}	304	Worst-case assumption
foc	0.02	Default
BCF_{worm}	2.19	$BCF_{worm/soil} = (PEC_{worm,ww}/PEC_{soil,dw})$ $= (0.84 + 0.012 \times P_{ow}) / foc \times K_{oc}$
PEC_{worm}	0.42	$PEC_{worm} = PEC_{soil} \times BCF_{worm/soil}$
Daily dietary dose (mg/kg bw/d)	0.44	$DDD = PEC_{worm} \times 1.05$

Parameter	folpet	comments
NOEL (mg/kg bw/d)	78.3	
TER _{lt}	176	Acceptable risk

TER values shown in bold fall below the relevant trigger.

Risk assessment for fish-eating birds via secondary poisoning

According to EFSA/2009/1438, the risk for piscivorous birds is assessed for a bird of 1000 g body weight with a daily food consumption of 159 g. Bioaccumulation in fish is estimated based on predicted concentrations in surface water as a limit value for admissible concentrations of folpet in water.

Table 9.2-5: Assessment of the risk for fish-eating birds due to exposure to folpet via bioaccumulation in fish (secondary poisoning) for the intended use in cereals

Parameter	folpet	comments
PEC _{sw} (twa = 21 d) (mg/L)	0.002495	Worst-case value: spring cereals, multiple applications, D1 scenario (set 2)
BCF _{fish}	56	Whole fish
BMF	-	biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	0.14	PEC _{fish} = PEC _{water} × BCF _{fish}
Daily dietary dose (mg/kg bw/d)	0.02	DDD = PEC _{fish} × 0.159
NOEL (mg/kg bw/d)	78.3	
TER _{lt}	3525	Acceptable risk

TER values shown in bold fall below the relevant trigger.

zRMS comments:

The Applicants' approach in evaluation of the risk of secondary poisoning is in line with EFSA (2009). Compounds selected for this assessment are agreed by the zRMS. Evaluation was not triggered for remaining metabolites of active substance due to their log Pow <3.

Despite all corrections of the zRMS, acceptable risk of secondary exposure from all relevant compound could be concluded for birds.

9.2.2.5 Biomagnification in terrestrial food chains

Not relevant.

9.2.3 Risk assessment for baits, pellets, granules, prills or treated seed

Not relevant.

9.2.4 Overall conclusions

The risk assessment to birds was conducted according to the EFSA Guidance Document for the Risk Assessment for Birds and Mammals.

An acceptable risk was obtained for SAP50SCF at the screening phase for acute exposure and at the first-tier for long-term exposure.

The risk assessment for drinking water was not triggered.

An acceptable risk was also obtained for the secondary poisoning scenarios.

Overall, birds present an acceptable risk towards SAP50SCF when used according to the proposed application patterns.

9.3 Effects on terrestrial vertebrates other than birds (KCP 10.1.2)

9.3.1 Toxicity data

Mammalian toxicity studies have been carried out with folpet. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on mammals of SAP50SCF were not evaluated as part of the EU assessment of folpet.

However, the provision of further data on the formulation SAP50SCF is not considered essential, because the toxicity of the formulation can reliably be predicted based on the active substance data.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.3-1: Endpoints and effect values relevant for the risk assessment for mammals

Species	Substance	Exposure System	Results	Reference
Rat	folpet	Acute	LD ₅₀ >2000 mg/kg bw	EFSA Scientific Report (2009) 297, 70-80
Rat	folpet	Reproductive toxicity	The EPCO meeting agreed on a NOEC of 1500 ppm	EFSA Scientific Report (2009) 297, 70-80

zRMS comments:

Mammalian toxicity data for folpet provided in Table 9.3-1 above has been validated by zRMS and confirmed that they are in line with EU agreed endpoints reported in EFSA Journal (2007) 124, 1-84 and EFSA Scientific Report (2007) 106, respectively. However, in case of NOEC value it should be noted that correct NOEC value of 140.9 mg a.s./kg b.w./d according to confirmatory data of August 2010 should be used in the long-term risk assessment.

9.3.1.1 Justification for new endpoints

Since the agreed NOEC is an overall from a 2-generation reproduction dietary study, a conversion factor of 0.1 will be applied to the NOEC and the correspondent endpoint for risk assessment is 150 mg/kg bw/d.

9.3.2 Risk assessment for spray applications

The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Mammals and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438).

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals covers the risk for mammals from all intended uses (see 9.1.2).

9.3.2.1 First-tier assessment (screening/generic focal species)

The results of the acute and reproductive first-tier risk assessments are summarised in the following tables.

Table 9.3-2: Screening step of the acute and long-term/reproductive risk for mammals due to the use of SAP50SCF in cereals

Intended use	Cereals
Active substance/product	folpet
Application rate (g/ha)	2 × 600
Acute toxicity (mg/kg bw)	2000
TER criterion	10

Crop scenario Growth stage	Indicator/generic focal species	SV ₉₀	MAF ₉₀	DDD ₉₀ (mg/kg bw/d)	TER _a
-	Small herbivorous mammal	118.4	1.2	85.25	23.5
Reprod. toxicity (mg/kg bw/d)		140.9 150			
TER criterion		5			
Crop scenario Growth stage	Indicator/generic focal species	SV _m	MAF _m × TWA	DDD _m (mg/kg bw/d)	TER _{lt}
-	Small herbivorous mammal	48.3	1.4 x 0.53	21.50	6.55 6.98

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

zRMS comments:

The acute risk assessment for exposure of folpet to mammals has been validated by zRMS.

~~Due to the change in reproductive endpoint (correct NOEC value of 140.9 mg a.s./kg b.w./d according to confirmatory data of August 2010) the long-term risk assessment has been amended by zRMS.~~

The calculated TER_A and TER_{LT} values are above the triggers of 10 and 5 respectively, indicating no unacceptable risk to mammals following application of SAP50SCF according to the proposed use pattern.

9.3.2.2 Higher-tier risk assessment

Not relevant as acceptable risks are observed in the first tier risk assessment.

9.3.2.3 Drinking water exposure

When necessary, the assessment of the risk for mammals due to uptake of contaminated drinking water is conducted for a small omnivorous mammal with a body weight of 21.7 g (*Apodemus sylvaticus*) and a drinking water uptake rate of 0.24 L/kg bw/d (cf. Appendix K of EFSA/2009/1438).

Puddle scenario

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances ($K_{oc} < 500$ L/kg) or 3000 in the case of more sorptive substances ($K_{oc} \geq 500$ L/kg).

With a $K(f)_{oc}$ of 304, folpet belongs to the group of less sorptive substances. To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals covers the risk for mammals from all intended uses (see 9.1.2).

Due to the rapid degradation of folpet in water (DT_{50} of 0.018 d), an effective rate of 600 g a.s./ha will be used in the calculations.

Effective application rate (g/ha)	=	600		
Acute toxicity (mg/kg bw)	=	2000	quotient =	0.3
Reprod. toxicity (mg/kg bw/d)	=	140.9 150	quotient =	4.0

zRMS comments:

The leaf scenario does not have to be considered taking into account the proposed uses (cereals).
The evaluation of the risk resulting from uptake of contaminated water in Puddle scenario was not required since ratio between effective application rate and endpoint relevant for acute risk and long-term assessment is <3000.
~~The reproductive toxicity endpoint used in the risk assessment should be 140.9 mg/kg bw/d and for this reason this value was considered by zRMS in the Table above.~~

9.3.2.4 Effects of secondary poisoning

The log P_{ow} of folpet amounts to 3.017 and thus exceeds the trigger value of 3. A risk assessment for effects due to secondary poisoning is required.

Risk assessment for earthworm-eating mammals via secondary poisoning

According to EFSA/2009/1438, the risk for vermivorous mammals is assessed for a small mammal of 10 g body weight with a daily food consumption of 12.8 g. Bioaccumulation in earthworms is estimated based on predicted concentrations in soil.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals covers the risk for mammals from all intended uses (see 9.1.2).

Table 9.3-3: Assessment of the risk for earthworm-eating mammals due to exposure to folpet via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

Parameter	folpet	comments
PEC _{soil} (tw _a = 21 d) (mg/kg soil)	0.193	
log P_{ow} / P_{ow}	3.017/1039.9	
K _{oc}	304	Worst-case assumption
f _{oc}	0.02	Default
BCF _{worm}	2.19	$BCF_{worm/soil} = (PEC_{worm,ww} / PEC_{soil,dw})$ $= (0.84 + 0.012 \times P_{ow}) / f_{oc} \times K_{oc}$
PEC _{worm}	0.42	$PEC_{worm} = PEC_{soil} \times BCF_{worm/soil}$
Daily dietary dose (mg/kg bw/d)	0.54	$DDD = PEC_{worm} \times 1.28$
NOEL (mg/kg bw/d)	150	
TER _{lt}	277	Acceptable risk

TER values shown in bold fall below the relevant trigger.

Risk assessment for fish-eating mammals via secondary poisoning

According to EFSA/2009/1438, the risk for piscivorous mammals is assessed for a mammal of 3000 g body weight with a daily food consumption of 425 g. Bioaccumulation in fish is estimated based on predicted concentrations in surface water as a limit value for admissible concentrations of folpet in water.

Table 9.3-4: Assessment of the risk for fish-eating mammals due to exposure to folpet via bioaccumulation in fish (secondary poisoning) for the intended use in cereals

Parameter	folpet	comments
PEC _{sw} (tw _a = 21 d) (mg/L)	0.002495	Worst-case value: spring cereals, multiple applications, D1 scenario (set 2)
BCF _{fish}	56	Whole fish
BMF	-	biomagnification factor (relevant for $BCF \geq 2000$)
PEC _{fish}	0.14	$PEC_{fish} = PEC_{water} \times BCF_{fish}$

Parameter	folpet	comments
Daily dietary dose (mg/kg bw/d)	0.02	DDD = PEC _{fish} × 0.142
NOEL (mg/kg bw/d)	150	
TER _{It}	7560	Acceptable risk

TER values shown in bold fall below the relevant trigger.

9.3.2.5 Biomagnification in terrestrial food chains

Not relevant.

9.3.3 Risk assessment for baits, pellets, granules, prills or treated seed

Not relevant.

9.3.4 Overall conclusions

The risk assessment to mammals was conducted according to the EFSA Guidance Document for the Risk Assessment for Birds and Mammals.

An acceptable risk was obtained for SAP50SCF at the screening phase for both acute and long-term exposure.

The risk assessment for drinking water was not triggered.

An acceptable risk was also obtained for the secondary poisoning scenarios.

Overall, mammals present an acceptable risk towards SAP50SCF when used according to the proposed application patterns.

zRMS comments:

The Applicants' approach in evaluation of the risk of secondary poisoning is in line with EFSA (2009). Compounds selected for this assessment are agreed by the zRMS. Evaluation was not triggered for remaining metabolites of active substance due to their log Pow <3.

Despite all corrections of the zRMS, acceptable risk of secondary exposure from all relevant compounds could be concluded for mammals.

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

No data available.

9.5 Effects on aquatic organisms (KCP 10.2)

9.5.1 Toxicity data

Studies on the toxicity to aquatic organisms have been carried out with folpet and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents, as well as in Appendix 2 of this document (new studies).

Effects on aquatic organisms of SAP50SCF were not evaluated as part of the EU assessment of folpet. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.5-1: Endpoints and effect values relevant for the risk assessment for aquatic organisms – folpet and relevant metabolites

Species	Substance	Exposure System	Results	Reference
Rainbow trout	folpet	96 h, s	LC ₅₀ = 233 µg a.s./L	EFSA Scientific Report (2009) 297, 70-80
Brown trout*	folpet	96 h, s	LC₅₀ = 98 µg a.s./L	EFSA Scientific Report (2009) 297, 70-80
Common carp	Folpet	96-h, s	LC ₅₀ = 1012 µg/L	Addendum to DAR, Folpet (2005)
3-spined stickleback	Folpet	96-h, s	LC ₅₀ = 229 µg/L	Addendum to DAR, Folpet (2005)
Roach	Folpet	96-h, s	LC ₅₀ = 211 µg/L	Addendum to DAR, Folpet (2005)
Bream	Folpet	96-h, s	LC ₅₀ = 114 µg/L	Addendum to DAR, Folpet (2005)
Rainbow trout	Folpan 500 SC	28 d, ss	LC ₅₀ = 110 µg a.s./L	EFSA Scientific Report (2009) 297, 70-80
<i>Rainbow trout (Oncorhynchus mykiss)</i>	Folpan 500 SC	28 d, ss	NOLC = 39 µg a.s./L	Addendum to Folpet DAR (2005)
<i>Daphnia magna</i>	Folpan 80 WDG	72 h	24h-EC₅₀ = 680 µg a.s./L	EFSA Scientific Report (2009) 297, 70-80
<i>Daphnia magna</i>	Folpet	28 d, f	28 d NOEC = 1.8 µg a.s./L (320 µg a.s./L) **	Section B9 of Folpet DAR (2005)
<i>Scenedesmus subspicatus</i>	folpet	21 d, ss	E_rC₅₀ > 10000 µg a.s./L E _b C ₅₀ > 10000 µg a.s./L	EFSA Scientific Report (2009) 297, 70-80
Bluegill sunfish	Phthalimide	96 h, ss	LC₅₀ = 38000 µg/L	EFSA Scientific Report (2009) 297, 70-80
<i>Daphnia magna</i>	Phthalimide	48 h, s	EC₅₀ = 39000 µg/L	EFSA Scientific Report (2009) 297, 70-80
Rainbow trout	Phthalic acid	96 h, s	LC₅₀ > 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
<i>Daphnia magna</i>	Phthalic acid	48 h, s	EC₅₀ ≥ 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
<i>Selenastrum capricornutum</i>	Phthalic acid	72 h, s	E_bC₅₀ > 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
Rainbow trout	Phthalamic acid	96 h, s	LC₅₀ > 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80

Species	Substance	Exposure System	Results	Reference
<i>Daphnia magna</i>	Phthalamic acid	48 h, s	EC ₅₀ ≥ 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
<i>Selenastrum capricornutum</i>	Phthalamic acid	72 h, s	E _b C ₅₀ > 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
Rainbow trout	Benzamide	96 h, s	LC ₅₀ > 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
<i>Daphnia magna</i>	Benzamide	48 h, s	EC ₅₀ ≥ 102000 µg/L	EFSA Scientific Report (2009) 297, 70-80
<i>Selenastrum capricornutum</i>	Benzamide	72 h, s	E _b C ₅₀ > 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
Rainbow trout	2-cyanobenzoic acid	96 h, s	LC ₅₀ > 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
<i>Daphnia magna</i>	2-cyanobenzoic acid	48 h, s	EC ₅₀ > 102000 µg/L	EFSA Scientific Report (2009) 297, 70-80
<i>Selenastrum capricornutum</i>	2-cyanobenzoic acid	72 h, s	E _b C ₅₀ > 100000 µg/L	EFSA Scientific Report (2009) 297, 70-80
Higher-tier studies (micro- or mesocosm studies)				
=				

s: static; ss: semi-static; f: flow-through; nom: based on nominal concentrations; mm: based on mean measured concentrations; im: based on initial measured concentrations

*Six species of fish were tested. Brown trout (*Salmo trutta*) was the most sensitive species tested, and this LC₅₀ should be used in the higher tier risk assessment. Uncertainty regarding interspecies variation in sensitivity has been reduced. Hence, a TER trigger of 10 should be used.

** In line with the recommendations in the PRAPER conclusion a new semi-static study on folpet technical (██████, 2007, ref. 33881221, submitted with post Annex I compliance dossier under IIA 8.3.2/02) was also conducted. The 21-day EC₅₀ of the test item for *Daphnia magna* under semi-static conditions with renewal every 2 to 3 days was determined to be 1.4 mg/L for mortality and 0.85 mg/L for reproduction. The NOECs were 1.0 mg/L and 0.32 mg/L for survival of adults and reproduction, respectively.

zRMS comments:

Aquatic toxicity data for a.s.- folpet and its metabolites included in Tables 9.5-1 above are in line with EU agreed endpoints reported in EFSA Scientific Report (2009) 297, 70-80.

Table 9.5-2: Endpoints and effect values relevant for the risk assessment for aquatic organisms – SAP50SCF

Species	Substance	Exposure System	Results	Reference
<i>Oncorhynchus mykiss</i>	SAP50SCF	96 h, ss	LC ₅₀ = 0.44 mg f.p./L _{nom} (equivalent to 0.22 mg a.s./L)	KCP 10.2.1/01, ██████
<i>Daphnia magna</i>	SAP50SCF**	48h, ss	48h-EC ₅₀ = 0.665* mg t.i./L _{nom} (equivalent to 0.34 mg a.s./L) 24h-EC ₅₀ = 1.683* mg t.i./L _{nom} (equivalent to 0.86 mg a.s./L) 48h-EC ₅₀ = 0.140 mg a.s./L _{mm} 24h-EC ₅₀ = 0.380 mg a.s./L _{mm}	KCP 10.2.1/05, Alves, 2023, amendment 2023 ⁴ CLOVER-A-01-2023

Species	Substance	Exposure System	Results	Reference
<i>Daphnia magna</i>	SAP50SCF***	48h,f	48h-EC ₅₀ > 0.600 mg t.i./L _{nom} (equivalent to 0.3066 mg a.s./L)	KCP 10.2.1/06, Wendling, 2024, S23-104263 ***
<i>Oncorhynchus mykiss</i>	Folpet 80 WG	96 h, ss	LC ₅₀ = 0.176 mg t.p./L _{nom} (equivalent to 0.14344 mg a.s./L)	KCP 10.2.1/02, [REDACTED] 2007, 33891230 Supplementary info
<i>Daphnia magna</i>	Folpet 80 WG	48 h, ss	EC ₅₀ = 0.67 mg t.p./L _{nom} (equivalent to 0.54605 mg a.s./L)	KCP 10.2.1/03, Grade and Wydra, 2007, 33892220 Supplementary info
<i>Daphnia magna</i>	Folpet technical	21 d, ss	NOEC = 0.32 mg t.i./L _{nom} (equivalent to 0.3136 mg a.s./L)	KCP 10.2.1/04, Grade and Wydra, 2007, 33881221
Higher-tier studies (micro- or mesocosm studies)				
-				

s: static; ss: semi-static; f: flow-through; nom: based on nominal concentrations; mm: based on mean measured concentrations

*calculated based on the content of active substance declared in the final report (511 g/L).

~~***Analytical phase still ongoing, endpoints derived based on nominal concentrations. Nevertheless, the endpoints derived based on mean measured concentrations should not bring any change to the risk assessment nor conclusions presented below as the comparison should be done with endpoints based on nominal concentrations (see arguments provided below).~~

***Additional information. The analytical report is still ongoing but the study is not necessary for the risk assessment.

An invertebrate flow-through study to confirm the results and conclusions obtained with the invertebrate semi-static study has been contracted with SAP50SCF. ~~with expected draft report in March 2024.~~

zRMS comment:

Studies on effects of the formulated product SAP50SCF on aquatic organisms for the most sensitive organism for a.s. (Fish and *Daphnia magna*) listed in Table 9.5-2 were evaluated by the zRMS and considered acceptable. Summaries of the performed studies together with zRMS evaluation may be found in Appendix 2.

The additional study for folpet technical to *Daphnia magna* by [REDACTED] 2007, 33881221 and data other formulation than SAP50SCF included in the Table 9.5-2 has not been used in the risk assessment by zRMS and for this reason was crossed out.

It should be noted that the study by [REDACTED] 2024, has not been evaluated by zRMS due to that analytical report is not available yet. However other studies for formulated product is available and was considered at this stage of evaluation of the product.

9.5.1.1 Justification for new endpoints

- Formulation studies:

SAP50SCF is a formulated product constituted by one active substance only (folpet). Since the active substance is the major constituent of this formulated product, it is expected that the toxicity of the product will be driven by the active substance. Looking at the active substance endpoints for fish acute, invertebrates acute and algae, it is clear that fish and invertebrates are more sensitive than algae by a factor of more than 10 and 100. Thus, studies with SAP50SCF were conducted with fish and invertebrates.

A comparison of the endpoints EU-agreed for the active substance and the endpoints obtained in the studies above with SAP50SCF is presented below. Since the EU-agreed data on the active substance is obtained based on static or semi-static studies and endpoints were derived based on nominal concentrations, the same approach was followed for describing SAP50SCF endpoints. Moreover, for *Daphnia magna*, the EU-agreed EC₅₀ is the one obtained at 24h (24h EC₅₀ of 680 µg/L and 48h EC₅₀ of 116 µg/L), the same approach with SAP50SCF was used for the comparison (24h EC₅₀ of 860 µg/L and 48h EC₅₀ of 340 µg/L).

Lowest endpoints obtained from active substance and SAP50SCF (nominal)

Organism	A.S. (EFSA Scientific Report, 2009)	SAP50SCF	Remarks
<i>Fish</i>	98 µg/L	220 µg a.s./L	Endpoints from a.s. and SAP50SCF are in the same order of magnitude. Thus, the risk assessment will be conducted based on the active substance data.
<i>Invertebrates</i>	680 µg/L (24h)	860 µg a.s./L (24h)	
	116 µg/L (48h)	340 µg/L (48h)	

As stated above, only endpoints derived based on nominal concentrations should be used for the comparison with the active substance data. Nevertheless, if the endpoints derived based on mean measured concentrations of folpet were to be used for this comparison, the same conclusion would be reached as:

Organism	A.S. (EFSA Scientific Report, 2009)	SAP50SCF (mean measured)	Remarks
<i>Invertebrates</i>	680 µg/L (24h)	380 µg a.s./L (24h) CI: 260-780 µg a.s./L	Looking at the results from 24h, SAP50SCF seems to be slightly more toxic. Nevertheless, this is only a result of the high variation in the results due to the abnormal behavior of fate (quick degradation). This is shown by the huge confidence interval derived where the value of 680 µg/L is included. At 48h, the confidence interval is quite robust and SAP50SCF endpoint is in the same order of magnitude as for the active substance. Thus, the risk assessment should still be conducted with the a.s. data.
	116 µg/L (48h)	140 µg/L (48h) CI: 110-180 µg a.s./L	

It should also be noted that several technical issues arouse for the performance of the flow-through study, namely: maintenance of folpet concentrations, possibility of having a stable stock solution, and adjusting the flow velocity so that daphnids were not washed.

Due to some difficulties, the concentrations to be tested were also influenced and so the highest concentration tested was 0.600 mg t.i./L (equivalent to 0.3066 mg a.s./L). No effects higher than 50% were observed during the entire study period. SAP50SCF is, thus, not more toxic than the active substance as at 48 hours the EC₅₀ of the active (0.116 mg a.s./L) is around half of the unbounded value obtained for SAP50SCF (0.3066 mg a.s./L). All these values are obtained using the nominal concentrations as the analytical phase of the flow-through study is still ongoing facing several technical issues as well.

zRMS comments:

zRMS agrees that based on the comparison of toxicity for aquatic invertebrates the active substance covers the risk assessment for formulation SAP50SCF.

- Folpet fish acute endpoint for risk assessment:

Species Sensitivity Distribution – SSD – Tier 2b approach

The fish acute endpoint previously presented and used for risk assessment as a higher tier RAC in EFSA Scientific Report for folpet (2009) was derived by using the lowest available LC₅₀ of 98 µg/L and reducing the Assessment Factor (AF) to 10. This approach is outdated after the entry into force of the EFSA Aquatic Guidance (2013) - “Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters”. The mentioned guidance document states that when data is available for more than five vertebrate species, then a tier 2b approach (i.e. Species Sensitivity Distribution – SSD) should be applied.

Looking at all the data available for folpet, six species were tested (see table below) and the SSD approach applies. Additionally, this approach was discussed during the pre-submission meeting and was agreed with the zonal Rapporteur Member State (zRMS) of this dossier.

Table 17: Folpet: acute fish toxicity studies on 6 species. Results of analytical measurements in relation to the derived LC50 from each study.

Species	Analysis of stocks compared to intended conc. (%)	Range of nominal test concs.	Analysis of test media		LC50 (nominal)	Is LC50 in range where nominals confirmed by analysis?	Ref.
			Measured concs in test media compared to nominal	Nominal tests concs. for which % nominal range applies			
rainbow trout	78 – 96%	24.3 - 568 µg/L	87 – 103%	117 – 568 µg/L	233 µg/L	YES	2002a
brown trout	91 – 100%	13.7 – 320 µg/L	139%	320 µg/L	98 µg/L	NO	2002b
common carp	85 – 94%	64 – 1500 µg/L	67 – 76%	320 – 1500 µg/L	1012 µg/L	YES	2002c
3-spined stickleback	97 – 121%	42.7 – 1000 µg/L	86 – 92%	207 – 1000 µg/L	229 µg/L	YES	2002d
roach	93 – 101%	42.7 – 1000 µg/L	71 – 83%	207 – 1000 µg/L	211 µg/L	YES	2002e
bream	97 – 121%	19.4 – 456 µg/L	92 – 101%	207 – 456 µg/L	114 µg/L	NO*	2002f

* LC50 was outside the range where analytical measurement of test media was possible. However, from the concentration-response at nominal 207 µg/L (71% mortality) and 465 µg/L (100% mortality) it is possible to judge that an LC50 of 114 µg/L is likely to be accurate.

However, zRMS proposed to perform the SSD with the LC₅₀ reported as measured concentrations instead of nominal values was also taken into account. (more information can be found in the minutes of such meeting). From the table above, the analysis of stock solutions resulted in acceptable (80-120%) recovery values for all tests with the exception of rainbow trout which failed by 2% (78%). This proves the correct preparation of the application solutions. The LC₅₀ values reported as nominal values are also inside the range where nominal concentrations were confirmed by analysis for almost all species (only brown trout and bream LC₅₀ did not fall inside the referred range). Therefore, only these two endpoints are should be corrected accounting for the measured concentrations.

For brown trout, 139% recovery was observed in the test media when compared to nominal, resulting in a LC₅₀ of 136.22 µg a.s./L (98 µg a.s./L x 139%). Thus, using the nominal value for the derivation of the SSD would be conservative. Nevertheless, both values were used, and two different SSD-curves were determined.

For bream, and as stated in the footnote of the table, “from the concentration-response at nominal 207 µg/L (71% mortality) and 465 µg/L (100% mortality) it is possible to judge that an LC₅₀ of 114 µg/L is likely to be accurate”. Therefore, no further correction is applicable in the Applicant’s point of view.

As agreed in the meeting, Both statistical tools - MOSAIC and ETX - were used for both set of data: endpoints derived using the measured recovery values or using the nominal recovery values. All derived SSD-curves and consequent Tier 2b-RACs are presented below.

1) Species Sensitivity Distribution curves derived using endpoints based on measured recovery values (LC₅₀)

As mentioned above, all LC₅₀ were inside the nominal range confirmed by analysis with the exception of brown trout and bream (for which no correction will be applied). For brown trout, an LC₅₀ of 136.2 µg/L would be obtained when considering 139% recovery of the 98 µg/L LC₅₀. The SSD’s are presented below, using both programs for the statistical analyses and the data described in the table below.

Table 1-1 – Measured values used in the SSD

Species	LC ₅₀ (derived with the measured recovery, µg/L)
Rainbow trout	233
Brown trout	136.2
Common carp	1012
3-spined stickleback	229
Roach	211
Bream	114

1.a) MOSAIC tool approach
(available at: <https://mosaic.univ-lyon1.fr/ssd>)

The SSD curve obtained is presented below alongside with both distribution characteristics (log- normal and log-logistic) and the derived Hazard Concentration (HC_x) values:

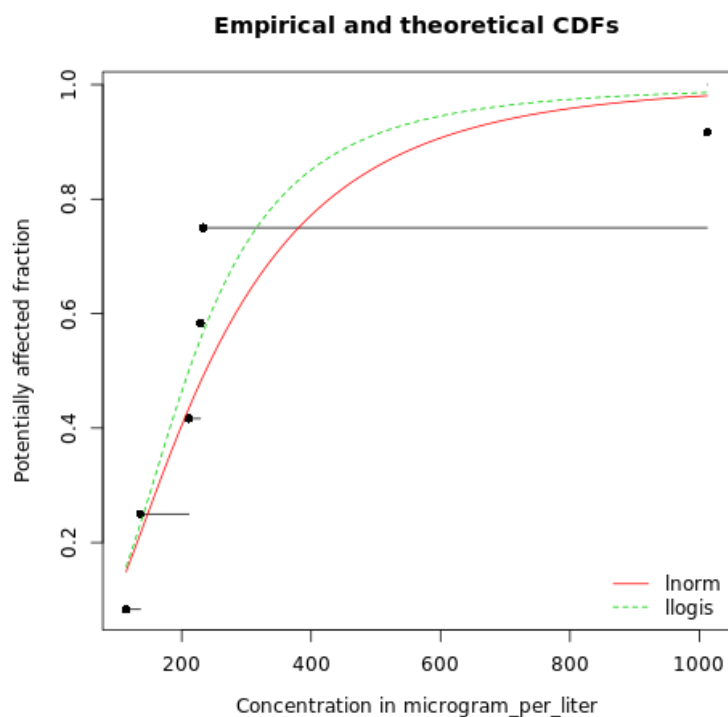


Figure 1-1 – SSD for fish lethal concentration endpoint (LC₅₀) derived based on measured recovery values of folpet using MOSAIC tool.

Respective SSD statistical parameters:

Log normal distribution (log-likelihood = -39.2)

meanlog: 5.5 [4.9; 6]

sdlog: 0.7 [0.27; 1]

Log logistic distribution (log-likelihood = -39.0)

shape: 2.1e+02 [1.3e+02; 3.6e+02]

scale: 2.7 [1.7; 7.9]

Table 1-2-Reported values from MOSAIC tool ran with LC₅₀ derived based on measured recoveries for the six fish species

HC	Log-normal	Log-logistic
HC₅	<u>75</u> <u>[35; 2e02]</u>	<u>72</u> <u>[31; 1.7e02]</u>
HC ₁₀	96 [49; 2.2e02]	94 [46; 1.9e02]
HC ₂₀	1.3e02 [73; 2.7e02]	1.3e02 [68; 2.3e02]
HC ₅₀	2.4e02 [1.4e02; 4.2e02]	2.1e02 [1.2e02; 3.5e02]

Based on the log-likelihood of both distributions used in MOSAIC tool (log-normal and log-logistic), the one that best suits the data, i.e. that presents the lowest result, is the log-logistic (-39.0). This is the distribution that results in the lowest HC₅ from the two tested and so, this would be the chosen endpoint to be used in the risk assessment.

1.b) ETX tool approach

(available at: Vlaardingen PLA, Traas TP, Wintersen AM, Aldenberg T. 2004. ETX 2.0. A program to calculate hazardous concentrations and fraction affected, based on normally distributed toxicity data. Bilt-hoven, the Netherlands: National Institute for Public Health and the Environment (RIVM). Report no. 601501028/2004, 68 pp)

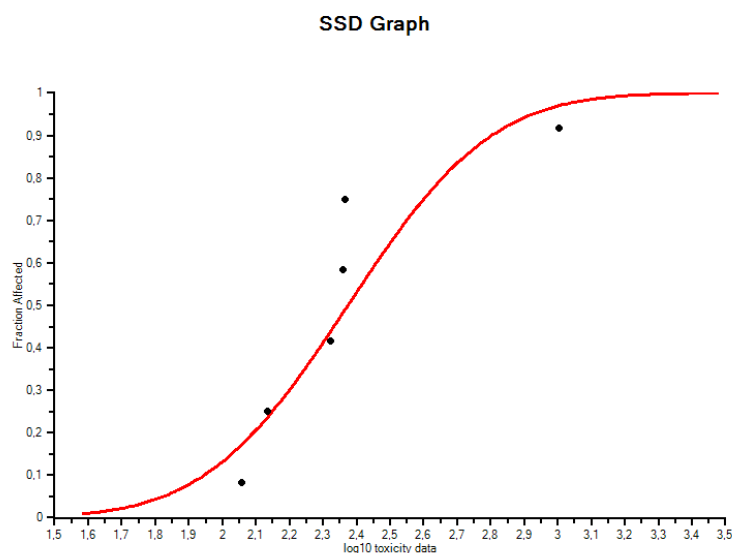


Figure 1-2 – SSD for fish lethal concentration endpoint (LC₅₀) derived based on measured recovery values of folpet using ETX tool.

Respective SSD statistical parameters:

Parameters of the normal distribution		
Mean	2.37e0	mean of the log toxicity values
s.d.	3.34e-1	Sample standard deviation
n	6.00e0	Sample size
Anderson-Darling test for normality		
Sign. level	Critical	Normality
0.1	0.631	Rejected
0.05	0.752	Accepted
0.025	0.873	Accepted
0.01	1.035	Accepted
Kolmogorov-Smirnov test for normality		
0.1	0.819	Rejected
0.05	0.895	Rejected

Parameters of the normal distribution		
0.025	0.995	Accepted
0.01	1.035	Accepted
Cramer von Mises test for normality		
0.1	0.104	Accepted
0.05	0.126	Accepted
0.025	0.148	Accepted
0.01	0.179	Accepted

Table 2-Reported values from ETX tool ran with LC₅₀ derived based on measured recoveries for the six fish species.

HC	Value
HC₅	6.155e1
HC ₅₀	2.369e2

As the goodness-of-fit indicates, the normal distribution derived by the ETX tool does not fit well the data available. Thus, the derived endpoints should not be used for the risk assessment.

2) Species Sensitivity Distribution curves derived using endpoints based on nominal recovery values (LC₅₀)

For this second set of SSD curves, only the nominal values collected from the Addendum DAR, 2005 for folpet, for the six fish species presented in the table below will be used.

Table 2-1 – Nominal values used in the SSD

Species	LC ₅₀ (nominal, µg/L)
Rainbow trout	233
Brown trout	98
Common carp	1012
3-spined stickleback	229
Roach	211
Bream	114

2.a) MOSAIC tool approach

The SSD curve obtained is presented below alongside with both distribution characteristics (log- normal and log-logistic) and the derived Hazard Concentration (HC_x) values:

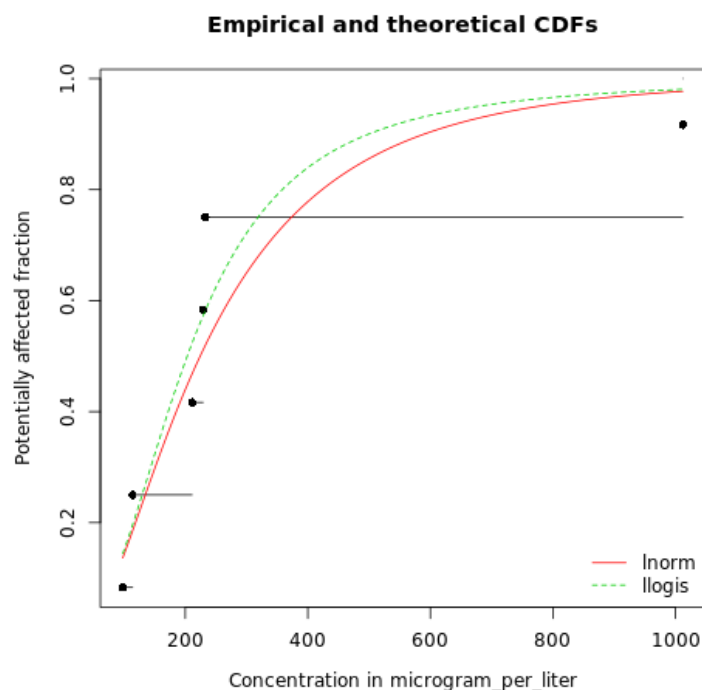


Figure 2-1 – SSD for fish lethal concentration endpoint (LC₅₀) of folpet using MOSAIC tool with nominal values from the Addendum DAR, 2005 for folpet.

Respective SSD statistical parameters:

Log normal distribution (log-likelihood = -39.3)

meanlog: 5.4 [4.8; 6]

sdlog: 0.75 [0.28; 1.1]

Log logistic distribution (log-likelihood = -39.2)

shape: 2e+02 [1.1e+02; 3.6e+02]

scale: 2.4 [1.5; 7]

Table 2-2-Reported values from MOSAIC tool ran with nominal values of LC₅₀ for the six fish species

HC	Log-normal	Log-logistic
<u>HC₅</u>	<u>65</u> <u>[30; 1.9e02]</u>	<u>61</u> <u>[23; 1.6e02]</u>
HC ₁₀	85 [42; 2.2e02]	83 [37; 1.9e02]
HC ₂₀	1.2e02 [64; 2.6e02]	1.2e02 [58; 2.3e02]
HC ₅₀	2.2e02 [1.2e02; 4.2e02]	2e02 [1.1e02; 3.6e02]

Based on the log-likelihood of both distributions used in MOSAIC tool (log-normal and log-logistic), the one that best suits the data, i.e. that presents the lowest result, is the log-logistic (-39.2). This is the distribution that results in the lowest HC₅ from the two tested and so, this would be the chosen endpoint to be used in the risk assessment.

2.b) ETX tool approach

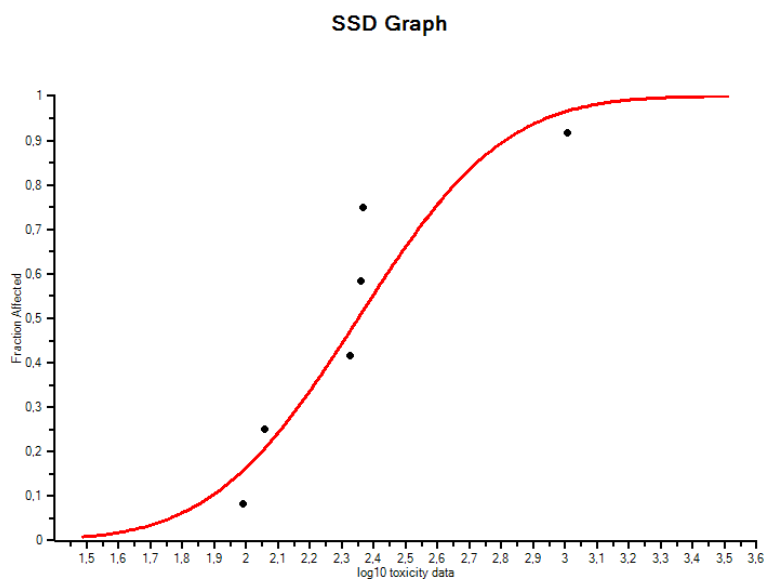


Figure 2-2 – SSD for fish lethal concentration endpoint (LC₅₀) of folpet using ETX tool with nominal values from the Addendum DAR, 2005 for folpet.

Respective SSD statistical parameters:

Parameters of the normal distribution		
Mean	2.35e0	mean of the log toxicity values
s.d.	3.59e-1	Sample standard deviation
n	6.00e0	Sample size
Anderson-Darling test for normality		
Sign. level	Critical	Normality
0.1	0.631	Accepted
0.05	0.752	Accepted
0.025	0.873	Accepted
0.01	1.035	Accepted
Kolmogorov-Smirnov test for normality		
0.1	0.819	Rejected
0.05	0.895	Accepted
0.025	0.995	Accepted
0.01	1.035	Accepted
Cramer von Mises test for normality		
0.1	0.104	Accepted
0.05	0.126	Accepted
0.025	0.148	Accepted
0.01	0.179	Accepted

Table 2-3-Reported values from ETX tool ran with nominal values of LC₅₀ for the six fish species.

HC	Value
<u>HC5</u>	<u>5.274e1</u>
HC50	2.243e2

The goodness-of-fit indicates of the normal distribution derived by the ETX tool fails for the significance level of 10% for only one statistical test. For the remaining significance levels and tests, the derived SSD curve is accepted. Therefore, this will be considered for the risk assessment.

Conclusion:

Using a Tier 2b-approach (SSD) according to the EFSA Aquatic Guidance (2013), the following HC₅ values that could be considered for risk assessment were derived: 72 (measured), 61 (nominal) and 52.7 (nominal) µg a.s./L. Using a conservative approach and since all these derived curves are fitting the data quite well, the lowest Tier 2b approach (SSD) derived HC₅ of 52.7 µg/L for fish acute endpoint will be used. This HC₅ will be coupled with an assessment factor of 9 with a final tier 2b-RAC of 5.9 µg/L for acute fish exposure (the most conservative approach).

zRMS comments:

zRMS agrees with Tier 2b approach (SSD) and derived HC₅ = 52.7 µg/L value with 9 giving RAC = 5.9 µg a.s./L for the acute risk assessment to fish.

9.5.2 Risk assessment

The evaluation of the risk for aquatic and sediment-dwelling organisms was performed in accordance with the recommendations of the “Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters in the context of Regulation (EC) No 1107/2009”, as provided by the Commission Services (SANTE-2015-00080, 15 January 2015).

The relevant global maximum FOCUS Step 1, 2 and 3 PEC_{SW} for risk assessments covering the proposed use pattern and the resulting PEC/RAC ratios are presented in the table below.

In the following table, the ratios between predicted environmental concentrations in surface water bodies (PEC_{SW}, PEC_{SED}) and regulatory acceptable concentrations (RAC) for aquatic organisms are given per intended use for each FOCUS scenario and each organism group and with consideration maximum and minimum application doses.

Table 9.5-3: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for folpet for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP50SCF in cereals

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Test-species		-	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Scenedesmus subspicatus</i>
Endpoint (µg/L)		HC ₅ 52.7	NOEC 39	EC ₅₀ 680	NOEC 320	EC ₅₀ 10000
AF		9	10	100	10	10
RAC (µg/L)		5.9	3.9	6.8	32	1000
FOCUS Scenario	PEC _{gl-max} (µg/L)					
Winter-cereals						
Step 1 (worst-case value between sets 1 and 2, further details refer to B8)						
-	147.83	25.1	37.9	21.7	4.6	0.1
Step 2 (worst-case value between sets 1 and 2, further details refer to B8)						
N-Europe	9.98	1.7	2.6	1.5	0.3	Ok-at-step-1.
S-Europe	8.45	1.4	2.2	1.2	0.3	
Step 3—Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.356	0.6	0.9	0.5	Ok-at-step-2.	Ok-at-step-1.
D1/stream	2.834	0.5	0.7	0.4		

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
D2/ditch	3.364	0.6	0.9	0.5		
D2/stream	2.941	0.5	0.8	0.4		
D3/ditch	3.325	0.6	0.9	0.5		
D4/pond	0.1597	0.0	0.0	0.0		
D4/stream	2.513	0.4	0.6	0.4		
D5/pond	0.1849	0.0	0.0	0.0		
D5/stream	2.899	0.5	0.7	0.4		
D6/ditch	3.34	0.6	0.9	0.5		
R1/pond	0.3032	0.1	0.1	0.0		
R1/stream	4.449	0.8	1.1	0.7		
R3/stream	5.952	1.009	1.5	0.9		
R4/stream	3.386	0.6	0.9	0.5		
Step 3—Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.814	0.6	0.98	0.6	Ok-at-step 2.	Ok-at-step 1.
D1/stream	2.964	0.5	0.8	0.4		
D2/ditch	3.838	0.7	0.98	0.6		
D2/stream	3.26	0.6	0.8	0.5		
D3/ditch	3.801	0.6	0.97	0.6		
D4/pond	0.1312	0.0	0.0	0.0		
D4/stream	2.807	0.5	0.7	0.4		
D5/pond	0.1312	0.0	0.0	0.0		
D5/stream	3.034	0.5	0.8	0.4		
D6/ditch	3.758	0.6	0.96	0.6		
R1/pond	0.1312	0.0	0.0	0.0		
R1/stream	2.504	0.4	0.6	0.4		
R3/stream	3.518	0.6	0.9	0.5		
R4/stream	2.515	0.4	0.6	0.4		
Spring-cereals						
Step 1 (worst-case value between sets 1 and 2, further details refer to B8)						
-	147.83	25.1	37.9	21.7	4.6	0.1
Step 2 (worst-case value between sets 1 and 2, further details refer to B8)						
N-Europe	5.52	0.9	1.4	0.8	0.2	Ok-at-step 1.
S-Europe	8.45	1.4	2.2	1.2	0.3	
Step 3—Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	4.488	0.8	1.2	0.7	Ok-at-step 2.	Ok-at-step 1.
D1/stream	2.91	0.5	0.7	0.4		
D3/ditch	3.326	0.6	0.9	0.5		
D4/pond	0.1764	0.0	0.0	0.0		
D4/stream	2.777	0.5	0.7	0.4		

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
D5/pond	0.1643	0.0	0.0	0.0		
D5/stream	2.87	0.5	0.7	0.4		
R4/stream	11.17	1.9	2.9	1.6		
Step 3—Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.848	0.7	0.99	0.6	Ok-at-step-2:	Ok-at-step-1:
D1/stream	3.365	0.6	0.9	0.5		
D3/ditch	3.805	0.6	0.98	0.6		
D4/pond	0.1312	0.0	0.0	0.0		
D4/stream	3.111	0.5	0.8	0.5		
D5/pond	0.1312	0.0	0.0	0.0		
D5/stream	3.194	0.5	0.8	0.5		
R4/stream	6.215	1.1	1.6	0.9		

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

April 2024

An updated risk assessment is presented below according to the requests done by zRMS PL in the data gaps (updated PEC_{sw} values):

Table 9.5-4a: Aquatic organisms: acceptability of risk ($PEC/RAC < 1$) for folpet for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP50SCF in cereals

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Test species		~	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Scenedesmus subspicatus</i>
Endpoint ($\mu\text{g/L}$)		HC ₅	NOEC	EC ₅₀	NOEC	EC ₅₀
AF		9	10	100	10	10
RAC ($\mu\text{g/L}$)		5.9	3.9	6.8	32	1000
FOCUS Scenario	$PEC_{gl-max}(\mu\text{g/L})$					
Winter cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.355	0.6	0.9	0.5	Ok-at-step-2:	Ok-at-step-1:
D1/stream	2.833	0.5	0.7	0.4		
D2/ditch	3.364	0.6	0.9	0.5		
D2/stream	2.941	0.5	0.8	0.4		
D3/ditch	3.324	0.6	0.9	0.5		
D4/pond	0.143	0.0	0.0	0.0		
D4/stream	2.510	0.4	0.6	0.4		
D5/pond	0.174	0.0	0.0	0.0		
D5/stream	2.898	0.5	0.7	0.4		
D6/ditch	3.339	0.6	0.9	0.5		
R1/pond	0.240	0.0	0.1	0.0		

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
R1/stream	3.572	0.6	0.9	0.5		
R3/stream	4.379	0.7	1.1	0.6		
R4/stream	2.536	0.4	0.7	0.4		
Step 3—Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.814	0.6	0.98	0.6	Ok-at-step-2.	Ok-at-step-1.
D1/stream	2.966	0.5	0.8	0.4		
D2/ditch	3.838	0.7	0.98	0.6		
D2/stream	3.260	0.6	0.8	0.5		
D3/ditch	3.800	0.6	0.97	0.6		
D4/pond	0.131	0.0	0.0	0.0		
D4/stream	2.809	0.5	0.7	0.4		
D5/pond	0.131	0.0	0.0	0.0		
D5/stream	3.034	0.5	0.8	0.4		
D6/ditch	3.757	0.6	0.96	0.6		
R1/pond	0.131	0.0	0.0	0.0		
R1/stream	2.504	0.4	0.6	0.4		
R3/stream	3.517	0.6	0.9	0.5		
R4/stream	2.515	0.4	0.6	0.4		
Spring cereals						
Step 3—Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	4.060	0.7	1.04	0.6	Ok-at-step-2.	Ok-at-step-1.
D1/stream	2.910	0.5	0.7	0.4		
D3/ditch	3.325	0.6	0.9	0.5		
D4/pond	0.167	0.0	0.0	0.0		
D4/stream	2.776	0.5	0.7	0.4		
D5/pond	0.150	0.0	0.0	0.0		
D5/stream	2.869	0.5	0.7	0.4		
R4/stream	8.846	1.5	2.3	1.3		
Step 3—Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.847	0.7	0.99	0.6	Ok-at-step-2.	Ok-at-step-1.
D1/stream	3.365	0.6	0.9	0.5		
D3/ditch	3.804	0.6	0.98	0.6		
D4/pond	0.131	0.0	0.0	0.0		
D4/stream	3.110	0.5	0.8	0.5		
D5/pond	0.131	0.0	0.0	0.0		
D5/stream	3.194	0.5	0.8	0.5		
R4/stream	4.639	0.8	1.2	0.7		

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

- Maximum dose

Table 9.5-3a: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for folpet for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP50SCF in cereals

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Test species		-	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Scenedesmus subspicatus</i>
Endpoint (µg/L)		HC ₅ 52.7	NOEC 39	EC ₅₀ 680	NOEC 320	E _r C ₅₀ 10000
AF		9	10	100	10	10
RAC (µg/L)		5.9	3.9	6.8	32	1000
FOCUS Scenario	PEC _{gl-max} (µg/L)					
Winter cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.363	0.6	0.9	0.5	0.1	0.0
D1/stream	2.838	0.5	0.7	0.4	0.1	0.0
D2/ditch	5.555	0.9	1.4	0.8	0.2	0.0
D2/stream	3.657	0.6	0.9	0.5	0.1	0.0
D3/ditch	3.324	0.6	0.9	0.5	0.1	0.0
D4/pond	0.143	0.0	0.0	0.0	0.0	0.0
D4/stream	2.510	0.4	0.6	0.4	0.1	0.0
D5/pond	0.174	0.0	0.0	0.0	0.0	0.0
D5/stream	2.898	0.5	0.7	0.4	0.1	0.0
D6/ditch	3.339	0.6	0.9	0.5	0.1	0.0
R1/pond	0.597	0.1	0.2	0.1	0.0	0.0
R1/stream	9.239	1.6	2.4	1.4	0.3	0.0
R3/stream	10.360	1.8	2.7	1.5	0.3	0.0
R4/stream	9.376	1.6	2.4	1.4	0.3	0.0
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.819	0.6	0.98	0.6	0.1	0.0
D1/stream	2.970	0.5	0.8	0.4	0.1	0.0
D2/ditch	5.546	0.9	1.4	0.8	0.2	0.0
D2/stream	3.651	0.6	0.9	0.5	0.1	0.0
D3/ditch	3.800	0.6	0.97	0.6	0.1	0.0
D4/pond	0.131	0.0	0.0	0.0	0.0	0.0
D4/stream	2.809	0.5	0.7	0.4	0.1	0.0
D5/pond	0.131	0.0	0.0	0.0	0.0	0.0
D5/stream	3.034	0.5	0.8	0.4	0.1	0.0
D6/ditch	3.757	0.6	0.96	0.6	0.1	0.0
R1/pond	0.176	0.0	0.0	0.0	0.0	0.0
R1/stream	2.504	0.4	0.6	0.4	0.1	0.0
R3/stream	3.517	0.6	0.9	0.5	0.1	0.0

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae
R4/stream	2.515	0.4	0.6	0.4	0.1	0.0
Spring cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	4.078	0.7	1.05	0.6	0.1	0.0
D1/stream	2.910	0.5	0.7	0.4	0.1	0.0
D3/ditch	3.325	0.6	0.9	0.5	0.1	0.0
D4/pond	0.167	0.0	0.0	0.0	0.0	0.0
D4/stream	2.776	0.5	0.7	0.4	0.1	0.0
D5/pond	0.151	0.0	0.0	0.0	0.0	0.0
D5/stream	2.869	0.5	0.7	0.4	0.1	0.0
R4/stream	13.350	2.3	3.4	2.0	0.4	0.0
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.851	0.7	0.99	0.6	0.1	0.0
D1/stream	3.365	0.6	0.9	0.5	0.1	0.0
D3/ditch	3.804	0.6	0.98	0.6	0.1	0.0
D4/pond	0.131	0.0	0.0	0.0	0.0	0.0
D4/stream	3.110	0.5	0.8	0.5	0.1	0.0
D5/pond	0.131	0.0	0.0	0.0	0.0	0.0
D5/stream	3.194	0.5	0.8	0.5	0.1	0.0
R4/stream	8.165	1.4	2.1	1.2	0.3	0.0

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

For the Step 4 calculations, only the comparison of the additional PEC_{SW} values with the lowest RAC of 3.9 µg/L will be presented here for maximum dose.

Maximum dose:

Table 9.5-3b: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for folpet based on FOCUS Step 4 calculations and toxicity data for fish chronic with mitigation of spray drift and run-off for the use of SAP50SCF in cereals

Intended use	Cereals
Active substance	folpet
Application rate (g/ha)	2 x 600
<i>Winter Cereals – Multiple applications – 15 meters of vegetated filter strip</i>	
D2/ditch	no further mitigation possible
R1/stream	3.221
R3/stream	3.634
R4/stream	3.273
RAC (µg/L)	
3.9	PEC/RAC ratio
R1/stream	0.8
R3/stream	0.9

R4/stream	1.8
Winter Cereals - Multiple applications –20 meters of vegetated filter strip	
R1/stream	2.198
R3/stream	2.482
R4/stream	2.235
RAC (µg/L) 3.9	PEC/RAC ratio
R1/stream	0.6
R3/stream	0.6
R4/stream	0.6
Winter Cereals - Single applications –5 meters of vegetated filter strip	
D1/ditch	1.040
D2/ditch	no further mitigation possible
RAC (µg/L) 3.9	PEC/RAC ratio
D1/ditch	0.3
Winter Cereals - Single applications –10 meters of vegetated filter strip	
D1/ditch	0.554
RAC (µg/L) 3.9	PEC/RAC ratio
D2/ditch	no further mitigation possible
D1/ditch	0.1
Spring Cereals - Multiple applications –20 m of vegetated filter strip	
D1/ditch	0.310
R4/strean	3.155
RAC (µg/L) 3.9	PEC/RAC ratio
D1/ditch	0.1
R4/strean	0.8
Spring Cereals - Single application –10 meters of vegetated filter strip	
R4/strean	3.684
RAC (µg/L) 3.9	PEC/RAC ratio
R4/strean	0.9

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

- Minimum dose

Table 9.5-3c: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for folpet for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP50SCF in cereals

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Test species		-	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Scenedesmus subspicatus</i>
Endpoint (µg/L)		HC ₅ 52.7	NOEC 39	EC ₅₀ 680	NOEC 320	E _r C ₅₀ 10000
AF		9	10	100	10	10
RAC (µg/L)		5.9	3.9	6.8	32	1000
FOCUS Scenario	PEC _{gl-max} (µg/L)					
Winter cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.522	0.4	0.6	0.4	0.1	0.0
D1/stream	2.129	0.4	0.5	0.3	0.1	0.0
D2/ditch	3.341	0.6	0.9	0.5	0.1	0.0
D2/stream	2.212	0.4	0.6	0.3	0.1	0.0
D3/ditch	2.493	0.4	0.6	0.4	0.1	0.0
D4/pond	0.107	0.0	0.0	0.0	0.0	0.0
D4/stream	1.882	0.3	0.5	0.3	0.1	0.0
D5/pond	0.130	0.0	0.0	0.0	0.0	0.0
D5/stream	2.173	0.4	0.6	0.3	0.1	0.0
D6/ditch	2.504	0.4	0.6	0.4	0.1	0.0
R1/pond	0.443	0.1	0.1	0.1	0.0	0.0
R1/stream	6.840	1.2	1.8	1.01	0.2	0.0
R3/stream	7.645	1.3	2.0	1.1	0.2	0.0
R4/stream	6.974	1.2	1.8	1.03	0.2	0.0
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.864	0.5	0.7	0.4	0.1	0.0
D1/stream	2.227	0.4	0.6	0.3	0.1	0.0
D2/ditch	3.335	0.6	0.9	0.5	0.1	0.0
D2/stream	2.445	0.4	0.6	0.4	0.1	0.0
D3/ditch	2.850	0.5	0.7	0.4	0.1	0.0
D4/pond	0.098	0.0	0.0	0.0	0.0	0.0
D4/stream	2.107	0.4	0.5	0.3	0.1	0.0
D5/pond	0.098	0.0	0.0	0.0	0.0	0.0
D5/stream	2.275	0.4	0.6	0.3	0.1	0.0
D6/ditch	2.818	0.5	0.7	0.4	0.1	0.0
R1/pond	0.131	0.0	0.0	0.0	0.0	0.0
R1/stream	1.878	0.3	0.5	0.3	0.1	0.0
R3/stream	2.638	0.4	0.7	0.4	0.1	0.0

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae
R4/stream	1.886	0.3	0.5	0.3	0.1	0.0
Spring cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.057	0.5	0.8	0.4	0.1	0.0
D1/stream	2.182	0.4	0.6	0.3	0.1	0.0
D3/ditch	2.494	0.4	0.6	0.4	0.1	0.0
D4/pond	0.125	0.0	0.0	0.0	0.0	0.0
D4/stream	2.082	0.4	0.5	0.3	0.1	0.0
D5/pond	0.113	0.0	0.0	0.0	0.0	0.0
D5/stream	2.152	0.4	0.6	0.3	0.1	0.0
R4/stream	9.871	1.7	2.5	1.5	0.3	0.0
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.888	0.5	0.7	0.4	0.1	0.0
D1/stream	2.523	0.4	0.6	0.4	0.1	0.0
D3/ditch	2.853	0.5	0.7	0.4	0.1	0.0
D4/pond	0.098	0.0	0.0	0.0	0.0	0.0
D4/stream	2.332	0.4	0.6	0.3	0.1	0.0
D5/pond	0.098	0.0	0.0	0.0	0.0	0.0
D5/stream	2.395	0.4	0.6	0.4	0.1	0.0
R4/stream	6.020	1.02	1.5	0.9	0.2	0.0

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

For the Step 4 calculations, only the comparison of the additional PEC_{SW} values with the lowest RAC of 3.9 µg/L will be presented here.

Table 9-5-3d: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for folpet based on FOCUS Step 4 calculations and toxicity data for fish chronic with mitigation of spray drift and run-off for the use of SAP50SCF in cereals

Intended use	Cereals
Active substance	folpet
Application rate (g/ha)	2 x 450
Winter Cereals - Multiple applications –10 m of vegetated filter strip	
R1/strean	3.107
R3/strean	3.489
R4/strean	3.173
RAC (µg/L)	
3.9	PEC/RAC ratio
R1/strean	0.8
R3/strean	0.9
R4/strean	0.8
Spring Cereals – Multiple applications –15 m of vegetated filter strip	
R4/strean	3.420

RAC (µg/L) 3.9	PEC/RAC ratio
R4/strean	0.9
Spring Cereals - Multiple applications –20 m of vegetated filter strip	
R4/strean	2.332
RAC (µg/L) 3.9	PEC/RAC ratio
R4/strean	0.6
Spring Cereals - Single applications –10 m of vegetated filter strip	
R4/strean	2.717
RAC (µg/L) 3.9	PEC/RAC ratio
R4/strean	0.7

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Dose	Application number	Crop	Mitigation measure
Maximum dose	Single	Winter cereals	D1 scenario: 5 meters of vegetated filter strip D2 scenario: restriction of application
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	D2 scenario: restriction of application R1, R3 and R4 scenarios: 15 meters of vegetated filter strip
		Spring cereals	D1, R4 scenario: 20 meters of vegetated filter strip
Minimum dose (see Appendix 3)	Single	Winter cereals	None
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	R1, R3 and R4 scenarios: 10 meters of vegetated filter strip
		Spring cereals	R4 scenario: 15 meters of vegetated filter strip

zRMS comments:

Based on the lowest RAC= 3.9 µg a.s./L value obtained for long-term toxicity to fish for folpet the following risk mitigation measures are required:

Dose	Application number	Crop	Mitigation measure
Maximum dose	Single	Winter cereals	D1 scenario: 10 meters of vegetated filter strip D2 scenario: restriction of application at MSs level
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	D2 scenario: restriction of application R1, R3 and R4 scenarios: 20 meters of vegetated filter strip
		Spring cereals	D1, R4 scenario: 20 meters of vegetated filter strip
Minimum dose	Single	Winter cereals	None
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip

	Multiple	Winter cereals	R1, R3 and R4 scenarios: 10 meters of vegetated filter strip
		Spring cereals	R4 scenario: 20 meters of vegetated filter strip

Based on the risk assessment for relevant scenarios for Poland such as: **D3, D4 and R1**, the following risk mitigation measures are required:

Multiple application at the maximum dose:

- 20-meter vegetative buffer zone (R1 scenario) for multiple application for winter and spring cereals

Multiple application at the minimum dose:

- 10-meter vegetative buffer zone (R1 scenario) for multiple application for winter and spring cereals

For single application for winter and spring cereals the risk mitigation measures is not required for scenarios relevant for Poland (D3, D4 and R1).

For the intended uses, calculated PEC/RAC ratios did not indicate an acceptable risk for the most sensitive group of aquatic organisms (risk for fish chronic as characterised by a NOEC of 39 µg/L in connection with an assessment factor of 10) in several FOCUS Steps 1-3 scenarios. Therefore, further PEC/RAC ratios were calculated based on FOCUS Step 4 PEC_{SW} considering reduced exposure of surface water bodies.

Table 9.5-5: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for folpet based on FOCUS Step 4 calculations and toxicity data for fish chronic with mitigation of spray drift and run-off for the use of SAP50SCF in cereals

Intended use	Cereals
Active substance	folpet
Application rate (g/ha)	2 x 600
<i>Winter Cereals – Multiple applications – 5 meters of vegetated filter strip</i>	
R1/stream	2.759
R3/stream	3.892
RAC (µg/L)	
5.9	PEC/RAC ratio
R3/stream	0.7
RAC (µg/L)	
3.9	PEC/RAC ratio
R1/stream	0.7
R3/stream	0.998
<i>Winter Cereals – Multiple applications – 10 meters of vegetated filter strip</i>	
R1/stream	1.870
R3/stream	2.717
RAC (µg/L)	
3.9	PEC/RAC ratio
R1/stream	0.5
R3/stream	0.7
<i>Spring Cereals – Multiple applications – 15 m buffer zone including 15 m of vegetated filter strip</i>	
D1/ditch	0.4592

R4/stream	3.873
RAC (µg/L)	
5.9	PEC/RAC ratio
R4/stream	0.7
RAC (µg/L)	
3.9	PEC/RAC ratio
D1/ditch	0.1
R4/stream	0.99
<i>Spring Cereals – Multiple applications – 20 m buffer zone including 20 m of vegetated filter strip</i>	
D1/ditch	0.3465
R4/stream	2.640
RAC (µg/L)	
3.9	PEC/RAC ratio
D1/ditch	0.1
R4/stream	0.7
<i>Spring Cereals – Single application – 10 meters of vegetated filter strip</i>	
R4/stream	2.805
RAC (µg/L)	
5.9	PEC/RAC ratio
R4/stream	0.5
RAC (µg/L)	
3.9	PEC/RAC ratio
R4/stream	0.7

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5-6a: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for folpet based on FOCUS Step 4 calculations and toxicity data for fish chronic with mitigation of spray drift and run-off for the use of SAP50SCF in cereals

Intended use	Cereals
Active substance	folpet
Application rate (g/ha)	2 x 600
<i>Winter Cereals – Multiple applications – 5 meters of vegetated filter strip</i>	
R3/stream	2.863
RAC (µg/L)	
3.9	PEC/RAC ratio
R3/stream	0.7
<i>Winter Cereals – Multiple applications – 10 meters of vegetated filter strip</i>	
R3/stream	1.999
RAC (µg/L)	
3.9	PEC/RAC ratio
R3/stream	0.5
<i>Spring Cereals – Multiple applications – 15 m buffer zone including 15 m of vegetated filter strip</i>	
D1/ditch	0.407

R4/stream	3.067
RAC (µg/L)	
5.9	PEC/RAC ratio
R4/stream	0.5
RAC (µg/L)	
3.9	PEC/RAC ratio
D1/ditch	0.1
R4/stream	0.8
RAC (µg/L)	
6.8	PEC/RAC ratio
R4/stream	0.5
<i>Spring Cereals – Multiple applications – 20 m buffer zone including 20 m of vegetated filter strip</i>	
D1/ditch	0.307
R4/stream	2.090
RAC (µg/L)	
5.9	PEC/RAC ratio
R4/stream	0.4
RAC (µg/L)	
3.9	PEC/RAC ratio
D1/ditch	0.1
R4/stream	0.5
RAC (µg/L)	
6.8	PEC/RAC ratio
R4/stream	0.3
<i>Spring Cereals – Single application – 5 meters of vegetated filter strip</i>	
R4/stream	3.013
RAC (µg/L)	
3.9	PEC/RAC ratio
R4/stream	0.8
<i>Spring Cereals – Single application – 10 meters of vegetated filter strip</i>	
R4/stream	2.094
RAC (µg/L)	
3.9	PEC/RAC ratio
R4/stream	0.5

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

9.5.3 Overall conclusions

An acceptable risk of SAP50SCF can be concluded when the appropriate mitigation measures are in place:

zRMS comments:

Based on the lowest RAC= 3.9 µg a.s./L value obtained for long-term toxicity to fish for folpet the following risk mitigation measures are required:

Dose	Application number	Crop	Mitigation measure
Maximum dose	Single	Winter cereals	D1 scenario: 10 meters of vegetated filter strip D2 scenario: restriction of application at MSs level.
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	D2 scenario: restriction of application R1, R3 and R4 scenarios: 20 meters of vegetated filter strip
		Spring cereals	D1, R4 scenario: 20 meters of vegetated filter strip
Minimum dose	Single	Winter cereals	None
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	R1, R3 and R4 scenarios: 10 meters of vegetated filter strip
		Spring cereals	R4 scenario: 20 meters of vegetated filter strip

Based on the risk assessment for relevant scenarios for Poland such as: D3, D4 and R1, the following risk mitigation measures are required:

Multiple application at the maximum dose:

- 20-meter vegetative buffer zone (R1 scenario) for multiple application for winter and spring cereals

Multiple application at the minimum dose:

- 10-meter vegetative buffer zone (R1 scenario) for multiple application for winter and spring cereals

For single application for winter and spring cereals the risk mitigation measures is not required for scenarios relevant for Poland.

For remained scenarios the risk mitigation measures are left for decision at MSs level.

Please note that additional aquatic risk assessment may be required by the concerned Member States that do not accept simulations performed according to FOCUS recommendations.

For remaining metabolites of active compound, the risk is acceptable with no need for risk mitigation measures.

It should be noted that risk assessment for metabolites is covered by the a.s. risk assessment. No additional calculations are required.

Dose	Application number	Crop	Mitigation measure
Maximum dose	Single	Winter cereals	None
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	R1 and R3 scenario: 5 meters of vegetated filter strip
		Spring cereals	R4 scenario: 15 meters of vegetated filter strip
Minimum dose (see Appendix 3)	Single	Winter cereals	None
		Spring cereals	R4 scenario: 5 meters of vegetated filter strip
	Multiple	Winter cereals	R3 scenario: 5 meters of vegetated filter strip
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip

April 2024

Dose	Application number	Crop	Mitigation measure
Maximum dose	Single	Winter cereals	None
		Spring cereals	R4 scenario: 5 meters of vegetated filter strip
	Multiple	Winter cereals	R3 scenario: 5 meters of vegetated filter strip
		Spring cereals	R4 scenario: 15 meters of vegetated filter strip
Minimum dose (see Appendix 3)	Single	Winter cereals	None
		Spring cereals	None
	Multiple	Winter cereals	None
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip

9.6 Effects on bees (KCP 10.3.1)

9.6.1 Toxicity data

Studies on the toxicity to bees have been carried out with folpet. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies). Effects on bees of SAP50SCF were not evaluated as part of the EU assessment of folpet. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.6-1: Endpoints and effect values relevant for the risk assessment for bees

Species	Substance	Exposure System	Results	Reference
<i>Apis mellifera</i>	folpet	Acute oral	LD ₅₀ > 236 µg a.s./bee	EFSA Scientific Report (2009) 297, 70-80
<i>Apis mellifera</i>	Folpan 80 WDG	Acute oral	LD ₅₀ > 179 µg a.s./bee	EFSA Scientific Report (2009) 297, 70-80
<i>Apis mellifera</i>	folpet	Acute contact	LD ₅₀ > 200 µg a.s./bee	EFSA Scientific Report (2009) 297, 70-80
<i>Apis mellifera</i>	Folpan 80 WDG	Acute contact	LD ₅₀ > 160 µg a.s./bee	EFSA Scientific Report (2009) 297, 70-80
<i>Apis mellifera</i>	Folpet 80 WG	Acute oral	LD ₅₀ > 104.8 µg a.s./bee	KCP 10.3.1.1/01, Schmitzer and

Species	Substance	Exposure System	Results	Reference
<i>Apis mellifera</i>	Folpet 80 WG	Acute contact	LD ₅₀ > 100 µg a.s./bee	Pavie, 2007, 33893035 Supplementary info
<i>Apis mellifera</i>	Folpet technical	Chronic oral	LDD ₅₀ > 16.29 µg a.s./bee/day	KCP 10.3.1.2/01, Ansaloni, 2015, TRC14-246BA
<i>Apis mellifera</i>	Folpet technical	Acute larvae	8 d LDD ₅₀ = 4.846 µg a.s./larvae/day developmental period NOED = 0.89 µg a.s./larvae/day developmental period 8d LD ₁₀ = 0.64 µg a.s./larvae/day developmental period (95% C.I. = 0.13-1.28)	KCP 10.3.1.3/01, Ansaloni, 2015, TRC14-245BA
<i>Apis mellifera</i>	Folpet technical	Chronic larvae	ED ₅₀ > 6.48 µg a.s./larvae/developmental period ED ₁₀ = could not be calculated NOED = 2.16 µg a.s./larvae/developmental period	KCP 10.3.1.3/02, Marín, 2022, S21-05947
<i>Bombus</i> sp.	Folpet technical	Acute oral	LD ₅₀ > 100 µg a.s./bee	KCP 10.3.1.1/02, Fauser-Misslin, 2015, 20140156
<i>Bombus</i> sp.	Folpet technical	Acute contact	LD ₅₀ > 100 µg a.s./bee	
<i>Bombus</i> sp.	Folpet 80 WG	Acute oral	LD ₅₀ > 389.3 µg a.s./bee	KCP 10.3.1.1/03, Amsel, 2015, 15-10-48-167-B
<i>Bombus</i> sp.	Folpet 80 WG	Acute contact	LD ₅₀ > 199.5 µg a.s./bee	
<i>Osmia bicornis</i>	Folpet 80 WG	Acute oral	LD ₅₀ > 104.1 µg a.s./bee	KCP 10.3.1.1/04, Schnurr, 2015, 15-10-48-114-B
<i>Osmia bicornis</i>	Folpet 80 WG	Acute contact	LD ₅₀ > 199.5 µg a.s./bee	
<i>Apis mellifera</i>	SAP50SCF	Acute oral Acute contact	LD ₅₀ > 302.41 µg a.s./bee LD ₅₀ > 571.22 µg a.s./bee	KCP 10.3.1.1/05, Ansaloni, 2023, S23-102834
Higher-tier studies (tunnel test, field studies)				
-				

zRMS comments:

Acute bee toxicity data for active substance provided in Table 9.6-1 are in line with EU agreed endpoints reported in EFSA Scientific Report (2009) 297, 70-80.

To fulfil the data requirements as set by Commission Regulation (EU) No 284/2013, studies on acute toxicity to adult bees and chronic and larvae toxicity to bees for formulated product should be submitted.

It should be noted that according to recommendation given in EFSA PPR Meeting on general recurring issues, (EFSA, 2019)), when a PPP appears to be more toxic, i.e. its toxicity endpoint is three times lower than the equivalent endpoint of the active substance, according to the data requirement the lower endpoint should be used for the risk assessment or risk assessments for both the active substance and PPP could be provided.

The results of acute toxicity data for the active substance and formulation are available and are summarized in the table above.

Toxicity	Folpet	SAP50SCF
Acute oral	LD ₅₀ > 236 µg a.s./bee	LD ₅₀ > 302.41 µg a.s./bee
Acute contact	LD ₅₀ > 200 µg a.s./bee	LD ₅₀ > 571.22 µg a.s./bee

All the available endpoints are unbound. The toxicity endpoint for formulation SAP50SCF expressed in a.s. unit is not three times lower than the equivalent endpoint of the active substance.

In the same time, it should be noted that the chronic studies for adult bees and larvae bees for the product SAP50SCF is not required as the chronic a.s. data are available and covers the chronic risk assessment for the current formulation.

Studies on acute effects of the formulated product to bees listed in Table above were evaluated by the zRMS and considered acceptable. The reported endpoints are confirmed.
Summary of the performed studies together with zRMS evaluation may be found in Appendix 2.

9.6.1.1 Justification for new endpoints

SAP50SCF is a formulated product constituted by one active substance only (folpet). Since the active substance is the major constituent of this formulated product, it is expected that the toxicity of the product will be driven by the active substance. Additionally, there are studies performed with Folpet 80 WG, which is a formulated product also constituted by the same active substance only. The data available for both formulations indicate that they present similar ecotoxicological profiles with Folpet 80 WG being slightly more toxic.

This means that conducting a risk assessment for SAP50SCF with the data from the active substance and Folpet 80 WG is reliable and conservative. For further details, please refer to bridging statement on Part C of this dossier.

9.6.2 Risk assessment

The evaluation of the risk for bees was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002).

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group cereals covers the risk for birds from all intended uses (see 9.1.2).

9.6.2.1 Hazard quotients for bees

- *Risk assessment according to SANCO/10329/2002 rev 2 final*

Table 9.6-2: First-tier assessment of the risk for bees due to the use of SAP50SCF in cereals

Table 3.6-2: First-tier assessment of the risk for bees due to the use of SAP50SCF in cereals			
Intended use		Cereals	
Active substance		folpet	
Application rate (g a.s./ha)		2 × 600	
Test design	LD ₅₀ (lab.) (µg a.s./bee)	Single application rate (g a.s./ha)	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	>236	600	<2.5
Contact toxicity	>200		<3.0
Product		SAP50SCF	
Application rate (g a.s./ha)		2 × 600	
Test design	LD ₅₀ (lab.) (µ a.s.g/bee)	Single application rate (g a.s./ha)	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	>302.41	600	<1.98
Contact toxicity	>571.22		<1.05

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

Chronic risk to honey bees

According to the new data requirements (Commission regulation No 283/2013 and 284/2013), a chronic toxicity test with honeybees is required where exposure to honeybees cannot be excluded.

The EPPO 2010 scheme does not recommend a chronic assessment for adults for foliar spray applications. However, as an approach, it is proposed an assessment based on the refinement for seed coatings/soil treatments (point 7 on the scheme). This approach can be adapted to provide a worst case assessment for foliar sprays.

A worst case of potential exposure via residues in pollen / nectar can be estimated based on the default worst case value of 1 mg a.s./kg proposed in the EPPO 2010 scheme (see Note 6), based on a database of measured values from aerial plant parts as a surrogate for nectar and pollen.

The default residues can then be combined with a measure of consumption in order to estimate the exposure of bees. Worst case data from Rortais *et al.*, 2005 as proposed in the EPPO 2010 scheme have been used to estimate the consumption by bee foragers:

Worst case: forager consuming 898.8 mg sugar for 7 days (= 128 mg sugar /day).

Assuming 40% sugar content of nectar: $(898.8 * 2.5)/7 = 321$ mg nectar/day

Thus considering residues of 1 mg a.s./kg sugar x consumption of 321 mg nectar/bee/day

Total exposure ETE = 0.32 µg a.s./bee/day

-

This can be compared to the adult LDD₅₀ of 16.29 µg a.s./bee/day.

TER = NOED (µg a.s./bee/day) / ETE (µg a.s./bee/day) (EPPO 2010 trigger = 1)

The chronic TER values are given in the table below.

Table 9.6.3: Chronic adult bees risk due to the use of SAP50SCF

Uses	Exposure Route	LDD ₅₀ [µg a.s./bee/day]	Maximum nectar consumption [mg nectar/bee/day]	Generic worst case residue intake of folpet [µg a.s./bee/day]	TER _{chronic}	Trigger
Cereals	Oral	16.29	321	0.32	50.9	1

Values in **bold** are above the trigger and indicate an acceptable risk to honey bees

The chronic TER based on worst case generic residue assumptions is 50.9 and higher than the respective trigger of 1.

The TER value of 50.9 is above the trigger (1), indicating that the proposed uses of SAP50SCF pose an acceptable chronic risk to adult bees.

Risk to honey bee larvae

According to the new data requirements (Commission regulation No 283/2013 and 284/2013), a honey bee brood study is required where exposure to honey bee brood cannot be excluded.

The toxicity of SAP50SCF to honeybee larvae (KCP 10.3.1.3/01 and 10.3.1.3/02) was determined in a 120 h and in a 22 d exposure study. In the first study, the LDD₅₀ and the NOED were calculated to be 4.846 and 0.89 µg a.s./larvae, respectively. Since this the test was stopped before the beginning of larvae emergence, the endpoint is considered valid as an acute (mortality) larvae endpoint. The second study presents a NOED of 2.16 µg a.s./larva. Since this study lasted for the entire developmental period of the larvae, the derived endpoints are considered valid as chronic ones. This endpoint will be used for the risk assessment. A worst case risk assessment to honeybee larvae can be conducted through the calculation of a TER value as set out in the EPPO 2010 scheme (point 5 on the scheme). A worst case potential exposure via residues in pollen / nectar can be estimated based on the default worst case residue of 1 mg a.s./kg proposed in the EPPO 2010 scheme (see Note 6). The default residues can then be combined with a measure of consumption in order to estimate the exposure of bees. Worst case data from Rortais *et al.*, 2005 as proposed in the EPPO scheme have been used to estimate the consumption by bee larvae:

-
Worst case: drone larvae consuming 98.2 mg sugar during 6.5 days (= 15.1 mg sugar /day).
Assuming a mean sugar content of 40% in nectar: $(98.2 * 2.5)/6.5 = 37.8$ mg nectar/larva/day
Thus, considering residues of 1 mg a.s./kg x consumption of 37.8 mg nectar/larva/day:
Total exposure ETE = 0.0378 µg a.s./larva/day
This can be compared to the larval NOED of 2.16 µg a.s./larva
 $TER = NOED (\mu\text{g a.s./larva}) / ETE (\mu\text{g a.s./larva})$ (EPPO 2010 trigger = 1)
According to the parameters above, the worst case consumption of nectar for a honey bee larvae values 37.8 mg nectar/larvae/day during its whole development and the generic worst case residue value is set to 1 mg a.s./kg in nectar as given in the revised EPPO scheme (2010).
Therefore, the maximum amount of folpet residues, a honeybee larvae could ingest by consumption of nectar is 0.0378 µg a.s./ larvae/day.

Table 9.6-4: Chronic larvae risk for bees due to the use of SAP50SCF

Use	Scenario	NOED [µg a.s./larvae]	Maximum consumption of pollen/nectar [mg/larvae/day]	Generic worst case residue intake of folpet [µg a.s./larvae/day]	TERlarvae	Trigger
Cereals	Nectar	2.16	37.8	0.0378	57.1	1

The TER based on the combined residues of worst case generic residue assumptions for the whole developmental period is higher than the trigger of 1 (TER=57.1).

zRMS comments:

The acute risk assessment for bees presented in Table 9.6-2 is agreed by the zRMS. HQ_{oral, contact} values for the active substances and the formulated product SAP50SCF are below the trigger of 50, indicating a low acute risk for bees.

Please note that the evaluation has been performed in line with SANCO/10329/2002 rev 2 final.

Overall, acceptable risk to bees may be concluded from the intended uses of SAP50SCF.

- **Risk assessment according to EFSA Journal 2013; 11(7):3295**

The Applicant would like to highlight that the guidance document used for this risk assessment is not yet noted and is currently under update. Therefore, the risk assessment is only presented for illustrative reasons and it is the Applicant's point of view that no conclusion should be drawn on the basis of these results until the updated and noted document is available.

Table 9.6-5: Screening step of the risk for bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use		Cereals			
Active substance		folpet			
Application rate (g a.s./ha)		2 × 600			
Test design	LD ₅₀ (lab.) (µg a.s./bee)	"Calculation factor"	HQ/ETR	Trigger	Risk indicator
Acute oral toxicity	>236	7.6	0.02	0.2	OK
Acute contact toxicity	>200	1	3.0	42	OK
Chronic oral toxicity	16.29	7.6	0.280	0.03	!
Chronic larvae toxicity	2.16	4.4	2.97	0.2	!

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

Table 9.6-6: First tier of the risk for bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use		Cereals							
Active substance		folpet							
Application rate (g a.s./ha)		2 × 600							
Application	BBCH	Category	Scenario	Ef	SV HB	TWA HB	ETR	trigger	Risk indicator
Spray DW	30-39	chronic	Treated crop	1	0.92	0.72	0.024	0.03	OK
	40-69	chronic	Treated crop	1	0.92	0.72	0.024	0.03	OK
	30-39	chronic	Weeds	0.5	2.9	0.72	0.038	0.03	!
	40-69	chronic	Weeds	0.3	2.9	0.72	0.023	0.03	OK
	30-39	chronic	Field margin	0.0092	2.9	0.72	0.001	0.03	OK
	40-69	chronic	Field margin	0.0092	2.9	0.72	0.001	0.03	OK
	30-39	chronic	Adjacent crop	0.0033	5.8	0.72	0.001	0.03	OK
	40-69	chronic	Adjacent crop	0.0033	5.8	0.72	0.001	0.03	OK
	30-39	chronic	Next crop	1	0.54	0.72	0.014	0.03	OK
	40-69	chronic	Next crop	1	0.54	0.72	0.014	0.03	OK
	30-39	larva	Treated crop	1	0.15	0.85	0.09	0.2	OK
	40-69	larva	Treated crop	1	0.15	0.85	0.09	0.2	OK
	30-39	larva	Weeds	0.5	2.2	0.85	0.63	0.2	!
	40-69	larva	Weeds	0.3	2.2	0.85	0.38	0.2	!
	30-39	larva	Field margin	0.0092	2.2	0.85	0.01	0.2	OK
	40-69	larva	Field margin	0.0092	2.2	0.85	0.01	0.2	OK
	30-39	larva	Adjacent crop	0.0033	4.4	0.85	0.01	0.2	OK
	40-69	larva	Adjacent crop	0.0033	4.4	0.85	0.01	0.2	OK
	30-39	larva	Next crop	1	0.4	0.85	0.23	0.2	!
	40-69	larva	Next crop	1	0.4	0.85	0.23	0.2	!

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

— Refinement of residue deposition on weeds:

At SAP50SCF application, the BBCH growth phase 30-59 is equivalent to the stem elongation, booting and inflorescence emergence, heading and covers the growth stages 3 to 5. EFSA Guidance takes into account the interception of the spray by the crop where values are derived from FOCUS 2001 (Appendix X, Table X2a).

The EFSA Guidance on the Risk Assessment for Bees is the most recent guidance document, although not yet noted. Even so, it is a 9 year old document and it is normal that it does not reflect the up-to-date available knowledge. Namely, the deposition factor to be used for the risk assessment at Tier 1 corresponds to crop interception values as used in the FOCUS surface water report (FOCUS, 2001). In the context of a higher-tier assessment, updated values could also be used. In fact, an updated document (Generic Guidance for Tier 1 FOCUS Ground Water Assessments, Version 2.3, 2021) was released recently (2021) presenting updated figures of Deposition Factors (see table Błąd! Nie można odnaleźć źródła odwołania.below); high should be accepted in the context of a higher tier Risk Assessment.

Therefore, an updated refined risk assessment based on EFSA Guidance recommendations considering a refined DF as a weight of evidence approach is proposed.

Table 1.5: Interception by other crops dependent on growth stage

Crop	Bare – emergence	Leaf development	Stem elongation		Flowering		Senescence Ripening
	BBCH [#]						
	0– 09	10–19	20–39		40–89		90–99
Beans (field + vegetable)	0	25	40		70		80
Cabbage	0	25	40		70		90
Carrots	0	25	60		80		80
Cotton	0	30	60		75		90
Grass ^{##}	0	40	60		90		90
Linseed	0	30	60		70		90
Maize	0	25	50		75		90
Oil seed rape (summer)	0	40	80		80		90
Oil seed rape (winter)	0	40	80		80		90
Onions	0	10	25		40		60
Peas	0	35	55		85		85
Potatoes	0	15	60		85		50
Soybean	0	35	55		85		65
Spring cereals	0	0	BBCH 20–29*	BBCH 30–39*	BBCH 40–69	BBCH 70–89	80–
			20	80	90	80	
Strawberries	0	30	50		60		60
Sugar beets	0	20	70 (rosette)		90		90
Sunflower	0	20	50		75		90
Tobacco	0	50	70		90		90
Tomatoes	0	50	70		80		50
Winter cereals	0	0	BBCH 20–29*	BBCH 30–39*	BBCH 40–69	BBCH 70–89	80
			20	80	90	80	

[#]The BBCH code is indicative (Meier, 2001).

^{##}A value of 90 is used for applications to established turf.

*BBCH code of 20–29 for tillering and 30–39 for elongation.

For BBCH 30–39, a crop interception of 80% is proposed, therefore an Ef of 0.2 will be considered. For BBCH 40–69, a crop interception of 90% is proposed, therefore an Ef of 0.1 will be considered.

—Refinement of TWA for next crop scenario:

Folpet degradation in soil and water is very quick, with DT₅₀ values of 1.38 (geomean of 4 values) and 0.018 days (highest value obtained), respectively. The TWA figure is calculated with a default DT₅₀ value of 10 days which is not at all representative of folpet. Therefore, a refinement of this value is considered below, which is especially relevant for the next crop scenarios:

	Chronic oral exposure	Larvae exposure
DT ₅₀	1.38	1.38
K	0.50228057	0.50228057
T	40	5
K*T	5.02280566	2.51140283
$1 - e^{-Kt}$	0.99341398	0.91884569
TWA	0.198	0.366

Refined risk assessment:

Table 9.6-7: Refined risk assessment for bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use		Cereals							
Active substance		folpet							
Application rate (g a.s./ha)		2 × 600							
Application	BBCH	Category	Scenario	Ef	SV HB	TWA HB	ETR	trigger	Risk indicator
Spray-DW	30-39	chronic	Weeds	0.2*	2.9	0.72	0.015	0.03	OK
	30-39	larva	Weeds	0.2*	2.2	0.85	0.104	0.2	OK
	40-69	larva	Weeds	0.1*	2.2	0.85	0.126	0.2	OK
	30-39	larva	Next crop	1	0.4	0.366*	0.099	0.2	OK
	40-69	larva	Next crop	1	0.4	0.366*	0.099	0.2	OK

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

*refined parameters

zRMS comments:

The chronic adult and larvae bees risk assessment is not required according to SANCO/10329/2002 rev 2 final.

Based on Tier 1 based on the EFSA Journal 2013; 11(7):329 (not approved at EU level) indicated an unacceptable chronic risk for adult bee (weed scenario) and larva bees (scenario weed and next crop).

Further refinement of the risk assessment presented by the Applicant has not been verified by zRMS and it is left at MSs level.

The chronic risk assessment for adults and larvae bees for PL registration of the product is not required yet until Bee GD document will be approved at EU level.

9.6.2.2 Higher-tier risk assessment for bees (tunnel test, field studies)

Not relevant.

9.6.3 Effects on bumble bees

- Risk assessment according to SANCO/10329/2002 rev 2 final

Table 9.6-8: First-tier assessment of the risk for bumble bees due to the use of SAP50SCF in cereals

Intended use		Cereals		
Active substance		folpet		
Application rate (g a.s./ha)		2 × 600		
Test design	LD ₅₀ (lab.) (µg a.s./bee)	Single application rate (g a.s./ha)		Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	>100	600		<6.0
Contact toxicity	>100			<6.0

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

zRMS comments:

The acute risk assessment for bees presented in Table 9.6-8 is agreed by the zRMS. HQ_{oral,contact} values for the active substance are below the trigger of 50, indicating a low acute risk for bumble bees.
Please note that the evaluation has been performed in line with SANCO/10329/2002 rev 2 final.

Overall, acceptable risk to bumble bees may be concluded from the intended uses of SAP50SCF.

- **Risk assessment according to EFSA Journal 2013; 11(7):3295**

Table 9.6-9: Screening step of the risk for bumble bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use	Cereals				
Active substance	folpet				
Application rate (g a.s./ha)	2 × 600				
Test design	LD₅₀ (lab.) (µg a.s./bee)	“Calculation factor”	HQ/ETR	Trigger	Risk indicator
Acute oral toxicity	>100	11.2	0.07	0.034	!
Acute contact toxicity	>100	1	6.0	7	OK

Table 9.6-10: First tier of the risk for bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use	Cereals								
Active substance	folpet								
Application rate (g a.s./ha)	2 × 600								
Application	BBCH	Category	Scenario	Ef	SV BB	TWA BB	ETR	trigger	Risk indicator
Spray DW	30-39	acute	Treated crop	1	2.3	1	0.0138	0.036	OK
	40-69	acute	Treated crop	1	2.3	1	0.0138	0.036	OK
	30-39	acute	Weeds	0.5	6.5	1	0.0195	0.036	OK
	40-69	acute	Weeds	0.3	6.5	1	0.0117	0.036	OK
	30-39	acute	Field margin	0.0092	6.5	1	0.0004	0.036	OK
	40-69	acute	Field margin	0.0092	6.5	1	0.0004	0.036	OK
	30-39	acute	Adjacent crop	0.0033	11.2	1	0.0002	0.036	OK
	40-69	acute	Adjacent crop	0.0033	11.2	1	0.0002	0.036	OK
	30-39	acute	Next crop	1	0.9	1	0.0054	0.036	OK
	40-69	acute	Next crop	1	0.9	1	0.0054	0.036	OK

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

zRMS comments:

The acute risk assessment for bumble bees presented in Table 9.6-9 and Table 9.6-10 is agreed by the zRMS. HQ oral,contact values for the active substance at Tier 1 are below the trigger values, indicating a low acute risk for bumble bees.

Overall, acceptable risk to bumble bees may be concluded from the intended uses of SAP50SCF according to EFSA Journal 2013; 11(7):3295 (not approved. at EU level).

9.6.4 Effects on solitary bees

~~— Risk assessment according to SANCO/10329/2002 rev 2 final~~

~~Table 9.6-11: First-tier assessment of the risk for solitary bees due to the use of SAP50SCF in cereals~~

Intended use	Cereals		
Active substance	folpet		
Application rate (g a.s./ha)	2 × 600		
Test design	LD ₅₀ (lab.) (µg a.s./bee)	Single application rate (g a.s./ha)	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	≥104.1	600	≤5.8
Contact toxicity	≥199.5		≤3.0

~~Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.~~

~~— Risk assessment according to EFSA Journal 2013; 11(7):3295~~

~~Table 9.6-12: Screening step of the risk for solitary bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329~~

Intended use	Cereals				
Active substance	folpet				
Application rate (g a.s./ha)	2 × 600				
Test design	LD ₅₀ (lab.) (µg a.s./bee)	"Calculation factor"	HQ/ETR	Trigger	Risk indicator
Acute oral toxicity	≥104.1	5.7	0.03	0.04	OK
Acute contact toxicity	≥199.5	1	3.0	8	OK

zRMS comments:

Currently the risk assessment is not required for solitary bees at zonal registration of plant protection products.

9.6.5 Overall conclusions

~~The risk assessment for bees was conducted according to SANCO/10329/2002 rev 2 final and according to EFSA Journal 2013;11(7):3295 for illustrative purposes only as the last mentioned guidance document is not yet noted. Acceptable acute and chronic risks were determined towards bees (honey, bumble and solitary ones) after exposure to SAP50SCF in the proposed application patterns.~~

zRMS comments:

The acute risk assessment for bees and bumble bees was conducted according to SANCO/10329/2002 rev 2 final and according to EFSA Journal 2013;11(7):3295 indicated an acceptable risk.
The chronic adult and larvae risk assessment is not required according to SANCO/10329/2002 rev 2 final.
Based on Tier 1 an unacceptable chronic risk based on the EFSA Journal 2013; 11(7):329(not approved at EU level) for adult bee and larva bees for scenario weed and next crop (only larvae) is identified.
Further refinement of the chronic risk assessment presented by the Applicant was not verified by zRMS and it is left at MSs level.

9.7 Effects on arthropods other than bees (KCP 10.3.2)

9.7.1 Toxicity data

Studies on the toxicity to non-target arthropods have been carried out with folpet. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on non-target arthropods of SAP50SCF were not evaluated as part of the EU assessment of folpet. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.7-1: Endpoints and effect values relevant for the risk assessment for non-target arthropods

Species	Substance	Exposure System	Results	Reference
<i>Typhlodromus pyri</i> (protonymphs)	Folpet 80 WG	Laboratory test glass plates (2D)	LR ₅₀ = 3063.6 g a.s./ha 2859.0 < ER ₅₀ < 5348.8 g a.s./ha	KCP 10.3.2.1/01, Moll, 2007, 33895063 Supplementary info
<i>Aphidius rhopalosiphi</i> (adults)	Folpet 80 WG	Laboratory test glass plates (2D)	LR ₅₀ > 6400 g a.s./ha ER ₅₀ > 6400 g a.s./ha	KCP 10.3.2.1/02, Luna, 2015, TRC14-253BA Supplementary info
<i>Aphidius rhopalosiphi</i> (adults)	SAP50SCF	Laboratory test glass plates (2D)	LR ₅₀ > 1809.50 g a.s./ha ER ₅₀ < 452.38 g a.s./ha and >226.19 g a.s./ha	KCP 10.3.2.1/04, Varela, 2023, S23-102835
<i>Typhlodromus pyri</i> (protonymphs)	SAP50SCF	Laboratory test glass plates (2D)	LR ₅₀ > 4000 g a.s./ha ER ₅₀ > 4000 g a.s./ha	KCP 10.3.2.1/03, Luna, 2023, S23-100376
<i>Typhlodromus pyri</i> (protonymphs)	SAP50SCF	Extended laboratory test Bean leaves (2D)	LR ₅₀ > 5250 g a.s./ha No effects on reproduction higher than 50% up to 5250 g a.s./ha	KCP 10.3.2.2/01, Schwarz, 2011, 63142062
<i>Chrysoperla carnea</i> (larvae)	Folpet 80 WG	Extended laboratory test Bean leaves (2D)	LR ₅₀ > 5348.8 g a.s./ha ER ₅₀ > 5348.8 g a.s./ha	KCP 10.3.2.2/02, Moll, 2007, 33898047 Supplementary info
<i>Coccinella septempunctata</i> (larvae)	Folpet 80 WG	Extended laboratory test Bean plants (2D)	LR ₅₀ > 5348.8 g a.s./ha ER ₅₀ > 5348.8 g a.s./ha	KCP 10.3.2.2/03, Moll, 2007, 33897012 Supplementary info
<i>Aphidius rhopalosiphi</i> (adults)	Folpet 80 WG	Extended aged residue laboratory test Bean leaves (2D)	LR ₅₀ > 5348.8 g a.s./ha ER ₅₀ > 5348.8 g a.s./ha	KCP 10.3.2.2/04, Moll, 2007, 33899003 Supplementary info
Field or semi-field tests				
-				

zRMS comments:

The studies performed with the formulated product SAP50SCF were evaluated and agreed by the zRMS (for details, please refer to respective points in Appendix 2). Endpoints reported in Table 9.7-1 are confirmed to be correct. The study for additional NTA species are not required and for this reason they have been shaded in the Table 9.7-1 above.

9.7.1.1 Justification for new endpoints

Not relevant.

9.7.2 Risk assessment

The evaluation of the risk for non-target arthropods was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002), and in consideration of the recommendations of the guidance document ESCORT 2.

9.7.2.1 Risk assessment for in-field exposure

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group field crops covers the risk for non-target arthropods from all intended uses (see 9.1.2).

Calculate $PER_{in-field}$ values according to ESCORT 2 as:

Application rate \times MAF.

Table 9.7-2: First- and higher-tier assessment of the in-field risk for non-target arthropods due to the use of SAP50SCF in cereals

Intended use	Cereals		
Active substance/product	folpet		
Application rate (g/ha)	2 x 600		
MAF	1.7		
Test species Tier I	LR₅₀ (lab.) (g a.s./ha)	PER_{in-field} (g/ha)	HQ_{in-field} criterion: HQ \leq 2
<i>Typhlodromus pyri</i>	>4000	1020	<0.26
<i>Aphidius rhopalosiphi</i>	>1809.50		<0.56

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment. Criteria values shown in bold breach the relevant trigger.

* If an LR₅₀ or ER₅₀ from a relevant extended laboratory test is available, it should be considered in place of the rate with \leq 50 % effect.

zRMS comments:

The risk assessment presented in Table 9.7-2 is agreed by the zRMS.

Based on calculations performed with consideration of the Tier I laboratory data acceptable in-field risk to non-target arthropods from all intended uses of SAP50SCF may be concluded.

In addition, one extended study for T.pyri has been conducted for formulation SAP50SCF indicating that no effects on reproduction higher than 50% up to 5250 g a.s./ha is expected after exposure of formulated product.

9.7.2.2 Risk assessment for off-field exposure

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the assessment for the use group field crops covers the risk for non-target arthropods from all intended uses (see 9.1.2).

Calculate $PER_{\text{off-field}}$ values according to ESCORT 2 as:

Application rate \times MAF \times (drift factor/vegetation distribution factor)

Calculate the corrected $PER_{\text{off-field}}$ values according to ESCORT 2 as:

corr. $PER_{\text{off-field}} = PER_{\text{off-field}} / \text{correction factor}$

Table 9.7-3: First- and higher-tier assessment of the off-field risk for non-target arthropods due to the use of SAP50SCF in cereals

Intended use	Cereals				
Active substance/product	folpet				
Application rate (g/ha)	2 x 600				
MAF	1.7				
vdf	10 (2D studies)				
Test species Tier I	LR₅₀ (lab.) (g a.s./ha)	Drift rate	PER_{off-field} (g/ha)	CF	HQ_{off-field} criterion: HQ \leq 2
<i>Typhlodromus pyri</i>	>4000	2.38%	2.4276	10	<0.006
<i>Aphidius rhopalosiphi</i>	>1809.50				<0.013

MAF: Multiple application factor; vdf: Vegetation distribution factor; (corr.) PER: (corrected) Predicted environmental rate; CF: Correction factor; HQ: Hazard quotient. Criteria values shown in bold breach the relevant trigger.

* If an LR₅₀ or ER₅₀ from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50 % effect.

zRMS comments:

The risk assessment presented in Table 9.7-3 is validated by the zRMS.

Overall, based on calculations performed with consideration of the Tier I laboratory data acceptable off-field risk to non-target arthropods from all intended uses of SAP50SCF may be concluded with no need for risk mitigation measures.

9.7.2.3 Additional higher-tier risk assessment

Not relevant.

9.7.2.4 Risk mitigation measures

No risk mitigation needed.

9.7.3 Overall conclusions

The risk assessment for non-target arthropods was conducted according to SANCO/10329/2002 rev 2 final. Acceptable in- and off-field risks were determined towards bees after exposure to SAP50SCF in the proposed application patterns.

9.8 Effects on non-target soil meso- and macrofauna (KCP 10.4)

9.8.1 Toxicity data

Studies on the toxicity to earthworms and other non-target soil organisms (meso- and macrofauna) have been carried out with folpet and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on earthworms and other non-target soil organisms (meso- and macrofauna) of SAP50SCF were not evaluated as part of the EU assessment of folpet. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.8-1: Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna)

Species	Substance	Exposure System	Results	Reference
<i>Eisenia foetida</i>	folpet	Mixed into substrate 14 d, acute	LC ₅₀ > 1,000 mg folpet/kg (LC ₅₀ -corrected > 500 mg folpet/kg ^a)	EFSA Scientific Report (2009) 297, 70-80
<i>Eisenia foetida</i>	Folpan 80 WDG	Mixed into substrate 14 d, acute	LC ₅₀ > 828 mg folpet/kg (Folpan 80 WDG) (LC ₅₀ corrected > 414 mg folpet/kg ^a)	EFSA Scientific Report (2009) 297, 70-80
<i>Eisenia foetida</i>	folpet	Mixed into substrate 56 d, chronic	NOEC = 5.18** mg folpet/kg soil	EFSA Scientific Report (2009) 297, 70-80
<i>Eisenia foetida</i>	Folpet 80 WG	Mixed into substrate 14 d, acute	LC ₅₀ > 1000 mg f.p./kg sdw	KCP 10.4.1.1/01, Witte, 2009, 51141021 Supplementary info
<i>Eisenia foetida foetida</i>	Folpet 80 WG	Mixed into substrate 56 d, chronic 2 % peat content	NOEC ≥ 39.99 mg f.p./mg sdw (31.99 mg a.s./kg sdw)	KCP 10.4.1.1/01, Ansaloni, 2014, TRC14 250BA Supplementary info
<i>Eisenia foetida foetida</i>	Folpet 80 WG	Mixed into substrate 56 d, chronic 5 % peat content	NOEC = 30.76 mg f.p./kg sdw (24.61 mg a.s./kg sdw)	KCP 10.4.1.1/02, Ansaloni, 2014, TRC14 251BA Supplementary info
<i>Eisenia foetida foetida</i>	Folpet 80 WG	Mixed into substrate 56 d, chronic 40 % peat content	NOEC ≥ 39.99 mg f.p./mg sdw (31.99 mg a.s./kg sdw)	KCP 10.4.1.1/03, Ansaloni, 2014, TRC14 252BA Supplementary info
<i>Eisenia foetida</i>	Folpet 80 WG	Overspray 56 d, chronic 5 % peat content	NOEC = 6.4 kg t.i./ha (equivalent to 6.95 mg a.s./kg sdw) ^{***}	KCP 10.4.1.1/04, Lührs, 2007, 33896022 Supplementary info
<i>Eisenia foetida</i>	BPC324F (Folpet 80 WG)	Mixed into substrate 56 d, chronic 5 % peat content	NOEC = 18.75 mg f.p./kg sdw (15.375 mg a.s./kg sdw)	KCP 10.4.1.1/05, Pavie, 2014, 84831022 Supplementary info
<i>Eisenia andrei</i>	SAP50SCF	Mixed into substrate 56 d, chronic 5 % peat content	NOEC ≥ 204.70 mg f.p./kg sdw (CV EC₁₀ > 204.70 mg f.p./kg sdw (86.75 mg a.s./kg sdw)	KCP 10.4.1.1/06, Queralt, 2023, S23- 102837

Species	Substance	Exposure System	Results	Reference
Field studies				
-				
Litter bag test				
-				

* ~~Corrected value derived by dividing the endpoint by a factor of 2 in accordance with the EPPO earthworm scheme 2002.~~

** It was agreed in the EPCO 22 experts' meeting on ecotoxicology that the lowest endpoint should be used without applying a correction factor.

*** ~~Calculated assuming a soil depth of 5 cm, a soil density of 1.5 g/cm³, and an active substance content of 81.5% w/w as mentioned in CoA of the sample used in the test.~~

zRMS comments:

Data for earthworms for active substance folpet provided in Table 9.8-1 are in line with EU agreed endpoints reported in EFSA Scientific Report (2009) 297, 70-80.

Only studies for technical a.s.- folpet and formulation SAP50SCF is considered by zRMS in the current risk assessment and for this reason data for other formulations is struck through in Tables above.

9.8.1.1 Justification for new endpoints

Not relevant.

9.8.2 Risk assessment

The evaluation of the risk for earthworms and other non-target soil organisms (meso- and macrofauna) was performed in accordance with the recommendations of the "Guidance Document on Terrestrial Ecotoxicology", as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

9.8.2.1 First-tier risk assessment

The relevant PEC_{soil} for risk assessments covering the proposed use pattern are taken from Section 8 (Environmental Fate), Chapter 8.7.2, Table 8.7-3. According to the assessment of environmental-fate data, multi-annual accumulation in soil does not need to be considered for folpet.

Table 9.8-2: First-tier assessment of the acute and chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use of SAP50SCF in cereals

Intended use		Cereals	
Acute effects on earthworms – no longer a data requirement			
Chronic effects on earthworms			
Product/active substance	NOEC (mg/kg dw)	PEC _{soil} (mg/kg dw)	TER _{lt} (criterion TER ≥ 5)
folpet	5.18	0.263	19.7
Phthalimide	0.518*	0.092	5.63
Phthalamic acid	0.518*	0.015	34.5
Phthalic acid	0.518*	0.016	32.4
SAP50SCF	43.75 ≥86.75	0.263	166.34 130.8
Chronic effects on other soil macro- and mesofauna – no data available			

TER values shown in bold fall below the relevant trigger.

*Assuming a worst-case situation of the metabolite being 10 times more toxic than parent.

zRMS comment:

The risk assessment for earthworms has been amended by the zRMS according to recommendation given in EFSA 2015. The NOEC value for product has been corrected because log Pow of folpet is higher than 2. No toxicity data are available for metabolites and for this reason a worst-case situation of the metabolite being 10 times more toxic than parent has been assumed.

All TER_{LT} values for earthworms for active substance, formulated product SAP50SCF as well as metabolites potentially relevant in soil are greater than the trigger of 5, indicating an overall acceptable risk.

9.8.2.2 Higher-tier risk assessment

Not relevant.

9.8.3 Overall conclusions

The risk assessment for soil macro- and mesofauna was conducted according to SANCO/10329/2002 rev 2 final. An acceptable risk is proven for earthworms when exposed to the active substance, its metabolites and the formulated product. No data on springtail and mites is submitted since no unacceptable risks were concluded for non-target terrestrial arthropods and earthworms. Therefore, springtail and mites are not expected to be affected at the proposed application rates.

9.9 Effects on soil microbial activity (KCP 10.5)

9.9.1 Toxicity data

Studies on effects soil microorganisms have been carried out with folpet. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on soil microorganisms of SPA50SCF were not evaluated as part of the EU assessment of folpet. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.9-1: Endpoints and effect values relevant for the risk assessment for soil microorganisms

Endpoint	Substance	Exposure System	Results	Reference
N-mineralisation	folpet	63 d, aerobic	No significant effects of folpet (< 25% effect compared to untreated control) when tested at 1.593 and 15.93 kg folpet/ha (equivalent to 21.24 mg/kg sdw)*.	EFSA Scientific Report (2009) 297, 70-80
C-mineralisation	folpet	63 d, aerobic	Dehydrogenase activity affected by < 25% compared to untreated control when tested at 1.593 and 15.93 kg folpet/ha.	EFSA Scientific Report (2009) 297, 70-80
N-mineralisation	Folpet 80 WG	28 d, aerobic sandy loam soil	No significant effects (< 25% effect compared to untreated control) when tested at 3.75 and 25	KCP 10.5/01, Gimeno, 2015, TRC14-299SM Supplementary info

Endpoint	Substance	Exposure System	Results	Reference
			mg/kg sdw	
N-mineralisation	SAP50SCF	28 d, aerobic sandy loam soil	No significant effects (< 25% effect compared to untreated control) when tested at 3.90 and 19.50 mg f.p./kg sdw	KCP 10.5/02, Queralt, 2023, S23-102838

*Calculated assuming a soil depth of 5 cm and a soil density of 1.5 g/cm³.

zRMS comments:

Data for soil microorganism for a.s., formulated product and folpet provided in Table 9.9-1 are in line with EU agreed endpoints reported in EFSA Scientific Report (2009) 297, 70-80.

Information regarding effects on carbon mineralisation is no longer a data requirement and for this reason is struck through in tables above.

9.9.1.1 Justification for new endpoints

Not relevant.

9.9.2 Risk assessment

The evaluation of the risk for soil microorganisms was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

The relevant PEC_{soil} for risk assessments covering the proposed use pattern are taken from Section 8 (Environmental Fate), Chapter 8.7.2, Table 8.7-3 and were already used in the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) (see 9.8).

Table 9.9-2: Assessment of the risk for effects on soil micro-organisms due to the use of SAP50SCF in cereals

Intended use	Cereals		
N-mineralisation			
Product/active substance	Max. conc. with effects ≤ 25 % (mg/kg dw)	PEC _{soil} (mg/kg dw)	Risk acceptable?
folpet	21.24 (at 63 d)	0.263	Yes
Phthalimide	2.124*	0.092	Yes
Phthalamic acid	2.124*	0.015	Yes
Phthalic acid	2.124*	0.016	Yes
SAP50SCF	19.50 (at 28 d)	0.394	Yes
C-mineralisation – no longer a data requirement			

*Assuming a worst-case situation of the metabolite being 10 times more toxic than parent.

zRMS comments:

The risk assessment presented in Table 9.9-2 above is in general agreed by the zRMS
The effects on the nitrogen transformations are acceptable (<25%) at concentration which is higher than the maximum relevant PECs for the maximum application rate of active substance and the product.
Overall, no unacceptable effects on soil microbial activity are expected following application of SAP50SCF.

9.9.3 Overall conclusions

The risk assessment for microorganisms was conducted according to SANCO/10329/2002 rev 2 final. An acceptable risk is proven for microorganisms when exposed to the active substance, its metabolites and the formulated product.

9.10 Effects on non-target terrestrial plants (KCP 10.6)

9.10.1 Toxicity data

Studies on the toxicity to non-target terrestrial plants have been carried out with folpet. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on non-target terrestrial plants of SAP50SCF were not evaluated as part of the EU assessment of folpet. New data submitted with this application are listed in Appendix 1 summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.10-1: Endpoints and effect values relevant for the risk assessment for non-target terrestrial plants

Species	Substance	Exposure System	Results	Reference
-	Folpan 80 WDG	Field conditions	Under field conditions, 'Folpan' 80 WDG was applied at 1.6, 4.8 and 8.0 kg product/ha to winter wheat, spring barley, winter oat, spring oat, winter rye, winter oilseed rape, linseed, peas, field beans and sugar beet. No phytotoxicity observed. An additional field trial resulted in no phytotoxicity on a range of crops at 6.4 kg folpet/ha ('Folpan' 80 WDG).	EFSA Scientific Report (2009) 297, 70-80
<i>Zea mays</i> <i>Lolium perenne</i> <i>Triticum aestivum</i> <i>Cucumis sativus</i> <i>Brassica napus</i> <i>Beta vulgaris</i> <i>Lycopersicon esculentum</i>	Folpet 80 % WG	21 d Seedling emergence (limit test)	At 1.6 kg a.s./ha, max 49.5% reduction on foliar fresh weight for <i>C. sativus</i>	KCP 10.6.2/01, Eley, 2009, ACE-08-259
<i>Zea mays</i> <i>Lolium perenne</i> <i>Triticum aestivum</i> <i>Cucumis sativus</i> <i>Brassica napus</i> <i>Beta vulgaris</i> <i>Lycopersicon esculentum</i>	Folpet 80 % WG	21 d Vegetative vigour	ER ₅₀ plant weight > 3.2 kg a.s./ha	KCP 10.6.2/02, Eley, 2009, ACE-08-260

m: monocotyledonous; d: dicotyledonous

9.10.1.1 Justification for new endpoints

SAP50SCF is a formulated product constituted by one active substance only (folpet). Since the active substance is the major constituent of this formulated product, it is expected that the toxicity of the product will be driven by the active substance. Additionally, there are studies performed with Folpet 80 WG, which is a formulated product also constituted by the same active substance only. The data available for both formulations indicate that they present similar ecotoxicological profiles with Folpet 80 WG being slightly more toxic.

This means that conducting a risk assessment for SAP50SCF with the data from the active substance and Folpet 80 WG is reliable and conservative. For further details, please refer to bridging statement on Part C of this dossier.

9.10.2 Risk assessment

9.10.2.1 Tier-1 risk assessment (based screening data)

Limit tests at rates up to 1.6 kg a.s./ha (seedling emergence) and 3.2 kg a.s./ha (vegetative vigour) were conducted with a similar formulation and effects were below the critical threshold as defined by the “Guidance Document on Terrestrial Ecotoxicology”, (SANCO/10329/2002 rev.2 final, 2002). The limit test rates exceed the highest field application rate of 600 g and are thus considered an indicator for an acceptable risk.

zRMS comments:

No toxicity endpoints are available for the product for SAP50SCF non-target terrestrial plants. However, based on the ecotoxicological data for both formulations (SAP50SCF and Folpet 80% WG), where formulation 80% WG is similar or more toxic than 500 SC and based on the higher content of the a.s., the endpoints from formulation 80% WG used in the risk assessment has been validated by zRMS.

In accordance with SANCO/10329 (17 October 2002), the risk to non-target terrestrial plants can be considered acceptable at the screening level if there were no effects on any species >50% at the maximum intended application rate.

The ER₅₀ values > 1.6 and 3.2. kg /ha for similar formulation from seedling emergence and vegetative vigour tests are above the maximum test rates, covering the maximum single application rate of in cereals (0.6 kg a.s./ha) indicating an acceptable risk to non-target crops from exposure of SAP50SCF.

9.10.2.2 Tier-2 risk assessment (based on dose-response data)

Not relevant.

9.10.2.3 Higher-tier risk assessment

Not relevant.

9.10.2.4 Risk mitigation measures

No risk mitigation needed.

9.10.3 Overall conclusions

The risk assessment for non-target terrestrial plants was conducted according to SANCO/10329/2002 rev 2 final. Since folpet is a fungicide, a tier 1 risk assessment was conducted, and an acceptable risk is proven when SAP50SCF is applied at the proposed application rates.

9.11 Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)

No available data.


9.12 Monitoring data (KCP 10.8)

No available data.

9.13 Classification and Labelling


Folpet: Classification and Labelling.

Classification and labelling in accordance with Regulation (EC) No 1272/2008

Environmental hazards	Aquatic Acute 1	
Hazard pictograms		
Signal word	Warning	
Hazard statements	H400	Very toxic to aquatic life.
Precautionary statements –	P273, P391, P501	

SAP50SCF: Classification and Labelling

Classification and labelling in accordance with Regulation (EC) No 1272/2008

Environmental hazards	Aquatic Chronic 2; Aquatic Acute 1	
Hazard pictograms		
Signal word	Warning	
Hazard statements	H400 H411 ¹	Very toxic to aquatic life. Toxic to aquatic life with long lasting effects. ²
Precautionary statements –	P273, P391, P501	

¹This classification is based on toxicity of Folpet 80 WG (LC₅₀ for *O. mykiss* = 0.176 mg/L; EC₅₀ for *D. magna* = 0.67 mg/L) according to the regulation (EC) n° 1272/2008 and (EC) n° 286/2011.

²Since the product is classified as H400 + H411, the hazard statement relevant for labeling is the H410: Very toxic to aquatic life with long lasting effects.

zRMS comments:

The following classification and labelling are proposed by zRMS.


Acute 1

H400: Hazard classification is based on the lowest acute toxicity endpoint of the studies with the formulation on the most sensitive species (fish).
No chronic toxicity data on the formulation are available.

Chronic 1

H410:

The summation method applies; a.s. is classified as Chronic 1 (M=1); sum of Chronic 1 components > 25% (considering the M factor)

Hazard category	Acute 1 Chronic 1
GHS pictogram	
Signal word	Warning
Hazard statement	H400: Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects Associated hazard statement that could appear on the label H410: Very toxic to aquatic life with long lasting effects
Precautionary statement response	P391: Collect spillage
Precautionary statement disposal	P501: Dispose of contents/container in accordance with local regulation
Supplemental hazard information	EUH401: To avoid risks to human health and the environment, comply with the instructions for use

The final classification on the label is H410.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.2.1/01	██████	2011	Acute toxicity of folpet Sapec 500 SC to Rainbow Trout (<i>Oncorhynchus mykiss</i>) in a 96-hour semi static test ██████ N°. 63141230 GLP Unpublished	Y	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.2.1/02	██████	2007	Acute toxicity of Folpet 80 WG to Rainbow Trout (<i>Oncorhynchus mykiss</i>) in a 96-hour semi static test ██████ N°. 33891230 GLP Unpublished	Y	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.2.1/03	Grade, R., Wydra, V.	2007	Acute toxicity of Folpet 80 WG to <i>Daphnia magna</i> in a semi static 48-hour immobilization test Ibacon Report N°. 33892220 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.2.1/04	Grade, R., Wydra, V.	2007	Influence of Folpet technical to <i>Daphnia magna</i> in a reproduction test Ibacon Report N°. 33881221 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.2.1/05	Alves, D.	2023	Toxicity of SAP50SCF to the Water Flea <i>Daphnia magna</i> under Laboratory Conditions (48h Acute Immobilisation Test with Semi-static design) CloverStrategy Report N°. CLOVER-A-01-2023 GLP Unpublished (biological phase, the analytical phase is still ongoing with draft report expected date for November 2023)	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.2.1/06	Wendling, K.	2024 Interim report	Folpec 50 SC: Toxicity to the Water Flea <i>Daphnia magna</i> Straus under Laboratory Conditions (Acute Immobilisation Test—Flow through) Eurofins Report N°. S23-104263 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.1/01	Schmitzer, S., Pavic, B.	2007	Effects of Folpet 80 WG (Acute Contact and Oral) on Honey Bees (<i>Apis mellifera</i> L.) in the laboratory Ibacon Report N°. 33893035	N	ASCENZA AGRO S.A.

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			GLP Unpublished		(formerly Sapec Agro S.A.)
KCP 10.3.1.1/02	Fausser-Misslin, A.	2015	Folpet: Acute Oral and Contact Toxicity to Bumble Bee (<i>Bombus terrestris</i> L.) under Laboratory Conditions IES Report N°. 20140156 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.1/03	Amsel, K.	2015	Acute toxicity of Folpet 80 WG to the bumblebee <i>Bombus terrestris</i> L. under laboratory conditions BioChem agrar Report N°. 15 10 48 167 B GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.1/04	Schnurr, A.	2015	Acute toxicity of Folpet 80 WG to the solitary bee <i>Osmia bicornis</i> L. under laboratory conditions BioChem agrar Report N°. 15 10 48 114 B GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.1/05	Ansaloni, T.	2023	SAP50SCF (Folpet 500 SC): Acute Oral and Contact Toxicity to the Honey bees (<i>Apis mellifera</i> L.), under Laboratory Conditions Eurofins Report N°. S23-102834 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.2/01	Ansaloni, T.	2015	Chronic toxicity of FOLPET TECHNICAL on honeybees (<i>Apis mellifera</i> L.) Trialcamp Report N°. TRC14-246BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.3/01	Ansaloni, T.	2015	Toxicity of FOLPET TECHNICAL on honey bee larvae (<i>Apis mellifera</i> L.) after repeated exposure under laboratory conditions Trialcamp Report N°. TRC14-245BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.3/01	Marín, M.	2022	Folpet Technical: Honey Bee (<i>Apis mellifera</i> L.) Larval Toxicity Test following Repeated Exposure under Laboratory Conditions Eurofins Report N°. S21-05947 GLP	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			Unpublished		
KCP 10.3.2.1/01	Moll, M.	2007	Effects of Folpet 80 WG on the Predatory Mite <i>Typhlodromus pyri</i> in the laboratory—Dose response test Ibacon Report N°. 33895063 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.1/02	Luna, F.	2015	A laboratory test to determine the LR50 of the formulation “FOLPET 80 WG” (Folpet 800 g/kg, WG) on the parasitic wasp <i>Aphidius rhopalosiphi</i> (Hymenoptera: Braconidae) Trialeamp Report N°. TRC14_253BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.1/03	Luna, F.	2023	SAP50SCF (Folpet 500 SC): Toxicity to the Predatory Mite, <i>Typhlodromus pyri</i> Scheuten (Acari, Phytoseiidae) under Standard Laboratory Conditions Eurofins Report N°. S23-100376 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.1/04	Varela, S.	2023	SAP50SCF (Folpet 500 SC): Toxicity to the Aphid Parasitoid <i>Aphidius rhopalosiphi</i> De Stefani Perez (Hymenoptera, Braconidae) under Laboratory Conditions Eurofins Report N°. S23-102835 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.2/01	Schwarz, A.	2011	Effects of Folpet Sapec 500 SC on the predatory mite <i>Typhlodromus pyri</i> , extended laboratory study – Dose response test Ibacon Report N°. 63142062 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.2/02	Moll, M.	2007	Effects of Folpet 80 WG on the Lacewing <i>Chrysoperla carnea</i> , extended laboratory study—Dose response test Ibacon Report N°. 33898047 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.2/03	Moll, M.	2007	Effects of Folpet 80 WG on the Ladybird Beetle <i>Coccinella septempunctata</i> , extended laboratory study—Dose response test Ibacon Report N°. 33897012	N	ASCENZA AGRO S.A. (formerly Sapec

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			GLP Unpublished		Agro S.A.)
KCP 10.3.2.2/04	Moll, M.	2007	Effects of Folpet 80 WG on the Parasitoid <i>Aphidius rhopalosiphii</i> , extended laboratory study—Aged residue test Ibacon Report N°. 33899003 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapee Agro S.A.)
KCP 10.4.1.1/01	Ansaloni, T.	2014	A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80 WG to the earthworm <i>Eisenia foetida</i> (Oligochaeta: Lumbricidae) in artificial substrate at 2% peat content Trialeamp Report N°. TRC14-250BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapee Agro S.A.)
KCP 10.4.1.1/02	Ansaloni, T.	2014	A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80 WG to the earthworm <i>Eisenia foetida</i> (Oligochaeta: Lumbricidae) in artificial substrate at 5% peat content Trialeamp Report N°. TRC14-251BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapee Agro S.A.)
KCP 10.4.1.1/03	Ansaloni, T.	2014	A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80 WG to the earthworm <i>Eisenia foetida</i> (Oligochaeta: Lumbricidae) in artificial substrate at 10% peat content Trialeamp Report N°. TRC14-252BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapee Agro S.A.)
KCP 10.4.1.1/04	Lühns, U.	2007	Effects of Folpet 80 WG on Reproduction and Growth of Earthworms <i>Eisenia fetida</i> in Artificial Soil with 5% peat Ibacon Report N°. 33896022 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapee Agro S.A.)
KCP 10.4.1.1/05	Pavic, B.	2014	Effects of BCP324F on Reproduction and Growth of Earthworms <i>Eisenia fetida</i> in Artificial Soil with 5% Peat Ibacon Report N°. 84831022 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapee Agro S.A.)
KCP 10.4.1.1/06	Queral, M.	2023	SAP50SCF (Folpet 500 SC): Sublethal Toxicity to the Earthworm <i>Eisenia andrei</i> (Oligochaeta, Lumbricidae) in Artificial Soil with 5 % Peat Eurofins Report N°. S23-102837	N	ASCENZA AGRO S.A. (formerly Sapee)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			GLP Unpublished		Agro S.A.)
KCP 10.5/01	Gimeno, C.	2015	Effects of the formulated product Folpet 80 WG on activity of the soil microflora under laboratory conditions Trialeamp Report N°. TRC14-299SM GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.5/02	Queralt, M.	2023	SAP50SCF (Folpet 500 SC): Effects on the Activity of Soil Microflora under Laboratory Conditions (Nitrogen Transformation) Eurofins Report N°. S23-102838 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.6.2/01	Eley, R.	2009	Evaluation of the Phytotoxicity of Folpet 80% WG Non Target Terrestrial Plant Seedling Emergence and Growth Test (Based on OECD Guideline 208) AgroChemex Report N°. ACE-08-259 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.6.2/02	Eley, R.	2009	Evaluation of the Phytotoxicity of Folpet 80% WG Non Target Terrestrial Plant Vegetative Vigour Test (Based on OECD Guideline 227) AgroChemex Report N°. ACE-08-260 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review (renewal process of the a.s.)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.3.1.1/01	Schmitzer, S., Pavic, B.	2007	Effects of Folpet 80 WG (Acute Contact and Oral) on Honey Bees (<i>Apis mellifera</i> L.) in the laboratory Îbacon Report N°. 33893035 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.3.1.1/02	Fausser-Misslin, A.	2015	Folpet: Acute Oral and Contact Toxicity to Bumble Bee (<i>Bombus terrestris</i> L.) under Laboratory Conditions IES Report N°. 20140156 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.3.1.1/03	Amsel, K.	2015	Acute toxicity of Folpet 80 WG to the bumblebee <i>Bombus terrestris</i> L. under laboratory conditions BioChem agrar Report N°. 15 10 48 167 B GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.3.1.1/04	Schnurr, A.	2015	Acute toxicity of Folpet 80 WG to the solitary bee <i>Osmia bicornis</i> L. under laboratory conditions BioChem agrar Report N°. 15 10 48 114 B GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.3.1.2/01	Ansaloni, T.	2015	Chronic toxicity of FOLPET TECHNICAL on honeybees (<i>Apis mellifera</i> L.) Trialcamp Report N°. TRC14-246BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.3.1.3/01	Marín, M.	2022	Folpet Technical: Honey Bee (<i>Apis mellifera</i> L.) Larval Toxicity Test following Repeated Exposure under Laboratory Conditions Eurofins Report N°. S21-05947 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.3.2.1/01	Moll, M.	2007	Effects of Folpet 80 WG on the Predatory Mite <i>Typhlodromus pyri</i> in the laboratory – Dose response test Ibacon Report N°. 33895063 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.3.2.2/04	Moll, M.	2007	Effects of Folpet 80 WG on the Parasitoid <i>Aphidius rhopalosiphi</i> , extended laboratory study – Aged residue test Ibacon Report N°. 33899003 GLP	N	ASCENZA AGRO S.A. (formerly

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			Unpublished		Saptec Agro S.A.)
KCP 10.3.2.2/02	Moll, M.	2007	Effects of Folpet 80 WG on the Lacewing <i>Chrysoperla carnea</i> , extended laboratory study – Dose response test Ibacon Report N°. 33898047 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.3.2.2/03	Moll, M.	2007	Effects of Folpet 80 WG on the Ladybird Beetle <i>Coccinella septempunctata</i> , extended laboratory study – Dose response test Ibacon Report N°. 33897012 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.2.1/04	Grade, R., Wydra, V.	2007	Influence of Folpet technical to <i>Daphnia magna</i> in a reproduction test Ibacon Report N°. 33881221 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.4.1/01	Witte, B.	2009	Acute Toxicity (14 Days) of FOLPET 80 WG to the Earthworm <i>Eisenia fetida</i> in Artificial Soil with 5% Peat Ibacon Report N°. 51141021 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP 10.2.1/02	██████	2007	Acute toxicity of Folpet 80 WG to Rainbow Trout (<i>Oncorhynchus mykiss</i>) in a 96-hour semi static test ██████ N°. 33891230 GLP Unpublished	Y	ASCENZA AGRO S.A. (formerly Saptec Agro S.A.)
KCP	Grade, R., Wydra, V.	2007	Acute toxicity of Folpet 80 WG to <i>Daphnia magna</i> in a semi static 48-hour immobilization test	N	ASCENZA

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
10.2.1/03			Ibacon Report N°. 33892220 GLP Unpublished		AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.1/01	Schmitzer, S., Pavic, B.	2007	Effects of Folpet 80 WG (Acute Contact and Oral) on Honey Bees (<i>Apis mellifera</i> L.) in the laboratory Ibacon Report N°. 33893035 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.1/03	Amsel, K.	2015	Acute toxicity of Folpet 80 WG to the bumblebee <i>Bombus terrestris</i> L. under laboratory conditions BioChem agrar Report N°. 15 10 48 167 B GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.1/04	Schnurr, A.	2015	Acute toxicity of Folpet 80 WG to the solitary bee <i>Osmia bicornis</i> L. under laboratory conditions BioChem agrar Report N°. 15 10 48 114 B GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.1.3/01	Ansaloni, T.	2015	Toxicity of FOLPET TECHNICAL on honey bee larvae (<i>Apis mellifera</i> L.) after repeated exposure under laboratory conditions Trialcamp Report N°. TRC14-245BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.2/02	Moll, M.	2007	Effects of Folpet 80 WG on the Lacewing <i>Chrysoperla carnea</i> , extended laboratory study – Dose response test Ibacon Report N°. 33898047 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.2/03	Moll, M.	2007	Effects of Folpet 80 WG on the Ladybird Beetle <i>Coccinella septempunctata</i> , extended laboratory study – Dose response test Ibacon Report N°. 33897012 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.3.2.2/04	Moll, M.	2007	Effects of Folpet 80 WG on the Parasitoid <i>Aphidius rhopalosiphi</i> , extended laboratory study – Aged residue test Ibacon Report N°. 33899003 GLP	N	ASCENZA AGRO S.A. (formerly Sapec)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			Unpublished		Agro S.A.)
KCP 10.4.1.1/01	Ansaloni, T.	2014	A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80 WG to the earthworm <i>Eisenia foetida</i> (Oligochaeta: Lumbricidae) in artificial substrate at 2% peat content Trialcamp Report N°. TRC14-250BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.4.1.1/02	Ansaloni, T.	2014	A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80 WG to the earthworm <i>Eisenia foetida</i> (Oligochaeta: Lumbricidae) in artificial substrate at 5% peat content Trialcamp Report N°. TRC14-251BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.4.1.1/03	Ansaloni, T.	2014	A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80 WG to the earthworm <i>Eisenia foetida</i> (Oligochaeta: Lumbricidae) in artificial substrate at 10% peat content Trialcamp Report N°. TRC14-252BA GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.4.1.1/04	Lühns, U.	2007	Effects of Folpet 80 WG on Reproduction and Growth of Earthworms <i>Eisenia fetida</i> in Artificial Soil with 5% peat Ibacon Report N°. 33896022 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.4.1.1/05	Pavic, B.	2014	Effects of BCP324F on Reproduction and Growth of Earthworms <i>Eisenia fetida</i> in Artificial Soil with 5%Peat Ibacon Report N°. 84831022 GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.5/01	Gimeno, C.	2015	Effects of the formulated product Folpet 80 WG on activity of the soil microflora under laboratory conditions Trialcamp Report N°. TRC14-299SM GLP Unpublished	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)
KCP 10.2.1/06	Wendling, K.	2024 Interim report	Folpec 50 SC: Toxicity to the Water Flea <i>Daphnia magna</i> Straus under Laboratory Conditions (Acute Immobilisation Test – Flow-through) Eurofins Report N°. S23-104263 GLP	N	ASCENZA AGRO S.A. (formerly Sapec Agro S.A.)

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			Unpublished		

List of data relied on not submitted by the applicant but necessary for evaluation

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
No data.					

Appendix 2 Detailed evaluation of the new studies

A 2.1 KCP 10.1 Effects on birds and other terrestrial vertebrates

A 2.1.1 KCP 10.1.1 Effects on birds

A 2.1.1.1 KCP 10.1.1.1 Acute oral toxicity

A 2.1.1.2 KCP 10.1.1.2 Higher tier data on birds

A 2.1.2 KCP 10.1.2 Effects on terrestrial vertebrates other than birds

A 2.1.2.1 KCP 10.1.2.1 Acute oral toxicity to mammals

A 2.1.2.2 KCP 10.1.2.2 Higher tier data on mammals

A 2.1.3 KCP 10.1.3 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)

A 2.2 KCP 10.2 Effects on aquatic organisms

A 2.2.1 KCP 10.2.1 Acute toxicity to fish, aquatic invertebrates, or effects on aquatic algae and macrophytes

A 2.2.1.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 203 with no deviation.</p> <p>The test concentration of active substance was <u>verified in 24 h intervals</u> from fresh and aged test solutions. In the freshly prepared samples of the test 99% of the nominal test concentrations were found. In the aged test media, all samples were below the limit of detection. Nevertheless, all reported results are related to nominal concentrations of the test item. The endpoints were evaluated based on nominal concentrations of the test item.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>96 h LC₅₀ = 0.44 mg product Folpet 500 SC/ L for rainbow trout (<i>Oncorhynchus mykiss</i>) (based on nominal concentration)</p>
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Reference: KCP 10.2.1/01

Report Acute Toxicity of Folpet Sapec 500 SC to Rainbow Trout (*Oncorhynchus mykiss*) in a 96-hour Semi Static Test, Kley, A., Deierling, T., 2011, Report No. 63141230

Guideline(s): Yes, Commission Regulation (EC) No 440/2008 and the OECD No. 203, 1992

Deviations: No

GLP: Yes

Acceptability: Yes

Duplication (if vertebrate study) No

Objective

The purpose of this 96 hour study was to evaluate the acute toxicity of the test item Folpet Sapec 500 SC to fish. For this purpose, juvenile rainbow trout were exposed in a semi static test to aqueous test media containing the test item at various concentrations under defined conditions. The recorded effects were mortality and sublethal effects of the test fish.

The used method is recommended by the test guidelines, and also rainbow trout is one of the fish species recommended by the international test guidelines of the OECD and EC.

The purpose of the analytical part of this study was to verify the concentrations of the test item in the test medium.

Materials and methods

Test item:	Folpet Sapec 500 SC; batch no.: S – MRA; content of active ingredient: Folpet 500 g/L (analytical).
Test species:	Juvenile rainbow trout (<i>Oncorhynchus mykiss</i>) mean length: 4.59 cm \pm 0.27 cm; source: Forellenzuchtbetrieb Störk, 88348 Bad Saulgau, Germany
Test design:	This study encompassed 6 treatment groups (5 dose rates of the test item, control) each containing 7 individuals. The acute toxicity to unfed juvenile rainbow trout was determined in an aerated, static semi static, 96-hour test. The test fish were observed after approximately 2, 24, 48, 72 and 96 hours test duration for sublethal effects and mortality. Dead fish were removed at least once daily and discarded. At test start and at day 3 samples of the freshly prepared test media were taken. Furthermore, samples of the aged test media were taken after 24 hours of test duration and at test end. These samples were analysed via HPLC-method.
Endpoints:	NOEC after 96 h, LOEC after 96 h; LC50: lethal concentration producing 50% mortality after 96 h of exposure.
Test concentrations:	2.4, 1.1, 0.5, 0.23 and 0.10 mg test item/L and a control.
Test conditions:	Water temperature: 14 °C; pH value: 7.7 to 8.1; dissolved oxygen concentration: 90 to 101 % of the air saturation value; photoperiod: 16 h light – 8 h dark; light intensity: 530 to 990 lux and thus were within the ranges requested by guideline OECD 203.

Results and discussions

Biological test results:

In the control and the nominal test concentration of 0.10 mg test item/L all fish survived until the end of the experiment and no signs of intoxication were observed. At the nominal test concentration of 0.23 mg test item/L no mortality was observed but all fish showed sublethal effects like extended gills and strong ventilation and the fish were mainly swimming at the water surface after 2 hours of exposure. After 24 hours of exposure until the end of the test no sublethal effects were observed at nominal 0.23 mg test item/L anymore. At nominal 0.5 mg test item/L all fish showed sublethal effects like extended gills and strong ventilation and the fish were mainly swimming at the water surface after 2 hours of exposure as well. After 24 hours two fish were mainly located at the bottom of the aquarium at nominal 0.5 mg/L and mucous secretion was observed. After 48 hours of test duration one fish was dead at nominal 0.5 mg test item/L and the remaining six fish showed strong ventilation and mucous secretion and were located mainly at the bottom of the aquarium. After 72 hours six fish were dead at nominal 0.5 mg test item/L and until the end of the test no further mortality or sublethal effects were observed. At the nominal test concentration of 1.1 and 2.4 mg test item/L all fish displayed hyperventilation and extended gills shortly after introducing in the test aquaria. After 2 hours additionally tumbling during swimming was observed at nominal 1.1 mg test item/L and the fish were swimming mainly at the bottom of the aquarium. At nominal 2.4 mg test item/L all fish were located at the bottom of the aquarium and at the water surface, respectively. After 24 hours of exposure all fish were dead at the nominal test concentrations of 1.1 and 2.4 mg test item/L.

All biological results are listed in the table below.

Table 1. Observed mortality of unfed rainbow trout (*Oncorhynchus mykiss*) exposed to Folpet Sapec 500 SC for 96 hours in a semi static test

Nominal concentration [mg/L]	Mortality					
	Exposure Time [h]					
	0	2	24	48	72	96
	#mort	#mort	#mort	#mort	#mort	#mort
Control	0	0	0	0	0	0
0.10	0	0	0	0	0	0
0.23	0	0	0	0	0	0
0.5	0	0	0	1	6	6
1.1	0	0	7	7	7	7
2.4	0	0	7	7	7	7
LC50 [mg/L]	n.d.	n.d.	0.73	0.57	0.44	0.44
95 % C.I.	n.d.	n.d.	0.58 – 0.92	n.d.	n.d.	n.d.

#mort: number of dead fish

n.d. = not determinable

C.I.: Confidence intervals

Values refer to nominal test concentrations

Analytical results:

The quantification of the test item Folpet Sapec 500 SC was performed using liquid chromatography (HPLC-method).

In the freshly prepared samples of the test 99% of the nominal test concentrations were found. In the aged test media all samples were below the limit of detection. Nevertheless, all reported results are related to nominal concentrations of the test item.

Conclusion

Based on the test results the 96-hour LC50 of Folpet Sapec 500 SC for rainbow trout (*Oncorhynchus mykiss*) was determined to be 0.44 mg test item/L based on the nominal test concentrations. The LC0 was determined to be 0.23 mg test item/L and the LC100 was determined to be 1.1 mg test item/L both values also based on nominal test concentrations.

Validity criteria

Control:	In the control no fish died until the end of the test.
Dissolved Oxygen Concentration:	The dissolved oxygen concentration in the test media did not fall below 90 % of air saturation value during the test.

A 2.2.1.2 Study 2

Comments of zRMS:	<p>The study was conducted in line with OECD 203 (1992) with one deviation. According to the study plan , if analysis directly after sampling is not possible, the samples will be stored in a freezer (≤ - 10°) immediately after sampling... and will be kept stored until analysis concerned on analysis of item concentrations: In the current study , the samples collected at the start of the test were prepared for analysis directly but measured after one day storage at room temperature.</p> <p>These deviations are considered to have no impact on the outcome of the study as all the validity criteria were met.</p> <p>The test concentration of active substance was verified in 24 h intervals from fresh and aged test solutions.</p> <p>The endpoints were evaluated based on nominal concentrations of the test item.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment: 96 h LC₅₀ = 0.176 mg product Folpet 80 WG/L for rainbow trout (<i>Oncorhynchus mykiss</i>) (based on nominal concentration)</p> <p>The study is not considered in the risk assessment.</p>
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Reference:	KCP 10.2.1/02
Report	Acute Toxicity of Folpet 80 WG to Rainbow Trout (<i>Oncorhynchus mykiss</i>) in a 96-hour Semi Static Test, Grade, R., Wydra, V., 2007, Report No. 33891230
Guideline(s):	Yes, Directive 92/69/EEC, C.1, 1992 and the OECD No. 203, 1992
Deviations:	None from guideline, one from study plan with no presumed effect on the study.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	No

Objective

The purpose of this study was to evaluate the acute toxicity of the test item Folpet 80 WG to fish. For this purpose, juvenile Rainbow trout were exposed in a semi static test to aqueous test media containing the test item at various concentrations under defined conditions. The recorded effects were mortality and symptoms of intoxication of the test fish. A dose-response test was performed to establish an LC50 value.

The used method is recommended by the test guidelines, and also Rainbow trout is one of the fish species recommended by the international test guidelines.

The purpose of the analytical part of this study was to verify the concentration of the active ingredient of this test item in the test medium.

Materials and methods

Water hardness: 2.5 mmol/L (=250.0 mg/L) as CaCO₃

Test concentrations: 0.031, 0.063, 0.125, 0.25 and 0.5 mg test item/L, and a control.

Results and discussions

Biological results: In the control and at the nominal test concentrations up to and including nominal 0.063 mg test item/L all fish survived until the end of the test.
96-hour LC50: 0.176 mg test item/L
95 % Confidence Intervals: n.d.
96-hour LC0: 0.063 mg test item/L
96-hour LC100: 0.50 mg test item/L
96-hour NOEC: 0.063 mg test item/L
96-hour LOEC: 0.125 mg test item/L
n.d. – not determined by statistic program (ToxRat Professional)

Analytical method:

The quantification of the test item was performed using liquid chromatography (HPLC-method with UV detection).

Analytical results:

Table. Summary of Analytical Results

Sample description [mg/L]	% of nominal ¹	RSD [%]	n
Control	n.a.	n.a.	4
0.031	117	6	4
0.063	105	7	4
0.125	106	3	4
0.25	104	5	4
0.5	101	2	2

¹mean value of the freshly prepared samples per treatment group

RSD relative standard deviation per treatment group

N number of analyzed samples

n.a. not applicable

Conclusion

The acute toxicity of Folpet 80 WG to Rainbow trout (*Oncorhynchus mykiss*) was assessed in a semi-static

dose-response test. The 96-hour LC₅₀ value was determined to be 0.176 mg test item/L.

Validity criteria

Control:	In the control no fish died until the end of the test.
Dissolved Oxygen Concentration:	The dissolved oxygen concentration in the test media did not fall below 60 % of air saturation value during the test.

A 2.2.1.3 Study 3

Comments of zRMS:	<p>The study was conducted in line with OECD 203 (2004) with no deviation.</p> <p>The test concentration of active substance was verified in 24 h intervals from fresh and aged test solutions.</p> <p>At the start of the test just before introduction of the <i>Daphnia</i>, average 106 % of the nominal test concentrations were found. In the aged test media after 24 hours test duration the concentrations were below the Limit of Quantification.</p> <p>The endpoints were evaluated based on nominal concentrations of the test item.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>48 h EC₅₀ = 0.67 mg Folpet 80 WG /L for <i>Daphnia magna</i></p> <p>The study is not considered in the risk assessment.</p>
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Reference:	KCP 10.2.1/03
Report	Acute Toxicity of Folpet 80 WG to <i>Daphnia magna</i> in a Semi Static 48-hour Immobilization Test, Grade, R., Wydra, V., 2007, Report No. 33892220
Guideline(s):	Yes, Commission Directive 92/69/EEC, C.2, 1992 and the OECD Guideline 202, adopted April 2004
Deviations:	No
GLP:	Yes
Acceptability:	Ye
Duplication (if vertebrate study)	N/A

Objective

The purpose of this study was to evaluate the influence of the test item Folpet 80 WG on the immobilisation of *Daphnia magna*. Young *Daphnia* (<24 hours old) were exposed in a semi static test to the test item for 48 hours, added to culture medium at a range of concentrations.

The test method of application and the test species *Daphnia magna* are recommended by the test guidelines. The purpose of the analytical part of this study was to verify the concentrations of the active ingredient of the test item in the test medium.

Materials and methods

Test concentrations:	0.0625, 0.125, 0.25, 0.50, 1.0 and 2.0 mg test item/L and a control.
Analytical method:	The quantification of the active ingredient of the test item was performed using liquid chromatography (HPLC-method) with UV detector.

Results and discussions

Biological results:	In the control and at the nominal test concentrations up to and including nominal 0.125 mg test item/L no daphnia were immobilized until the end of the test.
24-hour EC50:	1.88 mg test item/L
95% confidence values:	1.11 – 3.18 mg test item/L
24-hour EC0:	1.0 mg test item/L

24-hour EC100:	>2.0 mg test item/L
24-hour NOEC:	1.0 mg test item/L
24-hour LOEC:	2.0 mg test item/L
48-hour EC50:	0.67 mg test item/L
95% confidence values:	0.49 to 0.92 mg test item/L
48-hour EC0:	0.125 mg test item/L
48-hour EC100:	>2.0 mg test item/L
48-hour NOEC:	0.125 mg test item/L
48-hour LOEC:	0.25 mg test item/L

Analytical results:

Table. Summary of Analytical Results			
Sample description [mg/L]	% of nominal ¹	RSD [%]	N
Control	n.a.	n.a.	4
0.0625	103	17	4
0.125	117	11	4
0.25	111	19	4
0.5	106	6	4
1	106	2	4
2	91	20	4

¹Mean value of the freshly prepared samples per treatment group

RSD relative standard deviation per treatment group

N number of analysed samples

n.a. not applicable

At the start of the test just before introduction of the *Daphnia*, average 106 % of the nominal test concentrations were found. In the aged test media after 24 hours test duration the concentrations were below the Limit of Quantification.

All reported results are related to nominal concentrations of the test item.

Conclusion

The toxic effect of the test item Folpet 80 WG to *Daphnia magna* was assessed in a semi static dose-response test. The 48-hour EC50 value was 0.67 mg test item/L.

Validity criteria

Control immobilization rate:	%; Furthermore: 0.0% of the <i>Daphnia</i> showed signs of disease or stress; Validity criterion was met.
Dissolved oxygen concentration:	≥8.6 mg O ₂ /L in the control and test vessels at the end of the test; Validity criterion was met.

A 2.2.1.4 Study 4

Comments of zRMS:	The following study is with the technical active substance and therefore will not be evaluated by the zRMS-PL.
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Reference:	KCP 10.2.1/04
Report	Influence of Folpet technical to <i>Daphnia magna</i> in a Reproduction Test, Grade, R., Wydra, V., 2007, Report No. 33881221
Guideline(s):	Yes, Commission Directive 2001/59/EC, C.20, 2001 and OECD guideline 211, adopted September 1998
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The toxic effects of the test item Folpet technical on the survival and reproduction rate of *Daphnia magna* were determined during an exposure period of 21 days. Young *Daphnia* were exposed in a semi-static test to aqueous test media containing the test item at various concentrations. The mortality rate, the reproduction rate and symptoms of intoxication were compared with corresponding parameters in the control. The test method of application and the test species *Daphnia magna* are recommended by the test guidelines. The purpose of the analytical part of this study was to verify the concentrations of the test item in the test medium.

Materials and methods

Test concentrations:	0.032, 0.10, 0.32, 1.0 and 3.2 mg test item/L, a control and a solvent control (DMF).
Analytical method:	The quantification of the test item was performed using liquid chromatography (HPLC-method with UV-detection).

Results and discussions

Biological results:	21-days EC50 (Mortality):	1.2 mg test item/L
	21-days EC50 (Reproduction):	0.85 mg test item/L
	21-days NOEC (Reproduction rate):	0.32 mg test item/L
	21-days LOEC (Reproduction rate):	1.0 mg test item/L
	21-days NOEC (Survival of adults):	1.0 mg test item/L
	21-days LOEC (Survival of adults):	3.2 mg test item/L

According to the results of a Bonferroni-Welch-t test in comparison to the solvent control (one-sided, $\alpha = 0.05$) no significant toxic effect of the test item on the mean reproduction rate was determined up to and including the nominal test concentration of 0.32 mg test item/L.

Signs of intoxication:	No particular signs of intoxication were observed in the test animals during the test up to concentrations of 1.0 mg test item/L (statistical NOEC for the survival of adults). At the highest test concentration of 3.2 mg test item/L (LOEC for the survival of adults) all test animals died.
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Analytical results:

Table. Summary of Analytical results		
Sample description [mg/L]	% of nominal ¹	N
Control	n.a.	6
Solvent control	n.a.	6
0.032	121	6
0.10	115	6
0.32	94	6
1.0	96	6

3.2	96	2
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¹mean value of all measured samples of freshly prepared test medium per treatment group

n.a. not applicable

n number of samples analysed

The mean recovery rate in the freshly prepared test concentrations was 106% (average for all concentration). In the aged test media the measured concentrations were below the Limit of Detection, except for the 48 old test media samples of day two of concentration level 1 and 3.2 mg test item/L. The concentrations in the 1 mg test item/L samples were below the Limit of Quantification and in the 3.2 mg test item/L samples parent folpet was found with 4 % of the nominal values. Under the test conditions the test item was not stable during the test medium renewal periods of 48 and 72 hours. All reported results are related to nominal concentrations of the test item.

Conclusion

Taking into account the survival rates and the reproduction rates of the test animals, the highest concentration of Folpet technical tested without toxic effects after the exposure period of 21 days was 0.32 mg test item/L (21-days overall NOEC). The lowest concentration tested with adverse effects (21-days overall LOEC) was determined to be 1.0 mg test item/L.

Validity criteria

Survival rate of adult *Daphnia* in the control: 100%; validity criterion was met.

Mean number of alive offspring in the control after 21 days: 136 per surviving adult *Daphnia*; validity criterion was met.

A 2.2.1.5 Study 5

Comments of zRMS:	<p>The study was conducted in line with OECD 202 (2004) with minor deviations such as:</p> <ul style="list-style-type: none"> ○ The hardness of the test medium at the beginning of the definitive test was 17°dH. Instead of between 7.8 and 14°dH), ○ The reference test was performed one week earlier than the definitive test. ○ During the test, the room temperature fluctuated between 18,3 and 22,5 °C. ○ Before running the one-way ANOVA test to analyse definitive test data, the assumptions of normal distribution of data and the homogeneity of variances between treatments were checked by Shapiro-Wilk test and a Bartlett test, respectively. <p>These deviations are considered to have no impact on the outcome of the study as all the validity criteria were met.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>48 h EC₅₀ = 0.65 mg a.s./L for <i>Daphnia magna</i> (nominal concentration)</p> <p>The endpoint values estimated considering the concentrations of the test item measured in chemical analyses were lower than the endpoints considering the nominal concentrations, most probably due to the high degradability of the test item (DT50 = 0.02 days). The time period between the preparation of the test treatments and the beginning of the test/samplings (at 0h) varied between treatments from 39 to 86 minutes, which was enough time to partially degrade the test item.</p> <p>48 h EC₅₀ = 0.14 mg a.s./L for <i>Daphnia magna</i> (measured concentration)</p>
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Reference:	KCP 10.2.1/05
Report	Toxicity of SAP50SCF to the Water Flea <i>Daphnia magna</i> under Laboratory Conditions (48h Acute Immobilisation Test with Semi-static design), Alves, D., 2023, Report No. CLOVER-A-01-2023
Guideline(s):	Yes, OECD test guideline 202 (2004)
Deviations:	<p>Yes,</p> <p>The hardness of the test medium at the beginning of the definitive test was 17°dH. Although this value is out of the recommended interval in the study plan (between 7.8 and 14°dH), hardness medium is not a validity criteria for the test. Moreover, since the test medium was similar (i.e. the same batch) to that used for the organisms acclimatization and given the known non-significant influence of hardness medium in the survival of <i>Daphnia magna</i>, no relevant influence was expected from this parameter on the outcome of the study.</p> <p>The reference test was performed one week earlier than the definitive test. It is considered that, even though it was carried out a week earlier than expected, the sensitivity of the daphnids is the same between the two tests as the same batch of daphnia was used.</p> <p>During the test, the room temperature fluctuated between 18,3 and 22,5 °C. The room temperature was higher than 22,0°C only for 42 minutes in total. However, these 42 minutes were not continuous and, therefore, it was assumed that the short periods with temperature higher than 20,0°C did not influenced the outcome of the study.</p> <p>Before running the one-way ANOVA test to analyse definitive test data, the assumptions of normal distribution of data and the homogeneity of variances between treatments were checked by Shapiro-Wilk test and a Bartlett test, respectively. Since these assumptions were not fulfilled (data were not normally distributed and variances of treatments were heterogeneous even after transforming the data), a one-way ANOVA followed by a post-hoc Dunnett test could not be used and a Kruskal-Wallis test followed by a Dunn test with Bonferroni correction was used instead, for NOEC and LOEC estimation.</p>
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

- 1.To determine the immobilisation effect of SAP50SCF on the water flea *Daphnia magna*
- 2.To determine the no observed effect concentration (NOEC)
- 3.To determine the effect median concentration (EC50)

Materials and methods

Test item	SAP50SCF
Batch number	23D0018A
Density analysed	1.22 g/ ml
Expiry date	April 2025
Content of a.i. analysed	511g/L
Species/Variety	<i>Daphnia magna</i> Straus (Cladocera: Daphniidae)
Life stage at start of exposure	Less than 24 hours old

Source	<p>The organisms that were used in the tests came from traceable batches of dormant eggs (ephippia) of the <i>Daphnia magna</i> crustaceans, supplied by Microbiotests Inc. established as a spin-off in Kleimoer 15, 9030 Gent, Belgium, through the Portuguese representative company Ambifirst, Unip. Lda.</p> <p>These eggs are protected by a chitinous capsule called ephippium and can be stored for long periods of time without losing viability. When ephippians are placed under specific environmental conditions, eggs develop in about 3 days into hatchlings that can be used immediately for toxicity testing.</p>
Test design	<p>The batch number of used ephippia was DM220323</p> <p>Dose response test (2 range finder semi-static tests with different pH of test medium), 1 definitive semi-static test and 1 reference test</p>
Renewal of test solution(s)	Every 24 hours (semi-static test)
Duration of exposure phase	48 hours
Number of treatment groups	1 control group and 5 treatment concentrations
Test medium	<p>ISO test water according to annex 3 of the OECD guideline (Test No. 202: <i>Daphnia</i> sp. Acute Immobilisation Test).</p> <p>Four solutions were prepared. A solution of calcium chloride with 11,76g/L concentration, a magnesium sulphate solution with 4,93g/L concentration, a sodium bicarbonate with 2,59 g/L and a potassium chloride with 0.23 g/L.</p> <p>To prepare ISO water, 50ml of each solution were added in a 2000ml volumetric flask. Distilled water was added up to the 2000mL mark.</p>
pH	7,66 – 7,77
Oxygen saturation	125-128 % saturation.
Total hardness	17°dH
Temperature	18.3-22.5°C
Oxygen concentration	10.74-11.13 mg/L
Exposure to light	16 h light, 8 h dark
Feeding	None
Specific documentation	Test conditions were recorded using appropriate equipment
Test concentrations:	Definitive test (0, 0.10, 0.17, 0.31, 0.56, 1.00 mg a.i./L)
Mode of assessment	Immobilised daphnids were counted. All daphnids not able to swim after gentle agitation of the test vessel were considered to be immobile.
Statistics	<p>The following parameters were determined:</p> <p>NOEC The highest test item concentration causing no immobility to daphnids was calculated after evaluating the normality of data distribution with a Shapiro-Wilk test, and the homogeneity of variances with a Bartlett test. The assumptions of normality of data distribution and homogeneity of variances were not fulfilled (even after transforming the data), a one-way ANOVA could not be carried out.</p> <p>A Kruskal-Wallis test followed by a Dunn test with Bonferroni correction was performed with RStudio (v 2023.06.2) interface software with R (v 4.1.3) (package ‘dunn.test’ v 1.3.5).</p> <p>EC50 The test item concentration causing 50 % effect in the respective parameter of the test organism population was estimated by Probit analysis with the PriProbit software (v 1.63).</p> <p>NOEC and LOEC: The highest test item concentration to which no significant effect was observed (NOEC) and the</p>

lowest test item concentrations to which a significant effect was observed (LOEC) were estimated after evaluating the normality of data distribution with a Shapiro-Wilk test, and the homogeneity of variances with a Bartlett test. Since the assumptions of normality of data distribution and homogeneity of variances were not fulfilled, a one-way ANOVA could not be carried out.

A Kruskal-Wallis non-parametric test followed by a Dunn test with Bonferroni correction was performed using RStudio (v 2023.06.2) interface software with R v4.1.3 (package 'dunn.test' v 1.3.5).

EC₁₀ and EC₅₀: Concentration of the test item causing 10% and 50% effect, respectively, compared to control, in the respective parameter of the test organism population was estimated by Probit analysis with the PriProbit software (v 1.63).

Endpoints Estimation: NOEC, LOEC, EC₁₀ and EC₅₀ values were first estimated based on nominal concentrations. After chemical analysis, NOEC, LOEC, EC₅₀ and EC₁₀ values were estimated based on measured concentrations (considering mean concentrations measured in A1 0h samples for 24h estimations [n=3] and in A1 0h and A2 0h samples for 48h estimations [n=6]).

Results and discussions

The estimated NOEC, LOEC, EC₅₀ values for the active ingredient of the test item (and its limits) are presented in the table below.

	24h	48h
EC ₁₀	0.22 (0, -0.32) mg a.i./L (95% confidence level)	0.15 (0.09-0.19) mg a.i./L (95% confidence level)
EC ₅₀	0.86 (0.61-1.68) mg a.i./L (95% confidence level)	0.34 (0.28-0.43) mg a.i./L (95% confidence level)
NOEC	C3 (0.31mg a.i./L)	C3 (0.31mg a.i./L)
LOEC	C4 (0.56mg a.i./L)	C4 (0.56mg a.i./L)

NOEC, LOEC, EC₁₀ and EC₅₀ values (and the corresponding 95% confidence intervals) estimated considering the actual concentrations of the test item measured in chemical analyses are presented in the table below.

	24h	48h
NOEC	C3 (0.15 mg a.i./L)	C3 (0.14 mg a.i./L)
LOEC	C4 (0.25 mg a.i./L)	C4 (0.23 mg a.i./L)
EC ₁₀	0.095 (0.04-0.14) mg a.i./L	0.056 (0.03-0.08) mg a.i./L
EC ₅₀	0.38 (0.26-0.78) mg a.i./L	0.14 (0.11-0.18) mg a.i./L

Reference test results:

The estimated EC₅₀ values for the active ingredient of the reference test item is presented in the table below.

	24h	48h
EC ₅₀	0.91 (0.71-1.14) mg a.i./L	0.65 (0.54-0.78) mg a.i./L

Conclusion:

The no-observed-effect concentration (NOEC) of the test item is 0.31 mg a.i./L after 24 and 48h of application.

The effect median concentration (EC₅₀) of the test item is 0.86 (0.61-1.68) mg a.i./L after 24h of application, and after 48h the value decrease to 0.34 (0.28-0.43) mg a.i./L.

In the reference test, the concentration of potassium dichromate for a 50% of effect comparing to the control treatment (EC₅₀) at 24h is 0.91 (0.71-1.14) mg a.i./L and 0.65 (0.54-0.78) mg a.i./L after 48h of exposure.

This value is covered by the EC50 1.00 mg/L after 24h and 0.68 mg/L after 48h reported in the specification sheet of the batch of used daphnids.

NOEC and LOEC of the test item estimated considering the nominal concentrations were 0.31 and 0.56 mg a.i./L, respectively, for 24h and 48h of exposure.

EC10 and EC50 values based on nominal concentrations were 0.22 (0.11-0.32) and 0.86 (0.61-1.68) mg a.i./L after 24h of exposure, decreasing to 0.15 (0.09-0.19) and 0.34 (0.28-0.43) mg a.i./L after 48h, respectively.

Considering concentrations of the test item measured in the chemical analyses, the LOEC and NOEC values were 0.25 and 0.15 mg a.i./L, respectively, for 24h and, for 48h of exposure, the LOEC and NOEC values were 0.23 and 0.14 mg a.i./L, respectively.

EC10 and EC50 values, considering concentrations of the test item, were 0.095 (0.04-0.14) and 0.38 (0.26-0.78) mg a.i./L respectively, after 24h of exposure, decreasing to 0.056 (0.03-0.08) and 0.14 (0.11-0.18) mg a.i./L after 48h.

The endpoint values estimated considering the concentrations of the test item measured in chemical analyses were lower than the endpoints considering the nominal concentrations, most probably due to the high degradability of the test item (DT50 = 0.02 days). The time period between the preparation of the test treatments and the beginning of the test/samplings (at 0h) varied between treatments from 39 to 86 minutes, which was enough time to partially degrade the test item. Therefore, the endpoints based on chemical measurements can be seen as a worst-case scenario.

Validity criteria

The definitive test and reference test fulfilled the validity criteria of the study.

Control immobilisation	The percentage of immobilisation was ≤ 10 % in the control treatments (actual 0%).
Oxygen concentration	The dissolved oxygen concentration at the end of the test was ≥ 3 mg/L in all test units (actual 10.74-11.13 mg/L).

Study 6

Comments of zRMS:	The study is not evaluated by zRMS at this stage of evaluation due to the analytical report is still ongoing. Therefore, the endpoints could be not confirmed yet.
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Reference:	KCP 10.2.1/06
Report	Folpec 50 SC: Toxicity to the Water Flea Daphnia magna Straus under Laboratory Conditions (Acute Immobilisation Test – Flow-through, Wendling, K., 2024, Report No. S23-104263
Guideline(s):	Yes, OECD 202 (2004): OECD Guidelines for Testing of Chemicals No. 202. Daphnia sp., Acute Immobilisation Test. Adopted: 13 April 2004.
Deviations:	No
GLP:	Yes (study conducted under GLP, interim report non-GLP)
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

EC₅₀ at the end of the test period where possible

Materials and methods

Test item

Test item Folpec 50 SC
Batch number 23D0018A
Active ingredient Folpet

Test system

Test organism (species) *Daphnia magna* Straus, Clone V
Life stage at start of exposure Max. 24 hours old
Source The animals are continuously bred in the laboratory and were originally purchased in a healthy condition from the Federal Environment Agency in Berlin/Germany

Test design

Test design Dose-response test in flow through design. Flow rates were equivalent to at least 18 test chamber volumes per 24 hours
Duration of exposure phase 48 hours
Number of treatment groups 1 control group: Negative control (C)
5 test item groups (T1 to T5)
Replicates per treatment group 4
Test organisms per replicate 5

Test conditions

Temperature 20.2-20.6°C
pH 6.54-6.83
Oxygen saturation ≥ 8.98 mg/L
Light regime 16 hours photoperiod / 8 hours darkness daily

Application

Application mode Flow-through with diluting system
Treatment groups C: 0 µg/L
T1 to T5: 25.6, 56.3, 124, 273 and 600 µg/L (nominal)

Assessment

Immobilisation Immobilised daphnids were counted after 24 and 48 hours of exposure

Analytical verification

Samples analysed Analytical samples of all test item concentrations and control taken at test start, after 24 hours and after 48 hours will be analysed.

Statistics

Immobilisation The EC50 after 48 h of exposure could not be determined since the immobilisation was below 50% up to the highest concentration of 600 µg/L (nominal).

Dates of experimental work 13 Dec 2023 – Analytical Phase still ongoing

Results and discussions

Analytical: The analysis of samples is still ongoing and will be reported in the final report.

Biological

Summary of results for immobilisation of <i>Daphnia magna</i> after 24 and 48 h of exposure					
Nominal concentration [µg/L]	Total number of daphnids introduced	Total no. of immobile daphnids	Total Immobilisation [%]	Total no. of immobile daphnids	Total Immobilisation [%]
		24 h		48 h	
0 (C)	20	0	0	1	5
25.6	20	0	0	2	10
56.3	20	0	0	2	10
124	20	0	0	0	0
273	20	0	0	2	10
600	20	2	10	6	30

C: control

Abnormal behaviour or appearance:

Test organisms showed no behavioural abnormalities or abnormalities in appearance or pathological symptoms in the control group. 48 hours after exposure one daphnid stuck at the water surface in the test item treatment group of 25.6 µg/L and two in the test item treatment group of 273 µg/L.

Conclusion

The study is valid since all required criteria were met.

The EC₅₀ after 48 h of exposure could not be determined since the immobilisation was below 50% up to the highest concentration of 600 µg/L (nominal).

Validity criteria

The study is valid since the required criteria were met.

Parameters	Required	Actual
Control immobilisation [%]	≤10	5
Oxygen concentration at the end of the test [mg/L]	≥3 in all test units	≥8.98

A 2.2.2 KCP 10.2.2 Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms

A 2.2.3 KCP 10.2.3 Further testing on aquatic organisms

A 2.3 KCP 10.3 Effects on arthropods

A 2.3.1 KCP 10.3.1 Effects on bees

A 2.3.1.1 KCP 10.3.1.1 Acute toxicity to bees

A 2.3.1.1.1 Study 1

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal of the a.s.-folpet: Based on the evaluation, the acute oral and contact toxicity test is considered valid.</p> <p>48 h LD₅₀ > 100 µg a.s./bee (acute contact toxicity) 48 h LD₅₀ > 104.8 µg a.s./bee (acute oral toxicity)</p> <p>The zRMS-PL agrees with the evaluation and the derived endpoints for Folpet 80 WG formulation but it is not considered at the current risk assessment for Folpet 500 SC. It is additional information.</p>
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Reference: KCP 10.3.1.1/01

Report Effects of Folpet 80 WG (Acute Contact and Oral) on Honey Bees (*Apis mellifera* L.) in the laboratory, Schmitzer, S., Pavic, B., 2007, Report No. 33893035

Guideline(s): Yes, OECD 213 and 214 (1998)

Deviations: No

GLP: Yes

Acceptability: Yes

Duplication N/A
(if vertebrate study)

Objective

Honey bees (*A. mellifera*) can be affected by pesticide residues as a result of indirect contact on plant surfaces, via oral intake of contaminated food or water, via inhalation of vapour or by direct overspray in the course of an application in the field according to normal agriculture practice. If the proposed use pattern of Folpet 80 WG indicated such a possible exposure of honey bees, acute contact and oral toxicity data is necessary for the registration of the pesticide use in question. This study provides:

- The acute toxicity levels of the test item to honey bees;
- Toxicity information comparable to expected residues from standard rates, for assessment of the potential hazard to honey bees;
- Information to support precautionary label statements;
- Information to indicate the need for further testing e.g. semi-field or field studies.

Materials and methods

Test Item: Folept 80 WG, Batch No.: M-BOA, a.i. content 80.0 % (nominal), 81.5 % w/w (analysed) according to certificate of analysis

Test Species: Honey bee (*Apis mellifera* L.); female worker bees; obtained from a healthy and queen-right colony, bred by IBACON, collected on the morning of use.

Test Design: Limit test; acute oral and contact toxicity test; duration 48 h; 5 replicates, each consisting of 10 bees in one cage per test concentration; assessment of mortality after 4, 24 and 48 hours; reference item: Dimethoate 400 g/L (nominal).

Test Concentrations*: Contact test: 100.0 µg a.i./bee
Oral test: 104.8 µg a.i./bee

*in the following, e.g. 100.0 µg a.i./bee as Folpet 80 WG will be mentioned as 100.0 µg a.i./bee since throughout the report the test concentrations are expressed in µg active ingredient pre bee

Test Conditions: Temperature: 25 °C; relative humidity: 26 % - 46 %; photoperiod: 24 h darkness

Results and discussions

At the end of the contact toxicity test (48 hours after application), there was 0.0 % mortality at 100.0 µg a.i./bee. No mortality occurred in the control (water + 0.5 % Adhäsit).

In the oral toxicity test the maximum nominal test level of Folpet 80 WG (100 µg a.i./bee) correspond to an actual intake of 104.8 µg a.i./bee. After 48 hours this dose level led to a mortality of 2.0 %. A mortality of 2.0 % occurred as well in the control (50 % sugar solution).

No test item induced behavioural effects were observed at any time.

Table. Toxicity of Folpet 80 WG to honey bees (*Apis mellifera* L.) in contact and oral toxicity (limit test)

	Contact Test [48 h]	Oral Test [48 h]
LD50	>100.0 µg a.i./bee	>104.8 µg a.i./bee

The contact and oral LD50 (24 h) values of the reference item (dimethoate) were calculated to be 0.30 and 0.14 µg a.i./bee, respectively.

Conclusion

The toxicity of Folpet 80 WG was tested in both an acute contact and an oral toxicity test on honey bees. The LD50 (48 h) was > 100.0 µg a.i./bee in the contact toxicity test. The LD50 (48 h) was > 104.8 µg a.i./bee in the oral toxicity test.

Validity criteria

Control Mortality:	Contact Test CO2/water control: 0.0% Oral Test Water/sugar control: 2.0%
LD50 of Reference Item (24 hrs):	Contact Test: 0.30 µg a.i./bee Oral Test: 0.14 µg a.i./bee
Validity of the tests:	The contact and oral test are considered valid as the control mortality in each case was < 10% and the LD50 values obtained with the reference item (dimethoate), were within the required ranges.

A 2.3.1.1.2 Study 2

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal of a.s.- folpet: Based on the evaluation, the bumble bee acute oral and contact toxicity test is considered valid.</p> <p>96 h LD₅₀ > 100 µg a.s./bumble bee (acute oral and contact toxicity)</p> <p>The RMS - PL agrees with the evaluation and the derived endpoints for the a.s-folpet.</p>
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Reference:	KCP 10.3.1.1/02
Report	Folpet: Acute Oral and Contact Toxicity to Bumble Bee (<i>Bombus terrestris</i> L.) under Laboratory Conditions, Fauser-Misslin, A., 2015, Report No. 201401569.
Guideline(s):	<p>Yes, no official test guideline is currently available for side-effects testing of Plant Protection Products on bumblebees under laboratory conditions. Therefore, the study will be conducted according to presently valid honeybee guidelines and based on appropriate scientific literature on the topic of concern:</p> <ul style="list-style-type: none"> • OECD. 1998. Test no. 213: honey bees, acute oral toxicity. In OECD Guidelines for testing of chemical section 2: effects on biotic systems. OECD publishing. • OECD. 1998. Test no. 214: honey bees, acute contact toxicity. In OECD Guidelines for testing of chemical section 2: effects on biotic systems. OECD publishing. • Van der Steen, JM. 2001. Review of the methods to determine hazards and toxicity of pesticides to bumblebees (<i>Bombus terrestris</i> L.). Apidologie, 32: 399-406. • AFPP. 2012. CEB Method no. 230: Méthode d'évaluation des effets des préparations phytopharmaceutiques sur l'abeille domestique <i>Apis mellifera</i> L. AFPP publishing. • EFSA. 2013. Guidance on the risk assessment of plant protection products on bees (<i>Apis mellifera</i>, <i>Bombus</i> spp. and solitary bees)
Deviations:	None to the guideline, three to the study plan with no impact on the integrity and quality of the study.
GLP:	Yes
Acceptability:	Yes

Duplication N/A
(if vertebrate study)

Objective

The purpose of the study was to determine the acute oral and contact toxicity of Folpet to bumble bees, *Bombus terrestris* L., under laboratory conditions.

Mortality and sublethal effects of the bumble bees were assessed.

The LD50, NOED and LOED values were calculated.

Materials and methods

Test item:	Folpet technical
Content of a.i.(analysed):	978.2 g/kg
Test species:	Worker bumble bees (<i>Bombus terrestris</i>).
Test units oral test:	Plastic vials (for the feeding period) and then well-ventilated plastic boxes (10 × 9 × 5 cm) during the rest of the study.
Test unit contact test:	Well-ventilated plastic boxes (10 × 9 × 5 cm).
Test system:	Adult worker bumble bees.
Oral treatments:	Four treatments: a control, a solvent control, one test item and a reference item treatment.
Contact treatments:	Four treatments: a control, a solvent control, one test item and a reference item treatment.
Limit Test oral dose:	The target dose was 100 µg a.i./bee. The final dose tested was 100 µg a.i./bee.
Limit Test contact dose:	The target dose was 100 µg a.i./bee. The final dose tested was 100 µg a.i./bee.
Reference item oral dose:	The target dose was 10 µg dimethoate/bee. The final dose tested was 10 µg dimethoate/bee.
Reference item contact dose:	The target dose was 10 µg dimethoate/bee. The final dose tested was 10 µg dimethoate/bee.
Replicates:	Three replicate units, each consisting of 10 worker bees, were set up for control, solvent control and reference item. Six replicate units, each consisting of 10 worker bees, were set up for the test item.
Observations:	Mortality and abnormalities were determined after 4, 24, 48, 72 and 96 hours.
Test conditions:	Mean temperature: 25.3 °C (range 24.5 – 25.9 °C); mean relative humidity: 60.2 % (range 51.5 – 64.3 %) and constant darkness.
Statistics:	The solvent control was used for statistical analyses. For the oral and the contact test, Fisher's exact test with Bonferroni-Holm Adjustment, $\alpha = 0.05$, one-sided greater was performed at 48 and 96 hours to compare the mortality rates between the solvent control and test item treatment.

Results and discussions

Results 48h:

		Treatment			
		Control	Solvent control	Reference item	Folpet 100 µg/bee
Oral test (48 h)	Mortality (%)	0.0	6.7	100	4.0 ^a
	48h LD50	>100 µg/bee ^b			
	48h NOED	≥100 µg/bee			
	48h LOED	>100 µg/bee			
Contact test (48 h)	Mortality (%)	0.0	3.0	27	0.0 ^a
	48h LD50	>100 µg/bee ^b			
	48h NOED	≥100 µg/bee			
	48h LOED	>100 µg/bee			

^a not statistically significantly different when compared to the solvent control (Fisher's exact test with Bonferroni-Holm Adjustment, $\alpha = 0.05$, one-sided greater, $p = 0.146$).

^b Based on the low toxicity of the limit test dose of 100 µg a.i./bee in both the oral and contact test the 48h LD50 of Folpet was determined to be > 100 µg a.i./bee.

Results 96h:

		Treatment			
		Control	Solvent control	Reference item	Folpet 100 µg/bee
Oral test (96 h)	Mortality (%)	0	10	100	4.0 ^c
	96h LD50	>100 µg/bee ^d			
	96h NOED	≥100 µg/bee			
	96h LOED	>100 µg/bee			
Contact test (96 h)	Mortality (%)	0	3.3	70	3.3 ^c
	96h LD50	>100 µg/bee ^d			
	96h NOED	≥100 µg/bee			
	96h LOED	>100 µg/bee			

^c not statistically significantly different when compared to the solvent control (Fisher's exact test with Bonferroni-Holm Adjustment, $\alpha = 0.05$, one-sided greater, $p = 0.270$).

^d Based on the low toxicity of the limit test dose of 100 µg Folpet/bee in both the oral and contact test the 96h LD50 of Folpet was determined to be > 100 µg Folpet/bee.

Conclusion

Oral Test

After 48 and 96 hours acute oral exposure of adult worker bumble bee to Folpet technical, the cumulative mortality at 100 µg a.i./bee test item was 4 % and not statistically significantly different when compared to the solvent control.

The 48 and 96 hours LD₅₀ for the oral treatment was determined to be > 100 µg Folpet/bee. NOED and LOED for the oral test were determined to be ≥ 100 µg a.i./bee and > 100 µg a.i./bee, respectively.

Contact Test

After 48 and 96 hours acute contact exposure of adult worker bumble bee to Folpet technical, the cumulative mortality at 100 µg a.i./bee test item was 0.0 and 3.3%, respectively and not statistically significantly different when compared to the solvent control.

The 48 and 96 hours LD₅₀ for the contact treatment was determined to be > 100 µg Folpet/bee. NOED and LOED for the contact test were determined to be ≥ 100 µg a.i./bee and > 100 µg a.i./bee, respectively.

Validity criteria

Oral test

At 48 hours, bumble bee worker mortality in the control and solvent control treatment was 0.0 % and 6.7 %, respectively.

At 96 hours, bumble bee worker mortality in the control and solvent control treatment was 0.0 % and 10 %, respectively.

Mortality in the reference item treatment after 48 and 96 hours was 100 % at 10 µg dimethoate/bee.

All validity criteria were met, therefore, the study is valid.

Contact test

At 48 hours, bumble bee worker mortality in the control and solvent control treatment was 0.0 % and 3.0 %, respectively.

At 96 hours, bumble bee worker mortality in the control and solvent control treatment was 0.0 % and 3.3 %, respectively.

Mortality in the reference item treatment after 48 hours was 27 % and after 96 hours 70% at 10 µg dimethoate/bee.

All validity criteria were met, therefore, the study is valid.

A 2.3.1.1.3 Study 3

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal of a.s.-folpet: Based on the evaluation, the bumble bee acute oral and contact toxicity test is considered valid.</p> <p>96 h LD₅₀ > 250 µg product 80 WG./bumble bee correspond to 199.5 µg a.s./bumble bee (acute contact toxicity) 96 h LD₅₀ > 487.7 µg product 80 WG./bumble bee correspond to 389.3 µg a.s./bumble bee (acute oral toxicity)</p> <p>The RMS-PL agrees with the evaluation and the derived endpoints. This study is not considered in the risk assessment for the current formulation. Folpec 500 SC.</p>
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Reference:	KCP 10.3.1.1/03
Report	Acute toxicity of Folpet 80 WG to the bumblebee <i>Bombus terrestris</i> L. under laboratory conditions, Amsel, K., 2015, Report No. 15 10 48 167 B
Guideline(s):	Yes, Adapted from VAN DER STEEN (1996 & 2001), OECD 213 (1998), OECD 214 (1998) and HANEWALD et al. (2013)
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The purpose of this study was to determine the acute toxicity of Folpet 80 WG to the bumblebee *Bombus terrestris* L. in a laboratory test after oral and contact exposure.

As no approved guideline is available on the acute toxicity testing on bumblebees the method used in this study is adapted from the following internationally accepted publications and guidelines:

- VAN DER STEEN, J.J.M.; GRETENKORD, C.; SCHAEFER, H.:
Methods to determine the acute oral and contact LD50 of pesticides for bumble bees (*Bombus terrestris* L.)
Proceedings ICPBR 6th Symposium on the Hazard of Pesticides to Bees, Braunschweig, 1996
- OECD 213: OECD Guideline for the Testing of Chemicals, Honeybees, Acute Oral Toxicity Test (adopted 21st September 1998)
- OECD 214: OECD Guideline for the Testing of Chemicals, Honeybees, Acute Contact Toxicity Test (adopted 21st September 1998)
- VAN DER STEEN: Review of the methods to determine the hazard and toxicity of pesticides to bumblebees. *Apidologie* 32 (399–406), 2001
- HANEWALD, N. et al.: Optimizing laboratory toxicity test methods for Bumblebees (*Bombus terrestris* L.) (Presented by BASF SE on the SETAC Conference in Glasgow), 2013

Materials and methods

Test item:	Folpet 80 WG Batch code.: A-CXN Active substance(s)/Content: Folpet: 798.1 g/kg (analysed)
Test species:	<i>Bombus terrestris</i> L. (bumblebee), young adult worker bumblebees derived from queen-right standard-hives; source: Biobest Belgium N.V., Ilse Velden 18, 2260 Westerlo, Belgium delivered: Katz Biotech AG, An der

Test design:	Birkenpfuhlheide 10, 15837 Baruth, Germany; collected from the bumblebee micro-hive in the morning prior to use Contact: 96 hours; 1 dose rate of test item, 60 replicates with 1 bumblebees each; Oral: 96 hours; 1 dose rates of test item; 60 replicates with 1 bumblebee each; Reference item: 96 hours; 4 dose rates of test item, 30 replicates with 1 bumblebees each; Dimethoate EC 400 (Dimethoate 420.3 g/L analysed content); Dose rates for contact tets: 10.1, 6.4, 4.0, 2.5 µg a.s./bumblebee Dose rates for oral tets: 1.50, 0.82, 0.45, 0.25 µg a.s./bumblebee Assessments of mortality and behavioural effects were done after 4, 24, 48, 72 and 96 hours.
Endpoints:	Mortality, behaviour
Dose rates [product/bee]:	Contact test: 250.0 µg/bumblebee Oral test (offered): 500.0 µg/bumblebee Oral test (consumed): 487.8 µg/bumblebee
Dose rates [a.s./bee]:	Contact test: 199.5 µg/bumblebee Oral test (offered): 399.1 µg/bumblebee Oral test (consumed): 389.3 µg/bumblebee The unit [µg a.s./bumblebee] refers to the CoA analysed content of the active substance in the formulated product.
Test conditions:	Temperature: 24.3 – 25.5 °C Relative humidity: 52 – 70 % Illumination: constant darkness throughout the test (diffuse artificial light of about 100 lx only during handling and assessments) Food: 50 % w/v sucrose solution
Statistics:	Statistical program used: ToxRat Professional 3.1 (2015) Statistical significance of mortality values - Fisher`s Exact Binomial Test for test item - Fisher`s Exact Binomial Test with Bonferroni Correction for reference item LD50 values for reference item - Logit analysis (linear weight regression) for contact test - Logit analysis (linear maximum likelihood regression) for oral test
Date of work:	10 - 14 August 2015

Results and discussions

Contact test

Both control groups treated with deionised water or with TritonX solution showed no mortality within 96 hours. In the test item treatment, no mortality occurred after dorsal application of 250.0 µg Folpet 80 WG/bumblebee, after 96 hours

Therefore, the LD₅₀ (96 h) was estimated to be > 250.0 µg Folpet 80 WG/bumblebee, corresponding to > 199.5 µg a.s./bumblebee.

No effects on behaviour of surviving bumblebees occurred in all tested dose rates in the contact toxicity test when compared to the control.

Oral test

The control group fed with 50 % (w/v) sucrose solution showed no mortality within 96 hours. In the test item treatment, slight mortality of 1.7 % occurred after oral consumption of 487.8 µg Folpet 80 WG/bumblebee, after 96 hours.

Therefore, the LD₅₀ (96 h) was estimated to be > 487.8 µg consumed Folpet 80 WG/bumblebee, corresponding to > 389.3 µg consumed a.s./bumblebee.

No effects on behaviour of surviving bumblebees occurred in all tested dose rates in the oral toxicity test when compared to the control.

The respective LD₅₀ values of the contact and oral toxicity test are presented in Table I.

Table: LD₅₀-values of the contact and oral toxicity test

LD ₅₀	Contact toxicity test	Oral toxicity test ¹
	24 h, 48 h, 72 h, 96 h	24 h, 48 h, 72 h, 96 h
LD50 [µg product/bumblebee]	> 250.0	> 487.8
LD50 [µg a.s./bumblebee]	> 199.5	> 389.3

¹ Doses of the oral toxicity test are referring to consumed doses

The contact and oral LD₅₀ (96 h) of the reference item was calculated to be 5.0 µg dimethoate/bumblebee and 0.71 µg dimethoate/bumblebee, respectively. All validity criteria have been met in this study.

Conclusion

The toxicity of Folpet 80 WG was tested in both acute contact and acute oral toxicity tests on bumblebees. Based on the obtained results the LD₅₀ (96 h) in the contact toxicity test was estimated to be > 250.0 µg Folpet 80 WG/bumblebee, which corresponds to > 199.5 µg a.s./bee.

In the oral test the LD₅₀ (96 h) was estimated to be > 487.8 µg consumed Folpet 80 WG/bumblebee, which corresponds to > 389.3 µg consumed a.s./bee.

Validity criteria

The validity criteria of the acute bumblebee study with Folpet 80 WG are given in Table below. All recommended validity values were met.

Table: Validity of the acute bumblebee study

Validity criterion		Occurred / calculated	Recommended
Mean control mortality (96 h)	Contact test:	0.0 %	≤ 10 %
	- Deionised water	0.0 %	
	- 0.5% TritonX solution		
	Oral test: - Sucrose solution	0.0 %	≤ 10 %
LD50 value of the reference (96 h)	Contact toxicity test	5.0 µg a.s./bumblebee	Between 10.1 – 2.5 µg a.s./bumblebee
	Oral toxicity test	0.71 µg a.s./bumblebee	Between 1.47 – 0.25 µg a.s./bumblebee

A 2.3.1.1.4 Study 4

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal of a.s.-folpet: Based on the evaluation, the solitary bee acute oral and contact toxicity test is considered valid.</p> <p>96 h LD₅₀ > 200 µg a.s./bee (contact toxicity) 96 h LD₅₀ = 104.1 µg a.s./bee (oral toxicity)</p> <p>The zRMS-PL agrees with the evaluation and the derived endpoints. This study is not considered in the risk assessment for the current formulation Folpet 500 SC.</p>
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Reference:	KCP 10.3.1.1/04
Report	Acute toxicity of Folpet 80 WG to the solitary bee <i>Osmia bicornis</i> L. under laboratory conditions, Schnurr, A., 2015, Report No. 15 10 48 114 B
Guideline(s):	Yes, OECD 213 (1998), OECD 214 (1998), EFSA (2013)
Deviations:	No
GLP:	Yes

Acceptability: Yes

Duplication N/A
(if vertebrate study)

Objective

The purpose of this study was to determine the acute toxicity of Folpet 80 WG to the solitary bee *Osmia bicornis* L. in a laboratory test after oral and contact exposure.

This study is designed to comply with the following internationally accepted guidelines:

- OECD 213: OECD Guideline for the Testing of Chemicals, Honeybees, Acute Oral Toxicity Test (adopted 21st September 1998)
- OECD 214: OECD Guideline for the Testing of Chemicals, Honeybees, Acute Contact Toxicity Test (adopted 21st September 1998)
- EFSA Journal: Guidance on the risk assessment of plant production products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees (2013))

Data on the toxicity to *Osmia bicornis* L. were generated in order to comply with international regulations and the EFSA Guidance on Pollinators (2013).

Materials and methods

Test item:	Folpet 80 WG Batch No.: A-CXN Analysed content: 798.1 g/kg Folpet
Test species:	Solitary bee <i>Osmia bicornis</i> L. (Hymenoptera, Apoidea); females in good health condition; age: newly emerged; weight range: 70-150 mg; source: DSP (Dr. Schubert Pflanzenzucht), An den Linden 34, 06188 Landsberg, Germany.
Test design:	Contact (LD50 test): 96-h; 5 dose rates of test item, 3 replicates with 10 bees each; Oral (LD50 test): 96-h; 5 dose rates of test item; 30 replicates with 1 bee each; The mortality and the behaviour were assessed 4 h, 24 h, 48 h, 72 h and 96 h after application in the contact and oral toxicity tests. Reference item: Dimethoate EC 400 (analysed dimethoate of 420.3 g/L)
Endpoints:	Mortality, behavioural impairments
Dose rates:	Contact test: 200.0, 100.0, 50.0, 25.0, 12.5 µg a.s./solitary bee Oral test (offered): 400.0, 182.0, 82.8, 37.7, 17.1 µg a.s./solitary bee Oral test (consumed): 361.3, 162.3, 77.2, 34.1, 15.6 µg a.s./solitary bee The unit [µg a.s./bee] refers to the nominal content of the active ingredients in the formulated product.
Test conditions:	Temperature: 19.4 – 21.4 °C Relative humidity: 64.7 – 78.1 % Illumination: 12:12 h light-dark-cycle Food: 50 % (w/v) sucrose solution (500 g/L) with anise oil (20 µL/L)
Statistics:	Statistical program used: ToxRat Professional 3.1.0 (2015) LD50 - contact reference item: Probit analysis (linear weighted regression) - oral test item: Probit analysis (linear maximum likelihood regression) - oral reference item: Probit analysis (linear maximum likelihood regression) Statistical significance of mortality values - test item: Multiple Sequentially-rejective Fisher Test After Bonferroni-Holm Correction ($p \leq 0.05$) - reference item: Multiple Sequentially-rejective Fisher Test After Bonferroni-Holm Correction ($p \leq 0.05$)
Dates of work:	August 03 – August 07, 2015

Results and discussions

Contact test

The control group treated with 0.5 % Triton X solution revealed a low mortality of 6.7 % within 96 hours. In the test item group no statistically significant mortalities occurred after thoracal application of nominal

200.0, 100.0, 50.0, 25.0 and 12.5 µg Folpet/solitary bee after 96 h, respectively. Only low mortalities of 23.3, 16.7, 20.0, 16.7, and 16.7 % occurred after the application of nominal 200.0, 100.0, 50.0, 25.0 and 12.5 µg Folpet/solitary bee, which were not statistically significant in comparison to the control group.

The LD50 (96 h) was >200.0 µg Folpet/solitary bee.

No effects on behaviour of surviving bees occurred after thoracal application of nominal 200.0, 100.0, 50.0, 25.0 and 12.5 µg Folpet/solitary bee at any time.

Oral test

The control groups fed with 50 % (w/v) sucrose solution with anise oil (20 µL/L) showed a low mortality of 10.0 % within 96 hours.

In the test item group statistically significant mortalities of 90.0, 70.0 and 43.3 % occurred after oral consumption of nominal 361.3, 162.3 and 77.2 µg Folpet/solitary bee after 96 h. The consumption of 34.1 and 15.6 µg Folpet/solitary bee resulted in lower, not statistically significant mortalities of 10.0 % after 96 h, respectively.

The LD50 (96 h) based on the corrected mortality was 104.3 µg Folpet/solitary bee.

Effects on behaviour of surviving bees were observed in one bee (3.7 %) after the consumption of nominal 361.3 µg Folpet/solitary bee after 24 h. This was characterized by moribund behaviour.

All other bees showed no effects on behaviour after the consumption of 361.3, 162.3, 77.2, 34.1 and 15.6 µg Folpet/solitary bee, respectively, at any time.

The respective LD50 values of the contact and oral toxicity test are summarised in Table I.

Table I: LD50-values of the contact and oral toxicity test				
LD50¹ (95%-CL)²	Contact toxicity test		Oral toxicity test³	
	48 h	96 h	48 h	96 h
LD50 [µg a.s./s. bee]⁴ (95 %-CL / lower-upper)	>200.0	>200.0	305.1 (180.1 – 516.9)	104.3 (81.5 – 133.5)
LD50 [µg a.s./s. bee]⁵ (95 %-CL / lower-upper)	>199.5	>199.5	304.4 (179.7 – 515.6)	104.1 (81.3 – 133.1)

1 based on the corrected mortality; 2 CL: confidence limits; 3 Doses of the oral toxicity test are referring to consumed doses;

4 based on nominal content; 5 based on analysed content

The contact and oral LD50 (96-h) of the reference item was calculated to 0.704 µg dimethoate/solitary bee and 0.454 µg dimethoate/solitary bee, respectively. The control mortality in both tests was ≤10 %. All validity criteria have been met.

Conclusion

The toxicity of Folpet 80 WG was tested in both acute contact and acute oral toxicity tests on solitary bees. The LD50 (96 h) based on corrected mortality in the contact toxicity test was nominal >200.0 µg Folpet/solitary bee (analysed >199.5 µg Folpet/ solitary bee). In the oral toxicity test the LD50 (96 h) based on corrected mortality was nominal 104.3 µg consumed Folpet/solitary bee (analysed 104.1 µg consumed Folpet/solitary bee).

Validity criteria

The validity criteria of the acute solitary bee study with Folpet 80 WG are given in Table below.

Table: Validity criteria of the acute solitary bee study			
Validity criterion		Occurred / calculated	Recommended
Control mortality (96 h)	Contact test:		
	- deionised water	10.0 %	≤ 10 %
	- Triton X solution	6.7 %	
Oral test: - 50 % sucrose solution with anise oil (20µL/L)		10.0 %	≤ 10 %

A 2.3.1.1.5 Study 5

Comments of zRMS:	<p>The study was conducted in line with OECD 213 and 214 with no deviations.</p> <p>All validity criteria were met.</p> <p>Overall, the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>48 h LD₅₀ > 302.41 µg a.s./bee (oral)</p> <p>48 h LD₅₀ > 571.22 µg a.s./bee (contact)</p>
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Reference:	KCP 10.3.1.1/05
Report	SAP50SCF (Folpet 500 SC): Acute Oral and Contact Toxicity to the Honey bees (<i>Apis mellifera</i> L.), under Laboratory Conditions, Ansaloni, T., 2023, Report No. S23-102834
Guideline(s):	Yes, OECD Guidelines No. 213 and 214 (1998)
Deviations:	Yes, Behavioural abnormalities in the reference item treatment were not recorded since the reference item is known to be toxic to honeybees and therefore effects are expected. Moreover, the dose range covers the expected LD50 values.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

To determine the effects of SAP50SCF (Folpet 500 SC) on the honey bee (*Apis mellifera* L.), from acute oral and contact exposures, and to determine the Median Lethal Doses (LD₅₀) and the No Observed Effect Doses (NOED) at 24 and 48 hours, and furthermore at 72 and 96 hours if the study is prolonged, where possible.

Materials and methods

Test item:	SAP50SCF (Folpet 500 SC)
Batch No.:	22C3310A
Active ingredient:	Folpet
Density	1.22 g/mL
Content (analysed):	517 g/L
Reference item:	BAS 152 65 I (dimethoate, analysed content: 420.1 g/L; density 1.062 g/mL)
Place of test:	Eurofins Trialcamp S.L.U., Polígon Industrial l'Alter. Avda. Antic Regne de València, 25. 46290, Alcàsser (Valencia), Spain
Test Species:	<i>Apis mellifera</i> L.
Age:	Adult worker bees
Source:	Queen-right, healthy colony from our commercial apiary. Honey bees were collected from the outer combs of the beehive and distributed into test cages one day before start of exposure.
Collection:	
Acclimatisation:	The collected honey bees were kept under test conditions until test start. During the acclimatisation period they were fed ad libitum with untreated 50% (w/v) aqueous sucrose solution.
Test design:	Acute oral and contact toxicity dose response test; 48-hours test duration; one control in the oral and contact tests, five test doses of the test item, 4 doses of

	the reference item; 5 replicates, with 10 bees each, per control and test item group and 4 replicates of 10 bees each per reference group. Assessment of mortality 4, 24, and 48 hours after exposure start.
Test doses:	Control groups: Oral Toxicity Test: Untreated 50% (w/v) aqueous sucrose solution (C) Contact Toxicity Test: 0.1% (v/v) Triton X solution in deionised water (C)
	Test item groups: Oral Toxicity Test: 471.95, 613.54, 797.60, 1036.88 and 1347.95 µg test item (hereafter t.i.)/bee, equivalent to 200.00, 260.00, 338.00, 439.40 and 571.22 µg folpet (hereafter a.i.)/bee (nominal dose). Contact Toxicity Test: 471.95, 613.54, 797.60, 1036.88 and 1347.95 µg test item (hereafter t.i.)/bee, equivalent to 200.00, 260.00, 338.00, 439.40 and 571.22 µg folpet (hereafter a.i.)/bee (nominal dose).
	Reference Item groups: Oral Toxicity Test: 0.060, 0.090, 0.140 and 0.210 µg dimethoate/bee (nominal dose). Contact Toxicity Test: 0.080, 0.120, 0.180 and 0.270 µg dimethoate/bee (nominal dose).
Test conditions:	Oral Toxicity Test: Temperature: 25.1 – 25.8 °C Relative Humidity: 54.9 – 62.1 % Contact Toxicity Test: Temperature: 25.1 – 25.8 °C Relative Humidity: 54.9 – 62.1 % Exposure to light: 24-h darkness, except during application and assessments.
Dates of work	29 May 2023 – 01 Jun 2023 (Experimental Phase start to Experimental Phase end dates).
Statistics:	Statistical calculations were made using the statistical program ToxRatPro® Version 3.3.0. Since no mortality occurred in the test item treatments of the oral test, no statistical analysis was performed on these data and the 24-h and 48-h NOED and LD ₅₀ oral values were empirically estimated. Since no mortality occurred in the test item treatments of the contact test, no statistical analysis was performed on these data and the 24-h and 48-h NOED and LD ₅₀ oral values were empirically estimated. The 24-h LD ₅₀ values for the reference item in both the oral and the contact tests were estimated by means of Probit analysis using linear max. likelihood regression.

Results and discussions

In the oral toxicity test, 0.0% mortality was observed at the end of the observation period after 48 hours for the control treatment.

In the contact toxicity test, 0.0% mortality was observed at the end of the observation period after 48 hours for the control treatment.

In the oral toxicity test, in the test item nominal doses of 200.00, 260.00, 338.00, 439.40 and 571.22 µg a.i./bee, the actual consumed doses were 179.16, 209.97, 241.43, 302.41 and 274.57 µg a.i./bee, and the cumulative mean mortality was 0.0, 0.0, 0.0, 0.0 and 0.0%, respectively, 48 hours after start of exposure.

In the contact toxicity test, in the test item nominal doses of 200.00, 260.00, 338.00, 439.40 and 571.22 µg a.i./bee, the cumulative mean mortality was 0.0, 0.0, 0.0, 0.0 and 0.0%, respectively, 48 hours after start of exposure.

No behavioural abnormalities in the control and the treatments groups with the test item were observed both in the oral and in the contact tests throughout the study.

The 24-h oral Median Lethal Dose (LD₅₀) value with 95% confidence limits for the reference item was 0.106 [0.096 – 0.116] µg dimethoate/bee. The 24-h contact Medial Lethal Dose (LD₅₀) value with 95%

confidence limits for the reference item was 0.125 [0.113 – 0.137] µg dimethoate/bee.

The 24-h and 48-h oral median Lethal Dose (LD₅₀) values for the test item SAP50SCF (Folpet 500 SC) were empirically estimated to be higher than the highest consumed dose of 302.41 µg a.i./bee.

The 24-h and 48-h contact median Lethal Dose (LD₅₀) values for the test item SAP50SCF (Folpet 500 SC) were empirically estimated to be higher than the applied dose of 571.22 µg a.i./bee.

The 24-h and 48-h No Observed Effect Dose (NOED) values in the oral test for the test item SAP50SCF (Folpet 500 SC) were estimated to be equal to or higher than 302.41 µg a.i./bee based on the highest consumed dose.

The 24-h and 48-h NOED values in the contact test for the test item SAP50SCF (Folpet 500 SC) were estimated to be equal to or higher than 571.22 µg a.i./bee based on the nominal dose.

Conclusion

The oral and contact acute toxicity of SAP50SCF (Folpet 500 SC) was tested under laboratory conditions over a period of 48 hours.

The resulting endpoints of this oral and contact acute toxicity test to the honey bees (*Apis mellifera* L.) with the test item SAP50SCF (Folpet 500 SC) are presented below:

Endpoints	[µg t.i./bee] *	[µg a.i./bee]
24 h Oral LD ₅₀	> 713.62	> 302.41
48 h Oral LD ₅₀	> 713.62	> 302.41
24 h Oral NOED	≥ 713.62	≥ 302.41
48 h Oral NOED	≥ 713.62	≥ 302.41
24 h Contact LD ₅₀	> 1347.95	> 571.22
48 h Contact LD ₅₀	> 1347.95	> 571.22
24 h Contact NOED	≥ 1347.95	≥ 571.22
48 h Contact NOED	≥ 1347.95	≥ 571.22

* Endpoints equivalences based on the actual content of the active ingredient (folpet: 517 g/L and density 1.22 g/mL) according to the CoA.

The 24-h oral Median Lethal Dose (LD₅₀) value with 95% confidence limits for the reference item was 0.106 [0.096 – 0.116] µg dimethoate/bee. The 24-h contact Median Lethal Dose (LD₅₀) value with 95% confidence limits for the reference item was 0.125 [0.113 – 0.137] µg dimethoate/bee.

All validity criteria were met, and the sensitivity of the test organisms was confirmed. Accordingly, the study was deemed valid.

Validity criteria

The study is considered valid since the control and reference item validity criteria were met:

- The average control mortality was ≤ 10% at the end of the tests. Actual 0.0% mortality for the control group (C) in the oral toxicity test and 0.0% in the control group of the contact toxicity test.
- The 24-hour LD₅₀ of the reference item met the specified range of: 0.10 to 0.35 µg dimethoate/bee (actual: 0.106 µg dimethoate/bee) in the oral toxicity test, as well as the specified range of: 0.10 to 0.30 µg dimethoate/bee (actual: 0.125 µg dimethoate/bee) in the contact toxicity test.

- A 2.3.1.1.6 KCP 10.3.1.1.1 Acute oral toxicity to bees**
- A 2.3.1.1.7 KCP 10.3.1.1.2 Acute contact toxicity to bees**
- A 2.3.1.2 KCP 10.3.1.2 Chronic toxicity to bees**
- A 2.3.1.2.1 Study 1**

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal: Based on the evaluation, the honey bee chronic oral toxicity test is considered valid.</p> <p>10 d LDD₅₀ > 16.29 µg a.s./bee/d 10 d NOED > 16.29 µg a.s./bee/d</p>
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Reference:	KCP 10.3.1.2/01
Report	Chronic toxicity of FOLPET TECHNICAL on honeybees (<i>Apis mellifera</i> L.), Ansaloni, T., 2015, Report No. TRC14-246BA
Guideline(s):	Yes, Based on CEB (2012) method, adaptations of OECD Guidelines n° 213 (1998), publications of Decourty et al. (2005) and Suchail et al (2001), recommendations of the german ring test group (2013) and EPPO 170
Deviations:	<p>Yes,</p> <ul style="list-style-type: none"> - Maximum temperature was slightly above 35.00 °C for periods of less than two consecutive hours (Maximum temperature = 35.29 °C) during the acclimatization period and for periods less than two consecutive hours (Maximum temperature = 35.6 °C) during the test. - Minimum temperature was below 31.00 °C (26.13 °C) on a punctual lecture during the test. - Relative humidity was below 50% (min = 37.6%) on punctual lectures during the test <p>The aforementioned deviations have had no negative impact on the outcome of the study.</p>
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

A study was carried out under laboratory conditions with the objective to determine the chronic toxicity of FOLPET TECHNICAL to adult worker honeybees. The test was performed with a range of five rates with a spacing factor of 2. The study followed the CEB (2012) method, adaptations of OECD Guidelines n° 213 (1998), publications of Decourty et al. (2005) and Suchail et al (2001), recommendations of the German ring test group (2013) and EPPO 170 and was conducted under study code TRC14-246BA.

Materials and methods

Test item:

FOLPET TECHNICAL, batch XF20111023G, analytical content for Folpet 978.2 g/kg, expiry November 2016.

Test species:

Apis mellifera L. Var. Iberica; young adult worker honeybees (≤ 24 h old) collected from a healthy queen-right colony sourced from a commercial apiary. Honeybees were collected shortly after emergence two days prior to the first application and were maintained under test conditions in holding cages throughout the study.

Test design:

Application: The selection of test item doses for the definitive test were based on the maximum solubility of the test item in 50% aqueous sucrose solution (0.83 μg folpet/ μL) and under suggestion by the sponsor. Five doses in a geometric series (factor of 2) of the test item were assessed: 6.25, 12.5, 25, 50 and 100 μg Folpet/bee/day when considering consumption of all food provided. A stock solution was prepared daily by mixing a defined amount of the test item with acetone. Aliquots of these stock solutions were mixed with sucrose solution (50% w/v) to achieve the required test concentrations. Five replicates per treatment each enclosing ten bees, were group fed with one feeder per cage containing 1200 μL of test solution, thus providing 120 μL of test solution per bee. Feeders were weighed prior to their placement in the test cages and were changed on a daily basis with new feeders containing fresh test solutions. When removed each feeder was re-weighed and the daily mean dose consumption per bee was calculated taking into account the surviving individuals at the moment of replacement. Two control groups (untreated sucrose solution 50% w/v and sucrose solution 50% w/v + acetone), and the reference product Dimethoate 40% EC at a daily dose of 0.144 μg a.i./bee/day concurrently tested.

Assessments: Honeybees were observed daily at approximately the same time (when the feeders were changed) for mortality and behaviour assessments. Dead bees were removed from the test units. At the end of the test, surviving individuals of each treatment were frozen at $\leq 10^\circ\text{C}$.

Statistics: Daily mean consumption of each dose of the test item were compared with the pooled controls by means of pair-wise non parametric test (Mann-Whitney exact test). No statistical analysis was performed on mortality data. Statistics was performed using the software SPSS 19; SPSS©Onc, 1989-2010.

Results and discussions

Diet consumption and mortality: Mean daily consumption was 20.55 μL /bee of the offered diet in the negative control group and was 19.56 μL /bee in the solvent control group. No statistical significant difference in mean consumed diet was observed between the two control groups. Mean cumulative mortality after the ten days exposure was $2.00 \pm 2.00\%$ (mean \pm SE) in the negative control and it was 0.00 % in the solvent control.

Daily mean daily consumption of the bees exposed to the test item treatments ranged between 19.34 μL /bee to 20.23 μL /bee. As a consequence, the recalculated daily consumed doses ranged between 1.04 μg Folpet/bee/day and 16.29 μg Folpet/bee/day. Mean cumulative consumption (consumption over the ten days dosing period) ranged between 10.40 μg Folpet/bee and 162.86 μg Folpet/bee. No statistically significant difference in the daily mean consumed diet was observed between any of the test item treatments and the pooled control (Mann-Whitney exact test).

Mean cumulative mortality of the honeybees dosed orally with the test item for ten consecutive days ranged between 0.00% and $4.00 \pm 4.00\%$. Estimated LDD50-value at 10 days was higher than the highest consumed cumulative dose of 162.86 μg Folpet/bee corresponding to a daily mean consumed dose of 16.29 μg Folpet/bee/day, therefore, the NOED for mortality was determined to be ≥ 16.29 μg Folpet/bee/day and the LDD10 and LDD20 was estimated to be >16.29 μg Folpet/bee/day. Symptoms of intoxication were observed sporadically and on very few individuals starting on the third day of dosing (one individual showing uncoordinated movements in T5). Symptoms were apathy (little response to an external stimulus, i.e. a gentle air blow) and lack of coordination. By the end of the study (day 10) the percentage of affected bees based on the surviving individuals ranged between 2.04% at the lowest dose (T1 = 10.40 μg Folpet/bee, cumulative) and 10.00% at the second highest dose (T4 = 80.59 μg Folpet/bee, cumulative). Hence, the observed sublethal effects can be considered as not significant.

Conclusion

Food consumption of the treated diet with Folpet technical in all test item concentrations was not statistically significantly different when compared to the pooled control. Sublethal effects (i.e. apathy and lack of coordination) were observed sporadically and in few individuals starting on the third day of exposure ranging from 2.04% (T1 = 10.40 µg Folpet/bee, cumulative) to 10.00% (T4 = 80.59 µg Folpet/bee, cumulative) of the surviving individuals after 240h chronic exposure.

The estimated chronic LDD50-value for the Folpet technical was determined to be higher than the highest consumed dose of 162.86 µg Folpet/bee (cumulative), corresponding to a daily treatment LDD50 value of 16.29 µg Folpet/bee. Based on the mortality data, the NOED was determined to be ≥ 16.29 µg Folpet/bee/day, the highest achievable dose and the LDD10 and LDD20 was estimated to be >16.29 µg Folpet/bee/day.

	Mean Daily		Cumulative over ten days	
	Folpet technical	Folpet*	Folpet technical	Folpet*
LDD50-values (consumed µg/bee)	>16.65	>16.29	>166.49	>162.86

* Analytical content

The results obtained with the toxic reference substance (100% cumulative mortality) confirmed the sensitivity of the bees under the conditions of the test.

Validity criteria

The test was considered valid as the results obtained met the set validity criterion:

- Mortality observed in control treatments was equal or less than 15.00% for the duration of the test (final cumulated mortality = 2.00% for the negative control and 0.00% for the solvent control).
- Mean mortality in the reference product concentration was $\geq 50\%$ at the end of the test (final cumulated mortality = 100.00%).

A 2.3.1.3 KCP 10.3.1.3 Effects on honey bee development and other honey bee life stages

A 2.3.1.3.1 Study 1

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal of the a.s.-folpet: Based on the evaluation, the honey bee larvae toxicity test is considered valid.</p> <p>D8 LD₁₀ = 0.64 µg a.s./larva/developmental period (95% C.I. = 0.13-1.28) D8 LD₂₀ = 1.13 µg a.s./larva/developmental period (95% C.I. = 0.35-2.02) D8 LD₅₀ = 3.37 µg a.s./larva/developmental period (95% C.I. = 1.86-6.32) D8 NOED = 0.89 µg a.s./larva/developmental period</p> <p>Since the derived LD₁₀ is lower than the NOED, the reliability of the LD₁₀ should be checked, in line with EFSA Supporting publication 2019:EN-1673. Normalised width of confidence interval: NW = 1.79 (rating: poor) Steepness: 0.19 (shallow) Classification based on the relationship between EC₁₀ and EC₂₀ /EC₅₀ confidence intervals: High certainty (LD₁₀ < LD₂₀, low) The study was not used in the risk assessment as the OECD 239 study is more appropriate.</p>
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Reference:	KCP 10.3.1.3/01
Report	Toxicity of FOLPET TECHNICAL on honey bee larvae (<i>Apis mellifera</i> L.) after repeated exposure under laboratory conditions, Ansaloni, T., 2015, Report No. TRC14-245BA
Guideline(s):	Yes, OECD Guideline n° 237 (2013) and EPPO 170
Deviations:	<p>Yes</p> <ul style="list-style-type: none"> - Temperature in the incubator was slightly above 35 °C (Max = 35.28 °C) during intervals of more than 2 consecutive hours. Other short deviations in temperature and relative humidity occurred in concomitance with the opening of the incubator for manipulation of the test system (assessments and/or diet provisioning). - The analytical report is not annexed to these final report because it is not available. <p>The aforementioned deviations have had no negative impact on the outcome of the study.</p>
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

A study was carried out under laboratory conditions with the objective to determine the toxicity of Folpet technical to honey bees' larvae after repeated exposure. Based on non-GLP range finding the test was performed with a range of four doses. The study followed the OECD guideline 237 with modifications of the dose administration (repeated dosing based on OECD Draft Guidance Document "Honey Bee (*Apis mellifera*) Larval Toxicity Test, Repeated Exposure" (2014) and was conducted under study code TRC14-245BA.

Materials and methods

Test Item:

Folpet technical, batch XF20111023G, purity for Folpet 978.2g/kg, expiry November 2016.

Test species:

Apis mellifera L. Var. Iberica; larvae of honey bees collected from a healthy queen-right colony sourced from a commercial apiary. Honey bee larvae at the stage L1 were selected from three different colonies and individually placed into cellular well-plates where they were fed with a standardized amount of artificial diet.

Test procedure:

Selection of test larvae: Queens of a minimum of three colonies were confined within an empty comb or a comb with emerging worker bees and empty cells of their own colony with an exclusion cage 3 days before the beginning of the test (D -3). At Day -2 (D -2), and within a maximum of 30 hours after confinement, the queens were released after checking the presence of fresh laid eggs. The comb with the eggs was left in the cage near the brood combs until hatching (D1), when the first instar (L1) larvae were taken from the combs and individually placed in well-plates under controlled conditions.

Test Units: Larvae were reared in sterilised crystal polystyrene grafting cells placed individually into a well of a 48 well plate, with the top maintained at the level of the plate by means of a dental roll wetted with approximately 500 µl of the sterilising solution enhanced with 15% w/v glycerol. The plates were placed into a hermetic Plexiglass desiccator with a dish filled with potassium sulphate saturated solution in order to keep a water saturated atmosphere. The desiccator was placed into an incubator with forced ventilation at 34-35 °C and water saturated atmosphere for the duration of the test.

Diet composition: All larvae were fed once a day with the exception of D2. Three different diets, adapted to the needs of each larval stage, were prepared during the test: Diet A (D1, 20 µl/larva): 50% weight of fresh royal jelly + 50% weight of aqueous solution containing 2% weight of yeast extract, 12% weight of glucose and 12% weight of fructose. Diet B (D3, 20 µl/larva): 50% weight of fresh royal jelly + 50% weight of aqueous solution containing 3% weight of yeast extract, 15% weight of glucose and 15% weight of fructose. Diet C (D4 to D6): 50% weight of fresh royal jelly + 50% weight of aqueous solution containing 4% weight of yeast extract, 18% weight of glucose and 18% weight of fructose. The following volumes of diet were administered on days D4 to D6: D4 = 30 µl, D5 = 40 µl, D6 = 50 µl.

Application of the test substance: Six doses of the test item with a spacing factor of 2.2 were assessed daily for four consecutive days (D3 to D6). Each test dose was prepared daily from a fresh stock solution obtained by mixing a defined amount of the test item with a defined amount of an organic solvent (i.e. acetone) and then by mixing this solution with a defined amount the corresponding diet. To maintain constant concentrations in terms of mg a.i./mL diet/day, daily doses increased progressively in accordance to the increasing volume of diet administered each day. The final cumulative doses (total of four applications) were of 0.41, 0.89, 1.97, 4.32, 9.51 and 20.92 µg Folpet/larva. On D3, a minimum of twelve well-fed larvae from each of the three colonies (36 larvae per treatment) were selected for each treatment and dosed with 20 µl of the corresponding diet (diet B) containing the test solution with the corresponding concentration. Administration of the selected doses of test item continued on a daily basis until day 6 with the corresponding diets. Mixing of the test solution with the diet was performed just before administration.

Assessments: Mortality was assessed and recorded at feeding time at D4, D5, D6, D7 and D8. An immobile larva or a larva that did not react to the contact with the grafting tool was noted as dead. Dead larvae were removed at each assessment and anomalies in behaviour were recorded. On D8, the presence of uneaten food was qualitatively recorded.

Toxic reference treatment: A toxic standard reference product, Dimethoate (Dimethoate 40% EC) was applied at a constant concentration of 40 mg a.i./Kg diet/day on thirty six larvae on the same days the test item was applied. Procedures followed those described above for the test item.

Statistics: For mortality data of the test item, a standard probit analysis (Finney 1971) was performed for

the calculation of the LD50-values and a step down test for monotone response (Jonckheere-Terpstra exact test) for the estimation of the No Observed Effect Dose. All statistics were performed using the statistical software SPSS 19; SPSS©Onc, 1989-2010.

Results and discussions

Mean mortality in the control groups was 11.11% (negative control) and 13.89% (solvent control) 120 hours after the first application (D8).

Mean mortality of honey bees' larvae dosed orally with the test item ranged between 0.00% (T1 and T2 = 0.41 and 0.89 µg Folpet/larva/developmental period) and 44.44% (T6 = 20.92 µg Folpet/larva/developmental period) 24 hours after dosing, between 8.33% (T1= 0.41 µg Folpet/larva/developmental period) and 94.44% (T6 = 20.92 µg Folpet/larva/developmental period) 48 hours after dosing, between 11.11% (T1= 0.41 µg Folpet/larva/developmental period) and 100.00% (T6 = 20.92 µg Folpet/larva/developmental period) 72 and 96 hours after dosing and between 19.44% (T1= 0.41 µg Folpet/larva/developmental period) and 100.00% (T6 = 20.92 µg Folpet/larva/developmental period) 120 hours after dosing.

The estimated LD50-values are reported in the following table.

Oral Test	LDD*50 (µg Folpet/larva/developmental period)
Test item 96h (D3 to D7)	5.004
Test item 120h (D3 to D8)	4.846

* LDD: Lethal Dietary Dose

A significant effect (mortality significantly higher than the control mortality) both at 96 and 120 hours after the first application (D7 and D8, respectively) was observed starting with treatment T3 (1.97 µg Folpet/larva/developmental period). Therefore, cumulative NOED (No Observed Effect Dose over 4 and 5 days after the first application, cumulative dosing) corresponded to a cumulated dose of 0.89 µg Folpet/larva both at 96 and 120 hours after the first application.

Hours after the first application	NOED (µg Folpet/larva/developmental period D3 to D8)
96	0.89
120	0.89

At 120 hours after the first application, one individual of the surviving larvae in treatment T1 (0.41 µg Folpet/larva/developmental period) and two individuals of the surviving larvae of the negative and solvent controls and treatment T3 (1.97 µg Folpet/larva/developmental period) had unconsumed diet. In all other treatment doses, no abnormal symptoms were observed for the surviving individuals at 120 hours after dosing.

Reference treatment: Corrected mortality observed in the larvae exposed to the reference product was 93.75% both at 96 and 120 hours after dosing.

Conclusion

The estimated LDD50-value for Folpet technical corresponded to a cumulative (over 4 days of application) dietary dose of 5.004 µg Folpet/larva 96 hours after dosing and 4.846 µg Folpet/larva 120 hours after dosing.

A cumulative dietary dose of 0.89 µg Folpet/larva resulted in a NOED at the end of the study (No Observed effect Dose over the 4 days of exposure, cumulative dosing, both at 96 and 120 hours after the first application).

The results obtained with the toxic reference substance confirmed the sensitivity of the test system (bees' larvae) under the test conditions.

Validity criteria

The test is considered valid as the results obtained met the set validity criteria:

- Mortality observed in control treatments was 11.11% (negative control) and 13.89% (solvent control) 120 hours after dosing.
- Corrected mortality (Schneider-Orelli) observed in the larvae exposed to the reference product was 93.75% 120 hours after dosing.

A 2.3.1.3.2 Study 2

Comments of zRMS:	The study is acceptable as all validity criteria were met. NOED = 2.16 µg a.s./larvae/developmental period ED ₁₀ could not be determined.
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Reference:	KCP 10.3.1.3/02
Report	Folpet Technical: Honey Bee (<i>Apis mellifera</i> L.) Larval Toxicity Test following Repeated Exposure under Laboratory Conditions, Marín, M., 2022, Report No. S21-05947
Guideline(s):	Yes, OECD Guidance Document 239 (2021) & SANTE/2020/12830, Rev.1 (2021)
Deviations:	Yes The reduction of the relative humidity conditions from $95 \pm 5\%$ to $80 \pm 5\%$ was done on day 7 (D7) of the test instead of on day 8 (D8). The reported deviation to the guidance has no impact on the outcome of the study since validity criteria for the control were met.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

To determine the effects of Folpet Technical on honey bee (*Apis mellifera* L.) larvae, after a repeated exposure test. To determine the No Observed Effect Concentration/Dose (NOEC/NOED) and the Lowest Observed Effect Concentration/Dose (LOEC/LOED) for adult emergence (from D3 to D22). To determine the Median Effect Concentration/Dose (EC₅₀/ED₅₀) and any EC_x/ED_x (i.e., EC₁₀/ED₁₀ and EC₂₀/ED₂₀) for adult emergence (from D3 to D22), where possible.

Materials and methods

Test item: Folpet Technical; Batch code: 99138337; active substance: folpet; content of a.s.: 98.2 % w/w (content of active substance according to certificate of analysis); expiry date: 04 May 2024.

Reference item: BAS 152 I; Batch code: COD-002332; active ingredient: dimethoate; content of a.i. analysed: 99.1 % w/w; expiry date: 27 Jan 2023.

Test organisms: Honey bee (*Apis mellifera* L.), synchronized first instar (L1) larvae not older than 30 hours at grafting time.

Source: Commercial beehives from the in-house Test Facility stock, adequately fed, healthy and as far as possible disease-free and queen-right. The hives from which the larvae were obtained were not previously exposed to any chemical treatments within four weeks of test initiation.

Preparation of test organisms and larvae collection: On D-3, the queens from at least three colonies were isolated for one day within a queen excluder placed on a single frame with empty cells in their own hive, to provide knownaged eggs and subsequent larvae.

On D-2, maximum 30 hours after isolation, the queens were released. Frames containing eggs were left in the excluder cages until hatching (D1). Three frames from different hives, containing the highest number of synchronized larvae, were selected for grafting in the laboratory.

Test design: Dose response test with duration of 21 days from grafting on day 1 to the final assessment on day 22. From day 3 until day 6 of the test, 5 different concentrations of Folpet Technical were applied to the larvae of the test item groups and one single concentration of the reference item was applied to the

larvae of the reference item group. Both, test and reference item, were supplied in diet B (day 3) and C (days 4, 5 and 6). The daily feeding volume increased from 20 µL to 50 µL diet per larva over the application period. The cumulative feeding volume from day 3 until day 6 of 140 µL diet per larva was considered for the calculation of the cumulative doses per larva.

Two control groups (negative and solvent control) were included in the test and exposed for the same period of time under identical exposure conditions to the treatments. Each treatment group consisted of 48 larvae; 16 from each of three different colonies (each colony representing one replicate). Larval mortality assessments were on days 4, 5, 6, 7, and 8. The presence of uneaten food was qualitatively recorded on day 8. Assessment of mortality during pupation phase was on day 15 and assessment of emergence on day 22 was recorded.

Test concentrations and doses: Controls: C1: Negative control (untreated diet).

C2: Solvent control (diet + 0.5 % acetone).

Test item: 0.58, 1.75, 5.24, 15.71 and 47.13 mg test item/L diet (equivalent to 0.53, 1.59, 4.76, 14.28 and 42.85 mg test item/kg diet and 0.08, 0.24, 0.73, 2.20 and 6.60 µg test item/larva).

Reference item: R: 48.00 mg dimethoate/kg diet (equivalent to 7.39 µg dimethoate/larva).

Test conditions: Air Temperature: 33.5 – 35.1 °C*

Relative humidity: 37.7* – 98.5 %

* Short term deviations were recorded (temperatures out of range up to 30 min once every 24 h; relative humidity out of range up to 2 h).

Exposure to light: Constant darkness except during feeding and assessments.

Analytical verification: Samples of the negative control diet (C1), solvent control diet (C2), as well as of all the concentrations of the test item treated diets (T1 to T5) were taken from D3 to D6, directly after preparation, and placed in the freezer at ≤ -18 °C until shipment.

Only solvent control (C2) and the highest and lowest concentrations samples (T5 and T1 respectively) were analysed.

An Analytical Phase was performed to verify the concentration of test item in the samples taken. A method was validated and samples of diet were analysed for concentration determination of folpet. Quantification was performed by use of LC-MS/MS detection. The limit of quantification (LOQ) of the analytical method was 0.10 mg/kg for folpet in larval diet solution and with a limit of detection (LOD) set at 0.03 mg/kg (defined as the lowest calibration standard, which is 30 % of the LOQ).

Statistics: Statistical calculations were made using MS Excel 2016 v.16.0 and the statistical software Tox-Rat® Professional version 3.3.0. A statistical significance of $\alpha = 0.05$ was considered for all tests, except where stated. Solvent and negative control mortalities were compared by a Fisher's exact binomial test. The treated groups were compared to the solvent control to determine the endpoints. The NOEC for emergence at 22 days was determined by multiple Chi-square tests with Bonferroni correction. The NOED was considered to be the dose corresponding to the NOEC.

EC10,20/ED10,20 values could not be calculated since no clear dose response was obtained on larvae emergence when exposed to the active substance folpet. The EC50/ED50 values were empirically estimated from data.

Dates of work: 13 Sep 2021 – 09 May 2022 including analytical phase.

Results and discussions

The measured concentration in the samples was within ± 20 % of nominal test concentration used. Thus the concentrations of the test item were confirmed and the endpoints are based on nominal values.

On day 8, the cumulative larval mortality was 10.4 % for both the negative control and the solvent control. On day 22, the adult emergence rate of the initial grafted larvae was 87.5 % for the negative control and 85.4 % for the solvent control. Therefore, the validity criteria for the control groups were met for both test periods: the D8 mortality was lower than 15 % and the D22 days emergence rate was greater than 70 %, across all replicates. Cumulative mortality in the Reference Item group also met the validity criteria (> 50 % on day 8, actual value 93.8 %).

On day 8, one individual in the 4.76 mg t.i./kg diet group (T3) was observed with uneaten food. This individual was recorded as dead on the D15 assessment. At the end of the test, in the final assessment of the emergence on day 22, no emerged bees were recorded as being affected (i.e. malformation). Main results are shown in the following tables:

Analytical results

The following residues were determined in the samples:

Sample Code	Timing	Treatment ID	Folpet		
			R	Nominal Concentration	Recovery (% of nominal)
			mg/kg	mg/kg	
S21-05947-D3-C2-3-A	D3	C2	< LOD	-	na
S21-05947-D4-C2-3-A	D4	C2	< LOD		na
S21-05947-D5-C2-3-A	D5	C2	< LOD		na
S21-05947-D6-C2-3-A	D6	C2	< LOD		na
S21-05947-D3-T1-3-A	D3	T1	0.472	0.52	90.8%
S21-05947-D4-T1-3-A	D4	T1	0.456		87.7%
S21-05947-D5-T1-3-A	D5	T1	0.440		84.6%
S21-05947-D6-T1-3-A	D6	T1	0.438		84.2%
S21-05947-D3-T5-3-A	D3	T5	39.4	42.07	93.7%
S21-05947-D4-T5-3-A	D4	T5	38.7		92.0%
S21-05947-D5-T5-3-A	D5	T5	36.6		87.0%
S21-05947-D6-T5-3-A	D6	T5	38.4		91.3%

LOQ: 0.1 mg/kg; LOD: 0.03 mg/kg; na: not applicable

Residues are not corrected for procedural recoveries

C: Control (untreated); T1 and T5: Test item solutions taken on day 3 (D3), 4 (D4), 5 (D5) or 6 (D6); na: not applicable

An analytical verification of the test item during the exposure phase was performed. Recoveries were within the acceptable levels.

Treatment Group [mg t.i./kg diet]		Cumulative Mortality [%]						
		D4	D5	D6	D7	D8	D15	D22
C1	[-]	0.0	8.3	8.3	10.4	10.4	12.5	12.5
C2	[-]	2.1	8.3	8.3	10.4	10.4	10.4	14.6
T1	[0.53]	0.0	6.3	6.3	8.3	8.3	20.8	20.8
T2	[1.59]	0.0	0.0	0.0	2.1	4.2	12.5	12.5
T3	[4.76]	0.0	2.1	2.1	2.1	4.2	14.6	14.6
T4	[14.28]	2.1	4.2	6.3	10.4	10.4	14.6	14.6
T5	[42.85]	0.0	14.6	35.4	39.6	39.6	47.9	50.0
R	[48.00] ^a	20.8	68.8	91.7	93.8	93.8	100.0	100.0

t.i.: test item (Folpet Technical).

^a mg dimethoate/kg diet.

Treatment Group [mg t.i./kg diet]		Corrected Mortality [%] ^a						
		D4	D5	D6	D7	D8	D15	D22
C1	[-]	-2.1	0.0	0.0	0.0	0.0	2.3	-2.4
T1	[0.53]	-2.1	-2.3	-2.3	-2.3	-2.3	11.6	7.3
T2	[1.59]	-2.1	-9.1	-9.1	-9.3	-7.0	2.3	-2.4
T3	[4.76]	-2.1	-6.8	-6.8	-9.3	-7.0	4.7	0.0
T4	[14.28]	0.0	-4.5	-2.3	0.0	0.0	4.7	0.0
T5	[42.85]	-2.1	6.8	29.5	32.6	32.6	41.9	41.5

t.i.: test item (Folpet Technical).

^a Corrected for solvent control according to Abbott's formula (1925) modified by Schneider-Orelli (1947).

The No Observed Effect Concentration (NOEC) for emergence at 22 days was determined to be 14.28 mg test item/kg diet (corresponding to 14.02 mg active substance/kg diet according to the certificate of analysis). The corresponding No Observed Effect Dose (NOED), based on the total amount of diet supplied to the larvae, was determined to be 2.20 µg test item/larva (corresponding to 2.16 µg active substance/larva according to the certificate of analysis).

The Lowest Observed Effect Concentration (LOEC) for emergence at 22 days was determined to be 42.85 mg test item/kg diet (corresponding to 42.07 mg active substance/kg diet according to the certificate of analysis). The corresponding Lowest Observed Effect Dose (LOED), based on the total amount of diet supplied to the larvae, was determined to be 6.60 µg test item/larva (corresponding to 6.48 µg active substance/larva according to the certificate of analysis).

Results did not allow to calculate reliable EC10/20/50 values with 95 % confidence limits for emergence on day 22 (D22).

Since no corrected mortalities higher than 50 % were recorded, the EC50 was considered to be higher than the highest tested concentration (42.85 mg test item/kg diet, corresponding to 42.07 mg active substance/kg diet according to the certificate of analysis). The corresponding ED50 was considered to be higher than the highest tested dose (6.60 µg test item/larva, corresponding to 6.48 µg active substance/larva according to the certificate of analysis).

Conclusion

The repeated exposure of the test item 'Folpet Technical' to honey bee (*Apis mellifera* L.) was tested under laboratory conditions over a 21-day period.

All validity criteria were met and sensitivity of the test organisms was confirmed.

Accordingly, the study was deemed valid.

The test item concentrations were analytically confirmed and therefore the concentrations/doses were based on nominal values.

Main endpoints of the study are shown in the following table.

Endpoints

Endpoints	Concentration	Dose
NOEC/NOED	14.28 mg t.i./kg diet 14.02 mg a.s./kg diet ^a	2.20 µg t.i./larva ^b 2.16 µg a.s./larva ^{a, b}
LOEC/LOED	42.85 mg t.i./kg diet 42.07 mg a.s./kg diet ^a	6.60 µg t.i./larva ^b 6.48 µg a.s./larva ^{a, b}
EC10 / ED10	n.d.	n.d.
EC20 / ED20	n.d.	n.d.
EC50 / ED50	> 42.85 mg t.i./kg diet > 42.07 mg a.s./kg diet ^a	> 6.60 µg t.i./larva ^b > 6.48 µg a.s./larva ^{a, b}

t.i.: test item (Folpet Technical); a.s.: active substance (folpet); n.d.: not determined because no clear dose/response was found.

^a Based on the active substance content (folpet: 98.2 % w/w).

^b Based on the cumulative application volume of 140 µL/larva.

Validity criteria

The study was considered valid since validity criteria for both control and reference item groups mortality were met.

Control	The cumulative larval mortality from day 3 (D3) until day 8 (D8) was ≤ 15 % across all replicates (actual mean value 10.4 % for both the negative and the solvent control). On day 22 (D22) the adult emergence rate was ≥ 70 % across all replicates (actual mean value 87.5 % for the negative control and 85.4 % for the solvent control).
Refer- ence	The cumulative larval mortality was ≥ 50 % across all replicates on day 8 (D8) (actual mean value 93.8 %).

A 2.3.1.4	KCP 10.3.1.4	Sub-lethal effects
A 2.3.1.5	KCP 10.3.1.5	Cage and tunnel tests
A 2.3.1.6	KCP 10.3.1.6	Field tests with honeybees

A 2.3.2 KCP 10.3.2 Effects on non-target arthropods other than bees
A 2.3.2.1 KCP 10.3.2.1 Standard laboratory testing for non-target arthropods
A 2.3.2.1.1 Study 1

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal of the a.s.- folpet: Based on the evaluation, the laboratory glass plate toxicity test conducted with the predatory mite <i>T. pyri</i> is considered valid.</p> <p>7 d LR₅₀ = 3.759 kg product 80 WG /ha, corresponding to 3.064 kg a.s./ha.</p> <p>The RMS PL agrees with the evaluation. The results are not considered in the risk assessment for current product.</p>
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Reference:	KCP 10.3.2.1/01
Report	Effects of Folpet 80 WG on the Predatory Mite <i>Typhlodromus pyri</i> in the Laboratory – dose response test, Moll, M., 2007, Report No. 33895063
Guideline(s):	Yes, based on Blümel <i>et al.</i> , 2000
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The purpose of this study was to produce a concentration-response curve for mortality effects seen over 7 days of exposure. From these the LR50 value was calculated. The effect of Folpet 80 WG on the predatory mite *Typhlodromus pyri* was measured in the laboratory via contact on treated glass surfaces, compared to a water treated control and to a toxic reference item.

Typhlodromus pyri is recommended as one of the most sensitive standard species for non-target arthropod regulatory testing for plant protection products (Candolfi *et al.* 2001).

Materials and methods

Test item:	Folpet 80 WG; batch no. M-BOA; content of a.s.: Folpet: 80.0 % (nominal), 81.5 % w/w (analysed).
Test species:	Predatory Mite (<i>Typhlodromus pyri</i>), protonymphs less than 24 hours old; source: Katz Biotech AG, Baruth, Germany.
Test design:	This study encompassed 7 treatment groups (5 dose rates of the test item, control, reference item) with 3 replicates each containing 20 mites. The mites were exposed to dried residues on treated glass plates. Survival of the mites were assessed after 3 and 7 days.
Endpoints:	Mortality after 7 days of exposure; LR50: lethal rate producing 50 % mortality after exposure over 7 days.
Reference item:	Perfekthion (Dimethoate, 414.4 g/L (nominal: 400 g/L)).
Test rates:	Control, 536, 1002, 1875, 3508 and 6563 g product/ha and reference item. The reference item was applied at an application rate of 8.0 mL Perfekthion/ha. All treatments were applied in 200 L water/ha. The spraying dilutions were sprayed onto glass plates via laboratory spraying equipment, which were then air dried.
Test conditions:	Temperature: 24 °C – 25 °C; relative humidity: 60 % - 82 %; photoperiod: 16 h light

Statistics: : 8 h dark; light intensity: 480 lux – 1280 lux.
Mortality: Fisher Exact Test, LR50: Probit-Analysis

Results and discussions

All study validity criteria were met.

In the different Folpet 80 WG treatment groups mortalities between 10.0 % and 80.0 % were observed. This results in corrected mortalities between 1.8 % and 78.2 %. At 536, 1002 and 1875 g product/ha mortality was not statistically significantly different and at 3508 and 6563 g product/ha mortality was statistically significantly different compared to the control where 8.3 % mortality was observed (Fisher Exact Test, $\alpha = 0.05$).

The LR50 was determined to be 3759 g product/ha, the lower 95 % confidence limit was 3197 g product/ha, the upper 95 % confidence limit was 4420 g product/ha.

The results are summarized in the table below.

Table. Effects of Folpet 80 WG on mortality of the predatory mite, *Typhlodromus pyri*, exposed to fresh dried residue in the laboratory

	Rate ¹⁾ [g/ha]	Mortality ²⁾ [%]	Corrected Mortality ³⁾ [%]
Control	0	8.3	--
Folpet 80 WG	536	10.0 n.s.	1.8
Folpet 80 WG	1002	15.0 n.s.	7.3
Folpet 80 WG	1875	18.3 n.s.	10.9
Folpet 80 WG	3508	53.3 *	49.1
Folpet 80 WG	6563	80.0 *	78.2
Endpoint ⁴⁾			
LR50 (95 % CL): 3759 g product/ha (3197 – 4420 g product/ha)			

1) Application rate in 200 L water/ha

2) Mortality: after 7 days of exposure to spray residues on glass plates (Fisher Exact Test, $\alpha = 0.05$: n.s. = not significant, * = significant)

3) Corrected mortality according to Abbott and improvements by Schneider-Orelli

4) LR50 was calculated with Probit Analysis; CL = confidence limits

The reference item applied at a rate of 8.0 mL Perfekthion/ha produced a statistically significant mortality of 100.0 % after 7 days.

Conclusion

Under worst case laboratory conditions, the LR50 of Folpet 80 WG is 3759 g product/ha (95 % confidence limits: 3197 – 4420 g product/ha) in 200 L water/ha.

Validity criteria

Control Mortality: 8.3 %, validity criterion was met

Reference Item Mortality: 100.0 % corrected mortality, validity criterion was met

A 2.3.2.1.2 Study 2

Comments of zRMS:	<p>The study is considered reliable as all validity criteria were met.</p> <p>48 h LR₅₀ = 8.0 kg product Folpet 80 WG/ha</p> <p>The study is not considered in the risk assessment for the current formulation.</p>
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Reference: KCP 10.3.2.1/02

Report A laboratory test to determine the LR50 of the formulation “FOLPET 80 WG” (Folpet 800 g/kg, WG) on the parasitic wasp *Aphidius rhopalosiphi* (Hymenoptera: Braconidae), Luna, F., 2015, Report No. TRC14.253BA

Guideline(s): Yes, based on Mead-Briggs M.A. *et al.*, 2000

Deviations:	Yes, 1. The number of females and males introduced in the test units was 5 : 5 instead of 7 : 3 as the Study Plan indicates, due to there were not enough females available at the start of the exposure. No problems for the reproduction performance were observed, since more than 15 surviving females per treatment were obtained in the control and all test item groups. 2. Relative humidity was recorded outside the range established in the study plan of 60 to 90% for more than 2 hours continuously during the mortality period (48 hours of exposure). The relative humidity was recorded between 66.1% and 99.1% during the first and second day of the mortality period. The above mentioned deviations were considered by the Study Director to have not had any adverse effect on the outcome of the study.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

A standard laboratory study was carried out to generate data on dose-response toxicity of the formulation “FOLPET 80 WG” (Folpet 800 g/kg, WG) to *Aphidius rhopalosiphi* DeStephani Perez (Hymenoptera: Braconidae) under laboratory conditions in order to calculate the LR₅₀-values (application dose leading to 50 % mortality of the exposed organisms) and fecundity (number of offspring per surviving female). The application of test substance and exposure of the parasitoids was performed using glass plates as the test substrate.

The study was carried out under GLP conditions and according to OECD Good Laboratory Practice Standards. The trial was codified as TRC14-253BA. The protocol was employed using appropriate SOP's and conducted under the guideline: “A laboratory test for evaluating the effects of plant protection products on the parasitic wasp, *Aphidius rhopalosiphi* DeStephani-Perez (Hymenoptera: Braconidae)” (Mead-Briggs M.A. et al. 2000).

The endpoints were the following:

1. To study the mortality at 48 hours after application (lethal effect).
2. To study the fecundity of the survival females during one day in the presence of their hosts.

Materials and methods

Test Substance

“FOLPET 80 WG” (Folpet 800 g/kg, WG)

Batch: I-GVA;

Purity: 80% w/w (800 g folpet /kg)

Expiry: July 2016.

Test design

The proposed rates were obtained according to results from a preliminary non GLP range-finder test. A range of five rates of the test substance from 0.5 to 8.0 kg/ha of formulated product (FP) were sprayed with a laboratory track sprayer based on an application volume equivalent to 200 L/ha. *A. rhopalosiphi* were exposed for 48-h to freshly dried residues on glass plates. The test included, and was validated with a water control treatment and a reference substance (Dimethoate 400 g/L EC at 0.3 mL/ha) treatment.

For the mortality test, the exposure test unit (arenas) consisted of two treated glass plates (10x10 cm) fitted treated surface inwards to a square metal frame (with holes in each side) to which an air supply was connected to avoid pesticide vapour build-up. Four replicates for each treatment were used and 10 adult wasps per replicate were placed in each arena. Once the wasps were introduced in the arenas, the test units were placed into an environmental chamber at 20 ± 2 °C, 60-90% RH, with a 16:8h light-dark (L:D) photoperiod.

Assessments

Mortality assessments were carried out after 2, 24 and 48 hours of exposure. To assess any effects on the relative fecundity of the surviving insects, 15 surviving females per treatment were taken after the mortality

phase. This was possible with all five tested rates. These females were individually confined inside pots of aphid-infested cereal plants enclosed in plastic ventilated cylinders. After a period of 24h, females were removed again and the survivors were disposed of by means of freezing. The parasitized aphids within the fecundity arenas were left to develop in situ and the number of aphid mummies that developed was recorded 11 days after parasitization. Fecundity was expressed as number of mummies per female.

Results and discussions

Less than 10% mortality (5%) and acceptable reproductive capacity (34.13 mummies per female) were observed during the 48-hour exposure period and subsequent fecundity assessment in the control group. The toxic reference substance produced 87.50% mortality and confirmed the sensitivity of the test species and the test conditions.

Under these laboratory test conditions, the 48-hour LR₅₀ for the test product “FOLPET 80 WG” (Folpet 800 g/kg, WG) on the parasitic wasp *Aphidius rhopalosiphi* was estimated to be greater than the maximum assayed rate 8.0 kg FP/ha, equivalent to 6400 g folpet /ha (according to the analytical certificate), as corrected mortality was 23.68% compared to the control. Significant differences on mortality were found for the assayed rates 4.0 and 8.0 kg FP/ha (18.42% and 23.68% corrected mortality respectively).

No significant effects on the reproductive capacity of the parasitic wasp, *Aphidius rhopalosiphi*, were found for the assayed rates, 0.5 to 8.0 kg FP/ha (maximum 13.67% reduction compared to the control at the rate of 4.0 kg FP /ha). Therefore, the NOER (no-observed-effect rate) based on reproductive capacity was 8.0 kg FP /ha.

TRT	Product	Rate Kg product/ha	Mortality ⁽¹⁾ (%)	Corrected ⁽²⁾ mortality (%)	Fecundity Mummies per fe- male	% reduction ⁽²⁾
C	Control	0	5.0	--	34.13	--
T1	“FOLPET 80 WG” (Folpet 800 g/kg, WG)	0.5	0.0	-5.26	39.00	-14.26
T2		1.0	2.5	-2.63	35.53	-4.10
T3		2.0	12.5	7.89	32.29	5.41
T4		4.0	22.5*	18.42	29.47	13.67
T5		8.0	27.5*	23.68	31.14	8.76
R	Dimethoate 40% EC	0.3 mL/ha	87.5	86.84	--	--

(1): *= Significantly different compared to the water control (Jonckheere-Terpstra test, exact sig., 1-tailed).

Mortality of the reference product (R) was not statistically analyzed.

(2): Negative value indicates a decrease (mortality) or an increase (reproduction) compared to the control.

Conclusion

Less than 13% mortality (5%) and acceptable reproductive capacity (34.13 mummies per female) were observed during the 48-hour exposure period and subsequent fecundity assessment in the control group. The toxic reference substance produced 87.50% mortality and confirmed the sensitivity of the test species and the test conditions. The test is therefore judged as valid.

Under the laboratory test conditions, the 48 hour LR₅₀ of the test product “FOLPET 80 WG” (Folpet 800 g/kg, WG) on the parasitic wasp *Aphidius rhopalosiphi* was estimated to be greater than the maximum assayed rate 8.0 kg FP/ha, equivalent to 6400 g folpet /ha (according to the analytical certificate), as corrected mortality was 23.68% compared to the control. Significant differences on mortality were found for the assayed rates of 4.0 and 8.0 kg FP/ha (18.42% and 23.68% corrected mortality, respectively compared to control).

No significant effects on the reproductive capacity of the parasitic wasp, *Aphidius rhopalosiphi*, were found for the assayed rates of 0.5 to 8.0 kg FP/ha (maximum 13.67% reduction compared to the control at the rate of 4.0 kg /ha, and 8.76% reduction at 8 kg FP/ha, the highest dose tested). Therefore, the NOER (no-observed-effect rate) based on reproductive capacity was 8.0 kg FP /ha.

Validity criteria

For the test to be considered valid, the following performance criteria (Mead-Briggs *et al.* 2000) must be met:

- The 48-h mortality in the control treatment should not exceed 13%.

- The minimum value for reproduction is 5 mummies per female and no more than 2 females resulting in 0 mummies.
- The mortality in the reference substance should range from 50% to 100%.

A 2.3.2.1.3 Study 3

Comments of zRMS:	The study is considered reliable as all validity criteria were met. LR ₅₀ > 4000 g a.s./ha
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Reference:	KCP 10.3.2.1/03
Report	SAP50SCF (Folpet 500 SC): Toxicity to the Predatory Mite, <i>Typhlodromus pyri</i> Scheuten (Acari, Phytoseiidae) under Standard Laboratory Conditions, Luna, F., 2023, Report No. S23-100376
Guideline(s):	Yes, IOBC/WPRS (Blümel <i>et al.</i> , 2000) and Grimm, C. <i>et al.</i> (2001)
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The objective of the study was to determine the effects of SAP50SCF (Folpet 500 SC) on mortality and reproduction of the predatory mite *Typhlodromus pyri* Scheuten under standard laboratory conditions (exposure on glass plates); to determine the rate causing 50 % mortality (LR50) and 50 % reduction in reproduction (ER50), and to determine the No Observed Effect Rate (NOER), where possible.

Typhlodromus pyri was selected because it is a recommended sensitive indicator species for testing the side effects of plant protection products on non-target arthropods and it is one of the two standard species required for EU registration.

Materials and methods

Test item: SAP50SCF (Folpet 500 SC)
Batch No. 22C3310A
Content of a.i. (nominal): 500 g/L.
Content of a.i. (analysed): 517 g/L

Reference item: Dimethoate 40 % w/v EC; BAS 152 65 I
Batch No. 10248664A
Content of a.i. (nominal/analysed): 400.0 / 420.1 g/L

Test species: *Typhlodromus pyri* Scheuten,
Life stage at test start: protonymphs (\leq 24 hours old)

Endpoints: LR50 (median Lethal Rate) and ER50 (median Effect Rate), where possible.
The No Observed Effect Rate (NOER), where possible.

Test design: Test and reference items were diluted in deionised water and applied with a laboratory track sprayer to glass plates. A control group applied with deionised water was included in the study. All applications were performed with a spray volume of 200 L/ha. After assembling the test units, twenty protonymphs of *Typhlodromus pyri* were introduced into each test unit (5 replicates per treatment). Direct

treatment effects (mortality) and any change in behaviour, with respect to the control, were assessed after 1, 3 and 7 days. Reproduction was assessed on days 9, 11 and 14 for the control group and each test item group, where the corrected mortality was equal to or less than 50 %.

Test rates: SAP50SCF (Folpet 500 SC): 170.75, 375.66, 826.45, 1818.18 and 4000.00 g folpet/ha equivalent to 0.33, 0.73, 1.60, 3.52 and 7.74 L test item/ha (according to the analytical concentration).
Dimethoate 40 % w/v EC: 3.78 g dimethoate /ha equivalent to 0.009 L reference item/ha (according to the analytical concentration).

Test conditions: Temperature: 24.4 – 25.0° C

Relative humidity: 57.5 – 78.8 % *

*: Humidity below 60 % was not registered for longer than 2 hours continuously, not considered deviation

Light regime: 16 h light / 8 h darkness

Light intensity: 1426 - 1513 lux during exposure

Statistics: Step-down Cochran-Armitage Test with survival/escaped individuals at 7 d (one-sided greater, $\alpha = 0.05$) was used to detect significant differences between mortality data of the test item groups and the control in order to determine the NOER for lethal effects, after performing a qualitative trend by contrasts (monotonicity of rate/response); this analysis of contrasts revealed a linear trend.

It was not possible to determine the LR50 by probit or any other analysis since mortality data with the tested rates of the test item were less than 50%.

Reproduction data were not necessary to be statistically studied since the cumulative offspring/female at 14 d was higher in the test item treatment groups in comparison to the control group and therefore, it was not possible to determine the 14-day-ER50.

Dates of work: 20 February – 06 March 2023 [Experimental Phase]

Results and discussions

Treatment	Rates ^a [g a.i./ha]	Mean mortality ^b [%]	Corrected mortality [%]	Reproduction [eggs/female]	Reduction in reproduction rate ^c [%]
Control (deionised water)	--	9.00	--	7.00	--
Test item SAP50SCF (Folpet 500 SC)	170.75	9.00	0.00	7.66	-9.52
	375.66	15.00	6.59	7.60	-8.59
	826.45	25.00 ^{sd}	17.58	7.73	-10.53
	1818.18	29.00 ^{sd}	21.98	7.08	-1.27
	4000.00	44.00 ^{sd}	38.46	7.17	-2.50
Reference item Dimethoate 40% w/v EC	3.78	94.00	93.41	--	--

a Rates in g of active ingredient /ha

b sd: Statistically significantly increased compared to control (Step-down Cochran-Armitage Test with *Typhlodromus pyri* (mortality) at 7 d, one-sided greater, $\alpha = 0.05$)

c Negative values indicate an increase in number of eggs per female when compared to control

Conclusion

The study was conducted as a rate response test under standard laboratory test conditions with seven treatment groups on *Typhlodromus pyri*, including the test item SAP50SCF (Folpet 500 SC) at five application rates, the reference item (Dimethoate 40 % w/v EC) at a single application rate and the control applied with deionised water.

Mortality below 20% (9.0%) was achieved 7 days after the application, and an acceptable reproductive capacity (7.00 eggs/female) was assessed over a further 7 days in the control group, meeting the validity criteria. The toxic reference product caused 93.41 % mortality (corrected relative to control) and confirmed the sensitivity of the test species and the test conditions.

Under these standard laboratory test conditions, LR50 (rate producing 50 % mortality) was estimated to be

greater than the maximum tested rate of 4000.00 g folpet/ha (equivalent to 7.74 L test item/ha, according to the analysed content).

The 14-day-ER₅₀ (rate causing 50 % reduction in reproduction) was estimated to be greater than 4000.00 g folpet/ha (equivalent to 7.74 L test item/ha, according to the analysed content) based on the results in reproduction relative to the control, since the cumulative offspring/female at 14 d was higher in the test item treatment groups in comparison to the control group.

The LOER (Lowest Observed Effect Rate when compared to the control) for lethal effects was determined in 826.45 g folpet/ha (equivalent to 1.60 L test item/ha, according to the analysed content) since significant effects were obtained when compared to the control group at the tested rates of 826.45 to 4000.00 g folpet/ha test item/ha (Step-down Cochran-Armitage Test, one-sided greater, $\alpha = 0.05$). The NOER (No Observed Effect Rate when compared to the control) for lethal effects was therefore determined in 375.66 g folpet/ha (equivalent to 0.73 L test item/ha, according to the analysed content).

The NOER for sub-lethal effects (cumulative offspring/female) was estimated as higher than or equal to 4000.00 g folpet/ha (equivalent to 7.74 L test item/ha according to the analysed content) since the cumulative offspring/female at 14 d was even higher in the test item treatment groups than in the control group.

Endpoint	Rate	
	[g folpet/ha] a	[L test item/ha] b
LR ₅₀	n.d.; > 4000.00	n.d.; > 7.74
ER ₅₀	n.d.; > 4000.00	n.d.; > 7.74
LOER (mortality)	826.45	1.60
NOER (mortality)	375.66	0.73
NOER (reproduction)	n.d.; \geq 4000.00	n.d.; \geq 7.74

a Rate in g of active ingredient/ha

b Equivalent rate in L of formulated product/ha according to the certificate of analysis (Folpet 517 g/L)

n.d.: not determined

Validity criteria

Control mortality	The mean mortality (dead and escaped individuals) in the control should be \leq 20 % on day 7 of exposure (actual: 9.0 % mortality).
Reference item mortality	The corrected cumulative mean mortality in the reference item group should range between 50 % and 100 % on day 7 after application (actual: 93.41 % corrected mortality).
Control reproduction	The cumulative mean number of eggs per female in the control (from day 7 to day 14) should be \geq 4.0 eggs/female (actual: 7.00 eggs/female).

A 2.3.2.1.4 Study 4

Comments of zRMS:	The study is considered reliable as all validity criteria were met. LR ₅₀ > 1809.50 g a.s./ha ER ₅₀ < 452.38 g a.s./ha
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Reference:	KCP 10.3.2.1/04
Report	SAP50SCF (Folpet 500 SC): Toxicity to the Aphid Parasitoid <i>Aphidius rhopalosiphi</i> De Stefani Perez (Hymenoptera, Braconidae) under Laboratory Conditions, Varela, S., 2023, Report No. S23-102835
Guideline(s):	Yes, IOBC (Mead-Briggs, M. A. <i>et al.</i> , 2000)
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Duplication N/A
(if vertebrate study)

Objective

The objectives of the study were to determine the effects of SAP50SCF (Folpet 500 SC) on mortality and reproduction of the parasitoid *Aphidius rhopalosiphi* De Stefani Perez under worst-case laboratory conditions (exposure to glass plates) and to establish the rate producing 50 % mortality (LR₅₀), the 50 % reduction in reproduction rate (ER₅₀) and the No Observed Effect Rate (NOER), where possible.

Aphidius rhopalosiphi De Stefani Perez was selected because it is a recommended sensitive indicator species for testing the side effects of plant protection products on non-target arthropods and it is one of the two standard species required for EU registration.

Materials and methods

Test item:	SAP50SCF (Folpet 500 SC) Batch No.: 22C3310A Content of active ingredient (a.i.) (nominal / analysed): 500 / 517 g folpet/L
Reference item:	Dimethoate 40 % w/v EC; BAS 152 65 I Batch No. 10248664A Content of a.i. (nominal / analysed): 400.0 / 420.1 g/L
Test rates:	SAP50SCF (Folpet 500 SC): 113.09, 226.19, 452.38, 904.75 and 1809.50 g folpet/ha (Equivalent to 0.22, 0.44, 0.88, 1.75 and 3.50 L test item/ha, according to the analytical concentration, and calculated using unrounded values from highest to lowest value according to a geometric series with a factor of 2). Dimethoate 40 % w/v EC: 0.126 g dimethoate /ha (Equivalent to 0.0003 L of reference item/ha, according to the analytical concentration).
Test species:	<i>Aphidius rhopalosiphi</i> De Stefani Perez, Life stage at start of exposure: adult wasps (less than 48 hours old)
Endpoints:	LR ₅₀ (median Lethal Rate) and ER ₅₀ (median Effect Rate), where possible. The No Observed Effect Rate (NOER), where possible.
Test design:	Test and reference items were diluted in deionised water and applied with a laboratory track sprayer to glass plates. A control group applied with deionised water was included in the study. All applications were performed with a spray volume of 200 L/ha. After assembling of test units, ten adult wasps were introduced into each test unit (4 replicates per treatment). The repellent effect of the test item on the wasps was assessed once during the initial three hours after their release. Direct effects of treatment and any behavioral changes relative to control were assessed at approximately 2, 24, and hours. Reproduction (mummies/female) was assessed 11 days following a 24-hour parasitisation period. Reproduction was assessed for the control group and each test item group, where the corrected mortality was below 50%.
Test conditions:	Temperature: 20.1 – 21.3 °C Relative humidity: 73.5 – 85.4 % Light regime: 16 h light / 8 h darkness Light intensity: 1323 – 1436 lux during mortality 1653 – 2344 lux during parasitisation 8171 – 11098 lux during development of mummies
Statistics:	It was not possible to determine the LR ₅₀ by probit or any other analysis since corrected mortality data with the tested rates of the test item were less than 50 %. Step-down Rao-Scott-Cochran-Armitage Test Procedure with survival at 48 h (one-sided greater, $\alpha = 0.05$) was used to detect significant differences between response data of the test item groups and the control group in order to determine the NOER for lethal effects, after performing a qualitative trend by contrasts (monotonicity of rate/response); this analysis of contrasts revealed a linear trend and extra binomial variance resulted probable after Tarone's Test.

Chi² 2x2 Test with Bonferroni Correction was used with repellency (adults not seen on the treated glasses) in order to study any significant difference to the control as repellence effect; the analysis of contrasts did not reveal a linear trend.

Reduction of reproduction was above than 50% from the tested rate of 452.38 g a.i./ha, however it was not possible to determine the ER₅₀ by probit or any other analysis since not reliable confidence limits were obtained due to the small size of samples. Only three treatment groups could be included in the statistical analyses, those treatments groups in which at least 15 female wasps were recovered after parasitisation phase, control, T1 and T3.

Reproduction data met normality (Shapiro-Wilk's Test) and homoscedasticity (Levene Test) was passed. The analysis of contrasts revealed a linear trend, thus the Williams Multiple sequential t-test with number of offspring at 14 d (one-sided smaller, $\alpha = 0.05$) was used.

Dates of work: 25 Jul 2023 – 08 Aug 2023 [Experimental Phase]

Results and discussions

Treatment	Rates [g a.i./ha] ^a	Mean mortality [%] ^b	Corrected mortality [%]	Reproduction [eggs/female]	Reduction in repro- duction rate ^c [%]
Control (deionised water)	--	2.50	--	40.87	--
Test item SAP50SCF (Folpet 500 SC)	113.09	10.00	7.69	31.64	22.57
	226.19	27.50 ^{sd}	25.64	23.45	42.61
	452.38	17.50 ^{sd}	15.38	12.67 ^{sd}	69.00
	904.75	37.50 ^{sd}	35.90	19.50	52.28
	1809.50	40.00 ^{sd}	38.46	15.71	61.55
Reference item Dimethoate 40% w/v EC	0.126	100.00	100.00	--	--

a Rates of the test and reference items in g of active ingredient (a.i.)/ha.

b sd: Statistically significant increased compared to the control (Step-down Rao-Scott-Cochran-Armitage test, one-sided greater, $\alpha=0.05$).

c sd: Statistically significant increased compared to the control (Williams Multiple Sequential t-test, one-sided smaller, $\alpha=0.05$). Only control, T1 and T3 treatment groups were included in the statistical analysis.

Conclusion

The study was conducted as a rate response test under laboratory conditions with seven treatment groups on *Aphidius rhopalosiphii* De Stefani Perez, including the test item SAP50SCF (Folpet 500 SC) at five application rates, the reference item (Dimethoate 40 % w/v EC) at a single application rate and the control, applied with deionised water.

Mortality less than 13 % (2.50 %) and acceptable reproductive capacity (40.87 mummies per female and two females producing 0 mummies) were observed during the 48-hour exposure period and subsequent fecundity assessment in the control group.

The toxic reference item caused 100.00 % corrected mortality and confirmed the sensitivity of the test species and the test conditions.

Under these standard laboratory test conditions, LR₅₀ was estimated to be greater than the maximum tested rate of 1809.50 g folpet/ha (equivalent to 3.50 L test item/ha according to the analysed content).

Less than 15 female wasps were recovered from parasitisation phase in treatments T2, T4 and T5, with 11, 13 and 7 female wasps, respectively. Therefore, statistical analyses were only performed for control, T1 and T3 treatments.

It was not possible to determine the ER₅₀ based on the reproductive capacity (estimated application rate at which the fecundity is reduced by 50 % as compared to the control) by probit or any other analysis. Not reliable confidence limits were obtained due to the small size of samples (only three treatments groups with 15 females) and ER₅₀ was estimated to be below 452.38 g folpet/ha, equivalent to 0.88 L test item/ha, according to the analysed content.

The LOER (Lowest Observed Effect Rate when compared to the control) for lethal effects was determined

in 226.19 g folpet/ha (equivalent to 0.44 L test item/ha, according to the analysed content) since significant effects were obtained when compared to the control group at the tested rates from 226.19 to 1809.50 g folpet/ha (Step-down Rao-Scott-Cochran-Armitage Test, one-sided greater, $\alpha = 0.05$). The NOER (No Observed Effect Rate when compared to the control) for lethal effects was therefore determined in 113.09 g folpet/ha (equivalent to 0.22 L test item/ha, according to the analysed content).

Considering only control group, T1 and T3 treatments in the statistical analyses, the LOER for sublethal effects (fecundity) was determined in 452.38 g folpet/ha (equivalent to 0.88 L test item/ha, according to the analysed content) since significant effects was obtained when compared to the control group at this tested rate (Williams Multiple Sequential t-test, one-sided smaller, $\alpha=0.05$). The NOER for sublethal effects was determined in 113.09 g folpet/ha (equivalent to 0.22 L test item/ha, according to the analysed content).

SAP50SCF (Folpet 500 SC) on <i>Aphidius rhopalosiphi</i> De Stefani Perez. Laboratory Conditions		
Endpoint	Rate	
	[g folpet/ha] ^a	[L test item/ha] ^b
LR ₅₀ ^c	n.d.; [> 1809.50]	n.d.; [> 3.50]
ER ₅₀ ^d	n.d.; [< 452.38]	n.d.; [< 0.88]
LOER (mortality) ^e	226.19	0.44
NOER (mortality) ^e	113.09	0.22
LOER (reproduction) ^f	452.38	0.88
NOER (reproduction) ^f	113.09	0.22

a Rate in g active ingredient/ha

b Formulated product content according to the Certificate of Analysis (517 g folpet /L)

c n.d.: not determined as corrected mortality was below 50% up to and including 1809.50 g folpet/ha (relative to the control)

d n.d.: not determined as only control, T1 and T3 treatment groups recovered at least 15 female wasps from parasitisation period

e According to the Step-down Rao-Scott-Cochran-Armitage test, one-sided greater, $\alpha=0.05$

f According to the Williams Multiple Sequential t-test, one-sided smaller, $\alpha=0.05$. Only control, and T1 (113.09 g folpet/ha) and T3 (452.38 g folpet/ha) treatment groups were included in the statistical analysis

Validity criteria

Control mortality	The mean mortality in control should be ≤ 13 % after 48 hours of exposure (actual: 2.50 %).
Reference item mortality	The reference item should cause cumulative corrected 48-hour mortality ≥ 50 % (actual: 100.00 %).
Control reproduction	The mean number of mummies per female in the control should be ≥ 5.0 mummies/female (actual: 40.87). No more than 2 females should fail to produce mummies (actual: 2 females).

A 2.3.2.2 KCP 10.3.2.2 Extended laboratory testing, aged residue studies with non-target arthropods

A 2.3.2.2.1 Study 1

Comments of zRMS:	<p>The study is acceptable as all relevant validity criteria of the IOBC guideline were met.</p> <p>LR₅₀ > 5250 g a.s./ha</p> <p>There was no effect on reproduction up to and including 5250 g a.s./ha, the highest rate tested, compared to the control.</p>
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Reference:	KCP 10.3.2.2/01
Report	Effects of Folpet Sapec 500 SC on the Predatory Mite <i>Typhlodromus pyri</i> , Extended Laboratory Study – Dose Response Test, Schwarz, A., 2011, Report No. 63142062
Guideline(s):	Yes, based on Blümel <i>et al.</i> 2000 and Oomen 1998
Deviations:	Yes,

- Test conditions were not recorded for four days during reproduction due to a breakdown of the computer the data were not recorded
- The mentioned deviation has no presumed effect on the study as the air condition was running correctly.

GLP: Yes

Acceptability: Yes

Duplication (if vertebrate study) N/A

Objective

The purpose of this study was to produce a concentration-response curve for mortality effects seen over 7 days of exposure. From these the LR50 value was calculated. The effect of Folpet Sapec 500 SC on the predatory mite *Typhlodromus pyri* was measured via contact on treated leaf surfaces compared to a water treated control and to a reference item. Additionally, an assessment for significant sublethal effects (reproduction assessment) was done.

Typhlodromus pyri is recommended as one of the most sensitive standard species for non-target arthropod regulatory testing for plant protection products (Candolfi *et al.*, 2001).

Materials and methods

Test item: Folpet Sapec 500 SC; batch no.: C-MRA; content of a.s.: Folpet, 500 g/L.

Test species: Predatory mite (*Typhlodromus pyri*), protonymphs less than 24 hours old; source: Katz Biotech AG, Baruth, Germany.

Test design: This study encompassed 7 treatment groups (5 dose rates of the test item, control, reference item) with 6 replicates each containing 10 mites. The mites were exposed to dried residues on treated leaf surfaces (bean leaves). Survival of the mites was assessed after 3 and 7 days. For the reproduction assessment surviving mites from the control and from all test item groups where the corrected mortality was < 50 % were sexed and the number of eggs per females was recorded on 3 assessment days within one week.

Endpoints: Mortality after 7 days of exposure; LR50: lethal rate producing 50 % mortality after exposure over 7 days, additionally reproduction capacity for all variants with less than 50 % corrected mortality.

Reference item: Perfekthion (Dimethoate, 414.8 g/L (nominal: 400 g/L)).

Test rates: Control, 328, 656, 1312, 2625 and 5250 g a.s./ha and reference item. The reference item was applied at an application rate of 40 mL Perfekthion/ha. All treatments were applied in 200 L water/ha. The spraying dilutions were sprayed onto leaves via laboratory spraying equipment, which were then air dried.

Test conditions: Temperature: 23 °C – 27 °C; relative humidity: 66 % - 76 %; photoperiod: 16 h light : 8 h dark; light intensity: acclimatization: 990 lux; exposure: 210 lux – 940 lux.

Results and discussions

Table. Mortality and reproduction of *Typhlodromus pyri*

	Rate 1) [g a.s./ha]	Mortality 2) [%]	Mortality corr. 3) [%]	Reproduction 4) [eggs/female]	Effects on reproduction 5) [%]
Control	0	20.0	--	4.6	--
Folpet Sapec 500 SC	328	11.7 n.s.	-10.4	4.3 n.s.	7.6
Folpet Sapec 500 SC	656	21.7 n.s.	2.1	2.6 n.s.	43.8
Folpet Sapec 500 SC	1312	1.7 n.s.	-22.9	4.4 n.s.	4.6
Folpet Sapec 500 SC	2625	5.0 n.s.	-18.8	4.0 n.s.	13.0
Folpet Sapec 500 SC	5250	8.3 n.s.	-14.6	4.6 n.s.	1.7

Endpoint
LR50 > 5250 g a.s./ha
1) Application rate in 200 L water/ha
2) Mortality: after 7 days of exposure to spray residues on leaf surfaces (Fisher's Exact Test, $\alpha = 0.05$; n.s. = not significant)
3) Corrected mortality according to Abbott and improvements by Schneider-Orelli
4) Reproduction: mean number of eggs/female, (Dunnett's t-test, $\alpha = 0.05$; n.s. = not significant)
5) Calculated on the exact raw data

The reference item applied at a rate of 40 mL Perfekthion/ha produced a statistically significant mortality of 100.0 % after 7 days.

Conclusion

Under extended laboratory conditions the LR50 of Folpet Sapec 500 SC is estimated to be greater than 5250 g a.s./ha.

The reproductive capacity of *T. pyri* was tested at all dose rates. There was no effect on reproduction up to and including 5250 g a.s./ha, the highest rate tested, compared to the control.

Validity criteria

Control Mortality: 20.0 %, validity criterion was met

Reference Item Mortality: 100 % corrected mortality, validity criterion was met

Control Reproduction:

A 2.3.2.2.2 Study 2

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal: Based on the evaluation, the extended laboratory toxicity test conducted with the lacewing <i>Chrysoperla carnea</i> is considered valid.</p> <p>48 h LR₅₀ > 6.563 kg Folpet 80 WG/ha corresponding to 5.349 kg a.s./ha ER₅₀ > 6.563 kg Folpet 80 WG/ha corresponding to 5.349 kg a.s./ha</p> <p>The zRMS-PL agrees with the evaluation. The study is not considered in the risk assessment for current formulation.</p>
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Reference: KCP 10.3.2.2/02

Report Effects of Folpet 80 WG on the Lacewing *Chrysoperla carnea*, Extended Laboratory Study – Dose Response Test, Moll, M., 2007, Report No. 33898047

Guideline(s): Yes, based on Vogt *et al.* 2000

Deviations: No

GLP: Yes

Acceptability: Yes

Duplication (if vertebrate study) N/A

Objective

The purpose of this study was to determine the toxicity of Folpet 80 WG on the larvae of the lacewing *Chrysoperla carnea* in the laboratory through contact with substance-treated leaf surfaces (exposure period) compared to a water treated control and a reference item. Additionally an assessment for sublethal effects on reproduction of the survivors (reproduction) was made.

Chrysoperla carnea is recommended as standard species for non-target arthropod regulatory testing for

plant protection products (Candolfi *et al.* 2001).

Materials and methods

Test item:	Folpet 80 WG; batch no. M-BOA; content of a.s.: Folpet: 80.0 % (nominal), 81.5 % w/w (analysed).
Test species:	Lacewing (<i>Chrysoperla carnea</i>), larvae (2 to 3 days old); source: Katz Biotech AG, Baruth, Germany.
Test design:	This study encompassed 5 treatment groups (3 dose rates of the test item, control, reference item) with 40 replicates each containing 1 larva. The larvae were exposed to dried residues on treated leaf surfaces (bean leaves). Exposure time lasted as long as pupae were transferred to the reproduction units for development of adults. Mortality checks were carried out regularly until hatching of adult lacewings. In addition for the control and the test item treatment groups where the corrected mortality was < 50 % the reproduction performance, i.e. egg deposition and larval hatching rate, was determined (2 checks/week, 24 hours period each check).
Endpoints:	Larval and pupal mortality, additionally reproductive capacity for female survivors.
Reference item:	Perfekthion (Dimethoate, 414.4 g/L (nominal: 400 g/L)).
Test rates:	Control, 1875, 3508 and 6563 g product/ha and reference item. The reference item was applied at an application rate of 100 mL Perfekthion/ha. All treatments were applied in 400 L water/ha. The spraying dilutions were sprayed onto bean plants via laboratory spraying equipment, which were then air dried.
Test conditions:	Temperature: 23 °C – 27 °C; relative humidity: 60 % - 90 %; photoperiod: 16 h light : 8 h dark; light intensity: 1790 lux – 8030 lux.
Statistics:	Mortality: Fisher Exact Test

Results and discussions

All study validity criteria were met.

In the control and different Folpet 80 WG treatment groups mortalities between 5.0 % and 10.0 % were observed. This results in corrected mortalities of 0.0 % and 5.3 %. At all dose rates mortality was not statistically significant different compared to the control where 5.0 % mortality was observed (Fisher Exact Test, $\alpha = 0.05$). So there was no effect on mortality up to and including 6563 g product/ha.

Reproduction was > 15 eggs per female per day and the mean hatching rate was > 70 % at all dose rates (1875, 3508 and 6563 g product/ha). This indicates that there is no negative effect of the test item on reproductive performance of *Chrysoperla carnea* up to and including 6563 g product/ha.

The results are summarized in the table below.

Table. Effects of Folpet 80 WG on pre-imaginal mortality and reproduction of *Chrysoperla carnea*, exposed to fresh dried residue in the laboratory

	Rate [g/ha] 1)	Mortality [%] 2)	Mortality corr. [%] 3)	Reproduction [eggs/female/day]	Hatching rate [%]
Control	--	5.0	--	33.8	83.6
Folpet 80 WG	1875	10.0 n.s.	5.3	33.6	86.2
Folpet 80 WG	3508	7.5 n.s.	2.6	30.4	83.6
Folpet 80 WG	6563	5.0 n.s.	0.0	25.5	92.6

1) Application rate in 400 L deionised water/ha

2) Pre-imaginal mortality after exposure to spray residue on leaf surfaces (Fisher Exact Test, $\alpha = 0.05$; n.s. = not significant, * = significant)

3) Corrected pre-imaginal mortality according to Abbott and improvements by Schneider-Orelli

The reference item produced 62.5 % mortality (corrected mortality: 60.5 %) of exposed lacewings.

Conclusion

There was no effect on mortality and reproduction up to and including 6563 g product/ha, the highest dose rate tested.

Validity criteria

Control mortality: 5.0 %, validity criterion was met

Reference item mortality: 60.5 % corrected mortality, validity criterion was met
Fecundity in the control group: 33.8 eggs per female per day (mean number), validity criterion was met
Fertility in the control group: 83.6 % larval hatching rate (mean value), validity criterion was met.

A 2.3.2.2.3 Study 3

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal of the a.s.- folpet: Based on the evaluation, the extended laboratory toxicity test conducted with the ladybird beetle <i>C. septempunctata</i> is considered valid.</p> <p>48 h LR₅₀ > 6.563 kg Folpet 80 WG /ha corresponding to 5.349 kg a.s./ha ER₅₀ > 6.563 kg Folpet 80 WG /ha corresponding to 5.349 kg a.s./ha</p> <p>The zRMS -PL agrees with the evaluation. The study is not considered in the risk assessment for current formulation.</p>
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Reference: KCP 10.3.2.2/03
Report Effects of Folpet 80 WG on the Ladybird Beetle *Coccinella septempunctata*, Extended Laboratory Study – Dose Response Test, Moll, M., 2007, Report No. 33897012
Guideline(s): Yes, based on Schmuck *et al.* 2000
Deviations: No
GLP: Yes
Acceptability: Yes
Duplication N/A
(if vertebrate study)

Objective

The purpose of this study was to determine the toxicity of Folpet 80 WG on the ladybird beetle larvae and pupae of *C. septempunctata* in the laboratory through contact with substance-treated leaf surfaces (exposure period) compared to a water treated control and a reference item. Additionally an assessment for sublethal effects on reproduction of the survivors (reproduction) was made.

C. septempunctata is one of the general entomophagous predators. It is of cosmopolitan distribution and occurs in most crops and natural habitats. It is recommended as testing species for non-target arthropod regulatory testing for plant protection products (Candolfi *et al.* 2001).

Materials and methods

Test item: Folpet 80 WG; batch no. M-BOA; content of a.s.: Folpet: 80.0 % (nominal), 81.5 % w/w (analysed).
Test species: Ladybird beetle (*Coccinella septempunctata*), 4 – 5 days old larvae; source: Katz Biotech AG, Baruth, Germany.
Test design: This study encompassed 5 treatment groups (3 dose rates of the test item, control, reference item) with 40 replicates each and each containing 1 *C. septempunctata* larva. The larvae (4 – 5 days old) were exposed to dried residues on treated leaf surfaces (bean leaves). The duration of the pre-imaginal mortality part was 12 – 14 days. The reproductive performance of the survivors was examined over 2 weeks (oviposition period) using adults from the control and from those test item concentrations where the corrected mortality was < 50 %.
Endpoints: Pre-imaginal mortality of exposed larvae and pupae; LR50: lethal rate producing 50

	% mortality after exposure. Additionally reproductive capacity for adult survivors.
Reference item:	Perfekthion (Dimethoate, 414.4 g/L (nominal: 400 g/L)).
Test rates:	Control, 1875, 3508 and 6563 g product/ha and reference item. The reference item was applied at an application rate of 100 mL Perfekthion/ha. All treatments were applied in 400 L water/ha. The spraying dilutions were sprayed onto bean plants via laboratory spraying equipment, which were then air dried.
Test conditions:	Temperature: 23 °C – 27 °C; relative humidity: 60 % - 90 %; photoperiod: 16 h light : 8 h dark; light intensity: 1610 lux – 7280 lux.
Statistics:	Mortality: Fisher Exact Test, Reproduction: Welch-t-Test (eggs per female per day, fertile eggs per female per day), Dunnett-Test (larval hatching rate)

Results and discussions

All study validity criteria were met.

In the control and different Folpet 80 WG treatment groups mortalities between 0.0 % and 7.5 % were observed. This results in corrected mortalities of -5.3 % and 2.6 %. At all dose rates mortality was not statistically significant different compared to the control where 5.0 % mortality was observed (Fisher Exact Test, $\alpha = 0.05$). Therefore, there was no effect on mortality up to and including 6563 g product/ha.

Reproduction was > 2 fertile eggs per viable female per day in the control group and at dose rates of 1875, 3508 and 6563 g product/ha. There was no statistically significant difference in the reproduction rate between control and test item, and the reproductive output is within the historical data base for control beetles. Therefore, this parameter is considered as not impacted by the treatment (Schmuck *et al.* 2000) up to and including 6563 g product/ha.

The results are summarized in the table below.

Table. Pre-imaginal mortality and reproduction of *Coccinella septempunctata*

	Rate [g/ha] 1)	Mortality [%] 2)	Mortality corr. [%] 3)	Reproduction [fertile eggs per female per day] 4)
Control	--	5.0	--	10.1
Folpet 80 WG	1875	5.0 n.s.	0.0	10.5 n.s.
Folpet 80 WG	3508	0.0 n.s.	-5.3	11.2 n.s.
Folpet 80 WG	6563	7.5 n.s.	2.6	11.9 n.s.

1) Application rate in 400 L water/ha

2) Pre-imaginal mortality after exposure to spray residue on leaf surfaces (Fisher Exact Test, $\alpha = 0.05$: n.s. = not significant)

3) Corrected pre-imaginal mortality according to Abbott and improvements by Schneider-Orelli; negative value means lower mortality compared to the control

4) Reproduction: mean number of fertile eggs/female/day, (Welch-t-Test, $\alpha = 0.05$: n.s. = not significant)

The reference item produced 82.5 % mortality (corrected mortality: 81.6 %) of exposed ladybird beetles.

Conclusion

There was no effect on mortality and reproduction up to and including 6563 g product/ha, the highest dose rate tested.

Validity criteria

Control mortality:	5.0 %, validity criterion was met
Reference item mortality:	81.6 % (corrected mortality), validity criterion was met
Control reproduction rate:	10.1 fertile eggs per female per day (mean number), validity criterion was met

A 2.3.2.2.4 Study 4

Comments of zRMS:	<p>The study was evaluated at EU level in the context of the renewal of the active substance folpet.</p> <p>Conclusion of the RMS of the renewal of a.s.-folpet: Based on the evaluation, the extended laboratory toxicity test (aged residues) conducted with the parasitoid <i>A.rhopalosiphi</i> is considered valid.</p> <p>48 h LR₅₀ > 6.563 kg Folpet 80 WG /ha corresponding to 5.349 kg a.s./ha NOER = 6.563 kg Folpet 80 WG/ha corresponding to 5.349 kg a.s./ha The RMS PL agrees with the evaluation. The study is not considered in the risk assessment.</p>
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Reference:	KCP 10.3.2.2/04
Report	Effects of Folpet 80 WG on the Parasitoid <i>Aphidius rhopalosiphi</i> , Extended Laboratory Study – Aged Residue Test, Moll, M., 2007, Report No. 33899003
Guideline(s):	Yes, based on Mead-Briggs <i>et al.</i> 2000 and current improvements by the ring-test group (Mead-Briggs <i>et al.</i> 2002)
Deviations:	Yes, the age at test start was maximum 48 hours and 25 minutes instead of not older than 48 hours with no presumed effect on the study.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The purpose of this study was to determine acute toxicity of folpet 80 WG on the parasitoid *Aphidius rhopalosiphi* in the laboratory by contacting fresh and aged spray residues on bean leaves (*Phaseolus vulgaris* L.) compared to a water treated control and to a reference item. Additionally, an assessment for sub-lethal effects on parasitisation activity of the female survivors was made.

- A. *rhopalosiphi* is recommended as the most sensitive standard species for non-target arthropod regulatory testing for plant protection products (Barrett *et al.* 1994).

Materials and methods

Test item:	Folpet 80 WG; batch no. M-BOA; content of a.s.: Folpet: 80.0 % (nominal), 81.5 % w/w (analysed).
Test species:	Parasitoid (<i>Aphidius rhopalosiphi</i>), adults less than 48 hours old (reference item: less than 48 hours and 25 minutes old); source: Katz Biotech AG, Baruth, Germany.
Test design:	Two bioassays were performed in this aged residue study. The 1 st bioassay was started on the day of application and the 2 nd bioassay was started 13 days after application. The study encompassed 5 treatment groups (3 dose rates of the test item, control, reference item) in the 1 st bioassay and 4 treatment groups (3 dose rates of the test item, control) in the 2 nd bioassay with 4 replicates each containing 7 female and 3 male parasitoids. The parasitoids were exposed to freshly dried and aged residues on leaves from field treated bean plants. Survival of the parasitoids was assessed after 2, 24 and 48 hours. At 48 hours, for treatment groups with < 50 % corrected mortality survived females were removed and their reproductive capacity was assessed by confining them individually over untreated barley plants infested with the host cereal aphids, <i>Rhopalosiphum padi</i> . The adult parasitoids were removed after 24 hours and the aphid-infested plants left for further 11 days before the numbers of aphid mummies that had developed were assessed.
Endpoints:	Mortality of parasitoids after 48 h of exposure. Additionally reproductive capacity of

- female survivors.
- Reference item: Perfekthion (Dimethoate, 414.4 g/L (nominal: 400 g/L)).
- Test rates: Control, 1875, 3508 and 6563 g product/ha and reference item. The reference item was applied at an application rate of 50.0 mL Perfekthion/ha. All treatments were applied in 400 L water/ha. The test items were sprayed onto potted bean plants via field spraying equipment and air dried afterwards outdoors under natural conditions. The treated plants were protected against rain for 7 days after application.
- Test conditions: 1st and 2nd bioassay: Temperature: 18 °C – 22 °C; relative humidity: 70 % - 86 % (acclimatization, exposure and parasitisation period), 60 – 72 % (post-parasitisation period, within the test units); photoperiod: 16 h light : 8 h dark; light intensity: 400 lux – 6500 lux (acclimatization, exposure and parasitisation period), 13900 – 22135 lux (post-parasitisation period).
- Statistics: Mortality: Fisher Exact Test, settling rate and reproduction: Dunnett-Test (except settling rate, reference item: Student-t-Test)

Results and discussions

All study validity criteria were met.

In the different Folpet 80 WG treatment groups mortalities between 0.0 % and 5.0 % were observed in the 1st and 2nd bioassay. This results in corrected mortalities of -2.6 % and 2.6 %. There was no statistically significant difference in mortality at all dose rates in both bioassays compared to the control where 2.5 % mortality was observed (Fisher Exact Test, $\alpha = 0.05$).

During the initial 3 hours after release of the wasps 24.5 % - 27.5 % of the wasps settled on the leaves in the different Folpet 80 WG treatment groups compared to 16.0 % of the wasps in the control in the 1st bioassay. In the 2nd bioassay 15.5 % - 30.0 % of the wasps settled on the leaves in the different Folpet 80 WG treatment groups compared to 24.0 % of the wasps in the control. There was no statistically significant difference in the settling rate at all dose rates in both bioassays compared to the control (test item: Dunnett Test, $\alpha = 0.05$; reference item: Student-t-Test, $\alpha = 0.05$).

Reproduction of *Aphidius rhopalosiphii* was assessed in the control and in all Folpet 80 WG treatment groups in both bioassays. The mean number of mummies was between 31.0 and 43.3 in the test item treatment groups and 41.4 in the control treatment group in the 1st bioassay. In the 2nd bioassay the mean number of mummies was between 51.7 and 57.5 in the test item treatment groups and 61.6 in the control treatment group. A statistically significant difference to the control was not observed for all test item treatment groups in both bioassays (Dunnett-Test, $\alpha = 0.05$).

The results are summarized in the tables below.

Table. Mortality and parasitisation efficiency of the parasitoids – 1st bioassay: test start on the day of application

	Rate [mL/ha] 1)	Mortality [%] 2)	Mortality corr. [%] 3)	Reproduction [mummies/female] 4)	Effect on reproduction [%] 5)
Control	0	2.5	--	41.4	--
Folpet 80 WG	1875	0.0 n.s.	-2.6	40.4 n.s.	2.5
Folpet 80 WG	3508	2.5 n.s.	0.0	43.3 n.s.	-4.6
Folpet 80 WG	6563	0.0 n.s.	-2.6	31.0 n.s.	25.1
Reference Item (Perfekthion)	50.0	100.0 *	100.0	--	--

- 1) Application rate in 400 L water/ha; application was done in the field under outdoor conditions
- 2) Mortality after 48 hours of exposure to spray residue on leaf surfaces (Fisher Exact Test, $\alpha = 0.05$: n.s. = not significant, * = significant)
- 3) Corrected mortality according to Abbott and improvements by Schneider-Orelli; negative value means lower mortality compared to the control
- 4) Reproduction: mean number of parasitized aphids/female, (Dunnett-Test, $\alpha = 0.05$: n.s. = not significant)
- 5) Calculated on the exact raw data; negative value means increased reproduction compared to the control

Table. Mortality and parasitisation efficiency of the parasitoids – 2nd bioassay: test start 13 days after of application

	Rate [mL/ha] 1)	Mortality [%] 2)	Mortality corr. [%] 3)	Reproduction [mum- mies/female] 4)	Effect on reproduction [%] 5)
Control	0	2.5	--	61.6	--
Folpet 80 WG	1875	5.0 n.s.	2.6	56.0 n.s.	9.1

Folpet 80 WG	3508	0.0 n.s.	-2.6	57.5 n.s.	6.7
Folpet 80 WG	6563	0.0 n.s.	-2.6	51.7 n.s.	16.1

- 1) Application rate in 400 L water/ha; application was done in the field under outdoor conditions
- 2) Mortality after 48 hours of exposure to spray residue on leaf surfaces (Fisher Exact Test, $\alpha = 0.05$: n.s. = not significant)
- 3) Corrected mortality according to Abbott and improvements by Schneider-Orelli; negative value means lower mortality compared to the control
- 4) Reproduction: mean number of parasitized aphids/female, (Dunnett-Test, $\alpha = 0.05$: n.s. = not significant)
- 5) Calculated on the exact raw data

Conclusion

In the 1st bioassay on the day of application and in the 2nd bioassay 13 days after application there was no effect of Folpet 80 WG on mortality of *A. rhopalosiphi* compared to the control at all dose rates (1875, 3508 and 6563 g product/ha).

The reproductive capacity of *A. rhopalosiphi* was assessed in the 1st and 2nd bioassay for all dose rates of Folpet 80 WG. In the 1st bioassay many parasitoids died during the parasitisation period in the different Folpet 80 WG treatment groups, but there was no statistically significant difference compared to the control and the reduction was below the trigger value of 50 %. Because a dose dependent high mortality was observed during the parasitisation period in the 1st bioassay, the 2nd bioassay was performed although parasitisation was not affected in the 1st bioassay. In the 2nd bioassay there was no remarkable mortality during the parasitisation period and there was no statistically significant difference compared to the control and the reduction was below the trigger value of 50 % like in the 1st bioassay.

Because there were no effects of Folpet 80 WG on survival and reproduction of *A. rhopalosiphi* 13 days after application it was not necessary to make further testing with aged residues.

Validity criteria

Control mortality: 1st and 2nd bioassay: 2.5 %, validity criterion was met

Reference item mortality: 100 %, validity criterion was met

Control reproduction 1st bioassay:

- 41.4 mummies per female (mean value), validity criterion was met;
- There was no parasitoid producing zero values, validity criterion was met

2nd bioassay:

- 61.6 mummies per female (mean value), validity criterion was met;
- There was no parasitoid producing zero values, validity criterion was met

A 2.3.2.3	KCP 10.3.2.3	Semi-field studies with non-target arthropods
A 2.3.2.4	KCP 10.3.2.4	Field studies with non-target arthropods
A 2.3.2.5	KCP 10.3.2.5	Other routes of exposure for non-target arthropods

A 2.4 KCP 10.4 Effects on non-target soil meso- and macrofauna

A 2.4.1 KCP 10.4.1 Earthworms

A 2.4.1.1 KCP 10.4.1.1 Earthworms - sub-lethal effects

A 2.4.1.1.1 Study 1

Comments of zRMS:	Acute studies are no longer data requirement and therefore the following study is not evaluated by the zRMS.
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Reference:	KCP 10.4.1/01
Report	Acute Toxicity (14 Days) of FOLPET 80 WG to the Earthworm <i>Eisenia fetida</i> in Artificial Soil with 5% Peat, Witte, B., 2009, Report No. 51141021
Guideline(s):	Yes, based on OECD 207, 1984 and ISO 11268-1, 1993
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The purpose of this study was to determine the acute toxicity of FOLPET 80 WG to the earthworm *Eisenia fetida* after 7 and 14 days exposure and to estimate the LC₅₀.

Materials and methods

Test Item:
FOLPET 80 WG; batch no.: Q-CQF; content of a.i.: 78.1%

Test Species:

Clitellated adult earthworms (*Eisenia fetida*), 11 to 12 months old (weight range 300 to 600 mg) from cultures held at the laboratory.

Test Design:

14-days exposure in treated artificial soil. Different concentrations of the test item were mixed homogeneously into the soil which was filled in glass vessels before the earthworms were introduced on top of the soil; 5 concentrations and one control; 4 replicates per treatment group with 10 earthworms each. Assessment of worm mortality and behavioural effects after 7 and 14 days, measurement of weight change as sublethal parameter after 14 days.

Endpoints:

Effect on mortality of earthworms after exposure over 14 days, behavioural effects, weight change.

Test Rates:

Control, 62.5, 125, 250, 500 and 1000 mg FOLPET 80 WG/kg soil1.

Test Conditions:

Artificial soil according to OECD 207 but with reduced content of peat (5%); initial pH 5.6 to 5.7, pH at experimental end 5.5 to 5.6; water content of soil dry weight at test initiation 23.9% to 24.7% (53.1% to 54.9% of the maximum water holding capacity); at test termination 23.1% to 24.2% (51.3% to 53.8% of the maximum water holding capacity); temperature: 19°C to 21°C; continuous illumination (light intensity:

420 lux to 770 lux).

Statistics:

Standard procedures, Dunnett's test (weight change)

Results and discussions

After 14 days of exposure, no mortality was observed in the control or any test item concentration. No behavioural effects were observed in any treatment group. The body weight changes were not statistically significantly different compared to the control at the test concentration of 62.5 mg test item/kg soil. At the concentrations of 125 mg test item/kg soil and above the body weight was significantly reduced compared to the control. However, there was no clear dose-effect response and all values remained within the 20% accepted as validity criteria for control animals. The results are summarised in Table below.

Table. Effect of FOLPET 80 WG on Earthworm (*Eisenia fetida*) mortality and biomass (14 d)

Test Species	<i>Eisenia fetida</i>					
Exposure	artificial soil					
14 d NOEC (for mortality)	1000 mg/kg dry weight soil					
14 d LOEC (for mortality)	greater than 1000 mg/kg dry weight soil					
14 d NOEC (for biomass)	62.5 mg/kg dry weight soil					
14 d LOEC (for biomass)	125 mg/kg dry weight soil					
14 d LC50	greater than 1000 mg/kg dry weight soil					
14 d LC50Confidence Limits	not determinable					
Treatment Group	Control	FOLPET 80 WG [mg/kg soil dry weight]				
	deionised water	62.5	125	250	500	1000
Mortality after 14 days [%]	0	0	0	0	0	0
Significance	-	-	-	-	-	-
Body weight change after 14 days [%]	-9.3	-13.6	-16.9	-17.0	-16.3	-18.6
Significance (Dunnett's-test, $\alpha=0.05$)	-	n.s.	*	*	*	*

- not applicable n.s. = No statistically significant differences compared to the control * = statistically significantly different to the control

Reference Item Test:

In the most recent test with the reference item 2-Chloroacetamide (performed in July/August 2008 under IBACON study number 26884021) the LC50 after 14 days was determined to be 23.7 mg test item/kg soil dry weight (95% confidence limits not determinable, see Appendix 2). This value is within the range recommended by the guideline ISO 11268-1, 1993 (20 to 80 mg 2-chloroacetamide/kg soil).

Conclusion

In a 14-day acute toxicity study with FOLPET 80 WG to earthworms (*Eisenia fetida*) the 14-day LC50 was estimated to be greater than 1000 mg test item/kg soil.

The No Observed Effect Concentration (NOEC) related to mortality was determined to be 1000 mg FOLPET 80 WG/kg soil, i.e. the highest tested concentration. The No Observed Effect Concentration (NOEC) related to biomass was determined to be 62.5 mg FOLPET 80 WG/kg soil.

Validity criteria

Control Mortality: Was 0% at day 14, validity criterion was met.
Control Mean Loss of Biomass: Was 9.3% at day 14, validity criterion was met.

A 2.4.1.1.2 Study 2

Comments of zRMS:	<p>The study has been evaluated according to OECD 222 (2004) and is considered acceptable. All validity criteria are met.</p> <p>NOEC_{reproduction} = 39.99 mg formulation Folpet 80 WG/kg soil dry weight</p> <p>The study is not considered in the risk assessment for the current formulation.</p>
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Reference:	KCP 10.4.1.1/01
Report	A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80 WG to the earthworm <i>Eisenia foetida foetida</i> (Oligochaeta: Lumbricidae) in artificial substrate at 2% peat Content, Ansaloni, T., 2014, Report No. TRC14-250BA
Guideline(s):	Yes, ISO 11268-2: 1998 and OECD 222: 2004
Deviations:	<p>Yes,</p> <p>Temperature in the climatic chamber was slightly above 22 °C % for periods longer than 2 hours</p> <p>continuously, but without negative effects on the control treatment.</p> <p>The aforementioned deviation has had no negative impact on the outcome of the study.</p>
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

A dose response study was carried out under laboratory conditions with the objective to determine the effects on reproduction, growth and percentage mortality of the earthworm *Eisenia foetida foetida* (Oligochaeta: Lumbricidae) exposed to the formulated product Folpet 80 WG in artificial soil containing 2% peat (dry weight).

The study followed OECD guideline 222 and the ISO 11268 – 2: 1998 and was conducted under study code TRC14-250BA.

Materials and methods

Test product:

Folpet 80 WG, batch I-GVA, analytical content for Folpet 80% w/w, expiry July 2016.

Test species:

Adult earthworms of the species *Eisenia foetida* between two months and one year old, with clitellum and a wet mass between 250 mg and 600 mg. The test individuals were selected from a synchronized population and did not differ in age by more than 4 weeks. The earthworms were maintained in artificial substrate under conditions identical to the experimental conditions for 1 day before the start of the study.

Test design:

Test product concentrations: Adult earthworms were maintained in an artificial substrate treated with Folpet 80 WG at concentrations of 14.00, 18.20, 23.66, 30.76 and 39.99 mg formulated product/kg dry substrate and removed and evaluated on day 28 after exposure for mortality and weight variation.

Reproduction was then evaluated on day 54.

The concentrations of the test product were selected with a spacing factor of 1.3.

Experimental units: The experimental units consisted of glass containers, with a capacity of approximately 1.5 litres, filled with 500g (dry weight) of either the treated or untreated (control) artificial substrate mixed

with 60% of its water holding capacity (WHC) of de-ionized water. Eight replicates of the water control and four replicates per treatment with the test product consisting of 10 worms each were exposed at 20 ± 2 °C, 16:8 light/dark photoperiods and a light intensity of 400 to 800 lux.

Assessments: Assessments of adult mortality and weight variation were carried out on day 28 after the application at which point the adults were removed from the substrate, and assessment of offspring production was carried out on day 54 after the application.

Toxic reference: The toxic standard Carbendazim (OECD 222: 2004) is regularly tested; the last test was performed between January and March 2014 and resulted in an LC50 of 2.87 mg/kg dry soil and a statistical significant reduction in the number of offspring at concentrations ≥ 0.6 mg/kg.

Results and discussions

Mortality and weight variation: Mean mortality at 28 days after the application was 0.00% in the water control. Mean mortality at 28 days after the application was 2.50% in treatment T1 (14.00 mg f.p./kg dry soil) and 0.00% in all other treatments with the test product. No statistical analysis was performed for this

parameter. Average weight variation at 28 days after the application with respect to the initial weight was positive (body mass gain) for the control group and for all the treatments with the test product. No significant

difference in weight variation was observed for any of the treatments as compared to the test product.

Reproduction: After 56 days the mean number of offspring in the control treatment was of 325.63 ± 9.37 individuals (mean \pm SE). Mean offspring production in the treatments with the test product ranged between 289.75 ± 5.56 individuals at the highest concentration tested (39.99 mg f.p./kg dry substrate) and 329.25 ± 18.64 individuals at 23.66 mg f.p./kg dry substrate). No Significant difference in offspring production as compared to the control group was observed for any of the tested rates of the test substance. At the evaluation for reproduction a general decrease in size of the offspring with increasing concentration of the test product was observed

Conclusion

Survival, weight variation and reproduction of *Eisenia foetida* adults were not negatively affected after 28 days of exposure to the assayed concentrations of Folpet 80 WG as compared to the control group. Therefore, the ‘No Observed Effect Concentration’ (NOEC), under the conditions of this study, for the test product corresponded to the highest rate tested of 39.99 mg formulated product/kg dry substrate, equivalent to 31.99 mg Folpet/kg dry substrate.

Validity criteria

The results were considered valid as the validity criteria were fulfilled:

- The mean rate of juveniles’ production was of 325.63 ± 9.37 individuals per control container (mean \pm SE) (range per container was 289 to 364).
- The coefficient of variation of reproduction in the controls was 8.14%.
- The percent mortality of the adults observed in the control was 0.00%.

A 2.4.1.1.3 Study 3

Comments of zRMS:	<p>The study has been evaluated according to OECD 222 (2016) and is considered acceptable. All validity criteria are met.</p> <p>NOEC reproduction = 30.76 mg formulation Folpet 80 WG/kg soil dry weight.</p> <p>The study was not considered in the risk assessment for the current formulation.</p>
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Reference: KCP 10.4.1.1/02

Report A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80

WG to the earthworm *Eisenia foetida foetida* (Oligochaeta: Lumbricidae) in artificial substrate at 5% peat Content, Ansaloni, T., 2014, Report No. TRC14-251BA

Guideline(s):	Yes, ISO 11268-2: 1998 and OECD 222: 2004
Deviations:	Yes, Temperature in the climatic chamber was slightly above 22 °C % for periods longer than 2 consecutive hours, but without negative effects on the control treatment. The aforementioned deviation has had no negative impact on the outcome of the study.
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

A dose response study was carried out under laboratory conditions with the objective to determine the effects on reproduction, growth and percentage mortality of the earthworm *Eisenia foetida foetida* (Oligochaeta: Lumbricidae) exposed to the formulated product Folpet 80 WG in artificial soil containing 5% peat (dry weight).

The study followed OECD guideline 222 and the ISO 11268 – 2: 1998 and was conducted under study code TRC14-251BA.

Materials and methods

Test product:

Folpet 80 WG, batch I-GVA, analytical content for Folpet 80% w/w, expiry July 2016.

Test species:

Adult earthworms of the species *Eisenia foetida* between two months and one year old, with clitellum and a wet mass between 250 mg and 600 mg. The test individuals were selected from a synchronized population and did not differ in age by more than 4 weeks. The earthworms were maintained in artificial substrate under conditions identical to the experimental conditions for 1 day before the start of the study.

Test design:

Test product concentrations: Adult earthworms were maintained in an artificial soil treated with Folpet 80 WG at concentrations of 14.00, 18.20, 23.66, 30.76 and 39.99 mg formulated product/kg dry substrate and removed and evaluated on day 28 after exposure for mortality and weight variation.

Reproduction was then evaluated on day 56.

The concentrations of the test product were selected with a spacing factor of 1.3.

Experimental units: The experimental units consisted of glass containers, with a capacity of approximately 1.5 litres, filled with 500g (dry weight) of either the treated or untreated (control) artificial substrate mixed with 60% of its water holding capacity (WHC) of de-ionized water. Eight replicates of the water control and four replicates per treatment with the test product consisting of 10 worms each were exposed at 20 ± 2 °C, 16:8 light/dark photoperiods and a light intensity of 400 to 800 lux.

Assessments: Assessments of adult mortality and weight variation were carried out on day 28 after the application at which point the adults were removed from the substrate, and assessment of offspring production was carried out on day 56 after the application.

Toxic reference: The toxic standard Carbenfendazim (OECD 222: 2004) is regularly tested; the last test was performed between January and March 2014 and resulted in an LC50 of 2.87 mg/kg dry soil and a statistical significant reduction in the number of offspring at concentrations ≥ 0.6 mg/kg

Results and discussions

Mortality and weight variation: Mean mortality at 28 days after the application was 0.00% in the water control. Mean mortality at 28 days after the application was 2.50% in treatment T3 (23.66 mg f.p./kg dry soil) and 0.00% in all other treatments with the test product. No statistical analysis was performed for this parameter. Average weight variation at 28 days after the application with respect to the initial weight was

positive (body mass gain) for the control group and for all the treatments with the test product. Weight variation of the earthworms exposed to the test product was significantly higher than weight variation of the control earthworms for all treatments with the exception of T3 (23.66 mg f.p./kg dry substrate).

Reproduction: After 56 days the mean number of offspring in the control treatment was of 237.50 ± 15.63 individuals (mean \pm SE). Mean offspring production in the treatments with the test product ranged between 166.75 ± 12.11 individuals at the highest concentration tested (39.99 mg f.p./kg dry substrate) and 244.00 ± 12.50 individuals at 23.66 mg f.p./kg dry substrate). Significant difference in offspring production as compared to the control group was observed for the tested rate of 39.99 mg formulated product/kg dry substrate.

Conclusion

Survival and weight variation of *Eisenia foetida* adults were not negatively affected after 28 days of exposure to the assayed concentrations of Folpet 80 WG as compared to the control group.

Reproduction of the earthworms exposed to a rate of 39.99 mg f.p./kg dry substrate was significantly lower than offspring production of the control earthworms.

Therefore, the 'No Observed Effect Concentration' (NOEC), under the conditions of this study, for the test product corresponded to the second highest rate tested of 30.76 mg formulated product/kg dry substrate, equivalent to 24.61 mg Folpet/kg dry substrate.

Validity criteria

The results were considered valid as the validity criteria were fulfilled:

- The mean rate of juveniles' production was of 237.50 ± 15.63 individuals per control container (mean \pm SE) (range per container was 172 to 290).
- The coefficient of variation of reproduction in the controls was 18.61%.
- The percent mortality of the adults observed in the control was 0.00%.

A 2.4.1.1.4 Study 4

Comments of zRMS:	<p>The study has been evaluated according to OECD 222 (2004) and is considered acceptable. All validity criteria are met.</p> <p>NOEC reproduction = 39.99 mg formulation Folpet 80 WG/kg soil dry weight</p> <p>The study is not considered in the risk assessment.</p>
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Reference:	KCP 10.4.1.1/03
Report	A laboratory test to determine the chronic (sub-lethal) effects of Folpet 80 WG to the earthworm <i>Eisenia foetida foetida</i> (Oligochaeta: Lumbricidae) in artificial substrate at 10% peat content, Ansaloni, T., 2014, Report No. TRC14-252BA
Guideline(s):	Yes, ISO 11268-2: 1998 and OECD 222: 2004
Deviations:	<p>Yes,</p> <p>Temperature in the climatic chamber was slightly above 22 °C % for periods longer than 2 consecutive hours, but without negative effects on the control treatment.</p> <p>The aforementioned deviation has had no negative impact on the outcome of the study.</p>
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

A dose response study was carried out under laboratory conditions with the objective to determine the

effects on reproduction, growth and percentage mortality of the earthworm *Eisenia foetida foetida* (Oligochaeta: Lumbricidae) exposed to the formulated product Folpet 80 WG in artificial soil containing 10% peat (dry weight).

The study followed OECD guideline 222 and the ISO 11268 – 2: 1998 and was conducted under study code TRC14-252BA.

Materials and methods

Test product:

Folpet 80 WG, batch I-GVA, analytical content for Folpet 80% w/w, expiry July 2016.

Test species:

Adult earthworms of the species *Eisenia foetida* between two months and one year old, with clitellum and a wet mass between 250 mg and 600 mg. The test individuals were selected from a synchronized population and did not differ in age by more than 4 weeks. The earthworms were maintained in artificial substrate under conditions identical to the experimental conditions for 2 days before the start of the study.

Test design:

Test product concentrations: Adult earthworms were maintained in an artificial soil treated with Folpet 80 WG at concentrations of 14.00, 18.20, 23.66, 30.76 and 39.99 mg formulated product/kg dry substrate and removed and evaluated on day 28 after exposure for mortality and weight variation.

Reproduction was then evaluated on day 56.

The concentrations of the test product were selected with a spacing factor of 1.3.

Experimental units: The experimental units consisted of glass containers, with a capacity of approximately 1.5 litres, filled with 500g (dry weight) of either the treated or untreated (control) artificial substrate mixed with 60% of its water holding capacity (WHC) of de-ionized water. Eight replicates of the water control and four replicates per treatment with the test product consisting of 10 worms each were exposed at 20 ± 2 °C, 16:8 light/dark photoperiods and a light intensity of 400 to 800 lux.

Assessments: Assessments of adult mortality and weight variation were carried out on day 28 after the application at which point the adults were removed from the substrate, and assessment of offspring production was carried out on day 56 after the application.

Toxic reference: The toxic standard Carbendazim (OECD 222: 2004) is regularly tested; the last test was performed between January and March 2014 and resulted in an LC50 of 2.87 mg/kg dry soil and a statistical significant reduction in the number of offspring at concentrations ≥ 0.6 mg/kg.

Results and discussions

Mortality and weight variation: Mean mortality at 28 days after the application was 2.50% in the water control. Mean mortality at 28 days after the application was 0.0% in all treatments with the test product.

No statistical analysis was performed for this parameter. Average weight variation at 28 days after the application with respect to the initial weight was positive (body mass gain) for the control group and for all the treatments with the test product. Weight variation of the earthworms exposed to the test product was higher than weight variation of the control earthworms for all treatments, with significant statistical difference between the control and the treatment groups at 30.76 and 23.66 mg f.p./kg dry substrate.

Reproduction: After 56 days the mean number of offspring in the control treatment was of 295.50 ± 13.84 individuals (mean \pm SE). Mean offspring production in the treatments with the test product ranged between 240.25 ± 36.53 individuals at the highest concentration tested (39.99 mg f.p./kg dry substrate) and 339.25 ± 25.00 individuals at 30.76 mg f.p./kg dry substrate. No significant difference in offspring production as compared to the control group was observed for any of the tested rate of the test substance.

Conclusion

Survival, weight variation and reproduction of *Eisenia foetida* adults were not negatively affected after 28 days of exposure to the assayed concentrations of Folpet 80 WG as compared to the control group.

Therefore, the 'No Observed Effect Concentration' (NOEC), under the conditions of this study, for the test product corresponded to the highest rate tested of 39.99 mg formulated product/kg dry substrate, equivalent to 31.99 mg Folpet/kg dry substrate.

Validity criteria

The results were considered valid as the validity criteria were fulfilled:

- The mean rate of juveniles' production was of 295.50 ± 13.84 individuals per control container (mean \pm SE) (range per container was 227 to 346).
- The coefficient of variation of reproduction in the controls was 13.24%.
- The percent mortality of the adults observed in the control was 2.50%.

A 2.4.1.1.5 Study 5

Comments of zRMS:	<p>The study has been evaluated according to OECD 222 (2004) and is considered acceptable. All validity criteria are met. The study design was overspray.</p> <p>NOEC reproduction = 6400 g formulation Folpet 80 WG/ha = 8.533 mg formulation 80 WG/kg soil dry weight (6.95 mg a.s. kg soil dry weight)</p> <p>The study is not considered in the risk assessment for current formulation.</p>
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Reference:	KCP 10.4.1.1/04
Report	Effects of Folpet 80 WG on Reproduction and Growth of Earthworms <i>Eisenia fetida</i> in artificial Soil with 5% Peat, Lührs, U., 2007, Report No. 33896022
Guideline(s):	Yes, based on OECD 222, 2004 and ISO 11268.2, 1998
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The purpose of this study was to investigate the effects of Folpet 80 WG on the mortality, body weight, feeding activity and reproduction of adult *Eisenia fetida*.

Materials and methods

Test item:	Folpet 80 WG; batch no. M-BOA; content of a.s.: Folpet: 80.0 % (nominal), 81.5 % w/w (analysed).
Test species:	Earthworm (<i>Eisenia fetida</i>), adult worms (with clitellum and weight range 300 to 565 mg), approximately 10 months old, source: from an in-house culture.
Test design:	<p>Plastic boxes were filled with artificial soil prepared according to OECD 222 (but with reduced content of peat) before the earthworms were introduced on top of the soil; 5 rates of the test item (dose response test) were sprayed onto the soil surface and were compared to one control sprayed with deionised water; 4 replicates for the test item treatments and 8 replicates for the control, with 10 worms each.</p> <p>Assessment of mortality, behavioural effects and measurement of weight change was carried out after 28 days exposure of adult worms in treated artificial soil. After an additional 28 days, determination of number of offspring was conducted.</p>
Endpoints:	Mortality, weight change, feeding activity and reproduction rate were determined.
Reference item:	Brabant Carbendazim Flowable (Carbendazim, 500 g/L nominal). The effects of the reference item were investigated in a separate study.
Test rates:	Control, 1600, 3200, 4800, 6400 and 8000 g Folpet 80 WG/ha.
Test conditions:	Artificial soil according to OECD 222 (with reduced content of peat: 5%); pH 6.2 at test initiation, 5.9 – 6.0 at test termination; water content 21.1 % - 21.3 % (52.8 % to

Statistics: 53.3 % of maximum water holding capacity, WHC) at test termination; temperature: 19 °C – 22 °C; photoperiod: 16 h light : 8 h dark, light intensity: 490 lux to 800 lux. Standard procedures, Fisher exact test (mortality), Dunnett's test (weight changes and reproduction).

Results and discussions

All study validity criteria were met.

A slight mortality of 2.5 % was found at the rate of 3200 g test item/ha, which was not statistically significantly different compared to the control, where no worm died (Fisher exact test, $\alpha = 0.05$).

Body weight of the earthworms exposed to Folpet 80 WG were not statistically significantly different compared to the control up to the highest test rate of 8000 g test item/ha (Dunnett's test, $\alpha = 0.05$).

No statistically significant effects on reproduction were observed up to and including the test rate of 6400 g test item/ha. At the rate of 8000 g test item/ha a statistically significant reduction of reproduction was observed (Dunnett's test, $\alpha = 0.05$). No behavioural abnormalities were observed in any of the treatment groups and the feeding activity in all the treated groups was comparable to the control.

Table. Effect of Folpet 80 WG on earthworms (<i>Eisenia fetida</i>) in a 56-day reproduction study						
Folpet 80 WG [g test item/ha]	Control	1600	3200	4800	6400	8000
Mortality (day 28) 1) [%]	0.0	0.0	2.5 n.s.	0.0	0.0	0.0
Weight change (day 28) 2) [%]	43.1	48.6 n.s.	46.7 n.s.	47.7 n.s.	46.2 n.s.	44.6 n.s.
No. of juveniles (day 56) 2)	336	343 n.s.	325 n.s.	327 n.s.	314 n.s.	250 *
Reproduction in [%] of control (day 56)	--	102.2	96.9	97.4	93.4	74.5
Endpoints [mg/kg soil dry weight]						
NOEL (day 28 mortality and weight)	8000					
NOEL (day 56 reproduction)	6400					

n.s. = not significantly different compared to the control

* = significantly different compared to the control

1) Fisher-exact test, $\alpha = 0.05$

2) Dunnett-test, $\alpha = 0.05$

Reference item test:

In the most recent test with the reference item Brabant Carbendazim Flowable (performed under IBACON Study Number 21344022), there were statistically significant effects on reproduction at a concentration of 1.7 mg carbendazim/kg artificial soil (dry weight); the EC50 for reproduction was calculated as 1.57 mg carbendazim/kg soil dry weight. The results are shown in Appendix 2 indicating that the sensitivity of the worms was consistent with the level proposed by the OECD 222 guideline (significant effects between 1 and 5 mg carbendazim/kg soil dry weight).

Conclusion

In an earthworm reproduction and growth study with Folpet 80 WG the no-observed-effect-level (NOEL) of for mortality, growth and feeding activity of the earthworm *Eisenia fetida* was 8000 g test item/ha, i.e. the highest rate tested.

The NOEL for reproduction was determined to be equivalent to 6400 g test item/ha soil dry weight.

Validity criteria

Control Mortality:	Control mortality was 0 %.
Reproduction of Control:	The number of worms per replicate was 298 to 425
Coefficient of Variation of Reproduction in Control:	V = 13.1 %

A 2.4.1.1.6 Study 6

Comments of zRMS:	<p>The study has been evaluated according to OECD 222 (2004) and is considered acceptable. All validity criteria are met.</p> <p>NOEC reproduction = 13.75 mg formulation BCP324F/kg soil dry weight (11.28 mg a.s./kg soil dry weight)</p> <p>The study is not considered in the risk assessment for the current formulation.</p>
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Reference:	KCP 10.4.1.1/05
Report	Effects of BCP324F on Reproduction and Growth of Earthworms <i>Eisenia fetida</i> in Artificial Soil with 5% Peat, Pavic, B., 2014, Report No. 84831022
<u>Guideline(s):</u>	<u>Yes, based on OECD 222, 2004 and ISO 11268-2, 2012</u>
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The purpose of this study was to investigate the effects of BCP324F on the mortality, body weight, feeding activity and reproduction of the adult earthworm *Eisenia fetida*.

Materials and methods

Test Item:

BCP324F; batch no.: 2219-06; content of a.i.: Folpet: 80% (nominal), 82.00% w/w (analysed)

Test Species:

Earthworm (*Eisenia fetida*), adult worms (with clitellum and weight range 300 to 600 mg), approximately 10 months old, source: from an in-house culture.

Test Design:

56-day test in treated artificial soil prepared according to OECD 222 (5% peat only); different concentrations of the test item were incorporated into the soil; 6 treatment groups (5 test item concentrations, control); 4 replicates for the test item treatments and 8 replicates for the control with 10 worms each.

Assessment of adult worm mortality, behavioural effects and biomass development was carried out after 28 days exposure of adult worms in treated artificial soil. Reproduction rate (number of offspring) was assessed after additional 28 days (assessed 56 days after application).

Endpoints:

Mortality, weight change, feeding activity and reproduction rate were determined.

Reference Item:

Luxan Carbendazim 500 FC (Carbendazim, 500 g/L nominal). The effects of the reference item were investigated in a separate study.

Test Concentrations:

Control, 8.75, 11.25, 13.75, 16.25 and 18.75 mg BCP324F/kg soil1.

Test Conditions:

Artificial soil according to OECD 222 (with reduced content of peat: 5%); initial pH 5.8 to 5.9, pH at experimental end 6.0 to 6.3; water content 20.8% to 21.6% (50.8% to 52.8% of maximum water holding capacity, WHC) at experimental start and 21.8% to 25.5% (53.1% to 62.1% of the maximum WHC) at experimental end; temperature: within the range of 18 °C to 22 °C; photoperiod: 16 h light : 8 h dark, light

intensity: within the range of 400 lux to 800 lux.

Statistics:

Standard procedures, Williams t-test (weight changes and reproduction).

Results and discussions

All study validity criteria were met. No mortality was observed in any treatment group.

The body weight changes of the earthworms after 4 weeks exposure to BCP324F were not statistically significantly different compared to the control up to and including the test item concentration of 16.25 mg test item/kg soil. At the test item concentration of 18.75 mg test item/kg soil body weight changes were statistically significantly increased when compared to the control (Williams t-test, $\alpha = 0.05$, two-sided). Nevertheless, the statistical significant differences are not considered dose-related since worms in lower test item concentrations did also gain weight even if not as much as they did in the highest test item concentration.

No statistically significant effects on reproduction were observed up to concentration of 13.75 mg test item/kg soil but in the test item concentration of 16.25 mg test item/kg soil and above reproduction was statistically significantly reduced compared to the control group (Williams t-test, $\alpha = 0.05$, one-sided smaller). Nevertheless, the statistical significant differences are not considered dose-related since reproduction of worms at highest test item concentration is comparable with the reproduction output of worms in the lowest test item concentration. No behavioural abnormalities were observed in any of the treatment groups and the feeding activity in all the treated groups was comparable to the control (see Table below).

Table. Effect of BCP324F on earthworms (*Eisenia fetida*) in a 56-day reproduction study

BCP324F [mg/kg soil dry weight]	Control	8.75	11.25	13.75	16.25	18.75
Mortality (day 28) [%]	0.0	0.0	0.0	0.0	0.0	0.0
Significance	-	-	-	-	-	-
Weight change (day 28) [%]	14.4	20.9	22.8	21.7	22.5	26.5
Significance 1)	-	n.s.	n.s.	n.s.	n.s.	*
Mean No. of juveniles (day 56)	375	311	334	351	281	312
Significance 1)	-	n.s.	n.s.	n.s.	*	*
Reproduction in [%] of control (day 56)	-	82.9	89.0	93.4	74.8	83.2
Food consumption [g]	24.4	25.0	23.5	24.5	24.8	24.8
Endpoints [mg/kg soil dry weight]						
NOEC (day 28 mortality)	18.75					
NOAEC (day 28 weight)	18.75					
NOAEC (day 56 reproduction)	18.75					

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

Reference Item Test:

In the most recent test with the reference item Luxan Carbendazim 500 FC (performed under IBACON Study Number 46646022 from August 2013 to October 2013), there were statistically significant effects on reproduction at a concentration of 1.30 mg carbendazim/kg soil and higher; the EC50 for reproduction was calculated as 1.32 mg carbendazim/kg soil.

Conclusion

In an earthworm reproduction and growth study with BCP324F the No Observed Effect Concentration (NOEC) for mortality and feeding activity of the earthworm *Eisenia fetida* was determined to be 18.75 mg test item/kg soil, i.e. the highest concentration tested.

The No Observed Adverse Effect Concentration (NOAEC) for weight changes and reproduction was determined to be the concentration of 18.75 mg test item/kg soil.

Validity criteria

Control Mortality:

Control mortality was 0% and so this validity criterion was met.

Reproduction of Control:

The number of juvenile worms per replicate was 294 to 449 and so this validity criterion was met.

~~Coefficient of Variation of Reproduction in Control:
Was 12.5% and so this validity criterion was met.~~

A 2.4.1.1.7 Study 7

Comments of zRMS:	The study is considered valid. All validity criteria were met.
	NOEC _{reproductive} ≥ 204.70 mg product Folpet 500SC/kg dws correspond to ≥ 86.75 mg a.s./kg dws
	EC _{10, 20, 50} ≥ 204.70 mg product Folpet500 SC /kg dws correspond to ≥ 86.75 mg a.s./kg dws

Reference:	KCP 10.4.1.1/06
Report	SAP50SCF (Folpet 500 SC) Sublethal Toxicity to the Earthworm <i>Eisenia andrei</i> (Oligochaeta, Lumbricidae) in Artificial Soil with 5 % Peat, Queralt, M., 2023, Report No. S23-102837
Guideline(s):	Yes, OECD Guideline No. 222 (2016) and ISO 11268-2 (2012)
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

The objective of the study was to assess the effects of SAP50SCF (Folpet 500 SC) on mortality, weight variation and reproduction of *Eisenia andrei*, and to determine the NOEC (No Observed Effect Concentration) and the LOEC (Lowest Observed Effect Concentration) for mortality, reproduction and body weight change, the median Lethal Concentration (LC₅₀) for mortality and the EC₁₀, EC₂₀ and EC₅₀ for reproduction, where possible.

Materials and methods

Test item:	SAP50SCF (Folpet 500 SC); batch code: 22C3310A; active ingredient: Folpet; nominal content: 500 g/L; analysed content: 517 g/L; density: 1.22 g/mL; expiry date: Mar 2024.
Test organism:	<i>Eisenia andrei</i> (Oligochaeta, Lumbricidae), between 2 to 12 months old (adults), presence of well-developed clitellum, a wet mass between 250 - 600 mg, selected from a synchronized population and did not differ in age by more than 4 weeks. The earthworms were maintained in artificial substrate under conditions identical to the experimental conditions for 1 day before the start of the study.
Test design:	Concentration-response test, 56-days exposure in treated artificial soil. Eight different test item concentrations were mixed into the soil; four replicates per test item concentration as well as a water control (without test item) with eight replicates. Each replicate with ten adult worms. Assessment of worm mortality and body weight change after 28 days, assessment of reproduction after 56 days.
Test item concentrations:	0.00 (control), 3.34, 6.02, 10.83, 19.50, 35.10, 63.18, 113.72 and 204.70 mg test item/kg soil dry weight. Equivalent to: 0.00 (control), 1.42, 2.55, 4.59, 8.26, 14.87, 26.77, 48.19 and 86.75 mg of folpet/kg soil dry weight.
Endpoints:	LOEC (Lowest Observed Effect Concentration) and NOEC (No Observed Effect Concentration) for mortality, body weight variation and reproductive output; LC ₅₀ (median Lethal Concentration) for adult mortality and EC ₁₀ , 20, 50 (Effect Concentration of 10, 20, 50 %) for reproductive output, where possible.
Test conditions:	Artificial soil with 5 % sphagnum peat content; soil pH 5.94 to 6.08 at test initiation

	and pH 6.44 to 6.49 at test termination; water content between 27.30 and 27.94 % at test initiation (corresponding to 54.42 % and 55.69 % of the WHCmax) and 38.53 to 43.39 % at test termination; temperature during exposure: 19.9 °C to 21.1 °C; 16:8 light:dark cycles (long day conditions), and light intensity from 507.0 to 675.4 lux.
Statistics:	<p>Statistical calculations were performed with ToxRat Professional 3.3.0 and Microsoft Office Excel-2016® v.16.0. Calculation of treatment means and standard deviations.</p> <p>Level of significance $\alpha = 0.05$ for the final statistical comparison tests.</p> <p>Analysis of mortality was not performed due to no adult mortality was observed in any of the tested concentration. Similarly, the median Lethal Concentration (LC50) for adult mortality could not be calculated and it was empirically estimated from the results.</p> <p>The weight variation and reproductive output of the control group and the test item groups was pre-tested for normality of data distribution with Shapiro-Wilk's test ($\alpha = 0.01$) and for homoscedasticity with Levene's test ($\alpha = 0.01$). After performing a trend analysis by contrasts (monotonicity of concentration/response, $\alpha = 0.05$), both weight variation was analysed using Dunnett's Multiple t-test procedure ($\alpha = 0.05$, two-sided) and reproductive output was also analysed using Dunnett's Multiple t-test procedure ($\alpha = 0.05$, one-sided smaller).</p> <p>The EC10, 20, 50 for reproductive output could not be calculated and were empirically estimated from the results.</p>
Dates of work:	20 Apr 2023 (application) to 16 Jun 2023 (final pH and water content determination).

Results and discussions

In the control group, the mean mortality of adults was 0.00 %, the number of juveniles per replicate was between 244 and 364, and the coefficient of variation of reproductive output was 12.98 %. Therefore, the validity criteria for the control group were met.

No behaviour abnormalities were observed when the worms burrowed into the soil on the application day. At the 28-day assessment, one adult individual of the treatment 5 showed the symptom of being regenerating segments. In the control replicates and in the rest of tested concentrations, no pathological symptoms of the adult earthworms were observed.

Food consumption of the adult earthworms was estimated to be similar in all the test item groups compared to the control group during the first four weeks of the study.

A 0.00 % of mortality of adult earthworms was observed in the control and in all the test item treatments. In the control group, the mean body weight increased in 199.74 mg/worm. In the treatments, the mean body weight increased between 202.20 mg/worm, observed in T2 (6.02 mg test item/kg soil dry weight), and 223.05 mg/worm, observed in T6 (63.18 mg test item/kg soil dry weight). The body weight increase was not statistical significantly different between the control and any of the test item concentrations (Dunnett's Multiple t-test Procedure, $\alpha = 0.05$, two-sided).

The maximum reduction in reproductive output occurred at the fourth lowest test item concentration (19.50 mg test item/kg soil dry weight) with a 6.93 % of reduction compared to the control. The mean number of juveniles was 307.00. No statistical significant differences were observed between the control and the highest test item concentration (Dunnett's Multiple t-test Procedure, $\alpha = 0.05$, one-sided smaller).

The toxic reference item carbendazim (supplier: Sigma-Aldrich, analysed purity: 99.5 %) was tested in a separate study (S23-100246, dates of work: January – March 2023). A statistically significant reduction in the number of juveniles was determined at 1.74 mg test item/kg soil dry weight. This result is within the range expected from the OECD Test Guideline No 222 (2016) (1 – 5 mg carbendazim/kg soil dry weight) and, hence, acceptable sensitivity of the test system was assured.

Results of mortality, body weight change and reproductive output of *Eisenia andrei* summarised:

Treatment group	Test item concentration	Mean mortality	Mean body weight change	Mean no. of juveniles per replicate	CV	Variation in reproductive output ^a
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	[mg t.i./kg sdw]	[%]	[mg/worm]		[%]	[%]
C	0.00	0.00	199.74	329.88	12.98	-
T1	3.34	0.00	204.08	337.75	15.09	2.39
T2	6.02	0.00	202.20	352.25	6.11	6.78
T3	10.83	0.00	205.18	336.75	20.74	2.08
T4	19.50	0.00	210.40	307.00	14.81	-6.93
T5	35.10	0.00	216.23	317.75	19.65	-3.68
T6	63.18	0.00	223.05	356.75	9.73	8.15
T7	113.72	0.00	217.13	336.00	24.44	1.86
T8	204.70	0.00	217.63	337.50	18.62	2.31

t.i.: test item; sdw: soil dry weight; CV: Coefficient of Variation; T: treatment.
a negative values indicate lower reproduction compared to the control

Conclusion

In a 56-day *Eisenia andrei* reproduction test in artificial soil for the test item SAP50SCF (Folpet 500 SC), all validity criteria were met and sensitivity of the test organisms could be confirmed. Accordingly, the study was deemed valid.

No behaviour abnormalities were observed when the worms burrowed into the soil on the application day, and at the 28-day assessment, one adult individual of the treatment 5 showed the symptom of being regenerating segments was observed. In the control replicates and in the rest of tested concentrations, no pathological symptoms of the adult earthworms were observed.

Under the conditions of this study, the resulting endpoints are as presented below.

The LOEC for mortality, weight variation and reproductive output could not be determined and were estimated to be greater than the highest concentration tested of 204.70 mg test item/kg soil dry weight; equivalent to 86.75 mg folpet/kg soil dry weight. Accordingly, the NOEC for mortality, weight variation and reproductive output were determined to be equal to or greater than the highest concentration tested of 204.70 mg test item/kg soil dry weight; equivalent to 86.75 mg folpet/kg soil dry weight.

Since adult mortality was always below 50 %, LC₅₀ was estimated to be greater than the highest concentration tested of 204.70 mg test item/kg soil dry weight; equivalent to 86.75 mg folpet/kg soil dry weight.

Effects on reproduction were always below 10 %, therefore, the EC₁₀, EC₂₀ and EC₅₀ for reproductive output were estimated to be greater than the highest concentration tested of 204.70 mg test item/kg soil dry weight; equivalent to 86.75 mg folpet/kg soil dry weight.

Endpoints:

Endpoints	Concentration	
	Test item	Active ingredient
	[mg test item/kg sdw]	[mg folpet/kg sdw] a
LOEC mortality^b	> 204.70	> 86.75
NOEC mortality^b	≥ 204.70	≥ 86.75
LC₅₀^b	> 204.70	> 86.75
(95 %-confidence interval)	n.d.	n.d.
LOEC body weight change^c	> 204.70	> 86.75
NOEC body weight change^c	≥ 204.70	≥ 86.75
LOEC reproductive output^d	> 204.70	> 86.75
NOEC reproductive output^d	≥ 204.70	≥ 86.75
EC_{10, 20, 50}^b	> 204.70	> 86.75
(95 %-confidence interval)	n.d.	n.d.

sdw: soil dry weight; n.d.: not determined.

a Based on the active ingredient content from the CoA and test item density: 517 g/L and 1.22 g/mL, respectively.

b Empirically estimated from the results.

c Dunnett's multiple t-test procedure ($\alpha = 0.05$, two sided).

d Dunnett's multiple t-test procedure ($\alpha = 0.05$, one-sided smaller).

Validity criteria

All required validity criteria were met. Accordingly, the study is regarded as valid.
Study validity check for parameters in the control group

Parameter	Required	Observed
Adult mortality	≤ 10 %	0.00 %
Number of juveniles per vessel at the end of the test	≥ 30	244 - 364
Coefficient of variation of reproduction	≤ 30 %	12.98 %

A 2.4.1.2 KCP 10.4.1.2 Earthworms - field studies

A 2.4.2 KCP 10.4.2 Effects on non-target soil meso- and macrofauna (other than earthworms)

A 2.4.2.1 KCP 10.4.2.1 Species level testing

A 2.4.2.2 KCP 10.4.2.2 Higher tier testing

A 2.5 KCP 10.5 Effects on soil nitrogen transformation

A 2.5.1 Study 1

Comments of zRMS:	<p>The study has been evaluated according to OECD 216 (2000) and is considered acceptable. All validity criteria are met.</p> <p>No nitrogen transformation effects up to 25 mg formulation Folpet 80 WG /kg dry soil</p> <p>The study is not considered in the risk assessment.</p>
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Reference: KCP 10.5/01

Report Effects of the formulated product Folpet 80 WG on activity of the soil microflora under laboratory conditions, Gimeno, C., 2015, Report No. TRC14-299SM

Guideline(s): Yes, OECD Guidelines for Testing of Chemicals (No. 216, 2000)

Deviations: Yes,
Temperature during soil storage was occasionally above 6 °C. Maximum temperature during this period was 6.31°C.
The extractions and samples preparation were performed up to 84 after application. As no long -term effects were detected, only samples extracted at 0, 7, 14 and 28 days after the application were analysed and reported.
No records of temperature during first shipment of samples to the laboratory are available. The use of dry ice and the short duration of transport assured the optimum conditions during transport, samples arrived to destiny deep frozen.
The issue of the final report was delayed
The reported deviations had no impact on the outcome of the study.

GLP: Yes

Acceptability: Yes

Duplication (if vertebrate study) N/A

Objective

A Laboratory study was carried out to determine the effects of the test product Folpet 80 WG on the activity

(nitrogen transformation) of soil microflora under laboratory conditions.

Materials and methods

Test Substance

Folpet

Product Code: Folpet 80, WG

Batch: I-GVA

Purity: 80 % w/w

Expiry: July, 2016.

Test System

Sandy loam soil (59.9% sand) low in organic matter (organic carbon content 0.67%) was used. Soil pH was 6.4 and the microbial biomass carbon content was 1.23% of total soil organic carbon.

Test design

The study was conducted in a controlled environment chamber at a temperature of 20 ± 2 °C, high air humidity and under dark conditions for the duration of the test.

The moisture content of soil samples was maintained during the test at about 42 % of its WHC.

Two different concentrations of test substance were tested, 3.75 mg test product/kg soil (T1) and 25 mg test product/kg soil (T2).

A control group treated with an equivalent amount of de-ionized water was concurrently tested.

Four replicates per treatment and control were tested. The duration of the test was 28 days.

Assessments

Soil samples were analysed for nitrate formation rates on days 0, 7, 14 and 28. Effects on NO₃-production were evaluated.

Test endpoint

Nitrate formation rate (mg NO₃- /kg dry weight soil/day) and % of deviation from the control.

Results and discussions

Significant differences ($\alpha = 0.05$) between the treatments and the control for nitrate content in soil were found at day 0 and 28 for the treatment T1 and at day 7, 14 and 28 for the treatment T2. Significant differences ($\alpha = 0.05$) between the treatments and the control for nitrate formation rates were found at day 0-7 and 0-28 for treatment T1 and at day 0-7, 0-14 and 0-28 for treatment T2.

The difference in nitrate content and in nitrate formation rates between the 3.75 mg test product/kg soil dry weight treatment and the control did not exceed 25% on any day tested.

The difference in nitrate content between the 25 mg test product/kg soil dry weight treatment and the control was higher than 25 % at day 14, but not at day 28.

The differences in nitrate formation rates between the 25 mg test product/kg soil dry weight treatment and the control were higher than 25% at days 0-7 and 0-14 but not at day 0-28.

After 28 days of incubation, differences to the control in nitrate formation rates were 15.41 % and 10.97% in the 3.75 and 25 mg test product/kg soil dry weight treatment respectively.

NO ₃ - content (mg NO ₃ -/kg d.w.s.) Mean values									
	Control			T1 3.75 mg PF/kg d.w.s.			T2 25 mg PF/kg d.w.s.		
Evaluation	NO ₃ -content	SD	CV%	NO ₃ -content	SD	Deviation %	NO ₃ -content	SD	Deviation %
Day 0	56.21	0.49	0.87	57.15*	0.17	1.66	55.62	1.30	-1.05
Day 7	70.61	1.77	2.50	68.47	0.80	-3.03	54.26*	0.17	-23.15
Day 14	160.07	1.51	0.94	156.64	7.69	-2.14	67.69*	0.79	-57.71
Day 28	215.41	2.02	0.94	240.88*	2.47	11.82	232.29*	7.60	7.84

Whithin files figures followed by “*” are significantly different from the respective control at the 0.05 probability level.
(T-test $\alpha = 0.05$ for day 0, 14 and 28; Mann-Whitney exact test for day 7)

NO3- formation rate (mg NO3-/kg d.w.s./day) Mean values						
	Control		T1 3.75 mg PF/kg d.w.s.		T2 25 mg PF/kg d.w.s.	
Evaluation	NO3-for- mation rate	CV%	NO3-formation rate	Deviation %	NO3-formation rate	Deviation %
Day 0-7	2.06	10.13	1.62*	-21.34	-0.19*	-109.47
Day 0-14	7.42	1.12	7.11	-4.20	0.86*	-88.38
Day 0-28	5.69	1.16	6.56*	15.41	6.31*	10.97

Within files figures followed by ‘*’ are significantly different from the respective control at the 0.05 probability level.
(T-test $\alpha = 0.05$)

Conclusion

The test product ‘Folpet 80 WG’ at concentrations of 3.75 and 25 mg/kg soil dry weight was found to have no long term effect on the nitrogen transformation activity of soil microflora when tested over 28 days. There were statistically significant differences to the control in nitrate formation rates at day 28. Nevertheless, because the deviation between the control soil and that treated with Folpet 80 WG did not exceed 25% after 28 days of exposure, the impact of Folpet 80 WG on soil microflora is considered negligible.

Validity criteria

The coefficient of variation between control replicates remained below 15% throughout the study period for the nitrate content. The highest coefficient of variation in the control group was 2.5% for the nitrate content and 10.13% for the day 0 – 7 nitrate formation rate. Hence, the study was considered valid as the results obtained met the validity criteria.

A 2.5.2 Study 2

Comments of zRMS:	The study has been evaluated according to OECD 216 (2000) and is considered acceptable. All validity criteria are met. No nitrogen transformation effects up to 19.5 mg formulation Folpet 500 SC /kg dry soil.
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Reference:	KCP 10.5/02
Report	SAP50SCF (Folpet 500 SC): Effects on the Activity of Soil Microflora under Laboratory Conditions (Nitrogen Transformation), Queralto, M., 2023, Report No. S23-102838
Guideline(s):	Yes, OECD 216 (2000)
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

This test assesses the effect of chemicals of interest on nitrogen transformation in aerobic surface soils under laboratory conditions favorable to microbial metabolism. Soils are treated, homogenized and incubated in the dark at 20 ± 2 °C. Endpoint measured was nitrate formation rate (mg NO3-/kg soil dry weight/day).

Materials and methods

Test item:	SAP50SCF (Folpet 500 SC); batch code: 22C3310A; active ingredient: Folpet; nominal content: 500 g/L; analysed content: 517 g/L; density: 1.22 g/mL; expiry date: Mar 2024.
Test soil:	Sandy loam soil (59.7 ± 0.8 % sand), low in organic matter (organic carbon

Test design:	<p>content 0.66 ± 0.05 %) was used. Soil pH (in water) was 6.64 and the microbial biomass carbon content was 1.91 % of total soil organic carbon.</p> <p>2 test item groups and 1 control group with 4 replicates per test item treatment and control were tested.</p> <p>28-day exposure in treated soil with 3.90 mg test item/kg soil dry weight and 19.50 mg test item/kg soil dry weight. The test item solutions were mixed homogeneously into the soil. Deionised water was added for the control group; the treated soil was distributed in glass test units and incubated in controlled conditions.</p> <p>Soils were sampled for nitrate formation rates on days 0, 7, 14 and 28 after application. Effects on NO₃⁻ production were evaluated.</p> <p>Endpoint: Nitrate formation rate (mg NO₃⁻/kg soil dry weight/day) and % of deviation from the control. Calculations have been performed considering an accumulative approach and an incremental approach.</p>
Test item concentrations:	Control (deionised water), 3.90 mg test item/kg soil dry weight (equivalent to 1.65 mg folpet/kg soil dry weight) and 19.50 mg test item/kg soil dry weight (equivalent to 8.26 mg folpet/kg soil dry weight).
Test conditions:	Soil incubation was performed in a controlled environment chamber at a temperature range of 19.80 to 21.14 °C (target: 20 ± 2 °C) and under dark conditions; moisture content was 42 % of WHC at test start; the water content was maintained during the test.
Statistics:	Calculation of mean nitrate formation rates (considering accumulative and incremental approaches), Standard Deviation (SD) and Coefficient of Variation (CV). Statistical comparisons between each concentration and the control were performed for nitrate formation rates. All data were tested for normality with the Shapiro-Wilk's test and for homoscedasticity with the Levene's test before performing the appropriate statistical test. Student t-test was used for all data, as they showed normal distribution and homogeneity of variance. Level of significance was $\alpha = 0.05$ for hypothesis testing.
Dates of work:	25 Apr 2023 (Application) to 25 May 2023 (nitrate analysis).

Results and discussions

Difference to the control in nitrate content was 2.97 % in the 3.90 mg test item/kg soil dry weight treatments and 17.47 % in the 19.50 mg test item/kg soil dry weight treatments, respectively, on day 28.

The deviation of nitrate formation rate between the control and test item treatments at 3.90 and 19.50 mg test item/kg soil dry weight did not exceed 25 % (both accumulative and incremental approaches) on day 28.

Deviations from control in nitrate formation rates 28 days after the test start were 4.08 % for accumulative approach (0-28 days) and -4.76 % for incremental approach (14-28 days) at the 3.90 mg test item/kg soil dry weight treatment.

Deviations from the control in nitrate formation rates 28 days after the test start were 24.26 % for accumulative approach (0-28 days) and -8.35 % for incremental approach (14-28 days) at the 19.50 mg test item/kg soil dry weight treatment.

NO ₃ ⁻ content (mg NO ₃ ⁻ /kg d.w.s.) Mean values									
	Control			3.90 mg test item/kg sdw			19.50 mg test item/kg sdw		
Evaluation	NO ₃ ⁻ content	SD	CV%	NO ₃ ⁻ content	SD	Deviation from Control %	NO ₃ ⁻ content	SD	Deviation from Control %
Day 0	54.13	0.42	0.77	54.23	0.37	0.17	54.33	0.29	0.37
Day 7	109.70	1.10	1.00	103.54	2.86	-5.62	71.25	4.11	-35.05
Day 14	137.37	1.56	1.13	145.54	1.25	5.95	175.05	2.65	27.43
Day 28	190.39	2.97	1.56	196.04	2.55	2.97	223.65	3.12	17.47

sdw: soil dry weight; SD: Standard Deviation; CV: Coefficient of Variation

NO3- formation rate (mg NO3-/kg d.w.s./day). Accumulative approach. Mean values						
	Control		3.90 mg test item/kg sdw		19.50 mg test item/kg sdw	
Evaluation	NO3-for- mation rate	CV%	NO3-for- mation rate	Deviation from Control %	NO3-for- mation rate	Deviation from Control %
0-7 days	7.94	1.79	7.04 a	-11.25	2.42 ^a	-69.56
0-14 days	5.95	1.71	6.52 a	9.71	8.62 ^a	45.03
0-28 days	4.87	1.92	5.06 a	4.08	6.05 ^a	24.26

sdw: soil dry weight; CV: Coefficient of Variation

a Significant differences from the respective control at the 0.05 probability level (Student t-test, 2-tailed).

NO3- formation rate (mg NO3-/kg d.w.s./day). Incremental approach. Mean values						
	Control		3.90 mg test item/kg sdw		19.50 mg test item/kg sdw	
Evaluation	NO3-for- mation rate	CV%	NO3-formation rate	Deviation from Control %	NO3-formation rate	Deviation from Control %
0-7 days	7.94	1.79	7.04 ^a	-11.25	2.42 ^a	-69.56
7-14 days	3.95	6.94	6.00 ^a	51.80	14.836 ^a	275.15
14-28 days	3.79	3.70	3.61	-4.76	3.47 ^a	-8.35

sdw: soil dry weight; CV: Coefficient of Variation

a Significant differences from the respective control at the 0.05 probability level (Student t-test, 2-tailed).

Conclusion

The study was deemed valid as the results met the validity criteria.

The test item SAP50SCF (Folpet 500 SC) at the test concentration of 3.90 mg test item/kg soil dry weight (equivalent to 1.65 mg folpet/kg soil dry weight) was found to have a short term stimulation effect on nitrate formation at the assessment at 7-14 days (in terms of incremental approach), with a deviation respect to the control of 51.80 % (stimulation higher than 25 %). Nevertheless, this stimulation was temporary and it was counteracted by an inhibition in nitrate formation at 14-28 days, with a deviation respect to the control of -4.76 % (deviation respect to the control below 25 %). In terms of the accumulative approach, it was not found to have effect on nitrate formation throughout the study (deviation respect to the control always below 25%).

The test item concentration of 19.50 mg test item/kg soil dry weight (equivalent to 8.26 mg folpet/kg soil dry weight) was found to have a short-term inhibition effect on nitrate formation at the assessment 0-7 days with a deviation of -69.56 % (inhibition higher than 25 %). Nevertheless, this inhibition was temporary and it was counteracted by a stimulation in nitrate formation at 14 and 28 days. In terms of the accumulative approach at 0-14 and 0-28 days, the deviation respect to the control was 45.03 % and 24.26 %, respectively; and in terms of the incremental approach at 7-14 and 14-28 days, the deviation with respect to the control was 275.15 % and -8.35 %, respectively.

Therefore, it can be concluded that the test item SAP50SCF (Folpet 500 SC) had no impact on the nitrogen transformation activity of soil microflora at test concentrations up to 19.50 mg test item/kg soil dry weight (equivalent to 8.26 mg folpet/kg soil dry weight) at day 28, since deviation respect to the control was below 25%.

Validity criteria

The coefficient of variation between control replicates remained below 15 % throughout the study period for the nitrate content. The highest coefficient of variation in the control group was 1.56 % for the nitrate concentration on day 28. Hence, the study was considered valid as the results obtained met the validity criteria.

A 2.6 KCP 10.6 Effects on terrestrial non-target higher plants

A 2.6.1 KCP 10.6.1 Summary of screening data

A 2.6.2 KCP 10.6.2 Testing on non-target plants

A 2.6.2.1 Study 1

Comments of zRMS:	<p>The study has been evaluated according to OECD 208 and is considered acceptable since it followed in general the procedures indicated and fulfilled the corresponding validity criteria. Actual measured concentrations were within 80-120% of nominal concentrations.</p> <p>ER₅₀=1.6 kg a.s./ha</p> <p><u>Visual phytotoxicity:</u></p> <p>No plant mortality or visual signs of injury were recorded for any treatment in any species.</p>
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Reference:	KCP 10.6.2/01
Report	Evaluation of the Phytotoxicity of Folpet 80% WG Non Target Terrestrial Plant Seedling Emergence and Growth Test (Based on OECD Guideline 208), Eley, R., 2009, Report No. ACE-08-259
Guideline(s):	Yes, OECD Guideline 208
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	No

Objective

A study was carried out at Aldhams Farm between 17th November 2008 and 12th January 2009 (glasshouse phase) to generate dose response data for Folpet 80% WG, when applied pre-emergence to a range of monocotyledon and dicotyledon terrestrial plant species.

Materials and methods

Folpet 80% WG is formulated as a water dispersible granule (WG) containing 80% Folpet active ingredient and was applied at a single rate of 1.6 kilograms of active substance per hectare (kg as/ha) at a volume rate of 300 (+/-10%) litres per hectare (l/ha). The methodology is based on the OECD guideline 208 (adopted on 19 July 2006) for seedling emergence and growth. Data from the study can be used to assess the risk to non target terrestrial plants from pre emergence application of Folpet 80% WG. The study was conducted to GLP standards.

Results and discussions

Mean Final Fresh Weights (21 days after 50% emergence in the untreated controls) Expressed as a Percentage of the Untreated Control

Family	Species	Untreated	Folpet 80%WG 1.6 kg as/ha
Gramineae	<i>Zea mays</i>	100	105
Gramineae	<i>Lolium perenne</i>	100	98
Gramineae	<i>Triticum aestivum</i>	100	106
Cucurbitaceae	<i>Cucumis sativus</i>	100	50.5
Brassicaceae	<i>Brassica napus</i>	100	88
Chenopodiaceae	<i>Beta vulgaris</i>	100	107
Solonaceae	<i>Lycopersicon esculentum</i>	100	78

Conclusion

Three attempts to achieve the specified level of 70% emergence using untreated Brassica napus seed failed. Brassica napus seed pre-treated with insecticide and fungicide was also used at the third attempt and this emerged very well (95% in the untreated controls). The results from the pre-treated Brassica napus seed are used in this report. These results accurately reflect the phytotoxicity of Folpet 80% WG on Brassica napus and the use of pre-treated seed had no effect upon the study other than enabling us to achieve >70% emergence and produce healthy plants.

No plant mortality or visual signs of injury were recorded for any treatment in any species.

The only species to show any significant reduction in emergence in pots treated with Folpet 80% WG was *Cucumis sativus*. However, emergence was also relatively low in the control pots (70%) and may have influenced the results with Folpet 80% WG. All other species showed no significant differences between treated and untreated pots.

Cucumis sativus was also the only species to show a significant reduction in final fresh weights in treated pots. However, *Cucumis sativus* plants that emerged were healthy, showing no visual signs of phytotoxicity and this reduction appears to be related to the reduced levels of emergence.

Validity criteria

The validity criteria outlined in the study plan (as amended) were met i.e. there was at least 70% mean emergence in the untreated controls for all species, untreated plants did not exhibit any phytotoxic effects, the mean plant survival of untreated plants exceeded 90% for all species, and environmental conditions were identical for plants of each particular species.

A 2.6.2.2 Study 2

Comments of zRMS:	<p>The study has been evaluated according to OECD 227 and is considered acceptable. All validity criteria are met.</p> <p>Actual measured concentrations were within 80-120% of nominal concentrations.</p> <p>ER₅₀ > 3.2 kg a.s./ha</p> <p><u>Visual phytotoxicity:</u></p> <p>No symptoms of visual injury or plant mortality were recorded in any treatment of any species.</p>
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Reference:	KCP 10.6.2/02
Report	Evaluation of the Phytotoxicity of Folpet 80% WG Non Target Terrestrial Plant Vegetative Vigour Test (Based on OECD Guideline 227), Eley, R., 2009, Report No. ACE-08-260
Guideline(s):	Yes, OECD Guideline 227
Deviations:	No
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study)	N/A

Objective

A study was carried out at Aldhams Farm between 17th November 2008 and 8th December 2008 (glasshouse phase) to generate dose response data for Folpet 80% WG, when applied post-emergence to a range of monocotyledon and dicotyledon terrestrial plant species.

Materials and methods

Folpet 80% WG is formulated as a water dispersible granule (WG) containing 80% Folpet active ingredient. ER50 values have been calculated from the dose response data using final foliar fresh weight data for each species and can be used to assess the risk of Folpet 80% WG to terrestrial non-target plants. The methodology is based on the OECD guideline 227 (adopted on 19 July 2006) for vegetative vigour. The study was conducted to GLP standards.

ER₅₀, kg as/ha of Folpet 80% WG Based on Final Fresh Weights

Family	Species	Common Names	ER ₅₀ (kg as/ha)
Gramineae	<i>Zea mays</i>	Maize	> 3.2
Gramineae	<i>Lolium perenne</i>	Ryegrass	> 3.2
Gramineae	<i>Triticum aestivum</i>	Winter Wheat	> 3.2
Cucurbitaceae	<i>Cucumis sativus</i>	Cucumber	> 3.2
Brassicaceae	<i>Brassica napus</i>	Oilseed rape	> 3.2
Chenopodiaceae	<i>Beta vulgaris</i>	Sugar beet	> 3.2
Solanaceae	<i>Lycopersicon esculentum</i>	Tomato	> 3.2

All species tested showed a high level of tolerance to post-emergence application of Folpet 80% WG. Only *Triticum aestivum* showed a statistically significant reduction in fresh weight at the highest rate but this was only 6%. ER₅₀ values based on final fresh weights for all species are therefore concluded as being greater than the highest rate tested (3.2 kg as/ha). No symptoms of visual injury or plant mortality were recorded in any treatment of any species.

The validity criteria outlined in the study plan were met i.e. there was less than 2 x variation in the weights of untreated replicate pots for all species, untreated plants did not exhibit any phytotoxic effects, the mean plant survival exceeded 90% for all species, and environmental conditions were identical for plants of each particular species.

A 2.6.3	KCP 10.6.3	Extended laboratory studies on non-target plants
<p>1. Test species</p> <p>2. Test conditions</p> <p>3. Test results</p>	<p>1. Test species</p> <p>2. Test conditions</p> <p>3. Test results</p>	<p>1. Test species</p> <p>2. Test conditions</p> <p>3. Test results</p>

A 2.7 KCP 10.7 Effects on other terrestrial organisms (flora and fauna)

A 2.8 KCP 10.8 Monitoring data

Appendix 3 Calculations considering the minimum proposed application rate

zRMS comments:

Additional information has not been evaluated by zRMS except the calculations of the risk assessment for aquatic organism submitted in **Appendix 4**.
Remained calculation can be considered at MSs level if relevant.

Effects on birds (KCP 10.1.1)

Table A3-1: Screening step of the acute and long-term/reproductive risk for birds due to the use of SAP50SCF in cereals

Intended-use		Cereals				
Active substance/product		folpet				
Application rate (g/ha)		2 x 450				
Acute toxicity (mg/kg bw)		2150				
TER criterion		40				
Crop scenario	Indicator/generic focal species	SV ₉₀	MAF ₉₀	DDD ₉₀ (mg/kg bw/d)	TER _a	
Growth stage						
-	Small omnivorous bird	158.8	1.2	85.75	25.1	
Reprod. toxicity (mg/kg bw/d)		78.3				
TER criterion		5				
Crop scenario	Indicator/generic focal species	SV _m	MAF _m × TWA	DDD _m (mg/kg bw/d)	TER _{lt}	
Growth stage						
-	Small omnivorous bird	64.8	1.4 x 0.53	21.64	3.6	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table A3-2: First-tier assessment of the long-term/reproductive risk for birds due to the use of SAP50SCF in cereals

Intended-use		Cereals				
Active substance/product		folpet				
Application rate (g/ha)		2 x 450				
Reprod. toxicity (mg/kg bw/d)		78.3				
TER criterion		5				
Crop scenario	Indicator/generic focal species	SV _m	MAF _m × TWA	DDD _m (mg/kg bw/d)	TER _{lt}	
Growth stage						
Cereals BBCH ≥ 40	Small omnivorous bird "lark" Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods	3.3	1.4 x 0.53	1.10187	71.1	
Cereals BBCH 30–39	Small omnivorous bird "lark" Combination (invertebrates with interception) 25% crop leaves 25% weed seeds 50% ground arthropods	5.4	1.4 x 0.53	1.80306	43.4	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Puddle-scenario

Effective application rate (g/ha)	450		
Acute toxicity (mg/kg bw)	2150	quotient	2
Reprod. toxicity (mg/kg bw/d)	78.3	quotient	2

Risk assessment for earthworm-eating birds via secondary poisoning

Table A30-3: Assessment of the risk for earthworm-eating birds due to exposure to folpet via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

Parameter	folpet	comments
PEC _{soil} (twa = 21 d) (mg/kg soil)	0.145	
log P _{ow} / P _{ow}	3.017/1039.9	
K _{ee}	304	Worst case assumption
f _{ee}	0.02	Default
BCF _{worm}	2.19	$BCF_{worm/soil} = (PEC_{worm,ww} / PEC_{soil,dw}) = (0.84 + 0.012 \times P_{ow}) / f_{ee} \times K_{ee}$
PEC _{worm}	0.32	$PEC_{worm} = PEC_{soil} \times BCF_{worm/soil}$
Daily dietary dose (mg/kg bw/d)	0.33	$DDD = PEC_{worm} \times 1.05$
NOEL (mg/kg bw/d)	78.3	
TER _{it}	235	Acceptable risk

TER values shown in bold fall below the relevant trigger.

Risk assessment for fish-eating birds via secondary poisoning

Table A3-4: Assessment of the risk for fish-eating birds due to exposure to folpet via bioaccumulation in fish (secondary poisoning) for the intended use in cereals

Parameter	folpet	comments
PEC _{sw} (twa = 21 d) (mg/L)	0.001871	Worst case value: spring cereals, multiple applications; D1-scenario (set 2)
BCF _{fish}	56	Whole fish
BMF	–	biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	0.10	$PEC_{fish} = PEC_{water} \times BCF_{fish}$
Daily dietary dose (mg/kg bw/d)	0.02	$DDD = PEC_{fish} \times 0.159$
NOEL (mg/kg bw/d)	78.3	
TER _{it}	4700	Acceptable risk

TER values shown in bold fall below the relevant trigger.

Effects on terrestrial vertebrates other than birds (KCP 10.1.2)

Table A3-5: Screening step of the acute and long-term/reproductive risk for mammals due to the use of SAP50SCF in cereals

Intended use	Cereals					
Active substance/product	folpet					
Application rate (g/ha)	2 × 450					
Acute toxicity (mg/kg bw)	2000					
TER criterion	40					
Crop scenario Growth stage	Indicator/generic focal species	SV ₉₀	MAF ₉₀	DDD ₉₀ (mg/kg bw/d)	TER _a	

-	Small herbivorous mammal	118.4	1.2	63.94	31.3
Reprod. toxicity (mg/kg bw/d)	450				
TER criterion	5				
Crop scenario Growth stage	Indicator/generic focal species	SV _m	MAF _m × TWA	DDD _m (mg/kg bw/d)	TER _{it}
-	Small herbivorous mammal	48.3	1.4 x 0.53	16.13	9.30

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Puddle scenario

Effective application rate (g/ha) =	150		
Acute toxicity (mg/kg bw) =	2000	quotient =	1.3
Reprod. toxicity (mg/kg bw/d) =	150	quotient =	5.0

Risk assessment for earthworm-eating mammals via secondary poisoning

Table 0-6: Assessment of the risk for earthworm-eating mammals due to exposure to folpet via bioaccumulation in earthworms (secondary poisoning) for the intended use in cereals

Parameter	folpet	comments
PEC _{soil} (twa = 21 d) (mg/kg soil)	0.145	
log P _{ow} /P _{ow}	3.017/1039.9	
K _{oc}	304	Worst-case assumption
f _{oc}	0.02	Default
BCF _{worm}	2.19	$BCF_{worm/soil} = (PEC_{worm,ww} / PEC_{soil,dw}) = (0.84 + 0.012 \times P_{ow}) / f_{oc} \times K_{oc}$
PEC _{worm}	0.32	$PEC_{worm} = PEC_{soil} \times BCF_{worm/soil}$
Daily dietary dose (mg/kg bw/d)	0.41	$DDD = PEC_{worm} \times 1.28$
NOEL (mg/kg bw/d)	150	
TER _{it}	369	Acceptable risk

TER values shown in bold fall below the relevant trigger.

Risk assessment for fish-eating mammals via secondary poisoning

Table 0-7: Assessment of the risk for fish-eating mammals due to exposure to folpet via bioaccumulation in fish (secondary poisoning) for the intended use in cereals

Parameter	folpet	comments
PEC _{sw} (twa = 21 d) (mg/L)	0.001871	Worst-case value: spring cereals, multiple applications, D1 scenario (ste 2)
BCF _{fish}	56	Whole fish
BMF	-	biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	0.10	$PEC_{fish} = PEC_{water} \times BCF_{fish}$
Daily dietary dose (mg/kg bw/d)	0.01	$DDD = PEC_{fish} \times 0.142$
NOEL (mg/kg bw/d)	150	
TER _{it}	10082	Acceptable risk

TER values shown in bold fall below the relevant trigger.

Effects on aquatic organisms (KCP 10.2)

Table 0-8: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for folpet for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP50SCF in cereals

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Test species		-	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Scenedesmus subspicatus</i>
Endpoint (µg/L)		HC ₅ 52.7	NOEC 39	EC ₅₀ 680	NOEC 320	ErC ₅₀ 40000
AE		9	10	100	10	10
RAC (µg/L)		5.9	3.9	6.8	32	4000
FOCUS-Scenario	PEC _{gl-max} (µg/L)					
Winter-cereals						
Step 1 (worst-case value between sets 1 and 2, further details refer to B8)						
-	110.87	18.8	28.4	16.3	3.5	0.1
Step 2 (worst-case value between sets 1 and 2, further details refer to B8)						
N-Europe	7.48	1.3	1.9	1.1	0.2	Ok-at-step-1.
S-Europe	6.34	1.1	1.6	0.9	0.2	
Step 3—Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.517	0.4	0.6	0.4	Ok-at-step-2.	Ok-at-step-1.
D1/stream	2.126	0.4	0.5	0.3		
D2/ditch	2.523	0.4	0.6	0.4		
D2/stream	2.206	0.4	0.6	0.3		
D3/ditch	2.493	0.4	0.6	0.4		
D4/pond	0.1198	0.0	0.0	0.0		
D4/stream	1.884	0.3	0.5	0.3		
D5/pond	0.1387	0.0	0.0	0.0		
D5/stream	2.174	0.4	0.6	0.3		
D6/ditch	2.505	0.4	0.6	0.4		
R1/pond	0.2274	0.0	0.1	0.0		
R1/stream	3.337	0.6	0.9	0.5		
R3/stream	4.464	0.8	1.1	0.7		
R4/stream	2.54	0.4	0.7	0.4		
Step 3—Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.861	0.5	0.7	0.4	Ok-at-step-2.	Ok-at-step-1.
D1/stream	2.223	0.4	0.6	0.3		
D2/ditch	2.879	0.5	0.7	0.4		
D2/stream	2.445	0.4	0.6	0.4		
D3/ditch	2.851	0.5	0.7	0.4		
D4/pond	0.09837	0.0	0.0	0.0		
D4/stream	2.106	0.4	0.5	0.3		
D5/pond	0.09838	0.0	0.0	0.0		
D5/stream	2.276	0.4	0.6	0.3		

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
D6/ditch	2.818	0.5	0.7	0.4		
R1/pond	0.09838	0.0	0.0	0.0		
R1/stream	1.878	0.3	0.5	0.3		
R3/stream	2.638	0.4	0.7	0.4		
R4/stream	1.886	0.3	0.5	0.3		
Spring cereals						
Step 1 (worst-case value between sets 1 and 2, further details refer to B8)						
-	110.87	18.8	28.4	16.3	3.5	0.1
Step 2 (worst-case value between sets 1 and 2, further details refer to B8)						
N-Europe	4.14	0.7	1.06	0.6	0.1	Ok at step 1.
S-Europe	6.34	1.1	1.6	0.9	0.2	
Step 3—Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.366	0.6	0.9	Ok at step 2.	Ok at step 2.	Ok at step 1.
D1/stream	2.183	0.4	0.6			
D3/ditch	2.495	0.4	0.6			
D4/pond	0.1323	0.0	0.0			
D4/stream	2.083	0.4	0.5			
D5/pond	0.1232	0.0	0.0			
D5/stream	2.152	0.4	0.6			
R4/stream	8.38	1.4	2.1			
Step 3—Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.886	0.5	0.7	Ok at step 2.	Ok at step 2.	Ok at step 1.
D1/stream	2.524	0.4	0.6			
D3/ditch	2.854	0.5	0.7			
D4/pond	0.09842	0.0	0.0			
D4/stream	2.333	0.4	0.6			
D5/pond	0.09841	0.0	0.0			
D5/stream	2.396	0.4	0.6			
R4/stream	4.662	0.8	1.2			

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table A3-9: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for folpet based on FOCUS Step 4 calculations and toxicity data for fish chronic with mitigation of spray drift and run-off for the use of SAP50SCF in cereals

Intended use	Cereals
Active substance	folpet

Application rate (g/ha)	2 x 450
<i>Winter Cereals – Multiple applications – 5 meters of vegetated filter strip</i>	
R3/stream	1.658
RAC (µg/L)	
3.9	PEC/RAC ratio
R3/stream	0.4
<i>Winter Cereals – Multiple applications – 10 meters of vegetated filter strip</i>	
R3/stream	2.037
RAC (µg/L)	
3.9	PEC/RAC ratio
R3/stream	0.5
<i>Spring Cereals – Multiple applications – 15 m buffer zone including 15 m of vegetated filter strip</i>	
R4/stream	3.790
RAC (µg/L)	
5.9	PEC/RAC ratio
R4/stream	0.6
RAC (µg/L)	
3.9	PEC/RAC ratio
R4/stream	0.97
<i>Spring Cereals – Multiple applications – 20 m buffer zone including 20 m of vegetated filter strip</i>	
R4/stream	3.027
RAC (µg/L)	
3.9	PEC/RAC ratio
R4/stream	0.8
<i>Spring Cereals – Single application – 10 meters of vegetated filter strip</i>	
R4/stream	2.104
RAC (µg/L)	
3.9	PEC/RAC ratio
R4/stream	0.5

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 0-8a: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for folpet for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP50SCF in cereals

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Test-species		-	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Scenedesmus subspicatus</i>
Endpoint (µg/L)		HC ₅ 52.7	NOEC 39	EC ₅₀ 680	NOEC 320	E _c EC ₅₀ 10000
AE		9	10	100	10	10
RAC (µg/L)		5.9	3.9	6.8	32	1000
FOCUS Scenario	PEC _{gl-max} (µg/L)					
Winter-cereals						
Step 3— Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.516	0.4	0.6	0.4	Ok-at-step-2.	Ok-at-step-1.
D1/stream	2.125	0.4	0.5	0.3		
D2/ditch	2.523	0.4	0.6	0.4		
D2/stream	2.205	0.4	0.6	0.3		
D3/ditch	2.493	0.4	0.6	0.4		
D4/pond	0.107	0.0	0.0	0.0		
D4/stream	1.882	0.3	0.5	0.3		
D5/pond	0.130	0.0	0.0	0.0		
D5/stream	2.173	0.4	0.6	0.3		
D6/ditch	2.504	0.4	0.6	0.4		
R1/pond	0.178	0.0	0.0	0.0		
R1/stream	2.615	0.4	0.7	0.4		
R3/stream	3.213	0.5	0.8	0.5		
R4/stream	1.872	0.3	0.5	0.3		
Step 3— Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.860	0.5	0.7	0.4	Ok-at-step-2.	Ok-at-step-1.
D1/stream	2.224	0.4	0.6	0.3		
D2/ditch	2.878	0.5	0.7	0.4		
D2/stream	2.445	0.4	0.6	0.4		
D3/ditch	2.850	0.5	0.7	0.4		
D4/pond	0.098	0.0	0.0	0.0		
D4/stream	2.107	0.4	0.5	0.3		
D5/pond	0.098	0.0	0.0	0.0		
D5/stream	2.275	0.4	0.6	0.3		
D6/ditch	2.818	0.5	0.7	0.4		
R1/pond	0.098	0.0	0.0	0.0		
R1/stream	1.878	0.3	0.5	0.3		
R3/stream	2.638	0.4	0.7	0.4		
R4/stream	1.886	0.3	0.5	0.3		

Group		Fish-acute	Fish-prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Spring cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.044	0.5	0.8	Ok at step 2.	Ok at step 2.	Ok at step 1.
D1/stream	2.182	0.4	0.6			
D3/ditch	2.494	0.4	0.6			
D4/pond	0.125	0.0	0.0			
D4/stream	2.082	0.4	0.5			
D5/pond	0.113	0.0	0.0			
D5/stream	2.152	0.4	0.6			
R4/stream	6.499	1.1	1.7			
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.885	0.5	0.7	Ok at step 2.	Ok at step 2.	Ok at step 1.
D1/stream	2.523	0.4	0.6			
D3/ditch	2.853	0.5	0.7			
D4/pond	0.098	0.0	0.0			
D4/stream	2.332	0.4	0.6			
D5/pond	0.098	0.0	0.0			
D5/stream	2.395	0.4	0.6			
R4/stream	3.410	0.6	0.9			

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table A3-9a: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for folpet based on FOCUS Step 4 calculations and toxicity data for fish chronic with mitigation of spray drift and run-off for the use of SAP50SCF in cereals

Intended use	Cereals
Active substance	folpet
Application rate (g/ha)	2 x 450
Spring Cereals – Multiple applications – 10 m of vegetated filter strip	
R4/stream	2.937
RAC (µg/L)	
5.9	PEC/RAC ratio
R4/stream	0.5
RAC (µg/L)	
3.9	PEC/RAC ratio
R4/stream	0.8

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Effects on bees (KCP 10.3.1)

— Risk assessment according to SANCO/10329/2002 rev 2 final

Table A3-10: First tier assessment of the risk for bees due to the use of SAP50SCF in cereals

Intended-use	Cereals		
Active-substance	folpet		
Application rate (g a.s./ha)	2 × 450		
Test-design	LD ₅₀ (lab.) (µg a.s./bee)	Single-application rate (g a.s./ha)	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral-toxicity	>236	450	<1.9
Contact-toxicity	>200		<2.3
Product	SAP50SCF		
Application rate (g a.s./ha)	2 × 600		
Test-design	LD ₅₀ (lab.) (µ a.s.g/bee)	Single-application rate (g a.s./ha)	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral-toxicity	>302.41	450	<1.49
Contact-toxicity	>571.22		<0.79

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

Chronic risk to honey bees

Table A3-11: Chronic adult bees risk due to the use of SAP50SCF

Uses	Exposure Route	LDD ₅₀ [µg a.s./bee/day]	Maximum nectar consumption [mg nectar/bee/day]	Generic worst case residue intake of folpet [µg a.s./bee/day]	TER _{chronic}	Trigger
Cereals	Oral	16.29	321	0.32	50.9	+

Values in bold are above the trigger and indicate an acceptable risk to honey bees

Risk to honey bee larvae

Table A3-12: Chronic larvae risk for bees due to the use of SAP50SCF

Use	Scenario	NOED [µg a.s./larvae]	Maximum consumption of pollen/nectar [mg/larvae/day]	Generic worst case residue intake of folpet [µg a.s./larvae/day]	TER _{larvae}	Trigger
Cereals	Nectar	0.89	37.8	0.0378	23.5	+

— Risk assessment according to EFSA Journal 2013; 11(7):3295

Table A3-13: Screening step of the risk for bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use	Cereals					
Active substance	folpet					
Application rate (g a.s./ha)	2 × 450					
Test design	LD ₅₀ (lab.) (µg a.s./bee)	"Calculation factor"	HQ/ETR	Trigger	Risk indicator	
Acute oral toxicity	≥ 236	7.6	0.01	0.2	OK	
Acute contact toxicity	≥ 200	1	2.3	42	OK	

Chronic oral toxicity	16.29	7.6	0.210	0.03	!
Chronic larvae toxicity	2.16	4.4	2.22	0.2	!

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

Table A3-14: First tier of the risk for bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use		Cereals							
Active substance		folpet							
Application rate (g a.s./ha)		2 × 450							
Application	BBCH	Category	Scenario	Ef	SV-HB	TWA-HB	ETR	trigger	Risk indicator
Spray-DW	30-39	chronic	Treated crop	1	0.92	0.72	0.018	0.03	OK
	40-69	chronic	Treated crop	1	0.92	0.72	0.018	0.03	OK
	30-39	chronic	Weeds	0.5	2.9	0.72	0.029	0.03	OK
	40-69	chronic	Weeds	0.3	2.9	0.72	0.017	0.03	OK
	30-39	chronic	Field margin	0.0092	2.9	0.72	0.001	0.03	OK
	40-69	chronic	Field margin	0.0092	2.9	0.72	0.001	0.03	OK
	30-39	chronic	Adjacent crop	0.0033	5.8	0.72	0.000	0.03	OK
	40-69	chronic	Adjacent crop	0.0033	5.8	0.72	0.000	0.03	OK
	30-39	chronic	Next crop	1	0.54	0.72	0.011	0.03	OK
	40-69	chronic	Next crop	1	0.54	0.72	0.011	0.03	OK
	30-39	larva	Treated crop	1	0.15	0.85	0.06	0.2	OK
	40-69	larva	Treated crop	1	0.15	0.85	0.06	0.2	OK
	30-39	larva	Weeds	0.5	2.2	0.85	0.47	0.2	!
	40-69	larva	Weeds	0.3	2.2	0.85	0.28	0.2	!
	30-39	larva	Field margin	0.0092	2.2	0.85	0.01	0.2	OK
	40-69	larva	Field margin	0.0092	2.2	0.85	0.01	0.2	OK
	30-39	larva	Adjacent crop	0.0033	4.4	0.85	0.01	0.2	OK
	40-69	larva	Adjacent crop	0.0033	4.4	0.85	0.01	0.2	OK
	30-39	larva	Next crop	1	0.4	0.85	0.17	0.2	OK
	40-69	larva	Next crop	1	0.4	0.85	0.17	0.2	OK

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

Refined risk assessment:

Table A3-15: Refined risk assessment for bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use		Cereals							
Active substance		folpet							
Application rate (g a.s./ha)		2 × 450							
Application	BBCH	Category	Scenario	Ef	SV-HB	TWA-HB	ETR	trigger	Risk indicator
Spray-DW	30-39	larva	Weeds	0.2*	2.2	0.85	0.189	0.2	OK
	40-69	larva	Weeds	0.1*	2.2	0.85	0.095	0.2	OK

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

*refined parameters

Effects on bumble bees

~~— Risk assessment according to SANCO/10329/2002 rev 2 final~~

~~Table A3-16: First tier assessment of the risk for bumble bees due to the use of SAP50SCF in cereals~~

Intended use	Cereals		
Active substance	folpet		
Application rate (g a.s./ha)	2 × 450		
Test design	LD ₅₀ (lab.) (µg a.s./bee)	Single application rate (g a.s./ha)	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	≥ 100	450	< 4.5
Contact toxicity	≥ 100		< 4.5

~~Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.~~

~~— Risk assessment according to EFSA Journal 2013; 11(7):3295~~

~~Table A3-17: Screening step of the risk for bumble bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329~~

Intended use	Cereals				
Active substance	folpet				
Application rate (g a.s./ha)	2 × 450				
Test design	LD ₅₀ (lab.) (µg a.s./bee)	"Calculation factor"	HQ/ETR	Trigger	Risk indicator
Acute oral toxicity	≥ 100	1	4.5	2	OK
Acute contact toxicity	≥ 100	11.2	0.05	0.036	1

~~Table A3-18: First tier of the risk for bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329~~

Intended use	Cereals								
Active substance	folpet								
Application rate (g a.s./ha)	2 × 450								
Application	BBCH	Category	Scenario	Ef	SV BB	TWA BB	ETR	trigger	Risk indicator
Spray-DW	30-39	acute	Treated crop	1	2.3	1	0.0104	0.036	OK
	40-69	acute	Treated crop	1	2.3	1	0.0104	0.036	OK
	30-39	acute	Weeds	0.5	6.5	1	0.0146	0.036	OK
	40-69	acute	Weeds	0.3	6.5	1	0.0088	0.036	OK
	30-39	acute	Field margin	0.0092	6.5	1	0.0003	0.036	OK
	40-69	acute	Field margin	0.0092	6.5	1	0.0003	0.036	OK
	30-39	acute	Adjacent crop	0.0033	11.2	1	0.0002	0.036	OK
	40-69	acute	Adjacent crop	0.0033	11.2	1	0.0002	0.036	OK
	30-39	acute	Next crop	1	0.9	1	0.0041	0.036	OK
	40-69	acute	Next crop	1	0.9	1	0.0041	0.036	OK

~~Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.~~

Effects on solitary bees

~~— Risk assessment according to SANCO/10329/2002 rev 2 final~~

Table A3-19: First tier assessment of the risk for solitary bees due to the use of SAP50SCF in cereals

Intended use	Cereals		
Active substance	folpet		
Application rate (g a.s./ha)	2 x 450		
Test design	LD ₅₀ (lab.) (µg a.s./bee)	Single application rate (g a.s./ha)	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	>104.1	450	<4.3
Contact toxicity	>199.5		<2.3

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

— Risk assessment according to EFSA Journal 2013; 11(7):3295

Table A3-20: Screening step of the risk for solitary bees due to the use of SAP50SCF in cereals according to EFSA Journal 2013; 11(7):329

Intended use	Cereals				
Active substance	folpet				
Application rate (g a.s./ha)	2 x 450				
Test design	LD ₅₀ (lab.) (µg a.s./bee)	"Calculation factor"	HQ/ETR	Trigger	Risk indicator
Acute oral toxicity	>104.1	5.7	0.02	0.04	OK
Acute contact toxicity	>199.5	1	2.3	8	OK

Effects on arthropods other than bees (KCP 10.3.2)

Table A30-11: First and higher tier assessment of the in-field risk for non-target arthropods due to the use of SAP50SCF in cereals

Intended use	Cereals		
Active substance/product	folpet		
Application rate (g/ha)	2 x 450		
MAF	1.7		
Test species Tier I	LR ₅₀ (lab.) (g a.s./ha)	PER _{in-field} (g/ha)	HQ _{in-field} criterion: HQ ≤ 2
<i>Typhlodromus pyri</i>	>4000	765	<0.19
<i>Aphidius rhopalosiphii</i>	>1809.50		<0.42

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment. Criteria values shown in bold breach the relevant trigger.

* If an LR₅₀ or ER₅₀ from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50 % effect.

Table A3-22: First and higher tier assessment of the off-field risk for non-target arthropods due to the use of SAP50SCF in cereals

Intended use	Cereals		
Active substance/product	folpet		
Application rate (g/ha)	2 x 450		
MAF	1.7		
vdf	10 (2D studies)		

Test species Tier I	LR ₅₀ (lab.) (g a.s./ha)	Drift rate	PER _{off-field} (g/ha)	CF	HQ _{off-field} criterion: HQ ≤ 2
<i>Typhlodromus pyri</i>	>4000	2.38%	1.8207	10	<0.005
<i>Aphidius rhopalosiphi</i>	>1800-50				<0.010

MAF: Multiple application factor; vdf: Vegetation distribution factor; (corr.) PER: (corrected) Predicted environmental rate; CF: Correction factor; HQ: Hazard quotient. Criteria values shown in bold breach the relevant trigger.

*—— If an LR₅₀ or ER₅₀ from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50 % effect.

Effects on non-target soil meso- and macrofauna (KCP 10.4)

Table A3-13: First tier assessment of the acute and chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use of SAP50SCF in cereals

Intended use	Cereals		
Acute effects on earthworms — no longer a data requirement			
Chronic effects on earthworms			
Product/active substance	NOEC (mg/kg dw)	PEC _{soil} (mg/kg dw)	TER _{lit} (criterion TER ≥ 5)
folpet	5.18	0.198	26.2
Phthalimide	0.518*	0.069	7.51
Phthalamic acid	0.518*	0.011	47.1
Phthalic acid	0.518*	0.012	43.2
SAP50SCF	≥86.75	0.295	194.1
Chronic effects on other soil macro- and mesofauna			

TER values shown in bold fall below the relevant trigger.

*Assuming a worst case situation of the metabolite being 10 times more toxic than parent.

Effects on soil microbial activity (KCP 10.5)

Table A30-14: Assessment of the risk for effects on soil micro-organisms due to the use of SAP50SCF in cereals

Intended-use	Cereals		
N-mineralisation			
Product/active-substance	Max. conc. with effects ≤ 25 % (mg/kg dw)	PEC _{soil} (mg/kg dw)	Risk acceptable?
folpet	21.24 (at 63 d)	0.198	Yes
Phthalimide	2.124*	0.069	Yes
Phthalamie-acid	2.124*	0.011	Yes
Phthalic-acid	2.124*	0.012	Yes
SAP50SCF	19.50 (at 28 d)	0.295	Yes
C-mineralisation — no longer a data requirement			

*Assuming a worst case situation of the metabolite being 10 times more toxic than parent.

Effects on non-target terrestrial plants (KCP 10.6)

9.13.1.1 Tier 1 risk assessment (based screening data)

Limit tests at rates up to 1.6 kg a.s./ha (seedling emergence) and 3.2 kg a.s./ha (vegetative vigour) were conducted with a similar formulation and effects were below the critical threshold as defined by the “Guidance Document on Terrestrial Ecotoxicology”, (SANCO/10329/2002 rev.2 final, 2002). The limit test rates exceed the highest field application rate of 450 g and are thus considered an indicator for an acceptable risk.

Appendix 4 Additional calculations based on soil DT₅₀ of 4.68 days for folpet

zRMS comments:

The risk assessment provided by the Applicant has been evaluated by zRMS according to recommendation given by e-fate expert in Section 8.

Therefore, the risk assessment with PEC_{sw} calculations based on DT₅₀=5.68 days value has been accepted with and 10 m and 20 m VFS. The relevant calculation are copied to Point 9.5.2.

As indicated in section B8, the following calculations are provided for completeness and the Applicant stands by the risk assessment presented above.

- Maximum dose

Table A4-1: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for folpet for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP50SCF in cereals

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Test species		-	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Scenedesmus subspicatus</i>
Endpoint (µg/L)		HC ₅ 52.7	NOEC 39	EC ₅₀ 680	NOEC 320	E _r C ₅₀ 10000
AF		9	10	100	10	10
RAC (µg/L)		5.9	3.9	6.8	32	1000
FOCUS Scenario	PEC _{gl-max} (µg/L)					
Winter cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.363	0.6	0.9	0.5	0.1	0.0
D1/stream	2.838	0.5	0.7	0.4	0.1	0.0
D2/ditch	5.555	0.9	1.4	0.8	0.2	0.0
D2/stream	3.657	0.6	0.9	0.5	0.1	0.0
D3/ditch	3.324	0.6	0.9	0.5	0.1	0.0
D4/pond	0.143	0.0	0.0	0.0	0.0	0.0
D4/stream	2.510	0.4	0.6	0.4	0.1	0.0
D5/pond	0.174	0.0	0.0	0.0	0.0	0.0
D5/stream	2.898	0.5	0.7	0.4	0.1	0.0
D6/ditch	3.339	0.6	0.9	0.5	0.1	0.0
R1/pond	0.597	0.1	0.2	0.1	0.0	0.0
R1/stream	9.239	1.6	2.4	1.4	0.3	0.0
R3/stream	10.360	1.8	2.7	1.5	0.3	0.0
R4/stream	9.376	1.6	2.4	1.4	0.3	0.0
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.819	0.6	0.98	0.6	0.1	0.0
D1/stream	2.970	0.5	0.8	0.4	0.1	0.0
D2/ditch	5.546	0.9	1.4	0.8	0.2	0.0

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae
D2/stream	3.651	0.6	0.9	0.5	0.1	0.0
D3/ditch	3.800	0.6	0.97	0.6	0.1	0.0
D4/pond	0.131	0.0	0.0	0.0	0.0	0.0
D4/stream	2.809	0.5	0.7	0.4	0.1	0.0
D5/pond	0.131	0.0	0.0	0.0	0.0	0.0
D5/stream	3.034	0.5	0.8	0.4	0.1	0.0
D6/ditch	3.757	0.6	0.96	0.6	0.1	0.0
R1/pond	0.176	0.0	0.0	0.0	0.0	0.0
R1/stream	2.504	0.4	0.6	0.4	0.1	0.0
R3/stream	3.517	0.6	0.9	0.5	0.1	0.0
R4/stream	2.515	0.4	0.6	0.4	0.1	0.0
Spring cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	4.078	0.7	1.05	0.6	0.1	0.0
D1/stream	2.910	0.5	0.7	0.4	0.1	0.0
D3/ditch	3.325	0.6	0.9	0.5	0.1	0.0
D4/pond	0.167	0.0	0.0	0.0	0.0	0.0
D4/stream	2.776	0.5	0.7	0.4	0.1	0.0
D5/pond	0.151	0.0	0.0	0.0	0.0	0.0
D5/stream	2.869	0.5	0.7	0.4	0.1	0.0
R4/stream	13.350	2.3	3.4	2.0	0.4	0.0
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.851	0.7	0.99	0.6	0.1	0.0
D1/stream	3.365	0.6	0.9	0.5	0.1	0.0
D3/ditch	3.804	0.6	0.98	0.6	0.1	0.0
D4/pond	0.131	0.0	0.0	0.0	0.0	0.0
D4/stream	3.110	0.5	0.8	0.5	0.1	0.0
D5/pond	0.131	0.0	0.0	0.0	0.0	0.0
D5/stream	3.194	0.5	0.8	0.5	0.1	0.0
R4/stream	8.165	1.4	2.1	1.2	0.3	0.0

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

For the Step 4 calculations, only the comparison of the additional PEC_{SW} values with the lowest RAC of 3.9 µg/L will be presented here.

Table A4-2: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for folpet based on FOCUS Step 4 calculations and toxicity data for fish chronic with mitigation of spray drift and run-off for the use of SAP50SCF in cereals

Intended use	Cereals
Active substance	folpet
Application rate (g/ha)	2 x 600
<i>Winter Cereals - Multiple applications –15 meters of vegetated filter strip</i>	
D2/ditch	no further mitigation possible
R1/stream	3.221
R3/stream	3.634
R4/stream	3.273
RAC (µg/L)	
3.9	PEC/RAC ratio
R1/stream	0.8
R3/stream	0.9
R4/stream	0.8
<i>Winter Cereals - Multiple applications –20 meters of vegetated filter strip</i>	
R1/stream	2.198
R3/stream	2.482
R4/stream	2.235
RAC (µg/L)	
3.9	PEC/RAC ratio
R1/stream	0.6
R3/stream	0.6
R4/stream	0.6
<i>Winter Cereals - Single applications –5 meters of vegetated filter strip</i>	
D1/ditch	1.040
D2/ditch	no further mitigation possible
RAC (µg/L)	
3.9	PEC/RAC ratio
D1/ditch	0.3
<i>Winter Cereals - Single applications –10 meters of vegetated filter strip</i>	
D1/ditch	0.554
RAC (µg/L)	
3.9	PEC/RAC ratio
D1/ditch	0.1
<i>Spring Cereals - Multiple applications –20 m of vegetated filter strip</i>	
D1/ditch	0.310
R4/strean	3.155
RAC (µg/L)	
3.9	PEC/RAC ratio
D1/ditch	0.1
R4/strean	0.8

<i>Spring Cereals - Single application –10 meters of vegetated filter strip</i>	
R4/stream	3.684
RAC (µg/L) 3.9	PEC/RAC ratio
R4/stream	0.9

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

- Minimum dose

Table A4-3: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for folpet for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of SAP50SCF in cereals

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae
Test species		-	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Scenedesmus subspicatus</i>
Endpoint (µg/L)		HC ₅ 52.7	NOEC 39	EC ₅₀ 680	NOEC 320	E _t C ₅₀ 10000
AF		9	10	100	10	10
RAC (µg/L)		5.9	3.9	6.8	32	1000
FOCUS Scenario	PEC _{gl-max} (µg/L)					
Winter cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.522	0.4	0.6	0.4	0.1	0.0
D1/stream	2.129	0.4	0.5	0.3	0.1	0.0
D2/ditch	3.341	0.6	0.9	0.5	0.1	0.0
D2/stream	2.212	0.4	0.6	0.3	0.1	0.0
D3/ditch	2.493	0.4	0.6	0.4	0.1	0.0
D4/pond	0.107	0.0	0.0	0.0	0.0	0.0
D4/stream	1.882	0.3	0.5	0.3	0.1	0.0
D5/pond	0.130	0.0	0.0	0.0	0.0	0.0
D5/stream	2.173	0.4	0.6	0.3	0.1	0.0
D6/ditch	2.504	0.4	0.6	0.4	0.1	0.0
R1/pond	0.443	0.1	0.1	0.1	0.0	0.0
R1/stream	6.840	1.2	1.8	1.01	0.2	0.0
R3/stream	7.645	1.3	2.0	1.1	0.2	0.0
R4/stream	6.974	1.2	1.8	1.03	0.2	0.0
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.864	0.5	0.7	0.4	0.1	0.0
D1/stream	2.227	0.4	0.6	0.3	0.1	0.0
D2/ditch	3.335	0.6	0.9	0.5	0.1	0.0
D2/stream	2.445	0.4	0.6	0.4	0.1	0.0
D3/ditch	2.850	0.5	0.7	0.4	0.1	0.0
D4/pond	0.098	0.0	0.0	0.0	0.0	0.0

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae
D4/stream	2.107	0.4	0.5	0.3	0.1	0.0
D5/pond	0.098	0.0	0.0	0.0	0.0	0.0
D5/stream	2.275	0.4	0.6	0.3	0.1	0.0
D6/ditch	2.818	0.5	0.7	0.4	0.1	0.0
R1/pond	0.131	0.0	0.0	0.0	0.0	0.0
R1/stream	1.878	0.3	0.5	0.3	0.1	0.0
R3/stream	2.638	0.4	0.7	0.4	0.1	0.0
R4/stream	1.886	0.3	0.5	0.3	0.1	0.0
Spring cereals						
Step 3 – Multiple applications (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	3.057	0.5	0.8	0.4	0.1	0.0
D1/stream	2.182	0.4	0.6	0.3	0.1	0.0
D3/ditch	2.494	0.4	0.6	0.4	0.1	0.0
D4/pond	0.125	0.0	0.0	0.0	0.0	0.0
D4/stream	2.082	0.4	0.5	0.3	0.1	0.0
D5/pond	0.113	0.0	0.0	0.0	0.0	0.0
D5/stream	2.152	0.4	0.6	0.3	0.1	0.0
R4/stream	9.871	1.7	2.5	1.5	0.3	0.0
Step 3 – Single application (worst-case value between sets 1 and 2, further details refer to B8)						
D1/ditch	2.888	0.5	0.7	0.4	0.1	0.0
D1/stream	2.523	0.4	0.6	0.4	0.1	0.0
D3/ditch	2.853	0.5	0.7	0.4	0.1	0.0
D4/pond	0.098	0.0	0.0	0.0	0.0	0.0
D4/stream	2.332	0.4	0.6	0.3	0.1	0.0
D5/pond	0.098	0.0	0.0	0.0	0.0	0.0
D5/stream	2.395	0.4	0.6	0.4	0.1	0.0
R4/stream	6.020	1.02	1.5	0.9	0.2	0.0

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

For the Step 4 calculations, only the comparison of the additional PEC_{sw} values with the lowest RAC of 3.9 µg/L will be presented here.

Table A4-4: Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for folpet based on FOCUS Step 4 calculations and toxicity data for fish chronic with mitigation of spray drift and run-off for the use of SAP50SCF in cereals

Intended use	Cereals
Active substance	folpet
Application rate (g/ha)	2 x 450
Winter Cereals - Multiple applications –10 m of vegetated filter strip	
R1/strean	3.107
R3/strean	3.489
R4/strean	3.173

RAC (µg/L) 3.9	PEC/RAC ratio
R1/stream	0.8
R3/stream	0.9
R4/stream	0.8
<i>Spring Cereals - Multiple applications –15 m of vegetated filter strip</i>	
R4/stream	3.420
RAC (µg/L) 3.9	PEC/RAC ratio
R4/stream	0.9
<i>Spring Cereals - Multiple applications –20 m of vegetated filter strip</i>	
R4/stream	2.332
RAC (µg/L) 3.9	PEC/RAC ratio
R4/stream	0.6
<i>Spring Cereals - Single applications –10 m of vegetated filter strip</i>	
R4/stream	2.717
RAC (µg/L) 3.9	PEC/RAC ratio
R4/stream	0.7

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Dose	Application number	Crop	Mitigation measure
Maximum dose	Single	Winter cereals	D1 scenario: 5 meters of vegetated filter strip D2 scenario: restriction of application
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	D2 scenario: restriction of application R1, R3 and R4 scenarios: 15 meters of vegetated filter strip
		Spring cereals	D1, R4 scenario: 20 meters of vegetated filter strip
Minimum dose (see Appendix 3)	Single	Winter cereals	None
		Spring cereals	R4 scenario: 10 meters of vegetated filter strip
	Multiple	Winter cereals	R1, R3 and R4 scenarios: 10 meters of vegetated filter strip
		Spring cereals	R4 scenario: 15 meters of vegetated filter strip