

FINAL REGISTRATION REPORT

Part B

Section 9

Ecotoxicology

Detailed summary of the risk assessment

Product code: GLOB2106cF

Product name: Revus Pro

Chemical active substances:

Propamocarb-HCl, 450 g/L

Mandipropamid, 75 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Globachem NV

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MS Finalisation date: 06/03/2024

Version history

When	What
March 2023	Initial dossier submission by applicant for approval of new product
July 2023	Dossier sent for evaluation
November 2023	zRMS evaluation of dRR
March 2024	Final version prepared by zRMS after Commenting period

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Evaluator comments:

The text highlighted in grey was provided by the evaluator.

9 Ecotoxicology (KCP 10)

9.1 Critical GAP and overall conclusions

Table 9.1-1: 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 saf- ener/ 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	Soil organisms	Non-target plants
Zonal uses (field or outdoor uses, certain types of protected crops)																				
1	PL, BE, CZ, DE, NL	Seed, ware and starch potato (SOLTU)	F	<i>Phytophthora infestans</i> (PHYTIN)	Normal downward spraying	After emergence to shortly before harvest (BBCH21- 89)	a) 3 b) 3	7	a) 1.9 b) 5.7	a) Propamocarb- HCl: 0.855 + Mandipropamid: 0.1425 b) Propamocarb- HCl: 2.565 + Mandipropamid: 0.4275	150-300	14	/							

* 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

Explanation for column 15 – 21 “Conclusion”

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 for birds and mammals is acceptable when GLOB2106cF is applied according to the intended uses.

9.1.1.2 Effects on aquatic organisms (KCP 10.2)

The risk for aquatic organisms is acceptable when GLOB2106cF is applied according to the intended uses.

9.1.1.3 Effects on bees (KCP 10.3.1)

The risk for bees is acceptable when using GLOB2106cF according to the intended uses.

9.1.1.4 Effects on arthropods other than bees (KCP 10.3.2)

The risk for non-target arthropods is acceptable when using GLOB2106cF according to the intended uses. No risk mitigation measures are needed.

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 for soil macro- and mesofauna is acceptable when using GLOB2106cF according to the intended uses.

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

The risk is acceptable for non-target plant following exposure to GLOB2106cF according to the intended uses. No mitigation measures are needed.

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

Not required.

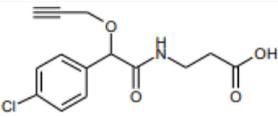
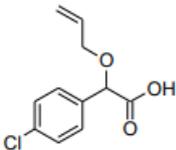
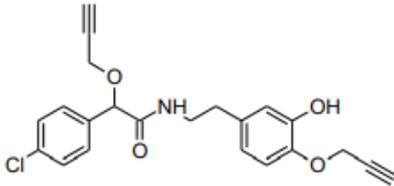
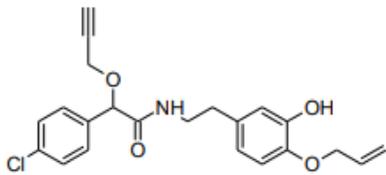
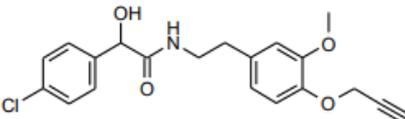
9.1.2 Grouping of intended uses for risk assessment

All risk assessments have been conducted at the dose rate of 3 x 1.9 L/ha applied between BBCH 21 and 89.

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 GLOB2106cF is indicated in the table.

Table 9.1-2 Metabolites of Mandipropamid

Metabolite	Molar mass	Chemical structure	Maximum observed occurrence in compartments	Exposure assessment required due to
SYN 500003	224.7 g/mol		Soil: <10% Water/sediment systems: - water: 9.2%, - sediment: 3.5%	PEC _{sw/sed} : risk to aquatic organisms
SYN 504851	226.7g/mol		Soil: <10% Water/sediment systems: - water: 21.0%, - sediment: 24.3%	PEC _{sw/sed} : risk to aquatic organisms
SYN 521195	397.9 g/mol		Water/sediment systems: - water: 3.4%, - sediment: 15.6%	PEC _{sw/sed} : risk to aquatic organisms
SYN 539678	399.9 g/mol		Water/sediment systems: - water: 1.9%, - sediment: 11.2%	PEC _{sw/sed} : risk to aquatic organisms
CGA 380778	373.8 g/mol		Soil: 6.0% Water/sediment systems: - total system: 0.001%	PEC _{soil} : risk to soil organisms PEC _{sw/sed} : risk to aquatic organisms

9.2 Effects on birds (KCP 10.1.1)

zRMS Comments:	<p>The risk assessment was performed in accordance with the B & M Guidance, EFSA (2009). All relevant used endpoints were agreed at the EU level.</p> <p>Propamocarb-HCl. The acute and long-term risk were submitted at screening and First Tier. The submitted acute and long-term risk to birds was accepted. The TER_A and TER_{LT} values exceed the trigger values of 10 and 5, respectively, indicating an acceptable risk for birds.</p> <p>Mandipropamid. The acute and long-term risk were submitted at screening step. The submitted acute and long-term risk to birds was accepted. The TER_A and TER_{LT} values exceed the trigger values of 10 and 5, respectively, indicating an acceptable risk for birds.</p> <p>Mixture toxicity. The submitted risk assessment was accepted.</p> <p>Secondary poisoning. For both active substances and mandipropamid relevant metabolite SYN 539678, the risk assessment for fish-eating and earthworm-eating birds was performed and the TER_{LT} values are above the trigger value of 5.</p>
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9.2.1 Toxicity data

Avian toxicity studies have been carried out with Propamocarb-HCl, Mandipropamid and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents. Effects on birds of GLOB2106cF were not evaluated as part of the EU assessment of Propamocarb-HCl and Mandipropamid. However, the provision of further data on the GLOB2106cF is not considered essential, because the risk for birds from GLOB2106cF can be adequately assessed from the risk assessment of the active substances. 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
Bobwhite quail	Propamocarb-HCl	Acute Oral	>1842 mg a.s./kg b.w.	EFSA Scientific Report (2006) 78, 1-80
Bobwhite quail	Propamocarb-HCl	Short-term dietary	>962 mg a.s./kg b.w./day*	EFSA Scientific Report (2006) 78, 1-80
Bobwhite quail	Propamocarb-HCl	Long-term dietary/reproductive	105 mg a.s./kg b.w./day	EFSA Scientific Report (2006) 78, 1-80
Mallard duck	Mandipropamid	Acute oral	>1000 mg a.s./kg	EFSA Scientific

Species	Substance	Exposure System	Results	Reference
			b.w.	Report (2012) 10(11), 2935
Bobwhite quail	Mandipropamid	Short-term dietary	> 2141 mg a.s./kg b.w./day	EFSA Scientific Report (2012) 10(11), 2935
Bobwhite quail	Mandipropamid	Sub-chronic and reproductive	83.6 mg/kg bw/d	EFSA Scientific Report (2012) 10(11), 2935

* According to the zRMS, no mortality or moribund effects were observed in the short-term dietary toxicity test providing an endpoint of >962 mg as/kg bw/day (corresponding to the maximal tested concentration of 5000 mg as/kg feed). Therefore, the LD50 >1842 mg a.s./kg b.w. can be used for the acute TER calculation for Propamocarb-HCl.

9.2.1.1 Justification for new endpoints

/

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

Not relevant.

9.2.3 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).

9.2.3.1 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 GLOB2106cF in potatoes

Intended use		Potatoes				
Active substance/product		Propamocarb-HCl				
Application rate (g/ha)		3 × 855 g a.i./ha				
Acute toxicity (mg/kg bw)		>1842				
TER criterion		10				
Crop scenario	Indicator/generic focal species	SV ₉₀	MAF ₉₀	DDD ₉₀ (mg/kg bw/d)	TER _a	
-	Small omnivorous bird	158.8	1.6	217.24	8.48	
Reprod. toxicity (mg/kg bw/d)		105				
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	2.0 x 0.53	58.72	1.79
Intended use		Potatoes			
Active substance/product		Mandipropamid			
Application rate (g/ha)		3 × 142.5 g a.i./ha			
Acute toxicity (mg/kg bw)		1000			
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	1.6	22.63	44.19
Reprod. toxicity (mg/kg bw/d)		83.6			
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	2.0 x 0.53	9.79	8.54

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.

Since the acute and chronic TER values of Propamocarb-HCl are below the thresholds, a first-tier assessment needs to be performed for this active only.

Table 9.2-3: First-tier assessment of the acute and long-term/reproductive risk for birds due to the use of GLOB2106cF in potato

Intended use		Potatoes			
Active substance		Propamocarb-HCl			
Application rate (g/ha)		3 × 855 g a.i./ha			
Acute toxicity (mg/kg bw)		>1842			
TER criterion		10			
Crop scenario Growth stage	Indicator/generic focal species	SV ₉₀	MAF ₉₀	DDD ₉₀ (mg/kg bw/d)	TER _a
BBCH ≥ 20	Small insectivorous bird “wagtail”	25.2	1.6	34.47	53.4
BBCH ≥ 40	Small omnivorous bird “lark”	7.2	1.6	9.85	187.0
BBCH 10 - 19	Small insectivorous bird “wagtail”	26.8	1.6	36.66	50.2
BBCH 10 - 39	Small omnivorous bird “lark”	24.0	1.6	32.83	56.1
Reprod. toxicity (mg/kg bw/d)		105			
TER criterion		5			
Crop scenario Growth stage	Indicator/generic focal species	SV _m	MAF _m × TWA	DDD _m (mg/kg bw/d)	TER _{lt}
BBCH ≥ 20	Small insectivorous bird “wagtail”	9.7	2.0 x 0.53	8.79	11.9

BBCH ≥ 40	Small omnivorous bird “lark”	3.3	2.0 x 0.53	2.99	35.1	
BBCH 10 - 19	Small insectivorous bird “wagtail”	11.3	2.0 x 0.53	10.24	10.3	
BBCH 10 - 39	Small omnivorous bird “lark”	10.9	2.0 x 0.53	9.88	10.6	
Intended use		Potatoes				
Active substance/product						
Application rate (g/ha)						
Acute toxicity (mg/kg bw)						
TER criterion						
		Mandipropamid				
		3 × 142.5 g a.i./ha				
		1000				
		10				
Crop scenario	Indicator/generic focal species	SV₉₀	MAF₉₀	DDD₉₀	TER_a	
Growth stage				(mg/kg bw/d)		
BBCH 10 - 19	Small insectivorous bird “wagtail”	26.8	1.6	6.11	163.7	
Reprod. toxicity (mg/kg bw/d)		83.6				
TER criterion		5				

$$rpf_{a.s.1} = \frac{1}{TER_{a.s.1}} / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} + \dots + \frac{1}{TER_{a.s.i}} \right)$$

Crop scenario	Indicator/generic focal species	SV_m	MAF_m × TWA	DDD_m	TER_{lt}
Growth stage				(mg/kg bw/d)	
BBCH 10 - 19	Small insectivorous bird “wagtail”	11.3	2.0 x 0.53	1.71	48.9

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.

Assessment of combined toxicity

As requested by the Central Zone when a product contains more than one active substance, an additional assessment on combined toxicity risk has to be presented. It is considered that a quantitative toxicity risk assessment according to concentration addition is not needed if one of the following points applies:

- The risk assessment for all active substances in the product passes with a high margin of safety
- One active substance clearly drives the risk assessment

These conditions are assessed following a step-wise approach. Note that for the calculation only the scenario with the lowest TER values was considered (most critical scenario). This safely covers all other scenarios.

1st step: Margin of safety

Condition: all TER values are > Trigger × n (n = number active substances in the mixture; in this case 2). For this reason, the applicant has calculated the first-tier TER values for Mandipropamid with regard to the worst-case scenario for Propamocarb-HCl at that level (Table 9.2-3).

2nd step: Risk per fraction

Condition: One a.s. contributes to ≥ 90% of the predicted combined toxicity of the product.

Assessment: The contribution of each individual a.s. to the combined toxicity (risk per fraction, rpf) is estimated based on the following equation:

The estimation is based on TER values from the same refinement level to assure comparability.

3rd step: TER_{MIX} calculation

Condition: The combined toxicity is acceptable if $TER_{MIX} \geq 10$ (acute) or 5 (long-term)

Assessment: The combined toxicity risk (TER_{MIX}) with concentration-addition is estimated based on the following equation:

$$TER_{mix} = 1 / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} + \dots + \frac{1}{TER_{a.s.i}} \right)$$

Table 9.2-4: Combined toxicity assessment – birds

Intended use	Potatoes, BBCH 21-89				
Active substances	Propamocarb-HCl, Mandipropamid				
Application rate	1.9 L/ha				
	TER values		Step 1 All TER ≥ trigger x n	Step 2 Rpf_{max}	Step 3 TER_{MIX}
	Propamocarb-HCl	Mandipropamid			
Acute	50.2	163.7	Yes	Not needed	Not needed
Chronic	10.3	48.9	Yes	Not needed	Not needed

An acceptable acute and chronic risk for birds from the combined exposure to all active substances in the product can be concluded due to a high margin of safety (all TER values > trigger × 2).

9.2.3.2 Higher-tier risk assessment

Not needed.

9.2.3.3 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 GLOB2106cF 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 263.65 mL/g, Propamocarb-HCl belongs to the group of less sorptive substances. With a $K(f)_{oc}$ of 795.4 mL/g, Mandipropamid belongs to the group of more sorptive substances. To achieve a concise risk assessment, the risk envelope approach is applied. To take into account the 3 applications, a MAF of 1.6 was used as a worst-case (effective application rate = application rate × 1.6).

Propamocarb-HCl				
Effective application rate (g/ha)=	1368			
Acute toxicity (mg/kg bw) =	1842	quotient	=	0.743

Reprod. toxicity (mg/kg bw/d) =	105	quotient =	13.03
Mandipropamid			
Effective application rate (g/ha)=	228		
Acute toxicity (mg/kg bw) =	1000	quotient =	0.228
Reprod. toxicity (mg/kg bw/d) =	83.6	quotient =	2.727

9.2.3.4 Effects of secondary poisoning

The log P_{ow} of Propamocarb-HCl amounts up to 0.67 at pH 9 (EFSA, 2006) and thus does not exceed the trigger value of 3. A risk assessment for effects due to secondary poisoning is not required.

The log P_{ow} of Mandipropamid amounts to 3.2 (EFSA, 2012) and thus exceeds the trigger value of 3. A risk assessment for effects due to secondary poisoning is required.

The log P_{ow} value of the Mandipropamid soil metabolite CGA 380778 is 2.6. The log P_{ow} of aquatic metabolites SYN 504851 and SYN 500003 are pH-dependent, being -0.86 and -1.2, respectively, at pH 6.8 and still under 3 when corrected to the neutral form only. The log P_{ow} of the sediment metabolites SYN 521195 and SYN 539678 were estimated to be 2.85 and 3.24, respectively. Consideration of bioaccumulation of SYN 539678 (sediment metabolite) is therefore required. The exposure to this metabolite will clearly be far lower than that for the parent. Furthermore, although the toxicity of this metabolite to birds has not been measured, its toxicity (measured or estimated) to soil or aquatic organisms is similarly low or lower than that of Mandipropamid. On this basis, risk of secondary poisoning from parent Mandipropamid provides a worst-case scenario. Since exposure to the parent poses a negligible secondary poisoning risk to earthworm-eating birds and fish-eating birds (see risk assessments below), the risk from the metabolite is also expected to be negligible. For the sake of completeness, the applicant performs the risk assessment for SYN 539678 (sediment metabolite) regarding fish-eating birds using the endpoint of Mandipropamid divided by 10.

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.

Table 9.2-5: Assessment of the risk for earthworm-eating birds due to exposure to Mandipropamid via bioaccumulation in earthworms (secondary poisoning) for the intended use in potatoes

Parameter	Mandipropamid	comments
PEC _{soil} (mg/kg soil)	0.2092	See dRR Part B8 Table 8.7-3
log P_{ow} / P_{ow}	3.2/1585	
K _{oc}	795.4	Geomean (n = 7)
f _{oc}	0.02	Default
BCF _{worm}	1.25	$BCF_{worm/soil} = (PEC_{worm,ww}/PEC_{soil,dw}) = (0.84 + 0.012 \times P_{ow}) / f_{oc} \times K_{oc}$
PEC _{worm}	0.2615	$PEC_{worm} = PEC_{soil} \times BCF_{worm/soil}$
Daily dietary dose (mg/kg bw/d)	0.275	DDD = PEC _{worm} × 1.05
NOEL (mg/kg bw/d)	83.6	
TER _{lt}	304	

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.

Table 9.2-6: Assessment of the risk for fish-eating birds due to exposure to Mandipropamid via bioaccumulation in fish (secondary poisoning) for the intended use in potatoes

Parameter	Mandipropamid	comments
PEC _{sw} (mg/L)	0.00247	dRR Section B8 Table 8.9-9 (Step 3), R3/stream worst-case value
BCF _{fish}	19.7	
BMF	-	biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	0.049	$PEC_{fish} = PEC_{water} \times BCF_{fish}$
Daily dietary dose (mg/kg bw/d)	0.008	$DDD = PEC_{fish} \times 0.159$
NOEL (mg/kg bw/d)	83.6	
TER _{lt}	10450	

TER values shown in bold fall below the relevant trigger.

Table 9.2-7: Assessment of the risk for fish-eating birds due to exposure to SYN 539678 via bioaccumulation in fish (secondary poisoning) for the intended use in potatoes

Parameter	SYN 539678	comments
PEC _{sw} (mg/L)	0.0025142	dRR Section B8 Table 8.9-21 (Step 2), worst-case value
BCF _{fish}	19.7	
BMF	-	biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	0.05	$PEC_{fish} = PEC_{water} \times BCF_{fish}$
Daily dietary dose (mg/kg bw/d)	0.008	$DDD = PEC_{fish} \times 0.159$
NOEL (mg/kg bw/d)	8.36	Parent endpoint divided by 10
TER _{lt}	1045	

TER values shown in bold fall below the relevant trigger.

9.2.3.5 Biomagnification in terrestrial food chains

Not relevant.

9.2.4 Overall conclusions

The risk for birds is acceptable when GLOB2106cF is applied according to the intended uses.

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

zRMS Comments:	<p>The submitted acute and long-term risk to mammals was accepted. The risk assessment was performed in accordance with the B & M Guidance, EFSA (2009). All relevant used endpoints were agreed at the EU level.</p> <p>Propamocarb-HCl and Mandipropamid. The acute and long-term risk were submitted at screening and First Tier. The submitted acute and long-term risk to birds was accepted. The TER_A and TER_{LT} values exceed the trigger values of 10 and 5, respectively, indicating an acceptable risk for mammals.</p> <p>Mixture toxicity. The submitted risk assessment for mammals due to use of formulation GLOB2106cF was accepted. For chronic risk assessment the higher tier assessment was provided. The refinement based on deposition factor (interception) was accepted. The refinement based on refined DT₅₀ values for both active substances was not necessary as the former one was sufficient. This approach was not evaluated. For both active substances and mandipropamid relevant metabolite SYN 539678, the risk assessment for fish-eating and earthworm-eating mammals was performed and the TER_{LT} values are above the trigger value of 5.</p>
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9.3.1 Toxicity data

Mammalian toxicity studies have been carried out with Propamocarb-HCl, Mandipropamid and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents. Effects on mammals of GLOB2106cF were not evaluated as part of the EU assessment of Propamocarb-HCl and Mandipropamid. However, the provision of further data on the formulation GLOB2106cF is not considered essential, because the risk for mammals from GLOB2106cF can be adequately assessed from the risk assessment for the active substances.

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	Propamocarb-HCl	Oral Acute	LC ₅₀ LD ₅₀ = 1330 mg/kg bw	EFSA, 2006
Rat	Propamocarb-HCl	Reproductive toxicity (long-term)	NOAEL = 104 mg/kg bw/day	EFSA, 2006
Rat	Mandipropamid	Oral Acute	LC ₅₀ LD ₅₀ > 5000 mg/kg bw	EFSA, 2012
Rat	Mandipropamid	Reproductive toxicity (long-term)	NOEL NOAEL = 20 mg/kg bw/day	EFSA, 2012

zRMS Comments	The abbreviation of endpoints was corrected in accordance with relevant EFSA scientific reports for both active substances.
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9.3.1.1 Justification for new endpoints

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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).

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 GLOB2106cF in potatoes

Intended use		Potatoes				
Active substance/product		Propamocarb-HCl				
Application rate (g/ha)		3 × 855				
Acute toxicity (mg/kg bw)		1330				
TER criterion		10				
Crop scenario	Indicator/generic focal species	SV₉₀	MAF₉₀	DDD₉₀ (mg/kg bw/d)	TER_a	
-	Small herbivorous mammal	118.4	1.6	161.97	8.2	
Reprod. toxicity (mg/kg bw/d)		104				
TER criterion		5				
Crop scenario	Indicator/generic focal species	SV_m	MAF_m × TWA	DDD_m (mg/kg bw/d)	TER_{lt}	
-	Small herbivorous mammal	48.3	2.0 x 0.53	51.20	2.03	

Intended use		Potatoes				
Active substance/product		Mandipropamid				
Application rate (g/ha)		3 × 142.5				
Acute toxicity (mg/kg bw)		5000				
TER criterion		10				
Crop scenario	Indicator/generic focal species	SV₉₀	MAF₉₀	DDD₉₀ (mg/kg bw/d)	TER_a	
-	Small herbivorous mammal	118.4	1.6	27.00	185.2	
Reprod. toxicity (mg/kg bw/d)		20				
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	2.0 x 0.53	7.30	2.74

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.

The TER_A value is greater than the trigger of 10 for Mandipropamid only. Also, the TER_{LT} values (first-tier) are lower than 5, triggering further chronic risk assessment for both active substances.

Table 9.3-3: First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of GLOB2106cF in potatoes

Intended use	Potatoes				
Active substance/product	Propamocarb-HCl				
Application rate (g/ha)	3 × 855				
Acute toxicity (mg/kg bw/d)	1330				
TER criterion	10				
Crop scenario Growth stage	Indicator/generic focal species	SV ₉₀	MAF ₉₀	DDD ₉₀ (mg/kg bw/d)	TER _a
BBCH ≥ 20	Small insectivorous mammal “shrew”	5.4	1.6	7.39	180.0
BBCH ≥ 40	Large herbivorous mammal “lagomorph”	10.5	1.6	14.36	92.6
BBCH ≥ 40	Small herbivorous mammal “vole”	40.9	1.6	55.95	23.8
BBCH ≥ 40	Small omnivorous mammal “mouse”	5.2	1.6	7.11	187.0
BBCH 10 - 19	Small insectivorous mammal “shrew”	7.6	1.6	10.40	127.9
BBCH 10 - 39	Small omnivorous mammal “mouse”	17.2	1.6	23.53	56.5
BBCH 10 - 40	Large herbivorous mammal “lagomorph”	35.1	1.6	48.02	27.7
Reprod. toxicity (mg/kg bw/d)	104				
TER criterion	5				
Crop scenario Growth stage	Indicator/generic focal species	SV _m	MAF _m × TWA	DDD _m (mg/kg bw/d)	TER _{lt}
BBCH ≥ 20	Small insectivorous mammal “shrew”	1.9	2.0 x 0.53	1.72	60.4
BBCH ≥ 40	Large herbivorous mammal “lagomorph”	4.3	2.0 x 0.53	3.90	26.7
BBCH ≥ 40	Small herbivorous mammal “vole”	21.7	2.0 x 0.53	19.67	5.3
BBCH ≥ 40	Small omnivorous mammal “mouse”	2.3	2.0 x 0.53	2.08	49.9
BBCH 10 - 19	Small insectivorous mammal “shrew”	4.2	2.0 x 0.53	3.81	27.3
BBCH 10 - 39	Small omnivorous mammal	7.8	2.0 x 0.53	7.07	14.7

	“mouse”				
BBCH 10 - 40	Large herbivorous mammal “lagomorph”	14.3	2.0 x 0.53	12.96	8.0
Intended use	Potatoes				
Active substance/product	Mandipropamid				
Application rate (g/ha)	3 × 142.5				
Acute toxicity (mg/kg bw)	5000				
TER criterion	10				
Crop scenario	Indicator/generic focal species	SV₉₀	MAF₉₀	DDD₉₀ (mg/kg bw/d)	TER_a
BBCH ≥ 40	Small herbivorous mammal “vole”	40.9	1.6	9.33	535.9
Reprod. toxicity (mg/kg bw/d)	20				
TER criterion	5				
Crop scenario	Indicator/generic focal species	SV_m	MAF_m × TWA	DDD_m (mg/kg bw/d)	TER_{it}
BBCH ≥ 20	Small insectivorous mammal “shrew”	1.9	2.0 x 0.53	0.29	69.7
BBCH ≥ 40	Large herbivorous mammal “lagomorph”	4.3	2.0 x 0.53	0.65	30.8
BBCH ≥ 40	Small herbivorous mammal “vole”	21.7	2.0 x 0.53	3.28	6.1
BBCH ≥ 40	Small omnivorous mammal “mouse”	2.3	2.0 x 0.53	0.35	57.6
BBCH 10 - 19	Small insectivorous mammal “shrew”	4.2	2.0 x 0.53	0.63	31.5
BBCH 10 - 39	Small omnivorous mammal “mouse”	7.8	2.0 x 0.53	1.18	17.0
BBCH 10 - 40	Large herbivorous mammal “lagomorph”	14.3	2.0 x 0.53	2.16	9.3

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.

Assessment of combined toxicity

As requested by the Central Zone when a product contains more than one active substance, an additional assessment on combined toxicity risk has to be presented. It is considered that a quantitative toxicity risk assessment according to concentration addition is not needed if one of the following points applies:

- The risk assessment for all active substances in the product passes with a high margin of safety
- One active substance clearly drives the risk assessment

These conditions are assessed following a step-wise approach. Note that for the calculation only the scenario with the lowest TER values was considered (most critical scenario). This safely covers all other scenarios.

1st step: Margin of safety

Condition: all TER values are $> \text{Trigger} \times n$ (n = number active substances in the mixture; in this case 2). For this reason, the applicant has calculated the first-tier acute TER values for Mandipropamid with regard to the worst-case scenario for Propamocarb-HCl at that level (Table 9.3-3).

2nd step: Risk per fraction

Condition: One a.s. contributes to $\geq 90\%$ of the predicted combined toxicity of the product.

Assessment: The contribution of each individual a.s. to the combined toxicity (risk per fraction, rpf) is estimated based on the following equation:

The estimation is based on TER values from the same refinement level to assure comparability.

3rd step: TER_{MIX} calculation

Condition: The combined toxicity is acceptable if TER_{MIX} ≥ 10 (acute) or 5 (long-term)

Assessment: The combined toxicity risk (TER_{MIX}) with concentration-addition is estimated based on the following equation:

$$TER_{mix} = 1 / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} + \dots + \frac{1}{TER_{a.s.i}} \right)$$

Table 9.3-4: Combined toxicity assessment – mammals

$$rpf_{a.s.1} = \frac{1}{TER_{a.s.1}} / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} + \dots + \frac{1}{TER_{a.s.i}} \right)$$

Intended use	Potatoes, BBCH 21-89				
Active substances	Propamocarb-HCl, Mandipropamid				
Application rate	1.9 L/ha				
	TER values		Step 1 All TER \geq trigger x n	Step 2 Rpf_{max}	Step 3 TER_{MIX}
	Propamocarb-HCl	Mandipropamid			
Acute	23.8	535.9	Yes	Not needed	Not needed
Chronic – small herbivorous mammal “vole”	5.3	6.1	No	0.54 (Propamocarb-HCl) ^a	2.84
Chronic – large herbivorous mammal “lagomorph”	8.0	9.3	No	0.54 (Propamocarb-HCl) ^b	4.30

a) Calculation of rpf for “vole”

	Propamocarb-HCl	Mandipropamid
TER	5.3	6.1
1/TER	0.19	0.16
rpf	0.54	0.46

b) Calculation of rpf for “lagomorph”

	Propamocarb-HCl	Mandipropamid
TER	8.0	9.3
1/TER	0.13	0.11
rpf	0.54	0.46

An acceptable acute risk for mammals from the combined exposure to all active substances in the product can be concluded due to a high margin of safety (all TER values $> \text{trigger} \times 2$).

For the chronic risk for mammals from combined exposure to all active substances in the product, further refinements are required as presented below. Note that for the calculation only the scenarios with the lowest TER values were considered (two scenarios with TER values below 10 for both actives *i.e.* BBCH ≥ 40 , *Small herbivorous mammal “vole”* and *BBCH 10-40 Large herbivorous mammal “lagomorph”*). For the other scenarios, the TER_{MIX} is higher than 10, showing an acceptable chronic risk for mammals from combined exposure to all active substances in the product.

9.3.2.2 Higher-tier risk assessment

Small herbivorous mammal “vole”, BBCH ≥ 40

Deposition factor:

For the refinement, the deposition values as described in EFSA GD, Appendix E were used. Interception can only be taken into account at later growth stages with high vegetation coverage. Interception values according to FOCUS groundwater (EFSA Journal 2014;12(5):3662) were used.

For the uses in potatoes at BBCH 40-89, the interception is 85 % leading to a deposition of 15% (used in the calculation of the refined SV, see Table 9.3-5).

Table 9.3-5: Refined reproductive risk assessment for small herbivorous mammals exposed in potatoes at BBCH 40-89, interval between applications 7 days

Intended use		Potatoes			
Active substance/product		Propamocarb-HCl			
Application rate (g/ha)		3 × 855			
Reprod. toxicity (mg/kg bw/d)		104			
TER criterion		5			
Crop scenario Growth stage	Indicator/generic focal species	Refined SV_m	MAF_m × TWA	DDD_m (mg/kg bw/d)	TER_{it}
BBCH ≥ 40	Small herbivorous mammal “vole”	FIRbw (1.33) × RUDmean (54.2) × deposition (0.15) = 10.8	2.0 × 0.53	9.79	10.6
Intended use		Potatoes			
Active substance/product		Mandipropamid			
Application rate (g/ha)		3 × 142.5			
Reprod. toxicity (mg/kg bw/d)		20			
TER criterion		5			
Crop scenario Growth stage	Indicator/generic focal species	SV_m	MAF_m × TWA	DDD_m (mg/kg bw/d)	TER_{it}
BBCH ≥ 40	Small herbivorous mammal “vole”	FIRbw (1.33) × RUDmean (54.2) × deposition (0.15) = 10.8	2.0 × 0.53	1.63	12.3

TER_{MIX} calculation

Condition: The combined toxicity is acceptable if $TER_{MIX} \geq 5$ (long-term)

Assessment: The combined toxicity risk (TER_{MIX}) with concentration-addition is estimated based on the following equation:

$$TER_{mix} = 1 / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} + \dots + \frac{1}{TER_{a.s.i}} \right)$$

After refinement, the TER_{MIX} equals to 5.7, showing an acceptable chronic risk for mammals from the combined exposure to all active substances in the product.

Large herbivorous mammal “lagomorph”, BBCH 10-40

Refinement 1: focal species

The generic focal species “lagomorph” in the potato scenario is cited as a rabbit, with bodyweight 1543 g and FIR/bw 0.50. In fact, either rabbit or hare may be present in any crop type (for rabbit, largely depending on the presence of warrens), and the more relevant focal species on the basis of vulnerability is the Brown hare, *Lepus europaeus* (Topping & Weyman 2018). In the EFSA guidance, the Brown hare is only used as a generic focal species in vineyards, eating non-grass herbs as for the “rabbit” in potato crops. Therefore, the FIR/bw for the hare in vineyards can be used directly for the hare in potatoes. The standard hare has bodyweight 3800 g and FIR/bw for eating non-grass herbs of 0.39. This is used in the refined risk assessment below.

Table 9.3-6: Refined reproductive risk assessment for large herbivorous mammals exposed in potatoes at BBCH 10-40, interval between applications 7 days

Intended use		Potatoes			
Active substance/product		Propamocarb-HCl			
Application rate (g/ha)		3 × 855			
Reprod. toxicity (mg/kg bw/d)		104			
TER criterion		5			
Crop scenario	Indicator/generic focal species	Refined SV_m	MAF_m × TWA	DDD_m (mg/kg bw/d)	TER_{it}
BBCH 10 - 40	Large herbivorous mammal “lagomorph”	FIRbw (0.39) × RUDmean (28.7) × deposition (1) = 11.2	2.0 × 0.53	10.2	10.2
Intended use		Potatoes			
Active substance/product		Mandipropamid			
Application rate (g/ha)		3 × 142.5			
Reprod. toxicity (mg/kg bw/d)		20			
TER criterion		5			
Crop scenario	Indicator/generic focal species	SV_m	MAF_m × TWA	DDD_m (mg/kg bw/d)	TER_{it}
BBCH 10 - 40	Large herbivorous mammal “lagomorph”	FIRbw (0.39) × RUDmean (28.7) × deposition (1) = 11.2	2.0 × 0.53	1.69	11.8

TER_{MIX} calculation

Condition: The combined toxicity is acceptable if TER_{MIX} ≥ 5 (long-term)

Assessment: The combined toxicity risk (TER_{MIX}) with concentration-addition is estimated based on the following equation:

$$TER_{mix} = 1 / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} + \dots + \frac{1}{TER_{a.s.i}} \right)$$

After refinement, the TER_{MIX} equals to 5.5, showing an acceptable chronic risk for mammals from the combined exposure to all active substances in the product.

Large herbivorous mammal “lagomorph”, BBCH 10-40

Refinement 2: DT₅₀

An alternative way to refine the risk for large herbivorous mammals is the use of refined DT₅₀ values for both active substances.

For Propamocarb-HCl, residue data on lettuce leaves are used. These data are presented in the DAR (Section B7, 2005) and in the Final Addendum to the DAR of Propamocarb (2006) and allow the determination of a realistic MAF and Ftwa value to refine the risk assessment as kinetic data have been collected.

Using a refined DT₅₀ value of 3.8 days (instead of the default 10 days), the MAF x twa is recalculated as presented in Appendix H of the EFSA Guidance 2009 using the moving time window approach for multiple applications (NL calculator):

# applic.	3									
applic. rate (g/ha)	855	855	855							1440
factor (optional)	1	1	1	1	1	1	1	1	1	1
interval (d)	7	7	7							
normalised to 1st applic.	1.00	1.00	1.00							
interval (d)	7	7								
	standard	refined a	refined b							
DT50	10	3.8								
k	0.06931	0.18241	#####							
length twa interval (d)	21									
MAF 90 %-ile (approx.)	1.64	1.21	#####							
standard MAF-mean	1.99	1.36	#####							
MAF x TWA (mean)	1.28	0.68	#####							

For Mandipropamid, a study on decline of residues on early cereal foliage (surrogate for grasses) is available (Cairns, 2013; VV-405547). The geometric mean DT₅₀ of 4.74 days is used to refine the risk assessment below, based on the data from 4 trials in Cairns (2013) but excluding trial 3 as rainfall may have affected the residues. The study by Cairns (2013) was conducted in central Europe.

Using a refined DT₅₀ value of 4.74 days (instead of the default 10 days), the MAF x twa is recalculated as presented in Appendix H of the EFSA Guidance 2009 using the moving time window approach for multiple applications (NL calculator):

# applic.	3									
applic. rate (g/ha)	142.5	142.5	142.5							1440
factor (optional)	1	1	1	1	1	1	1	1	1	1
interval (d)	7	7	7							
normalised to 1st applic. interval (d)	1.00	1.00	1.00							
	7	7								
	standard	refined a	refined b							
DT50	10	4.74								
k	0.06931	0.14623	#####							
length twa interval (d)	21									
MAF 90 %-ile (approx.)	1.64	1.29	#####							
standard MAF-mean	1.99	1.49	#####							
MAF × TWA (mean)	1.28	0.80	#####							

Table 9.3-7: Refined reproductive risk assessment for large herbivorous mammals exposed in potatoes at BBCH 10-40, interval between applications 7 days

Intended use		Potatoes			
Active substance/product		Propamocarb-HCl			
Application rate (g/ha)		3 × 855			
Reprod. toxicity (mg/kg bw/d)		104			
TER criterion		5			
Crop scenario	Indicator/generic focal species	SV _m	MAF _m × TWA	DDD _m (mg/kg bw/d)	TER _{it}
Growth stage					
BBCH 10 - 40	Large herbivorous mammal “lagomorph”	14.3	0.68	8.31	12.5
Intended use		Potatoes			
Active substance/product		Mandipropamid			
Application rate (g/ha)		3 × 142.5			
Reprod. toxicity (mg/kg bw/d)		20			
TER criterion		5			
Crop scenario	Indicator/generic focal species	SV _m	MAF _m × TWA	DDD _m (mg/kg bw/d)	TER _{it}
Growth stage					
BBCH 10 - 40	Large herbivorous mammal “lagomorph”	14.3	0.80	1.63	12.3

TER_{MIX} calculation

Condition: The combined toxicity is acceptable if TER_{MIX} ≥ 5 (long-term)

Assessment: The combined toxicity risk (TER_{MIX}) with concentration-addition is estimated based on the following equation:

$$TER_{mix} = 1 / \left(\frac{1}{TER_{a.s.1}} + \frac{1}{TER_{a.s.2}} + \dots + \frac{1}{TER_{a.s.i}} \right)$$

After refinement, the TER_{MIX} equals to 6.2, showing an acceptable chronic risk for mammals from the combined exposure to all active substances in the product.

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 263.65 mL/g, Propamocarb-HCl belongs to the group of less sorptive substances. With a $K(f)_{oc}$ 795.4 mL/g, Mandipropamid belongs to the group of more sorptive substances. To achieve a concise risk assessment, the risk envelope approach is applied. To take into account the 3 applications, a MAF of 1.6 was used as a worst-case (effective application rate = application rate x 1.6).

Propamocarb-HCl			
Effective application rate (g/ha) =	1368		
Acute toxicity (mg/kg bw) =	1330	quotient =	1.029
Reprod. toxicity (mg/kg bw/d) =	104	quotient =	13.15
Mandipropamid			
Effective application rate (g/ha) =	228		
Acute toxicity (mg/kg bw) =	5000	quotient =	0.046
Reprod. toxicity (mg/kg bw/d) =	20	quotient =	11.40

9.3.2.4 Effects of secondary poisoning

The log P_{ow} of Propamocarb-HCl amounts up to 0.67 at pH 9 (EFSA, 2006) and thus does not exceed the trigger value of 3. A risk assessment for effects due to secondary poisoning is not required.

The log P_{ow} of Mandipropamid amounts to 3.2 (EFSA, 2012) and thus exceeds the trigger value of 3. A risk assessment for effects due to secondary poisoning is required.

The log P_{ow} value of the Mandipropamid soil metabolite CGA 380778 is 2.6. The log P_{ow} of aquatic metabolites SYN 504851 and SYN 500003 are pH-dependent, being -0.86 and -1.2, respectively, at pH 6.8 and still under 3 when corrected to the neutral form only. The log P_{ow} of the sediment metabolites SYN 521195 and SYN 539678 were estimated to be 2.85 and 3.24, respectively. Consideration of bioaccumulation of SYN 539678 (sediment metabolite) is therefore required. The exposure to this metabolite will clearly be far lower than that for the parent. Furthermore, although the toxicity of this metabolite to mammals has not been measured, its toxicity (measured or estimated) to soil or aquatic organisms is similarly low or lower than that of Mandipropamid. On this basis, risk of secondary poisoning from parent Mandipropamid provides a worst-case scenario. Since exposure to the parent poses a negligible secondary poisoning risk to earthworm-eating mammals and fish-eating mammals (see risk assessments below), the risk from the metabolite is also expected to be negligible. For the sake of completeness, the applicant performs the risk assessment for SYN 539678 (sediment metabolite) regarding fish-eating mammals using the endpoint of Mandipropamid divided by 10.

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 measured/predicted concentrations in soil/porewater / is based on experimental data.

Table 9.3-8: Assessment of the risk for earthworm-eating mammals due to exposure to Mandipropamid via bioaccumulation in earthworms (secondary poisoning) for the intended use in potatoes

Parameter	Mandipropamid	comments
PEC _{soil} (mg/kg soil)	0.2092	See dRR Part B8 Table 8.7-3
log P _{ow} / P _{ow}	3.2/1585	
Koc	795.4	Geomean (n = 7)
foc	0.02	Default
BCF _{worm}	1.25	$BCF_{worm/soil} = (PEC_{worm,ww}/PEC_{soil,dw}) = (0.84 + 0.012 \times P_{ow}) / foc \times Koc$
PEC _{worm}	0.2615	$PEC_{worm} = PEC_{soil} \times BCF_{worm/soil}$
Daily dietary dose (mg/kg bw/d)	0.335	$DDD = PEC_{worm} \times 1.28$
NOEL (mg/kg bw/d)	20	
TER _{It}	59.7	

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.

Table 9.3-9: Assessment of the risk for fish-eating mammals due to exposure to Mandipropamid via bioaccumulation in fish (secondary poisoning) for the intended use in potatoes

Parameter	Mandipropamid	comments
PEC _{sw} (mg/L)	0.00247	dRR Section B8 Table 8.9-9 (Step 3), R3/stream worst-case value
BCF _{fish}	19.7	
BMF	-	biomagnification factor (relevant for $BCF \geq 2000$)
PEC _{fish}	0.049	$PEC_{fish} = PEC_{water} \times BCF_{fish}$
Daily dietary dose (mg/kg bw/d)	0.007	$DDD = PEC_{fish} \times 0.142$
NOEL (mg/kg bw/d)	20	
TER _{It}	2857	

TER values shown in bold fall below the relevant trigger.

Table 9.3-10: Assessment of the risk for fish-eating mammals due to exposure to SYN 539678 via bioaccumulation in fish (secondary poisoning) for the intended use in potatoes

Parameter	SYN 539678	comments
PEC _{sw} (mg/L)	0.0025142	dRR Section B8 Table 8.9-21 (Step 2)
BCF _{fish}	19.7	
BMF	-	biomagnification factor (relevant for $BCF \geq 2000$)
PEC _{fish}	0.049	$PEC_{fish} = PEC_{water} \times BCF_{fish}$

Daily dietary dose (mg/kg bw/d)	0.007	DDD = PEC _{fish} × 0.142
NOEL (mg/kg bw/d)	2	Parent endpoint divided by 10
TER _{lt}	285.7	

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 for mammals is acceptable when GLOB2106cF is applied according to the intended uses.

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

Birds and mammals are regarded as adequate surrogates for terrestrial stages of amphibians and reptiles. For the aquatic stages of amphibians, please refer to the risk assessment for fish presented in KCP 10.2.

9.5 Effects on aquatic organisms (KCP 10.2)

zRMS Comments:	<p>The submitted risk assessment was accepted.</p> <p>All relevant used endpoints for both active substances and mandipropamid metabolites were agreed at the EU level All relevant metabolites of mandipropamid were taken into consideration.</p> <p>Propamocarb-HCl. The risk assessment for aquatic organisms indicate an acceptable risk from acute and chronic exposure to the active substance: the PEC/RAC values are below the trigger values of 1, indicating an acceptable risk for aquatic organisms.</p> <p>No mitigation measures were proposed in risk assessment.</p> <p>Mandipropamid. The early and late application and single and multiple applications were taken into consideration. The risk assessment for aquatic organisms indicate an acceptable risk from acute and chronic exposure to the active substance and its metabolites metabolites SYN 504851, SYN 500003, CGA380778, SYN 521195 and SYN 539678. The risk assessment based on PEC_{sw} assessment in Step 3 (please refer to dRR Section B8) was sufficient and no mitigation measures were proposed.</p> <p>The TER-values were well above the trigger of 100 for acute exposure and the trigger of 10 for long-term exposure.</p>
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<p>Mixture toxicity. The submitted risk assessment was accepted. No mitigation measure is required.</p> <p>Formulation toxicity. The toxicity studies were submitted and accepted. The relevant endpoints for fish, aquatic invertebrates and algae were used in risk assessment. The PEC_{sw} for formulation were corrected in accordance with recalculated values provided in Section B8. No mitigation measure is required.</p> <p>An acceptable risk to aquatic organisms is expected if the application of the GLOB2106cF is in accordance with proposed pattern use.</p>

9.5.1 Toxicity data

Studies on the toxicity to aquatic organisms have been carried out with Propamocarb-HCl, Mandipropamid and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on aquatic organisms of GLOB2106cF were not evaluated as part of the EU assessment of Propamocarb-HCl and Mandipropamid. 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 – Propamocarb-HCl, Mandipropamid and relevant metabolites

Species	Substance	Exposure System	Results	Reference
<i>Fish</i>				
Rainbow trout (<i>Onchoryhynchus mykiss</i>)	Propamocarb-HCl	96 hours	Mortality, LC ₅₀ > 99 mg/L	EFSA Scientific Report (2006) 78, 1-80
Bluegill Sunfish (<i>Lepomis macrochirus</i>)	Propamocarb-HCl	96 hours	Mortality, LC ₅₀ > 92 mg/L	EFSA Scientific Report (2006) 78, 1-80
Bluegill sunfish (<i>Lepomis macrochirus</i>)	Propamocarb-HCl	32 days	NOEC > 6.3 mg/L	EFSA Scientific Report (2006) 78, 1-80
<i>Oncorhynchus mykiss</i>	Mandipropamid	96 hours	LC ₅₀ > 2.9 mg/L _{mm}	EFSA Scientific Report (2012) 10(11), 2935
<i>Oncorhynchus mykiss</i>	CGA 380778	96 hours	LC ₅₀ > 43 mg/L	Maynard & Swarbrick, 2005 (DAR 2006)
<i>Pimephales promelas</i>	Mandipropamid	28 d Flow-through	Growth & hatchability NOEC= 0.5 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Oncorhynchus mykiss</i>	SYN 504851	96 hours	Mortality, LC ₅₀ > 100 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Oncorhynchus mykiss</i>	SYN 500003	96 hours	Mortality, LC ₅₀	EFSA Scientific

Species	Substance	Exposure System	Results	Reference
			> 100 mg/L	Report (2012) 10(11), 2935
<i>Aquatic invertebrates</i>				
<i>Daphnia magna</i>	Propamocarb-HCl	48 hours	48 hours Mortalities, EC ₅₀ > 100 mg/L	EFSA Scientific Report (2006) 78, 1-80
<i>Daphnia magna</i>	Propamocarb-HCl	21 days	NOEC = 12.3 mg/L	EFSA Scientific Report (2006) 78, 1-80
<i>Daphnia magna</i>	Mandipropamid	48 hours	48 hours Mortalities, EC ₅₀ 7.1 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Crassostrea virginica</i>	Mandipropamid	96 h (flow-through)	48 hours Mortalities, EC ₅₀ 0.97 mg/L_{mm}	EFSA Scientific Report (2012) 10(11), 2935
<i>Crassostrea virginica</i>	CGA 380778	48 hours	48 hours Mortalities, EC ₅₀ 56 mg/L_{nom}	Maynard & Swarbrick, 2005 (DAR 2006)
<i>Daphnia magna</i>	Mandipropamid	21 days (semi-static)	Reproduction NOEC = 0.87 mg/L Length NOEC = 0.28 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Daphnia magna</i>	Mandipropamid	21 days (semi-static)	Reproduction & length NOEC = 0.076 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Daphnia magna</i>	SYN 504851	48 hours	EC ₅₀ > 100 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Daphnia magna</i>	SYN 500003	48 hours	EC ₅₀ > 100 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Chironomus riparius</i>	Mandipropamid	28 days (spiked sediment, static)	NOEC = 31.3 mg/kg	Kimmel, 2011; VV-397081
<i>Algae</i>				
<i>Pseudokirchneriella subcapitata</i>	Propamocarb-HCl	72 hours	Growth Rate, EC ₅₀ > 85 mg/L	EFSA Scientific Report (2006) 78, 1-80
<i>Anabaena flos-aquae</i>	Mandipropamid	96 hours static	Growth Rate, biomass EC ₅₀ > 19.8 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Pseudokirchneriella subcapitata</i>	CGA 380778	72 hours	Growth Rate, EC ₅₀ 33 mg/L	Maynard & Swarbrick, 2005 (DAR 2006)
<i>Pseudokirchneriella subcapitata</i>	SYN 504851	72 h static 96h static	Growth Rate, E _r C ₅₀ = 31.3 mg/L Biomass E _b C ₅₀ = 26.7 mg/L	EFSA Scientific Report (2012) 10(11), 2935

Species	Substance	Exposure System	Results	Reference
<i>Pseudokirchneriella subcapitata</i>	SYN 500003	72 h static	Growth Rate, E _r C ₅₀ = 39.8 mg/L Biomass E _b C ₅₀ =27.1 mg/L	EFSA Scientific Report (2012) 10(11), 2935
<i>Aquatic macrophytes</i>				
<i>Lemna gibba</i>	Propamocarb-HCl	14 days	Frond No., EC ₅₀ > 18 mg/L	EFSA Scientific Report (2006) 78, 1-80
<i>Lemna gibba</i>	Mandipropamid	7 days (static)	Frond, EC ₅₀ 4.2 mg/L	EFSA Scientific Report (2012) 10(11), 2935
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

Table 9.5-2: Endpoints and effect values relevant for the risk assessment for aquatic organisms – GLOB2106cF

Species	Substance	Exposure System	Results	Reference
<i>Oncorhynchus mykiss</i>	GLOB2106cF	96 h, s	LC ₅₀ > 100 mg/L _{nom}	xxxxxxxxxx, 2023 169461230
<i>Daphnia magna</i>	GLOB2106cF	48 h, s	EC ₅₀ > 85.8 mg/L _{mm}	Ganßmann M., 2023a 169461220
<i>Pseudokirchneriella subcapitata</i>	GLOB2106cF	72 h, s	E _r C ₅₀ > 100 mg/L _{nom}	Ganßmann M., 2023b 169461210
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

9.5.1.1 Justification for new endpoints

Since there is no aquatic organism that is clearly more sensitive to Propamocarb-HCl or Mandipropamid, formulation studies on all three aquatic groups, *i.e.* fish, aquatic invertebrates and algae, were performed. The necessity of a study evaluating the acute toxicity to fish following exposure to the formulation GLOB2106cF has been confirmed by the French authorities and permission has been given in the pre-submission sheet.

Regarding the soil metabolite CGA 380778 and the sediment metabolites SYN 521195 and SYN 539678, existing and ongoing acute studies on *Daphnia magna* have shown that these metabolites are less toxic than the parent. Therefore, the risk assessment of Mandipropamid covers the risk of the metabolites. For the sake of completeness, the applicant has assessed the acute risk for these metabolites where endpoints are available.

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.

Table 9.5-3: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Propamocarb-HCl for each organism group based on FOCUS Steps 1 and 2 calculations for the use of GLOB2106cF in potatoes

Group		Fish acute	Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants
Test species		<i>Oncorhynchus mykiss</i>	<i>Lepomis macrochirus</i>	<i>Lepomis macrochirus</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Lemna gibba</i>
Endpoint (µg/L)		LC ₅₀ >99000	LC ₅₀ >92000	NOEC >6300	EC ₅₀ >100000	NOEC 12300	E _r C ₅₀ >85000	EC ₅₀ 18000
AF		100	100	10	100	10	10	10
RAC (µg/L)		990	920	630	1000	1230	8500	1800
FOCUS Scenario	PEC _{gl-max} (µg/L)							
Step 1								
	656.2043	0.66283263	0.713266	1.041594	0.656204	0.533499	0.077201	0.364558
Step 2								
N-Europe	171.2359	0.17296556	0.186126	0.271803	0.171236	0.139216	0.020145	0.095131
S-Europe	138.8808	0.14028364	0.150957	0.220446	0.138881	0.112911	0.016339	0.077156

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 9.5-4: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Mandipropamid for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of GLOB2106cF in potatoes – early – multiple applications – Set 1

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Pimephales promelas</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Anabaena flos-aquae</i>	<i>Lemna gibba</i>	<i>Chironomus riparius</i>
Endpoint (µg/L)		LC ₅₀ 2900	NOEC 500	EC ₅₀ 970	NOEC 76	E _r C ₅₀ 19800	EC ₅₀ 4200	NOEC 31300 (µg/kg)
AF		100	10	100	10	10	10	10
RAC (µg/L)		29	50	9.7	7.6	1980	420	3130
FOCUS Scenario	PEC _{gl-max} (µg/L)							
Step 1								
	73.0884 (PEC _{sediment} 550.0736 µg/kg)	2.52028966	1.461768	7.534887	9.616895	0.036913	0.17402	0.17574
Step 2								
N-Europe	25.7593	0.88825172	0.515186	2.655598	3.389382	0.01301	0.06133167	-
S-Europe	20.798	0.71717241	0.41596	2.144124	2.736579	0.010504	0.04951905	-
Step 3								
D3/ditch	0.5423	0.0187	0.010846	0.055907	0.071355	0.000274	0.00129119	-
D4/pond	0.1346	0.00464138	0.002692	0.013876	0.017711	6.8E-05	0.00032048	-
D4/stream	0.4355	0.01501724	0.00871	0.044897	0.057303	0.00022	0.0010369	-
D6 ₁ /ditch	0.5401	0.01862414	0.010802	0.05568	0.071066	0.000273	0.00128595	-
D6 ₂ /ditch	1.893	0.06527586	0.03786	0.195155	0.249079	0.000956	0.00450714	-

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
R1/pond	0.1675	0.00577586	0.00335	0.017268	0.022039	8.46E-05	0.00039881	-
R1/stream	1.538	0.05303448	0.03076	0.158557	0.202368	0.000777	0.0036619	-
R2/stream	0.7669	0.02644483	0.015338	0.079062	0.100908	0.000387	0.00182595	-
R3/stream	1.594	0.05496552	0.03188	0.16433	0.209737	0.000805	0.00379524	-

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 9.5-5: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Mandipropamid for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of GLOB2106cF in potatoes – early – single application – Set 1

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Pimephales promelas</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Anabaena flos-aquae</i>	<i>Lemna gibba</i>	<i>Chironomus riparius</i>
Endpoint (µg/L)		LC ₅₀ 2900	NOEC 500	EC ₅₀ 970	NOEC 76	E _r C ₅₀ 19800	EC ₅₀ 4200	NOEC 31300 (µg/kg)
AF		100	10	100	10	10	10	10
RAC (µg/L)		29	50	9.7	7.6	1980	420	3130
FOCUS Scenario	PEC _{gl-max} (µg/L)							
Step 1								
	73.0884 (PEC _{sediment} 550.0736 µg/kg)	2.52028966	1.461768	7.534887	9.616895	0.036913	0.17402	0.17574
Step 2								
N-Europe	9.8096	0.33826207	0.196192	1.011299	1.290737	0.004954	0.02335619	-

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
S-Europe	7.9701	0.27483103	0.159402	0.82166	1.048697	0.004025	0.01897643	-
Step 3								
D3/ditch	0.7457	0.02571379	0.014914	0.076876	0.098118	0.000377	0.00177548	-
D4/pond	0.03009	0.00103759	0.000602	0.003102	0.003959	1.52E-05	7.1643E-05	-
D4/stream	0.5824	0.02008276	0.011648	0.060041	0.076632	0.000294	0.00138667	-
D6 ₁ /ditch	0.7374	0.02542759	0.014748	0.076021	0.097026	0.000372	0.00175571	-
D6 ₂ /ditch	0.7352	0.02535172	0.014704	0.075794	0.096737	0.000371	0.00175048	-
R1/pond	0.09205	0.00317414	0.001841	0.00949	0.012112	4.65E-05	0.00021917	-
R1/stream	1.034	0.03565517	0.02068	0.106598	0.136053	0.000522	0.0024619	-
R2/stream	0.683	0.02355172	0.01366	0.070412	0.089868	0.000345	0.00162619	-
R3/stream	0.7346	0.02533103	0.014692	0.075732	0.096658	0.000371	0.00174905	-

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 9.5-6: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Mandipropamid for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of GLOB2106cF in potatoes – late – multiple applications – Set 1

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Pimephales promelas</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Anabaena flos-aquae</i>	<i>Lemna gibba</i>	<i>Chironomus riparius</i>
Endpoint (µg/L)		LC ₅₀ 2900	NOEC 500	EC ₅₀ 970	NOEC 76	E _r C ₅₀ 19800	EC ₅₀ 4200	NOEC 31300 (µg/kg)
AF		100	10	100	10	10	10	10
RAC (µg/L)		29	50	9.7	7.6	1980	420	3130

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
FOCUS Scenario	PEC^{gl-max} (µg/L)							
Step 1								
	73.0884 (<i>PEC_{sediment}</i> 550.0736 µg/kg)	2.52028966	1.461768	7.534887	9.616895	0.036913	0.17402	0.17574
Step 2								
N-Europe	25.7593	0.88825172	0.515186	2.655598	3.389382	0.01301	0.06133167	-
S-Europe	20.798	0.71717241	0.41596	2.144124	2.736579	0.010504	0.04951905	-
Step 3								
D3/ditch	0.5431	0.01872759	0.010862	0.05599	0.071461	0.000274	0.0012931	-
D4/pond	0.1095	0.00377586	0.00219	0.011289	0.014408	5.53E-05	0.00026071	-
D4/stream	0.4468	0.0154069	0.008936	0.046062	0.058789	0.000226	0.00106381	-
D6 ₁ /ditch	0.5395	0.01860345	0.01079	0.055619	0.070987	0.000272	0.00128452	-
D6 ₂ /ditch	2.764	0.09531034	0.05528	0.284948	0.363684	0.001396	0.00658095	-
R1/pond	0.3556	0.01226207	0.007112	0.03666	0.046789	0.00018	0.00084667	-
R1/stream	1.422	0.04903448	0.02844	0.146598	0.187105	0.000718	0.00338571	-
R2/stream	0.9918	0.0342	0.019836	0.102247	0.1305	0.000501	0.00236143	-
R3/stream	2.47	0.08517241	0.0494	0.254639	0.325	0.001247	0.00588095	-

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 9.5-7: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Mandipropamid for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of GLOB2106cF in potatoes – late – single application – Set 1

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Pimephales promelas</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Anabaena flos-aquae</i>	<i>Lemna gibba</i>	<i>Chironomus riparius</i>
Endpoint (µg/L)		LC ₅₀ 2900	NOEC 500	EC ₅₀ 970	NOEC 76	E _r C ₅₀ 19800	EC ₅₀ 4200	NOEC 31300 (µg/kg)
AF		100	10	100	10	10	10	10
RAC (µg/L)		29	50	9.7	7.6	1980	420	3130
FOCUS Scenario	PEC _{gl-max} (µg/L)							
Step 1								
	73.0884 (PEC _{sediment} 550.0736 µg/kg)	2.52028966	1.461768	7.534887	9.616895	0.036913	0.17402	0.17574
Step 2								
N-Europe	9.8096	0.33826207	0.196192	1.011299	1.290737	0.004954	0.02335619	-
S-Europe	7.9701	0.27483103	0.159402	0.82166	1.048697	0.004025	0.01897643	-
Step 3								
D3/ditch	0.746	0.02572414	0.01492	0.076907	0.098158	0.000377	0.00177619	-
D4/pond	0.03008	0.00103724	0.000602	0.003101	0.003958	1.52E-05	7.1619E-05	-
D4/stream	0.5606	0.01933103	0.011212	0.057794	0.073763	0.000283	0.00133476	-
D6 ₁ /ditch	0.742	0.02558621	0.01484	0.076495	0.097632	0.000375	0.00176667	-
D6 ₂ /ditch	0.7415	0.02556897	0.01483	0.076443	0.097566	0.000374	0.00176548	-
R1/pond	0.07824	0.00269793	0.001565	0.008066	0.010295	3.95E-05	0.00018629	-

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
R1/stream	1.035	0.03568966	0.0207	0.106701	0.136184	0.000523	0.00246429	-
R2/stream	0.683	0.02355172	0.01366	0.070412	0.089868	0.000345	0.00162619	-
R3/stream	1.047	0.03610345	0.02094	0.107938	0.137763	0.000529	0.00249286	-

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 9.5-8: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Mandipropamid for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of GLOB2106cF in potatoes – early – multiple applications – Set 2

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Pimephales promelas</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Anabaena flos-aquae</i>	<i>Lemna gibba</i>	<i>Chironomus riparius</i>
Endpoint (µg/L)		LC ₅₀ 2900	NOEC 500	EC ₅₀ 970	NOEC 76	E _r C ₅₀ 19800	EC ₅₀ 4200	NOEC 31300 (µg/kg)
AF		100	10	100	10	10	10	10
RAC (µg/L)		29	50	9.7	7.6	1980	420	3130
FOCUS Scenario	PEC _{gl-max} (µg/L)							
Step 1								
	73.0884 (PEC _{sediment} 550.0736 µg/kg)	2.52028966	1.461768	7.534887	9.616895	0.036913	0.17402	0.17574
Step 2								
N-Europe	25.7593	0.88825172	0.515186	2.655598	3.389382	0.01301	0.06133167	-
S-Europe	20.798	0.71717241	0.41596	2.144124	2.736579	0.010504	0.04951905	-

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Step 3								
D3/ditch	0.5426	0.01871034	0.010852	0.055938	0.071395	0.000274	0.0012919	-
D4/pond	0.1258	0.00433793	0.002516	0.012969	0.016553	6.35E-05	0.00029952	-
D4/stream	0.4355	0.01501724	0.00871	0.044897	0.057303	0.00022	0.0010369	-
D6 ₁ /ditch	0.5402	0.01862759	0.010804	0.055691	0.071079	0.000273	0.00128619	-
D6 ₂ /ditch	1.891	0.0652069	0.03782	0.194948	0.248816	0.000955	0.00450238	-
R1/pond	0.1507	0.00519655	0.003014	0.015536	0.019829	7.61E-05	0.00035881	-
R1/stream	2.033	0.07010345	0.04066	0.209588	0.2675	0.001027	0.00484048	-
R2/stream	0.9905	0.03415517	0.01981	0.102113	0.130329	0.0005	0.00235833	-
R3/stream	2.023	0.06975862	0.04046	0.208557	0.266184	0.001022	0.00481667	-

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 9.5-9: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Mandipropamid for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of GLOB2106cF in potatoes – early – single application – Set 2

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Pimephales promelas</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Anabaena flos-aquae</i>	<i>Lemna gibba</i>	<i>Chironomus riparius</i>
Endpoint (µg/L)		LC ₅₀ 2900	NOEC 500	EC ₅₀ 970	NOEC 76	E _r C ₅₀ 19800	EC ₅₀ 4200	NOEC 31300 (µg/kg)
AF		100	10	100	10	10	10	10
RAC (µg/L)		29	50	9.7	7.6	1980	420	3130
FOCUS Scenario	PEC ^{gl-max} (µg/L)							

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Step 1								
	73.0884 (PEC _{sediment} 550.0736 µg/kg)	2.52028966	1.461768	7.534887	9.616895	0.036913	0.17402	0.17574
Step 2								
N-Europe	9.8096	0.33826207	0.196192	1.011299	1.290737	0.004954	0.02335619	-
S-Europe	7.9701	0.27483103	0.159402	0.82166	1.048697	0.004025	0.01897643	-
Step 3								
D3/ditch	0.7457	0.02571379	0.014914	0.076876	0.098118	0.000377	0.00177548	-
D4/pond	0.03009	0.00103759	0.000602	0.003102	0.003959	1.52E-05	7.1643E-05	-
D4/stream	0.5824	0.02008276	0.011648	0.060041	0.076632	0.000294	0.00138667	-
D6 ₁ /ditch	0.7374	0.02542759	0.014748	0.076021	0.097026	0.000372	0.00175571	-
D6 ₂ /ditch	0.7352	0.02535172	0.014704	0.075794	0.096737	0.000371	0.00175048	-
R1/pond	0.08477	0.0029231	0.001695	0.008739	0.011154	4.28E-05	0.00020183	-
R1/stream	1.034	0.03565517	0.02068	0.106598	0.136053	0.000522	0.0024619	-
R2/stream	0.683	0.02355172	0.01366	0.070412	0.089868	0.000345	0.00162619	-
R3/stream	0.7339	0.0253069	0.014678	0.07566	0.096566	0.000371	0.00174738	-

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 9.5-10: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Mandipropamid for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of GLOB2106cF in potatoes – late – multiple applications – Set 2

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Pimephales promelas</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Anabaena flos-aquae</i>	<i>Lemna gibba</i>	<i>Chironomus riparius</i>

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Endpoint (µg/L)		LC ₅₀ 2900	NOEC 500	EC ₅₀ 970	NOEC 76	E _r C ₅₀ 19800	EC ₅₀ 4200	NOEC 31300 (µg/kg)
AF		100	10	100	10	10	10	10
RAC (µg/L)		29	50	9.7	7.6	1980	420	3130
FOCUS Scenario	PEC _{gl-max} (µg/L)							
Step 1								
	73.0884 (PEC _{sediment} 550.0736 µg/kg)	2.52028966	1.461768	7.534887	9.616895	0.036913	0.17402	0.17574
Step 2								
N-Europe	25.7593	0.88825172	0.515186	2.655598	3.389382	0.01301	0.06133167	-
S-Europe	20.798	0.71717241	0.41596	2.144124	2.736579	0.010504	0.04951905	-
Step 3								
D3/ditch	0.5435	0.01874138	0.01087	0.056031	0.071513	0.000274	0.00129405	-
D4/pond	0.09612	0.00331448	0.001922	0.009909	0.012647	4.85E-05	0.00022886	-
D4/stream	0.4468	0.0154069	0.008936	0.046062	0.058789	0.000226	0.00106381	-
D6 ₁ /ditch	0.5395	0.01860345	0.01079	0.055619	0.070987	0.000272	0.00128452	-
D6 ₂ /ditch	2.761	0.0952069	0.05522	0.284639	0.363289	0.001394	0.00657381	-
R1/pond	0.3131	0.01079655	0.006262	0.032278	0.041197	0.000158	0.00074548	-
R1/stream	1.419	0.04893103	0.02838	0.146289	0.186711	0.000717	0.00337857	-
R2/stream	0.9911	0.03417586	0.019822	0.102175	0.130408	0.000501	0.00235976	-
R3/stream	2.468	0.08510345	0.04936	0.254433	0.324737	0.001246	0.00587619	-

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 9.5-11: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Mandipropamid for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of GLOB2106cF in potatoes – late – single application – Set 2

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Pimephales promelas</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Anabaena flos-aquae</i>	<i>Lemna gibba</i>	<i>Chironomus riparius</i>
Endpoint (µg/L)		LC ₅₀ 2900	NOEC 500	EC ₅₀ 970	NOEC 76	E _r C ₅₀ 19800	EC ₅₀ 4200	NOEC 31300 (µg/kg)
AF		100	10	100	10	10	10	10
RAC (µg/L)		29	50	9.7	7.6	1980	420	3130
FOCUS Scenario	PEC _{gl-max} (µg/L)							
Step 1								
	73.0884 (PEC _{sediment} 550.0736 µg/kg)	2.52028966	1.461768	7.534887	9.616895	0.036913	0.17402	0.17574
Step 2								
N-Europe	9.8096	0.33826207	0.196192	1.011299	1.290737	0.004954	0.02335619	-
S-Europe	7.9701	0.27483103	0.159402	0.82166	1.048697	0.004025	0.01897643	-
Step 3								
D3/ditch	0.746	0.02572414	0.01492	0.076907	0.098158	0.000377	0.00177619	-
D4/pond	0.03008	0.00103724	0.000602	0.003101	0.003958	1.52E-05	7.1619E-05	-
D4/stream	0.5606	0.01933103	0.011212	0.057794	0.073763	0.000283	0.00133476	-
D6 ₁ /ditch	0.742	0.02558621	0.01484	0.076495	0.097632	0.000375	0.00176667	-
D6 ₂ /ditch	0.7415	0.02556897	0.01483	0.076443	0.097566	0.000374	0.00176548	-

Group		Fish acute	Fish prolonged	Inverteb. acute	Inverteb. prolonged	Algae	Aquatic plants	Sed. dwell. prolonged
R1/pond	0.0666	0.00229655	0.001332	0.006866	0.008763	3.36E-05	0.00015857	-
R1/stream	1.034	0.03565517	0.02068	0.106598	0.136053	0.000522	0.0024619	-
R2/stream	0.683	0.02355172	0.01366	0.070412	0.089868	0.000345	0.00162619	-
R3/stream	1.047	0.03610345	0.02094	0.107938	0.137763	0.000529	0.00249286	-

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 9.5-12: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for SYN 504851 for each organism group based on FOCUS Steps 1 and 2 calculations for the use of GLOB2106cF in potatoes

Group		Fish acute	Inverteb. acute	Algae	Sed. dwell. prolonged
Test species		<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>
Endpoint (µg/L)		LC ₅₀ 100000	EC ₅₀ 100000	E _r C ₅₀ 31300	NOEC 31300 (µg/kg)*
AF		100	100	10	10
RAC (µg/L)		1000	1000	3130	3130
FOCUS Scenario	PEC _{gl-max} (µg/L)				
Step 1					
	26.6781 (PEC _{sediment} 1.1940 µg/kg)	0.026678	0.026678	0.008523	0.000381
Step 2					
N-Europe	9.8333	0.009833	0.009833	0.003142	-
S-Europe	7.9711	0.007971	0.007971	0.002547	-

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
 * 1x parent toxicity based on acute toxicity data showing that the metabolite is less toxic than the parent

Table 9.5-13: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for SYN 500003 for each organism group based on FOCUS Steps 1 and 2 calculations for the use of GLOB2106cF in potatoes

Group		Fish acute	Inverteb. acute	Algae
Test species		<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>
Endpoint (µg/L)		LC ₅₀ 100000	EC ₅₀ 100000	E _r C ₅₀ 39800
AF		100	100	10
RAC (µg/L)		1000	1000	3980
FOCUS Scenario	PEC _{gl-max} (µg/L)			
Step 1				
	7.4179	0.007418	0.007418	0.001864
Step 2				
N-Europe	2.6538	0.002654	0.002654	0.000667
S-Europe	2.1458	0.002146	0.002146	0.000539

Table 9.5-14: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for CGA 380778 for each organism group based on FOCUS Steps 1 and 2 calculations for the use of GLOB2106cF in potatoes

Group		Fish acute	Inverteb. acute	Algae
Test species		<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>
Endpoint (µg/L)		LC ₅₀ 43000	EC ₅₀ 56000	E _r C ₅₀ 33000
AF		100	100	10
RAC (µg/L)		430	560	3300
FOCUS Scenario	PEC _{gl-max} (µg/L)			
Step 1				
	4.8771	0.011342	0.008709	0.001478
Step 2				
N-Europe	1.2945	0.00301	0.002312	0.000392
S-Europe	1.0356	0.002408	0.001849	0.000314

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 9.5-15: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for SYN 521195 for each organism group based on FOCUS Steps 1 and 2 calculations for the use of GLOB2106cF in potatoes

Group		Sed. dwell. prolonged
Test species		<i>Chironomus riparius</i>
Endpoint (µg/L)		NOEC 31300 (µg/kg)*
AF		10
RAC (µg/L)		3130
FOCUS Scenario	PEC_{gl-max} (µg/L)	
Step 1		
	<i>PEC_{sediment}</i> <i>113.3094</i> <i>µg/kg</i>	0.036201

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

* 1x parent toxicity based on acute toxicity data showing that the metabolite is less toxic than the parent

Table 9.5-16: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for SYN 539678 for each organism group based on FOCUS Steps 1 and 2 calculations for the use of GLOB2106cF in potatoes

Group		Sed. dwell. prolonged
Test species		<i>Chironomus riparius</i>
Endpoint (µg/L)		NOEC 31300 (µg/kg)*
AF		10
RAC (µg/L)		3130
FOCUS Scenario	PEC_{gl-max} (µg/L)	
Step 1		
	<i>PEC_{sediment}</i> 80.9098 µg/kg	0.025850

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

* 1x parent toxicity based on acute toxicity data showing that the metabolite is less toxic than the parent

Combined risk assessment for the formulation GLOB2106cF

The Regulation (EC) No 1107/2009, in Article 29, requires that ‘interaction between the a.s., safeners, synergists and co-formulants shall be taken into account’ in the evaluation and authorisation. Guidance is provided in EFSA (2013¹) to perform the risk assessment for formulations containing more than one active substance.

The first step is to check if measured data on the product exist for the given endpoint (**Step1**). If yes, comparison between product data and active ingredient data will be possible. For GLOB2106cF, there is data available on the formulation for fish, Daphnia and algae, so the below scheme can be followed.

Concentration addition model (MDR) (step 2)

Therefore, the LD₅₀ of the formulated product is compared to the predicted mixture toxicity assuming concentration additivity according to the concentration addition model (CA model). The CA model is based on the following equation^[1], for deriving a predicted ECx or NOEC value for a mixture of (active) substances with known toxicity (ECx_{mix-CA} or NOEC_{mix-CA}), assuming concentration additivity:

$$\text{Equation 13: } ECx_{mix-CA} = \left(\sum_{i=1}^n \frac{p_i}{ECx_i} \right)^{-1}$$

where:

- n: number of mixture components
- i: index from 1...n mixture components
- p_i: the ith component as a relative fraction of the mixture composition (note: $\sum p_i$ must be 1)
- ECx_i: concentration of component i provoking x % effect (pragmatically, NOEC_i may be inserted, too).

When the formulation is more toxic than that predicted from the toxicity of the individual compounds, the use of the endpoint of the formulation is recommended for the first-tier assessment because it cannot be excluded that such effects would also occur after exposure of the aquatic organism to residues in the environment.

¹ Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Panel on Plant Protection Products and their Residues (PPR). Scientific opinion, EFSA Journal 2013;11(7):3290.

Table 9.5-17: Comparison of the toxicity of GLOB2106cF to the predicted one based on Propamocarb-HCl and Mandipropamid

Aquatic organisms	Fraction of Propamocarb-HCl in mixture	Fraction of Mandipropamid in mixture	Propamocarb-HCl EC ₅₀ (mg a.s./L)	Mandipropamid EC ₅₀ (mg a.s./L)	EC _{xmix-CA} . Predicted EC ₅₀ of GLOB2106cF based on the a.s. toxicity (mg as/L)	EC _{xppp} . EC ₅₀ of GLOB2106cF from the studies (mg a.s./L)	EC _{xppp} . EC ₅₀ of GLOB2106cF from the studies (mg sum of a.s./L)	MDR (model deviation ratio)	Comparison toxicity of the formulation and the predicted one
Fish	0.86	0.14	92	2.9	17.07	100	48.6	0.35	MDR= 0.2-5
<i>Daphnia</i>	0.86	0.14	100	0.97	6.42	85.8	41.7	0.15	MDR < 0.2
Daphnia-refined*	0.86	0.14	100	7.1	34.85	85.8	41.7	0.84	MDR= 0.2-5
Algae	0.86	0.14	85	19.8	57.8	100	48.6	1.19	MDR= 0.2-5

* In this line, the endpoints for *Daphnia magna* for both active substances were used in the analysis. In the previous line, endpoints of different species (*i.e.* *Daphnia magna* and *Crassostrea virginica*) were used, which does not allow a valid comparison and calculation of the MDR.

The predicted toxicity endpoint has been compared to the formulated product endpoint to derive a MDR by the formula ($MDR = EC_{xmix-CA} / EC_{xppp}$). If MDR is between 0.2 and 5, the observed and calculates toxicities are considered in agreement. If MDR is > 5, the observed toxicity of mixture is higher than that calculated assuming dose additivity. If MDR is < 0.2, the mixture is less toxic than expected.

The MDR for fish, *Daphnia* and algae are between 0.2 and 5, thus the measured and calculated toxicity are in agreement. It means that the toxicity of GLOB2106cF is not higher than the predicted one. In this case, EFSA (2013) recommends that the measured toxicity of the mixture be considered in the aquatic risk assessment (see below).

Combined toxicity based on Propamocarb-HCl and Mandipropamid

Mixture composition in the formulation versus mixture composition at PEC_{mix} (step 3)

The aim of this step is to check whether the mixture composition in the formulation study giving the measured mixture toxicity (EC_{xPPP}) in terms of the relative proportions of the individual active substances is similar to the mixture composition at the PEC_{mix} (proportion of each active in the environment (part of the PEC)). The same equation (equation 13) as for step 2 is used, with the difference that here the pi is PEC_i/PEC_{mix}. PEC_{mix} is simply the sum the each PEC_i. Using the same EC_{xmix-CA} (a.s. in PPP) as the one used in step 2 for MDR, the new EC_{xmix-CA} (a.s. in PEC_{mix}) (representing the mixture as it is in the environment) is calculated.

The following results were obtained for Step 1 and 2 (from the AGD_Aquamix_v1.15).

Fish	
ECxmix-CA (a.s. in PPP)/ ECxmix-CA (a.s. in PECmix)	
Step 1	0.76
Step 2	
N-Europe	0.93
S-Europe	0.93

Invertebrates	
ECxmix-CA (a.s. in PPP)/ ECxmix-CA (a.s. in PECmix)	
Step 1	0.81
Step 2	
N-Europe	0.94
S-Europe	0.94

Algae	
ECxmix-CA (a.s. in PPP)/ ECxmix-CA (a.s. in PECmix)	
Step 1	0.90
Step 2	
N-Europe	0.97
S-Europe	0.97

The ECxmix-CA (a.s. in PPP)/ECxmix-CA (a.s. in PECmix) is between 0.8 and 1.2 at Step 2 (mixture similar). Therefore, as a next step, a mixture risk assessment based on measured mixture toxicity is performed (see below).

Measured risk assessment (ETRmix-PPP based on product data) (step 4)

Step 4 (calculation of ETR) is only applicable for standard endpoints (tier 1 standard laboratory data). This is the case for fish, invertebrate (daphnia) and algae endpoints.

In EFSA guidance (2013), the risk assessment based on measured toxicity is using the following equation:

$$\text{Equation 17: } ETR_{PPP} = \frac{PEC_{mix}}{ECx_{PPP}}$$

With $PEC_{mix} = \sum PEC_i$

And ECx_{PPP} is the endpoints of the studies conducted with the PPP and expressed as $\mu\text{g sum a.s./L}$.

As a first approach, it is assumed that the $PEC_{mix,max}$ of all active substance present in the formulation will occur at the same moment. The results of AGD are presented below.

ETR-PPP calculation for fish, daphnia and algae (step 4 of AGD) based on Step1,2-Potatoes

Fish	
ETRmix-PPP	
Step 1	Go to 5/8
Step 2	
N-Europe	0.00
S-Europe	0.00

Invertebrates	
ETRmix-PPP	
Step 1	0.02
Step 2	
N-Europe	0.00
S-Europe	0.00

Algae	
ETRmix-PPP	
Step 1	0.02
Step 2	
N-Europe	0.00
S-Europe	0.00

ETR are below the trigger for fish, daphnia and algae at Step 2.

PECsw from FOCUS Drift Swash Tool

For completeness, the endpoints obtained in the aquatic studies with GLOB2106cF were also compared to the PECsw of the formulation calculated using the Drift Swash Calculator.

Table 9.5-18: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for GLOB2106cF for each organism group based on FOCUS drift calculations for the use of GLOB2106cF in potatoes

Group		Fish	Inverteb. acute	Algae
Test species		<i>Onchorynchus mykiss</i>	<i>Daphnia magna</i>	<i>Pseudokirchn. subcapitata</i>
Endpoint (µg/L)		LC ₅₀ 100000	EC ₅₀ 85800	E _r C ₅₀ 100000
AF		100	100	10
RAC (µg/L)		1000	858	10000
FOCUS Scenario	PEC _{gl-max} (µg/L)			
1 m	7.9186 10.899	0.007919 0.0109	0.009229 0.013	0.000792 0.00109

AF: Assessment factor; 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 is concluded for Propamocarb-HCl at Step 2.

An acceptable risk is concluded for Mandipropamid at Step 3.
 The risk of the relevant metabolites is acceptable at Step 1/2.

An acceptable risk for the formulation GLOB2106cF following spray drift is concluded without risk mitigation measures.

9.6 Effects on bees (KCP 10.3.1)

zRMS Comments:	<p>The submitted risk assessment based on SANCO/10329/2002 rev.2 (final), October 17, 2002 was accepted.</p> <p>New studies for acute and chronic toxicity on formulation were submitted and accepted. The EU agreed endpoints and accepted endpoints from submitted studies were used in risk assessment.</p> <p>The hazard quotients are below the trigger value of 50 considering SANCO guidance indicating that the active substances and formulation pose an acceptable acute risk to bees.</p> <p>The hazard quotients are below the trigger value of 1 considering the modified EPPO 2010 approach according to the ECPA proposal of 9 June 2017 (POS/17/LO/28028) indicating that the active substances and formulation pose an acceptable chronic risk to honey bee larvae and adult honey bees.</p>
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9.6.1 Toxicity data

Studies on the toxicity to bees have been carried out with Propamocarb-HCl, Mandipropamid and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related. Effects on bees of GLOB2106cF were not evaluated as part of the EU assessment of Propamocarb-HCl and Mandipropamid. New data submitted with this application are listed 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>	Propamocarb-HCl	Acute, oral	LD ₅₀ >84 µg a.s./bee	EFSA Scientific Report (2006) 78, 1-80
<i>Apis mellifera</i>	Propamocarb-HCl	Acute, contact	LD ₅₀ >100 µg a.s./bee	EFSA Scientific Report (2006) 78, 1-

Species	Substance	Exposure System	Results	Reference
				80
<i>Apis mellifera</i>	Mandipropamid	Acute, oral	LD ₅₀ >200 µg a.s./bee	EFSA Scientific Report (2012) 10(11), 2935
<i>Apis mellifera</i>	Mandipropamid	Acute, contact	LD ₅₀ >200 µg a.s./bee	EFSA Scientific Report (2012) 10(11), 2935
<i>Apis mellifera</i>	GLOB2106cF	Oral, acute, 48 h	LD ₅₀ > 445 µg/bee	Schabio S., 2023 169461035
<i>Apis mellifera</i>	GLOB2106cF	Contact, acute, 48 h	LD ₅₀ > 1000 µg/bee	Schabio S., 2023 169461035
<i>Bombus terrestris</i>	GLOB2106cF	Oral, acute	LD ₅₀ > 523.8 µg/bee	Chwiesko D., 2023 169461105
<i>Bombus terrestris</i>	GLOB2106cF	Contact, acute	LD ₅₀ > 600 µg/bee	Chwiesko D., 2023 169461105
<i>Apis mellifera</i>	GLOB2106cF	Adult, chronic	LDD ₅₀ = 76.87 µg/bee/d NOEDD = 30.82 µg/bee/d	Venturi S., 2023 BT262/22
<i>Apis mellifera</i>	GLOB2106cF	Larvae, chronic	NOED = 200 µg/larva	Colli M., 2023 BT126/22
Higher-tier studies (tunnel test, field studies)				
-				

9.6.1.1 Justification for new endpoints

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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).

9.6.2.1 Hazard quotients for bees

Table 9.6-2: First-tier assessment of the risk for bees due to the use of GLOB2106cF in potatoes

Intended use	Potatoes		
Active substance	Propamocarb-HCl		
Application rate (g/ha)	3 × 450		
Test design	LD ₅₀ (lab.) (µg/bee)	Single application rate (g/ha)	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50

Oral toxicity	84	450	5.36
Contact toxicity	100		4.50
Active substance	Mandipropamid		
Application rate (g/ha)	3 x 75		
Test design	LD₅₀ (lab.) (µg/bee)	Single application rate (g/ha)	Q_{HO}, Q_{HC} criterion: Q_H ≤ 50
Oral toxicity	200	75	0.375
Contact toxicity	200		0.375
Product	GLOB2106cF		
Application rate (g/ha)	3 × 2051.81		
Test design	LD₅₀ (lab.) (µg/bee)	Single application rate (g/ha)	Q_{HO}, Q_{HC} criterion: Q_H ≤ 50
Oral toxicity	445	2051.81	4.61
Contact toxicity	1000		2.05

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

9.6.3 Chronic risk assessment (KCP 10.3.1.2)

9.6.3.1 Larval chronic risk assessment

A chronic larval study is available and the potential acceptable risk can be further demonstrated by carrying out a worst-case risk assessment through the calculation of a TER value as set out in the modified EPPO 2010 approach according to the ECPA proposal of 9 June 2017 (POS/17/LO/28028).

A worst-case of potential exposure via residues in pollen and 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), 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. Worst case data from *Rortais et al., 2005*², as proposed in the EPPO scheme, have been used to estimate the consumption by bee larvae:

Worker larvae consuming 59.4 mg sugar in 5 days Assuming 30% sugar content of nectar the worst-case consumption with worker larvae is:

$$59.4/0.30 = 198 \text{ mg nectar in 5 days.}$$

In addition, worker larvae are considered to consume 2 mg pollen during their development phase (EFSA 2013).

Thus, considering the mean RUD values for nectar and pollen in EFSA 2013, exposure can be estimated for the whole development period.

$$\text{Nectar dose: } 2.05 \times 2.9 \times 198/1000 = 1.1771 \text{ µg/larva}$$

$$\text{Pollen dose: } 2.05 \times 6.1 \times 2/1000 = 0.025 \text{ µg/larva}$$

² Agnès RORTAIS, Gérard ARNOLD, Marie-Pierre HALM, Frédérique TOUFFET-BRIENS (2005). Modes of honeybees exposure to systemic insecticides: estimated amounts of contaminated pollen and nectar consumed by different categories of bees. *Apidologie* 36 (2005) 71–83

Total exposure ETE = 1.2021 µg/larvae (as a default worst-case residue at 2.05 kg a.s./ha)

This can be compared to the larval NOED of 200 µg/larva.

$$\text{TER} = \text{NOEDD} (\mu\text{g/larva}) / \text{ETE} (\mu\text{g/larva}) = 200/1.2021 = 166.4$$

The EPPO 2010 scheme proposes a trigger of 1 for assessment of the chronic risk to honey bees. It is clear that with a TER value of 166.4, the proposed uses of GLOB2106cF pose an acceptable risk to bee larval development.

9.6.3.2 Adult chronic risk assessment

The adult chronic risk assessment is performed using the modified EPPO 2010 approach according to the ECPA proposal of 9 June 2017 (POS/17/LO/28028).

This is based upon the method of EPPO 2010 risk assessment for systemic substances which is cited in the regulation as a current risk assessment scheme. It uses NOEDD values for the endpoint so avoids the issues associated with the generation of LDD₅₀ values for substances of low toxicity, and calculates exposure in a similar way to EFSA 2013. The approach is also in line with other chronic risk assessments (e.g. birds and mammals). EPPO 2010 recommended the calculation of a TER using the following equation:

$$\text{TER} = \text{NOEDD}/\text{daily dose}$$

Where daily dose (DD) is based on the worst case a sugar need of 128 mg/bee/day (Rortais et al 2005) of a bee feeding exclusively from nectar containing 30% sugar using the following equation:

$$\text{Daily dose} (\mu\text{g a.i./bee}) = \text{A.R.} \times [128 \text{ mg}/(1000 \times 0.3)] \times \text{RUD} = 2.05 \times [128/(1000 \times 0.3)] \times 2.9 = 2.5365 \mu\text{g/bee}$$

A.R. = application rate in kg a.i./ha

RUD = residue per unit dose from the EFSA bee guidance. Mean RUD_{nectar} = 2.9 mg a.i./kg (foliar sprays).

$$\text{TER} = \text{NOEDD}/\text{daily dose} = 30.82/2.5365 = 12.2$$

The EPPO 2010 scheme proposes a trigger of 1 for assessment of the chronic risk to honey bees. It is clear that with a TER value of 12.2, the proposed uses of GLOB2106cF pose an acceptable chronic risk to adult bees.

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

Not relevant.

9.6.4 Effects on bumble bees

9.6.4.1 Hazard quotients for bumble bees

Table 9.6-3: First-tier assessment of the risk for bumble bees due to the use of GLOB2106cF in potatoes

Product	GLOB2106cF		
Application rate (g/ha)	3 × 2051.81		
Test design	LD₅₀ (lab.) (µg/bee)	Single application rate (g/ha)	Q_{HO}, Q_{HC} criterion: Q_H ≤ 50
Oral toxicity	523.8	2051.81	3.92
Contact toxicity	600		3.42

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

9.6.5 Effects on solitary bees

Not required.

9.6.6 Overall conclusions

The risk for bees is acceptable when using GLOB2106cF according to the intended uses.

9.7 Effects on arthropods other than bees (KCP 10.3.2)

zRMS Comments:	<p>The submitted risk assessment based on the “Guidance Document on Terrestrial Ecotoxicology”, 2002, was accepted.</p> <p>New studies for formulation at Tier 1 and Tier 2 were submitted and accepted.</p> <p>The risk assessment is based on accepted studies endpoints for formulation GLOB2106cF.</p> <p>The hazard quotients are lower than trigger value ($HQ \leq 1$) indicating that the formulation poses an acceptable risk to arthropods other than bees.</p> <p>Therefore, an acceptable risk to arthropods other than bees is expected if the application of the GLOB2106cF is in accordance with intended uses.</p>
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9.7.1 Toxicity data

Studies on the toxicity to non-target arthropods have been carried out with Propamocarb-HCl, Mandipropamid and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on non-target arthropods of GLOB2106cF were not evaluated as part of the EU assessment of Propamocarb-HCl and Mandipropamid. 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)	GLOB2106cF	Extended laboratory test Bean leaves (2D)	LR ₅₀ > 6080 mL/ha ER ₅₀ > 6080 mL/ha	Leopold J., 2023a 169461062
<i>Aphidius rhopalosiphi</i> (adults)	GLOB2106cF	Extended laboratory test Barley plants (3D)	LR ₅₀ > 6080 mL/ha ER ₅₀ > 6080 mL/ha	Leopold J., 2022 169461002
<i>Chrysoperla carnea</i>	GLOB2106cF	Extended laboratory test Bean leaves (2D)	LR ₅₀ > 6080 mL/ha ER ₅₀ > 6080 mL/ha	Leopold J., 2023b 169461047
<i>Coccinella septempunctata</i>	GLOB2106cF	Extended laboratory test Bean leaves (2D)	LR ₅₀ > 6080 mL/ha ER ₅₀ > 6080 mL/ha	Leopold J., 2023c 169461012
Field or semi-field tests				
-				

9.7.1.1 Justification for new endpoints

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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

Table 9.7-2: First- and higher-tier assessment of the in-field risk for non-target arthropods due to the use of GLOB2106cF in potatoes

Intended use		Potatoes		
Active substance/product	GLOB2106cF			
Application rate (L/ha)	3 × 1.9			
MAF	2.3			
Test species	LR ₅₀ (lab.) (L/ha)	PER _{in-field} (L/ha)	HQ _{in-field} criterion: HQ ≤ 1	
<i>Typhlodromus pyri</i>	6.080	4.37	0.7	
<i>Aphidius rhopalosiphi</i>	6.080		0.7	
<i>Chrysoperla carnea</i>	6.080		0.7	

<i>Coccinella septempunctata</i>	6.080		0.7
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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.

9.7.2.2 Risk assessment for off-field exposure

Table 9.7-3: First- and higher-tier assessment of the off-field risk for non-target arthropods due to the use of GLOB2106cF in potatoes

Intended use		Potatoes			
Active substance/product	GLOB2106cF				
Application rate (L/ha)	3 × 1.9				
MAF	2.3				
vdf	5*				
Test species	LR ₅₀ (lab.) (L/ha)	Drift rate	PER _{off-field} (L/ha)	CF	HQ _{off-field} criterion: HQ ≤ 1
<i>Typhlodromus pyri</i>	6.080	0.0277	0.0242	5	0.02
<i>Aphidius rhopalosiphi</i>	6.080				0.02
<i>Chrysoperla carnea</i>	6.080				0.02
<i>Coccinella septempunctata</i>	6.080				0.02

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.

* A vdf of 5 was used in accordance with the proposal made in the EFSA Recurring Issues in Ecotoxicology (EFSA Supporting publication 2019: EN-1673).

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 for non-target arthropods is acceptable when using GLOB2106cF according to the intended uses. No risk mitigation measures are needed.

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

zRMS Comments:	<p>The submitted risk assessment based on Guidance Document on Terrestrial Ecotoxicology, 2002, was accepted.</p> <p>New laboratory studies were submitted and accepted.</p> <p>The risk assessment to earthworms and other non-target soil organisms (meso- and</p>
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	<p>macrofauna) is based on accepted endpoints. The PECsoil values for active substances, their metabolites and formulation were corrected in accordance with recalculations provided on Section B8.7. The recalculations are presented below the Table 9.8-2 (Table 9.8-2A). For risk assessment the PECsoil accum were used, if relevant.</p> <p>Since risk assessment for non-target soil meso- and macrofauna (earthworm and other organisms) is acceptable at Tier 1, then no further assessment was required.</p> <p>An acceptable risk to non-target soil organisms meso- and macrofauna is expected if the GLOB2106cF formulation is used in accordance with proposed uses.</p>
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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 Propamocarb-HCl, Mandipropamid and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on earthworms and other non-target soil organisms (meso- and macrofauna) of GLOB2106cF were not evaluated as part of the EU assessment of Propamocarb-HCl and Mandipropamid. 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 fetida</i>	Propamocarb-HCl	56 d, chronic	NOEC = 362 mg/kg dw	EFSA Scientific Report (2006) 78, 1-80
<i>Eisenia fetida</i>	Mandipropamid	56 d, chronic (artificial substrate)	NOEC = 32 mg/kg dw NOEC _{corr} = 16 mg/kg dw*	EFSA Scientific Report (2012) 10(11), 2935
<i>Eisenia fetida</i>	CGA 380778	No data available Toxicity assumed to be 10 times higher than parent	NOEC = 3.2 mg/kg dw NOEC _{corr} = 1.6 mg/kg dw*	-
<i>Folsomia candida</i>	Mandipropamid	Mixed into substrate 28d, chronic	NOEC = 20 mg/kg dw NOEC _{corr} = 10 mg/kg dw*	EFSA Scientific Report (2012) 10(11), 2935
<i>Folsomia candida</i>	CGA 380778	No data available Toxicity assumed to be 10 times higher than parent	NOEC = 2 mg/kg dw NOEC _{corr} = 1 mg/kg dw*	-
<i>Eisenia fetida</i>	GLOB2106cF	Mixed into substrate 56 d, chronic 10% peat content	NOEC = 309 mg/kg dw NOEC _{corr} = 154.5 mg/kg dw* EC ₁₀ = n.d. EC ₂₀ = n.d. EC ₅₀ > 1000 mg/kg dw	Straube D., 2022a 169461022

Species	Substance	Exposure System	Results	Reference
<i>Folsomia candida</i>	GLOB2106cF	Mixed into substrate 28 d, chronic 5% peat content	NOEC ≥ 1000 mg/kg dw NOEC _{corr} ≥ 500 mg/kg dw* EC ₁₀ = n.d. EC ₂₀ > 1000 mg/kg dw EC ₅₀ > 1000 mg/kg dw	Straube D., 2022b 169461016
<i>Hypoaspis aculeifer</i>	GLOB2106cF	Mixed into substrate 14 d, chronic 5% peat content	NOEC ≥ 1000 mg/kg dw NOEC _{corr} ≥ 500 mg/kg dw* EC ₁₀ > 1000 mg/kg dw EC ₂₀ > 1000 mg/kg dw EC ₅₀ > 1000 mg/kg dw	Straube D., 2022c 169461089
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.

9.8.1.1 Justification for new endpoints

For the Mandipropamid metabolite CGA 380778, no EU data are available so the worst case assumption was made by dividing the available endpoints of the parent by 10.

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 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 GLOB2106cF in potatoes

Intended use	Potatoes		
Chronic effects on earthworms			
Product/active substance	NOEC (mg/kg dw)	PEC _{soil} (mg/kg dw)	TER _{tt} (criterion TER ≥ 5)
Propamocarb-HCl	362	1.3057	277
Mandipropamid	16	0.2092	76.5
CGA 380778	1.6	0.0087	183

GLOB2106cF	154.5	3.3175	46.6
Chronic effects on other soil macro- and mesofauna			
Product/active substance	NOEC (mg/kg dw)	PEC_{soil} (mg/kg dw)	TER_{It} (criterion TER ≥ 5)
<i>Folsomia candida</i>			
Mandipropamid	10	0.2092	47.8
CGA 380778	1	0.0087	114.9
GLOB2106cF	500	3.3175	150.7
<i>Hypoaspis aculeifer</i>			
GLOB2106cF	500	3.3175	150.7

TER values shown in bold fall below the relevant trigger.

Table 9.8-3A: 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 GLOB2106cF in potatoes

Intended use	Potatoes		
Chronic effects on earthworms			
Product/active substance	NOEC (mg/kg dw)	PEC_{soil} (mg/kg dw)	TER_{It} (criterion TER ≥ 5)
Propamocarb-HCl	362	1.582	229
Mandipropamid	16	0.2092	76.5
CGA 380778	1.6	0.011	145
GLOB2106cF	154.5	1.0943	141
Chronic effects on other soil macro- and mesofauna			
Product/active substance	NOEC (mg/kg dw)	PEC_{soil} (mg/kg dw)	TER_{It} (criterion TER ≥ 5)
<i>Folsomia candida</i>			
Mandipropamid	10	0.2092	47.8
CGA 380778	1	0.011	90.9
GLOB2106cF	500	1.0943	457
<i>Hypoaspis aculeifer</i>			
GLOB2106cF	500	1.0943	457

9.8.2.2 Higher-tier risk assessment

Not relevant.

9.8.3 Overall conclusions

The risk for soil macro- and mesofauna is acceptable when using GLOB2106cF according to the intended uses.

9.9 Effects on soil microbial activity (KCP 10.5)

zRMS Comments:	<p>The submitted information and data were accepted. New study conducted on formulation was submitted and accepted.</p> <p>The risk assessment for effects on soil micro-organisms is based on accepted endpoints. The PECsoil values for active substances, their metabolites and formulation were corrected in accordance with recalculations provided on Section B8.7. The recalculations are presented below the Table 9.9-2 (Table 9.9-2A). For risk assessment the PECsoil accum were used, if relevant.</p> <p>The formulation GLOB2106cF pose no adverse effect on nitrate formation in soil.</p> <p>An acceptable risk to soil microorganisms is expected if the application of the GLOB2106cF is in accordance with proposed pattern use.</p>
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9.9.1 Toxicity data

Studies on effects soil microorganisms have been carried out with Propamocarb-HCl, Mandipropamid and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on soil microorganisms of GLOB2106cF were not evaluated as part of the EU assessment of Propamocarb-HCl and Mandipropamid. 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	Propamocarb-HCl	Study duration 28 d	≥ 28.9 mg a.s./kg dw	EFSA Scientific Report (2006) 78, 1-80
C-mineralisation	Propamocarb-HCl	Study duration 28 d	≥ 28.9 mg a.s./kg dw	EFSA Scientific Report (2006) 78, 1-80
N-mineralisation	Mandipropamid (based on product A1294B)	28 d, aerobic	19% effect at day 28 at ≥ 6 mg a.s./kg dw soil	EFSA Scientific Report (2012) 10(11), 2935
N-mineralisation	CGA 380778	No data available Toxicity assumed to be 10 times higher than parent	19% effect at day 28 at ≥ 0.6 mg a.s./kg dw soil	-
N-mineralisation	GLOB2106cF	70 d, aerobic	No effects ≥ 25% at 28.8 mg/kg dw	Hammesfahr U., 2022 169461080

9.9.1.1 Justification for new endpoints

For the Mandipropamid metabolite CGA 380778, no EU data are available so the worst case assumption was made by dividing the available endpoint of the parent by 10.

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 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 GLOB2106cF in potatoes

Intended use		Potatoes		
N-mineralisation				
Product/active substance	Max. conc. with effects ≤ 25 % (mg/kg dw)	PEC _{soil} (mg/kg dw)	Risk acceptable?	
Propamocarb-HCl	28.9 (at 28 d)	1.3057	yes	
Mandipropamid	6 (at 28 d)	0.2092	yes	
CGA 380778	0.6 (at 28 d)	0.0087	yes	
GLOB2106cF	28.8 (at 70 d)	3.3175	yes	
C-mineralisation				
Product/active substance	Max. conc. with effects ≤ 25 % (mg/kg dw)	PEC _{soil} (mg/kg dw)	Risk acceptable?	
Propamocarb-HCl	28.9 (at 28 d)	1.3057	yes	

Table 9.9-3A: Assessment of the risk for effects on soil micro-organisms due to the use of GLOB2106cF in potatoes

Intended use		Potatoes		
N-mineralisation				
Product/active substance	Max. conc. with effects ≤ 25 % (mg/kg dw)	PEC _{soil} (mg/kg dw)	Risk acceptable?	
Propamocarb-HCl	28.9 (at 28 d)	1.582	yes	
Mandipropamid	6 (at 28 d)	0.2092	yes	
CGA 380778	0.6 (at 28 d)	0.011	yes	
GLOB2106cF	28.8 (at 70 d)	1.0943	yes	
C-mineralisation				
Product/active substance	Max. conc. with effects ≤ 25 % (mg/kg dw)	PEC _{soil} (mg/kg dw)	Risk acceptable?	
Propamocarb-HCl	28.9 (at 28 d)	1.582	yes	

9.9.3 Overall conclusions

The risk is acceptable for soil micro-organisms following exposure to GLOB2106cF according to the intended uses.

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

zRMS Comments:	<p>The new studies were submitted and accepted.</p> <p>Toxicity effects of GLOB2106cF formulation on the vegetative vigour and seedling emergence were tested.</p> <p>An acceptable risk to non-target terrestrial plants is expected if the application of the GLOB2106cF is in accordance with proposed use pattern.</p> <p>No mitigation measure is required.</p>
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9.10.1 Toxicity data

Studies on the toxicity to non-target terrestrial plants have been carried out with Propamocarb-HCl, Mandipropamid and its relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on non-target terrestrial plants of GLOB2106cF were not evaluated as part of the EU assessment of active substance 1. 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
<i>Avena sativa</i> _m ¹⁾ <i>Triticum aestivum</i> _m ²⁾ <i>Cucumis sativus</i> _d ³⁾ <i>Glycine max</i> _d ⁴⁾ <i>Lactuca sativa</i> _d ⁵⁾ <i>Raphanus sativus</i> _d ⁶⁾	GLOB2106cF	21 d Seedling emergence	1) ER ₅₀ > 5.7 L/ha 2) ER ₅₀ > 5.7 L/ha 3) ER ₅₀ > 5.7 L/ha 4) ER ₅₀ > 5.7 L/ha 5) ER ₅₀ > 5.7 L/ha 6) ER ₅₀ > 5.7 L/ha	Stead A., 2023a STC/22/E1576
<i>Avena sativa</i> _m ¹⁾ <i>Triticum aestivum</i> _m ²⁾ <i>Cucumis sativus</i> _d ³⁾ <i>Glycine max</i> _d ⁴⁾ <i>Lactuca sativa</i> _d ⁵⁾ <i>Raphanus sativus</i> _d ⁶⁾	GLOB2106cF	21 d Vegetative vigour	1) ER ₅₀ > 5.7 L/ha 2) ER ₅₀ > 5.7 L/ha 3) ER ₅₀ > 5.7 L/ha 4) ER ₅₀ > 5.7 L/ha 5) ER ₅₀ > 5.7 L/ha 6) ER ₅₀ > 5.7 L/ha	Stead A., 2023b STC/22/E1575

m: monocotyledonous; d: dicotyledonous

9.10.1.1 Justification for new endpoints

/

9.10.2 Risk assessment

9.10.2.1 Tier-1 risk assessment (based screening data)

Not relevant.

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

The risk assessment is based on the “Guidance Document on Terrestrial Ecotoxicology”, (SANCO/10329/2002 rev.2 final, 2002). It is restricted to off-field situations, as non-target plants are non-crop plants located outside the treated area.

Table 9.10-2: Assessment of the risk for non-target plants due to the use of GLOB2106cF in potatoes

Intended use		Potatoes		
Active substance/product		GLOB2106cF		
Application rate (L/ha)		3 × 1.9		
MAF		2.3		
Test species	ER ₅₀ (L/ha)	Drift rate	PER _{off-field} (L/ha)	TER criterion: TER ≥ 5
<i>All species tested</i>	5.7	0.0277	0.121049	47.1

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

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 is acceptable for non-target plants following exposure to GLOB2106cF according to the intended uses. No mitigation measures are needed.

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

Not required.

9.12 Monitoring data (KCP 10.8)

Not relevant.

9.13 Classification and Labelling

See Part C.

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
KCA1 8.2.5.3	Kimmel, S.	2011	Mandipropamid – Effects on the development of sediment-dwelling larvae of <i>Chironomus riparius</i> in water-sediment systems with spiked sediment Report No. D13764 Document No. VV-397081 , NOA446510_10741 Test Facility Harlan Laboratories Ltd. GLP Unpublished	N	Syngenta (LoA Globachem NV)
KCP 10.1.2.2	Cairns, S.	2013	Mandipropamid – Foliage Decline Study with A12946B on Cereals in Northern France, Germany and the United Kingdom in 2013 Report No. 34472 Document No. VV-405547 , A12946B_11634 Test Facility Charles River Laboratories GLP Unpublished	N	Syngenta (LoA Globachem NV)
KCP 10.2.1	xxxxxxx	2023	GLOB2106cF: acute toxicity to Rainbow Trout (<i>Oncorhynchus mykiss</i>) in a 96-hour static test xxxxxxxxxxxxx GLP Unpublished	N	Globachem NV
KCP 10.2.1	Ganßmann M.	2023a	GLOB2106cF: Acute toxicity to <i>Daphnia magna</i> in a static 48-hour immobilisation test 169461220 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.2.1	Ganßmann M.	2023b	GLOB2106cF: Toxicity to <i>Pseudokirchneriella subcapitata</i> in an algal growth inhibition test 169461210 Ibacon GmbH GLP	N	Globachem NV

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 10.3.1.1	Schabio S.	2023	GLOB2106cF: Effects (acute contact and oral) on honey bees (<i>Apis mellifera</i> L.) in the laboratory 169461035 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.3.1.1	Chwiesko D.	2023	GLOB2106cF: acute contact and oral toxicity to bumblebees (<i>Bombus terrestris</i> L.) in the laboratory 169461105 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.3.1.2	Venturi S.	2023	Chronic oral effects of GLOB2106cF to adult worker honeybees (<i>Apis mellifera</i> L.) in a 10-day feeding laboratory test BT262/22 BioTecnologie BT S.r.l. GLP Unpublished	N	Globachem NV
KCP 10.3.1.3	Colli M.	2023	Effects of GLOB2106cF on honeybees (<i>Apis mellifera</i> L.) 22-day larval toxicity test with repeated exposure BT126/22 BioTecnologie BT S.r.l. GLP Unpublished	N	Globachem NV
KCP 10.3.2.2	Leopold, J.	2023a	GLOB2106cF: Effects on the predatory mite <i>Typhlodromus pyri</i> (Acari: Phytoseiidae), Extended laboratory study – Dose response test 169461062 Ibacon GmbH GLP Unpublished	N	Globachem NV

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 10.3.2.2	Leopold, J.	2022	GLOB2106cF: Effects on the parasitoid <i>Aphidius rhopalosiphi</i> (Hymenoptera, Braconidae), Extended laboratory study – Dose response test 169461002 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.3.2.2	Leopold, J.	2023b	GLOB2106cF: Effects on the lacewing <i>Chrysoperla carnea</i> (Neuroptera, Chrysopidae), Extended laboratory study – Dose response test 169461047 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.3.2.2	Leopold, J.	2023c	GLOB2106cF: Effects on the ladybird beetle <i>Coccinella septempunctata</i> (Coleoptera, Coccinellidae), Extended laboratory study – Dose response test 169461012 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.4.1.1	Straube, D.	2022a	GLOB2106cF: Effects on reproduction and growth of earthworms <i>Eisenia andrei</i> in artificial soil 169461022 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.4.2.1	Straube, D.	2022b	GLOB2106cF: Effects on reproduction of the Collembola (<i>Folsomia candida</i>) in artificial soil 169461016 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.4.2.1	Straube, D.	2022c	GLOB2106cF: Effects on reproduction of the predatory mite <i>Hypoaspis aculeifer</i> in artificial soil 169461089	N	Globachem NV

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
			Ibacon GmbH GLP Unpublished		
KCP 10.5	Hammesfahr, U.	2022	GLOB2106cF: Effects on the Activity of the Soil Microflora in the Laboratory (Nitrogen Transformation) 169461080 Ibacon GmbH GLP Unpublished	N	Globachem NV
KCP 10.6	Stead, A.	2023a	GLOB2106cF: OECD Terrestrial Plant Test - Seedling Emergence and Seedling Growth Test STC/22/E1576 Stockbridge Technology Centre Ltd GLP Unpublished	N	Globachem NV
KCP 10.6	Stead, A.	2023b	GLOB2106cF: OECD Terrestrial Plant Test - Vegetative Vigour Test STC/22/E1575 Stockbridge Technology Centre Ltd GLP Unpublished	N	Globachem NV

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

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
None					

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 XX	Author	YYYY	Title Company Report N Source GLP/non GLP/GEP/non GEP Published/Unpublished	Y/N	Owner

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
KCP 10.1.2.2	Cairns, S.	2013	Mandipropamid – Foliage Decline Study with A12946B on Cereals in Northern France, Germany and the United Kingdom in 2013 Report No. 34472 Document No. VV-405547 , A12946B_11634 Test Facility Charles River Laboratories GLP Unpublished	N	Syngenta (LoA Globachem)

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

No new studies submitted.

A 2.1.2 KCP 10.1.2 Effects on terrestrial vertebrates other than birds

No new studies submitted.

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

No new studies submitted.

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

Comments of zRMS:	<p>The submitted study was accepted. The validity criteria were met. No deviation was noted. The formulation GLOB2106cF was the test item.</p> <p>The following endpoints were derived: LC₅₀ > 100 mg test item/L; NOEC ≥ 100 mg test item/L</p> <p>These values will be used in risk assessment.</p>
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Reference:	KCP 10.2.1
Report	GLOB2106cF: Acute toxicity to Rainbow Trout (<i>Oncorhynchus mykiss</i>) in a 96-hour static test, xxxxxx, 2023, 169461230
Guideline(s):	Yes, OECD 203
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to evaluate the acute toxicity of the test item GLOB2106cF to fish. For this purpose, juvenile rainbow trout were exposed in a static test to various concentrations under defined conditions for 96 hours. The recorded effects were the mortality and sublethal effects on the fish.

Based on the test results, the 96-hour LC₅₀ could not be determined but was estimated to be > 100mg test item/L based on nominal concentrations. The NOEC was determined to be ≥ 100 mg test item/L also based on nominal concentrations.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content of a.i.: Propamocarb-HCl: 450 g/L (nominal), 448.0 g/L (analytical) ¹ Mandipropamid: 75 g/L (nominal), 76.21 g/L (analytical) ¹ according to certificate of analysis ¹ values of pre-accelerated storage
Test Species:	Juvenile rainbow trout (<i>Oncorhynchus mykiss</i>) mean length: 4.69 cm ± 0.2 cm; source: Forellenzuchtbetrieb Störk, 88348 Bad Saulgau, Germany
Test Design:	This study encompassed 6 treatment groups (5 dose rates of the test item and a control) each containing 7 individuals. The acute toxicity to unfed juvenile rainbow trout was determined in an aerated, static 96-hour test. The test fish were observed at test start and after approximately 2, 4, 24, 28.5, 48, 52, 72, 76 and 96 hours test duration for sublethal effects and mortality.
Endpoints:	NOEC after 96 h, LOEC after 96 h; LC ₅₀ : lethal concentration producing 50 % mortality after 96 h of exposure.
Test Concentrations:	100, 62.5, 39.1, 24.4 and 15.3 mg test item/L (spacing factor 1.6) and a control.
Test Conditions:	Water temperature: 11.7 to 12.1 °C (target: 10 – 14 °C); pH value: 7.2 to 7.7 (target: 6.0 – 8.5); dissolved oxygen concentration: 92 to 99 % of the air saturation value (target: ≥ 60 %); photoperiod: 12 h light - 12 h dark; light intensity: 690 to 800 lux (target: 540 – 1000 lux). Thus, test conditions were within the ranges requested by guideline OECD 203.
Statistical Analysis:	No statistical analysis was performed. The LC ₅₀ could not be quantified due to the absence of mortality in the test item treated groups but was estimated to be above the highest test concentration. The NOEC and the LOEC were determined directly from the raw data.

Results and Discussion

Experimental dates: 12 September 2022 – 21 October 2022

Validity Criteria:	In the control no fish died. The dissolved oxygen concentration in the test media of all treatment groups did not fall below 92 % of air saturation value. The test concentration was analysed. Thus, all validity criteria were met.
Biological test results:	In the control and all test item treated groups, all fish survived until the end of the experiment. At the concentrations of 100 and 62.5 mg test item/L, some fish showed the symptoms of abnormal ventilatory function and abnormal skin pigmentation after 96 hours exposure and additionally temporary loss of equilibrium and abnormal swimming behaviour on other assessment time points. The mortality observed is summarised in the table below.

Observed Mortality of unfed Rainbow Trout (*Oncorhynchus mykiss*) exposed to GLOB2106cF for 96 hours

Time weighted average concentration [mg test item/L]	Mortality (No. of dead fish)				
	0 h	24 h	48 h	72 h	96 h
Control	0	0	0	0	0
15.3	0	0	0	0	0
24.4	0	0	0	0	0
39.1	0	0	0	0	0
62.5	0	0	0	0	0
100	0	0	0	0	0
LC ₅₀ [mg test item/L]	-	> 100	> 100	> 100	> 100
95% CI.	-	n.d.	n.d.	n.d.	n.d.

- not relevant

n.d. not determinable

CI.: Confidence interval

Values refer to nominal test concentrations.

Analytical Test Results: The quantification of the active ingredients Mandipropamid and Propamocarb-HCl, based on its parent Propamocarb, of the test item GLOB2106cF in the test samples was performed using liquid chromatography with MS/MS detection.

At the start of the test, 108 % of the nominal test concentrations of Mandipropamid were found (average of all test concentrations). After 96 hours test duration, 95 % of the nominal value was determined (average of all test concentrations). During the test the fish were exposed to a mean of 102 % of nominal.

At the start of the test, 106 % of the nominal test concentrations of Propamocarb-HCl were found (average of all test concentrations). After 96 hours test duration, 109 % of the nominal value was determined (average of all test concentrations). During the test, the fish were exposed to a mean of 108 % of nominal.

Conclusions

The study is valid since all required validity criteria were met.

The acute effect of the test item GLOB2106cF to rainbow trout (*Oncorhynchus mykiss*) was assessed in a static concentration-response test. Based on the test results, the 96-hour LC₅₀ could not be determined but was estimated to be > 100mg test item/L based on nominal concentrations. The NOEC was determined to be ≥ 100 mg test item/L also based on nominal concentrations.

The initial concentrations and the maintenance of the exposure concentrations during the test were verified in the analytical part. All reported results refer to nominal values since the concentrations of the test item were within ± 20 % of the nominal concentrations during the test.

Comments of zRMS:	<p>The submitted study was accepted. The validity criteria were met. No deviation was noted. The formulation GLOB2106cF was the test item.</p> <p>During the test, the daphnids were exposed to a mean of 93 % and 95 % of nominal concentration of Mandipropamid and Propamocarb-HCl, respectively.</p>
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	<p>All reported results of Propamocarb-HCl refer to nominal values since the concentrations of the test item were within $\pm 20\%$ of the nominal concentrations during the test.</p> <p>All reported results of Mandipropamid refer to geometric mean concentrations, since the test item concentrations were not within $\pm 20\%$ of the nominal concentrations during the test.</p> <p>The following endpoints were derived: 48h EC₅₀ > 100 mg formulation/L (based on nominal concentration) 48h EC₅₀ > 85.8 mg formulation/L (based on measured concentration) NOEC = 9.4 mg formulation/L (based on nominal concentration) NOEC = 9.18 mg formulation/L (based on measured concentration) LOEC = 20.7 mg formulation/L (based on nominal concentration) LOEC = 19.8 mg formulation/L (based on measured concentration)</p> <p>The endpoints based on measured concentration will be used in risk assessment.</p>
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Reference:	KCP 10.2.1
Report	GLOB2106cF: Acute toxicity to <i>Daphnia magna</i> in a static 48-hour immobilisation test, Ganßmann M., 2023a, 169461220
Guideline(s):	Yes, OECD 202
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to determine the influence of the test item GLOB2106cF on the mobility of *Daphnia magna*.

For this purpose, young daphnids (< 24 hours old) were exposed in a static test to various concentrations under defined conditions for 48 hours. The recorded effects were the mobility of the daphnids after 24 and 48 hours.

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

The 48-hour NOEC was determined to be 9.4 mg test item/L. The 48-hour LOEC was determined to be 20.7 mg test item/L and the 48-hour EC₅₀ value was determined to be greater than 100 mg test item/L.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content of a.i.: Propamocarb-HCl: 450 g/L (nominal), 448.0 g/L (analytical) ¹ , Mandipropamid: 75 g/L (nominal), 76.21 g/L (analytical) ¹
Test Species:	according to certificate of analysis; ¹ values of pre storage <i>Daphnia magna</i> , clone 5; 1.25 to 20.25 hours old. Source: The daphnids introduced in the test were taken from ibacon's in-house laboratory culture.
Test Design:	This study encompassed 6 treatment groups (5 dose rates of the test item, and a control) each containing 20 individuals. The mobility of the daphnids was determined in a static 48-hour test by visual observation after 24 and 48 hours.

Endpoints:	Number of immobile organisms after 24 and 48 hours
Test Concentrations:	100, 45.5, 20.7, 9.4 and 4.3 mg test item/L (spacing factor 2.2) and a control
Test Conditions:	Water temperature: 19.7 to 20.0 °C (target: 18 °C – 22 °C; ± 1 °C within this range); pH value: 7.9 to 8.1 (target: 6 - 9); dissolved oxygen concentration: 8.3 to 9.0 mg/L (target: ≥ 3 mg/L); photoperiod: 16 h light: 8 h dark; light intensity: 530 to 690 lux (target: ≤ 1500 lux); Thus, test conditions were within the ranges requested by guideline OECD 202.
Statistics:	The NOEC and LOEC after 24 and 48 hours were determined directly from the raw data. Due to the low effects observed, only the EC ₂₀ values could be calculated by Probit Analysis (for nominal test concentrations) and Weibull Analysis (geometric mean measured test concentrations). The software used to perform the statistical analysis was ToxRat Professional, Version 3.3.0, ToxRat® Solutions GmbH.

Results and Discussion

Experimental dates: 15 November 2022 – 23 November 2022

Validity Criteria:	Control immobilisation rate: Achieved: 5 % (target: ≤ 10 %), Dissolved oxygen concentration at test end: Achieved: ≥ 8.3 mg O ₂ /L (target: ≥ 3 mg O ₂ /L)
	Thus, the validity criteria were met.

Biological Test Results:	After 48 hours of exposure, no statistically significant immobilisation of the test daphnids was observed. However, despite the statistical findings, the immobility at 20.7, 45.5 and 100 mg test item/L was clearly increased and the Daphnids were negatively affected. The NOEC and LOEC were therefore determined directly from the raw data. No sublethal effects on the daphnids were observed in any treatment after 48 hours.
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Summary of Biological Results

Concentrations		% of immobilised daphnids after	
Nominal [mg test item/L]	Geometric mean measured ¹	24 hours	48 hours
Control		0	5
4.3	4.39	0	10
9.4	9.18	0	10
20.7	19.8	5	35
45.5	37.8	0	35
100	85.8	0	35

	Based on nominal concentrations		Based on mean measured concentrations ¹	
	24 hours	48 hours	24 hours	48 hours
EC ₅₀ [mg test item/L]:	n.d.	> 100	n.d.	>85.8
95 % CI [mg test item/L]:	n.d.	n.d.	n.d.	n.d.
EC ₂₀ [mg test item/L]:	n.d.	14.1	n.d.	13.6
95 % CI [mg test item/L]:	n.d.	< 4.3 - 34.3	n.d.	< 4.39 - 31.1
EC ₁₀ [mg test item/L]:	n.d.	< 4.3	n.d.	n.d.
95 % CI [mg test item/L]:	n.d.	n.d.	n.d.	n.d.
NOEC [mg test item/L]:	≥100	9.4	≥85.8	9.18
LOEC [mg test item/L]:	>100	20.7	>85.8	19.8

Values refer to nominal and geometric mean measured test concentrations

CI: Confidence interval, n.d.: not determinable,

NOEC and LOEC were determined directly from the raw data.

¹ = geometric mean concentrations are based on the measured values of Mandipropamid.

Analytical Test Results:

The quantification of the active ingredients Mandipropamid and Propamocarb, which is the parent of Propamocarb-HCl, of the test item GLOB2106cF in the test samples was performed using liquid chromatography with MS/MS detection.

Mandipropamid:

At the start of the test, 101 % of the nominal test concentrations were found (average of all test concentrations). After 48 hours test duration, 86 % of the nominal value was determined (average of all test concentrations). During the test, the daphnids were exposed to a mean of 93 % of nominal.

Propamocarb-HCl:

At the start of the test, 94 % of the nominal test concentrations were found (average of all test concentrations). After 48 hours test duration, 95 % of the nominal value was determined (average of all test concentrations). During the test, the daphnids were exposed to a mean of 95 % of nominal.

Conclusions

The study was valid since all required validity criteria were met.

The toxic effect of the test item GLOB2106cF to *Daphnia magna* was assessed in a static concentration-response test. The 48-hour NOEC was determined to be 9.4 mg test item/L. The 48-hour LOEC was determined to be 20.7 mg test item/L and the 48-hour EC₅₀ value was determined to be greater than 100 mg/L.

The initial concentrations and the maintenance of the exposure concentrations during the test were determined in the analytical part. All reported results of Propamocarb-HCl refer to nominal values since the concentrations of the test item were within ± 20% of the nominal concentrations during the test.

All reported results of Mandipropamid refer to geometric mean concentrations, since the test item concentrations were not within ± 20 % of the nominal concentrations during the test.

Comments of zRMS:	<p>The submitted study was accepted. The validity criteria were met. No deviation was noted. The formulation GLOB2106cF was the test item.</p> <p>The following endpoints were derived: 72 h ErC₅₀ > 100 mg test item/L ErC₁₀ > 100 mg test item/L NOEC = 32 mg test item/L LOEC = 100 mg test item/L</p>
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Reference:	KCP 10.2.1
Report	GLOB2106cF: toxicity to <i>Pseudokirchneriella subcapitata</i> in an algal growth inhibition test, Ganßmann M., 2023b, 169461210
Guideline(s):	Yes, OECD 201
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this test is to determine the inhibitory effect of the test item GLOB2106cF on the growth of the freshwater unicellular green algal species *Pseudokirchneriella subcapitata*.

For this purpose, exponentially growing cultures of this unicellular green algal species were exposed to various concentrations of the test item under defined conditions. The inhibition of growth in relation to control cultures was determined over a test period of 72 hours and thus over several algal generations.

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

The 72-hour E_yC₅₀ was determined to be > 100 mg test item/L and the 72-hour E_rC₅₀ value was determined to be > 100 mg test item/L. The 72-hour NOE_yC was determined to be 32 mg test item/L and the associated 72-hour LOE_yC was 100 mg test item/L. The 72-hour NOE_rC was determined to be 32 mg test item/L and the associated 72-hour LOE_rC was 100 mg test item/L.

Materials and Methods

Test Item:	GLOB2106cF; Batch No.: BRN 3891; content of a.i.: Propamocarb-HCl: 450 g/L (nominal), 448.0 g/L (analytical) ¹ ; Mandipropamid: 75 g/L (nominal), 76.21 g/L (analytical) ¹ ; according to certificate of analysis ¹ values of pre accelerated storage
Test Species:	<i>Pseudokirchneriella subcapitata</i> , Strain No. 61.81 SAG formerly known as <i>Selenastrum capricornutum</i> , and recently renamed as <i>Raphidocelis subcapitata</i> (KORSHIKOV). Cultivated in the laboratories of ibacon; original source: "Culture Collection of Algae at Goettingen University (SAG)", 37073 Göttingen, Germany.
Test Design:	This study encompassed 6 treatment groups (5 concentrations of the test item and a control) with three replicates per test concentration and six replicates for the control. At test start 50 mL of the test media were inoculated with nominal 5000 algal cells per mL test medium and defined volumes of the algal suspensions were sampled after 24, 48

and 72 hours for determination of cell densities by spectrophotometric measurement.

Endpoints: Yield and growth rate of the algae

Test Concentrations: 100, 32, 10, 3.2 and 1.0 mg test item/L (spacing factor 3.16), and a control.

Test Conditions: Water temperature: observed: 21.2 to 22.2 °C (target: 21 – 24 °C, controlled at ± 2 °C);
 pH value in the control at test start: 8.0,
 pH value in the control at test end: 8.1;
 pH values in the test item treatments at test start: 7.9 to 8.0,
 pH values in the test item treatments at test end: 8.1 to 8.2;
 (target pH: 8.1 ± 0.1 at test start in untreated test water)
 continuous illumination:
 observed mean light intensity: 6622 lux (5980 to 6900 lux)
 (target: 4440 – 8880 lux, ± 15 % of mean value)

Statistics: Based on the calculated cell densities, the EC₁₀ value for Yield and the 95 %-confidence limits were calculated by Probit analysis.
 Due to the low effects of the test item the 72-hour E_rC₅₀ and the 72-hour E_yC₅₀ (see Definitions) as well as the corresponding EC₂₀ and the EC₁₀ value for growth could not be calculated but were determined directly from the raw data.
 For the determination of the 72-hour LOEC and the 72-hour NOEC, the calculated growth rates and yields at each test concentration were tested for significant differences compared to the control values by Williams t-test (yield and growth rate).
 The software used to perform the statistical analysis was ToxRat Professional, Version 3.3.0, ToxRat® Solutions GmbH.

Results and Discussion

Experimental dates: 19 September 2022 – 5 October 2022

Biological Results:

Validity Criteria: Cell density in the control:
 Achieved: 98.9-fold increase (criterion: ≥ 16) within 72 hours;
 Coefficient of Variation (CV) of sectional (daily) growth rate of the control:
 Achieved: 17.3 % (criterion: $\leq 35\%$);
 CV of average growth of control replicates:
 Achieved: 1.7 % (criterion: $\leq 7\%$);
 and thus, the validity criteria were met.

Biological results

Parameter	Yield [mg test item/L]	Growth rate [mg test item/L]
72-hour EC ₅₀	> 100 ¹	>100 ¹
95 % conf. interval	n.d.	n.d.
72-hour EC ₂₀	> 100 ¹	>100 ¹
95 % conf. interval	n.d.	n.d.
72-hour EC ₁₀	26.4	>100 ¹
95 % conf. interval	14.5 - 55.2	n.d.

72-hour NOEC	32	32
72-hour LOEC	100	100

n.d. = not determinable. Values refer to nominal test concentrations

¹ = values were determined directly from the raw data.

Analytical Results: The quantification of the active ingredients Mandipropamid and Propamocarb-HCl, based on its parent Propamocarb, of the test item GLOB2106cF in the test samples was performed using liquid chromatography with MS/MS detection.

At the start of the test, 110 % of the nominal test concentrations of Mandipropamid were found (average of all test concentrations). After 72 hours test duration, 97 % of the nominal value was determined (average of all test concentrations). During the test, the fish were exposed to a mean of 103 % of nominal.

At the start of the test, 83 % of the nominal test concentrations of Propamocarb-HCl were found (average of all test concentrations). After 72 hours test duration, 86 % of the nominal value was determined (average of all test concentrations). During the test, the algae were exposed to a mean of 85 % of nominal.

Conclusions

The study is valid since all required validity criteria were fulfilled. The influence of GLOB2106cF on the growth of the freshwater green algae *Pseudokirchneriella subcapitata* was assessed in a static concentration-response test. The 72-hour E_yC_{50} was determined to be > 100 mg test item/L and the 72-hour E_rC_{50} value was determined to be > 100 mg test item/L. The 72-hour NOE_yC was determined to be 32 mg test item/L and the associated 72-hour LOE_yC was 100 mg test item/L. The 72-hour NOE_rC was determined to be 32 mg test item/L and the associated 72-hour LOE_rC was 100 mg test item/L.

The initial concentrations and the maintenance of the exposure concentrations during the test were determined in the analytical part. All reported results refer to nominal values since the concentrations of the test item were within $\pm 20\%$ of the nominal concentrations during the test.

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

No new studies submitted.

A 2.2.3 KCP 10.2.3 Further testing on aquatic organisms

No new studies submitted.

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

Comments of zRMS:	The study was accepted. The study was conducted in accordance with OECD guidances 213 (acute oral)
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	<p>and 214 (acute contact).</p> <p>The validity criteria were met:</p> <ul style="list-style-type: none"> oral test: the mean mortality of the control groups was 0% (recommended $\leq 10\%$); contact test: the mean mortality of the control groups was 0%, (recommended $\leq 10\%$); <p>The following endpoints were derived</p> <p>Oral:</p> <p style="padding-left: 40px;">LD₅₀ 48 h > 445 µg formulation/bee NOED 48 h \geq 445 µg formulation/bee</p> <p>Contact:</p> <p style="padding-left: 40px;">LD₅₀ 96 h = 1000 µg formulation/bee NOED 48 h = 1000 µg formulation/bee</p>
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Reference:	KCP 10.3.1.1
Report	GLOB2106cF: Effects (acute contact and oral) on honey bees (<i>Apis mellifera</i> L.) in the laboratory, Schabio S., 2023, 169461035
Guideline(s):	Yes, OECD 213 and 214
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to determine the acute contact and oral toxicity of GLOB2106cF to the honey bee (*A. mellifera* L.). Mortality of the bees was used as the toxic endpoint. Sublethal effects, such as changes in behaviour, were also assessed.

The contact LD₅₀ values (24 and 48 h) of GLOB2106cF were determined to be > 1000.0 µg product/bee, respectively. The oral LD₅₀ values (24 and 48 h) were estimated to be both > 445.0 µg product/bee. The contact and oral NOED were estimated to be ≥ 1000.0 and ≥ 445.0 µg product/bee, respectively.

Materials and Methods

Test Item:	<p>GLOB2106cF, Batch No.: BRN 3891, content: Propamocarb HCl: Declared: 450 g/L Pre Storage: 448.0 g/L (equivalent to 99.56 % of the declared content), Post Accelerated Storage: 449.4 g/L (equivalent to 99.86 % of the declared content)</p> <p>Mandipropamid: Declared: 75 g/L Pre Storage: 76.21 g/L (equivalent to 101.6 % of the declared content), Post Accelerated Storage: 74.60 g/L (equivalent to 99.47 % of the declared content), according to GLP certificate of analysis.</p>
Test Species:	Honey bee (<i>Apis mellifera</i> L.); female worker bees; obtained from a healthy and queen-right colony, bred by ibacon, collected in the morning of use.
Test Design:	Acute contact and oral limit test; duration 48 hours (contact test and oral test); 5 replicates for the contact and oral test for the test item and control group, 3 for the reference item group, each consisting of 10 bees per cage per treatment; assessment of mortality after 4, 24 and 48 hours (oral and

	contact test); reference item: dimethoate 417 g/L (analysed).
Food	50 % w/v sucrose solution <i>ad libitum</i>
Test Dose Levels:	<u>Contact test:</u> 1000.0 µg product/bee* <u>Oral test (nominal):</u> 1000.0 µg product/bee * <u>Oral test (measured):</u> 445.0 µg product/bee *
	* The dose level of the test item was based on the product without taking into consideration active substances content.
Target Dose Levels of the Reference Item:	0.30, 0.20, 0.15 and 0.10 µg dimethoate per bee (contact test) 0.30, 0.15, 0.08 and 0.05 µg dimethoate per bee (oral test)
Consumed Dose Levels of the Reference Item:	0.27, 0.15, 0.08 and 0.06 µg dimethoate per bee (oral test)
Control:	Contact test: tap water + Triton X-100 treated control (applied after anaesthetization with CO ₂) Oral test: 50 % w/v sucrose solution
Anaesthetization:	Bees were anaesthetized for <i>ca.</i> 20 seconds with CO ₂ until they were completely immobilized immediately before application (only in the contact test).
Starvation Time:	25 minutes for all treatment groups in the oral test, prior to application
Application in the Contact Test:	A single 5 µL droplet of GLOB2106cF in an appropriate carrier (tap water + 0.1 % Triton X-100*) was placed on the dorsal bee thorax using a calibrated pipette (Multipette©, Eppendorf). For the control one 5 µL droplet of tap water containing 0.1 % Triton X-100* was used. The reference item was also applied in 5 µL tap water (dimethoate made up in tap water containing 0.1 % Triton X-100*). A 5 µL droplet was chosen in deviation to the guideline recommendation of a 1 µL droplet, since a higher volume ensured a more reliable dispersion of the test item; ibacon experience has proven that higher volumes are suitable and no adverse effects on the outcome of the study are to be expected [presented as a poster by Schmitzer et al. on the ICPBR Bee Protection Group meeting in Bologna, 2002]. *The Triton X-100 was used to improve the spreading of the test item droplet on the bee body. Triton X-100 is non-toxic to honey bees.
Application in the Oral Test:	The test item and reference item were applied in 50 % w/v sucrose solution, which was used as carrier (food) in the oral test. For the control pure 50 % w/v sucrose solution was offered to the bees. The treated food was offered in syringes, which were weighed before and after introduction into the cages. After a maximum duration of 6 hours, the syringes containing the treated food were removed, weighed and replaced by ones containing fresh, untreated food. The mean target dose levels (e.g. 1000.0 µg product/bee nominal) would have been obtained if exactly 20 mg/bee of the treated food were ingested. In practice, uptake of the treated sugar solutions differed slightly from the nominal 20 mg/bee and results are given based on the measured consumption.
Test Conditions:	Temperature: 23 - 25 °C; relative humidity: 54 - 61 %; photoperiod: 24 h darkness.
Test Parameters:	Mortality: Number of dead bees after 4 (± 0.5) hours (first day); 24 and 48 (± 2) hours (contact and oral test).

Behavioural abnormalities were assessed after 4 (\pm 0.5) hours (first day); 24 and 48 (\pm 2) hours (contact and oral test).

Sub-lethal effects such as symptoms of poisoning or any abnormal behaviour in comparison to the control were recorded according to the following categories: m = moribund (bees cannot walk and show only very feeble movements of legs and antennae, only weak response to stimulation; e.g. light or blowing; bees may recover but usually die) a = affected (bees still upright and attempting to walk but showing signs of reduced coordination; hyperactivity; aggressiveness; increased self-cleaning behaviour; rotations; shivering) c = cramps (bees contracting abdomen or entire body) ap = apathy (bees show only low or delayed reactions to stimulation e.g. light or blowing; bees are sitting motionless in the unit) v = vomiting.

Statistical analysis: The software used to perform the statistical analysis was ToxRat Professional, Version 3.2.1.

Results obtained from the bees treated with the test item were compared to those obtained from the water control group. As no test item treatment group showed mortality above 50.0 %, no statistical evaluation on the LD50 has been carried out. The contact and oral LD50 values of the reference item were determined according to Probit Analysis (according to Finney 1971).

Results and Discussion

Contact Test:

The tested dose of 1000 μ g product/bee led to a mortality of 4.0 % at test termination (48 hours). There was no mortality in the water control group (water + 0.1 % Triton X-100). No behavioural abnormalities occurred throughout the test. A prolongation of the test was not necessary.

Oral Test:

The target dose level of the test item (1000 μ g product/bee) was not achieved. Actual oral consumed doses of 445.0 μ g product/bee led to 10 % mortality at test termination (48 hours). No mortality occurred in the water control (50 % w/v sucrose solution = 500 g sucrose/L tap water). During the first 4 hours moribund and affected were observed in the test item group. After 48 hours one affected bee was observed in the test item treated group. A prolongation of the test was not necessary.

Toxicity of GLOB2106cF to honey bees; laboratory test

Test Item	GLOB2106cF	
Test Species	<i>Apis mellifera</i> L.	
Exposure	contact (solution in Triton X-100 (0.1 %)/water)	oral (50 % w/v sucrose solution)
Application rate [μ g product/bee]	1000.0	Target: 1000.0 Consumed: 445.0
LD ₅₀ [μ g product/bee]	24 hours: > 1000.0 48 hours: > 1000.0	24 hours: > 445.0 48 hours: > 445.0
NOED [μ g product/bee]	24 hours: \geq 1000.0 48 hours: \geq 1000.0	24 hours: \geq 445.0 48 hours: \geq 445.0

Validity criteria:

Control Mortality:	<u>Contact Test</u> untreated control: 0.0 % <u>Oral Test</u> untreated control 0.0 %
LD ₅₀ of Reference Item (24 hrs):	<u>Contact Test:</u> 0.19 µg a.i./bee <u>Oral Test:</u> 0.15 µg a.i./bee
Validity of the Tests:	The contact and oral tests are considered valid as the control mortality in each case was ≤ 10 % and the LD ₅₀ values obtained with the reference item (dimethoate) were within the required ranges.

Conclusions

The acute toxicity of GLOB2106cF on adult honey bees (*Apis mellifera* L.) was investigated in an acute contact and an acute oral limit study under laboratory conditions. The contact LD₅₀ values (24 and 48 h) of GLOB2106cF were determined to be 1000.0 µg product/bee, respectively. The oral LD₅₀ values (24 and 48 h) were estimated to be both > 445.0 µg product/bee. The contact and oral NOED were estimated to be ≥ 1000.0 and ≥ 445.0 µg product/bee, respectively.

Comments of zRMS:	The study was accepted. The study was conducted in accordance with OECD guidances 246 (acute oral) and 247 (acute contact). The validity criteria were met: <ul style="list-style-type: none"> • the mean mortality of the control groups was 0% (recommended ≤ 10 %); • contact test: water control mortality at test end was 0% (recommended ≤ 10 %); • oral test: water control mortality at test end was 3.0% (recommended ≤ 10%). The following endpoints were derived Oral: LD ₅₀ 48 h > 523.8 µg formulation/bee NOED 48 h ≥ 523.8 µg formulation/bee Contact: LD ₅₀ 96 h > 600 µg formulation/bee NOED 48 h ≥ 600 µg formulation/bee
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Reference:	KCP 10.3.1.1
Report	GLOB2106cF: acute contact and oral toxicity to bumblebees (<i>Bombis terrestris</i> L.) in the laboratory, Chwiesko D., 2023, 169461105
Guideline(s):	Yes, OECD 246 and 247
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to determine the acute contact and oral toxicity of GLOB2106cF to the bumblebee (*Bombus terrestris* L.).

Mortality of the bumblebees was used as the endpoint related to toxicity. Sub-lethal effects, such as changes in behaviour, were also assessed.

The purpose of the analytical part of this study was to verify proper dosing of the test item.

As there was no mortality in the test item treatment group in the contact test, the contact LD₅₀ (Lethal Dose causing 50 % mortality) (48 h) values were estimated to be > 600 µg product/bumblebee. The contact NOED (No Observed Effect Dose) (48 h) value was calculated to be ≥ 600 µg product/bumblebee.

As there was no mortality in the test item treatment group in the oral test, the oral LD₅₀, (48 h) values were estimated to be > 523.8 µg product/bumblebee. The oral NOED (48 h) value was calculated to be ≥ 523.8 µg product/bumblebee.

Materials and Methods

Test Item:	GLOB2106cF, Batch No.: BRN 3891, content: Propamocarb-HCl: Declared: 450 g/L, Pre Storage: 448.0 g/L (equivalent to 99.56 % of the declared content), Post Accelerated Storage: 449.4 g/L (equivalent to 99.86 % of the declared content), Mandipropamid: Declared: 75 g/L, Pre Storage: 76.21 g/L (equivalent to 101.6 % of the declared content), Post Accelerated Storage: 74.60 g/L (equivalent to 99.47 % of the declared content), according to certificate of analysis
Test Species:	Bumblebee (<i>Bombus terrestris</i> L.); female worker bumblebees; obtained from a commercial bumblebee breeding company (Koppert Deutschland GmbH, Zeppelinstr. 32, D-47638 Straelen, Germany).

Test Design:

Acute Contact Limit Test:

Duration: 48 h;

replicates: 50 for the test item and 50 for the water control treatment group, 30 for the reference item treatment group, each consisting of 1 bumblebee per cage per treatment; assessment of mortality and behavioural abnormalities: after 4 (± 0.5); 24 (± 2) and 48 (± 2) hours;

reference item: dimethoate 417 g/L (analytical).

Analytical verification of the concentration of the active ingredients Mandipropamid and Propamocarb-HCl, based on its parent

Propamocarb, of the test item GLOB2106cF in the contact application solution of the single concentration.

Acute Oral Limit Test:

Duration: 48 h;

replicates: 35 per each dose of the test item treatment group (five doses), 35 for the water control and 35 for the reference item treatment group, each consisting of 1 bumblebee per cage per treatment (individual bumblebees which did not take up at least 80 % of the mean food uptake per treatment group were excluded from the evaluation; assessment of mortality and behavioural abnormalities: after 4 (± 0.5); 24 (± 2) and 48 (± 2) hours;

reference item: dimethoate 417 g/L (analytical).

Analytical verification of the concentration of the active ingredients Mandipropamid and Propamocarb-HCl, based on its parent Propamocarb, of the test item GLOB2106cF in the oral feeding solutions of the highest and the lowest concentrations.

Test Item Dose Levels:

Contact Limit Test (nominal):

600 μg product/bumblebee

Oral Dose Response Test (target):

600, 300, 150, 75 and 37.5 μg product/bumblebee

Oral Dose Response Test achieved (mean consumption):

523.8, 327.4, 166.1, 87.8 and 44.7 μg product/bumblebee

Analytical Results of the Contact Test:

Contact application solution (600 µg product/bumblebee):	
Propamocarb-HCl: A-sample	131 %
Propamocarb-HCl: A-sample (re-analysis)	99 %
Propamocarb-HCl: B-sample	103 %
Mandipropamid: A-sample	85 %
Mandipropamid: A-sample (re-analysis)	89 %
Mandipropamid: B-sample	83 %

Analytical Results of the Oral Test:

Oral feeding solution (37.5 µg product/bumblebee):	
Propamocarb-HCl:	86 %
Mandipropamid:	88 %
Oral feeding solution (600 µg product/bumblebee):	
Propamocarb-HCl:	88 %
Mandipropamid:	94 %

Test Conditions:

Contact Test:

Acclimatisation:	Temperature: 24 - 26 °C Relative Humidity: 56 – 60 %
Exposure:	Temperature: 24 – 26 °C Relative Humidity: 56 – 62 %

Oral Test:

Acclimatisation:	Temperature: 24 - 26 °C Relative Humidity: 56 – 62 %
Exposure:	Temperature: 23 – 26 °C Relative Humidity: 56 – 62 %

Photoperiod:

Photoperiod: 24 h darkness (except handling procedures, including treatment and observations).

Study Validity:

This study met the OECD 246 (2017) and OECD 247 (2017) validity criteria as the control mortality in both the oral and contact tests was $\leq 10\%$ and the mortality due to the reference item (dimethoate) was $\geq 50\%$ at test end.

Statistics:

As the test item treatment groups in the contact and oral tests did not show any mortality, the LD50 values could not be calculated by statistical evaluation. The contact and oral LD50 values were considered to be higher than the highest dose rates tested.

The contact NOED values were determined using Fisher's Exact Binomial Test (one-sided greater, $\alpha = 0.05$). The oral NOED values were determined using Fisher's Exact Binomial Test with Bonferroni Correction (one-sided greater, $\alpha = 0.05$)

The software used to perform the statistical analysis was ToxRat Professional, Version 3.3.0, ® ToxRat Solutions GmbH.

Results and Discussion

Experimental dates: 06 September 2022 – 11 January 2023

Biological Results:

Contact Test:

In the contact test a droplet of 5 µL* containing the targeted dose level of 600 µg product/bumblebee was applied on the dorsal thorax of each exposed bumblebee. At the end of the contact toxicity test (48 hours after application), no mortality occurred in the test item treatment group. No mortality occurred also in the water control group (tap water containing 0.1 % v/v Triton X-100).

No test item related behavioural effects were observed at any time in the contact test.

The contact target dose level of the reference item of 10 µg dimethoate/bumblebee was applied on the dorsal thorax of each exposed bumblebee. The mortality in the reference item treatment group was 86.7 % (48 hours after application).

The contact test is considered valid as the water control mortality (tap water containing 0.1 % v/v Triton X-100) was ≤ 10 % and the reference item mortality (dimethoate) was ≥ 50 %.

*A 5 µL droplet was chosen in deviation to the guideline recommendation of 2 µL, since a higher volume ensures a more reliable dispersion of the test item; ibacon experience has proven that higher volumes are suitable and no adverse effects on the outcome of the study are to be expected; [according to internal ibacon experiments 2016 and 2022].

Oral Test:

In the oral test, the targeted dose levels of 600, 300, 150, 75 and 37.5 µg product/bumblebee would have been achieved if an exact amount of 40 mg treated feeding solution had been consumed by each exposed bumblebee. This was not the case and the actual food uptake per bumblebee in the different treatment groups varied between 0 and 68 mg. Therefore, bumblebees which did not consume at least 80 % of the mean food uptake were excluded from the derivation of the end points, as well as from the calculation of the actual mean oral doses in the test and reference item treatment groups. This was done to avoid potentially overestimating the final endpoints.

The actual mean consumed oral doses of the test item were 523.8, 327.4, 166.1, 87.8 and 44.7 µg product/bumblebee. There was no mortality in any of the test item treatment groups at test end (48 hours after application). For the 523.8, 327.4, 166.1, 87.8 and 44.7 µg product/bumblebee test item treatment groups, 13, 17, 17, 21 and 28 bumblebees respectively were considered for the evaluation (≥ 80 % of the mean food uptake). There was no mortality in the test item treatment group at test end (48 hours after application). One affected bumblebee was observed in the 166.1 µg product/bumblebee test item treatment group 48 hours after dosing.

For the water control group, 33 bumblebees were considered for the evaluation. 3.0 % mortality occurred in the water control group (50 % w/v aqueous sucrose solution).

Similarly, the reference item targeted dose level of 4.0 µg dimethoate/bumblebee would have been achieved if exactly 40 mg treated feeding solution had been consumed by each bumblebee. Considering bumblebees consuming a food uptake of at least 80 % of the mean food uptake, the mean consumption corresponded to an actual mean oral dose of 4.3 µg dimethoate/bumblebee. For the reference item treatment group, 23 bumblebees were considered for the evaluation. Under this condition, the mortality in the reference item treatment group was 100.0 % 24 hours after application.

The oral test is considered valid as the water control (50 % w/v sucrose solution) mortality was ≤ 10 % and the reference item (dimethoate) mortality was ≥ 50 %.

Toxicity to Bumblebees; Laboratory Tests

Test Item	GLOB2106cF	
Test Species	<i>Bombus terrestris</i> L.	
Exposure	Contact (tap water containing 0.1 % v/v Triton X-100)	Oral ¹ (50 % w/v sucrose solution)

Target dose rate [µg product/bumblebee]	600		600, 300, 150, 75 and 37.5	
Actual achieved dose rate [µg product/bumblebee]	n.a.		523.8, 327.4, 166.1, 87.8 and 44.7	
Test Duration:	24 h	48 h	24 h	48 h
LD ₅₀ [µg product/bumblebee] ^{2,3}	> 600	> 600	> 523.8	> 523.8
NOED [µg product/bumblebee] ^{2,4}	≥ 600	≥ 600	≥ 523.8	≥ 523.8

¹ For the 523.8, 327.4, 166.1, 87.8 and 44.7 µg product/bumblebee, 13, 17, 17, 21 and 28 bumblebees were considered for the evaluation, respectively.

² Results obtained from test item treated groups were compared to those obtained from the water control group.

³ As the test item treatment groups in the contact and oral tests did not show any mortality, the LD₅₀ values could not be calculated by statistical evaluation. The contact and oral LD₅₀ values were considered to be higher than the highest dose rates tested.

⁴ The contact NOED values were determined using Fisher's Exact Binomial Test (one-sided greater, $\alpha = 0.05$). The oral NOED values were determined using Fisher's Exact Binomial Test with Bonferroni Correction (one-sided greater, $\alpha = 0.05$).

n.a.= not applicable

Analytical Results:

The analytical recovery rates of the active substances Propamocarb-HCl and Mandipropamid in the testing solutions were as follows:

Concentration/bumblebee	Nominal concentration in the solution	Recovery of the nominal value in the solution
<u>Contact Test:</u> Application solution (600 µg product/bumblebee*)	120 g product/L application solution	Propamocarb-HCl: A-sample 131 % A-sample (re-analysis) 99 % B-sample 103 % Mandipropamid: A-sample 85 % A-sample (re-analysis) 89 % B-sample 83 %
<u>Oral Test:</u> Feeding solution (600 µg product/bumblebee*)	15 g product/kg feeding solution	Propamocarb-HCl: 86 % Mandipropamid: 88 %
<u>Oral Test:</u> Feeding solution (37.5 µg product/bumblebee*)	0.938 g product/kg feeding solution	Propamocarb-HCl: 88 % Mandipropamid: 94 %

* The dose levels of the test item were based on the product without taking into consideration active substance content.

Conclusions

The toxicity of GLOB2106cF to bumblebees was tested in an acute contact and oral toxicity test. As there was no mortality in the test item treatment group in the contact test, the contact LD₅₀ (Lethal Dose causing 50 % mortality) (48 h) values were estimated to be > 600 µg product/bumblebee. The contact NOED (No Observed Effect Dose) (48 h) value was calculated to be ≥ 600 µg product/bumblebee. As there was no mortality in the test item treatment group in the oral test, the oral LD₅₀, (48 h) values were estimated to be > 523.8 µg product/bumblebee. The oral NOED (48 h) value was calculated to be ≥ 523.8 µg product/bumblebee.

A 2.3.1.2 KCP 10.3.1.2. Chronic toxicity to bees

Comments of zRMS:	<p>The study was accepted. The validity criteria were met:</p> <ul style="list-style-type: none"> • mortality in reference item group was being 100 % at the end of the test (10 d); • mortality in the control group was 3.3% at the end of the test (after 10 days of exposure) below the threshold of 15 %. <p>No deviation was noted.</p> <p>The following endpoints were calculated: LC₅₀ = 4.724 g formulation/kg food NOEC = 1.562 g formulation/kg food</p> <p>LDD₅₀ = 76.78 µg formulation/bee/d NOEDD = 30.82 µg formulation/bee/day</p>
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Reference:	KCP 10.3.1.2
Report	Chronic oral effects of GLOB2106cF to adult worker honeybees (<i>Apis mellifera</i> L.) in a 10-day feeding laboratory test, Venturi S., 2023, BT262/22
Guideline(s):	Yes, OECD 245
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The objective of this study was to assess the chronic oral effects of the test item GLOB2106cF on adult worker honeybees *Apis mellifera* L. under laboratory conditions over a period of 10 days.

The study was carried out with 5 test item concentrations to establish the no observed effect concentration (NOEC), the no observed effect dietary dose (NOEDD), the lethal concentrations (LC_{10,20,50}) and lethal dietary doses (LDD_{10,20,50}) after 10 days of exposure.

The purpose of the analytical phase of this study was to verify the test item content in the feeding solutions at the highest and lowest concentrations, prepared and sampled on Day 0 of the test.

The test item **GLOB2106cF** had significant lethal effects on adult honeybees after being administered for 10 consecutive days starting from the concentration of 3125.00 mg/kg, corresponding to the effective dose of 47.99 µg/bee/day. The NOEC and the NOEDD were determined as 1562.50 mg/kg and 30.82

µg/bee/day, respectively. In terms of concentration, the LC₅₀ value was calculated as 4723.92 mg/kg. In terms of dose related to the consumptions, the LDD₅₀ was calculated as 76.87 µg/bee/day.

Materials and Methods

Test item

Name: GLOB2106cF
 Batch: BRN 3891
 Active substances: Mandipropamid: 76.21 g/L
 Propamocarb-HCl: 448.0 g/L

Test system

Species: *Apis mellifera* L.
 Age: Adult worker bees (maximum 2 days old)
 Source: Healthy colonies (hives no. 2, 5 and 6) maintained at BioTecnologie BT S.r.l.
 Acclimation: 24 hours
 Diet: 50% (w/v) aqueous sucrose solution

Experimental conditions

Temperature: min 31.0°C – max 35.2°C (average measured: 34.2°C)
 Humidity: min 41.5% – max 70.4% (average measured: 62.0%)
 Photoperiod: 24 h darkness (except during observations)

Study design

The 10-day chronic oral feeding test in the laboratory was performed as a dose-response test: the test item was diluted in 50% (w/v) aqueous sucrose solution (which is prepared every 4 days at the latest), to obtain the feeding solutions. The feeding solutions were prepared every day of the test. The reference item Dimethoate was tested at 1.00 mg a.s./kg diet (solution was prepared once and used daily). A control with untreated sucrose solution was run in parallel.

Trial layout of the 10-day Chronic Oral Toxicity Test with GLOB2106cF

Groups	Concentrations [mg prod./kg f.s.]	Doses ¹ [µg prod./bee/day]	Number of bees/cage	Number of cages	ID Code	
					From	To
Negative control	-	-	10	3	CTRLa	CTRLc
Test item (T1)	1562.5	31.3	10	3	T1a	T1c
Test item (T2)	3125	62.5	10	3	T2a	T2c
Test item (T3)	6250	125	10	3	T3a	T3c
Test item (T4)	12500	250	10	3	T4a	T4c
Test item (T5)	25000	500	10	3	T5a	T5c
Reference item	1.00	0.03	10	3	Ra	Rc
Evaporation	-	-	0	3	EVAa	EVAc

f.s. = feeding solution. ¹Theoretical doses; the effective doses were calculated based on actual food consumption.

Observations

Mortality and sub-lethal effects were recorded every 24 ± 2 h, from Day 1 to Day 10 of the test. The amount of feeding solution consumed was determined by weighing separate feeders at the start and at the end of each 24-h period of feeding.

Statistics

The LDD_x and LC_x values were both calculated with Weibull analysis using linear max. likelihood regression. The Step-down Cochran-Armitage Test Procedure (one-sided greater, α = 0.05) was used to determine the NOEDD/NOEC values. The software ToxRatPro 3.3.0 was used for the statistical analysis.

Results and Discussion

Biological phase: from 06th to 17th September 2022

Analytical phase: from 19th September 2022 to 24th February 2023

According to the OECD Guideline 245 (2017), the test is considered valid because:

- the average mortality across replicates of the control was 3.3% at the end of the test (10 days after exposure)
- the average mortality in the reference item group was 100% at the end of the test (10 days after exposure).

The results at the end of the test period are summarised in the following tables.

Summarized mean food uptake and cumulative mortality at the end of the test

Groups	Concentrations [mg prod./kg f.s.]	Mean daily uptake of ¹		Mean Mortality		
		Feeding solution [mg/bee/day]	Test item [µg/bee/day]	%M	%CM	S ²
Control	-	23.49	n/a	3.3	n/a	n/a
T1	1562.5	19.73	30.824	6.7	3.4	-
T2	3125	15.36	47.991	16.7	13.8	+
T3	6250	17.21	107.554	83.3	82.8	+
T4	12500	9.59	119.832	100.0	100.0	+
T5	25000	6.42	160.588	100.0	100.0	+
R	1.00	13.59	0.014	100.0	100.0	n/a

f.s. = feeding solution; %M = Mean Mortality; %CM = Corrected Mean Mortality; S = statistical significance; "+" = significant; "-" = not-significant. ¹Adjusted for evaporation from the feeders.

²Step-down Cochran-Armitage Test Procedure ($\alpha = 0.05$, one-sided greater).

Cumulative mean mortality for each day of the test

Group	Concentration [mg/kg f.s.]	Cumulative Mean Mortality [%]									
		D1	D2	D3	D4	D5	D6	D7	D8	D9	D10
Negative control	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.3	3.3
T1	1562.50	0.0	0.0	0.0	3.3	3.3	3.3	3.3	3.3	6.7	6.7
T2	3125.00	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.7	6.7	16.7
T3	6250.00	0.0	0.0	3.3	3.3	3.3	13.3	30.0	56.7	73.3	83.3
T4	12500.00	0.0	3.3	3.3	3.3	30.0	33.3	80.0	86.7	100.0	100.0
T5	25000.00	0.0	30.0	46.7	86.7	100.0	100.0	100.0	100.0	100.0	100.0
R	1.00	0.0	0.0	26.7	63.3	93.3	100.0	100.0	100.0	100.0	100.0

The test item **GLOB2106cF** had significant lethal effects on adult honeybees after being administered for 10 consecutive days starting from the concentration of 3125.00 mg/kg, corresponding to the effective dose of 47.99 µg/bee/day. The NOEC and the NOEDD were determined as 1562.50 mg/kg and 30.82 µg/bee/day, respectively. In terms of concentration, the LC₅₀ value was calculated as 4723.92 mg/kg. In terms of dose related to the consumptions, the LDD₅₀ was calculated as 76.87 µg/bee/day.

A summary of the results is provided in the table below.

The content of active substances, analysed in the highest and lowest test item concentrations of the feeding solutions sampled on Day 0 of the test, was determined to be within 20% of the nominal value, therefore the endpoints were calculated with the nominal concentrations and doses.

10-day Chronic Oral Toxicity of GLOB2106cF to young honey bees in the laboratory test

		GLOB2106cF
Critical dose [µg/bee/day]	LDD ₁₀	44.49 (31.44-54.33)
	LDD ₂₀	55.32 (42.45-64.73)
	LDD ₅₀	76.87 (65.98-85.38)
	NOEDD	30.82
Critical concentration [mg/kg diet]	LC ₁₀	2640.05 (1729.02-3264.59)
	LC ₂₀	3328.67 (2459.31-3915.92)
	LC ₅₀	4723.92 (4046.45-5333.43)
	NOEC	1562.5

95% confidence limits are in brackets.

The reference item dimethoate tested at 1.0 mg a.s./kg diet (corresponding to 0.014 µg/bee/day) caused 100% mortality by Day 6. The test fulfilled the validity criteria of OECD 245 (2017).

A summary of the results of the analytical verification of the active substances content in the test samples is reported in the following tables.

Results of the analysis of Mandipropamid in the feeding solutions (T1) sampled on D0

Code	Nominal conc. [g/kg]		Sample Weight [g]	Final Volume [mL]	Dilution Factor	Measured Conc.		Recovery [%]
	Test item	A.s.				[µg/L]	[g/kg]	
T1D0 001	1.56	0.110	1.00069	10	500.00	19.2214	0.0960	87.24
T1D0 002						19.5650	0.0978	88.80
						Mean	0.10	88.02
						SD	0.001	1.10
						RSD%	1.25	1.25

Results of the analysis of Mandipropamid in the feeding solutions (T5) sampled on D0

Code	Nominal conc. [g/kg]		Sample Weight [g]	Final Volume [mL]	Dilution Factor	Measured Conc.		Recovery [%]
	Test item	A.s.				[µg/L]	[g/kg]	
T5D0 001	25.0	1.76	1.00115	10	2000.00	81.7558	1.6332	92.57
T5D0 002						82.0174	1.6385	92.87
						Mean	1.64	92.72
						SD	0.004	0.21
						RSD%	0.23	0.23

Results of the analysis of Propamocarb-HCl in the feeding solutions (T1) sampled on D0

Code	Nominal Conc. [g/kg]		Sample Weight [g]	Final Volume [mL]	Dilution Factor	Measured Conc.			Recovery [%]
	Test item	A.S.				A.S. [µg/L] ¹	Prop-HCl [µg/L] ²	A.S. [g/kg]	
T1D0 001	1.56	0.647	1.00509	10	500.00	101.6602	121.3484	0.6037	93.28
T1D0 002						101.6030	121.2801	0.6033	93.23
						Mean	0.60	93.25	
						SD	0.0002	0.04	

¹A.S. content quantified as propamocarb.

²A.S. content converted in propamocarb-HCl (conversion factor = 1.21).

RSD%	0.04	0.04
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Results of the analysis of Propamocarb-HCl in the feeding solutions (T5) sampled on D0

Code	Nominal Conc. [g/kg]		Sample Weight [g]	Final Volume [mL]	Dilution Factor	Measured Conc.			Recovery [%]
	Test item	A.S.				A.S. [$\mu\text{g/L}$] ¹	Prop-HCl [$\mu\text{g/L}$] ²	A.S. [g/kg]	
T5D0 001	25.0	10.37	1.00044	10	2000.00	376.4592	449.3667	8.9834	86.62
T5D0 002						384.9097	459.4538	9.1850	88.56
						Mean	9.08	87.59	
						SD	0.14	1.37	
						RSD%	1.57	1.57	

¹A.S. content quantified as propamocarb.

²A.S. content converted in propamocarb-HCl (conversion factor = 1.21).

The analytical results demonstrate that the active substances content in the highest and lowest concentrated feeding solutions sampled on D0 was in the range of $\pm 20\%$ of nominal concentrations.

So, it was demonstrated that the procedure for the preparation of the solutions was correct and consequently that the bees were treated with the corresponding dose of test item. Therefore, the endpoints were calculated based on the nominal content of test item.

Conclusions

The effects of **GLOB2106cF** on adult worker honeybees (*Apis mellifera* L.) were assessed in a 10-day oral chronic test. The relevant endpoints are summarized below.

10-day Chronic Oral Toxicity of GLOB2106cF to young honey bees in the laboratory test

		GLOB2106cF
Critical dose [$\mu\text{g}/\text{bee}/\text{day}$]	LDD₁₀	44.49 (31.44-54.33)
	LDD₂₀	55.32 (42.45-64.73)
	LDD₅₀	76.87 (65.98-85.38)
	NOEDD	30.82
Critical concentration [mg/kg diet]	LC₁₀	2640.05 (1729.02-3264.59)
	LC₂₀	3328.67 (2459.31-3915.92)
	LC₅₀	4723.92 (4046.45-5333.43)
	NOEC	1562.50

95% confidence limits are in brackets.

The reference item dimethoate tested at 1.0 mg a.s./kg diet (corresponding to 0.014 $\mu\text{g}/\text{bee}/\text{day}$) caused 100% mortality by day 6. The test fulfilled the validity criteria of OECD 245 (2017).

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

Comments of zRMS:	<p>The study was accepted. The validity criteria were met:</p> <ul style="list-style-type: none"> larvae mortality in the control was below 15%; observed 14.6%; larvae mortality in the reference item mortality was $\geq 50\%$; observed 93.8%; <p>The following deviations were noted:</p> <ul style="list-style-type: none"> the mortality assessment on D7 was not carried out for the following
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	<p>reason: on D7 no operation is required (there are no treatments and there is no feeding of the larvae) and performing a mortality assessment would have involved opening the dryer with a consequent decrease of temperature and humidity. Therefore, to avoid stress to the larvae (in a very delicate stage such as the transition to pre-pupa) the assessment was performed directly on D8. This deviation did not affect the final conclusion and results;</p> <ul style="list-style-type: none">• short term deviations from the specified range in temperature and humidity (less than 2 h/d) were observed. This deviation did not affect the final conclusion and results. <p>The following endpoints were calculated: 22-d NOED = 200 µg formulation/larva</p> <p>On D22 the ED-EC₅₀ were evaluated to be greater than the maximum tested dose/concentration, equivalent to 400.00 µg test item/larva and 2597.40 mg test item/kg diet, respectively. No reliable LC-EC_{10,20,50} LD-ED_{10,20,50} were calculated.</p>
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Reference:	KCP 10.3.1.3
Report	Effects of GLOB2106cF on honeybees (<i>Apis mellifera</i> L.) 22-day larval toxicity test with repeated exposure, Colli M., 2023, BT126/22
Guideline(s):	Yes, OECD 239
Deviations:	Deviation No. 1 issued on 09th September 2022 Description: - 03rd August 2022 (day 3 of the test - during the treatments) the temperature was lower than 34°C for about 4 hours (minimum value 32.7°C), and the humidity was lower than 90% for about 2 hours (minimum value 76.8%) this was due to the operations carried out for the selection of the larvae for each treatment plate. - 04 th August 2022, (day 4 of the test) the temperature was lower than 34°C for about 2 hours (minimum value 33.0°C), this occurred during the assessment and treatment operations. - 05 th August 2022, (day 5 of the test) the temperature was lower than 34°C for about 2 hours (minimum value 32.7°C), this occurred during the assessment and treatment operations. Impact on the Study: None, the validity criteria were met, and the deviations are not considered to have affected the outcome of the study.
GLP:	Yes
Acceptability:	Yes

Executive summary

The objective of this study was to assess the effects on adult emergence of honeybees *Apis mellifera ligustica* L., following a repeated exposure of larvae to the test item GLOB2106cF. The study was carried out with five test item concentrations in order to establish the no observed effect concentration/dose (NOEC/NOED) and the EC_{10,20,50}/ ED_{10,20,50}, on day 22 (D22) and additionally on day (D8), where possible.

The purpose of the analytical phase of this study was to verify the concentrations of the test item in the stock solutions (at the lowest and highest concentration) used to treat the diet administered to the larvae prepared on D3. Moreover, the water used to treat the control was analysed.

The content of active substances was determined to be within 20% of the nominal values for all tested samples, therefore the endpoints were calculated based on nominal concentrations and doses. The control was also analysed, and no contamination was detected (<LOD).

Regarding the effects on larvae on D8, the test item GLOB2106cF did not cause statistically significant mortality up to the highest tested dose. Therefore, the NOED for larvae on D8 was determined to be $\geq 400.0 \mu\text{g}$ test item/larva equivalent to a NOEC of 2597.40 mg test item/kg diet.

Regarding the effects on adult emergence on D22, the test item GLOB2106cF caused a statistically significant mortality at the highest tested dose. Thus, the NOED and the NOEC for adult emergence was determined to be 200.00 μg test item/larva and 1298.70 mg test item/kg diet, respectively.

Materials and Methods

Test item

Name: GLOB2106cF
Batch: BRN 3891
Active substances: Mandipropamid: 76.21 g/L
Propamocarb-HCl: 448.0 g/L

Test system

Species: *Apis mellifera ligustica*
Age: 3 days old bee larvae (D3)
Source: Healthy colony maintained at BioTecnologie BT S.r.l. (colonies no. 6, 8, 15)
Diet: Dependent on developmental stage: Diet A, Diet B and Diet C
- Diet A (D1): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 2% weight of yeast extract, 12% weight of glucose and 12% weight of fructose.
- Diet B (D3): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 3% weight of yeast extract, 15% weight of glucose and 15% weight of fructose.
- Diet C (from D4 to D6): 50% weight of fresh royal jelly + 50% weight of an aqueous solution containing 4% weight of yeast extract, 18% weight of glucose and 18% weight of fructose.

Experimental conditions

Temperature: 32.0 – 34.7°C (average measured during the test: 34.3°C)
Humidity: from D1 to D8 = 76.8 – 94.1% (average measured during the test: 93.0%)
from D8 to D15 = 81.8 – 85.1% (average measured during the test: 82.5%)
from D15 to D22 = 53.5 – 64.3% (average measured during the test: 63.1%)
Photoperiod: 24 h darkness (except during observations)

Study design

The 22-day larval toxicity test with repeated exposure in the laboratory was performed as dose-response test: the test item was dissolved in water and then in the larval food (aqueous sugar solution mixed with royal jelly) and administered daily to the larvae from day 3 (D3) to 6 (D6) of the test.

The stock solutions and the treated diet were prepared freshly each day of administration.

The reference item Dimethoate was tested at a cumulative dose of 7.39 μg /larva. An untreated control was run in parallel with the royal jelly-based diet.

For each test item treatment group, for the control group and the reference item treatment group, 3 replicates of 12 larvae each were set up.

The cumulative doses and the concentrations of test item and reference item used for the test are shown in the tables below.

Trial layout - treatments expressed as doses

Groups	Cumulative doses		
	[µg test item/larva]	[µg Mandipropamid /larva]	[µg Propamocarb-HCl/larva]
Water control	0	0	0
Test item (T1)	25.00	1.764	10.371
Test item (T2)	50.00	3.529	20.743
Test item (T3)	100.00	7.057	41.485
Test item (T4)	200.00	14.114	82.971
Test item (T5)	400.00	28.229	165.941
Reference item	-	7.39 Dimethoate	

Trial layout - treatments expressed as concentrations

Groups	Concentrations		
	[mg test item/kg diet]	[mg Mandipropamid/kg diet]	[mg Propamocarb-HCl/kg diet]
Water control	0	0	0
Test item (T1)	162.338	11.456	67.346
Test item (T2)	324.675	22.913	134.693
Test item (T3)	649.351	45.826	269.385
Test item (T4)	1298.701	91.651	538.770
Test item (T5)	2597.403	183.302	1077.541
Reference item	-	Dimethoate: 48.0	

Observations

Assessments of mortality and any developmental/behavioral abnormality were performed daily from D4 to D8 (except on D7) and on D15 and on D22.

Pupal mortality and the emergence rate of adults were also assessed on D22.

Statistics

The Software Tox Rat Pro 3.3.0 was used to perform the statistics. To evaluate the statistical significance of the D8 and D22 data and the NOED/NOEC, the Chi² 2x2 Table Test with Bonferroni Correction test was applied. ED_x for emergence at 22 days were calculated using Weibull analysis using linear max. likelihood regression but no reliable data were found.

Deviation from the guidance document

The mortality assessment on D7 was not carried out for the following reason: on D7 no operation is required (there are no treatments and there is no feeding of the larvae) and performing a mortality assessment would have involved opening the dryer with a consequent decrease of temperature and humidity. Therefore, to avoid stress to the larvae (in a very delicate stage such as the transition to pre-pupa) the assessment was performed directly on D8.

Results and Discussion

Experimental period: 3rd August 2022 to 24th February 2023 (including the analytical phase)

Validity criteria:

- in the control plate(s) the cumulative larval mortality from D3 to D8 is ≤ 15% across all replicates (actual value 11.11%);
- in the control plate(s) the adult emergence rate on D22 is ≥ 70% across all replicates (actual value 83.33%);

- in the reference item group (dimethoate) the larval mortality is $\geq 50\%$ on D8 across all replicates (actual value 100%).

The results at the end of the test period are summarised in the following tables.

In addition, the results for the chemical analysis of the test item stock solutions are reported.

The qualitative observations carried out during the test (e.g. larval and pupal behaviour and morphological differences) did not show abnormalities in the surviving treated bees.

The following tables show the mean mortalities on D8 and D22, the pupal mortality and the effects on adult emergence on D8 and D22.

Mortality (M) and Corrected Mortality (CM) of larvae (on D8)

Treatment	Cumulative dose [µg test item/larva]	Concentration [mg test item/kg diet]	Larvae mortality on D8		
			M - Mean [%]	CM - Mean [%]	Sign.
Water control	0.00	0.00	11.11	n.a.	n.a.
Test item (T1)	25.00	162.338	8.33	0.00	-
Test item (T2)	50.00	324.675	11.11	0.00	-
Test item (T3)	100.00	649.351	8.33	0.00	-
Test item (T4)	200.00	1298.701	11.11	0.00	-
Test item (T5)	400.00	2597.403	22.22	12.50	-

n.a. = not applicable

+ : significant; - : non-significant (Chi² 2x2 Table test with Bonferroni Correction- $\alpha = 0.05$, one-sided greater)

*: negative values are replaced with 0.

Until D8 the test item did not cause statistically significant mortality of the treated larvae at all the tested dose and the NOED at D8 was estimated to be ≥ 400.0 µg test item/larva.

Pupal Mortality

Treatment	Cumulative dose [µg test item/larva]	Concentration [mg test item/kg diet]	Pupal mortality from D8 to D15*	Pupal mortality from D8 to D22**
			Mean [%]	Mean [%]
Water control	0.00	0.00	0.00	6.36
Test item (T1)	25.00	162.338	8.59	11.92
Test item (T2)	50.00	324.675	3.03	9.70
Test item (T3)	100.00	649.351	5.81	21.62
Test item (T4)	200.00	1298.701	6.36	18.79
Test item (T5)	400.00	2597.403	14.44	24.81

*calculated as a percentage comparing the number of dead pupae from D8 to D15 with the number of alive pupae on D8

**calculated as a percentage comparing the number of dead pupae from D8 to D22 with the number of alive pupae on D8

Total mortality (M) and corrected mortality (CM) from D3 to D22 and emergence (E) on D22

Treatment	Cumulative dose [µg test item/larva]	Concentration [mg test item/kg diet]	Mortality (larvae + pupae) on D22			Adult emergence on D22	
			M - Mean [%]	CM - Mean [%]	Sign.	E - Mean [%]	Sign.
Water control	0.00	0.00	16.67	n.a.	n.a.	83.33	n.a.
Test item (T1)	25.00	162.338	19.44	3.33	-	80.56	-
Test item (T2)	50.00	324.675	19.44	3.33	-	80.56	-
Test item (T3)	100.00	649.351	27.78	13.33	-	72.22	-
Test item (T4)	200.00	1298.701	27.78	13.33	-	72.22	-
Test item (T5)	400.00	2597.403	41.67	30.00	+	58.33	+

n.a. = not applicable

+ : significant; - : non-significant (Chi² 2x2 Table test with Bonferroni Correction- $\alpha = 0.05$, one-sided greater)

The adult emergence on D22 was statistically significant reduced at the highest tested dose, so the NOED was 200.00 µg test item/larva at the end of the test.

Reference item - mean mortality

Treatment	Dose [µg a.s./larva]	Concentration [mg a.s./kg diet]	Mortality on D8 Mean [%]
Reference item	7.39	48.00	100.00

A summary of the results of the analytical verification of the active substances content in the test samples is reported in the following tables.

Results of the analysis of the Mandipropamid content in S1D3 and S5D3 samples

Code	Recovery [%]	Mean Recovery [%]	±SD	RSD [%]
S1D3-r001	109.27	111.13	2.63	2.36
S1D3-r002	112.98			
S5D3-r001	100.28	99.88	0.68	0.68
S5D3-r002	99.32			

SD = standard deviation
 RSD = relative standard deviation

Results of the analysis of the Propamocarb-HCl content in S1D3 and S5D3 samples

Code	Recovery [%]	Mean Recovery [%]	±SD	RSD [%]
S1D3-r001	96.20	96.19	0.01	0.01
S1D3-r002	96.19			
S5D3-r001	96.42	96.88	0.65	0.67
S5D3-r002	97.35			

SD = standard deviation
 RSD = relative standard deviation

The analytical results demonstrate that the GLOB2106cF content in the water solutions prepared on D3 at the highest and lowest concentration was in the range of ± 20% of nominal concentrations and consequently that the procedure for the preparation of the treated diet was correct.

Conclusions

The effects of the test item GLOB2106cF on the larval development and subsequent adult emergence of honeybees (*Apis mellifera* L.), were tested in a GLP compliant laboratory study. The validity criteria of the GD OECD No. 239 (2021) with regards to control larval mortality on D8, control adults' emergence on D22 and toxicity on the reference item were met. Thus, the study is valid. The content of active substances was analysed in the lowest and highest test item concentrations of the stock solutions (prepared on D3) used to treat the diets and was determined to be within 20% of the nominal values for all tested samples, therefore the endpoints were calculated based on nominal concentrations and doses. The control was also analysed, and no contamination was detected (<LOD). Regarding the effects on larvae on D8, the test item GLOB2106cF did not cause statistically significant mortality up to the highest tested dose. Therefore, the NOED for larvae on D8 was determined to be ≥ 400.0 µg test item/larva (≥ 28.229 µg Mandipropamid/larva and 165.941 µg Propamocarb-HCl/larva) equivalent to a NOEC of 2597.403 mg test item/kg diet (183.302 mg Mandipropamid/kg and 1077.541 mg Propamocarb-HCl/kg).

Regarding the effects on adult emergence on D22, the test item GLOB2106cF caused a statistically significant mortality at the highest tested dose. Thus, the NOED and the NOEC for adult emergence was determined to be 200.00 µg test item/larva (14.114 µg Mandipropamid/larva and 82.971 µg Propamocarb-HCl/larva) and 1298.701 mg test item/kg diet (91.651 mg Mandipropamid/kg and 538.770 mg Propamocarb-HCl/kg), respectively.

On D22 the ED-EC50 were evaluated to be greater than the maximum tested dose/concentration, equivalent to 400.00 µg test item/larva and 2597.40 mg test item/kg diet, respectively.

No reliable LC-EC_{10,20,50}/LD-ED_{10,20,50} were calculated.

A 2.3.1.4 KCP 10.3.1.4 Sub-lethal effects

No new studies submitted.

A 2.3.1.5 KCP 10.3.1.5 Cage and tunnel tests

No new studies submitted.

A 2.3.1.6 KCP 10.3.1.6 Field tests with honeybees

No new studies submitted.

A 2.3.2 KCP 10.3.2 Effects on arthropods other than bees

A 2.3.2.1 KCP 10.3.2.1 Using artificial substrates

No new studies submitted.

A 2.3.2.2 KCP 10.3.2.2 Extended laboratory tests

Comments of zRMS:	<p>The study was accepted. The validity criteria were met.</p> <p>No significant deviations were observed.</p> <p>The following endpoints for <i>Typhlodromus pyri</i> were derived: 7-day LR₅₀ > 6080 mL formulation/ha in 200 L water/ha; ER50 > 6080 mL formulation/ha in 200 L water/ha; NOER = 2027 mL formulation/L in 200 L water/ha.</p> <p>The endpoints were used for risk assessment.</p>
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Reference: KCP 10.3.2.2

Report GLOB2106cF: Effects on the predatory mite *Typhlodromus pyri* (Acari: Phytoseiidae), Extended laboratory study – Dose response test, Leopold J., 2023a, 169461062

Guideline(s): Yes, Blümel *et al.*, 2000 and Oomen, 1988

Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to determine the effect of GLOB2106cF in the laboratory on mortality of the predatory mite *Typhlodromus pyri* 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.

Under extended laboratory conditions the LR₅₀ of GLOB2106cF is estimated to be > 6080 mL product/ha in 200 L water/ha. The NOER (no observed effect rate) for mortality effects was 2027 mL product/ha and the LOER (lowest observed effect rate) for mortality effects was 6080 mL product/ha in 200 L water/ha.

Reproduction of *Typhlodromus pyri* was assessed in the control and in all dose rates. There were no effects on reproduction up to and including the highest test item application rate of 6080 mL product/ha. Therefore, the ER₅₀ was estimated to be greater than 6080 mL product/ha in 200 L water/ha. The NOER for reproduction effects was equal to or greater than 6080 mL product/ha and the LOER for reproduction effects was greater than 6080 mL product/ha in 200 L water/ha.

All validity criteria were met. The study is considered valid.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; authenticated content (pre storage): 448.0 g/L propamocarb HCl (equivalent to 99.56% of the declared content), 76.21 g/L mandipropamid (equivalent to 101.6% of the declared content).
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 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; additionally, reproduction capacity for all variants with less than 50 % corrected mortality.
Validity Criteria:	<ul style="list-style-type: none">- Control mortality should not exceed 20 % at day 7 after exposure.- Reference Item mortality should result in at least 50 % corrected mortality at day 7 after exposure.- Control reproduction should be ≥ 4 eggs per female for the second week.
Reference Item:	Danadim Progress (nominal: 400 g dimethoate/L).
Test Rates: *	Control, 75.1, 225, 676, 2027 and 6080 mL product/ha and reference item. The reference item was applied at an application rate of 40 mL Danadim Progress/ha. All treatments were applied in 200 L spray volume/ha. The spraying solutions were sprayed onto leaves via laboratory spraying equipment, which were then air dried.
Test Conditions:	Temperature: 24 - 25 °C; relative humidity: 66 - 70 %; photoperiod: 16 h light : 8 h dark; light intensity: 320 - 400 lux.
Statistics:	Standard procedures, mortality: Chi ² 2x2 Table Test with Bonferroni Correction, Fisher Exact Binomial Test (both one-sided greater, α = 0.05),

* The test item rates were originally calculated based on the relative density of 1.45 given by the MSDS, but were recalculated later with the density of 1.4257 g/mL given by the GLP CoA.

reproduction: Dunnett's t-Test (one-sided smaller, $\alpha = 0.05$).

Results and Discussion

The mean mortality of *Typhlodromus pyri* was 16.7 % in the control treatment. In the test item treatments, it ranged from 18.3 to 45.0 % (corresponding to 2.0 to 34 % corrected mortality). There was no statistically significant increase of mortality compared to the control up to and including the application rate of 2027 mL product/ha (Chi² 2x2 Table Test with Bonferroni Correction, one-sided greater, $\alpha = 0.05$).

The reference item applied at a rate of 40 mL Danadim Progress/ha produced a statistically significant mortality of 100.0 % (corrected mortality 100.0 %) after 7 days.

The mean reproduction of *T. pyri* was assessed in the control and in all test item application rates. In the control treatment, the mean reproduction was 5.1 eggs per female. In the test item treatments, 3.2 to 5.7 eggs per female were recorded, corresponding to a reduction of reproduction of -11.7 to 37.6 %. Reproduction was not statistically significantly reduced compared to the control up to and including the highest application rate of 6080 mL product/ha (Dunnett's t-Test, one-sided smaller, $\alpha = 0.05$).

The results are summarized in the table below.

Mortality and reproduction of *Typhlodromus pyri*

	Rate ¹⁾ [mL product/ha]	Mortality ²⁾ [%]	Mortality corr. ₃₎ [%]	Reproduction ⁴⁾ [eggs/female]	Effect on reproduction ⁵⁾ [%]
Control	0	16.7	--	5.1	--
GLOB2106cF	75.1	25.0 n.s.	10.0	3.5 n.s.	32.3
GLOB2106cF	225	20.0 n.s.	4.0	4.3 n.s.	15.7
GLOB2106cF	676	18.3 n.s.	2.0	5.7 n.s.	-11.7
GLOB2106cF	2027	20.0 n.s.	4.0	3.5 n.s.	31.6
GLOB2106cF	6080	45.0 *	34.0	3.2 n.s.	37.6
Endpoints ⁶⁾					
	test item [mL product/ha]	propamocarb HCl [g a.s./ha]	mandipropamid [g a.s./ha]		
Mortality: LR ₅₀ Value:	> 6080	> 2724	> 463		
NOER for Mortality:	2027	908	154		
LOER for Mortality:	6080	2724	463		
Reproduction: ER ₅₀ Value:	> 6080	> 2724	> 463		
NOER for Reproduction:	≥ 6080	≥ 2724	≥ 463		
LOER for Reproduction:	> 6080	> 2724	> 463		

1) Application rate in 200 L spray volume/ha

2) Mortality: after 7 days of exposure to spray residues on leaf surfaces

(Chi² 2x2 Table Test with Bonferroni Correction; one-sided greater; $\alpha = 0.05$; 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; one-sided smaller; $\alpha = 0.05$; n.s. = not significant)

5) Calculated on the exact raw data; negative values indicate better performance compared to the control

6) The LR₅₀ and ER₅₀ value could not be calculated as no mortality or effect on reproduction above 50% was noted.

Validity criteria:

The reference item applied at a rate of 40 mL Danadim Progress/ha produced a statistically significant corrected mortality of 100.0 % after 7 days (should be ≥ 50 % corrected mortality). The control mortality was 16.7 % after 7 days (should not exceed 20 %). The mean control reproduction rate was 5.1 eggs per female after 14 days (should be ≥ 4 eggs per female in the second week). All validity criteria were met.

Conclusions

Under extended laboratory conditions the LR₅₀ of GLOB2106cF is estimated to be > 6080 mL product/ha in 200 L water/ha. The NOER (no observed effect rate) for mortality effects was 2027 mL product/ha and the LOER (lowest observed effect rate) for mortality effects was 6080 mL product/ha in 200 L water/ha. Reproduction of *Typhlodromus pyri* was assessed in the control and in all dose rates. There were no effects on reproduction up to and including the highest test item application rate of 6080 mL product/ha. Therefore, the ER₅₀ was estimated to be greater than 6080 mL product/ha in 200 L water/ha. The NOER for reproduction effects was equal to or greater than 6080 mL product/ha and the LOER for reproduction effects was greater than 6080 mL product/ha in 200 L water/ha. All validity criteria were met. The study is considered valid.

Comments of zRMS:	<p>The study was accepted.</p> <p>The validity criteria were met. No significant deviations were observed.</p> <p>The following endpoints for <i>Aphidius rhopalosiphi</i> were derived: 48-h LR₅₀ > 6080 mL formulation/ha in 400 L water/ha; ER₅₀ > 6080 mL formulation/ha in 400 L water/ha; NOER ≥ 6080 mL formulation/L in 400 L water/ha.</p> <p>The endpoints were used for risk assessment.</p>
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Reference:	KCP 10.3.2.2
Report	GLOB2106cF: Effects on the parasitoid <i>Aphidius rhopalosiphi</i> (Hymenoptera, Braconidae), Extended laboratory study – Dose response test, Leopold J., 2022, 169461002
Guideline(s):	Yes, IOBC (Mead-Briggs <i>et al.</i> , 2010)
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to determine the effect of GLOB2106cF in the laboratory on the parasitoid *Aphidius rhopalosiphi* via contact on treated plant surfaces (exposure period), compared to a water treated control and to a reference item. Additionally, an assessment for sublethal effects on parasitisation activity of the female survivors (post-exposure period) was done.

Under extended laboratory conditions, the LR₅₀ of GLOB2106cF is estimated to be greater than 6080 mL product/ha in 400 L water/ha. For mortality effects, the NOER (No Observed Effect Rate) is equal to or higher than 6080 mL product/ha and the LOER (Lowest Observed Effect Rate) is higher than 6080 mL product/ha in 400 L water/ha.

Reproduction of *A. rhopalosiphi* was assessed in the control and in all test item treatments. There was no statistically significant effect on reproduction up to and including the highest test item rate of 6080 mL product/ha. The ER₅₀ value for reproduction is estimated to be greater than 6080 mL product/ha in 400 L water/ha. For reproduction effects, the NOER is equal to or greater than 6080 mL product/ha and the LOER is greater than 6080 mL product/ha in 400 L water/ha.

All validity criteria were met. The study is considered valid.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content of a.s.: 450 g/L propamocarb HCl, 75 g/L mandipropamid (nominal); 448.0 g/L propamocarb HCl (equivalent to 99.56% of the declared content), 76.21 g/L mandipropamid (equivalent to 101.6% of the declared content) (authenticated (pre storage)).
Test Species:	Parasitoid (<i>Aphidius rhopalosiphi</i>), adults not older than 48 hours; 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 5 female parasitoids. The parasitoids were exposed to dried residues on treated plant surfaces (barley 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 - 12 days before the numbers of aphid mummies that had developed were assessed.
Endpoints:	Mortality of exposed parasitoids; additionally, reproductive capacity for female survivors was assessed.
Validity Criteria:	<ul style="list-style-type: none">– Control mortality should be ≤ 10 %.– Reference item mortality should be > 50 % corrected mortality.– Mean reproduction rate of control treatment should be ≥ 5 mummies per surviving female. <p>No more than 2 surviving female parasitoids should be producing zero values in the control treatment.</p>
Reference Item:	Danadim Progress (nominal: 400 g dimethoate/L).
Test Rates:	Control, 75.1, 225, 676, 2027 and 6080 mL product/ha and reference item. The reference item was applied at an application rate of 10.0 mL Danadim Progress/ha. All treatments were applied in 400 L spray volume/ha. The spraying solutions were sprayed onto barley plants <i>via</i> laboratory spraying equipment, which were then air dried.
Test Conditions:	Temperature: 20 - 21 °C; relative humidity: 73 - 76 % (acclimatisation and exposure period), 70 - 83 % (post-exposure period, within the test units); photoperiod: 16 h light : 8 h dark; light intensity: 690 - 860 lux (acclimatisation and exposure period), 1150 - 1190 lux (parasitisation period), 8720 - 17860 lux (post-parasitisation period).

Results and Discussion

The mean mortality of *Aphidius rhopalosiphi* was 0.0 % in the control treatment and was between 0.0 and 6.7 % in the test item treatments. Mortality was not statistically significantly increased in the test item treatments compared to the control up to and including the highest application rate of 6080 mL product/ha (Fisher's Exact Binomial Test after Bonferroni-Holm, one-sided greater, $\alpha = 0.05$).

The reference item applied at a rate of 10.0 mL Danadim Progress/ha produced a statistically significant corrected mortality of 100.0 % after 48 hours (Fisher's Exact Binomial Test; one-sided greater, $\alpha = 0.05$). No behavioural abnormalities (affected and/or moribund parasitoids) were observed at any test item application rate after 24 and 48 hours.

During the initial 2.5 hours the mean settling rate of the parasitoids on the plants was between 57.3 and 88.0 % in the test item treatments. The settling rate was not statistically significantly reduced compared to the control at any test item treatment (Williams t-Test, one-sided smaller, $\alpha = 0.05$). In the control and reference item treatment, it was 72.0 and 60.7 %, respectively and for the reference item it was not

statistically significantly reduced compared to the control (Student t-Test, one-sided smaller, $\alpha = 0.05$). As the settling rate was above the threshold value of 30% for repellent effects, no further assessments of the settling behaviour were carried out.

Reproduction of *A. rhopalosiphi* was assessed in the control and at all test item treatments. The mean reproduction rate was 66.1 mummies per surviving female in the control and ranged from 55.6 to 68.2 mummies per female in the test item treatments, corresponding to reductions of 15.8 % to -3.2 %. Reproduction was not statistically significantly reduced compared to the control up to and including the highest application rate of 6080 mL product/ha (Multiple Sequentially-rejective U-Test after Bonferroni-Holm, one-sided smaller, $\alpha = 0.05$).

The results are summarized in the table below.

Mortality and parasitisation efficiency of *Aphidius rhopalosiphi*

	Rate ¹⁾ [mL product/ha]	Mortality ²⁾ [%]	Mortality corr. ³⁾ [%]	Reproduction ⁴⁾ [mummies/female]	Effect on reproduction ⁵⁾ [%]
Control	-	0.0	--	66.1	--
GLOB2106cF	75.1	3.3 n.s.	3.3	67.6 n.s.	-2.3
GLOB2106cF	225	0.0 n.s.	0.0	62.2 n.s.	5.9
GLOB2106cF	676	0.0 n.s.	0.0	68.2 n.s.	-3.2
GLOB2106cF	2027	3.3 n.s.	3.3	64.8 n.s.	1.9
GLOB2106cF	6080	6.7 n.s.	6.7	55.6 n.s.	15.8
Endpoints ⁶⁾					
	test item [mL product/ha]	propamocarb HCl [g a.s./ha]	mandipropamid [g a.s./ha]		
Mortality: LR ₅₀ Value	> 6080	>2724	> 463		
NOER for Mortality	≥ 6080	≥ 2724	≥ 463		
LOER for Mortality	> 6080	> 2724	> 463		
Reproduction: ER ₅₀ Value	> 6080	> 2724	> 463		
NOER for Reproduction	≥ 6080	≥ 2724	≥ 463		
LOER for Reproduction	> 6080	> 2724	> 463		

1) Application rate in 400 L spray volume/ha

2) Mortality: after 48 hours of exposure to spray residues on plant surfaces

(Fisher's Exact Binomial Test after Bonferroni-Holm; one-sided greater; $\alpha = 0.05$; n.s. = not significant)

3) Corrected mortality according to Abbott and improvements by Schneider-Orelli, negative values indicate better survivorship compared to the control

4) Reproduction: mean number of parasitised aphids/female

(Multiple sequentially-rejective U-Test after Bonferroni-Holm; one-sided smaller; $\alpha = 0.05$; n.s. = not significant)

5) Calculated on the exact raw data, negative values indicate better performance compared to the control

6) LR50 and ER50 could not be calculated since there were no effects on mortality and/or reproduction above 50%.

Validity criteria:

The reference item applied at a rate of 10.0 mL Danadim Progress/ha produced a statistically significant corrected mean mortality of 100.0 % after 48 hours (should be > 50 % corrected mortality). The mean control mortality was 0.0 % after 48 hours of exposure (should not exceed 10 %). The mean control reproduction rate was 66.1 mummies per female (should be ≥ 5.0 mummies per surviving female). No female parasitoid produced zero values in the control treatment (no more than 2 surviving female parasitoids producing zero values). All validity criteria were met.

Conclusions

Under extended laboratory conditions, the LR₅₀ of GLOB2106cF is estimated to be higher than 6080 mL product/ha in 400 L water/ha. For mortality effects, the NOER (No Observed Effect Rate) is equal to or higher than 6080 mL product/ha and the LOER (Lowest Observed Effect Rate) is higher than 6080 mL product/ha in 400 L water/ha.

Since the settling rate of the parasitoids on the plants was > 30 % at all test item application rates during the initial 2.5 hours and the parasitoids were therefore sufficiently exposed to the treatment residues on the plants, no further assessments were carried out according to Mead-Briggs *et al.* 2010.

Reproduction of *A. rhopalosiphi* was assessed in the control and in all test item treatments. There was no statistically significant effect on reproduction compared to the control at any test item rate. The ER₅₀ value for reproduction is estimated to be higher than 6080 mL product/ha in 400 L water/ha. For reproduction effects, the NOER is equal to or higher than 6080 mL product/ha and the LOER is higher than 6080 mL product/ha in 400 L water/ha.

All validity criteria were met. The study is considered valid.

Comments of zRMS:	<p>The study was accepted. The validity criteria were met.</p> <p>No significant deviations were observed.</p> <p>The following endpoints for <i>Chrysoperla carnea</i> were derived: 7-day LR₅₀ > 6080 mL formulation/ha in 200 L water/ha; ER₅₀ > 6080 mL formulation/ha in 200 L water/ha; NOER ≥ 6080 mL formulation/L in 200 L water/ha.</p> <p>The endpoints were used for risk assessment.</p>
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Reference:	KCP 10.3.2.2
Report	GLOB2106cF: Effects on the lacewing <i>Chrysoperla carnea</i> (Neuroptera, Chrysopidae), Extended laboratory study – Dose response test, Leopold J., 2023b, 169461047
Guideline(s):	Yes, Vogt <i>et al.</i> , 2000, modified for exposure of <i>C. carnea</i> on natural substrate
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to determine the effect of GLOB2106cF in the laboratory on the mortality of larvae of the lacewing *C. carnea* via contact on test item treated leaf discs (exposure period) compared to a water treated control and a reference item. Additionally, an assessment for sublethal effects on reproduction of the survivors was made.

Under extended laboratory conditions the LR₅₀ of GLOB2106cF is estimated to be higher than 6080 mL product/ha in 200 L water/ha. The NOER (no observed effect rate) for mortality effects is equal to or higher than 6080 mL product/ha and the LOER (lowest observed effect rate) is greater than 6080 mL product/ha in 200 L water/ha.

The reproductive capacity of *C. carnea* was tested in the control and in all test item application rates. The mean hatching rate was comparable to the control in all test item application rates and was always > 70 %. Reproduction was > 15 eggs per female per day at all test item application rates and in the control. This indicates that there was no negative effect of the test item on reproductive performance of *C. carnea* up to and including the highest application rate of 6080 mL product/ha. The ER₅₀ value for effects on reproduction is estimated to be higher than 6080 mL product/ha in 200 L water/ha.

All validity criteria were met. The study is considered valid.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; authenticated content (pre storage): 448.0 g/L propamocarb HCl (equivalent to 99.56% of the declared content), 76.21 g/L mandipropamid (equivalent to 101.6% of the declared content).
Test Species:	Lacewing (<i>Chrysoperla carnea</i>), 2 - 3 days old larvae; 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 40 replicates each containing 1 larva. The larvae were exposed to dried residues on treated leaf surfaces (bean leaves). Exposure lasted until 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>i.e.</i> egg deposition and larval hatching rate, was determined (two checks per week, 24 hours period each check).
Endpoints:	Larval and pupal mortality. Additionally, reproductive capacity of female survivors for treatment groups with ≤ 50 % corrected mortality.
Validity Criteria:	<ul style="list-style-type: none">- Pre-imaginal control mortality should not exceed 20 %.- Pre-imaginal mortality of the reference item group should result in at least 50 % (preferably < 100 %) corrected mortality.- Mean fecundity in the control group should be at least 15 eggs per female per day.- Mean larval hatching rate of the control group should be at least 70 %.
Reference Item:	Danadim Progress (nominal: 400 g dimethoate/L).
Test Rates: *	Control, 75.1, 225, 676, 2027 and 6080 mL product/ha and reference item. The reference item was applied at an application rate of 170 mL Danadim Progress/ha. All treatments were applied in 200 L spray volume/ha. The spraying solutions were sprayed onto leaves <i>via</i> laboratory spraying equipment, which were then air dried.
Test Conditions:	Temperature: 23 - 27 °C; relative humidity: 62 - 72 %; photoperiod: 16 h light : 8 h dark; light intensity: 1020 - 1620 lux.
Statistics:	Mortality: Chi ² 2x2 Table Test with Bonferroni Correction, Fisher's Exact Binomial Test (both one-sided greater, $\alpha = 0.05$). Reproduction: In agreement with the guideline, no statistical evaluation was performed.

Results and Discussion

The mortality of *Chrysoperla carnea* was 17.5 % in the control treatment and was between 5.0 % (75.1 mL product/ha) and 20.0 % (225 mL product/ha) in the test item treatments, corresponding to corrected mortalities of -15.2 to 3.0 %. Mortality was not statistically significantly increased compared to the control up to and including the highest application rate of 6080 mL product/ha (Chi² 2x2 Table Test with Bonferroni Correction, one-sided greater, $\alpha = 0.05$).

The reference item applied at a rate of 170 mL Danadim Progress/ha produced a statistically significant mortality of 87.5 % (84.8 % corrected mortality; Fisher's Exact Binomial Test, one-sided greater, $\alpha = 0.05$).

Reproduction of *C. carnea* was assessed in the control and at all test item application rates. The mean number of eggs per female and day was 23.1 in the control treatment. In the test item treatments, reproduction ranged from 17.4 eggs per female and day (75.1 mL product/ha) to 30.5 eggs per female and

* The test item rates were originally calculated based on the relative density of 1.45 given by the MSDS, but were recalculated later with the density of 1.4257 g/mL given by the GLP CoA.

day (676 mL product/ha) and was > 15 eggs per female and day at all test item rates. No clear dose-response relationship was recognizable.

The mean hatching rate was higher than 70 % in the control and at all test item application rates and ranged from 95.8 % (2027 mL product/ha) to 96.7 % (75.1 mL product/ha).

The results are summarized in the table below.

Pre-imaginal mortality and reproduction of *Chrysoperla carnea*

	Rate ¹⁾ [mL product/ha]	Mortality ²⁾ [%]	Mortality corr. ³⁾ [%]	Reproduction ⁴⁾ [eggs/female/day]	Effect on Reproduction ⁵⁾ [%]	Larval hatching rate ⁶⁾ [%]
Control	--	17.5	--	23.1	--	96.0
GLOB2106cF	75.1	5.0 n.s.	-15.2	17.4	24.5	96.7
GLOB2106cF	225	20.0 n.s.	3.0	26.1	-13.1	96.5
GLOB2106cF	676	7.5 n.s.	-12.1	30.5	-32.1	95.9
GLOB2106cF	2027	15.0 n.s.	-3.0	27.5	-19.4	95.8
GLOB2106cF	6080	10.0 n.s.	-9.1	29.9	-29.6	96.3
Endpoints ⁷⁾						
	test item [mL product/ha]	propamocarb HCl [g a.s./ha]	mandipropamid [g a.s./ha]			
Mortality: LR ₅₀ value	> 6080	> 2724	> 463			
NOER for mortality	≥ 6080	≥ 2724	≥ 463			
LOER for mortality	> 6080	> 2724	> 463			
Reproduction: ER ₅₀ value	> 6080	> 2724	> 463			

1) Application rate in 200 L spray volume/ha

2) Pre-imaginal mortality after exposure to spray residues on leaf surfaces

(Chi² 2x2 Table Test with Bonferroni Correction; one-sided greater; α = 0.05; n.s. = not significant; * = significant)

3) Corrected mortality according to Abbott and improvements by Schneider-Orelli; negative values indicate better survivorship compared to the control

4) Reproduction: mean number of eggs per female per day;

5) Calculated on the exact raw data; negative values indicate better performance compared to the control

6) For the determination of the hatching rate only eggs were considered which were laid on the gauze of the oviposition cages due to technical reasons.

7) The LR₅₀ value could not be calculated as no mortalities above 50 % and no clear dose-relationship were observed; the ER₅₀ value for reproduction was determined by expert judgement.

Validity criteria

The reference item applied at a rate of 170 mL Danadim Progress/ha produced a statistically significant corrected mean mortality of 84.8 % after 22 days (should be ≥ 50 % corrected mortality). The pre-imaginal control mortality was 17.5 % (should not exceed 20 %). The mean control fecundity was 23.1 eggs per female per day (should be ≥ 15 eggs per female per day). Mean larval hatching rate of the control group was 96.0 % (should be at least 70 %). All validity criteria were met.

Conclusions

Under extended laboratory conditions the LR₅₀ of GLOB2106cF is estimated to be higher than 6080 mL product/ha in 200 L water/ha. The NOER (no observed effect rate) for mortality effects is equal to or higher than 6080 mL product/ha and the LOER (lowest observed effect rate) is greater than 6080 mL product/ha in 200 L water/ha.

The reproductive capacity of *C. carnea* was tested in the control and in all test item application rates. The mean hatching rate was comparable to the control in all test item application rates and was always > 70 %. Reproduction was > 15 eggs per female per day at all test item application rates and in the control. This indicates that there was no negative effect of the test item on reproductive performance of *C. carnea* up to and including the highest application rate of 6080 mL product/ha. The ER₅₀ value for effects on reproduction is estimated to be higher than 6080 mL product/ha in 200 L water/ha. All validity criteria were met. The study is considered valid.

Comments of zRMS:	<p>The study was accepted.</p> <p>The validity criteria were met. No significant deviations were observed.</p> <p>The following endpoints for <i>Coccinella septempunctata</i> were derived: LR₅₀ > 6080 mL formulation/ha in 200 L water/ha; ER₅₀ > 6080 mL formulation/ha in 200 L water/ha; NOER ≥ 6080 mL formulation/L in 200 L water/ha.</p> <p>The endpoints were used for risk assessment.</p>
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Reference:	KCP 10.3.2.2
Report	GLOB2106cF: Effects on the ladybird beetle <i>Coccinella septempunctata</i> (Coleoptera, Coccinellidae), Extended laboratory study – Dose response test, Leopold J., 2023c, 169461012
Guideline(s):	Yes, Schmuck <i>et al.</i> 2000; modified for exposure of <i>C. septempunctata</i> on natural substrate
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to produce a concentration-response curve for mortality effects seen during larval and pupal development. From these the LR₅₀ value was estimated.

The effect of GLOB2106cF on the ladybird beetle larvae and pupae of *C. septempunctata* L. was determined in the laboratory by 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.

Under extended laboratory conditions the LR₅₀ value of GLOB2106cF is estimated to be greater than 6080 mL product/ha in 200 L water/ha

For mortality effects, the NOER (No Observed Effect Rate) is equal to or higher than 6080 mL product/ha and the LOER (Lowest Observed Effect Rate) is higher than 6080 mL product/ha in 200 L water/ha.

The reproductive capacity of *C. septempunctata* was tested in all test item application rates. Reproduction was > 2 fertile eggs per viable female per day at all test item application rates, so the reproductive output is within the historical data base for control beetles and therefore this parameter is considered as not impacted by the treatment (Schmuck *et al.* 2000) up to and including 6080 mL product/ha. The ER₅₀ value for reproduction is estimated to be higher than 6080 mL product/ha in 200 L water/ha since no effect on reproduction above 50 % was recorded for any test item application rate.

All validity criteria were met. The study is considered valid.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content: 450 g/L propamocarb HCl, 75 g/L mandipropamid (nominal); 448.0 g/L propamocarb HCl (equivalent to 99.56% of the declared content), 76.21 g/L mandipropamid (equivalent to 101.6% of the declared content) (authenticated (pre storage)).
Test Species:	Ladybird beetle (<i>Coccinella septempunctata</i>), 4 - 5 days old larvae; egg 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 40 replicates each and each containing one <i>C. septempunctata</i> larva. The larvae were exposed to dried residues on treated leaf surfaces (bean leaves). Exposure time lasted until the hatching of the adults. The reproductive performance of the survivors was examined over two weeks (oviposition period) using adults from the control and from those test item concentrations where the corrected mortality was $\leq 50.0\%$.
Endpoints:	Pre-imaginal mortality of exposed larvae and pupae; additionally, reproductive capacity of adult survivors.
Validity Criteria:	<ul style="list-style-type: none">- Pre-imaginal mortality of the control treatment should not exceed 30 %.- Pre-imaginal mortality of the reference item treatment should be $> 40\%$ corrected mortality.- The control reproduction rate should be ≥ 2 fertile eggs per viable female per day (mean value).
Reference Item:	Danadim Progress (nominal: 400 g dimethoate/L).
Test Rates: *	Control, 75.1, 225, 676, 2027 and 6080 mL product/ha and reference item. The reference item was applied at an application rate of 8.0 mL Danadim Progress/ha. All treatments were applied in 200 L spray volume/ha. The spraying solutions were sprayed onto leaves <i>via</i> laboratory spraying equipment, which were then air dried.
Test Conditions:	Temperature: 24 - 27 °C; relative humidity: 62 - 72 %; photoperiod: 16 h light : 8 h dark; light intensity: 1000 - 1300 lux.
Statistics:	Mortality: Chi ² 2x2 Table Test with Bonferroni Correction, Fisher's Exact Binomial Test (both one-sided greater, $\alpha = 0.05$). Reproduction: In agreement with the guideline, no statistical evaluation was performed.

Results and Discussion

The mean mortality of *Coccinella septempunctata* was 5.0 % in the control treatment and ranged from 2.5 to 7.5 % in the test item treatments. Mortality was not statistically significantly increased compared to the control up to and including the highest application rate of 6080 mL product/ha (Chi² 2x2 Table Test with Bonferroni Correction, one-sided greater, $\alpha = 0.05$).

The reference item Danadim Progress applied at 8.0 mL product/ha produced a statistically significant corrected mortality of 100.0 % of exposed ladybird beetles (Fisher's Exact Binomial Test, one-sided greater, $\alpha = 0.05$).

Reproduction of *C. septempunctata* was assessed in the control and in all test item application rates. The mean number of fertile eggs per female ranged from 9.0 to 11.7 in the test item treatments, corresponding to reductions between 36.8 and 17.7 % compared to the control treatment. Reproduction was > 2 fertile eggs per viable female per day in all test item application rates. In the control treatment, reproduction was 14.2 fertile eggs per female per day.

* The test item rates were originally calculated based on the relative density of 1.45 given by the MSDS, but were recalculated later with the density of 1.4257 g/mL given by the GLP CoA.

Pre-imaginal mortality and reproduction of *Coccinella septempunctata*

	Rate ¹⁾	Mortality ²⁾	Mortality corr. ³⁾	Reproduction	Effect on reproduction ⁴⁾
	[mL product/ha]	[%]	[%]	[fertile eggs per female per day]	[%]
Control	0	5.0	--	14.2	--
GLOB2106cF	75.1	5.0 n.s.	0.0	10.7	24.6
GLOB2106cF	225	5.0 n.s.	0.0	11.7	17.7
GLOB2106cF	676	2.5 n.s.	-2.6	9.0	36.8
GLOB2106cF	2027	7.5 n.s.	2.6	11.0	22.6
GLOB2106cF	6080	2.5 n.s.	-2.6	9.9	30.1
Endpoints ⁵⁾					
	test item [mL product/ha]	propamocarb HCl [g a.s./ha]	mandipropamid [g a.s./ha]		
Mortality: LR ₅₀ Value (95% CL)	> 6080	>2724	> 463		
NOER for Mortality	≥ 6080	≥ 2724	≥ 463		
LOER for Mortality	> 6080	> 2724	> 463		
Reproduction: ER ₅₀ Value	> 6080	> 2724	> 463		

1) Application rate in 200 L spray volume/ha

2) Pre-imaginal mortality after exposure to spray residues on leaf surfaces

(Chi² 2x2 Table Test with Bonferroni Correction, $\alpha = 0.05$: n.s. = not significant)

3) Corrected pre-imaginal mortality according to Abbott and improvements by Schneider-Orelli; negative values indicate better survivorship compared to the control

4) Calculated on the exact raw data; percentage reduction compared to the control treatment

5) The LR₅₀ value could not be calculated as no mortalities above 50 % were noted; ER₅₀ for reproduction was not statistically evaluated and was therefore determined by expert judgement.

Validity criteria

The reference item applied at a rate of 8.0 mL Danadim Progress/ha produced a statistically significant corrected mean mortality of 100.0 % (should be > 40 % corrected mortality). The pre-imaginal control mortality was 5.0 % (should not exceed 30 %). The mean control fecundity was 14.2 fertile eggs per viable female per day (should be ≥ 2 eggs per viable female per day). All validity criteria were met.

Conclusions

Under extended laboratory conditions the LR₅₀ value of GLOB2106cF is estimated to be greater than 6080 mL product/ha in 200 L water/ha

For mortality effects, the NOER (No Observed Effect Rate) is equal to or higher than 6080 mL product/ha and the LOER (Lowest Observed Effect Rate) is higher than 6080 mL product/ha in 200 L water/ha.

The reproductive capacity of *C. septempunctata* was tested in all test item application rates. Reproduction was > 2 fertile eggs per viable female per day at all test item application rates, so the reproductive output is within the historical data base for control beetles and therefore this parameter is considered as not impacted by the treatment (Schmuck *et al.* 2000) up to and including 6080 mL product/ha. The ER₅₀ value for reproduction is estimated to be higher than 6080 mL product/ha in 200 L water/ha since no effect on reproduction above 50 % was recorded for any test item application rate.

All validity criteria were met. The study is considered valid.

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

Comments of zRMS:	<p>The study was accepted. The validity criteria were met:</p> <ul style="list-style-type: none"> • adult control mortality 4 weeks: less than 10 % (being 0 % after 4 weeks); • number of juveniles per replicate: more than 30; (being 90 to 158) • coefficient of variation of reproduction: less than 30 % (being 21.7 %) <p>The following endpoints for mortality were derived: NOEC \geq 1000 mg formulation/kg d.w.; LC₅₀ > 1000 mg formulation/kg d.w. and for reproduction the following endpoints were derived: NOEC = 309 mg formulation/kg d.w.; EC₅₀ > 1000 mg formulation/kg d.w.</p>
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Reference:	KCP 10.4.1.1
Report	GLOB2106cF: Effects on reproduction and growth of earthworms <i>Eisenia andrei</i> in artificial soil, Straube D., 2022a, 169461022
Guideline(s):	Yes, OECD 222 and ISO 11268-2
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to investigate the effects of GLOB2106cF on the mortality, body weight, feeding activity and reproduction of the adult earthworm *Eisenia andrei*.

The No Observed Effect Concentration (NOEC) for mortality and weight changes of the earthworm *Eisenia andrei* was determined to be \geq 1000 mg test item/kg soil dry weight, *i.e.* the highest concentration tested. The Lowest Observed Effect Concentration (LOEC) for mortality and weight changes was estimated to be >1000 mg test item/kg soil dry weight. The LC₅₀ was estimated to be >1000 mg test item/kg soil dry weight. The NOEC for reproduction was determined to be 309 mg test item/kg soil dry weight. The LOEC for reproduction was determined to be 556 mg test item/kg soil dry weight. The EC₁₀ and the EC₂₀ values could not be determined statistically due to the lacking concentration response. The EC₅₀ was estimated to be >1000 mg test item/kg soil dry weight as no reduction above 50% was observed.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content: 450 g/L Propamocarb HCl, 75 g/L Mandipropamid (nominal); 448.0 g/L Propamocarb HCl (equivalent to 99.56% of the declared content), 76.21 g/L Mandipropamid (equivalent to 101.6% of the declared content) (authenticated (pre storage))
Test Species:	Earthworm (<i>Eisenia andrei</i> , Bouché, 1972), adult earthworms (with clitellum and weight range 300 to 577 mg), approximately 7 to 8 months old, source: from an in-house culture.

Test Design:	56-day test in treated artificial soil prepared according to OECD 222; different concentrations of the test item were incorporated into the soil; 9 treatment groups (8 test item concentrations, control); 4 replicates for the test item treatments and 8 replicates for the control with 10 earthworms each. Assessment of adult earthworm mortality, behavioural effects and biomass development was carried out after 28 days exposure of adult earthworms 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:	Carbendazim (600 g/L nominal). The effects of the reference item were investigated in a separate GLP study.
Test Concentrations:	Control, 16.3, 29.4, 52.9, 95.3, 171, 309, 556 and 1000 mg GLOB2106cF/kg soil dry weight.
Test Conditions:	Artificial soil according to OECD 222; initial pH 5.8 to 6.4, pH at experimental end 6.0 to 6.2; water content 26.5% to 27.8% (53.1% to 55.6% of maximum water holding capacity, WHC) at experimental start and 24.4% to 26.3% (48.8% to 52.7% 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, Fisher's Exact Test (mortality), Dunnett's t-test (body weight changes), Williams t-test and 3-param. normal CDF (reproduction).

Results and Discussion

All study validity criteria were met:

Mean Control Mortality:	Should not exceed 10% over initial 4-week test period. The mean control mortality was 0%.
Reproduction of Control:	Should be ≥ 30 earthworms per replicate container. The number of juvenile earthworms per replicate was 90 to 158.
Coefficient of Variation of Reproduction in Control:	Should not exceed 30%. Was 21.7%.

A slight mortality of 2.5% was found at the test concentration of 29.4 mg test item/kg soil dry weight, which was not statistically significantly different compared to the control, where 0% of the earthworms died (Fisher's Exact Test, $\alpha = 0.05$, one-sided greater).

The body weight changes of the earthworms after 28 days exposure to GLOB2106cF were not statistically significantly different compared to the control up to and including the highest test concentration of 1000 mg test item/kg soil dry weight (Dunnett's t-test, $\alpha = 0.05$, two-sided).

The reproduction rates were not statistically significantly different compared to the control up to and including the test concentration of 309 mg test item/kg soil dry weight (Williams t-test, $\alpha = 0.05$, one-sided smaller). At the test concentration of 556 mg test item/kg soil dry weight and above, reproduction was statistically significantly reduced compared to the control.

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

The feeding activity in all the treated groups was comparable to the control.

Effect of GLOB2106cF on earthworms (*Eisenia andrei*) in a 56-day reproduction study

GLOB2106cF [mg test item/kg soil dry weight]	Control	16.3	29.4	52.9	95.3	171	309	556	1000
Mortality (day 28) [%]	0	0	2.5	0	0	0	0	0	0
Statistical Significance ¹⁾	-	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Body weight change (day 28) [%]	32.4	39.1	31.7	31.3	35.1	37.3	36.8	31.9	41.3
Statistical Significance ²⁾	-	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Mean No. of juveniles (day 56)	123	125	103	106	96	127	111	89	68
Statistical Significance ³⁾	-	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	*	*
Reproduction in [%] of control (day 56)	-	101	84	86	77	103	90	72	55
Food consumption [g]	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0
Endpoints [mg test item/kg soil dry weight]									
NOEC (day 28 mortality)	≥1000								
LOEC (day 28 mortality)	>1000								
LC ₅₀ ⁴⁾	>1000								
NOEC (day 28 weight)	≥1000								
LOEC (day 28 weight)	>1000								
NOEC (day 56 reproduction)	309								
LOEC (day 56 reproduction)	556								
EC ₁₀	n.d.								
EC ₂₀	n.d.								
EC ₅₀ ⁴⁾	>1000								

The results represent rounded values calculated from the exact raw data. - = not applicable n.s. = not significantly different compared to the control n.d. = The EC₁₀ and EC₂₀ values could not be determined statistically due to the lacking concentration response * = significantly different compared to the control 1) Fisher's Exact Test, $\alpha = 0.05$, one-sided greater 2) Dunnett's t-test, $\alpha = 0.05$, two-sided 3) Williams t-test, $\alpha = 0.05$, one-sided smaller 4) estimated value

Reference Item Test:

In the most recent test with the reference item Carbendazim (performed under ibacon Study No. 105688022 from May to July 2022), there were statistically significant effects on reproduction at a concentration of 1.00 mg a.i./kg soil dry weight and above, which is in line with the guideline OECD 222 (effects should be observed between 1 and 5 mg a.i./kg soil dry weight). The EC₅₀ for reproduction was calculated as 1.30 mg a.i./kg soil dry weight.

Conclusions

In an earthworm reproduction and growth study with GLOB2106cF, the No Observed Effect Concentration (NOEC) for mortality and weight changes of the earthworm *Eisenia andrei* was determined to be ≥1000 mg test item/kg soil dry weight, *i.e.* the highest concentration tested. The Lowest Observed Effect Concentration (LOEC) for mortality and weight changes was estimated to be >1000 mg test item/kg soil dry weight. The LC₅₀ was estimated to be >1000 mg test item/kg soil dry weight. The NOEC for reproduction was determined to be 309 mg test item/kg soil dry weight. The LOEC for reproduction was determined to be 556 mg test item/kg soil dry weight. The EC₁₀ and the EC₂₀ values could not be determined statistically due to the lacking concentration response. The EC₅₀ was estimated to be >1000 mg test item/kg soil dry weight as no reduction above 50% was observed.

A 2.4.1.2 KCP 10.4.1.2 Earthworms - field studies

No new studies submitted.

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

Comments of zRMS:	<p>The submitted study was accepted. The validity criteria were met:</p> <ul style="list-style-type: none"> • mean adult mortality: $\leq 20\%$; observed 1.0 %; • mean number of juveniles per test vessel: ≥ 100; observed: 808 to 1033; • coefficient of variation for the mean number of juveniles: $< 30\%$; observed 8.4%. <p>The following endpoints were derived:</p> <ul style="list-style-type: none"> • mortality: NOEC ≥ 1000 mg test item/kg soil d.w. LC₅₀ > 1000 mg test item/kg soil d.w. • reproduction: NOEC ≥ 1000 mg test item/kg soil d.w. EC₅₀ > 1000 test item/kg soil d.w. <p>The study results can be used in risk assessment.</p>
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Reference:	KCP 10.4.2.1
Report	GLOB2106cF: Effects on reproduction of the Collembola (<i>Folsomia candida</i>) in artificial soil, Straube D., 2022b, 169461016
Guideline(s):	Yes, OECD 232 and ISO 11267
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of the study was to determine the effects of GLOB2106cF on mortality and reproduction of Collembola (*Folsomia candida*) in artificial soil.

GLOB2106cF caused no statistically significant effects on mortality and reproduction of *Folsomia candida* up to and including the concentration of 1000 mg GLOB2106cF/kg soil dry weight.

Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be ≥ 1000 mg GLOB2106cF/kg soil dry weight. The overall Lowest Observed Effect Concentration (LOEC) was estimated to be > 1000 mg GLOB2106cF/kg soil dry weight. The LC₅₀ was estimated to be > 1000 mg GLOB2106cF/kg soil dry weight. The EC₁₀ and EC₂₀ values could not be determined by statistical analysis since there was no adequate concentration response, the EC₅₀ value was estimated to be > 1000 mg GLOB2106cF/kg soil dry weight as no adequate concentration response was observed.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content: 450 g/L Propamocarb HCl, 75 g/L Mandipropamid (nominal); 448.0 g/L Propamocarb HCl (equivalent to 99.56% of the declared content), 76.21 g/L Mandipropamid (equivalent to 101.6% of the declared content) (authenticated (pre storage))
Test Species:	Collembola <i>Folsomia candida</i> , 9 - 12 days old, from cultures held at the laboratory.

Test Design:	28-day exposure in treated artificial soil. Different concentrations of the test item were mixed homogeneously into the soil which was placed into glass vessels before the Collembola were introduced on top of the soil; 8 concentrations and one control were tested; 4 replicates/concentration with 10 Collembola each (8 replicates for the control). Feeding of Collembola with approximately 2 mg dry yeast for each test vessel at the beginning of the test and on day 14. Assessment of adult mortality, behavioural effects and reproduction was performed after 28 days.
Endpoints:	Mortality of adult Collembola, behavioural effects, number of juveniles.
Reference Item:	Boric acid (the effects of the reference item were investigated in a separate GLP study).
Test Concentrations:	Control, 16.3, 29.4, 52.9, 95.3, 171, 309, 556 and 1000 mg GLOB2106cF/kg soil dry weight.
Test Conditions:	Artificial soil according to OECD 232; pH at experimental start pH 5.8 to 5.9, pH at experimental end 5.9 to 6.1; water content at experimental start 17.1% to 18.1% (50.3% to 53.3% of the maximum water holding capacity); water content at experimental end 16.4% to 17.4% (48.3% to 51.3% of the maximum water holding capacity); temperature: within the range of 18°C to 22°C; illumination: 16 h light : 8 h dark, light intensity within the range of 400 to 800 lux.
Statistics:	Standard procedures, Fisher's Exact Test (mortality), Dunnett's t-test (reproduction).

Results and Discussion

Experimental dates: 13 July 2022 – 11 August 2022

All validity criteria for the study were met:

Control Mortality:	Should be $\leq 20\%$ (observed: 1%)
Control Reproduction:	Should reach ≥ 100 juveniles per container (observed: 808-1033 per replicate)
Coefficient of Variation of the Control Reproduction:	Should be less than 30% (was 8.4%)

A mortality of up to 5% was observed in the test item treated groups, which was not statistically significantly different compared to the control, where 1% of the Collembola died (Fisher's Exact test, $\alpha = 0.05$, one-sided greater).

Reproduction of the Collembolan exposed to GLOB2106cF was not statistically significantly different compared to the control up to and including the highest test concentration of 1000 mg test item/kg soil dry weight (Dunnett's t-test, $\alpha = 0.05$, one-sided smaller).

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

The results are shown in the table below.

Summary of the Effects of GLOB2106cF on Collembola (*Folsomia candida*) in a 28-day Reproduction Study

GLOB2106cF [mg test item/kg soil dry weight]	Control	16.3	29.4	52.9	95.3	171	309	556	1000
Mean mortality (day 28) [%]	1	3	0	0	3	3	3	3	5
Significance 1)	-	n.s.							
Mean no. of juveniles (day 28)	912	846	870	862	907	1002	895	863	732
Reproduction in [%] of control (day 28)	-	93	95	95	99	110	98	95	80
Statistical significance 2)	-	n.s.							
Endpoints [mg/kg soil dry weight]									
NOEC (mortality)	≥1000								
LOEC (mortality)	>1000								
LC ₅₀ (mortality) ³⁾	>1000								
NOEC (reproduction)	≥1000								
LOEC (reproduction)	>1000								
EC ₁₀ (reproduction)	n.d.								
EC ₂₀ (reproduction) ³⁾	n.d.								
EC ₅₀ (reproduction) ³⁾	>1000								

n.s. = not significantly different compared to the control

n.d. = not determined

¹⁾ Fisher's Exact Test, $\alpha = 0.05$, one-sided greater

²⁾ Dunnett's t-test, $\alpha = 0.05$, one-sided smaller

³⁾ estimated value

- not applicable

Reference Item Test:

In a separate study, the reference item Boric acid showed statistically significant effects on reproduction at concentrations of ≥ 48.8 mg/kg soil dry weight. The EC₅₀ for reproduction was calculated to be 81.6 mg/kg soil dry weight.

Conclusions

GLOB2106cF caused no statistically significant effects on mortality and reproduction of *Folsomia candida* up to and including the concentration of 1000 mg GLOB2106cF/kg soil dry weight. Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be ≥ 1000 mg GLOB2106cF/kg soil dry weight. The overall Lowest Observed Effect Concentration (LOEC) was estimated to be >1000 mg GLOB2106cF/kg soil dry weight. The LC₅₀ was estimated to be >1000 mg GLOB2106cF/kg soil dry weight. The EC₁₀ and EC₂₀ values could not be determined by statistical analysis since there was no adequate concentration response, the EC₅₀ value was estimated to be >1000 mg GLOB2106cF/kg soil dry weight as no adequate concentration response was observed.

Comments of zRMS:	<p>The submitted study was accepted.</p> <p>The validity criteria were met:</p> <ul style="list-style-type: none"> • mean mortality of adult females: ≤ 20 %; observed 4%; • mean number of juveniles per replicate: ≥ 50; observed 173 to 213; • coefficient of variation (mean number of juveniles per replicate): ≤ 30 %; observed 6.7 %.
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	<p>The following endpoints were derived:</p> <ul style="list-style-type: none"> • mortality: NOEC \geq 1000 mg test item/kg soil d.w. LC₅₀ > 1000 mg test item/kg soil d.w. • reproduction: NOEC \geq 171 mg test item/kg soil d.w. EC₅₀ > 1000 mg test item/kg soil d.w. <p>The study results can be used in risk assessment.</p>
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Reference:	KCP 10.4.2.1
Report	GLOB2106cF: Effects on reproduction of the predatory mite <i>Hypoaspis aculeifer</i> in artificial soil, Straube D., 2022c, 169461089
Guideline(s):	Yes, OECD 226
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of the study was to determine the effects of GLOB2106cF on mortality and reproduction of the predatory mite *Hypoaspis aculeifer*.

GLOB2106cF caused no statistically significant effects on mortality and reproduction of *Hypoaspis aculeifer* up to and including the highest test concentration of 1000 mg GLOB2106cF/kg soil dry weight. Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be \geq 1000 mg GLOB2106cF/kg soil dry weight. The overall Lowest Observed Effect Concentration (LOEC) was estimated to be >1000 mg GLOB2106cF/kg soil dry weight. The LC₅₀ was estimated to be >1000 mg GLOB2106cF/kg soil dry weight. The EC₁₀, EC₂₀ and EC₃₀ values were estimated to be >1000 mg GLOB2106cF/kg soil dry weight as no adequate concentration response was observed.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content: 450 g/L Propamocarb HCl, 75 g/L Mandipropamid (nominal); 448.0 g/L Propamocarb HCl (equivalent to 99.56% of the declared content), 76.21 g/L Mandipropamid (equivalent to 101.6% of the declared content) (authenticated (pre storage))
Test Species:	Predatory mite <i>Hypoaspis aculeifer</i> , adult females, approximately 12 days after reaching the adult stage (33 days after placing adult females in clean rearing vessels and the start of the egg laying period in the synchronisation), cultured by ibacon.
Test Design:	14 days exposure in treated artificial soil. Different concentrations of the test item were mixed homogeneously into the soil, which was filled into glass vessels before the predatory mites were introduced on top of the soil; 8 concentrations and one control were tested; 4 replicates per test item

	concentration and 8 replicates for the control, with 10 female predatory mites in each replicate. Feeding of the mites with cheese mites (<i>Tyrophagus putrescentiae</i>) <i>ad libitum</i> at test start and on day 2, 5, 7, 9 and 12. Assessment of adult mortality and reproduction performed after 14 days.
Endpoints:	Adult mortality, number of juveniles.
Reference Item:	Dimethoate (the effects of the reference item were investigated in a separate GLP study).
Test Concentrations:	Control, 16.3, 29.4, 52.9, 95.3, 171, 309, 556 and 1000 mg GLOB2106cF/kg soil dry weight.
Test Conditions:	Artificial soil based on OECD 226; initial pH 5.8 to 5.9, pH at experimental end 5.8; water content at experimental start 17.1% to 18.1% (50.3% to 53.3% of the maximum water holding capacity); at experimental end 16.8% to 17.6% (49.4% to 51.7% of the maximum water holding capacity); temperature: within the range of 18°C to 22°C; illumination: 16 h light : 8 h dark (within the range of 400 to 800 lux).
Statistics:	Standard procedures, Fisher's Exact Test (mortality), Dunnett's t-test (reproduction).

Results and Discussion

All validity criteria for the study were met:

Control Mortality:	≤ 20% of the introduced adult female animals (Mean mortality was 4%)
Control Reproduction:	≥ 50 juveniles per test unit (number of juveniles per replicate was 173 to 213)
Coefficient of Variation (CV) of the Control Reproduction:	Should be ≤30% (was 6.7%)

A mortality of up to 10% was observed in the test item treated groups, which was not statistically significantly different compared to the control, where 4% of the adult mites died (Fisher's Exact Test, $\alpha = 0.05$, one-sided greater).

Reproduction of the predatory mites exposed to GLOB2106cF was not statistically significantly different compared to the control up to and including the highest test concentration of 1000 mg/kg soil dry weight (Dunnett's t-test, $\alpha = 0.05$, one-sided smaller).

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

The results are shown in the table below.

Summary of the Effects of GLOB2106cF on the Predatory Mite *Hypoaspis aculeifer* in a 14-day Reproduction Study

GLOB2106cF [mg test item/kg soil dry weight]	Control	16.3	29.4	52.9	95.3	171	309	556	1000
Mortality (day 14) [%]	4	8	0	3	3	5	10	5	5
Statistical significance 1)	-	n.s.							
No. of juveniles (day 14)	197	194	219	193	206	194	215	190	193
Reproduction in [%] of control (day 14)	-	99	111	98	105	98	109	96	98
Statistical significance 2)	-	n.s.							
Endpoints [mg/kg soil dry weight]									
NOEC (mortality)	≥1000								
LOEC (mortality)	>1000								
LC ₅₀ (mortality) ³⁾	>1000								
NOEC (reproduction)	≥1000								
LOEC (reproduction)	>1000								
EC ₁₀ (reproduction)	>1000								
EC ₂₀ (reproduction) ³⁾	>1000								
EC ₅₀ (reproduction) ³⁾	>1000								

n.s. = not significantly different compared to the control

n.d. = not determined

¹⁾ Fisher's Exact Test, $\alpha = 0.05$, one-sided greater

²⁾ Dunnett's t-test, $\alpha = 0.05$, one-sided smaller

³⁾ estimated value

- not applicable

The reference item Dimethoate showed statistically significant treatment related effects on reproduction at a concentration of 2.23 mg a.i./kg soil dry weight and above. The EC₅₀ for reproduction was 2.95 mg a.i./kg soil dry weight.

Conclusions

GLOB2106cF caused no statistically significant effects on mortality and reproduction of *Hypoaspis aculeifer* up to and including the concentration of 1000 mg test item/kg soil dry weight.

Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be ≥1000 mg test item/kg soil dry weight. The overall Lowest Observed Effect Concentration (LOEC) was estimated to be >1000 mg test item/kg soil dry weight. The LC₅₀ was estimated to be >1000 mg test item/kg soil dry weight. The EC₁₀ value was not determined by statistical analysis since there was no adequate concentration response. The EC₂₀ and EC₅₀ values were estimated to be >1000 mg test item/kg soil dry weight as no reduction above 20% was observed.

A 2.4.2.2 KCP 10.4.2.2 Higher tier testing

No new studies submitted.

A 2.5 KCP 10.5 Effects on soil nitrogen transformation

Comments of zRMS:	<p>The submitted study was accepted.</p> <p>The validity criteria were met.</p> <p>No adverse effects on soil nitrogen transformation (measured as NO₃-N-production) at the end of the 28-day incubation period were observed.</p> <p>The effect less than 25% was observed at application rate of 2.88 and 28.8 mg GLOB2106cF /kg dw soil.</p>
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Reference:	KCP 10.5
Report	GLOB2106cF: Effects on the activity of soil microflora in the laboratory (nitrogen transformation), Hammesfahr U., 2022, 169461080
Guideline(s):	Yes, OECD 216 (2000)
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The purpose of this study was to determine the effects of the test item on the activity (nitrogen transformation) of soil microflora in a laboratory test over a period of 70 days of exposure. The test was performed in accordance with the OECD Guideline 216 (2000) by measuring the nitrogen turnover. The test item had no long-term impact on nitrogen transformation (nitrate content, mineral nitrogen content and nitrate formation rate) of soil microorganisms when applied at 2.88 mg and 28.8 mg test item/kg soil dry weight treatment.

Materials and Methods

Test Item:	GLOB2106cF, Batch No. BRN3891
Test System:	Biologically active agricultural soil: Loamy sand
Test Design:	Determination of nitrogen-transformation in soil enriched with lucerne meal. Comparison of test item treated soil with a non-treated soil. Three replicates per treatment. NH ₄ ⁻ , NO ₂ ⁻ and NO ₃ ⁻ -nitrogen formed in the nitrification process was determined by continuous flow analysis. Sampling scheme: 0, 7, 14, 28, 42, 56 and 70 days after treatment
Test Rates:	Control 2.88 mg GLOB2106cF/kg soil dry weight 28.8 mg GLOB2106cF/kg soil dry weight
Endpoints:	Effects on NO ₃ -nitrogen production after 70 days exposure (soil nitrogen transformation).
Reference Item:	Effects of sodium chloride were determined at a rate of 16 g/kg dry soil in a separate study (ibacon study code: 116526080) once a year.
Test Conditions:	Moisture: 45% to 50% of maximum water holding capacity (WHC _{max}). Temperature: 20°C ± 2°C, in the dark.
Statistics:	Calculation of mean values per treatment, standard deviation and coefficient of variation. Normality and homogeneity of variances were tested using the R/S-Test ($\alpha = 0.01$) and Levene's test ($\alpha = 0.01$), respectively and pair-wise comparisons of treated and control values according to Student t-test ($\alpha = 0.05$) were conducted.

Results and Discussion

Experimental dates: 02 May 2022 – 13 July 2022

All validity criteria were met. The variation between the replicate control samples for nitrate-N did not exceed the validity criterion of 15% throughout the study.

No adverse effects of the test item on nitrate content in soil were observed at day 28. At day 28, differences to the control were 24.25% and 24.13% in the 2.88 mg and 28.8 mg test item/kg soil dry weight treatment, respectively.

At test end at day 70, no adverse effects of the test item on nitrate content in soil were observed. At day 70, differences to the control were 8.19% and 10.27% in the 2.88 mg and 28.8 mg test item/kg soil dry weight treatment, respectively.

The mineral nitrogen contents in soil were within the trigger range of $\pm 25\%$ set by Eppo and SETAC guidelines at day 28. At day 28 differences to the control were 23.49% and 23.29% in the 2.88 mg and 28.8 mg test item/kg soil dry weight treatment, respectively.

At test end at day 70, no adverse effects of the test item on the cumulative soil nitrate formation rates were observed. At the 0 - 70 day determination, differences to the control were 15.61% and 22.43% in the 2.88 mg and 28.8 mg test item/kg soil dry weight treatment, respectively.

The incremental soil nitrate formation rates did exceed the trigger range of $\pm 25\%$ set by OECD guideline 216 at the 14 - 28 day determination for the high test rate only. Differences to the control were 21.83% and 47.48% in the 2.88 mg and 28.8 mg test item/kg soil dry weight treatment, respectively. The deviations were within the trigger range of $\pm 25\%$ deviation to the control for all sampling points of the prolongation for the incremental nitrate formation rate. The incremental soil nitrate formation rates did not exceed the trigger range of $\pm 25\%$ set by OECD guideline 216 at the 56 - 70 day determination for both test rates. Differences to the control were -20.14% and -20.00% in the 2.88 mg and 28.8 mg test item/kg soil dry weight treatment, respectively.

Effects of the test item on Nitrogen Transformation in a Loamy Sand Soil

Nitrogen Transformation - NO ₃ – Nitrogen (mg / kg soil dry weight) Mean Values						
	Control		2.88 mg GLOB2106cF/kg soil dw		28.8 mg GLOB2106cF/kg soil dw	
Sampling	Nitrate-N Content	Replicate Variation ¹	Nitrate-N Content	Deviation ²	Nitrate-N Content	Deviation ²
Day 0	21.404	0.07	20.023	-6.45	18.472*	-13.70
Day 7	11.733	11.28	16.786*	43.07	17.468*	48.88
Day 14	19.595	7.32	24.569	25.38	22.174	13.16
Day 28	28.759	4.45	35.734*	24.25	35.698*	24.13
Day 42	47.790	2.99	55.385*	15.89	55.025*	15.14
Day 56	53.803	11.73	60.970	13.32	62.269	15.74
Nitrogen Transformation - Mineral Nitrogen ³ (mg / kg soil dry weight) Mean Values						
	Control		2.88 mg GLOB2106cF/kg soil dw		28.8 mg GLOB2106cF/kg soil dw	
Sampling	Mineral-N Content	Replicate Variation ¹	Mineral -N Content	Deviation ²	Mineral -N Content	Deviation ²
Day 0	29.832	0.44	28.099	-5.81	26.133*	-12.40
Day 7	13.851	8.85	18.823*	35.90	19.346*	39.67
Day 14	20.583	6.85	25.489	23.84	23.046	11.97
Day 28	29.454	4.38	36.374*	23.49	36.313*	23.29
Day 42	49.896	2.83	57.491*	15.22	56.987*	14.21
Day 56	55.888	11.04	62.936	12.61	64.806*	15.96
Day 0	65.423	3.13	70.488	7.74	71.681*	9.57
Nitrogen Transformation - NO ₃ – Nitrogen Formation Rate (mg / kg soil dry weight per day) ⁴						

	Control	2.88 mg GLOB2106cF/kg soil dw		28.8 mg GLOB2106cF/kg soil dw	
Interval ⁴	Nitrate-N Formation	Nitrate-N Formation	Deviation ²	Nitrate-N Formation	Deviation ²
Day 0 - 7	-1.382	-0.462*	-66.57	-0.144*	-89.58
Day 0 - 14	-0.129	0.325	-351.94	0.264	-304.65
Day 0 - 28	0.263	0.561*	113.31	0.615*	133.84
Day 0 - 42	0.628	0.842*	34.08	0.871*	38.69
Day 0 - 56	0.578	0.731	26.47	0.782*	35.29
Day 0 - 70	0.602	0.696*	15.61	0.737*	22.43
Nitrogen Transformation - NO ₃ – Nitrogen Formation Rate (mg / kg soil dry weight per day) ⁵					
	Control	2.88 mg GLOB2106cF/kg soil dw		28.8 mg GLOB2106cF/kg soil dw	
Interval ⁵	Nitrate-N Formation	Nitrate-N Formation	Deviation ²	Nitrate-N Formation	Deviation ²
Day 0 - 7	-1.382	-0.462*	-66.57	-0.144*	-89.58
Day 7 - 14	1.123	1.112	-0.98	0.672	-40.16
Day 14 - 28	0.655	0.798	21.83	0.966	47.48
Day 28 - 42	1.359	1.404	3.31	1.380	1.55
Day 42 - 56	0.430	0.399	-7.21	0.518	20.47
Day 56 - 70	0.695	0.555	-20.14	0.556	-20.00

¹ = % variation within control replicates (coefficient of variation, calculated as standard deviation / mean value x 100)

² = % deviation to control

³ = mineral nitrogen = sum of nitrite- nitrate- and ammonium-nitrogen

⁴ = related to test start

⁵ = related to successive intervals between samplings

positive values = stimulatory effect; negative values = inhibitory effect

dw = dry weight

* statistically significantly different from control (Student t-test; $\alpha = 0.05$)

In a separate study the reference item sodium chloride had a retarding effect of more than $\pm 25\%$ compared to the control at days 28 and 99 after application. The results of the study proved sensitivity of the test system and provided assurance that the laboratory test conditions are adequate.

Conclusions

The test item had no long-term impact on nitrogen transformation (nitrate content, mineral nitrogen content and nitrate formation rates) of soil microorganisms when applied at 2.88 mg and 28.8 mg test item/kg soil dry weight treatment.

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

No new data submitted.

A 2.6.2 KCP 10.6.2 Testing on non-target plants

Comments of zRMS:	The study is considered acceptable; all validity criteria were fulfilled. No visual injury and effect on plant survival could be detected after application
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	of 5.7 L GLOB2106cF. The NOER for plant survival and biomass is higher or equal than the highest tested application rate of 5.7 L GLOB2106cF/ha for all tested plant species.
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Reference:	KCP 10.6
Report	GLOB2106cF: OECD Terrestrial Plant Test - Seedling Emergence and Seedling Growth Test, Stead A., 2023a, STC/22/E1576
Guideline(s):	Yes, OECD 208 (2006)
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The objective of this study was to generate data to assess the risk of GLOB2106cF to terrestrial non-target plants. This was achieved by determining pre-emergence phytotoxicity of GLOB2106cF, when applied to two monocotyledon and four dicotyledon species from five different plant families and ascertaining ER₁₀, ER₂₅, ER₅₀, NOEC and LOEC values based on shoot fresh weight reduction at harvest. Based on shoot fresh weight reduction, all six species had an ER₁₀, ER₂₅ and ER₅₀ value of > 5.7 L product/ha, a NOEC value of ≥ 5.7 L product/ha and a LOEC value of > 5.7 L product/ha.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content of a.s.: Mandipropamid 76.21 g/L, Propamocarb HCl 448.0 g/L.
Test Species and Rate:	Six plant species from five different plant families were tested: Oat (<i>Avena sativa</i>), Wheat (<i>Triticum aestivum</i>), Cucumber (<i>Cucumis sativus</i>), Soybean (<i>Glycine max</i>), Lettuce (<i>Lactuca sativa</i>), Radish (<i>Raphanus sativus</i>) The following rate beside a control with deionised water was tested: 5.7 L test item/ha.
Test Design:	Applications were made pre-emergence to all six species. All species were treated with the test item on 21 st July 2022. GLOB2106cF was applied at 5.7 L product/ha to all six species and compared with an untreated water only control. The water volume was 200 L/ha. Thirty seeds were tested per rate and species. The exposure time was 21 days after 50% emergence in the respective control depending on the growth of the seedlings. The concentration of the active ingredients in the dosing solution was verified analytically.
Test Conditions:	The study was performed in a glasshouse. Exposure conditions were as follows: target temperature was 22.0 °C ± 10 °C, target humidity was 70% ± 25%, a daily photoperiod of 16 hours was achieved by using supplementary lighting from 4am to 7am and 7pm to 8pm (21 st July to 16 th August 2022) to provide a minimum of 5000 lux.
Endpoints:	ER ₁₀ , ER ₂₅ and ER ₅₀ values (with corresponding R-Sq. values), NOEC and LOEC values, based on shoot fresh weight reduction. Observation of emergence, mortality, phytotoxicity.
Statistical analysis:	Statistical regression analyses to determine ER ₁₀ , ER ₂₅ , ER ₅₀ and Dunnett's Test to determine NOEC and LOEC values based on shoot fresh weight reduction were not required due to <10% reduction compared to the untreated control.

Results and Discussion

Experimental dates: 21 July 2022 – 16 August 2022

All validity criteria were met:

Emergence Rate of the Control Seeds: Was at least 70%.
 Mean Survival of Emerged Control Seedlings: Was at least 90%.
 Growth and Morphology of the Control Plants: Untreated control seedlings did not exhibit visible phytotoxic effects (e.g. chlorosis, necrosis, wilting, leaf and stem deformation) and plants exhibited only normal variation in growth and morphology for that particular species. Environmental conditions for a particular species were identical and the growing media contained the same amount of soil matrix, support media or substrate was from the same source.

Analytical verification of the dosing and control solutions:

The analytical recovery rates of the active ingredients Propamocarb-HCl and Mandipropamid in the dosing solution were 97% and 100% of the nominal values.

Biological observations:

For all species tested, there was no visual injury. Emergence was not affected at any treatment rate. Survival was not affected at any treatment rate.

Summary of effect rates (based on fresh weight)

ER₁₀, ER₂₅ and ER₅₀ values (with corresponding R-Sq. values) and NOEC and LOEC values, based on shoot fresh weight reduction, are summarized below.

Species	ER ₁₀ (L GLOB2106cF/ha)	ER ₂₅ (L GLOB2106cF/ha)	ER ₅₀ (L GLOB2106cF/ha)	R-Sq.
Oat	>5.7	>5.7	>5.7	N/A
Wheat	>5.7	>5.7	>5.7	N/A
Cucumber	>5.7	>5.7	>5.7	N/A
Soybean	>5.7	>5.7	>5.7	N/A
Lettuce	>5.7	>5.7	>5.7	N/A
Radish	>5.7	>5.7	>5.7	N/A

N/A = not appropriate owing to tolerance of these species to GLOB2106cF.

Species	NOEC (L GLOB2106cF/ha)	LOEC (L GLOB2106cF/ha)
Oat	≥5.7	>5.7
Wheat	≥5.7	>5.7
Cucumber	≥5.7	>5.7
Soybean	≥5.7	>5.7
Lettuce	≥5.7	>5.7
Radish	≥5.7	>5.7

Conclusions

Visual injury

- None of the six species displayed visual injury.

Based on shoot fresh weight reduction:

- All six species had an ER₁₀, ER₂₅ and ER₅₀ value of > 5.7 L product/ha, a NOEC value of ≥ 5.7 L product/ha and a LOEC value of > 5.7 L product/ha.

Comments of zRMS:	The study is considered acceptable; all validity criteria were fulfilled. No visual injury and effect on plant survival could be detected after application of 5.7 L GLOB2106cF. The NOER for plant survival and biomass is higher or equal than the highest tested application rate of 5.7 L GLOB2106cF/ha for all tested plant species.
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Reference:	KCP 10.6
Report	GLOB2106cF: OECD Terrestrial Plant Test – Vegetative Vigour Test, Stead A., 2023a, STC/22/E1575
Guideline(s):	Yes, OECD 227 (2006)
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Executive summary

The objective of this study was to generate data to assess the risk of GLOB2106cF to terrestrial non-target plants. This was achieved by determining post-emergence phytotoxicity of GLOB2106cF, when applied to two monocotyledon and four dicotyledon species from five different plant families and ascertaining ER₁₀, ER₂₅, ER₅₀, NOEC and LOEC values based on shoot fresh weight reduction at harvest.

Based on shoot fresh weight reduction, all six species had an ER₁₀, ER₂₅ and ER₅₀ value of > 5.7 L product/ha, a NOEC value of ≥ 5.7 L product/ha and a LOEC value of > 5.7 L product/ha.

Materials and Methods

Test Item:	GLOB2106cF; batch no.: BRN 3891; content of a.s.: Mandipropamid 76.21 g/L, Propamocarb HCl 448.0 g/L.
Test Species and Rate:	Six plant species from five different plant families were tested: Oat (<i>Avena sativa</i>), Wheat (<i>Triticum aestivum</i>), Cucumber (<i>Cucumis sativus</i>), Soybean (<i>Glycine max</i>), Lettuce (<i>Lactuca sativa</i>), Radish (<i>Raphanus sativus</i>) The following rate beside a control with deionised water was tested: 5.7 L test item/ha.
Test Design:	Treatment applications were made post-emergence to all six species at growth stage BBCH 12-14 (2-4 true leaves). GLOB2106cF was applied at 5.7 L product/ha to all six species and compared with an untreated water only control. The water volume was 200 L/ha. Twenty seeds were tested per rate and species. The exposure time was 21 days after 50% emergence in the respective control depending on the growth of the seedlings. The

concentration of the active ingredients in the dosing solution was verified analytically.

Test Conditions: The study was performed in a glasshouse. Exposure conditions were as follows: target temperature was 22.0 °C ± 10 °C, target humidity was 70% ± 25%, a daily photoperiod of 16 hours was achieved by using supplementary lighting from 4am to 7am and 7pm to 8pm (21st July to 16th August 2022) to provide a minimum of 5000 lux.

Endpoints: ER₁₀, ER₂₅ and ER₅₀ values (with corresponding R-Sq. values), NOEC and LOEC values, based on shoot fresh weight reduction. Observation of emergence, mortality, phytotoxicity.

Statistical analysis: Statistical regression analyses to determine ER₁₀, ER₂₅, ER₅₀ and Dunnett's Test to determine NOEC and LOEC values based on shoot fresh weight reduction were not required due to <10% reduction compared to the untreated control.

Results and Discussion

All validity criteria were met:

Emergence Rate of the Control Seeds: Was at least 70%.

Mean Survival of Emerged Control Seedlings: Was at least 90%.

Growth and Morphology of the Control Plants: Untreated control seedlings did not exhibit visible phytotoxic effects (e.g. chlorosis, necrosis, wilting, leaf and stem deformation) and plants exhibited only normal variation in growth and morphology for that particular species. Environmental conditions for a particular species were identical and the growing media contained the same amount of soil matrix, support media or substrate was from the same source.

Analytical verification of the dosing and control solutions:

The analytical recovery rates of the active ingredients Propamocarb-HCl and Mandipropamid in the dosing solution were 97% and 100% of the nominal values.

Biological observations:

Except for soybean (minor brown spotting and yellowing), there was no visual injury. Survival was not affected at any treatment rate.

Based on fresh weight the following effect rates were determined:

Summary of effect rates (based on fresh weight)

ER₁₀, ER₂₅ and ER₅₀ values (with corresponding R-Sq. values) and NOEC and LOEC values, based on shoot fresh weight reduction, are summarized below.

Species	ER ₁₀ (L GLOB2106cF/ha)	ER ₂₅ (L GLOB2106cF/ha)	ER ₅₀ (L GLOB2106cF/ha)	R-Sq.
Oat	>5.7	>5.7	>5.7	N/A
Wheat	>5.7	>5.7	>5.7	N/A
Cucumber	>5.7	>5.7	>5.7	N/A
Soybean	>5.7	>5.7	>5.7	N/A
Lettuce	>5.7	>5.7	>5.7	N/A

Radish	>5.7	>5.7	>5.7	N/A
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N/A = not appropriate owing to tolerance of these species to GLOB2106cF.

Species	NOEC (L GLOB2106cF/ha)	LOEC (L GLOB2106cF/ha)
Oat	≥5.7	>5.7
Wheat	≥5.7	>5.7
Cucumber	≥5.7	>5.7
Soybean	≥5.7	>5.7
Lettuce	≥5.7	>5.7
Radish	≥5.7	>5.7

Conclusions

Based on shoot fresh weight reduction:

- All six species had an ER₁₀, ER₂₅ and ER₅₀ value of > 5.7 L product/ha, a NOEC value of ≥ 5.7 L product/ha and a LOEC value of > 5.7 L product/ha.

A 2.6.3 KCP 10.6.3 Extended laboratory studies on non-target plants

No new data submitted.

A 2.7 KCP 10.7 Effects on other terrestrial organisms (flora and fauna)

Not required.

A 2.8 KCP 10.8 Monitoring data

Not required.