Bayer CropScience

Document Title

Tier 2 Summary
of Ecotoxicological studies
for the Plant Protection Product
Iprovalicarb & Folpet WG 65.3 (90+563 g/kg)

(Specification number 102000011659-04)

Substance(s)

IPROVALICARB
(Annex I renewal)

Data Requirements

Regulation EC/1141/2010

on the renewal of the inclusion of AIR2 active substances

in conjunction with

Directive 91/414/EEC and **Regulation EC/1107/2009**

According to OECD format guidance for industry data submissions

(SANCO/10387/2010 rev. 8 - on the renewal of active substances included in Annex I)

Annex IIIA
Section 6, Point 10
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IIIA 10 Ecotoxicological studies on the plant protection product

General Remarks

Throughout this dossier, references are made to study reports and statements on a 65.25 WG formulation of Iprovalicarb and Folpet, in which the composition had been incorrectly assigned. Any reference to this formulation is analogous to Iprovalicarb + Folpet WG 65.3 (9% Iprovalicarb & 56.3% Folpet), the true and accurate product description for this dossier.

Recent changes in the production of the WG 63.5 formulation of Iprovalicarb + Folpet have led to a change in the lignosulfonate component. This is considered only a minor change as explained in a bridging statement and therefore studies carried out with the former formulation are valid for the new one (see Edition No. M-246642-03-1 in confidential Document JIII).

Toxicity data is provided in this dossier on the WG 65.3 product from aquatic organism studies (fish, *Daphnia*, and algae), acute bee studies, non-target arthropod studies, chronic earthworm studies, soil micro-organisms and non-target terrestrial plants. This will be compared in the case of aquatic organisms to a mixture toxicity calculation according to Finney's formula (GIFAP, 1990) based on the active substance endpoints. The lower of the two values will be used for risk assessment purposes, to give an added level of protection. Active substance studies are not available for non-target arthropods and non-target terrestrial plants so and the risk assessments will be based solely on the WG 65.3 findings. Mixture toxicity calculations are not appropriate for chronic exposures and for the risk assessment for earthworm reproduction; the findings form the WG 65.3 study will be used.

Iprovalicarb
Iprovalicarb (chemical code SZX 0722) is a new fungicidal active substance. In March 1998, an Annex II dossier for this a.s. was submitted to the Irish PSD acting as rapporteur for the EU. In the dossier, the use of the compound was supported in grapes (data from studies conducted with the solo product, WG 50) and potatoes (data from studies conducted with a combination product with Mancozeb, WP 69).

Folpet
Folpet is manufactured by [redacted]., and an Annex II dossier was submitted in 2003 as part of the second stage of the EU review programme with Italy acting as the rapporteur for the EU. The conclusion from the peer review process was published in July 2006. Full details can be obtained from the manufacturers and from the EFSA Scientific Report (2006) 70, 1-78, Conclusion of the Peer Review.

Access to Folpet data
The representative formulation in the application for Annex I Renewal of iprovalicarb is a combination with folpet, which – from a Bayer perspective - is a 3rd party substance, procured from [redacted]. ([redacted]). Bayer CropScience AG has the right of reference to files, data, studies, summaries and assessments owned by [redacted] which were submitted in the EU for

the support of the registration of the active substance folpet and the representative formulation Folpan 80 WDG. The right to references of Bayer CropScience AG extends to all EU countries. A separate Letter of Access is included in this supplementary dossier (M-428625-01-1).

Bayer CropScience AG is using a risk envelope approach for the risk assessment of the representative formulation. Within the scope of this supplementary dossier, up to 4 applications at 1.35 kg/ha folpet are proposed as a safe use in grapes. This is much below the critical GAP that [redacted] currently defends in this crop in the EU, where 10 applications of up to 1.6 kg/ha have been approved, with all other parameters such as interval between applications or pre-harvest interval being identical or very similar. Therefore, Bayer CropScience AG considers it justified to refer to folpet data owned by [redacted] wherever appropriate. A folpet-specific risk assessment is not considered necessary to defend the Annex I listing of iprovalicarb.

Intended application pattern

The product is intended for use as a fungicide on grapes. The use pattern for this formulation is summarised in Table 10- 1.

Table 10- 1: Application pattern of Iprovalicarb + Folpet WG 65.3 as used for the risk assessment

Crop	Country	Timing of application BBCH	Max. number of applications	Application interval [d]	Maximum label rate [kg product/ha]	Maximum application rate, individual treatment [kg a.s./ha]	
						Iprovalicarb	Folpet
Grapes	Germany	16-75	**1-4**	**10-14**	**2.4**	**0.216**	**1.3512**
Grapes	Czech Republic	16-61	1-4	10-14	1.8	0.162	1.0134
Grapes	Spain	**15-85**	1-4	10-12	1.67	0.150	0.940

Bold letters: artificial worst case GAP considered for risk assessment

The risk assessments throughout this dossier are conducted with an artificial GAP that provides a risk envelope for the intended uses, i.e. 4 applications of 2.4 kg product/ha with an interval between applications of 10 days at BBCH 15-85.

Ecotoxicologically significant metabolites

Metabolites, for which analytical methods have to be established for monitoring purposes, have to be addressed as significant metabolites. For these metabolites, significant quantities have been observed in at least one environmental compartment of either soil, water, plant or air.
However, none of the metabolites can be considered as hazardous or poses a higher risk to terrestrial and aquatic organisms than the parent compound.

Ecotoxicologically relevant metabolites

None of the metabolites, which are addressed within this dossier and the corresponding Annex II for the active ingredients, is considered as ecotoxicologically relevant. None of the metabolites poses a higher risk to terrestrial and aquatic organisms than the parent compound.

IIIA 10.1 Effects on birds

Toxicity of iprovalicarb to birds

The summary of the toxicity profile of the active substance iprovalicarb to birds is provided in the following table.

Table 10.1- 1: Avian toxicity data of iprovalicarb

Test Species	Test design	Ecotoxicological endpoint	Reference
Bobwhite quail	acute, oral	**LD_{50} > 2000 mg a.s./kg bw**	[redacted] (1995) VB-034 M-000077-01-1 IIA 8.1.1/01 (EU point IIA, 8.1.1/01)
Bobwhite quail	5-day feeding	LC_{50} > 5000 mg a.s./kg feed DDD_{50} > 1351 mg a.s./kg bw/d	[redacted] (1997) SXR/VB 059 M-000066-01-1 IIA 8.1.2/01 (EU point IIA, 8.1.2/01)
Mallard duck	5-day feeding	LC_{50} > 5000 mg a.s./kg feed DDD_{50} > 2414 mg a.s./kg bw/d	[redacted] (1997) SXR/VE 009 M-000326-01-1 IIA 8.1.2/02 (EU point IIA, 8.1.2/02)
Bobwhite quail	22-weeks feeding chronic, reproduction	NOEC 2000 mg a.s./kg feed **NOAEL 161 mg a.s./kg bw/d**	[redacted] (1997) 177738 M-000124-01-1 IIA 8.1.4/01 (EU point IIA, 8.1.3/01)

Bold letters: endpoints used in risk assessment

Metabolites

The parent compound was the major component found in all residue studies, and the only metabolites of quantitative significance (4-hydroxymethyl-SZX 0722 and its glucoside [*M01* and *M02*]) found in any study were determined in very minor absolute quantities and represent a metabolic pathway also seen in animals.

The main metabolite in rotational crops was p-methyl-phenethylamine (PMPA, *M10*), but it is highly unlikely that this metabolite poses a risk to birds, even if its toxicity to birds would be in the same range as for the parent compound.

Toxicity of folpet to birds

The summary of the toxicity profile of the active substance folpet to birds is provided in the following table.

Table 10.1-2: Avian toxicity data of folpet

Test Species	Test design	Ecotoxicological endpoint			Reference
Bobwhite quail	acute, oral	**LD_{50}**	**> 2510**	**mg a.s./kg bw**	See list of endpoints (EFSA Scientific Report for Folpet 2006)
Bobwhite quail	5-day feeding	LC_{50} DDD_{50}	> 5000 > 1127	mg a.s./kg feed mg a.s./kg bw/d	
Mallard duck	5-day feeding	LC_{50} DDD_{50}	> 5000 > 746	mg a.s./kg feed mg a.s./kg bw/d	
Bobwhite quail	screening, reproduction	NOEC	4640	mg a.s./kg feed	
Bobwhite quail	18-weeks feeding chronic, reproduction	NOEC **NOAEL**	1000 **78.3**	mg a.s./kg feed **mg a.s./kg bw/d**	
Mallard duck	18-weeks feeding chronic, reproduction	NOEC NOAEL	1000 90.0	mg a.s./kg feed mg a.s./kg bw/d	

Bold letters: endpoints used in risk assessment

Metabolites

The main metabolites of folpet in plants are phthalimide and phthalic acid (EFSA Scientific Report for Folpet 2006). Bird studies and separate risk assessment were not performed for these metabolites. Initial residues in food items are assumed to be not more than for the parent compound. A risk to birds is unlikely, even if the toxicity to birds would be in the same range as for the parent compound. Further details can be obtained from Makhteshim.

Toxicity of the formulated product

The acute TER values - Tier 1 or refined - (see overview Table 10.1- 7 as well as Point 10.1.1 below) are above the trigger of 10. There is no indication that the formulation is more toxic than expected based on concentration additivity of its active substances (see Point 10.1.6).
For this reason and also considering animal welfare, no acute oral toxicity study with the preparation was deemed necessary. Instead the toxicity of the formulated product was calculated according to Finney's formula.

Table 10.1- 3: Avian toxicity data of the formulated Iprovalicarb + Folpet WG 65.3

Test species	Test design	Ecotoxicological endpoint			Reference
Bobwhite quail	acute, oral	LD_{50}	3713	mg/kg bw	calculated according to Finney

For more details reference is made to Point 10.1.6 of this dossier.

Selection of endpoints for the risk assessment

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

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

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

Data on more than one species will cause an increasingly conservative risk assessment if the same fixed assessment factors are applied to the most sensitive species' toxicity value. In methods are described that allow maintaining the level of protection when more than the required number of species has been tested.

For that reason the endpoints for risk assessment depicted in the table above have been established in accordance with the following criteria:

- If acute tests for more than one species are available the geometric mean should be used for the refined assessment, except when the endpoint for the most sensitive species is more than a factor 10 below the geometric mean of all the tested species. Where this is the case, the most sensitive species will be used for the risk assessment but generally without any assessment factor.
- If more than one acute study on the same species is available, the geometric mean of the endpoints of the same species should be taken. This endpoint is then used in the overall geometric mean for refinement.
- For reproductive studies, the endpoint from the most sensitive tested species should be used.
- If more than one reproductive study has been conducted according to a similar protocol or guideline on the same species, the two datasets are merged as if it were one study. Doing so, large spacing between the concentration steps may be diminished and more adequate LO(A)ELs and NO(A)ELs can be identified. This endpoint will be used for refinement.

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

Short-term endpoints

According to the risk assessment scheme of EFSA GD birds and mammals (2009) a short-term risk assessment is not required. However, the endpoint from short-term dietary studies, e.g. 5-day dietary study in birds (OECD 205) should be used in an acute risk assessment when indicating a higher toxicity via the dietary exposure route (lower LD_{50}).

But there is no indication that 5-day exposure via dietary route might provoke higher toxicity than one application via gavage in acute study.

Therefore, in acute risk assessment the acute endpoint will be used.

Reproductive endpoints

The acute oral LD_{50} value used in the acute avian assessment (either the LD_{50} for a single species, or the geometric mean for multiple species) divided by 10 to obtain $LD_{50}/10$ will be compared with the lowest NOAED from the reproduction study (studies) ignoring purely parental effects (e.g. changes in parental body weight and food consumption).

The lower endpoint from the reproduction study will be used in avian reproductive risk assessment.

Conversion of endpoints from ppm to mg a.s./kg bw/d

The TER figures for long-term exposure of birds are calculated on the basis of a dietary dose or level as recommended by "Guidance Document on Risk Assessment for Birds and Mammals under Council Directive 91/414/EEC" (SANCO/4145/2000-final).

Therefore dietary concentrations have to be converted into a daily dose. For this purpose generally the

mean body weight and the mean food consumption over the exposure period have to be calculated.

Risk assessment for birds

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

Calculation of Toxicity Exposure Ratio (TER)

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

Acute risk: $TER_A = LD_{50}$ [mg a.s./kg bw] / DDD

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

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

Calculation of Daily Dietary Dose (DDD)

Acute exposure:

The daily dietary dose for a single application is given by the following equation:

$DDD_{single\ application}$ = application rate [kg/ha] × shortcut value (SV_{90})

In case of multiple applications the $DDD_{single\ application}$ should be multiplied with an appropriate multiple application factor (MAF_{90}).

$DDD_{multiple\ applications} = DDD_{single\ application} \times MAF_{90}$

Long-term exposure:

For a single application the daily dietary dose is given by the following equation:

$DDD_{single\ application}$ = application rate [kg/ha] × shortcut value (SV_m) × TWA

For multiple applications the $DDD_{single\ application}$ should be multiplied with an appropriate multiple application factor (MAF_m).

$DDD_{multiple\ applications} = DDD_{single\ application} \times MAF_m$

Where

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

Standard exposure scenario for risk assessment on screening level

The main potential exposure route for birds is expected to be consumption of contaminated feed. Accordingly this will be main part of the risk assessment in the following under Sections 10.1.1 and 10.1.2.

The risk assessment on screening level as well as the Tier 1 risk assessment is based on standard scenarios (combination of indicator species (screening level) or generic focal species (Tier 1) and crop.

Default (“shortcut”-) values for the exposure estimate will be used as provided in Appendix A of the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009) representing a worst case assessment.

It is assumed that

- animals satisfy their entire food demand in the treated area (PT = 1),
- animals feed on a single food type only (PD = 1),
- over an acute time frame (hours) the animals feed on items containing maximum residues (90th percentile), whereas they would ingest food containing mean residues over a long-term period (days to weeks),
- the multiple application factor (MAF) for the acute or long-term exposure is based on default values based on a generic DT_{50} value of 10 days, considering the actual (maximum) number of applications and the interval between them,
- long-term predicted environmental concentrations to be compared with chronic endpoints can be calculated as the time-weighted average concentration. Default assumptions are a time window of 21 days and a DT_{50} of 10 days leading to a time weighted average factor (= f_{twa}) of 0.53.
  This factor is equally valid for feed items consisting of vegetation as well as of arthropods.
- The ‘indicator species’ used on screening level is not a real species but, by virtue of its size and feeding habits is considered to have higher exposure than other species that occur in a particular crop at a particular time and is therefore protective for all other species in that particular crop.

Avian indicator species for risk assessment on screening level

The product Iprovalicarb + Folpet WG 65.3 is intended to be used in grapes with four applications of 2.4 kg product/ha corresponding to 0.216 kg iprovalicarb/ha and 1.3512 kg folpet/ha at BBCH 15-85 with a minimum interval of 10 days. This is an artificial GAP that provides a risk envelope for the intended uses.

Folpet is a 3[rd] party substance procured from [redacted], ([redacted]). Bayer CropScience AG is using a risk envelope approach for the risk assessment of the representative formulation. Within the scope of this supplementary dossier, up to 4 applications at 1.35 kg/ha folpet are proposed as a safe use in grapes. This is much below the critical GAP that [redacted] currently defends in this crop in the EU, where 10 applications of up to 1.6 kg/ha have been approved, with all other parameters such as interval between applications or pre-harvest interval being identical or very similar. Therefore, Bayer CropScience AG considers it justified to refer to folpet data owned by [redacted] wherever appropriate. A folpet-specific risk assessment is not considered necessary to defend the Annex I listing of iprovalicarb.

According to the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009) the following indicator species have to be addressed in risk assessment on screening level.

Table 10.1- 4: Relevant avian indicator species for risk assessment on screening level

Crop	Indicator species	Shortcut value	
		For long-term RA based on RUD_m	For acute RA based on RUD_{90}
Grapes	Small omnivorous bird	38.9	95.3

Summary of calculated TER values for birds

Table 10.1- 5: Summary of all acute TER calculations as given under point 10.1.1

Crop	Indicator species	Active substance	SV_{90}	TER_A	Result needs refinement?
Grapes	Small omnivorous bird	Iprovalicarb	95.3	> 65	no

Table 10.1- 6: Summary of all reproductive (long-term) TER calculations as given under point 10.1.2

Crop	Indicator species	Active substance	SV_m	TER_{LT}	Result needs refinement?
Grapes	Small omnivorous bird	Iprovalicarb	38.9	19	no

Conclusion: According to the presented risk assessment, the risk to birds from the use of the product in grapes is acceptable.

IIIA 10.1.1 Acute toxicity exposure ratio (TER_A) for birds

Acute toxicity exposure ratio on screening level for birds

The risk assessment at the screening level has been performed for grapes for an application rate of 4 × 0.216 kg iprovalicarb/ha at a minimum application interval of 10 days.

Table 10.1.1- 1: Acute DDD and TER calculation on screening level for birds

Crop	Indicator species	LD_{50} [mg/kg bw]	DDD			DDD	TER_A	Annex VI Trigger
			Appl. rate [kg/ha]	SV_{90}	MAF_{90}			
Iprovalicarb								
Grapes	Small omnivorous bird	> 2000	0.216	95.3	1.5	30.9	65	10

All TER values are above the Annex VI trigger of 10 for acute exposure. Accordingly an unacceptable acute risk to birds from the use of the product according to the proposed use pattern can be excluded.

Acute risk assessment for birds drinking contaminated water

An assessment of the risk potentially posed by consumption of contaminated drinking water is required according to the EFSA Guidance Document for Birds and Mammals (2009). For details see point 10.1.2 of this dossier.
As Iprovalicarb + Folpet WG 65.3 is applied in grapes, no pools in leaf axils where an acute exposure possibly might occur are to be expected. Therefore the assessment is not relevant.

The acute risk from water in puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil is covered by the long-term risk assessment under point 10.1.2 of this dossier.

IIIA 10.1.2 Short-term toxicity exposure ratio (TERST) for birds

According to the risk assessment scheme of EFSA GD birds and mammals (2009) a short-term risk assessment is not required. However, the endpoint from short-term dietary studies, e.g. 5-day dietary study in birds (OECD 205) should be used in an acute risk assessment when indicating a higher toxicity via the dietary exposure route (lower LDD_{50}). But there is no indication that 5-day exposure via dietary route with bispyribac-sodium might provoke higher toxicity than one application via gavage in acute study.

Long-term toxicity exposure ratio on screening level for birds

The risk assessment at the screening level has been performed for grapes for an application rate of 4 × 0.216 kg iprovalicarb/ha at a minimum application interval of 10 days.

Table 10.1.2- 1: Long-term DDD and TER calculation on screening level for birds

Crop	Indicator species	NO(A)EL [mg/kg bw]	DDD				DDD	TER_{LT}	Annex VI Trigger
			Appl. rate [kg/ha]	SV_m	MAF_m	f_{twa}			
Iprovalicarb									
Grapes	Small omnivorous bird	161	0.216	38.9	1.9	0.53	8.5	19	5

The TER value is above the Annex VI trigger of 5 for reproductive/long-term exposure. Accordingly, safe use of the product in grapes can be concluded.

Long-term risk assessment for birds drinking contaminated water

An assessment of the risk potentially posed by consumption of contaminated drinking water is required according to the EFSA Guidance Document for Birds and Mammals (2009).

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

Two scenarios were identified as relevant for assessing the risk of pesticides via drinking water to birds and mammals:

- Leaf scenario, only relevant for birds possibly drinking water from puddles in leaf whorls after application of a pesticide to a crop and subsequent rainfall or irrigation. This scenario is only relevant for acute exposure.
  As Iprovalicarb + Folpet WG 65.3 is applied in grapes, no pools in leaf axils where an acute exposure possibly might occur are to be expected.
- Puddle scenario. Birds and mammals taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. This scenario is only relevant for acute and long-term exposure.

An "escape clause" recommended in the EFSA Guidance Document for Birds and Mammals (2009) allows for screening the need for a quantitative risk assessment by a comparison between the application rate and the toxicity of the respective substance. This escape clause specifies that *"due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals … no specific calculations of exposure and TER are necessary when the ratio of effective application rate* (= application rate × MAF) *(in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 30 in the case of less sorptive substances (Koc < 500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥ 500 L/kg)."* [2].

Table 10.12- 2: Evaluation of potential concern for exposure of birds drinking water (escape clause)

Compound	Koc [L/kg]	Application rate × MAF_m [g a.s./ha]	NO(A)EL [mg a.s./ kg bw/d]	Ratio (Application rate × MAF) / NO(A)EL	"Escape clause" No concern if ratio	Conclusion
Iprovalicarb	113.9	216 × 1.9	161	2.5	≤ 50	No concern

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

[2] EFSA (2009): Guidance Document on Risk Assessment for Birds & Mammals on request from EFSA, p. 69

IIIA 10.1.3 In case of bait, the concentration of active substance in the bait

Not applicable for spray application.

IIIA 10.1.4 In case of pellets, granules, pills or treated seed

Not applicable for spray application.

IIIA 10.1.4.1 Amount of a.s. in or on each pellet, granule, pill or treated seed

Not applicable for spray application.

IIIA 10.1.4.2 Proportion of the LD_{50} for the a.s. in 100 particles / gram particles

Not applicable for spray application.

IIIA 10.1.5 In the case of pellets, granules and pills, their size and shape

Not applicable for spray application.

IIIA 10.1.6 Acute oral toxicity of the preparation to the more sensitive species

The risk assessment based on the active substances revealed TER values well above the respective triggers indicating acceptable acute and long-term risk to birds (see Points 10.1.1 and 10.1.2 of this dossier).

A comparison of the acute endpoints of the formulation Iprovalicarb + Folpet WG 65.3 derived from a study on rats with calculated theoretical endpoints (calculated according to Finney's formula GIFAP, 1990) is shown in Table 10.1.6-1.

Table 10.1.6- 1: Comparison of acute toxicity: active ingredients vs. formulation

Species	iprovalicarb 9% + folpet 56.3%	Iprovalicarb + Folpet WG 65.3
	Calculated [mg product/kg]	Study results [mg product/kg]
Bird (Bobwhite quail)	3713 [1]	not available
Mammal (Rat)	3339 [2]	LD_{50} > 2500

[1] based on: iprovalicarb – LD_{50} > 2000 mg/kg bw; folpet – LD_{50} > 2510 mg/kg bw

[2] based on: iprovalicarb – LD_{50} > 5000 mg/kg bw; folpet – LD_{50} > 2000 mg/kg bw

The comparison of results of this testing with the results of mixed toxicity calculation according to Finney showed that the preparation can be expected to be not more toxic than on its active ingredient content base.
Thus a risk assessment based on the product would not change the conclusion derived from the risk assessment based on the individual active substances and is therefore omitted.

IIIA 10.1.7 Supervised cage or field trials

The risk assessment based on the active substance indicates acceptable acute, short-term and long-term risks to birds (see Points 10.1.1 and 10.1.2 of this dossier). For this reason and also considering animal

welfare, no supervised cage or field study with the preparation was deemed necessary.

IIIA 10.1.8 Acceptance of bait, granules or treated seed by birds

Not applicable for spray application.

IIIA 10.1.9 Effects of secondary poisoning

Substances with a high bioaccumulation potential could theoretically bear a risk of secondary poisoning for birds if feeding on contaminated prey like fish or earthworms. For organic chemicals, a log K_{OW} > 3 is used to trigger an in-depth evaluation of the potential for bioaccumulation.
The octanol/water partition coefficients (Log P_{ow}) for iprovalicarb have been determined as 3.18 (Diastereomer A) and 3.20 (Diastereomer B). Therefore, a risk assessment for a generic earthworm-eating bird and a generic fish-eating bird for the iprovalicarb component has been performed.

Risk assessment for bioaccumulation and food chain behaviour for birds

The risk assessment according to EFSA (2009) follows a tiered approach to assess the effects of plant protection products on birds and mammals.
The risk is considered acceptable, if the 'Long-term Toxicity Exposure Ratio' (TER_{LT}) value pass the trigger values of ≥ 5 for long-term exposure.
If the TER values are below the trigger values, a refined risk assessment based on more relevant and realistic conditions is performed for those particular areas.

Calculation of Toxicity Exposure Ratio (TER)

The long-term Toxicity to Exposure Ratio (TER) depends on the selection of the suitable endpoint and is defined as follows (EFSA 2009):

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

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

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

Residues in earthworms are calculated according to the following equation:

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

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

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

Where

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

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

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

Residues in fish are calculated according to the following equation:

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

Avian generic focal species for Tier 1 risk assessment

According to the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) the following generic focal species have to be addressed in the Tier 1 risk assessment.

Table 10.1.9- 1: Avian generic focal species for the Tier 1 risk assessment of secondary poisoning

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

Long-term TER calculation for earthworm-eating birds

Table 10.1.9- 2: Tier 1 long-term TER calculation for earthworm-eating birds

Compound	Iprovalicarb	Origin of value
BCF_{worm} calculation:		
P_{OW}	1550	AII 2.8
K_{OC} [mL/g]	113.9	IIA 7.4 / IIIA 9.3
f_{OC}	0.02	default
BCF_{worm}	8.534	
PEC_{worm} calculation:		
PEC_{soil} (twa, 21 d)[mg/kg]	0.359	IIIA 9.4
PEC_{worm} [mg/kg]	3.064	
DDD calculation:		
FIR/bw	1.05	Default
DDD [mg/kg bw/d]	3.22	
TER_{LT} calculation:		
NO(A)EL [mg/kg bw/d]	16[1]	IIIA 10.1
TER_{LT}	50	
Trigger	5	
Refined risk assessment required?	No	

[1] mean of both diastereomers

[2] Worst case PEC_{soil} (twa, 21 d) for the use in vines, early, 4 × 216 g a.s./ha, 4 × 60% interception, 10 days interval

The TER value is above the trigger of 5. Accordingly the risk to earthworm eating birds from the use of the product according to the proposed use pattern is acceptable.

Long-term TER calculation for fish-eating birds

Table 10.1.9- 3: Tier 1 long-term TER calculation for fish-eating birds

Compound	Iprovalicarb	Origin of value
PEC_{fish} calculation:		
BCF_{fish}	1.4	IIA 8.2.6.1/02
PEC_{SW} (twa, 21 d)[mg/L] [1)]	0.01993	AIII 9.7
PEC_{fish} [mg/kg]	0.028	
DDD calculation:		
FIR/bw	0.159	Default
DDD [mg/kg bw/d]	0.004	
TER_{LT} calculation:		
NO(A)EL [mg/kg bw/d]	161	IIIA 10.1
TER_{LT}	40250	
Trigger	5	
Refined risk assessment required?	No	

[1] Worst case PEC_{sw} (twa, 21 d) for the use in vines, early, 4 × 216 g a.s./ha, 4 × 50% interception, 10 days interval

The TER value is above the trigger of 5. Accordingly the risk to fish eating birds from the use of the product according to the proposed use pattern is acceptable.

IIIA 10.2 Effect on aquatic organisms

Toxicity of iprovalicarb to aquatic organisms

A summary of the aquatic toxicity profile is provided below for iprovalicarb.

Table 10.2- 1: Toxicity of iprovalicarb to aquatic organisms

Test species	Test system	Test duration	Endpoint [mg as/L]	Reference
Iprovalicarb				
Oncorhynchus mykiss (rainbow trout)	Static acute	96 h	LC_{50} > 22.7 (mm)	[redacted] (1995) DOM 95060 M-000056-01-1 IIA 8.2.1.1/01 (EU point IIA, 8.2.1/01)
Lepomis macrochirus (Bluegill sunfish)	Static acute	96 h	**LC_{50} > 20.7 (mm)**	[redacted] (1995) DOM 59059 M-000050-01-1 IIA 8.2.1.2/01 (EU point IIA, 8.2.1/02)
Oncorhynchus mykiss (rainbow trout)	Chronic semi static	28 d	NOEC ≥ 9.89 (nom)	[redacted] (1997) DOM 96053 M-000032-01-1 IIA 8.2.3/01 (EU point IIA, 8.2.2.1/01)
Oncorhynchus mykiss (rainbow trout)	ELS flow-through	88 d	**NOEC 5 (mm)**	[redacted] (2000) 443A-105 M-030681-01-1 IIA 8.2.4/01
Daphnia magna (water flea)	Static acute	48 h	**EC_{50} > 19.8 (mm)**	[redacted] (1996) HBF/DM 157 M-000039-01-1 IIA 8.3.1.1/01 (EU point IIA, 8.2.4/01)
Daphnia magna (water flea)	Reproduction test semi static	21 d	**NOEC 1.89 (mm)**	[redacted] (1996) HBF/RDM 57 M-000036-01-1 IIA 8.3.2.1/01 (EU point IIA, 8.2.5/01)
Chironomus riparius (chironomid)	Static, spiked sediment	28 d	**$EC_{15\ emerg.}$ 128 (nom)** $EC_{15\ develop.}$ > 250 (nom)	[redacted] (2010) EBSZL026 M-398870-01-1 IIA 8.5.2/01
Pseudokirchneriella subcapitata (green alga)	Growth inhibition test	72 h	**E_rC_{50} > 10 (nom)** **E_bC_{50} > 10 (nom)**	[redacted] (1996) AJO/141195 M-000034-01-1 IIA 8.4/01 (EU point IIA, 8.2.6/01)

Test species	Test system	Test duration	Endpoint [mg as/L]	Reference
M03 (Iprovalicarb-carboxylic acid)				
Oncorhynchus mykiss (rainbow trout)	Static acute	96 h	**LC_{50} > 10 mg p.m./L (nom)**	[redacted] (2011) EBSZX156 M-409113-01-1 IIA 8.2.1.3/03
Daphnia magna (water flea)	Static acute	48 h	**EC_{50} > 10 mg p.m./L (nom)**	[redacted] (2011) EBSZX157 M-409052-01-1 IIA 8.3.1.1/04
Pseudokirchneriella subcapitata (green alga)	Static acute	72 h	**E_bC_{50} > 10 mg p.m./L (nom)** **E_rC_{50} > 10 mg p.m./L (nom)**	[redacted] (2011) EBSZX 158 M-411009-01-1 IIA 8.4/04
M10 (PMPA)				
Oncorhynchus mykiss (rainbow trout)	Static acute	96 h	**LC_{50} > 100 mg p.m./L (nom)**	[redacted] (1997) DOM 96063 M-000114-01-1 IIA 8.2.1.3/01 (EU point IIA, 8.2.1/03)
Daphnia magna (water flea)	Static acute	48 h	**EC_{50} 36.5 mg p.m./L (nom)**	[redacted] (1997) HBE/DM 170 M-000119-01-1 IIA 8.3.1.1/02 (EU point IIA, 8.2.4/02)
Chironomus riparius (chironomid)	Static, spiked sediment	28 d	**$EC_{15\ emerg.}$ > 100 mg p.m./kg (nom)**	[redacted] (2010) EBSZL022 M-368933-01-1 IIA 8.5.2/02
Pseudokirchneriella subcapitata (green alga)	Growth inhibition test	72 h	E_rC_{50} 15.09 mg p.m./L (nom) **E_bC_{50} 7.18 mg p.m./L (nom)**	[redacted] (1997) AJO/151796 M-000079-01-1 IIA 8.4/02 (EU point IIA, 8.2.6/02)
M15 (N-acetyl-PMPA)				
Oncorhynchus mykiss (rainbow trout)	Static acute	96 h	**LC_{50} > 100 mg p.m./L (nom)**	[redacted] (1997) DOM 97048 M-000751-01-1 IIA 8.2.1.3/02 (EU point IIA, 8.2.1/04)
Daphnia magna (water flea)	Static acute	48 h	**$EC_{50} \geq$ 100 mg p.m./L (nom)**	[redacted] (1997) HBF/DM 185 M-000601-01-1 IIA 8.3.1.1/03 (EU point IIA, 8.2.4/03)
Pseudokirchneriella subcapitata (green algae)	Growth inhibition test	72 h	**E_rC_{50} > 100 mg p.m./L (nom)** **E_bC_{50} > 100 mg p.m./L (nom)**	[redacted] (1997) AJO/167297 M-000624-01-1 IIA 8.4/03 (EU point IIA, 8.2.6/03)

Bold values: Endpoints considered relevant for risk assessment

Metabolites

M10 (= PMPA) and M15 (=N-acetyl-PMPA) are aquatic metabolites of iprovalicarb of major importance that could be detected in the water/sediment study. In addition, the toxicity of the metabolite iprovalicarb-carboxylic acid (M03) was also tested.

Toxicity of folpet to aquatic organisms

A summary of the aquatic toxicity profile is provided below for folpet.

Table 10.2- 2: Toxicity of folpet to aquatic organisms

Test species	Test system	Test duration	Endpoint [mg as/L]	Reference
Folpet				
Oncorhynchus mykiss (Rainbow trout)	Static acute	96 h	**LC_{50} = 0.233**[1]	EFSA Scientific Report for Folpet, 2006
Salmo trutta (Brown trout)	Static acute	96 h	**LC_{50} = 0.098**[2]	
Oncorhynchus mykiss (Rainbow trout)	Chronic semi-static	28 d	24-h LC_{50} >0.156 96-h LC_{50} = 0.133 28-day LC_{50} = **0.110**[3]	
Daphnia magna (water flea)	Semi-static acute	48 h	**EC_{50} 0.680**[4]	
Scenedesmus subspicatus (green alga)	Growth inhibition test	72 h	**E_rC_{50} > 10** **E_bC_{50} > 10**	
Phthalimide				
Lepomis machrochirus (Bluegill sunfish)	Static acute	96 h	LC_{50} = 38 mg p.m./L	EFSA Scientific Report for Folpet, 2006
Daphnia magna (water flea)	Static acute	48 h	EC_{50} = 39 mg p.m./L	
Phthalic acid				
Oncorhynchus mykiss (rainbow trout)	Static acute	96 h	LC_{50} > 100 mg p.m./L	EFSA Scientific Report for Folpet, 2006
Daphnia magna (water flea)	Static acute	48 h	EC_{50} ≥ 100 mg p.m./L	
Pseudokirchneriella subcapitata (green algae)	Growth inhibition test	72 h	E_bC_{50} > 100 mg p.m./L	

Test species	Test system	Test duration	Endpoint [mg as/L]	Reference
Phthalamic acid				
Oncorhynchus mykiss (rainbow trout)	Static acute	96 h	LC_{50} > 100 mg p.m./L	EFSA Scientific Report for Folpet, 2006
Daphnia magna (water flea)	Static acute	48 h	EC_{50} > 100 mg p.m./L	
Pseudokirchneriella subcapitata (green algae)	Growth inhibition test	72 h	E_bC_{50} > 100 mg p.m./L	
Benzamide				
Oncorhynchus mykiss (rainbow trout)	Static acute	96 h	LC_{50} > 100 mg p.m./L	EFSA Scientific Report for Folpet, 2006
Daphnia magna (water flea)	Static acute	48 h	EC_{50} > 102 mg p.m./L	
Pseudokirchneriella subcapitata (green algae)	Growth inhibition test	72 h	E_bC_{50} > 100 mg p.m./L	
2-cyanobenzoic acid				
Oncorhynchus mykiss (rainbow trout)	Static acute	96 h	LC_{50} > 100 mg p.m./L	EFSA Scientific Report for Folpet, 2006
Daphnia magna (water flea)	Static acute	48 h	EC_{50} > 100 mg p.m./L	
Pseudokirchneriella subcapitata (green algae)	Growth inhibition test	72 h	E_bC_{50} > 100 mg p.m./L	

Bold values: Endpoints considered relevant for risk assessment

[1] value to be used for the Tier 1 risk assessment

[2] Six species of fish were tested (see Table 10.2-3). Brown trout (*Salmo trutta*) was the most sensitive species tested and this LC_{50} should be used in the higher tier risk assessment. Uncertainty regarding interspecies variation in sensitivity has been reduced. Hence, a TER trigger of 10 should be used.

[3] Test conducted with the product Folpan 500 SC

[4] Test conducted with the product Folpan 80 WDG

A multiple single species acute fish study has also been conducted for folpet and is summarised in the following table:

Table 10.2- 3: Multiple single-species acute toxicity tests with fish

Species	Exposure time	LC_{50} (mg a.s./L)	Reference
Brown trout *(Salmo trutta)*	24 h 96 h	0.098 0.098	Data provided by Makhteshim
Bream *(Abramis brama)*	24 h 96 h	0.155 0.114	
Roach (*Rutilus rutilus*)	24 h 96 h	0.211 0.211	
3- Spined stickleback (*Gasterosteus aculeatus*)	24 h 96 h	0.229 0.229	
Rainbow trout (*Oncorhynchus mykiss*)	24 h 96 h	0.233 0.233	
Carp (*Cyprinus carpio*)	24 h 96 h	1.471 1.012	

Metabolites

In the sediment water fate study five metabolites of Folpet were formed, which were themselves transient. These were (with highest % applied radioactivity for whole system) phthalimide up to 26.0% in water phase, phthalic acid up to 37.5% in water, phthalamic acid up to 13.3% in water, benzamide up to 10.2% in water and 2-cyanobenzoic acid up to 39.7% in water (see EFSA Scientific Report for Folpet, Appendix 1 list of endpoints). They have a low toxicity to aquatic organisms and are significantly less toxic than Folpet (see Table 10.2- 2). In addition, these compounds would have been present in the static toxicity tests on Folpet. The low metabolite toxicity explains how hydrolysis is such an effective detoxification mechanism. In terms of exposure, metabolite PEC values will be lower than Folpet. Therefore, the risk to aquatic organisms from these metabolites will be significantly lower than for Folpet itself, and no risk assessment is conducted with them.

Summary of data derived from studies with the formulated product

A summary of the aquatic toxicity profile of Iprovalicarb + Folpet WG 65.3 is provided in Table 10.2-4. For more details on the respective studies, reference is made to Point 10.2.2 of this dossier.

Table 10.2- 4: Toxicity of Iprovalicarb + Folpet WG 65.3 to aquatic organisms

Test organism	Test system	Endpoint [mg product/L]		Reference
Acute toxicity to fish				
Oncorhynchus mykiss (rainbow trout)	Semi-static 96 h	LC_{50}	0.088	[redacted] (2003) DOM 22067 M-079959-01-1 KIIIA 10.2.2.1/01
Acute toxicity to aquatic invertebrates				
Daphnia magna (water flea)	Static 48 h	EC_{50}	1.60	[redacted] (2003) DOM 22055 M-078438-01-1 KIIIA 10.2.2.2/01

Test organism	Test system	Endpoint [mg product/L]		Reference
Effects on algal growth				
Pseudokirchneriella subcapitata (green alga)	Static 72 h	E_bC_{50} E_rC_{50}	16.0 > 100	[redacted] (2002) 844711 M-065958-01-1 KIIIA 10.2.3.3/01

In addition, the acute mixture toxicity of the formulated product was calculated according to the formula of Finney (Finney, GIFAP, 1990):

$$1 / LC_{50\ expected} = \sum ct_{as} / LC_{50}$$

ct_{as} = w/w fraction of active substance in %
active substances = iprovalicarb, folpet

Table 10.2- 5: Calculation of the acute mixed toxicity of the formulation according to Finney

	Iprovalicarb	Folpet	Iprovalicarb + Folpet WG 65.3
Content within the product [%]	9	56.3	-
Effects on fish (*Oncorhynchus mykiss*)			
LC_{50} [mg as/L]	> 22.7	0.233	
LC_{50} – mixed toxicity [mg product/L]	Expected LC_{50} = 0.413		Measured LC_{50} = 0.088
Effects on *Daphnia magna*			
EC_{50} [mg as/L]	> 19.8	0.680	
EC_{50} – mixed toxicity [mg product/L]	Expected EC_{50} = 1.201		Measured EC_{50} = 1.60

Based on Finney's formula, the maximum deviation of the expected toxicity of the formulated product from the measured toxicity is a factor of 4.7 for fish and a factor of 1.3 for *Daphnia* from the measured toxicity values. This variation is within the experimental variability of biological systems and below the factor of 10 used in the Aquatic Guidance Document as indication for significant differences. Thus, the risk assessment for the formulated product can be safely based on the data generated on its active ingredients.

Selection of algae endpoints for risk assessment

Processes in ecosystems are dominantly rate driven and therefore, the unit development per time (growth rate) appears more suitable to measure effects in algae. Also, growth rates and their inhibition can easily be compared between species, test durations and test conditions, which is not the case for biomass. After numerous discussions, the current test guidelines OECD TG 201, the EU-Method C3, the EC regulation for Classification and Labeling (EC regulation 1272/2008) and the PPR Opinion (EFSA Journal 461, 1-44, 2007) list growth rate as the most suitable endpoint of the algae inhibition test. Only the current Guidance Document on Aquatic Toxicology (SANCO/3268/2001 rev. 4) still states that "*As there is no clear evidence available to indicate which is the most relevant endpoint for the field situation the lower figure should be used in the risk assessment*". In order to avoid unnecessary delays in dossier reviews, toxicity-exposure-ratios in this assessment are built on the

lower of the two values, the E_bC_{50} or the E_rC_{50} in case both values are available, unless justification is available.

IIIA 10.2.1 Toxicity exposure ratios for aquatic species

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

Predicted Environmental Concentrations in surface water bodies

Predicted environmental concentrations for the active substances and their relevant metabolites were calculated in surface water (PEC_{sw}) and in sediment (PEC_{sed}) according to FOCUS surface water scenarios as described in detail in Point 9.7 (active substances) and 9.8 (metabolites).

Concentrations in groundwater are also considered, as groundwater might become surface water, leading to exposure of aquatic organisms. However, the PEC values for the active substance and the soil metabolites are < 0.1 µg/L in groundwater for all relevant FOCUS scenarios and application rates (for details see Point 9.6), and thus not relevant for the risk assessment.

Table 10.2.1- 1: Maximum PEC_{sw} and PEC_{sed} values for iprovalicarb at FOCUS Steps 1 and 2

Crop	Step	Iprovalicarb		
		$PEC_{sw, max}$ [µg/L]	$PEC_{sw, 21\ d\ TWA}$ [µg/L]	$PEC_{sed, max}$ [µg/kg]
Vine, early 4 × 0.216 kg/ha, 50% interception	1	273.1	220.7	284.8
	2 (N-EU Multi)	18.54	14.72	20.11
	2 (S-EU Multi)	**24.92**	**19.93**	**27.23**
	2 (N-EU Single)	8.999	7.182	9.809
	2 (S-EU Single)	13.15	10.57	14.45

Bold letters: values used in risk assessment

Table 10.2.1- 2: Maximum PEC_{sw} and PEC_{sed} values for iprovalicarb metabolites at FOCUS Steps 1 and 2

Crop	Step	M03	M10		M15
		$PEC_{sw, max}$ [µg/L]	$PEC_{sw, max}$ [µg/L]	$PEC_{sed, max}$ [µg/kg]	$PEC_{sw, max}$ [µg/L]
Vine, early 4 × 0.216 kg/ha, 50% interception	1	32.78	46.34	128.9	45.43
	2 (N-EU Multi)	0.561	4.835	13.61	1.131
	2 (S-EU Multi)	**0.561**	**8.629**	**24.50**	**1.155**
	2 (N-EU Single)	0.329	1.440	4.036	0.362
	2 (S-EU Single)	0.352	2.513	7.119	0.386

Bold letters: values used in risk assessment

Risk assessment

Folpet is a 3rd party substance procured from [redacted]. ([redacted]). Bayer CropScience AG is using a risk envelope approach for the risk assessment of the representative formulation. Within the scope of this supplementary dossier, up to 4 applications at 1.35 kg/ha folpet are proposed as a safe use in grapes. This is much below the critical GAP that [redacted] currently

defends in this crop in the EU, where 10 applications of up to 1.6 kg/ha have been approved, with all other parameters such as interval between applications or pre-harvest interval being identical or very similar. Therefore, Bayer CropSciences AG considers it justified to refer to folpet data owned by [redacted] wherever appropriate. A folpet-specific risk assessment is not considered necessary to defend the Annex I listing of iprovalicarb.

Based on the representative most sensitive endpoint values (Table 10.2- 1) and the PEC_{sw} values (Table 10.2.1- 1 and Table 10.2.1- 2; highest values selected as worst case), the TER-values have been calculated, based on the following equations:

$TER_a = LC_{50}$ or EC_{50} / initial PEC_{water}
$TER_{lt} = E_rC_{50}$ / initial PEC_{water}
TER_{lt} = chronic NOEC / long-term PEC_{water}
The risk is considered acceptable, if the TER_a values for fish and invertebrates are >100 and the TER_{lt} values >10.

Summary of calculated TER values for aquatic organisms

Table 10.2.1- 3: Summary of all TER calculations as given under points 10.2.1.1 to 10.2.1.11 (based on most relevant endpoints)

Appl. rate [g as/ha]	Organism	Time-scale	Distance [m]	TER	Trigger	Assessment level
Iprovalicarb						
4 x 216	Fish	acute	-	831	100	Step 2
	Fish	long-term	-	201	10	
	Invertebrates	acute	-	> 795	100	
	Invertebrates	long-term	-	76	10	
	Sediment dweller (spiked sediment)	long-term	-	4701	10	
	Green algae	long-term	-	> 401	10	
M03						
-	Fish	acute	-	> 17825	100	Step 2
	Invertebrates	acute	-	> 17825	100	
	Green algae	long-term	-	> 17825	10	
M10						
-	Fish	acute	-	> 11589	100	Step 2
	Invertebrates	acute	-	> 4230	100	
	Sediment dweller (spiked sediment)	long-term	-	> 4082	10	
	Green algae	long-term	-	832	10	
M15						
-	Fish	acute	-	> 86580	100	Step 2
	Invertebrates	acute	-	≥ 86580	100	
	Green algae	long-term	-	> 86580	10	

Conclusion: According to the presented risk assessment, a risk to aquatic organisms from exposure after the use of the product as described in this dossier is unlikely.

IIIA 10.2.1.1 TER_A for fish

Table 10.2.1.1- 1: TER_A calculations for fish based on maximum PEC_{sw} values according to FOCUS Step 2

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_A	Annex VI Trigger
Iprovalicarb				
L. macrochirus	LC_{50} > 20700	24.92	> 831	100
M03				
O. mykiss	LC_{50} > 10000	0.561	> 17825	100
M10				
O. mykiss	LC_{50} > 100000	8.629	> 11589	100
M15				
O. mykiss	LC_{50} > 100000	1.155	> 86580	100

The TER_A values for the active substance iprovalicarb and its metabolites meet the required trigger as set in Annex VI of Council Directive 91/414/EEC indicating an acceptable acute risk to fish for application of the product.

IIIA 10.2.1.2 TER_{LT} for fish

Table 10.2.1.2- 1: TER_{LT} calculation for fish based on maximum PEC_{sw} values according to FOCUS Step 2

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Annex VI Trigger
Iprovalicarb				
O. mykiss	NOEC 5000	24.92	201	10

The TER_{LT} value for the active substance iprovalicarb meets the required trigger as set in Annex VI of Council Directive 91/414/EEC indicating an acceptable long-term risk to fish for application of the product.

IIIA 10.2.1.3 TER_A for Daphnia

Table 10.2.1.3- 1: TER_A calculation for *Daphnia* based on max. PEC_{sw} values according to FOCUS Step 2

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_A	Annex VI Trigger
Iprovalicarb				
D. magna	EC_{50} > 19800	24.92	> 795	100
M03				
D. magna	EC_{50} > 10000	0.561	> 17825	100
M10				
D. magna	EC_{50} > 36500	8.629	> 4230	100
M15				
D. magna	EC_{50} ≥ 100000	1.155	≥ 86580	100

The TER_A values for the active substance iprovalicarb and its metabolites meet the required trigger as set in Annex VI of Council Directive 91/414/EEC, indicating an acceptable acute risk to *Daphnia* for application of the product.

IIIA 10.2.1.4 TER_{LT} for Daphnia

Table 10.2.1.4- 1: TER_{LT} calculation for *Daphnia* based on max. PEC_{sw} values according to FOCUS Step 2

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Annex VI Trigger
Iprovalicarb				
D. magna	NOEC 1890	24.92	76	10

The TER_{LT} value for the active substance iprovalicarb meets the required trigger as set in Annex VI of Council Directive 91/414/EEC, indicating an acceptable long-term risk to *Daphnia* for application of the product.

IIIA 10.2.1.5 TER_A for an aquatic insect species

No specific studies on the acute toxicity of iprovalicarb to aquatic insect species were conducted. However, chronic studies addressing long-term effects on the sediment dwelling insect *Chironomus riparius* were performed with the active substance iprovalicarb and the metabolite M10 (please refer to Point 10.2.1.6 of this dossier).

IIIA 10.2.1.6 TER_{LT} for an aquatic insect species

Table 10.2.1.6- 1: TER_{LT} calculations for *C. riparius* based on max. PEC_{sed} values according to FOCUS Step 2

Species	Endpoint [µg/kg]	$PEC_{sed,max}$ [µg/kg]	TER_{LT}	Annex VI Trigger
Iprovalicarb				
C. riparius	EC_{15} 128000	27.23	4701	10
M10				
C. riparius	EC_{15} > 100000	24.50	> 4082	10

The TER_{LT} values for the active substance iprovalicarb and its metabolite M10 meet the required trigger as set in Annex VI of Council Directive 91/414/EEC, indicating an acceptable long-term risk to aquatic insects for application of the product.

IIIA 10.2.1.7 TER_A for an aquatic crustacean species

No studies on aquatic crustaceans other than daphnids are required since the product is not an insecticide and the active substances do not show an insecticidal mode of action. The risk for these organisms is covered by the aquatic risk assessment provided in this dossier.

IIIA 10.2.1.8 TER_{LT} for an aquatic crustacean species

Please refer to point IIIA 10.2.1.7.

IIIA 10.2.1.9 TER_A for an aquatic gastropod mollusc species

No studies on aquatic gastropod molluscs are deemed necessary according to current requirements. The risk for these organisms is covered by the aquatic risk assessment provided in this dossier.

IIIA 10.2.1.10 TER_{LT} for an aquatic gastropod mollusc species

Please refer to point IIIA 10.2.1.9.

IIIA 10.2.1.11 TER_{LT} for algae

Table 10.2.1.11- 1: TER_{LT} calculations for algae based on maximum PEC_{sw} values according to FOCUS Step 2

Species	Endpoint [µg/L]	$PEC_{sw,max}$ [µg/L]	TER_{LT}	Annex VI Trigger
Iprovalicarb				
P. subcapitata	E_bC_{50} > 10000	24.92	> 401	10
M03				
P. subcapitata	E_bC_{50} > 10000	0.561	> 17825	10
M10				
P. subcapitata	E_bC_{50} 7180	8.629	832	10
M15				
P. subcapitata	E_bC_{50} > 100000	1.155	> 86580	10

The TER_{LT} values for the active substance iprovalicarb and its metabolites meet the required trigger as set in Annex VI of Council Directive 91/414/EEC, indicating an acceptable long-term risk to algae for application of the product.

IIIA 10.2.2 Acute toxicity (aquatic) of the preparation

IIIA 10.2.2.1 Fish acute toxicity LC_{50}, freshwater cold-water species

Report:	**KIIIA 10.2.2.1/01; [redacted] 2003**
Title:	Acute toxicity of Iprovalicarb 9.0 WG + Folpet 56.3 to fish *(Oncorhynchus mykiss)*.
Document No:	M-079959-01-1 (Report No: DOM 22067)
Guidelines:	OECD Guideline No. 203 "OECD-Guideline for Testing of Chemicals", "Fish, Acute Toxicity Test", updated and adopted version of July 17, 1992
GLP	Yes (certified laboratory)

Material and methods:

Test item Iprovalicarb 9.0 WG + Folpet 56.3, content: Iprovalicarb 10.0% / Folpet 55.4%, specification: (batch no.: 07373/0048 (0046), development-no.: 3000244654), rainbow trout (*Oncorhynchus mykiss*, mean body length 5.5 cm, mean body weight 2.1 g), 10 fish per test concentration were exposed for 96 h under static test conditions to nominal concentrations of 0.0313, 0.0625, 0.125, 0.25 and 0.50 mg test item / L.

Findings:
Acute toxicity to fish (based on nominal concentrations)

Test item	Iprovalicarb 9.0 WG + Folpet 56.3
Test object	Rainbow Trout *(Oncorhynchus mykiss)*
Exposure	96h, static
minimum concentration causing 100%	0.125 mg test item / L

mortality (96 h)	
LC_{50} (96h) (95 % C.I.)	**0.088 mg test item / L** (0.063 – 0.125)
NOLEC* (96h)	0.0625 mg test item / L

*no-observed-lethal-effect concentration (NOLEC)

Observations:

There were neither adverse effects nor any mortality in the control group. The no-observed-effect concentration (NOEC) was 0.0313 mg test item / L. Up to five fish showed the following transient symptoms at 0.0625 mg test item / L: Remained for unusually long periods at the water surface, showed labored respiration, were inactive or displayed abnormally low activity.

IIIA 10.2.2.2 Acute toxicity (24 & 48 h) for Daphnia preferably Daphnia magna

Report:	**KIIIA 10.2.2.2/01 [redacted] 2003**
Title:	Acute toxicity of Iprovalicarb 9.0 WG & Folpet 56.3 to water fleas (*Daphnia magna)*
Document No:	M-078438-01-1 (Report No: DOM 22055)
Guidelines:	OECD 202 and EPA FIFRA 72-2
GLP	Yes (certified laboratory)

Material and methods:

Iprovalicarb 9.0 WG & Folpet 56.3, a.s. content 10.0 % Iprovalicarb, 55.4 % Folpet, Fl-No.: 07373/0048(0046), article No.: 0005539447), young *Daphnia magna* (1st instars < 24 h old, 3 x 10 animals per concentration) in a static test system were exposed for 48 h to nominal concentrations of 0, 0.10, 0.22, 0.48, 1.1, 2.3, 5.2 and 11 mg formulation/L. Measured concentrations of the a.s. were 100 to 120 % (on average 104 %) of nominal during this study.

Findings:

Toxicity to Waterfleas (based on nominal concentrations).

Test substance	Iprovalicarb 9.0 WG & Folpet 56.3	
Test object	*Daphnia magna*	
	mg formulation/L	
Exposure	24 h, static	48 h, static
EC_{50}	7.9	1.6
(95 % confidence limits)	4.9 – 13	1.2 – 2.3

Observations:

Statistically significant immobilisation occurred in concentrations ≥ 2.3 mg formulation/L after 24 hours. After 48 hours statistically significant immobilisation occurred at concentrations ≥ 0.22 mg formulation/L. There was no concentration causing 100 % immobility. Highest immobilities were 93 % after 48 hours. Abnormal behaviour or appearance of symptoms were not observable at concentrations which showed no significant immobilisation

IIIA 10.2.2.3 Effects on algal growth and growth rate

Report:	**KIIIA 10.2.2.3/01; [redacted] 2002**
Title:	Toxicity of Iprovalicarb WG 9 & Folpet 56.3 to *Pseudokirchneriella subcapitata* (formerly *Selenastrum capricornutum*) in a 72-hour algal growth inhibition test
Document No:	M-065958-01-1 (Report No: 844711)
Guidelines:	OECD 201 Directive 92/69/EEC C.3
GLP	Yes (certified laboratory)

Materials and methods:

Test item: Iprovalicarb WG 9 & Folpet 56.3; contents of active ingredients: Folpet (ENT 26539) 55.4%, Iprovalicarb (SZX 0722) 10.0%, specification: Batch no. 07373/0048(0046); Tox. no. 6124-00; *Pseudokirchneriella subcapitata* was exposed under static conditions (stirring cultures) for 72 hours. The following nominal test item concentrations were tested: 0.32, 1.0, 3.2, 10, 32, and 100 mg formulation/L. Calculations are based on nominal concentrations of the formulation. Measured concentrations of the a.s. were 94 to 100 % of nominal during this study.

Findings and observations:

Effects on algal average growth rate r (results based on nominal test item concentrations):

Test item	Iprovalicarb WG 9 & Folpet 56.3	
Test system	*Pseudokirchneriella subcapitata*	
Exposure	72 h, static	
	Biomass	Growth rate
EC_{50} (0-72 hours) [mg formulation/L]	16	>100
Lowest observed effect concentration (0-72 hours LOE_rC) [mg formulation/L]	3.2	3.2
Highest tested concentration without effects (0-72 hours NOE_rC) [mg formulation/L]	1.0	1.0

Growth rate related values are preferred because the validity criteria according to exponential growth are fulfilled.

Conclusion:

The E_bC_{50} for the WG formulation of Folpet + Iprovalicarb was 16 mg product/L and the E_rC_{50} value was >100 mg product/L

IIIA 10.2.2.4 Marine or estuarine organisms acute toxicity LC_{50}/EC_{50}

According to the current data requirements, no studies on marine or estuarine organisms are necessary. The potential risk for these organisms is covered by the aquatic risk assessment provided in this dossier.

IIIA 10.2.2.5 Marine sediment invertebrates, acute toxicity LC_{50}/EC_{50}

According to the current data requirements, no studies on marine or estuarine organisms are necessary. The potential risk for these organisms is covered by the aquatic risk assessment provided in this dossier.

IIIA 10.2.3 Microcosm or mesocosm study

No microcosm or mesocosm studies were performed with the formulated product. Based on the toxicity data and application rate of the product, the risk assessment (TER calculations) presented above indicates acceptable risk to aquatic organisms. Therefore, microcosm or mesocosm studies with the formulated product are not deemed necessary.

IIIA 10.2.4 Residue data in fish (long term)

Iprovalicarb:

The steady state bioconcentration factor for iprovalicarb in a laboratory study with Bluegill sunfish was determined to be in the range of 8.56-11.4 (mean 10, see Annex II, chapter 8.2.6). Iprovalicarb is bio-concentrated very rapidly by Bluegill sunfish. When exposure ceases, the radioactivity is depurated very quickly with a half-life of less than half a day. Additionally, it was considered that the BCFs obtained may have been overestimated because all calculations referred to total radioactivity (including parent compound and metabolites). This was confirmed by a residue analysis. The BCF for the parent compound in whole fish was determined as 1.4 (additional submission to AII, point 8.2.6).

Folpet

Folpet does not accumulate in fish. The overall BCF value was 56 (whole fish) (see EFSA Scientific Report for Folpet, Appendix 1 list of endpoints).

IIIA 10.2.5 Chronic fish toxicity data

Chronic studies with the formulated product were not considered necessary, as the relevant information can be obtained from studies with the active ingredient.

IIIA 10.2.5.1 Chronic toxicity (28 day exposure) to juvenile fish

See statement provided under Point IIIA 10.2.5.

IIIA 10.2.5.2 Fish early life stage toxicity test

See statement provided under Point IIIA 10.2.5.

IIIA 10.2.5.3 Fish life cycle test

See statement provided under Point IIIA 10.2.5.

IIIA 10.2.6 Chronic toxicity to aquatic invertebrates

Chronic studies with the formulated product were not considered necessary, as the relevant information can be obtained from studies with the active substances.

IIIA 10.2.6.1 Chronic toxicity to Daphnia magna (21-day)

See statement provided under Point IIIA 10.2.6.

IIIA 10.2.6.2 Chronic toxicity for a representative species of aquatic insects

See statement provided under Point IIIA 10.2.6.

IIIA 10.2.6.3 Chronic toxicity for a representative species of aquatic gastropod molluscs

See statement provided under Point IIIA 10.2.6.

IIIA 10.2.7 Accumulation in aquatic non-target organisms

Based on the information given under Point IIIA 10.2.4, considerable accumulation of residues of the product and/or metabolites in aquatic organisms is unlikely to occur.

IIIA 10.3 Effects on terrestrial vertebrates other than birds

Toxicity of iprovalicarb to mammals

A summary of the toxicity of iprovalicarb to mammals is provided in the following table:

Table 10.3- 1: Toxicity of iprovalicarb to mammals (selected studies)

Test species	Test design	Ecotoxicological endpoint		Reference
Rat	acute, oral	**LD_{50}**	**> 5000 mg a.s./kg bw**	[redacted] (1993) 22110 M-000355-01-1 IIA 5.2.1/01 (EU point IIA, 5.2.1/01)
Rat	Two-generation study	**$NOAEL_{reproduction}$** NOEC	**146.3 mg a.s./kg bw/day** 2000 mg a.s./kg feed	[redacted] (1997) 26391 M-001052-01-1 IIA 5.6.1/01 (EU point IIA, 5.6.1/01)

Bold letters: endpoints used in risk assessment

Metabolites of iprovalicarb

The parent compound was the major component found in all residue studies, and the only metabolites of quantitative significance (4-hydroxymethyl-SZX 0722 and its glucoside [*M01* and *M02*]) found in any study were determined in very minor absolute quantities and represent a metabolic pathway also seen in animals.

The main metabolite in rotational crops was p-methyl-phenethylamine (PMPA, *M10*). It is highly unlikely that this metabolite poses a risk to mammals, even as its toxicity is in the same range as for the parent compound. However, an acute feeding study with M10 has been conducted and a tier 1 risk assessment will be carried out assuming 100% conversion of iprovalicarb to M10.

Table 10.3- 2: Toxicity of the iprovalicarb metabolite M10 to mammals

Test species	Test design	Ecotoxicological endpoint			Reference
Rat	acute, oral	**LD_{50}**	**300**-500	**mg pm/kg bw**	[redacted] (1996) 25319 M-000505-01-1 IIA 5.8.1.1/01 (EU point IIA, 5.8.1.1/01)

Bold letters: endpoints used in risk assessment

Toxicity of folpet to mammals

A summary of the toxicity of folpet to mammals is provided in the following table:

Table 10.3- 3: Toxicity of folpet to mammals (selected studies)

Test species	Test design	Ecotoxicological endpoint		Reference
Rat	acute, oral	**LD_{50}**	**> 2000 mg a.s./kg bw**	(see EFSA Scientific Report for Folpet, Appendix 1 list of endpoints)
Rat	Two-generation study	**$NOAEL_{reproduction}$** NOEC	**140.9 mg a.s./kg bw/day** 1500 mg a.s./kg feed	

Bold letters: endpoints used in risk assessment

Metabolites of folpet

Phthalimide, phthalamic acid and phthalic acid are confirmed mammalian metabolites of folpet (see EFSA Scientific Report for Folpet, Appendix 1 list of endpoints) and their toxicity was accounted for in the acute and long term studies of folpet in mammals. Therefore, the mammalian risk assessment for folpet adequately addresses risk for folpet metabolites.

Toxicity of the formulated product

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

Table 10.3- 4: Mammalian toxicity data of the formulated product Iprovalicarb + Folpet WG 65.3

Test species	Test design	Ecotoxicological endpoint		Reference
Rat	acute, oral	LD_{50}	> 2500 mg/kg bw	[redacted] (2000) 30395 M-026075-01-1 KIIIA 7.7.1/01

For more details reference is made to Point 10.3.2.1 of this dossier.

Selection of endpoints for risk assessment

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

Risk Assessment for mammals

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

The screening step before the real risk assessment as described in the guidance based on indicator species level will be omitted.

Mammalian generic focal species for Tier 1 risk assessment

The product Iprovalicarb + Folpet WG 65.3 is intended to be used in grapes with four applications of 2.4 kg product/ha corresponding to 0.216 kg iprovalicarb/ha and 1.3512 kg folpet/ha at BBCH 15-85 with a minimum interval of 10 days. This is an artificial GAP that provides a risk envelope for the intended uses.

Folpet is a 3rd party substance procured from [redacted]. Bayer CropScience AG is using a risk envelope approach for the risk assessment of the representative formulation. Within the scope of this supplementary dossier, up to 4 applications at 1.35 kg/ha folpet are proposed as a safe use in grapes. This is much below the critical GAP that [redacted] currently defends in this crop in the EU, where 10 applications of up to 1.6 kg/ha have been approved, with all other parameters such as interval between applications or pre-harvest interval being identical or very similar. Therefore, Bayer CropScience AG considers it justified to refer to folpet data owned by [redacted] wherever appropriate. A folpet-specific risk assessment is not considered necessary to defend the Annex I listing of iprovalicarb.

According to the EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009) the following generic focal species have to be addressed in Tier 1 risk assessment.

Table 10.3- 5: Relevant generic mammalian focal species for Tier 1 risk assessment

Crop	Growth stage (BBCH)	Generic focal species	Representative species	Shortcut value	
				For long-term RA based on RUD mean	For acute RA based on RUD 90th perc.
Vineyard	10-19	Large herbivorous mammal “lagomorph”	Brown hare	**6.7**	**16.3**
Vineyard	20-39	Large herbivorous mammal “lagomorph”	Brown hare	5.5	13.6
Vineyard	≥ 40	Large herbivorous mammal “lagomorph”	Brown hare	3.3	8.1
Vineyard	10-19	Small insectivorous mammal “shrew”	Common shrew	**4.2**	**7.6**
Vineyard	≥ 20	Small insectivorous mammal “shrew”	Common shrew	1.9	5.4
Vineyard	10-19	Small herbivorous mammal “vole”	Common vole	**43.4**	**81.9**
Vineyard	20-39	Small herbivorous mammal “vole”	Common vole	36.1	68.2
Vineyard	≥ 40	Small herbivorous mammal “vole”	Common vole	21.7	40.9
Vineyard	10-19	Small omnivorous mammal “mouse”	Wood mouse	**4.7**	**10.3**
Vineyard	20-39	Small omnivorous mammal “mouse”	Wood mouse	3.9	8.6
Vineyard	≥ 40	Small omnivorous mammal “mouse”	Wood mouse	2.3	5.2

Bold values: reference unit doses that constitute the worst case exposure of a species. Subsequent risk assessments are presented for worst cases only.

IIIA 10.3.1 Toxicity exposure ratios for terrestrial vertebrates other than birds

Summary of calculated TER values for mammals

Table 10.3.1-1: Summary of TER values for acute toxicity

Crop (BBCH)	Generic focal species	Compound	SV_{90}	TER_A	Refinement
Vineyard (10-19)	Large herbivorous mammal "lagomorph"	Iprovalicarb	16.3	943	no
Vineyard (10-19)	Small insectivorous mammal "shrew"		7.6	> 2000	no
Vineyard (10-19)	Small herbivorous mammal "vole"		81.9	> 189	no
Vineyard (10-19)	Small omnivorous mammal "mouse"		10.3	> 1515	no
Vineyard (10-19)	Large herbivorous mammal "lagomorph"	M10	16.3	57	no
Vineyard (10-19)	Small insectivorous mammal "shrew"		7.6	120	no
Vineyard (10-19)	Small herbivorous mammal "vole"		81.9	11	no
Vineyard (10-19)	Small omnivorous mammal "mouse"		10.3	91	no

Table 10.3.1-2: Summary of TER values for long-term toxicity

Crop (BBCH)	Generic focal species	Compound	SV_m	TER_{LT}	Refinement
Vineyard (10-19)	Large herbivorous mammal "lagomorph"	Iprovalicarb	6.7	98	no
Vineyard (10-19)	Small insectivorous mammal "shrew"		4.2	163	no
Vineyard (10-19)	Small herbivorous mammal "vole"		43.4	16	no
Vineyard (10-19)	Small omnivorous mammal "mouse"		4.7	146.3	no

Conclusion: According to the presented risk assessment, the risk to mammals from the use of the product in grapes is acceptable.

IIIA 10.3.1.1 Acute toxicity exposure ratio (TER_A)

Tier 1 acute toxicity exposure ratio for mammals

The tier 1 risk assessment has been performed for grapes for an application rate of 4 × 0.216 kg iprovalicarb/ha at a minimum application interval of 10 days.

Table 10.3.1.1- 1: Tier 1 acute TER calculation for mammals

Crop	Generic focal species	LD_{50} [mg/kg bw]	DDD			DDD	TER_A	Trigger
			Appl. rate [kg/ha]	SV_{90}	MAF_{90}			
Iprovalicarb								
Grapes	Large herbivorous mammal "lagomorph"	> 5000	0.216	16.3	1.5	5.3	> 943	10
	Small insectivorous mammal "shrew"			7.6		2.5	> 2000	
	Small herbivorous mammal "vole"			81.9		26.5	> 189	
	Small omnivorous mammal "mouse"			10.3		3.3	> 1515	
M10								
Grapes	Large herbivorous mammal "lagomorph"	300	0.216	16.3	1.5	5.3	57	10
	Small insectivorous mammal "shrew"			7.6		2.5	120	
	Small herbivorous mammal "vole"			81.9		26.5	11	
	Small omnivorous mammal "mouse"			10.3		3.3	91	

All TER values are above the trigger of 10 for acute exposure. Accordingly an unacceptable acute risk to mammals from the use of the product according to the use pattern can be excluded.

Acute risk assessment for mammals drinking contaminated water

For further details, reference is made to Point 10.1.1 of this dossier. However, according to EFSA Guidance Document for Birds and Mammals (2009), unlike for birds the scenario of pools formed in leaf axils is not relevant for mammals. Therefore the risk assessment for mammals is limited to the scenario of puddles formed on the ground after application.

The acute risk from water in puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil is covered by the long-term risk assessment under Point 10.3.1.3 of this dossier.

IIIA 10.3.1.2 Short-term toxicity exposure ratio (TER_{ST})

Not required under Directive 91/414/EEC.

IIIA 10.3.1.3 Long-term toxicity exposure ratio (TER_{LT})

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

The tier 1 risk assessment has been performed for grapes for an application rate of 4 × 0.216 kg iprovalicarb/ha at a minimum application interval of 10 days.

Table 10.3.1.3- 1: Tier 1 long-term TER calculation for mammals

Crop	Generic focal species	NO(A)EL [mg/kg bw/d]	DDD				DDD	TER_{LT}	Trigger
			Appl. Rate [kg/ha]	SV_m	MAF_m	f_{ma}			
Iprovalicarb									
Grapes	Large herbivorous mammal "lagomorph"	146.3	0.216	6.7	1.9	0.53	1.5	98	5
	Small insectivorous mammal "shrew"			4.2			0.9	163	
	Small herbivorous mammal "vole"			43.4			9.4	16	
	Small omnivorous mammal "mouse"			4.7			1.0	146.3	

All TER values are above the trigger of 5 for the long-term exposure. Accordingly an unacceptable acute risk to mammals from the use of the product according to the use pattern can be excluded.

Long-term risk assessment for mammals drinking contaminated water

For further details, reference is made to Point 10.1.1 of this dossier.

Table 10.3.1.3- 2: Evaluation of potential concern for exposure via drinking water of mammals (escape clause)

Compound	Koc [L/kg]	Application rate * MAF [g as/ha]	NO(A)EL [mg as/ kg bw/d]	Ratio (Application rate * MAF) / NO(A)EL	"Escape clause" No concern if ratio	Conclusion
Iprovalicarb	113.9	216 × 1.9	146.3	2.8	≤ 50	No concern

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

IIIA 10.3.2 Effects on terrestrial vertebrates other than birds

IIIA 10.3.2.1 Acute oral toxicity of the preparation

The findings of an acute oral study with the formulation with rat are summarised in the following table:

Table 10.3.2.1- 1:Mammalian toxicity data of the formulated product Iprovalicarb + Folpet WG 65.3

Test species	Test design	Ecotoxicological endpoint			Reference
Rat	acute, oral	LD_{50}	> 2500	mg/kg bw	[redacted] (2000) 30395 M-026075-01-1 KIIIA 7.7.1/01

A comparison of the acute endpoints of the formulation Iprovalicarb + Folpet WG 65.3 derived from a

study on rats with calculated theoretical endpoints (calculated according to Finney's formula GIFAP, 1990) is shown in Table 10.3.2.1- 2.

Table 10.3.2.1- 2: Comparison of acute toxicity: active ingredients vs. formulation

Species	iprovalicarb 9% + folpet 56.3%	Iprovalicarb + Folpet WG 65.3
	Calculated [mg product/kg]	Study results [mg product/kg]
Mammal (Rat)	3339 [1]	LD_{50} > 2500

1 based on: iprovalicarb – LD_{50} > 5000 mg/kg bw; folpet – LD_{50} > 2000 mg/kg bw

The comparison of results of this testing with the results of mixed toxicity calculation according to Finney showed that the preparation can be expected to be not more toxic than on its active ingredient content base.
Thus a risk assessment based on the product would not change the conclusion derived from the risk assessment based on the individual active substances and is therefore omitted.

IIIA 10.3.2.2 Acceptance of bait, granules or treated seed

Not applicable for spray application.

IIIA 10.3.2.3 Effects of secondary poisoning

The octanol/water partition coefficients (Log P_{ow}) for iprovalicarb have been determined as 3.18 (Diastereomer A) and 3.20 (Diastereomer B), so iprovalicarb will be evaluated for potential effects of secondary poisoning of mammals. For details please refer to IIIA 10.1.9.

Risk assessment for bioaccumulation and food chain behaviour for mammals

The risk assessment procedure for wild mammals follows the same principles as described in detail under Point 10.1.9 for birds, i.e. EFSA Guidance Document on Risk Assessment for Birds & Mammals (2009).

Mammalian generic focal species for Tier 1 risk assessment

According to the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) the following generic focal species have to be addressed in the Tier 1 risk assessment.

Table 10.3.2.3- 1: Mammalian generic focal species for the Tier 1 risk assessment of secondary poisoning

Generic focal species	Body weight [g]	Example	FIR/bw
Earthworm eater	100	Common shrew	1.28
Fish eater	1000	Otter	0.142

Long-term TER calculation for earthworm-eating mammals

Table 10.3.2.3- 2: Tier 1 long-term TER calculation for earthworm-eating mammals

Compound	Iprovalicarb	Origin of value
PEC_{worm} [mg/kg]	3.064	Table 10.3.9- 2
DDD calculation:		
FIR/bw	1.28	Default
DDD [mg/kg bw/d]	3.92	
TER_{LT} calculation:		
NO(A)EL [mg/kg bw/d]	146.3	IIIA 10.3
TER_{LT}	37	
Trigger	5	
Refined risk assessment required?	No	

The TER value is above the trigger of 5. Accordingly an unacceptable risk to earthworm-eating mammals from the use of the product according to the proposed use pattern can be excluded.

Long-term toxicity exposure ratio for fish-eating mammals

Table 10.3.2.3- 3: Tier 1 long-term TER calculation for fish-eating mammals

Compound	Iprovalicarb	Origin of value
PEC_{fish} [mg/kg]	0.028	Table 10.3.9- 3
DDD calculation:		
FIR/bw	0.142	Default
DDD [mg/kg bw/d]	0.004	
TER calculation:		
NO(A)EL [mg/kg bw/d]	146.3	IIIA 10.3
TER_{LT}	36575	
Trigger	5	
Refined risk assessment required?	No	

The TER value is above the trigger of 5. Accordingly an unacceptable risk to fish-eating mammals from the use of the product according to the proposed use pattern can be excluded.

IIIA 10.3.3 Supervised cage or field trials or other appropriate studies

The risk assessment based on the active substances indicates acceptable acute and long-term risks to mammals (see Points 10.3.1.1 and 10.3.1.3 of this dossier). For this reason and also considering animal welfare, no supervised cage or field study with the preparation was deemed necessary.

IIIA 10.4 Effects on bees

Studies on effects on bees are available for the product Iprovalicarb + Folpet WG 65.3 and the active substances iprovalicarb and folpet. The results are summarised in the following table.

Table 10.4- 1: Acute toxicity to honey bees

Test species	Test design	Ecotoxicological endpoint	Reference
Iprovalicarb			
Honey bee	acute, 48 h oral acute, 48 h contact	LD_{50} > 199 µg a.s./bee LD_{50} > 200 µg a.s./bee	[redacted] (1995) 95 10 48 061 M-000086-01-1 IIA 8.7.1/01 (EU point IIA, 8.3.1.1/01)
Folpet			
Honey bee	acute, 48 h oral acute, 48 h contact	LD_{50} > 236 µg a.s./bee LD_{50} > 200 µg a.s./bee	See list of endpoints (EFSA Scientific Report 2006)
Iprovalicarb + Folpet WG 65.3			
Honey bee	acute, 48 h oral acute, 48 h contact	LD_{50} > 213 µg prod./bee LD_{50} > 200 µg prod./bee	[redacted] (2008) 42361035 M-302284-01-1 KIIIA 10.4.2.1/01

IIIA 10.4.1 Hazard Quotients for bees

An indication of hazard (Hazard Quotient Q_H) can be derived according to the EPPO risk assessment scheme, by calculating the ratio between the maximum single application rate (expressed in g or mL/ha) and the lowest laboratory contact and oral LD_{50} (expressed in µg/bee).

Q_{HO} and Q_{HC} resp. = Application rate [g or mL/ha] / LD_{50} oral or LD_{50} contact [µg/bee]

Q_H values can be calculated using data from the studies performed with each of the active ingredients and with the formulation. Q_H values higher than 50 are assumed to reflect levels of concern which trigger higher tiered tests for clarification of the risk to honey bees.

The product Iprovalicarb + Folpet WG 65.3 is intended to be used in grapes with four applications of 2400 g product/ha corresponding to 216 g iprovalicarb/ha and 1351.2 g folpet/ha. This application is worst case and covers all other GAP applications.

Folpet is a 3rd party substance procured from [redacted]. ([redacted]). Bayer CropScience AG is using a risk envelope approach for the risk assessment of the representative formulation. Within the scope of this supplementary dossier, up to 4 applications at 1.35 kg/ha folpet are proposed as a safe use in grapes. This is much below the critical GAP that [redacted] currently defends in this crop in the EU, where 10 applications of up to 1.6 kg/ha have been approved, with all other parameters such as interval between applications or pre-harvest interval being identical or very similar. Therefore, Bayer CropScience AG considers it justified to refer to folpet data owned by [redacted] wherever appropriate. A folpet-specific risk assessment is not considered necessary to defend the Annex I listing of iprovalicarb.

IIIA 10.4.1.1 Oral exposure Q_{HO}

Table 10.4.1.1- 1: Hazard quotients for bees – oral exposure

Crop	Exposure route	LD_{50} [µg/bee]	Application rate [g/ha]	Hazard quotient Q_{HO}	Trigger	Refined risk assessment
Iprovalicarb + Folpet WG 65.3						
Grapes	Oral	> 213	2400	< 11.3	50	No
Iprovalicarb						
Grapes	oral	> 199	216	< 1.1	50	No

The hazard quotient for oral exposure is below the trigger of concern (Q_{HO} < 50). Therefore, no unacceptable risk to bees is expected using the product according to the proposed use pattern.

IIIA 10.4.1.2 Contact exposure Q_{HC}

Table 10.4.1.2- 1: Hazard quotients for bees – contact exposure

Crop	Exposure route	LD_{50} [µg/bee]	Application rate [g/ha]	Hazard quotient Q_{HC}	Trigger	Refined risk assessment
Iprovalicarb + Folpet WG 65.3						
Grapes	contact	> 200	2400	12	50	No
Iprovalicarb						
Grapes	contact	> 200	216	< 1.1	50	No

The hazard quotient for contact exposure is below the trigger of concern (Q_{HC} < 50). Therefore, no unacceptable risk to bees is expected using the product according to the proposed use pattern.

IIIA 10.4.2 Acute toxicity of the preparation to bees

IIIA 10.4.2.1 Acute oral toxicity

Report:	**KIIIA 10.4.2.1/01; [redacted]; 2008**
Title:	Effects of Folpet + Iprovalicarb WG 9 + 56.3 % w/w (Acute Contact and Oral) on Honey Bees (*Apis mellifera* L.) in the Laboratory
Document No:	M-502284-01-1 (Report No: 42361035)
Guidelines:	OECD Guideline 213 and 214 (1998)
GLP	Yes (certified laboratory)

Executive Summary:

The aim of the study was to determine the effects of Folpet + Iprovalicarb WG 9 + 56.3% w/w on the mortality of the honeybee (*Apis mellifera*) after contact and oral exposure. For the assessment of contact toxicity, 50 worker bees per treatment were exposed for 48 hours to a single dose of 200 µg product per bee for topical application as a single 5µL droplet to the thorax (contact limit test). There was no mortality in the study and the LD_{50} (48h) was 200 µg product/bee in the contact toxicity test. For the assessment of oral toxicity, 5 replicates each consisting of 10 bees in which 50 worker bees were exposed for 48 hours to a single dose of 200 µg product per bee for feeding (oral limit test, value based on the actual intake of the test item). Mortality was used to determine the endpoints. There was no mortality in the study and the 48-hour LD_{50} was >213 µg a.i./bee. Dimethoate was included as the referenced item and the contact and oral LD_{50} (48h) values were calculated to be 0.17 and 0.12 µg a.i./bee, respectively.

Objective:
Honey bees (*A. mellifera*) can be affected by pesticide residues as a result of indirect contact on plant surfaces, via oral intake of contaminated food or water, via inhalation of vapour or by direct overspray in the course of an application in the field according to normal agricultural practice. If the proposed use pattern of Folpet + Iprovalicarb WG 9 + 56.3% w/w indicates such a possible exposure of honey bees, acute contact and oral toxicity data is necessary for the registration of the pesticide use in question. This study provides:

- the acute toxicity levels of the formulated test item and the corresponding toxicity levels of its active ingredients to honeybees;
- toxicity information comparable to expected residues from standard rates, for assessment of the potential hazard to honey bees;
- information to support precautionary label statements;
- information to indicate the need for further testing e.g. semi-field or field studies.

Material and methods:

Test item	A WG formulation of Folpet + Iprovalicarb WG 56.3+9A W
Specification No.:	102000011659;
TOX-No.:	TOX08081-00;
Batch ID.:	EM20002600;
content of a.s. (analysed):	Folpet (SR-407) 54.9 %w/w Iprovalicarb (SZX 0722) 9.00 %w/w
	date of completed analysis: 11 OCT 2007, BCS-D-FT Analysis & Services, D- [redacted]

Reference Item

Name	Dimethoate product
Batch No.:	1814
Formulation:	Perfekthion EC (BAS 152 11 I)
Active ingredient/content:	Dimethoate 400 g/L

Test Species
Honeybees (*Apis mellifera* carnica): female worker bees collected from local hives.

Test Design
Folpet + Iprovalicarb WG 9 + 56.3% w/w (Iprovalicarb (SZX 0722) 9.00 % w/w, folpet (SR-407) 54.9 % w/w analytical), Specification: Batch ID.: EM20002600; under laboratory conditions *Apis mellifera* (50 worker bees per dose) were exposed for 48 hours to a single dose of 213.0 µg product per bee for feeding (oral value based on the actual intake of the test item) and for topical application (contact) with a single dose of 200.0 µg product per bee.

Test Conditions
Temperature: 25°C; relative humidity: 38% - 58%; darkness (except during observation)

Validity Criteria:
The control mortality should not exceed 10% at test end.
The 24h LD_{50} of the reference item (dimethoate) should be within the range of 0.10 - 0.30 µg a.i./bee (contact test) and 0.10 - 0.35 µg a.i./bee (oral test)
The following table summarises the validity of the study:

Control Mortality:	Contact Test CO_2/water control:	 0.0 %
	Oral Test Water/sugar control:	 0.0 %
LD_{50} of Reference Item (24 hrs):	Contact Test:	0.17 µg a.i./bee
	Oral Test:	0.12 µg a.i./bee
Validity of the Tests:	The contact and oral test are considered valid as the control mortality in each case was < 10% and the LD_{50} values obtained with the reference item (dimethoate), were within the required ranges.	

Findings:

Toxicity to Honey Bees; laboratory test

Test Item	Folpet + Iprovalicarb WG 9 + 56.3 % w/w	
Test object	*Apis mellifera*	
Application rate µg product/bee	213.0	200.0
Exposure	oral (sugar solution)	contact (solution in Adhäsit (0.5 %)/water)
LD_{50} µg product/bee	> 213.0	> 200.0

Observations

At the end of the contact toxicity test (48 hours after application), there was 0.0 % mortality at 200.0 µg product/bee. No mortality occurred in the control (water + 0.5 % Adhäsit).

In the oral toxicity test the maximum nominal test level of Folpet + Iprovalicarb WG 9 + 56.3 % w/w (200 µg product/bee) corresponded to an actual intake of 213.0 µg product/bee. This dose level led to no mortality after 48 hours. No mortality occurred in the control (50 % sugar solution).

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

Conclusion

The toxicity of Folpet + Iprovalicarb WG 9 + 56.3% w/w was tested in both an acute contact and an oral toxicity test on honey bees. The LD_{50} (48 h) was >200.0 µg product/bee in the contact toxicity test. The LD_{50} (48 h) was > 213.0 µg product/bee in the oral toxicity test.

IIIA 10.4.2.2 Acute contact toxicity

Please refer to point Point 10.4.2.1.

IIIA 10.4.3 Effects on bees of residues on crops

In view of the findings reported under 10.4.1 and 10.4.2, and based on the requirements of Directive 91/414/EEC (Annex III, Point 10), no further studies are required. The Q_{HC} value is <50.

IIIA 10.4.4 Cage tests

Please refer to point Point 10.4.3.

IIIA 10.4.5 Field tests

Please refer to point Point 10.4.3.

IIIA 10.4.6 Investigation of special effects

Please refer to point Point 10.4.3.

IIIA 10.4.6.1 Larval toxicity

Please refer to point Point 10.4.3.

IIIA 10.4.6.2 Long residual effects

Please refer to point Point 10.4.3.

IIIA 10.4.6.3 Disorienting effects on bees

Please refer to point Point 10.4.3.

IIIA 10.4.7 Tunnel tests - effects of feeding on contaminated honey dew or flowers

Please refer to point Point 10.4.3.

IIIA 10.5 Effects on arthropods other than bees

Toxicity tests on non-target arthropods have been carried out with Iprovalicarb + Folpet WG 65.3 on the two indicator species *Typhlodromus pyri* and *Aphidius rhopalosiphi*. Further studies have been conducted on two additional species, *Coccinella septempunctata* and *Chrysoperla carnea*. A summary of the results is provided in Table 10.5- 1.

Table 10.5- 1: Iprovalicarb & Folpet WP 65.3: Ecotoxicological endpoints for arthropods other than bees

Test species, Dossier-file-No., reference	Tested Formulation, study type, exposure	Ecotoxicological Endpoint
Aphidius rhopalosiphi M-065136-01-1 Rep.No: 20021105/01-NLAp [redacted].; 2002 KIIIA 10.5.1/01	IPV + FLP WG 65.3 Laboratory, glass plates	
	0.725 kg prod./ha	Corr. Mortality [%]: 0 Effect on Reproduction [%]: 37.1
	10.50 kg prod./ha	Corr. Mortality [%]: 17.5 Effect on Reproduction [%]: 33.3
Aphidius rhopalosiphi M-071277-02-1 Rep.No: 14871002 [redacted]; 2003 KIIIA 10.5.2/01	IPV + FLP WG 65.3 Extended lab., exposure on potted barley plants	LR_{50} [kg prod./ha]: 1.964 Corr. Mortality [%] / Effect on Reproduction [%] / Repellency rel. to control [%]
	0.325 kg prod./ha	0.0 / 11.1 / -19.6 [A]
	0.725 kg prod./ha	16.7 / 70.6 / -18.8 [A]
	1.80 kg prod./ha	53.3 / n.a. / -19.6 [A]
	4.80 kg prod./ha	80.0 / n.a. / 9.2
	10.50 kg prod./ha	86.7 / n.a. / 1.5
Aphidius rhopalosiphi M-311332-01-1 Rep.No.: CW08/048 [redacted]2008 KIIIA 10.5.3/01	IPV + FLP WG 65.3 Aged residues, spray deposits on potted maize plants, 1 appl. of 5.1 kg prod./ha	Corr. Mortality [%] / Effect on Reproduction [%] / Repellency rel. to control [%]
	Residues aged for 0 days:	0 / 3.6 / 2.6 n.sign.
	Residues aged for 7days:	3.3 / n.a. / 8.7 n.sign.
Aphidius rhopalosiphi M-391612-01-1 Rep.No.: S10-02746 [redacted], 2010 KIIIA 10.5.3/02	IPV + FLP WG 65.3 Semi-field, spray deposits on barley plants 5.1 kg prod./ha	Effect on Reproduction [%] 23.2
Typhlodromus pyri M-066828-01-1 Rep.No.: 20021105/01-NLTp [redacted].; 2002 KIIIA 10.5.1/02	IPV + FLP WG 65.3 Laboratory, glass plates	Corr. Mortality [%] / Effect on Reproduction [%]
	6.9 kg prod./ha	2.1 / 18.6
	10.5 kg prod./ha	-1.0 [B] / 14.2
Typhlodromus pyri M-296923-01-1 Rep.No.: CW 07/064 [redacted]2008 KIIIA 10.5.2/02	IPV + FLP WG 65.3 Extended lab., spray deposits on detached bean leaves	LD_{50} [kg prod./ha]: > 8.5 Corr. Mortality [%] / Effect on Reproduction [%]
	0.5 kg prod./ha	-1.1 [B] / 11.2
	1.015 kg prod./ha	-8.9 [B] / -19.1 [C]
	2.062 kg prod./ha	-4.4 [B] / 13.4
	4.186 kg prod./ha	-8.9 [B] / 12.1
	8.5 kg prod./ha	1.1 / 8.4

Test species, Dossier-file-No., reference	Tested Formulation, study type, exposure	Ecotoxicological Endpoint		
Typhlodromus pyri M-073796-01-1 Rep.No.: 02 10 48 057 [redacted]2002 KIIIA 10.5.3/03	IPV + FLP WG 65.3 Aged residues, spray deposits on potted wine plants, 1 appl. of 5.42 kg prod./ha Residues aged for 0 days: Residues aged for 7 days: Residues aged for 14 days:	Corr. Mortality [%] 48.5 14.0 1.0	Effect on Reproduction [%] n.a. 9.2 0.5	
Coccinella septempunctata M-295911-01-1 Rep.No.: CW 07/065 [redacted]2008 KIIIA 10.5.2/03	IPV + FLP WG 65.3 Extended lab., spray deposits on detached bean leaves	LD_{50} [kg prod./ha]: > 8.5 Corr. Mortality [%]	Fertile eggs/Female/Day	
	Control	-	13.9	
	0.5 kg prod./ha	41.4	22.6	
	1.015 kg prod./ha	3.4	15	
	2.062 kg prod./ha	10.3	16.2	
	4.186 kg prod./ha	-10.3 [B]	19.8	
	8.5 kg prod./ha	0.0	10.2	
Chrysoperla carnea M-295914-01-1 Rep.No.: CW07/066 [redacted]2008 KIIIA 10.5.2/04	IPV + FLP WG 65.3 Extended lab., spray deposits on detached bean leaves	LD_{50} [kg prod./ha]: > 8.5 Corr. Mortality [%]	Eggs/Female/Day	Hatching [%]
	Control	-	17.2	74.3
	0.5 kg prod./ha	-2.9 [B]	10.3	68.1
	1.015 kg prod./ha	-2.9 [B]	12.2	71.6
	2.062 kg prod./ha	5.7	16.8	79.1
	4.186 kg prod./ha	-5.7 [B]	13.3	70
	8.5 kg prod./ha	2.9	18	74.5

A: A negative value indicates a higher percentage of wasps found on plants in the treatment than in the control.
B: A negative value indicates a higher mortality rate in the control than in the treatment.
C: A negative value indicates a higher reproduction rate in the treatment than in the control.
n.a.: not assessed
n.sign: not statistically significant at 5% level

Risk assessment procedures

The risk assessment was performed according to Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002) and to the Guidance Document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods (ESCORT 2, Candolfi et al. 2000[3]).

As data from Tier 2 tests for 4 species are available for the product the Tier 1 risk assessment was skipped and a Tier 2 risk assessment was conducted.

Potential exposure

The exposure scenario is based on the use pattern as given in Table 10- 1. Iprovalicarb + Folpet WG

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

65.3 is intended to be applied four times with an application rate of 2.4 kg product/ha in grapes. This application is worst case and covers all other GAP applications.

According to ESCORT2 and the Terrestrial Guidance Document the exposure is calculated as:
in-field: Application rate x MAF x 0.5 [4]
off-field: Application rate x MAF x (drift factor / VDF) x correction factor

- Application rate: 2.4 kg product/ha (grapes)
- Drift factor = 6.71% (74th percentile for four applications in grapes, late; ESCORT2)
- MAF (multiple application factor) = 2.7
- VDF (vegetation distribution factor) = 10 (default value as recommended by the Terrestrial Guidance Document, to take into account the 3-dimensional structure of the off-field vegetation; it can only be applied in the context of 2D-test systems)
- A correction factor is intended to cover uncertainty with regard to species sensitivity in the off-crop scenario. As proposed by the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002) a default value of 5 is used in the Tier 2 risk assessment.

Table 10.5-2: Exposure calculation for in-field risk assessment

Crop / no. of applications	Appl. rate [kg/ha]	Corr. factor (high crops) [4]	MAF	in-field PEC_{max}. [kg/ha]
Grapes / 4	2.4	0.5	2.7	3.24

Table 10.5- 3: Corrected exposure for off-field risk assessment

Crop	Application rate [kg/ha]	MAF	Drift [%]	Veg. distr. factor	Correction factor	off-field PEC_{max} [kg/ha]	Remark
Grapes	2.4	2.7	6.71	10	5	0.22	in case of 2-D study design
Grapes	2.4	2.7	6.71	-	5	2.17	in case of 3-D study design

[4] Correction factor of 0.5 for the in-field exposure assessment in high crops according to ESCORT2 (see footnote "a" in legend on page 19 of the ESCORT2 document)

In-field risk assessment

Table 10.5- 4: In-field risk assessment based on study results from Iprovalicarb + Folpet WG 65.3

Crop	Species	in-field PEC_{max} [kg prod./ha]	LR_{50} or ER_{50} [kg prod./ha]	Risk acceptable if:	Refined assessment required?
Grapes	*Aphidius rhopalosiphi*	3.24	> 0.325	Effects are < 50%	Yes
	Typhlodromus pyri	3.24	> 8.5	Effects are < 50%	No
	Coccinella septempunctata	3.24	> 8.5	Effects are < 50%	No
	Chrysoperla carnea	3.24	> 8.5	Effects are < 50%	No

The higher tier in-field risk assessment for *Typhlodromus*, *Coccinella* and *Chrysoperla* indicates that no unacceptable adverse effects are to be expected in the in-field area for arthropod species with a similar sensitivity as these species. The in-field risk assessment for *Aphidius rhopalosiphi* indicates that initial effects in the in-field area can not be excluded. Therefore, a further refinement is needed.

Refined in-field risk assessment

The results of the tier 2 risk assessment indicated that initial effects on species with a sensitivity like *Aphidius rhopalosiphi* can not be excluded. As a consequence, an aged residue study and a semi-field study were performed to demonstrate the potential for recovery for *Aphidius rhopalosiphi*, the most sensitive tested species.

An extended laboratory aged residue study has been performed on *Aphidius rhopalosiphi* ([redacted], 2008; M-311332-01-1, KIIIA 10.5.3/01). In this study, Iprovalicarb + Folpet WG 65.3 was applied once at a rate of 5.1 kg product/ha on potted maize plants. Spray residues were aged under semi-field conditions. Bioassays with freshly dried residues and residues aged for 7 days resulted in a corrected mortality of 0% and 3.3%, respectively. Reproduction of *A. rhopalosiphi* was tested in the first bioassay with freshly dried residues. No negative effects on reproduction were observed. In both bioassays the test item showed no repellent effects.
Additionally, a semi-field study was performed on *Aphidius rhopalosiphi* ([redacted], 2010; M-391612-01-1, KIIIA 10.5.3/02) to further assess the effects of Iprovalicarb + Folpet WG 65.3 under more realistic conditions. Females wasps were exposed to barley plants which had been treated with Iprovalicarb + Folpet WG 65.3 at an application rate of 5.1 kg product/ha for 48 hours. Afterwards, the reproductive capacity of the treated wasps was assessed. No adverse effects on the reproduction of *Aphidius rhopalosiphi* were observed.

These two studies indicate that no unacceptable effects (>50%) on mortality or reproduction of the most sensitive species *Aphidius rhopalosiphi* are to be expected after an application of 5.1 kg product/ha. Since the intended use pattern results in an in-field PEC_{max} of only 3.24 kg product/ha, it can be concluded that no unacceptable in-field risk for non-target arthropods has to be expected from the use of Iprovalicarb + Folpet WG 65.3 according to the proposed use pattern.

Off-field risk assessment

Table 10.5- 5: Off-field risk assessment based on study results from Iprovalicarb + Folpet WG 65.3

Crop	Species	off-field PEC_{max} [kg prod./ha]	LR_{50} or ER_{50} [kg prod./ha]	Risk acceptable if:	Refined assessment required?
Grapes	*Aphidius rhopalosiphi*	2.17	< 0.325	Effects are < 50%	Yes
	Typhlodromus pyri	0.22	> 8.5	Effects are < 50%	No
	Coccinella septempunctata	0.22	> 8.5	Effects are < 50%	No
	Chrysoperla carnea	0.22	> 8.5	Effects are < 50%	No

The off-field PEC is calculated to be 0.22 kg/ha for 2D-test systems and 2.17 kg/ha for 3D-test systems. For *Typhlodromus pyri*, *Coccinella septempunctata,* and *Chrysoperla carnea* there are no effects > 50% neither on mortality nor on reproduction at the expected off-field exposure rates. The off-field risk assessment for *Aphidius rhopalosiphi* indicates that initial effects in the off-field area can not be excluded. Therefore, a further refinement is needed.

Refined off-field risk assessment

For the most sensitive species *Aphidius rhopalosiphi*, effects on reproduction > 50% were observed in an extended laboratory study at rates exceeding 0.325 kg product/ha, which is lower than the off-field PEC_{max} of 2.17 kg product/ha for 3D test systems. Therefore, a semi-field study ([redacted], 2010; M-391612-01-1, KIIIA 10.5.3/02) was performed to test for effects Iprovalicarb + Folpet WG 65.3 under more realistic conditions (see in-field risk assessment above). In this study, an application of 5.1 kg product/ha did not lead to adverse effects on the reproduction of *A. rhopalosiphi*. In addition, an aged residue study on *A. rhopalosiphi* ([redacted], 2008; M-311332-01-1, KIIIA 10.5.3/01) showed that already in the first bioassay with freshly dried residues no adverse effects on mortality or reproduction occurred. Therefore, it can be concluded that at an application rate of 5.1 kg product/ha, which clearly exceeds the off-field PEC_{max} of 2.17 kg, no unacceptable off-field risk for non-target arthropods has to be expected.

Conclusion

Based on the provided risk assessment it can be concluded that the application of Iprovalicarb + Folpet WG 65.3 according to the proposed use pattern does not result in unacceptable adverse effects on NTA species in the in-field or the off-field area.

IIIA 10.5.1 Effects on sensitive species already tested, artificial substrates

Report:	**KIIIA 10.5.1/01, [redacted] 2002**
Title:	Folpet + Iprovalicarb WG 65.25: Acute Toxicity to the Aphid Parasitoid, *Aphidius rhopalosiphi* DeStefani Perez (Hymenoptera, Braconidae) in the Laboratory
Document No:	M-065136-01-1 (20021105/01-NLAp)
Guidelines:	IOBC guideline Mead-Briggs et al (2000)
GLP:	Yes

Materials and methods:
Folpet + Iprovalicarb WG 65.25 (Batch No. 07373/0048(0046), Article No. 00-05539447, Sample No. TOX05905-00, purity: 9.8 % Iprovalicarb and 55.7 % Folpet was diluted in water and applied with a spray application volume of 200 L water/ha to glass plates at rates equivalent to 0.725 kg product/ha and 10.50 kg product/ha. When dry, the glass plates (length of edges: 13 cm) were used to form the floor and the ceiling (treated surfaces inwards) of shallow arenas into which adult wasps were introduced. 10 wasps of equal sex ratio were placed into each exposure unit (n = 6 per treatment). Deionized water was applied as control (200 L/ha) and Perfekthion (content of a.i.: 417.5 g/L) was applied at 0.30 mL product/200 L water/ha as a toxic reference treatment. Assessments of direct treatment effects were made after 0.5, 2, 24 and 48 h. To assess any impact on the fecundity of surviving individuals, 15 females from the control group and also from the two test substance treatment groups were taken after 48 h and confined individually over aphid-infested barley plants for a further 24 h period. The numbers of parasitised aphids that developed was recorded 10 days later.
The mortality of the toxic standard group was 100%.

Findings:

Test substance	Folpet + Iprovalicarb WG 65.25			
Test object	*Aphidius rhopalosiphi*			
Exposure	Glass plates			
Application	Mortality* after 48 h [%]		Fecundity (mummies/female)	
Control	0		26.40	
Application rate	Mortality* after 48 h [%]	Corrected mortality* after 48 h [%]	mummies/ female	Reproduction relative to the control [%]
0.725 kg product/ha	0.0	0.0	16.60 (2)	62.88
10.50 kg product/ha	17.50 (1)	17.50	17.60	66.67

* based on the number of dead organisms
(1): Statistically significantly different from the control (Fisher's Exact Test, $p < 0.05$)
(2): Statistically significantly different from the control (Kruskal-Wallis Test, $p < 0.05$)

Discussion and Conclusions:
The results of the control group indicate that test organisms were in good conditions (0.00 % mortality and 26.40 mummies/female). The results of the toxic reference group indicate that the test system was sensitive to harmful substances (mortality: 100 %).
Statistically significant effects were observed on mortality in the 10.50 kg product/ha treatment group Folpet + Iprovalicarb WG 65.25.

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Report:	**KIHA 10.5.1/02, [redacted] 2002**
Title:	Acute Toxicity to the Predatory Mite, *Typhlodromus pyri* SCHEUTEN (Acari, Phytoseiidae) in the Laboratory
Document No:	M-066828-01-1 (20021105/01-NLTp)
Guidelines:	IOBC (Blümel et al. 2000)
GLP:	Yes

Materials and methods:
Folpet + Iprovalicarb WG 65.25 (Batch No. 07373/0048(0046), Article No. 00-05539447, Sample No. TOX05905-00, purity: 9.8 % Iprovalicarb and 55.7 % Folpet) was diluted in water and applied with a spray application volume of 200 L water/ha to glass plates at rates equivalent to 6.9 kg product/ha and 10.5 kg product/ha. Deionized water was used as control and Perfekthion (analysed content of a.i.: 417.5 g/L) was applied at 12 mL product in 200 L water/ha as a toxic reference treatment.
The test units consist of two glass cover slides. They were fixed together by means of two glass bars which were glued on them in the horizontal direction. In order to prevent the mites from escaping, a non-drying glue gel barrier was set on the glass plates. The glue barrier was formed as a square arena which resulted in an exposure area of approximately 10 - 12 cm^2. After application when residues were dry, the glass plates were placed treated surface upwards on wet filter paper. The thin gap between the two cover slides was filled with water by capillary forces and served as drinking water supply. Twenty protonymphs were placed with a fine-bristled brush onto each replicate unit (units: n = 5 per treatment).
Assessments of direct treatment effects (mortality assessments) were made after 3 and 7 days. The fertility test was conducted with those treatment groups where the corrected mortality was ≤ 50 %. Fecundity assessments were carried out 10, 12 and 14 days after treatment by counting the number of eggs and juveniles present in each test unit and determining the cumulative number of eggs per female.
Corrected mortality in the toxic standard was 89.7 %. For mortality and reproduction of control and test groups, see the table below.

Findings:
Summarised results of the study:

Test substance	Folpet + Iprovalicarb WG 65.25		
Test organism	*Typhlodromus pyri*		
Exposure	glass plates		
Application	Mortality[1] after 7 days [%]	Reproduction [eggs/female]	
Control	3.0	11.3	
Application rate	Corrected mortality[1] after 7 days [%]	Reproductive performance relative to control [%]	Reduction in reproduction relative to control [%]
6.9 kg product/ ha	2.1	81.4	18.6
10.5 kg product/ ha	0.0*	85.8	14.2

[1] Mortality based on the number of dead and missing organisms
* Negative value means that the mortality in the control group was higher as in the test group

Conclusions:
Up to the 10.5 kg product/ha application rate no statistically significant effects neither on mortality nor on fecundity were observed. The reduction in reproduction was below 19 %.
Corrected number of escapees in all treatment groups was below 6.5 % (escape rate in control was 3.0 %).

IIIA 10.5.2 Effects on non-target terrestrial arthropods in ext. laboratory tests

Report:	**KIIIA 10.5.2/01, [redacted].; 2002**
Title:	Effects of Folpet + Iprovalicarb WG 65.25 on the Parasitoid *Aphidius rhopalosiphi*, Extended Laboratory Study - Dose Response Test
Document No:	M-071277-01-1 (14871002)
Guidelines:	IOBC guideline Mead-Briggs et al (2000)
GLP:	Yes

Material and methods:
Folpet + Iprovalicarb WG 65.25 (active ingredients: Folpet, purity: 55.4 %; Iprovalicarb (SZX 0722), purity: 10.0 %; article no.: 0005539447, batch no.: 07373-0048(0046), sample no.: TOX06124-00); under extended laboratory conditions approximately 48 h old adult *Aphidius rhopalosiphi* (5 females per replicate) were exposed to dried spray deposits of 0.325 - 10.5 kg product/ha (diluted in 400 L deionised water/ha) on treated potted barley seedlings (6 replicates per treatment group). Deionised water was used as a control treatment and Perfekthion (8.5 ml product/ha diluted in 400 L deionised water/ha) as a reference treatment. The duration of the mortality part was
48 hours. The reproductive performance of the survivors was examined for another 24 hour period using females from the control and from those test item concentrations where corrected mortality was < 50.0 %. The toxic standard treatment caused 63.3 % corrected mortality.

Findings:
Aphidius rhopalosiphi, extended laboratory testing - dose response test

Test item	Folpet + Iprovalicarb WG 65.25			
Test object	*Aphidius rhopalosiphi*			
Exposure	Barley seedlings			
Treatment	Mortality after 48 h[a] [%]	Corrected mortality after 48 h [%]	Mummies per female[b]	Reduction in reproduction relative to control [%]
Control	0.0	-	37.7	-
0.325 kg product/ha	0.0	0.0	33.5	11.1
0.725 kg product/ha	16.7	16.7	11.1 *	70.6
1.80 kg product/ha	53.3 *	53.3	not assessed	-
4.80 kg product/ha	80.0 *	80.0	not assessed	-
10.5 kg product/ha	86.7 *	86.7	not assessed	-
8.5 ml Perfekthion/ha (Toxic Reference)	63.3 *	63.3	not assessed	-
LR$_{50}$ (CL 95 %)[c]	1.964 kg product/ha (1.413 - 2.731 kg product/ha)			

[a] * = significant; Fisher Exact Test, $\alpha = 0.05$
[b] * = significant; Bonferroni-U-Test, $\alpha = 0.05$
[c] CL = Confidence Limits

Observations:
At 1.80 kg product/ha 1 parasitoid, at 4.80 kg product/ha 2 parasitoids and at 10.5 kg product/ha 1 parasitoid showed behavioural abnormalities (moribund and affected) after 48 hours of exposure. No repellent effect was observed.

Conclusions:
The LR_{50} for mortality is 1.964 kg product/ha with no effects on either mortality or reproduction at 0.325 kg product/ha.

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Report:	**KIIIA 10.5.2/02, [redacted] 2008**
Title:	Toxicity to the predatory mite *Typhlodromus pyri* SCHEUTEN (Acari, Phytoseiidae) using an extended laboratory test Folpet + Iprovalicarb WG 56.3+9A W
Document No:	M-296923-01-1 (CW07064)
Guidelines:	IOBC (Blümel et al. 2000)
GLP:	Yes

Executive Summary:
The objective of this study was to investigate the lethal and sublethal toxicity of Folpet + Iprovalicarb WG 56.3+9A W to the predatory mite *Typhlodromus pyri* when exposed to detached treated leaf surfaces.
Survival and reproduction were determined at the rates of 0.5, 1.015, 2.062, 4.186 and 8.5 kg product/ha applied to detached bean leaves.
No significant dose related effect on mortality and reproduction could be observed. In the highest dose rate of 8.5 kg product/ha test item there was 1.1% corrected mortality. The reduction of reproduction relative to the control was 8.4%. At the lower rates of 0.5, 1.015, 2.062 and 4.186 kg product/ha -1.1, -8.9, -4.4 and -8.9% corrected mortality were found and the reduction of reproduction was 11.2, -19.1, 13.4 and 12.1%.
The figures obtained for the reproduction fulfil the validity criteria of laboratory method using glass plates.
The LD_{50} was estimated to be > 8.5 kg product/ha.

Objective:
The objective of this study was to investigate the lethal and sublethal toxicity of Folpet + Iprovalicarb WG 56.3+9A W to the predatory mite *Typhlodromus pyri* when exposed to detached treated leaf surfaces

Material and methods:
Test item: A WG formulation of Folpet + Iprovalicarb WG 56.3+9A W
Specification No.: 102000011659;
TOX-No.: TOX08081-00;
Batch ID.: EM20002600;
content of a.s. (analysed): Folpet (SR-407) 54.9 %w/w
Iprovalicarb (SZX 0722) 9.00 %w/w

date of completed analysis: 11 OCT 2007, BCS-D-FT Analysis & Services, D- [redacted] Monheim

The test item was applied at rates of 0.5, 1.015, 2.062, 4.186 and 8.5 kg product/ha and the effects were compared to a water treated control. A toxic reference (a.i.: dimethoate) applied at 0.1038 kg product/ ha was included to indicate the relative susceptibility of the test organisms and the test system.
Mortality of 100 protonymphs was assessed 1, 4, 7, 10, 12 and 14 days after exposure by counting the number of living and dead mites. The number of escaped mites was calculated as the difference from the total number exposed.
The reproduction rate of surviving mites was then evaluated over the period of 7-14 days after treatment by counting the total number of offspring (eggs and larvae) produced.

Validity Criteria:

The validity criteria are based on those of the laboratory method with glass plates (BLÜMEL ET AL., 2000).

	Validity criteria	Finding
MortEsc.-rate in the control group on day 7	< 20%	10 %
Average mortality in the reference item	> 50%.	100 %
Average number of eggs/female (calculated as sum of 4 assessment dates – from day 7 on) in the control group	≥ 4	4.3

Findings:
The mortality / escaping rate in the control chambers up to day 7 after treatment was 10.0%. The mean corrected mortality of the nymphs, and the mean reproduction rate of the surviving females exposed to the test item and the toxic reference is given below.

Mortality (7 days after treatment) / Reproduction

		Mortality [%]				Reproduction		
Treatment	kg product / ha	Uncorr.	Corr.	P-Value(*)		Rate	Red. rel. to Control [%]	P-Value(#)
Control	0	10.0	0.0			4.3	0	
Test item	0.5	9.0	-1.1	1.000	n.sign.	3.8	11.2	0.84 n.sign.
Test item	1.015	2.0	-8.9	0.165	n.sign.	5.1	-19.1	0.852 n.sign.
Test item	2.062	6.0	-4.4	1.000	n.sign.	3.7	13.4	0.972 n.sign.
Test item	4.186	2.0	-8.9	0.165	n.sign.	3.8	12.1	0.979 n.sign.
Test item	8.5	11.0	1.1	1.000	n.sign.	3.9	8.4	0.997 n.sign.
Reference item	0.1038	100.0	100.0			n.d.	n.d.	

LD_{50}: > 8.5 kg product/ha
* Fisher`s Exact test, two-sided, p-values are adjusted according to Bonferroni-Holm
# one-way ANOVA, p-values are adjusted according to Dunnett
n.d. not detected
n.sign. not significant
sign. significant

No significant dose related effect on mortality and reproduction could be observed. In the highest dose rate of 8.5 kg product/ha test item there was 1.1% corrected mortality. The reduction of reproduction relative to the control was 8.4%. At the lower rates of 0.5, 1.015, 2.062 and 4.186 kg product/ha -1.1, -8.9, -4.4 and -8.9% corrected mortality were found and the reduction of reproduction was 11.2, -19.1, 13.4 and 12.1%.
The figures obtained for the reproduction fulfil the validity criteria of laboratory method using glass plates.

Conclusion
The LD_{50} was estimated to be > 8.5 kg product/ha.

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Report:	**KIIIA 10.5.2/03, [redacted] 2008**
Title:	Toxicity to the ladybird beetle *Coccinella septempunctata* L. (Coleoptera, Coccinellidae) using an extended laboratory test Folpet + Iprovalicarb WG 56.3 + 9A W
Document No:	M-295911-01-1 (CW07/065)
Guidelines:	IOBC guideline [redacted] et al (2000)
GLP:	Yes

Executive Summary:
The aim of the study was to determine the toxicity of freshly dried residues of Folpet + Iprovalicarb WG 56.3+9A W applied onto leaves of *Phaseolus vulgaris* to the ladybird beetle *Coccinella septempunctata*.
Survival and reproduction were determined at the rates of 0.5, 1.015, 2.062, 4.186 and 8.5 kg product/ha applied to detached bean leaves.
At the dose rate of 0.5 kg product/ha 41.4% corrected mortality occurred. The dose rates of 1.015, 2.062, 4.186 and 8.5 kg product/ha had no influence on preimaginal mortality. Therefore it can be assumed that the effect at 0.5 kg product/ha was not test item related.
Reproduction was assessed in all rates of Folpet + Iprovalicarb WG 56.3+9A W. The mean number of fertile eggs per female and day was 13.9 in the control and 22.6 and 15, respectively, in the 0.5 and 1.015 kg product/ha rate. At the rates of 2.062, 4.186 and 8.5 kg product/ha rates 16.2, 19.8 and 19.2 fertile eggs per female and day, respectively were found. Because the reproductive performance was within the historical data base for control beetles (≥ 2 fertile eggs per female and day, [redacted] ET AL. 2000) this parameter is considered as not impacted by all test item rates.
The LD_{50} was estimated to be > 8.5 kg product/ha.

Objective:
The aim of the study was to determine the toxicity of freshly dried residues of Folpet + Iprovalicarb WG 56.3+9A W applied onto leaves of *Phaseolus vulgaris* to the ladybird beetle *Coccinella septempunctata*.

Material and methods:

Test item: A WG formulation of Folpet + Iprovalicarb WG 56.3+9A W
Specification No.: 102000011659;
TOX-No.: TOX08081-00;
Batch ID.: EM20002600;
content of a.s. (analysed): Folpet (SR-407) 54.9 %w/w
Iprovalicarb (SZX 0722) 9.00 %w/w
date of completed analysis: 11 OCT 2007, BCS-D-FT Analysis & Services, D- 40789 Monheim

The test item was applied to leaves of *Phaseolus vulgaris* at rates of 0.5, 1.015, 2.062, 4.186 and 8.5 kg product/ha and the effects were compared to a water treated control. A toxic reference (a.i.: dimethoate) applied at 0.0804 kg product/ha was included to indicate the relative susceptibility of the test organisms and the test system.
The preimaginal mortality was monitored over the duration of the study. The toxicity of the test item residues to the larvae and pupae are summarised below.
The fertility and fecundity of the surviving hatched adults were then evaluated over the period of 14 days.

Validity Criteria:
The validity criteria are based on those of the laboratory method with glass plates ([redacted] ET AL., 2000).

	Validity criteria	Finding
Mortality in water control	≤ 30%	27.5%
Corrected mortality reference item	> 40%	96.6%
Mean number of fertile eggs per female and day in water control	≥ 2	13.9

Findings:
Mortality and reproduction in each of the treatments are summarized as follows:

Mortality / Reproduction							
		Mortality [%]				Reproduction	
Treatment	kg product/ha	Uncorr.	Corr.	P-Value(*)		Fertile eggs per female and day	Fertility [hatching rate in %]
Control	0	27.5	0.0			13.9	95
Test item	0.5	57.5	41.4	0.061	n.sign.	22.6	91.8
Test item	1.015	30.0	3.4	1.000	n.sign.	15	89.2
Test item	2.062	35.0	10.3	1.000	n.sign.	16.2	91.9
Test item	4.186	20.0	-10.3	1.000	n.sign.	19.8	92.9
Test item	8.5	27.5	0.0	1.000	n.sign.	19.2	88.7
Reference item	0.0804	97.5	96.6			n.d.	n.d.

Mortality / Reproduction						
		Mortality [%]			Reproduction	
Treatment	kg product/ha	Uncorr.	Corr.	P-Value(*)	Fertile eggs per female and day	Fertility [hatching rate in %]
LD_{50}: > 8.5 kg product/ha						
* Fisher`s Exact test, two-sided, p-values are adjusted according to Bonferroni-Holm						
n.d. not detected						
n.sign. not significant						
sign. significant						

At the dose rate of 0.5 kg product/ha 41.4% corrected mortality occurred. The dose rates of 1.015, 2.062, 4.186 and 8.5 kg product/ha had no influence on preimaginal mortality. Therefore it can be assumed that the effect at 0.5 kg product/ha was not test item related.
Reproduction was assessed in all rates of Folpet + Iprovalicarb WG 56.3+9A W. The mean number of fertile eggs per female and day was 13.9 in the control and 22.6 and 15, respectively, in the 0.5 and 1.015 kg product/ha rate. At the rates of 2.062, 4.186 and 8.5 kg product/ha rates 16.2, 19.8 and 19.2 fertile eggs per female and day, respectively were found. Because the reproductive performance was within the historical data base for control beetles (≥ 2 fertile eggs per female and day, [redacted] ET AL. 2000) this parameter is considered as not impacted by all test item rates.

Conclusion
The LD_{50} was estimated to be > 8.5 kg product/ha.

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Report:	**KIIIA 10.5.2/04, [redacted] 2008**
Title:	Toxicity to the green lacewing *Chrysoperla carnea* Steph. (Neuroptera, Chrysopidae) using an extended laboratory test; Folpet + Iprovalicarb WG 56.3 + 9A W
Document No:	M-295914-01-1 (CW07/066)
Guidelines:	IOBC guideline Vogt et al (2000)
GLP:	Yes

Executive Summary:
The aim of the study was to determine the toxicity of freshly dried residues of Folpet + Iprovalicarb WG 56.3+9A W applied onto bean leaves, to the green lacewing *Chrysoperla carnea*.
The test item was applied to detached bean leaves at rates of 0.5, 1.015, 2.062, 4.186 and 8.5 kg product/ha and the effects were compared to a toxic reference (a.i.: dimethoate) applied at 0.0415 kg product/ha, and a water treated control.
The preimaginal mortality was monitored over the duration of the study. The toxicity of the test item residues to the larvae and pupae are summarised below.
The fertility and fecundity of the surviving hatched adults were then evaluated over the period of one week.
The dose rates of 0.5, 1.015, 2.062, 4.186 and 8.5 kg product/ha had no influence on mortality and reproduction and the LD_{50} was estimated to be > 8.5 kg product/ha.

Objective:
The aim of the study was to determine the toxicity of freshly dried residues of Folpet + Iprovalicarb WG 56.3+9A W applied onto bean leaves, to the green lacewing *Chrysoperla carnea*.

Material and methods:

Test item:	A WG formulation of Folpet + Iprovalicarb WG 56.3+9A W
Specification No.:	102000011659;
TOX-No.:	TOX08081-00;
Batch ID.:	EM20002600;
content of a.s. (analysed):	Folpet (SR-407) 54.9 %w/w
	Iprovalicarb (SZX 0722) 9.00 %w/w
	date of completed analysis: 11 OCT 2007, BCS-D-FT Analysis & Services, D- [redacted]

The test item was applied to detached bean leaves at rates of 0.5, 1.015, 2.062, 4.186 and 8.5 kg product/ha and the effects were compared to a toxic reference (a.i.: dimethoate) applied at 0.0415 kg product/ha, and a water treated control.
The preimaginal mortality was monitored over the duration of the study. The toxicity of the test item residues to the larvae and pupae are summarised below.
The fertility and fecundity of the surviving hatched adults were then evaluated over the period of one week.

Validity Criteria:
The validity criteria are based on those of the laboratory method with glass plates (VOGT ET AL. 2000).

	Validity criteria	Finding
Mortality in water control	≤ 20%	12.5%
Corrected mortality reference item	50 – 100%	57.1%
Mean number of eggs per female and day in water control	≥ 15	17.2
Mean Hatching Rate of the eggs (fertility) in water control	≥ 70%	74.3%

Findings:
Mortality and reproduction in each of the treatments are summarized as follows:

Mortality / Reproduction						
		Mortality [%]			Reproduction	
Treatment	kg product/ha	Uncorr.	Corr.	P-Value(*)	Eggs per female and day	Fertility [hatching rate in %]
Control	0	12.5	0.0		17.2	74.3
Test item	0.5	10.0	-2.9	1.000 n.sign.	10.3	68.1
Test item	1.015	10.0	-2.9	1.000 n.sign.	12.2	71.6
Test item	2.062	17.5	5.7	1.000 n.sign.	16.8	79.1
Test item	4.186	7.5	-5.7	1.000 n.sign.	13.3	70
Test item	8.5	15.0	2.9	1.000 n.sign.	18	74.5
Reference item	0.0415	62.5	57.1		n.d.	n.d.

Mortality / Reproduction						
		Mortality [%]			Reproduction	
Treatment	kg product/ha	Uncorr.	Corr.	P-Value(*)	Eggs per female and day	Fertility [hatching rate in %]
LD_{50}: > 8.5 kg product/ha						
* Fisher`s Exact test, two-sided, p-values are adjusted according to Bonferroni-Holm						
n.d. not detected						
n.sign. not significant						
sign. significant						

The dose rates of 0.5, 1.015, 2.062, 4.186 and 8.5 kg product/ha had no influence on mortality and reproduction.

Conclusion
The LD_{50} was estimated to be > 8.5 kg product/ha.

IIIA 10.5.3 Effects on non-target terrestrial arthropods in semi-field tests

Report:	**KIIIA 10.5.3/01; [redacted] 2008**
Title:	Toxicity to the parasitoid wasp *Aphidius rhopalosiphi* (DESTEPHANI-PEREZ) (Hymenoptera: Braconidae) using an extended laboratory test (under semi-field conditions aged residues on *Zea mays*). Folpet + Iprovalicarb WG 56.3 + 9 A W
Document No:	M-311332-01-1 (Report-No: CW08/048)
Guidelines:	Mead-Briggs et al. (2000), Mead-Briggs et al. (Draft 2006), Candolfi et al. (2001)
GLP	Yes (certified laboratory)

Objective:
The aim of the study was to determine the toxicity of Folpet + Iprovalicarb WG 56.3 + 9 A W to the parasitoid wasp *Aphidius rhopalosiphi* in an extended laboratory test after residual contact exposure to under semi-field conditions aged residues on potted plants of Zea mays.

Materials and methods:
A water dispersible granule formulation of Folpet + Iprovalicarb WG 56.3 + 9 A W was tested, specified by sample description: TOX-08081-00; specification no.: 102000011659, batch ID: EM20002600 [analysed content of active ingredients: Folpet: 54.9 %w/w and Iprovalicarb: 9.00 %w/w; date of analysis completed: 11 OCT 2007, BCS-D-FT Analysis & Services, D-40789 Monheim;].

The test item was applied with 5.1 kg product/ha in 400 L water/ha on potted maize plants. The control was treated with deionised water in the same way as the test item. The toxic reference Dimethoate was applied at 0.0136 kg product/ha (5 g a.i./ha) in 400 L water/ha on potted maize plants as well. For the further exposure dates it was applied directly on the cut maize leaves. It was included to indicate the relative susceptibility of the test organisms and the test system.
Aging of the spray residues of the test item on the potted maize plants took place under natural semi-field conditions with rain protection during the whole study.

Mortality of 30 females was assessed 2, 24 and 48 hours after exposure on maize leaves for each bioassay started on day 0 and 7 after application.
Repellency of the test item in both bioassays was determined during the initial 3 h after the release of the females. Five separate observations were made at 30-minute intervals starting immediately after the introduction of all wasps.
For the bioassays started on day 0 and day 7 after application 15 impartially chosen females from the water control and the treated group were each transferred to a cylinder containing untreated cereal plants infested with *Rhopalosiphum padi* for a period of 24 hours. The number of mummies was assessed 11 days later.
From these data the endpoints mortality and effects on reproduction were calculated and are summarized on the next table.

Findings:

Test item	Folpet + Iprovalicarb WG 56.3 + 9 A.W	
Test object	*Aphidius rhopalosiphi*	
Exposure	Dried spray deposits on maize leaves	
Start of bioassay	**0 DAA**[a]	**7 DAA**[a]
	Mortality (%) after 48 h	
Control	0	0
Test item	0	3.3
Reference item	93.3	100.0
	Corrected Mortality (%)	
Test item	0 (p-value 1.000, not significant) [b]	3.3 (p-value 1.000, not significant) [b]
Reference item	93.3	100.0
	Repellency (comparison per mean values)	
	% Wasps on plant	
Control	45.5	71.0
Test item	44.3	64.8
Reference item	43.5	32.7
	Rel. to control (%)	
Control	0	0
Test item	2.6 (p-value 0.982, not significant) [c]	8.7 (p-value 0.181, not significant) [c]
Reference item	4.4	25.8
	Reproduction	
	Number of mummies per female	
Control	21.9	- [d]
Test item	21.1	-
	Reduction rel. to control (%)	
Test item	3.6 (p-value 0.851, not significant) [c]	-

[a] Days after application
[b] Fisher's Exact test, two-sided, p-values adjusted according to Bonferroni-Holm
[c] Wilcoxon test, two-sided, p-values adjusted according to Bonferroni-Holm
[d] invalid results, see validity criteria, chapter 5.4

Conclusion:
In this extended laboratory test the lethal and sublethal effects of Folpet + Iprovalicarb WG 56.3 + 9 A W residues (aged under semi-field conditions) on the parasitoid wasp *Aphidius rhopalosiphi* were determined after application of 5.1 kg product/ha onto Zea mays.
In this study no mortality of the test item was found in the first bioassay started on day 0 after application. The reduction in reproductive success relative to the control in this bioassay was 3.6%.
A second bioassay was started 7 days after application and showed a corrected mortality of 3.3%. In this bioassay the observations on potential reproduction effects were not valid due to insufficient control performance (5 wasps produced zero reproduction in water control). Since the first bioassay indicated low mortality with low effects on reproduction the study was not prolonged.
No statistically significant repellent effect of the test item could be observed in both bioassays.

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Report:	**KIIIA 10.5.3/02; [redacted] 2010**
Title:	Iprovalicarb + Folpet WG 65.3 (9 + 56.3 % w/w): Effects on the reproduction of *Aphidius rhopalosiphi* (De Stephani Perez) (Hymenoptera, Braconidae) under semi-field conditions.
Document No:	M-391612-01-1 (Report-No: EBSZX159)
Guidelines:	Barrett et al. (1994), Mead-Briggs et al. (2000), Candolfi et al. (2001)
GLP	Yes (certified laboratory)

Objective: The objective of the study was to determine the effects of fresh residues of Iprovalicarb + Folpet WG 65.3 on the reproduction of the aphid parasitoid *Aphidius rhopalosiphi* (De Stefani Perez) (Hymenoptera, Braconidae) under semi-field exposure conditions.

Materials and methods: Test item: Iprovalicarb + Folpet WG 65.3 (9 + 56.3 % w/w), specified by sample description: TOX 09082-00; specification no.: 102000011659-02, batch ID: EM20082600, analysed content of active ingredients: 54.4% w/w folpet and 8.88 % w/w iprovalicarb.
Test organism: the parasitoid wasp *Aphidius rhopalosiphi*, approx. 48 h old adults.
The test item was diluted in water and applied with a spray application volume of 400 L water/ha to barley seedlings at 5.1 kg product/ha. Deionized water was used as control and Perfekthion (analysed content of dimethoate: 414.8 g/L) was applied at 40.0 g product/ha in 400 L water/ha as a reference treatment.
5 replicates per treatment contained 4 female wasps each. The adults were provided with artificial food. The parasitoids were exposed to the treated barley plants for 48 h under semi-field conditions, before the reproduction units for the fertility test were inserted into the cages for 24 h of oviposition. Counting of parasitised aphids was carried out 12 days after the start of the fertility test.
The parasitic capacity of the treated females was compared to that of the control.

Findings: The results can be considered as valid, as all validity criteria of the test were met. Corrected mortality of the reference item was 100% (> 50% required) and the mean reproduction per female in water control was 9.9 (≥ 5 required).

Test object	*Aphidius rhopalosiphi*		
Exposure	Barley seedlings		
Treatment groups	Total mummies	Mean mummies per female ± SD	R [%]
Control	197	9.9 ± 20.2	-
Iprovalicarb + Folpet WG 65.3 at 5.1 kg product/ha	151	7.6 ± 13.7	23.2
Reference item (Perfekthion) at 40.0 g product/ha	0	0.0 ± 0.0	100.0

SD: Standard deviation
R: Reduction in reproduction rate compared to the control

Conclusion: With respect to the test results it can be concluded that Iprovalicarb + Folpet WG 65.3 caused no adverse effects on reproduction of *Aphidius rhopalosiphi* under semi-field conditions at an application rate of 5.1 kg product/ha when applied on barley seedlings.

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Report:	**KIIIA 10.5.3/03, [redacted] 2002**
Title:	Toxicity of Folpet + Iprovalicarb WG 65.25 to the predatory mite *Typhlodromus pyri* SCHEUTEN under extended laboratory conditions (aged-residue test).
Document No:	M-073796-01-1 (02 10 48 057)
Guidelines:	IOBC guideline Blumel et al (2000)
GLP:	Yes

Material and methods:

The fungicide Folpet + Iprovalicarb WG 65.25 (purity: 10 % SZX 0722 + 55.4 % Folpet; specification: Development No.: 3000244654; TOX No.: 06124-00; Batch No.: 07373/0048(0046) was tested under extended laboratory conditions on the predatory mite *Typhlodromus pyri* SCHEUTEN after residual contact exposure to freshly applied under semi-field conditions aged residues on excised wine leaves. The test item was applied at a rate of 5.42 kg product/ha in 400 l deionized water/ha to potted wine plants. The control was treated with deionized water (400 l/ha). Dimethoate EC 400 (30 ml product/ha in 400 l/ha of water) was used as a toxic reference treatment. Aging of the spray residues on potted wine plants took place under natural field conditions with rain protection (UV-permeable) from the application (DAT 0) until DAT 7.
After that time, rain protection was necessary, because frequent showers were predicted, i.e. plants were protected against rain in a carport. Over a time of tree days, it was possible, to place the treated plants outdoor, because there was no rainfall (see Appendix 4). Protonymphs of the predatory mite *Typhlodromus pyri* SCHEUTEN were exposed in 5 replicates of 20 mites (per treatment group) to the spray residues of the test item, reference item and control, respectively. During the assessments the mites were fed with pollen (pine and birch). The number of surviving, dead and escaped predatory mites, behaviour and the number of eggs laid per evaluation period were recorded for each exposure over a period of 14 days. From these data the endpoints mortality and the effect on reproduction were calculated. The toxic reference treatment resulted in 51.5 % (DAT 0), 52.0 % (DAT 7) and 51.0 % (DAT 14) corrected mortality within 7 days.

Findings

Mortality

Test item	Folpet + Iprovalicarb WG 65.25		
Test object	*Typhlodromus pyri* SCHEUTEN		
Exposure	Dried spray deposits on excised wine leaves		
Treatment	% Mortality after 7 days		
Exposure time (DAT)	0	7	14
Control	3	0	2
Application rate [kg product/ha]	Corrected Mortality [%]		
5.42	48.5*	14.0*	1.0

Fecundity

Test item	Folpet + Iprovalicarb WG 65.25					
Test object	*Typhlodromus pyri* SCHEUTEN					
Exposure	Dried spray deposits on excised wine leaves					
Treatment	Fecundity (mean No. of eggs per surviving female)					
	mean No. of eggs/ female	**Reduction relative to control (%)**	**mean No. of eggs/ female**	**Reduction relative to control (%)**	**mean No. of eggs/ female**	**Reduction relative to control (%)**
Exposure time **DAT**	0		7		14	
Control	n.d	-	6.01	-	6.20	
Application rate [kg product/ha]						
5.42	n.d.	-	5.46	9.2	6.17	0.5

* statistically significantly different ($p < 0.05$)
n.d. = not determined (corrected mortality in the test item group > 30 %)
DAT = Day(s) After Treatment

Conclusions:
The results of the control group indicated that the test organisms were in a good condition (mortality: 3 % (DAT 0); 0 % (DAT 7), 2 % (DAT 14)).
The results of the toxic standard group indicated that the test system was sensitive to harmful substances (corrected mortality: 51.5 % (DAT 0); 52 % (DAT 7); 51 % (DAT 14)).

Mortality:
7 days after the 1st exposure (DAT 0) and the 2nd (DAT 7) exposure, respectively, statistically significantly differences in mortality were observed in the test item group compared to the control group.
No poisoning symptoms and anomalous behaviour of the treated predatory mites were recorded in comparison with the control group for all exposures.

Reproduction:
No statistically significant difference in reproduction (mean number of eggs/surviving female) was observed in the test item group (DAT 7 and DAT 14) when compared to the control group.
The reduction of reproduction relative to control was 9.2 % (DAT 7) and 0.5 % (DAT 14).

IIIA 10.5.4 Field tests on arthropods species

In view of the findings reported above, and based on the current requirements, no semi-field studies with the preparation have been conducted.

IIIA 10.6 Effects on earthworms and other soil macro-organisms

The toxicity data for Iprovalicarb + Folpet WG 65.3 and the individual active substances and their soil metabolites are shown in the following table.

Table 10.6- 1: Effect on soil macro-organisms – earthworms

Test species	Test design	Ecotoxicological endpoint			Reference
Iprovalicarb					
Eisenia fetida	acute, 14 d (10 % peat in test soil)	**LC_{50}**	**> 500** [1)]	**mg a.s./kg dws**	[redacted] (1996) HBF/Rg 222 M-000083-01-1 IIA 8.9.1/01 (EU point IIA, 8.4.1/01)
Eisenia fetida	chronic, 56 d (10% peat in test soil)	NOEC	≥ 0.5 [1, 2, 3)]	mg a.s./kg dws	[redacted] (1998) HBF/Rg 262 M-000750-01-1 IIA 8.9.2/01 (EU point IIA 8.4.2/01)
Eisenia fetida	chronic, 56 d (10% peat in test soil)	NOEC	≥ 5 [1, 2, 4)]	mg a.s./kg dws	[redacted] (2001) MPE/Rg 370/01 M-053073-01-1 IIA 8.9.2/02
Eisenia fetida	chronic, 56 d (5% peat in test soil)	**NOEC**	**≥ 64**	**mg a.s./kg dws**	[redacted] (2011) LRT-Rg-R-85/11 M-405822-01-1 IIA 8.9.2/03
Iprovalicarb-carboxylic acid (M03)					
Eisenia fetida	chronic, 56 d (5% peat in test soil)	**NOEC**	**≥ 100**	**mg pm/kg dws**	[redacted] (2011) 59691022 M-406133-01-1 IIA 8.9.2/04
PMPA (M10)					
Eisenia fetida	acute, 14 d (10 % peat in test soil)	**LC_{50}**	**> 500** [1)]	**mg pm/kg dws**	[redacted] (1999) HBF/Rg 302 M-016516-01-1 IIA 8.9.1/02 (EU point IIA, 8.4.1/02)
Eisenia fetida	chronic, 56 d (10% peat in test soil)	**NOEC**	**158** [1)]	**mg pm/kg dws**	[redacted] (2001) MPE/Rg 369/01 M-043357-01-1 IIA 8.9.2/05
N-acetyl-PMPA (M15)					
Eisenia fetida	chronic, 56 d (5% peat in test soil)	**NOEC**	**60.2**	**mg pm/kg dws**	[redacted] (2010) 52291022 M-368040-01-1 IIA 8.9.2/06
Folpet					
Eisenia fetida	acute, 14 d (10 % peat in test soil)	**LC_{50}**	**> 500** [1)]	**mg a.s./kg dws**	EFSA Scientific Report for Folpet (2006)
Eisenia fetida	chronic, 56 d (10% peat in test soil)	**NOEC**	**5.18** [5)]	**mg a.s./kg dws**	

Test species	Test design	Ecotoxicological endpoint	Reference
Iprovalicarb + Folpet WG 65.3			
Eisenia fetida	chronic, 56 d (5% peat in test soil)	**NOEC 1000 mg prod./kg dws**	[redacted] (2002) 14872002 M-066524-01-1 KIIIA 10.6.3/01

Bold letters: endpoints used in the risk assessment
[1] endpoint corrected to allow for log $P_{ow} > 2$
[2] study conducted with the formulation Iprovalicarb WG 50
[3] Calculated considering a soil depth of 5 cm and a bulk density of the soil of 1.5 g/cm³ (standard conversion)
[4] Calculated considering the actual test conditions (surface of the test vessels: approx. 200 cm², and the actual soil dry weight: 500 g in the test containers). Conversion according to the "Guidance Document on Terrestrial Ecotoxicology", SANCO/10329/2002 of October 17, 2002.
[5] study conducted with 10% organic matter but no correction necessary (see EFSA Scientific Report (2006) 70, 1-78, Conclusion of the peer review of Folpet)
dws = dry weight soil
pm = pure metabolite

Exposure in soil

Folpet is a 3rd party substance procured from [redacted]. ([redacted]). Bayer CropScience AG is using a risk envelope approach for the risk assessment of the representative formulation. Within the scope of this supplementary dossier, up to 4 applications at 1.35 kg/ha folpet are proposed as a safe use in grapes. This is much below the critical GAP that [redacted] currently defends in this crop in the EU, where 10 applications of up to 1.6 kg/ha have been approved, with all other parameters such as interval between applications or pre-harvest interval being identical or very similar. Therefore, Bayer CropScience AG considers it justified to refer to folpet data owned by [redacted] wherever appropriate. A folpet-specific risk assessment is not considered necessary to defend the Annex I listing of iprovalicarb.

Predicted environmental concentrations in soil (PEC_{soil}) values were calculated for the active substance iprovalicarb and its metabolites as described in detail in Point 9.4 and Point 9.5 of this dossier. A soil layer of 5 cm with a bulk density of 1.5 g/cm³, and conservative DT_{50} values of 68.56 days for iprovalicarb, 1.852 days for M03, 187.33 days for M10 and 0.929 days for M15 were considered. The accumulation potential of M10 after long term use was also assessed considering a soil mixing depth of 10 cm. The highest maximum PEC_{soil} values were calculated for the use in vines, early (4 × 216 g a.s./ha, 4 × 60% interception, 10 days interval). The PEC_{soil} values used for the risk assessment are presented in Table 10.6- 2.

Table 10.6- 2: Maximum PEC_{soil} values

Crop	Grapes	
	PEC_{soil} [mg/kg]	**PEC_{soil} (twa, 21 d) [mg/kg]**
Iprovalicarb + Folpet WG 65.3	5.120[1]	-
Iprovalicarb	0.398	0.359
M03	0.013	0.002
M10	0.110[2]	0.090
M15	0.019	0.001

[1] based on an application rate of 4 × 2400 g product/ha and 4 × 60% interception

[2] $PEC_{soil, total}$ (background $PEC_{plateau}$ in 10 cm depth + maximum residue of one year in 5 cm depth)

IIIA 10.6.1 Toxicity exposure ratios for earthworms, TER_A and TER_{LT}

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

Based on most sensitive endpoints (see Table 10.6- 1) the TER values are calculated using the following equations:

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

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

For lipophilic substances (log P_{OW} > 2) the Terrestrial Guidance Document recommends to apply an additional assessment factor of 2 for the ecotoxicological endpoints (LC_{50}, NOEC), if the study was conducted in artificial soil with a high content of organic matter (i.e. 10% peat), to consider the possible sorption of these compounds to the organic matter.

Table 10.6.1- 1: TER calculations for earthworms

Compound test design	Endpoint	[mg/kg soil]	PEC_{max} [mg/kg soil]	TER_A / TER_{LT}	Trigger	Refined risk assessment?
Iprovalicarb + Folpet WG 65.3	NOEC	1000	5.120	195	5	No
Iprovalicarb, acute	LC_{50}	500	0.398	≥ 1256	10	No
Iprovalicarb, chronic	NOEC	≥ 64	0.398	≥ 161	5	No
M03, chronic	NOEC	≥ 100	0.013	≥ 7692	5	No
M10, acute	LC_{50}	> 500 [1]	0.110	> 4545	10	No
M10, chronic	NOEC	158 [1]	0.110	1436	5	No
M15, chronic	NOEC	60.2	0.019	3168	5	No

[1] Study endpoint divided by factor 2

Conclusion:
The TER values are above the trigger of concern, indicating no unacceptable risk for earthworms from the application of the product according to the intended GAP.

IIIA 10.6.2 Acute toxicity to earthworms

No study on acute toxicity was performed with the formulation. Please refer to Point IIIA 10.6.3 for the reproduction study conducted with the formulation.

IIIA 10.6.3 Sublethal effects on earthworms

Report:	**KIIIA 10.6.3/01, [redacted] 2002**
Title:	Folpet + Iprovalicarb WG 65.25: Effects on Reproduction and Growth of Earthworms *Eisenia fetida* in Artificial Soil with 5 % Peat in the Test Substrate
Document No:	M-066524-01-1 (Rep. No.: 14872002)
Guidelines:	BBA 1994, ISO 11268-2 (1998)
GLP:	Yes

Materials and methods:
Folpet + Iprovalicarb WG 65.25 (Development No.: 3000244654, Batch No.: 07373/0048(0046), Tox No.: 06124-00) was mixed into the soil at 100, 178, 316, 562 and 1000 mg product/kg artificial soil (dry weight). The soil was based on OECD 207 but with reduced organic matter content (5 % peat). It contained 5 % Sphagnum-peat, air-dried and finely ground (2 mm), 20 % Kaolin clay (Kaolinite content >30 %); approximately 0.2 % chalk ($CaCO_3$) added to adjust pH to 6.0 ± 0.5; approximately 74.8 % fine quartz-sand (F34) containing more than 50 % by mass of particle size 0.05 mm to 0.2 mm. Earthworms *Eisenia fetida* (40 worms per treatment group) were exposed at 19 - 22 °C, light 450 - 800 lux, 16 h light : 8 h dark, fed weekly with dried cattle manure, initial soil water content 23.6 % - 25.4 % (51.2 % to 55.1 % of the water holding capacity), water content at experimental end 23.6 % to 28.3 % (50.3 % to 61.4 % of the water holding capacity), initial pH 5.5 to 5.6; pH at experimental end 5.7 to 5.9. Derosal SC 360 (active ingredient carbendazim) was tested as the toxic standard at least once a year in a dose response study control: untreated and the most recent study resulted in an EC_{50} for reproduction was calculated as 1.46 mg carbendazim/kg soil dry weight
Endpoints were mortality, body weight change, feeding activity and reproduction.

Findings:
Summary of Results

Test Item:	Iprovalicarb & Folpet WG 65.25					
Test Species:	*Eisenia fetida*					
Exposure:	test item mixed into the soil					
	control	Iprovalicarb & Folpet WG 65.25				
		100 mg product/kg	178 mg product/kg	316 mg product/kg	562 mg product/kg	1000 mg product/kg
mortality [%][1]	0.0 ± 0.0	0.0 - ± 0.0	0.0 - ± 0.0	2.5 n.s.[3] ± 5.0	5.0 n.s.[3] ± 5.8	0.0 ± 0.0
body weight change [%][1]	37.2 ± 6.6	43.1 n.s.[3] ± 6.6	41.8 n.s.[3] ± 4.1	40.9 n.s.[3] ± 8.0	37.6 n.s.[3] ± 1.8	35.3 n.s.[3] ± 2.5
reproduction # of juveniles[1]	400 ± 57	291 n.s.[3] ± 134	400 n.s.[3] ± 74	292 n.s.[3] ± 63	176 *[3] ± 155	287 n.s.[3] ± 93
amount of food added [g][1]	25.0 ± 0.0	25.0 ± 0.0	25.0 ± 0.0	25.0 ± 0.0	24.5 ± 0.7	24.6 ± 0.5

[1] mean ± SD = mean ± Standard Deviation from 4 replicates; the results represent rounded values calculated on the exact raw data
n.s = not significantly different compared to the control
* = significantly different compared to the control
- = not relevant
[3] = Fisher-exact test, $\alpha = 0.05$
= Dunnett test, $\alpha = 0.05$

Conclusion:
The no-observed-effect-concentration (NOEC) of Folpet + Iprovalicarb WG 65.25 for mortality, growth, reproduction and feeding activity of the earthworm *Eisenia fetida* found was 1000 mg product/kg dry artificial soil, the highest concentration tested. The statistically reduced number of juvenile earthworms in the concentration of 562 mg product/kg soil dry weight was not considered to be treatment related since the higher concentration of 1000 mg product/kg soil dry weight did not lead to a statistically significant reduction.

IIIA 10.6.4 Field tests (effects on earthworms)

Considering the findings reported above no further studies are required.

IIIA 10.6.5 Residue content of earthworms

As no significant acute or sub-lethal effects have been observed at relevant concentrations (see: 10.6.2 and 10.6.3) no further studies have to be considered.
Based on the information given under Annex Point 10.2.4, this Section 6, a considerable accumulation (bioconcentration) of residues of the product and/or metabolites is unlikely.

An estimated BCF for earthworms is addressed under Annex Point 10.1.9, this Section 6.

IIIA 10.6.6 Effects on other soil non-target macro-organisms

The toxicity data for iprovalicarb and its soil metabolites are shown in the following table.

Table 10.6.6- 1: Effects on other soil non-target macro-organisms

Test species	Test design	Ecotoxicological endpoint	Reference
Iprovalicarb			
Folsomia candida	chronic, 28 d (5% peat in test soil)	NOEC ≥ 1000 mg as/kg dws	[redacted] (2010) M-368058-01-1 FRM-COLL-80/10 IIA 8.14/01
Hypoaspis aculeifer	chronic, 14 d (5% peat in test soil)	NOEC ≥ 1000 mg as/kg dws	[redacted] (2010) M-366603-01-1 kra-HR-25/10 IIA 8.14/05
Iprovalicarb-carboxylic acid (M03)			
Folsomia candida	chronic, 28 d (5% peat in test soil)	NOEC ≥ 100 mg pm/kg dws	[redacted] (2011) M-405347-01-1 59692016 IIA 8.14/02
Hypoaspis aculeifer	chronic, 14 d (5% peat in test soil)	NOEC ≥ 100 mg pm/kg dws	[redacted] (2011) M-405048-01-1 59693089 IIA 8.14/06
PMPA (M10)			
Folsomia candida	chronic, 28 d (5% peat in test soil)	NOEC ≥ 1000 mg pm/kg dws	[redacted] (2010) M-361572-01-1 FRM-COLL-78/10 IIA 8.14/03
Hypoaspis aculeifer	chronic, 14 d (5% peat in test soil)	NOEC ≥ 1000 mg pm/kg dws	[redacted] (2009) M-358751-01-1 kra-HR-18/09 IIA 8.14/07
N-acetyl-PMPA (M15)			
Folsomia candida	chronic, 28 d (5% peat in test soil)	NOEC ≥ 100 mg pm/kg dws	[redacted] (2010) M-366743-01-1 FRM-COLL-81/10 IIA 8.14/04
Hypoaspis aculeifer	chronic, 14 d (5% peat in test soil)	NOEC ≥ 100 mg pm/kg dws	[redacted] (2010) M-364283-01-1 kra-HR-24/10 IIA 8.14/08

dws = dry weight soil
pm = pure metabolite

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

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

$TER = NOEC / PEC_{soil}$

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

Table 10.6.6- 2: TER calculations for soil macro-organisms

Compound Test design	Endpoint	[mg/kg soil]	PEC_{max} [mg/kg soil]	TER	Annex VI Trigger	Refined risk assessment?
Folsomia candida						
Iprovalicarb, chronic	NOEC	≥ 1000	0.398	≥ 2513	5	No
M03, chronic	NOEC	≥ 100	0.013	≥ 7692	5	No
M10, chronic	NOEC	≥ 1000	0.110	≥ 9091	5	No
M15, chronic	NOEC	≥ 100	0.019	≥ 5263	5	No
Hypoaspis aculeifer						
Iprovalicarb, chronic	NOEC	≥ 1000	0.398	≥ 2513	5	No
M03, chronic	NOEC	≥ 100	0.013	≥ 7692	5	No
M10, chronic	NOEC	≥ 1000	0.110	≥ 9091	5	No
M15, chronic	NOEC	≥ 100	0.019	≥ 5263	5	No

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

IIIA 10.6.7 Effects on organic matter breakdown

A study on the organic matter breakdown is not required based on the DT_{90} value of the active substance and acceptable TER values for earthworms, soil macro-organisms and soil micro-organisms.

IIIA 10.7 Effects on soil microbial activity

Studies are available for the product Iprovalicarb + Folpet WG 65.3, the active substances iprovalicarb and folpet, and the metabolites of iprovalicarb. The results are summarised in the following table.

Table 10.7- 1: Effects on soil non-target micro-organisms

Test design		Ecotoxicological endpoint			Reference
Iprovalicarb + Folpet WG 65.3					
N-cycle	28 d	no influence	22.67 17	mg/kg dws kg/ha	[redacted] (2009) M-359102-01-1 09 10 48 052 N KIIIA 10.7.1/01
Iprovalicarb					
C-cycle	91 d	no influence	6.6 4.95	mg/kg dws kg a.s./ha	[redacted] (1996) M-000096-01-1 AJO/142896 IIA 8.10.2/01 (EU point IIA, 8.5/01)
N-cycle	91 d	no influence	6.6 4.95	mg/kg dws kg a.s./ha	[redacted] (1996) M-000094-01-1 AJO/142996 IIA 8.10.1/01 (EU point IIA, 8.5/02)
Iprovalicarb-carboxylic acid (M03)					
N-cycle	28 d	no influence	13.33 10	mg pm/kg dws kg pm/ha	[redacted] (2011) M-404388-01-1 10 10 48 055 N IIA 8.10.1/02
PMPA (M10)					
N-cycle	28 d	no influence	0.93 0.7	mg pm/kg dws kg pm/ha	[redacted] (2010) M-366832-01-1 FRM-N-139/10 IIA 8.10.1/03
N-acetyl-PMPA (M15)					
N-cycle	28 d	no influence	1.21 0.913	mg pm/kg dws kg pm/ha	[redacted] (2010) M-366828-01-1 FRM-N-138/10 IIA 8.10.1/04
Folpet					
C-cycle	28 d	no influence	15.93	kg a.s./ha	EFSA Scientific Report for Folpet (2006)
N-cycle	28 d	no influence	15.93	kg a.s./ha	

Risk assessment

According to current regulatory requirements the risk is acceptable, if the effect of the recommended application rate of a compound/product on nitrogen or carbon mineralisation is < 25% after days.
In no case deviations from the control exceeded 25% after 28 days, indicating low rik to soil micro-organisms.

Thus, no unacceptable risks to soil non-target micro-organisms is to be expected from the use of

Iprovalicarb + Folpet WG 65.3, if the product is used according to the recommended use pattern.

IIIA 10.7.1 Laboratory test to investigate impact on soil microbial activity

Report:	**KIIIA 10.7.1/01; [redacted].; 2009**
Title:	Folpet + iprovalicarb WG 65.3 (56.3+9)A W: Effects on the activity of soil microflora (Nitrogen transformation test)
Document No:	M-359102-01-1 (Rep. No: 09 10 48 052 N)
Guidelines:	OECD 216; adopted January 21, 2000, OECD Guideline for the Testing of Chemicals, Soil Microorganisms: Nitrogen Transformation Test.
GLP	Yes (certified laboratory)

Objectives: The objective of the test was to determine the influence of 2.27 and 22.67 mg Folpet + Iprovalicarb WG 65.3 (56.3+9)A W/kg dry weight soil on nitrogen transformation in an agricultural soil.

Materials and Methods: Folpet + iprovalicarb WG 65.3 (56.3+9)A W (analytical findings: Folpet (SR-407) 54.9 % w/w, Iprovalicarb (SZX 0722) 9.00 % w/w; Specification No.: 102000011659, Batch ID: EM20002600, Sample description: TOX08081-00) was used in the test. A loamy sand soil (DIN 4220) was exposed for 28 days to 2.27 and 22.67 mg test item/kg soil dry weight. Application rates were equivalent to 1.7 and 17 kg test item/ha. Determination of the nitrogen transformation (NO_3-nitrogen production) in soil enriched with lucerne meal (concentration in soil 0.5 %). NH_4-nitrogen, NO_3- and NO_2-nitrogen were determined using the Autoanalyzer II (BRAN+LUEBBE) at different sampling intervals (0, 7, 14 and 28 days after treatment).
The coefficients of variation in the control (NO_3-N) were maximum 3 % and thus fulfilled the demanded range (≤15 %).

Findings: Effects on non-target soil microorganisms.

Time Interval (days)	Application rates											
	FLP+IPV WG 65.3 (56.3+9)A W											
	Control			2.27 mg/kg dry weight soil				22.67 mg/kg dry weight soil				
	Nitrate-N [1)]			Nitrate-N [1)]			% difference to control	Nitrate-N [1)]			% difference to control	
0-7	1.93	±	0.11	2.00	±	0.12	**3** n.s.	2.14	±	0.05	**11***	
7-14	0.20	±	0.16	0.43	±	0.04	**109** n.s.	0.42	±	0.17	**107** n.s.	
14-28	0.67	±	0.10	0.67	±	0.12	**1** n.s.	0.77	±	0.13	**14** n.s.	

The calculations were performed with unrounded values
1) Rate: Nitrate-N in mg/kg dry weight soil/time interval/day, mean of 3 replicates and standard deviation
n.s. = No statistically significant difference to the control (Student-t-test for homogeneous variances, 2-sided, $p \leq 0.05$).
* = statistically significantly different to control (Student-t-test for homogeneous variances, 2-sided, $p \leq 0.05$)

In a separate study the reference item Dinoterb caused a stimulation of nitrogen transformation of +37.9 % and +48.3 % at 16.00 and 27.00 mg Dinoterb per kg soil dry weight, respectively, 28 days after application (Appendix 4: Reference test, 5. Results of the reference test, page 28).

Observations: At time interval 7-14 days after treatment both test concentrations caused a temporary stimulation of the daily nitrate rate. No adverse effects of Folpet + iprovalicarb WG 65.3 (56.3+9)A W on nitrogen transformation in soil were observed in both test concentrations (2.27 mg/kg dry soil and 22.67 mg/kg dry soil) after 28 days.
Only negligible differences to control of 1 % (test concentration 2.27 mg/kg dry soil) and +14 % (test concentration 22.67 mg/kg dry soil) were measured at the end of the 28-day incubation period.

Conclusion: Folpet + iprovalicarb WG 65.3 (56.3+9)A W caused no adverse effects (difference to control < 25 %, OECD 216) on the soil nitrogen transformation (measured as NO_3-N production) at the end of the 28-day incubation period. The study was performed in a field soil at concentrations equivalent up to an application rate of 67 kg test item/ha.

IIIA 10.7.2 Further testing to investigate impact on soil microbial activity

Since laboratory testing has demonstrated that the active substances and their metabolites would not be expected to cause any significant effects on either soil microflora respiration or nitrogen transformation at concentrations above the maximum field rate, no additional testing has been performed.

IIIA 10.8 Effects on non-target plants

IIIA 10.8.1 Effects on non-target terrestrial plants

The risk assessment is based on the "Guidance Document on Terrestrial Ecotoxicology", (SANCO/10329/2002 rev2 final, 2002). It is restricted to off-field situations, as non-target plants are non-crop plants located outside the treated area. Spray drift from the treated areas may lead to residues of a product in off-crop areas.
In the case of a non-herbicides screening results and/or Tier 1 studies give first information about the likelihood for terrestrial plant effects. The risk can be considered acceptable if there are no data indicating more than 50% phytotoxic effect at the maximum application rate.

Seedling emergence and vegetative vigour studies have been conducted with Iprovalicarb + Folpet WG 65.3 following OECD testing guidelines 208 and 227, respectively (see Annex Points IIIA 10.8.1.3 and 10.8.1.2). They each involved 10 species tested at the maximum application rate of 2.55 kg product/ha.

Table 10.8.1- 1: Ecotoxicological endpoints for non-target terrestrial plants

Iprovalicarb + Folpet WG 65.3				
Plant species	Seedling emergence		Vegetative vigour	
	Max. effects at highest rate tested [2.55 kg/ha]	Parameter	Max. effects at highest rate tested [2.55 kg/ha]	Parameter
Buckwheat	10.5 % reduction	emergence	no negative impact	-
Cucumber	0.8 % reduction	shoot biomass	no negative impact	-
Oilseed rape	7.3 % reduction	shoot biomass	no negative impact	-
Soybean	11.5 % reduction	shoot biomass	12.0 % reduction	shoot biomass
Sugar beet	23.5 % reduction	survival	no negative impact	-
Sunflower	0.5 % reduction	shoot biomass	no negative impact	-
Tomato	5.4 % reduction	shoot biomass	no negative impact	-
Corn	5 % reduction	emergence	no negative impact	-
Oat	6 % reduction	shoot biomass	no negative impact	-
Onion	6.3 % reduction	survival	no negative impact	-
Reference	[redacted] (2009) Report No. SE 09/047 Doc No. M-357371-01-1 KIIIA 10.8.1.3/01		[redacted] (2009) Report No. VV 09/048 Doc No. M-357376-01-1 KIIIA 10.8.1.2/01	

In the case of Iprovalicarb + Folpet WG 65.3, neither the seedling emergence nor the vegetative vigour studies showed phytotoxic effects >50% at the maximum rate of 2.4 kg product/ha.
Thus, no unacceptable risks to non-target terrestrial plants are to be expected from the use of Iprovalicarb + Folpet WG 65.3, when used according to the recommended GAP.

IIIA 10.8.1.1 Seed germination

Please refer to Annex Point IIIA 10.8.1.2.

IIIA 10.8.1.2 Vegetative vigour

Report:	**KIIIA 10.8.1.2/01, [redacted] 2009**
Title:	Iprovalicarb + Folpet WG 9 + 56.3 % w/w: Effects on the vegetative vigour of ten species of non-target terrestrial plants (Tier 1)
Document No:	M-357376-01-1 (Rep. No: VV 09/048)
Guidelines:	OECD 227: OECD Guidelines for the testing of Chemicals, Terrestrial Plant Test: Vegetative Vigour Test (July 2006)
GLP	yes

Objective:
The purpose of this specific study is to evaluate the effect of Iprovalicarb + Folpet WG 9 + 56.3 % w/w on the vegetative vigour of ten plant species representing a broad range of both dicotyledonous and monocotyledonous plant families.

Materials and Methods:
Test item: Iprovalicarb + Folpet WG 9 + 56.3 % w/w, workorder: 07035734, sample description: TOX 08081-00, product: FLP + IPV WG 56.3 + 9A W, batch-ID: EM20002600, material no.: 06361579, specification no.: 102000011659, content for release: Folpet 54.9% w/w and Iprovalicarb 9.00% w/w, appearance: dark brown granules.
In total, plants of ten species including seven dicotyledonous species buckwheat (*Fagopyrum esculentum*), cucumber (*Cucumis sativus*), oilseed rape (*Brassica napus*), soybean (*Glycine max*), sugar beet (*Beta vulgaris*), sunflower (*Helianthus annuus*) and tomato (*Lycopersicon esculentum*) plus three monocotyledonous species; oat (*Avena sativa*), onion (*Allium cepa*) and corn (*Zea mays*) were grown in pots in the glasshouse.
At the 2-4 leaf stage plants were treated with Iprovalicarb + Folpet WG 9 + 56.3 % w/w using a laboratory track sprayer applied at 2.55 kg product / ha and a volume rate of 200 L/ha. Each pot contained 4 plants and there were 20 plants treated i.e. 5 replicates. Control pots were treated with deionised water.
Pots were grown and maintained under glasshouse conditions with a temperature control set at 23 ± 8°C during day and 18 ± 8°C at night with a 16 h photoperiod.
Survival and phytotoxicity were recorded 7, 14 and 21 days after application and assessment were made against the water treated controls.
The study was terminated 21 days after application. The parameters measured were survival, visual phytotoxicity, plant growth stage and shoot dry weight.
Statistical analysis of data was performed to obtain significance, carried out using the Pairwise Mann-Whitney-U-Test (one sided smaller; $p \leq 0.05$) by ToxRat statistics.

Findings:
Analysis of iprovalicarb of the highest application rate revealed it to be 95.6 % of nominal.
This study can be considered valid as the validity criteria of 90% survival at the end of the test in the untreated controls were achieved for all species.
A summary of the findings for each species is summarised in the following table:

Effects of Iprovalicarb + Folpet WG 9 + 56.3 % w/w in the 21 days vegetative vigour test

	buck-wheat	cucum-ber	oilseed rape	soy-bean	sugar beet	sun-flower	toma-to	corn	oat	onion
Survival * (% inhibition)	0	0	0	0	0	0	0	0	0	0
Phytotoxicity **	0	0 – A *f*	0	0 – A *f*	0 – A *f*	0	0	0	0	0
Shoot Dry Weight *** (% inhibition)	(12.8)	(3.6)	(22.6)	**12.0**	(4.2)	(9.5)	(8.4)	(13.7)	(0.9)	(5.9)

* survival is a measure of treated plants that survived at the end of the study and is expressed as an inhibition compared to the untreated control
** see materials and methods for a description of the phytotoxicity rating
*** inhibition or reduction is expressed on a per plant basis
( ) figures in parentheses indicate that there was an increase when compared to the untreated control
Bold figures are statistically significant (Pairwise Mann-Whitney-U-test, one sided smaller; $p \leq 0.05$).

Observations:

In general this study revealed a very low level of phytotoxicity as a result of a foliar application of Iprovalicarb + Folpet WG 9 + 56.3 % w/w at 2.55 kg product/ha.
There was no mortality in any species following an application of Iprovalicarb + Folpet WG 9 + 56.3 % applied at 2.55 kg product/ha.
Slight stunting was observed as visible phytotoxicity in soybean, sugar beet and cucumber.
Shoot dry weight was not adversely affected in any species apart from soybean were there was a 12% reduction, which was statistically significant.

Conclusion:

Following a foliar application of Iprovalicarb + Folpet WG 9 + 56.3 % w/w applied at 2.55 kg product/ha to ten terrestrial plant species at the 2 to 4 leaf stage, no adverse effects on survival and shoot dry weight exceeding the 50% effect trigger for further testing were obtained in this vegetative vigour study.

IIIA 10.8.1.3 Seedling emergence

Report:	**KIIIA 10.8.1.3/01, [redacted] 2009**
Title:	Iprovalicarb + Folpet WG 9 + 56.3 % w/w: Effects on the seedling emergence and growth of ten species of non-target terrestrial plants (Tier 1)
Document No:	M-357371-01-1 (Rep. No: SE 09/047)
Guidelines:	OECD 208: OECD Guidelines for the testing of Chemicals, Terrestrial Plant Test: Seedling emergence and Seedling Growth Test (July 2006):
GLP	yes

Objective:

The purpose of this specific study is to evaluate the effect of Iprovalicarb + Folpet WG 9 + 56.3 % w/w on the seedling emergence and growth of ten plant species representing a broad range of both dicotyledonous and monocotyledonous plant families.

Materials and Methods:

Test item: Iprovalicarb + Folpet WG 9 + 56.3 % w/w, workorder: 07035734, sample description: TOX 08081-00, product: FLP + IPV WG 56.3 + 9A W, batch-ID: EM20002600, material no.: 06361579, specification no.: 102000011659, content for release: Folpet 54.9% w/w and Iprovalicarb 9.00% w/w, appearance: dark brown granules.
In total, plants of ten species including seven dicotyledonous species buckwheat (*Fagopyrum esculentum*), cucumber (*Cucumis sativus*), oilseed rape (*Brassica napus*), soybean (*Glycine max*), sugar beet (*Beta vulgaris*), sunflower (*Helianthus annuus*) and tomato (*Lycopersicon esculentum*) plus three monocotyledonous species, oat (*Avena sativa*), onion (*Allium cepa*) and corn (*Zea mays*) were sown in pots in the glasshouse. The soil surface of the pots were treated with Iprovalicarb + Folpet WG 9 + 56.3 % w/w using a laboratory track sprayer applied at 2.55 kg product / ha and a volume rate of 200 L/ha. Each pot contained 5 seeds and there were 20 seeds treated i.e. 4 replicates. Control pots were treated with deionised water.
Pots were grown and maintained under glasshouse conditions with a temperature control set at 23 ± 8°C during day and 18 ± 8°C at night with a 16 h photoperiod.

Following the spray application to the soil surface of the pots, emergence was assessed daily until 70% emergence of control seedlings. Emergence, survival and phytotoxicity were recorded 7 and 14 days after this time and assessment were made against the water treated controls.
The study was terminated 14 days after 70% emergence of each species. The parameters measured were emergence, survival of emerged seedlings, visual phytotoxicity, plant growth stage and shoot dry weight.
Statistical analysis of data was performed to obtain significance, carried out using the Pairwise Mann-Whitney-U-Test (one sided smaller; $p \leq 0.05$) by ToxRat statistics.

Findings:
Analysis of iprovalicarb of the highest application rate revealed it to be 95.6% of nominal.
This study can be considered valid as the validity criteria of 70% emergence and 90% survival of the emerged seedlings at the end of the test in the untreated controls were achieved for all species.
A summary of the findings for each species is summarised in the following table:

Effects of Iprovalicarb + Folpet WG 9 + 56.3 % w/w on seedling emergence

	buck-wheat	cucum-ber	oilseed rape	soy-bean	sugar beet	sun-flower	toma-to	corn	oat	onion
Emergence (% inhibition)	10.5	0	0	0	10.5	0	(5.3)	5	0	(14.3)
Survival * (% inhibition)	0	0	0	0	23.5	0	0	0	0	6.3
Phytotoxicity **	0	0	0	0-A *f*	0	0-A *f*	0	0	0	A *b*
Shoot Dry Weight *** (% inhibition)	(16.6)	0.8	7.3	**11.5**	(11.7)	0.5	5.4	0.4	6.0	(6.6)

* survival is a measure of treated plants that survived at the end of the study, and is expressed as an inhibition compared to the untreated control
** see materials and methods for a description of the phytotoxicity rating
*** inhibition or reduction is expressed on a per plant basis
( ) figures in parentheses indicate that there was an increase when compared to the untreated control
Bold figures are statistically significant (Pairwise Mann-Whitney-U-test, one sided smaller; $p \leq 0.05$).

Observations:
In general this study revealed a very low level of phytotoxicity as a result of a soil application of Iprovalicarb + Folpet WG 9 + 56.3 % w/w at 2.55 kg product/ha.
The most sensitive species for emergence were buckwheat and sugar beet with 10.5% reductions.
The species showing the greatest effect on survival was sugar beet where there was a 23.5% reduction.
There were limited phytotoxic symptoms in this study with only slight stunting with soybean and sunflower and a slight necrosis of onion.
Soybean was the most sensitive species for shoot dry weight, with a 11.5% reduction which was statistically significant.

Conclusion:
Following a soil surface application of Iprovalicarb + Folpet WG 9 + 56.3 % w/w applied at 2.55 kg product/ha to ten terrestrial plant species, no adverse effects on emergence, seedling survival and shoot

dry weight exceeding the 50% effect trigger for further testing were obtained in this seedling emergence and growth study.

IIIA 10.8.1.4 Terrestrial field testing

Further studies were not considered necessary.

IIIA 10.8.2 Effects on non-target aquatic plants

The toxicological spectrum of the active substances towards aquatic plants is presented under Annex Point IIIA 10.2.

IIIA 10.8.2.1 Aquatic plant growth – Lemna

Due to the use of the product as a fungicide and since the product is not used as plant growth regulator, tests on aquatic plants are not required.

IIIA 10.8.2.2 Aquatic field testing

The spectrum of the biological activity of the product is well represented by the results and the risk assessments in Point 10.2. Therefore, further studies are not considered necessary.

IIIA 10.9 Effects on other non-target organisms believed to be at risk

The spectrum of the biological activity of the product is well represented by the results and the risk assessments in Point 10.2 to 10.8 of this dossier. Therefore, further data from biological primary screening or other preliminary tests are not considered relevant for the risk assessment.

IIIA 10.9.1 Summary of preliminary data: biological activity & dose range finding

Not relevant. See statement provided under Point 10.9.

IIIA 10.9.2 Assessment of relevance to potential impact on non-target species

Not relevant. See statement provided under Point 10.9.

IIIA 10.10 Other/special studies

The spectrum of the biological activity of the product is well represented by the results and the risk assessments in Point 10.2 to 10.8 of this dossier. Therefore, further data from biological primary screening or other preliminary tests are not considered relevant for the risk assessment.

IIIA 10.10.1 Other/special studies - laboratory studies

Not relevant. See statement provided under Point 10.10.

IIIA 10.10.2 Other/special studies - field studies

Not relevant. See statement provided under Point 10.10.

IIIA 10.11 Summary and evaluation of points IIIA 9 and IIIA 10.1 to 10.10

IIIA 10.11.1 Predicted distribution and fate in the environment and time courses

Summary on the fate and behaviour in soil

From the studies on the route of degradation in soil, it can be concluded that iprovalicarb was thoroughly degraded in soil under aerobic conditions to the final degradation product CO_2. Three metabolites were identified in the soil along with the parent compound and $^{14}CO_2$. The major metabolites (> 10% of the applied radioactivity (AR)) were SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)*. Terephthalic acid *(M23)* was found as minor metabolite. Unextractable residues reached 29.5 to 33.9% of AR at study end (valine-label, day 21) and up to 27.9% of AR and 31.5% of AR (phenyl label, 20°C, day 100 / day 365). Iprovalicarb was metabolised to the endpoint CO_2 via two routes. In one route the breakdown of the molecule started with the cleavage of the amide bond between the L valine and PMPA moieties. This led to the main metabolite PMPA *(M10)*. The other route proceeded via oxidation of the methyl group on the phenyl ring to a carboxylic group (SZX 0722-carboxylic acid *(M03)*) and further oxidation.

Under anaerobic conditions iprovalicarb was degraded appreciably in soil and would not be expected to persist in this type of environment. Iprovalicarb degraded to two major degradates. One major degradate, PMPA *(M10)*, formed under aerobic conditions and increased under anaerobic conditions. During the anaerobic phase, N-acetyl-PMPA *(M15)* was formed as major metabolite. In addition, SZX 0722-aminoacetonitrile *(M50)* was formed as minor degradate later in the study under anaerobic conditions. Unextractable residues reached 39.8% by the end of the study.

It can be concluded from the study concerning the photodegradation of iprovalicarb on soil surfaces that photodegradation will not significantly contribute to the degradation of iprovalicarb. A total of five degradation products including CO_2 were detected in the soil extracts. Two of these degradates were identified as SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)*. All individual degradates accounted for less than 5% of the applied radioactivity in the irradiated samples, with CO_2 representing 2.8% of AR following the irradiation period. The breakdown of iprovalicarb proceeded oxidation of the 4-methyl group to SZX 0722-carboxylic acid, cleavage of the amide bond to PMPA and ring cleavage followed by formation of CO_2.

The rate of degradation of iprovalicarb in soil has been investigated in laboratory trials, which were run with different soil types under aerobic conditions at 20°C and with one soil under 10°C. The degradation under anaerobic conditions and the soil photodegradation were also estimated based on laboratory trials. Furthermore, 6 field trials were conducted at different sites in northern and southern Europe. To derive kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation of these data was performed according to FOCUS kinetics (FOCUS, 2006) for the parent compound the major soil metabolites.

For iprovalicarb the non-normalised $DT_{50\ mod}$ for modelling purpose were in the range of 1.99 to 68.56 days and the normalised $DT_{50\ mod}$ in the range of 1.77 to 68.56 days (geom. mean 6.78 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 1.99 to 18.00 days and the $DT_{90\ initial}$ in the range of 6.62 to 252.12 days.
For SZX 072-carboxylic acid *(M03)* the non-normalised $DT_{50\ mod}$ for modelling purpose were in the range of 0.56 to 1.852 days and the normalised $DT_{50\ mod}$ in the range of 0.45 to 1.85 days (geom. mean 0.97 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 0.58 to 1.97 days and the $DT_{90\ initial}$ in the range of 1.94 to 6.53 days.
For PMPA *(M10)* the non-normalised $DT_{50\ mod}$ for modelling purpose were in the range of 44.28 to 187.33 days and the normalised $DT_{50\ mod}$ in the range of 39.39 to 187.4 days (geom. mean 81.08 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 44.28 to 239.32 days and the $DT_{90\ initial}$ in the range of 147.1 to 759.0 days.
For N-acetyl-PMPA *(M10)* the non-normalised $DT_{50\ mod}$ for modelling purpose were in the range of 0.422 to 0.929 days and the normalised $DT_{50\ mod}$ in the range of 0.42 to 0.93 days (geom. mean 0.72 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 9.0 to 22.3 hours (0.4 to 0.9 days) and the $DT_{90\ initial}$ in the range of 39.0 to 74.1 hours (1.6 to 3.1 days).

Iprovalicarb did degrade appreciably under anaerobic conditions in soil and would not be expected to persist in this type of environment. Iprovalicarb did degrade appreciably under anaerobic conditions in soil and would not be expected to persist in this type of environment. To derive kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation of these data was performed according to FOCUS kinetics (FOCUS, 2006). The degradation of iprovalicarb and two major metabolites in anaerobic soil was evaluated assuming different kinetic models. Best fit of the parent for the persistence purpose could be reached using a DFOP model ($DT_{50\ initial}$ = 25.4 days). For modelling purpose according to FOCUS kinetics, the degradation of iprovalicarb is well described assuming SFO decay ($DT_{50\ modelling}$ = 30.8 days). The metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* were fitted together with the parent compound, to describe best its total degradation pathways. PMPA *(M10)* shows very good to reasonable fits, assuming SFO decay (DT_{50} for modelling purpose: 38.6 days) and DFOP decay (DT_{50} for persistence endpoints: 43.1 days). N-acetyl-PMPA *(M15)* shows very good to reasonable fits, assuming SFO decay (DT_{50} for modelling purpose: 76.2 days) and DFOP decay (DT_{50} for persistence endpoints: 105.7 days).

It can be concluded from the study concerning the photodegradation of iprovalicarb on soil surfaces that photodegradation will not significantly contribute to the degradation of iprovalicarb. The DT_{50} values in the irradiated and dark samples were 62 and 53 days, respectively.

The kinetic evaluation of six field dissipation trials for persistence or trigger purpose according to FOCUS kinetics (FOCUS, 2006) resulted in non-normalised half-lives of 3.7 to12.5 days for iprovalicarb and 22.2 to 228.4 days for the metabolite PMPA *(M10)*. The corresponding DT_{90} values were in the range of 12.8 to 61.7 days and 73.6 to 758.9 days, respectively.

The adsorption constants K_d for iprovalicarb calculated by means of the Freundlich adsorption isotherm ranged from 0.60 - 4.64 mL/g. The corresponding K_{oc} were in the range of 44 - 221 mL/g

with an arithmetic mean of 114 mL/g. For the major soil metabolites SZX 0722-carboxylic acid *(M03)*, PMPA *(M10)* and N-acetyl-PMPA *(M15)* the K_d values were in the range of 0.012 - 0.354 mL/g, 0.67 - 11.09 mL/g and 0.34 - 0.56 mL/g and the corresponding K_{oc} values were in the range of 0.6 - 13.1 mL/g (mean 5.2 mL/g), 117.9 - 574.6 mL/g (mean 290.2 mL/g) and 32.2 - 53.4 mL/g (mean 39.7 mL/g), respectively.
The results of the field dissipation trials show no mobility of the compound when used in the field was observed in any of the trials; neither residues of iprovalicarb nor of PMPA *(M10)* were detected in soil horizons below 0 - 10 cm.
Based on the results of a lysimeter study it can be concluded with a high probability that iprovalicarb and its metabolites will not contaminate deeper soil layers or groundwater at concentrations $\geq$ 0.1 µg/L.

Summary on the fate and behaviour in water
In sterile aquatic systems iprovalicarb was stable to hydrolysis. Under the experimental conditions no formation of hydrolysis products was observed. Considering the hydrolytic stability determined under environmental pH and temperature conditions, it is not expected that hydrolytic processes will contribute to the degradation of iprovalicarb in the environment.

The UV-VIS absorption data in the environmentally relevant pH range showed that iprovalicarb in aqueous solutions does not absorb any light at wavelengths above 281 nm. Therefore no contribution of the direct photodegradation to the overall elimination of iprovalicarb in the aqueous environment is to be expected.

Studies with iprovalicarb in four different natural water/sediment systems under aerobic conditions showed that the compound was thoroughly degraded leading to CO_2 as the end product of the mineralisation process. PMPA *(M10)* was identified as major metabolite (> 10% of the applied radioactivity) in the water and sediment layers and N-acetyl-PMPA *(M15)* as major metabolite in the water layer. SZX 0722-carboxylic acid *(M03)* was found in amounts of 5.2% of the applied radioactivity in one entire system and N-acetyl-N-methyl-PMPA *(M16)* was found in very small amounts (< 0.5% of the applied radioactivity). Iprovalicarb was metabolised to the endpoint CO_2 via several routes. In one route iprovalicarb was degraded via oxidation of the methyl group of the aromatic system yielding the SZX 0722 carboxylic acid *(M03)*. In the other route the breakdown of the molecule started with cleavage in one of the amide bonds which led to the main metabolite PMPA *(M10)*. Subsequently PMPA reacted with an activated acidic acid derivative yielding N-acetyl-PMPA *(M15)*. This metabolite was methylated in very small amounts to form N-acetyl-N-methyl-PMPA *(M16)*. Ultimately the breakdown of iprovalicarb led to total mineralisation of the aromatic nucleus in the form of carbon dioxide.
To derive kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation of the data from the two water-sediment studies was performed according to FOCUS kinetics (FOCUS, 2006) for the parent compound the major metabolites.
For iprovalicarb the $DisT_{50}$ for modelling purpose in the water phase were in the range of 16.65 to 57.28 days (geom. mean 24.61 days) and in the range of 24.20 to 78.99 days (geom. mean 46.78 days) for the sediment phase. In the total system the $DegT_{50}$ for modelling purpose were in the range of

19.93 to 58.67 days (geom. mean 34.73 days). For persistence trigger evaluation the $DisT_{50}$ in the water phase were in the range of 14.84 to 57.28 days and in the range of 24.20 to 78.99 days for the sediment phase. In the total system the $DegT_{50}$ for persistence trigger evaluation were in the range of 19.17 to 58.67 days. The corresponding $DisT_{90}$ in the water phase were in the range of 58.2 to 190.3 days and in the range of 80.4 to 262.4 days for the sediment phase. In the total system the $DegT_{90}$ were in the range of 66.9 to 194.9 days.

For SZX 0722-carboxylic acid *(M03)* the $DegT_{50}$ in the total systems for modelling purpose and trigger evaluation were in the range of 5.64 to 25.15 days (geom. mean 12.15 days, arith. mean 15.89 days). The corresponding $DegT_{90}$ were in the range of 18.74 to 86.85 days.

For PMPA *(M10)* a $DegT_{50}$ in the total systems for modelling purpose and trigger evaluation of 66.34 days is considered appropriate. The corresponding $DegT_{90}$ is 220.4 days.

For N-acetyl-PMPA *(M15)* no reliable and statistically significant degradation parameters could be evaluated. So, for predictive modelling, a conservative default DT_{50} of 1000 days might be assumed in a total water-sediment system for N-acetyl-PMPA.

Summary on the fate and behaviour in air

Based on the results concerning vapour pressure, Henry law constant and volatilisation in a field experiment it can be concluded that significant volatilisation of iprovalicarb is not to be expected. In addition, estimates of the chemical lifetime in the troposphere resulted in half-lives > 1 day. According to these results an accumulation of iprovalicarb in the air and a contamination by wet or dry deposition is not to be expected.

IIIA 10.11.2 Non-target species at risk and extent of potential exposure

Terrestrial Vertebrates

The risk assessment showed that all toxicity-to-exposure-ratios (TER) for birds and mammals meet the a-priori acceptability criteria. Thus, an unacceptable risk to birds and mammals from dietary exposure after use of the product as described in this dossier is unlikely.

It was also shown that no unacceptable risk to birds and mammals resulted from exposure via drinking water and from secondary poisoning via earthworms or fish is given.

The risk from metabolites to vertebrates is considered to be low.

Aquatic Organisms

The TER values for aquatic organisms based on PEC_{sw} and PEC_{sed} values are in correspondence with the trigger values indicating that the use of the product according to the proposed use pattern does not raise any direct concern. No mitigation measures are required.

Honey Bees

Tier 1 risk assessment showed that the hazard quotients (oral and contact) are below the EU-trigger value. Therefore the use of the product according to the proposed use pattern does not constitute an unacceptable risk towards bees.

Terrestrial Non-Target Arthropods

The risk assessment indicated that no adverse effects on non-target arthropods are to be expected in the in-field and off-field area from the use of the product.

Earthworms and other soil not-target macro-organisms

As has been demonstrated by acute and chronic studies no unacceptable effects on earthworms are to be expected following the application according to the proposed use pattern.

Non-target soil micro-organisms

The risk consideration indicates that no adverse effects on soil micro-organisms are to be expected following the application according to the proposed use pattern.

Terrestrial Non-Target Plants

Overall, it can be concluded that terrestrial non-target plants are not at risk when the product is applied at rates recommended according to good agricultural practice. No mitigation measures are required.

IIIA 10.11.3 Short and long term risks for non-target organisms

Please refer to point 10.11.2.

IIIA 10.11.4 Risk of fish kills and fatalities in large vertebrates

According to the aquatic risk assessment provided under Point 10.2, application of the product according to the proposed use pattern and recommended mitigation measures will not result in unacceptable adverse effects for fish.

Based on the information presented under Points 10.1 and 10.3, it is most unlikely that unacceptable risks will occur in large vertebrates and terrestrial predators when the product is used in accordance with the label recommendations.

IIIA 10.11.5 Precautions necessary to avoid or minimize contamination

No unacceptable risk to non-target organisms is to be expected from the application of the product according to good agricultural practice.

Abbreviations

Abbreviation	Explanation	Definition
a.s.	Active substance	
a.i.	Active ingredient	
AR	Applied Radioactivity	
AV	Avoidance Factor	
BCF	Bioconcentration factor	
bw	Body weight	
calc.	Calculated	
C.L.	Confidence limit	
d	Day	
DDD	Daily dietary exposure	
DT_{50}	Half-life of disappearance	Period required for 50 % dissipation
DT_{90}		Period required for 90 % dissipation
d.wt.s.	Dry weight substrate	
EAC	Ecologically acceptable concentration	
EC_{50}	Median effective concentration	Effective concentration for 50 % of test organisms
ELS	Early life stage	
E_bC_{50}	EC related to biomass	
E_dC_{50}	EC related to cell density	
E_rC_{50}	EC related to growth rate	
E_yC_{50}	EC related to yield	
ER_{50}	Median effective rate	
f	female	
FIR / bw	Food Intake Rate	daily food intake per body weight of animal
h	Hour	
ha	Hectare	
HC_5	Hazardous concentration 5%	Concentration (HCp) derived from a distribution of species sensitivities, that indicates that a certain percentage (p) of all species have a sensitivity at or below this concentration. In the case of HC_5, p=5%.
HQ	Hazard Quotient	
LC_{50}	Lethal concentration, median	Lethal concentration for 50 % of test organisms
LD_{50}	Lethal dose, median	Lethal dose for 50 % of test organisms
LDD_{50}	Lethal dietary dose, median	Lethal dietary dose for 50 % of test organisms
LLC	Lowest lethal concentration	
LLD	Lowest lethal dose	
LOAEC	Lowest observed adverse effect concentration	
LOEC	Lowest observed effect concentration	
LOEL	Lowest observed effect level	
LOER	Lowest observed effect rate	
LR_{50}	Lethal rate 50%	
log P_{ow}	N-Octanol/Water partition coefficient	expressed as logarithm to base ten
m	male	
MAF	Multiple application factor	

Abbreviation	Explanation	Definition
met.	metabolite	
NOAEC	No observed adverse effect concentration	
NOEAEC	No observed environmental adverse effect concentration	
NOEC	No observed effect concentration	
NOEL	No observed effect level	
NOER	No observed effect rate	
NOLEC	No observed lethal effect concentration	
PEC	Predicted environmental concentration	
PEC_{GW}	PEC in ground water	
PEC_i	PEC initial	
PEC_{max}	PEC maximal	Maximal PEC during multiple applications
PEC_{soil}	PEC in soil	
PEC_{sw}	PEC in surface water	
PEC_{twa}	PEC time weighted average	
p.m.	Pure metabolite	
PD	Portion of Diet	Proportion of different food types in the diet
PT	Portion of Time	Proportion of diet obtained in treated area
Q_{HC}	Hazard quotient contact	Dose/contact LD_{50} (dose = field application rate)
Q_{HO}	Hazard quotient oral	Dose/oral LD_{50}
RUD	Residue per Unit Dose	Estimates (from literature) of residues in food sources converted to an application rate of 1 kg/ha
SV	Shortcut value	
TER	Toxicity exposure ratio	
TER_A	TER acute	Toxicity exposure ratio for acute exposure
TER_{ST}	TER short term	Toxicity exposure ratio for short-term exposure
TER_{LT}	TER long term	Toxicity exposure ratio for chronic exposure
TG	Technical Grade	
TRR	Total Radioactive Residues	
TWA	Time weighted average	
w	Week	
<	less than	
≤	less than or equal to	
>	greater than	
≥	greater than or equal to	