Document Title

Tier 2 Summary
of Ecotoxicological Studies
for the active substance Iprovalicarb (SZX 0722)

(Specification No.: 102000006810-05)

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 II

Document M

Section 6, Point 8

Date

2012-05-14

Author(s)

[redacted]

[redacted]

OWNERSHIP STATEMENT

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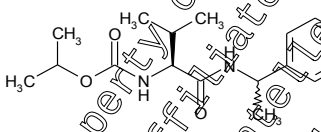
IIA 8 ECOTOXICOLOGICAL STUDIES

Identity of the active substance

ISO common name:	Iprovalicarb
Company Code	SZX 0722
Chemical name (IUPAC):	{2-Methyl-1-[1-(4-methylphenyl)ethylcarbonyl]propyl}-carbamic acid isopropylester
Chemical name (CA):	Carbamic acid, [2-methyl-1-[[[1-(4-methylphenyl)ethyl]amino] carbonyl] propyl]-, 1-methylethylester
CAS No.:	140923-17-7
CIPAC No.:	620
Structural formula:	

Tested metabolites

M03 = SZX 0722-carboxylic acid (synonym: Iprovalicarb-carboxylic acid)
M10 = SZX 0722-p-methylphenethylamine (synonyms: Iprovalicarb-p-methyl-phenetylamine, KUX 2365, SZX 0722 DBMA)
M15 = Iprovalicarb-N-acetyl-PMPA (synonym: WAK 7312)

IIA 8.1 Avian toxicity

No further studies with birds were required or conducted to address safety of iprovalicarb.

IIA 8.1.1 Acute oral toxicity to a quail species, mallard duck or other bird species

Please refer to point IIA 8.1.1 (EU point IIA 8.1.1) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.1.2 Avian dietary toxicity (5-day) test in a quail species or in a mallard duck

Please refer to point IIA 8.1.2 (EU point IIA 8.1.2) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.1.3 Avian dietary toxicity (5-day) test in a second unrelated species

Please refer to point IIA 8.1.3 (EU point 8.1.2) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.1.4 Subchronic and reproductive toxicity to birds

Please refer to point IIA 8.1.4 (EU point 8.1.3) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.2 Fish toxicity

In order to complete the aquatic risk assessment several acute toxicity studies to fish have been conducted with metabolites that can be formed in the aquatic environment. Short summaries of these studies are given below.

IIA 8.2.1 Acute toxicity of the active substance to fish

IIA 8.2.1.1 Rainbow trout

Please refer to point IIA 8.2.1.1 (EU point IIA 8.2.1) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.2.1.2 Warm water fish species

Please refer to point IIA 8.2.1.2 (EU point IIA 8.2.1) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.2.1.3 Acute toxicity of metabolites, degradation or reaction products

After Annex I listing of iprovalicarb an additional study with the metabolite M03 was performed. A short summary of this study is given below. Former studies performed with metabolites M10 and M15 are given under point IIA 8.2.1.3 (EU point IIA 8.2.1) of the EU dossier submitted for Annex I listing.

Metabolite M03

Report:	**IIA 8.2.1.3 /03, [redacted] (2011)**
Title:	Acute toxicity of SZX 0722-carboxylic acid (tech.) to fish (*Oncoryhnchus mykiss*) under static conditions (limit test)
Document No:	M-409113-01-1 (Rep. No: EBSZX156)
Guidelines:	EPA-FIFRA § 72-1/SEP-EPA-540/9-85-006 (1982/1985), OPPTS 850.1075 (Public Draft, 1996), EU Directive 92/69/EEC, C.1 (1992), OECD-Guideline No. 203 (1992).
GLP	Yes (certified laboratory)

Objective: A limit test at 100 mg pure metabolite (p.m.)/L was performed in order to show that fish (*Oncorhynchus mykiss*) were not affected by the test item at this test level.

Material and methods: Test item: SZX 0722-carboxylic acid (tech.), analyzed content of active substance: 98.9% w/w, specified by origin batch no.: BCOO 6249-10-3, Batch code: BCS-CR79590-01-01, tox no.: 09087-00.
Test organism: Rainbow trout (*Oncorhynchus mykiss*), mean body length 4.4 cm, mean body weight 0.9 g. Lot F11/06 was delivered on February 10, 2011. The biomass loading for this test was 0.675 g fish / L test medium
Thirty fish were exposed in a limit test for 96 h under static test conditions to a nominal concentration of 10.0 mg p.m./L against a water control with further 30 fish. A further control group of thirty fish was exposed to test water with the highest solvent concentration.
Dissolved oxygen concentrations ranged from 87 to 99% oxygen saturation, the pH values ranged from 6.6 to 6.9 and the water temperature ranged from 10.9°C to 11.2°C in all aquaria over the whole testing period.
Recoveries of SZX 0722-carboxylic acid were measured in all test levels on day 0, day 2 and day 4 of the exposure period to confirm nominal concentrations.

Findings: The analytical determination of SZX 0722-carboxylic acid (in water by HPLC – MS/MS) revealed mean recovery measured values of 108% of nominal over the whole testing period of 96 hours at the limit test concentration of 10.0 mg p.m./L. Therefore all results are given as nominal values.
Test conditions met all validity criteria given by the mentioned guidelines.
There were neither any sub-lethal effects nor any mortality in the control group.
Cumulative mortality was observed as follows (with a total number of 30 fish tested in each test level):

Exposure time	4 h		24 h		48 h		72 h		**96 h**	
Test level	No. of dead	% dead	No. of dead	% dead	No. of dead	% dead	No. of dead	% dead	**No. of dead**	**% dead**
Control	0	0	0	0	0	0	0	0	**0**	**0**
Solvent control	0	0	0	0	0	0	0	0	**0**	**0**
10.0 mg p.m/L	0	0	0	0	0	0	0	0	0	0

Conclusion: A limit test at 10.0 mg/L of metabolite SZX 0722-carboxylic acid (tech.) did not cause any mortality or sub-lethal effects on Rainbow trout (*Oncorhynchus mykiss*). The 96 h-LC_{50} is > 10.0 mg p.m./L and the 96 h-NOEC is ≥ 10.0 mg p.m./L.

IIA 8.2.2 Chronic toxicity to fish

Not performed with iprovalicarb, as chronic toxicity test (28 day exposure) to juvenile fish is available.

IIA 8.2.3 Chronic toxicity test (28 day exposure) to juvenile fish

Please refer to point IIA 8.2.3 (EU point IIA 8.2.2.1) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.2.4 Fish early life stage toxicity test

In view of the findings during the chronic toxicity test on juvenile fish (see IIA 8.2.3) and the low BCF value (see 8.2.3), an ELS toxicity test is not required. However, for registration purpose in USA a study has been conducted with iprovalicarb.

Report:	**IIA 8.2.4 /01, [redacted] (2000)**
Title:	TM-210: An early life-stage toxicity test with the rainbow trout (*Oncorhynchus mykiss*)
Document No:	M-030681-01-1 (Rep. No: 443A-105)
Guidelines:	OPPTS number 850.1400; ASTM Standard E1241-88a
GLP	Yes (certified laboratory)

Material and methods:

- Iprovalicarb tech. (= TM-210), purity: 97.61%, batch no. # 898809124,
- newly fertilised Rainbow Trout (*Oncorhynchus mykiss*, embryos, unfertilised eggs and sperm received from Mt. [redacted], [redacted], California)
- endpoints: hatching success, time to hatch, time for larvae to swim-up, post-hatch growth and survival
- study duration was 88 days under flow through conditions (60 days post-hatch)
- 4 replicate test chambers/treatment and control group (15 embryos/incubation cup = 30 embryos/replicate = 120 embryos/experimental group)
- nominal concentrations (mean measured) were negative control, solvent control, 0.63 (0.65), 1.3 (1.3), 2.5 (2.6), 5.0 (5.0) and 10 (9.1) mg a.s./L; mean measured concentrations represent 103, 100, 104, 100 and 91% of nominal, the results of the test are reported based on mean measured concentrations;
- temperature: 12 + 1°C; dissolved oxygen: >7.4 mg/L (69% saturation); pH: 7.9 to 8.4

Findings: Chronic toxicity of iprovalicarb to fish

Test substance	a.s.	
Test object	Rainbow Trout	
Exposure	88d, flow-through ELS	
	NOEC [mg a.s./L]	LOEC [mg a.s./L]
Egg hatch	9.1	>9.1
Time to swim-up	9.1	>9.1
Survival of larvae and fry (post-hatch)	9.1	>9.1
Growth: total length (day 31 and 60 post-hatch)	9.1	>9.1
Growth: wet weight (day 60 post-hatch)	5.0	9.1
Growth: dry weight (day 60 post-hatch)	5.0	9.1
Overall	5.0	9.1

Observations: All surviving fish in the controls and the treatment groups appeared normal and healthy during the test.

Conclusion: The overall NOEC has been determined as 5.0 mg a.s./L.

IIA 8.2.5 Fish life cycle test

Not performed with iprovalicarb, as a chronic toxicity test to juvenile fish test is available.

IIA 8.2.6 Bioconcentration potential in fish

IIA 8.2.6.1 Bioconcentration potential of the active substance in fish

Iprovalicarb was investigated with respect to bioconcentration in fish in view of the fact that the octanol/water partition coefficients (Log Pow) have been determined as 3.18 (Diastereomer A) and 3.20 (Diastereomer B).

Please refer to point IIA 8.2.6.1 (EU point IIA 8.2.3) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

After Annex I listing of iprovalicarb an additional study was performed to investigate the metabolism of iprovalicarb in bluegill sunfish.

Report:	**IIA 8.2.6.1 /02, [redacted] (2001)**
Title:	Nature of residues of [phenyl-UL-14C]SZX 0722 in bluegill sunfish
Document No.	M-064491-01-1 (Rep. No: MR-066/01)
Guidelines:	US EPA requirements (EPA pesticide Assessment Guidelines, Subdivision N, 8165-1)
GLP	Yes (certified laboratory)

Objectives: The current study was conducted to determine the nature of the residues in edible and non-edible tissues (viscera) of bluegill sunfish exposed to [Phenyl-UL-14C] iprovalicarb in a flow-through system for a fish metabolism study and to quantify the metabolites to the extent possible.

Material and methods: [phenyl-UL-14C]-SZX 0722 (= iprovalicarb), radiopurity: >99 %, chemical purity: >99%, specification: protocol THS 6017, specific radioactivity: 5.11 MBq/mg (3.066x108 dpm/mg; 138 µCi/mg)

The metabolism of [PhenyI-UL-14C]SZX 0722 was investigated in bluegill sunfish. Fish was exposed to water with a parent compound concentration of approximately 200 µg/L (flow through conditions) for 3 and 7 days. Analyses of water samples of day 0 and 7 ensured that the fish was exposed to the parent compound iprovalicarb, and not to iprovalicarb related metabolites. Fish were sampled at day 3 and day 7 and dissected into edible (fillets) and non-edible (viscera) parts, extracted with acetonitrile/water and analysed by HPLC.

The total radioactive residues (TRR) in the edible samples ranged between 0.822 mg/kg and 1.781 mg/kg fresh weight and amounted to 5.569 mg/kg and 9.746 mg/kg, respectively in viscera at day 3 and at day 7.

The main amount of the TRR in all fish samples was represented by the diastereomers of 4-hydroxymethyl-SZX 0722 glucuronide (including the diastereomers of the methylated 4-hydroxymethyl-SZX 0722-glucuronides formed prior to HPLC analysis due to the use of methanol as solvent), followed by the diastereomers of the taurine conjugate of SZX 0722 carboxylic acid. (An exception was the edible sample of day 3 in which the parent compound iprovalicarb was represented in a higher concentration than the taurine conjugate.) Further metabolites were 4-hydroxymethyl-SZX 0722 and SZX 0722 carboxylic acid, detected in varying concentrations. The presence of 3-hydroxyphenyl-SZX 0722-glucuronide could be possible, but was not confirmed; 3-hydroxyphenyl-SZX 0722 was not identified in any sample. Unchanged iprovalicarb was found in concentrations ranging between 0.157 mg/kg and 0.443 mg/kg. In the different samples the parent compound was represented by 4% to 24% of the TRR. This shows that iprovalicarb metabolised rather quickly.
Based on the residues of the parent compound iprovalicarb in edibles and viscera and on the concentration of iprovalicarb measured in water (nominal concentration 0.2 mg/L) the following bioconcentration factors were calculated for the parent compound:

BCFparent, edible, day 3	1.0	BCFparent, edible. day 7	0.9
BCFparent, viscera, day 3	2.1	BCFparent, viscera, day 7	2.3
BCFparent, whole fish day 3	1.4	BCFparent, whole fish day 7	1.4

The parent compound iprovalicarb used in this study was an approximately 1:1 mixture of S,R and S,S diastereomers, but it was not possible to detect the diastereomers separately by HPLC analysis. Nevertheless, it can be assumed that the residues of the parent compound iprovalicarb in fish are a mixture of diastereomers similar to the initial composition, because most of the metabolites formed were detected as a mixture of diastereomers in an approximately 1:1 ratio.

The following tables show the amounts of radioactivity (in % of TRR) and the corresponding equivalent concentrations (in mg/kg fresh weight) of a.s. in the fish samples investigated.

Test A (3 days)				
	Edible tissues		Viscera	
	% TRR	mg/kg	% TRR	mg/kg
TRR	100.00	**0.848**	100.00	**5.720**
bound residues	2.08	0.018	0.48	0.027
not analysed	0.97	0.008	2.17	0.124
taurine conjugate of SZX 0722 carboxylic acid	7.58	0.064	18.16	1.039
4-hydroxymethyl-SZX 0722 glucuronide*	28.01	0.238	49.21	2.815
4-hydroxymethyl-SZX 0722	15.46	0.131	11.42	0.653
SZX 0722 carboxylic acid	9.53	0.081	6.52	0.373
SZX 0722	24.09	0.204	7.74	0.443
Total identified	**84.67**	**0.718**	**93.05**	**5.323**
Total characterised	12.27	0.104	4.30	0.246
Sum identified + characterised	**96.94**	**0.822**	**97.35**	**5.569**

* sum of 4-hydroxymethyl-SZX 0722-glucuronide and methylated 4-hydroxymethyl-SZX 0722-glucuronide

Test B (7 days)				
	Edible tissues		Viscera	
	% TRR	mg/kg	% TRR	mg/kg
TRR	100.00	**1.838**	100.00	**9.926**
bound residues	1.29	0.024	0.50	0.049
not analysed	1.80	0.033	1.32	0.131
taurine conjugate of SZX 0722 carboxylic acid	29.59	0.544	20.18	2.003
4-hydroxymethyl-SZX 0722 glucuronide*	34.20	0.628	59.22	5.878
4-hydroxymethyl-SZX 0722	5.86	0.108	4.07	0.404
SZX 0722 carboxylic acid	8.83	0.162	4.80	0.477
SZX 0722	8.52	0.157	4.33	0.430
Total identified	**87.00**	**1.599**	**92.59**	**9.191**
Total characterised	9.91	0.182	5.59	0.555
Sum identified + characterised	**96.91**	**1.781**	**98.18**	**9.746**

* sum of 4-hydroxymethyl-SZX 0722-glucuronide and methylated 4-hydroxymethyl-SZX 0722-glucuronide

The biotransformation path of iprovalicarb in bluegill sunfish is characterised by hydroxylation of the methyl group attached to the aromatic ring to yield 4-hydroxymethyl-SZX 0722. 4-Hydroxymethyl-SZX 0722 was rapidly metabolised via conjugation to yield the corresponding glucuronide or via oxidation to yield SZX 0722 carboxylic acid, which was further metabolised via conjugation with taurine.

IIA 8.2.6.2 Bioconcentration potential of metabolites, degradation and reaction products

The log Pow values for metabolites M03, M10 and M15 are < 3 (please refer to IIA, 2.8). Therefore, bioconcentration of these metabolites is considered to be unlikely and studies are not necessary.

IIA 8.2.7 Aquatic bioavailability/biomagnification/depuration

No data requirement according to Regulation 1107/2009/EEC or Directive 91/414/EEC.

IIA 8.3 Aquatic species other than fish and aquatic species field testing

IIA 8.3.1 Acute toxicity to aquatic invertebrates

IIA 8.3.1.1 Acute toxicity (24 and 48 hour) for Daphnia preferably (*Daphnia magna*)

After Annex I listing of iprovalicarb an additional study with iprovalicarb metabolite M03 was performed. A short summary of the study is given below. Studies performed with the active substance and metabolites M10 and M15 are presented under point IIA 8.3.1.1 (EU point IIA 8.2.4) of the EU dossier submitted for Annex I listing.

Metabolite M03

Report:	**IIA 8.3.1.1 /04; [redacted] 2011**
Title:	Acute toxicity of SZX 0722-carboxylic acid (tech.) to the waterflea *Daphnia magna* in a static laboratory test system – Limit test
Document No:	M-409052-01-1 (Rep. No: EBSZX157)
Guidelines:	OECD Guideline 202, (2004) U.S. EPA Pesticide Assessment Guidelines, Subdivision E, § 72-2 (1982) EC Council Regulation No 440/2008, Method C.2 (2008) OPPTS Guideline 850.1010 Draft (1996), modified JMAFF 12 Nousan No. 8147 (2000)
GLP	Yes (certified laboratory)

Objective: The study was performed, to verify the absence of treatment-related effects on mobility of *Daphnia magna* over 48 hours under static exposure conditions, when exposed to a limit concentration of 10 mg/L of metabolite SZX0722-carboxylic acid.

Material and methods: SZX0722-carboxylic acid (tech.), batch BCS-CR79590-01-01, purity 98.9% w/w (TOX 09087-00); *Daphnia magna* (1st instars < 24 h old, 10 × 5 animals per concentration), exposed in a static test system for 48 hours to nominal concentrations of 0 (pure water control + solvent control) and 10 mg pure metabolite (p.m.)/L without feeding.
The content of SZX0722-carboxylic acid in exposure media was measured for verification of the test item concentrations.

Findings: Toxicity to *Daphnia magna* (based on nominal concentrations):

Treatment group	Exposed daphnids (=100%)	Immobilised daphnids			
		24 h		48 h	
		n	%	n	%
Pure water control	50	0	0	0	0
Solvent control	50	0	0	0	0
10 mg SZX0722-carboxylic acid /L	50	0	0	0	0

The accompanying chemical analysis of SZX0722-carboxylic acid revealed recoveries of 112% of nominal at the start and 118% of nominal at the end of the exposure period.
No contaminations of SZX0722-carboxylic acid were detected in samples from untreated water control.
Since the nominal concentration of 10 mg p.m./L has been successfully maintained over the entire test period all reported results are based on the nominal concentration.

Observations: No immobilities or other effects on behaviour occurred in untreated control within 48 hours of exposure.

Conclusions: Due to the absence of treatment related effects up to a nominal concentration of 10 mg/L, the EC_{50} for immobilisation after 24 and 48 hours of static exposure was > 10 mg p.m./L.

IIA 8.3.1.2 Acute toxicity (24 and 48 hour) for representative species of aquatic insects

As the products containing the active substance iprovalicarb are not to be used directly on surface water, studies on representative species from the groups of aquatic insects are not triggered.

IIA 8.3.1.3 Acute toxicity (24 and 48 hour) for representative species of aquatic crustaceans (species unrelated to Daphnia)

As the products containing the active substance iprovalicarb are not to be used directly on surface water, studies on representative species from the groups of aquatic insects, aquatic crustaceans (species unrelated to Daphnia) are not triggered.

IIA 8.3.1.4 Acute toxicity (24 and 48 hour) for representative species of aquatic gastropod molluscs.

As the products containing the active substance iprovalicarb are not to be used directly on surface water, studies on representative species from the group of aquatic gastropod molluscs are not triggered.

IIA 8.3.2 Chronic toxicity to aquatic invertebrates

IIA 8.3.2.1 Chronic toxicity in Daphnia magna (21-day)

Please refer to point IIA 8.3.2.1 (EU point IIA 8.2.5) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.3.2.2 Chronic toxicity for representative species of aquatic insects

As products containing the active substance iprovalicarb are not to be used directly on surface water, chronic toxicity studies with representative species of aquatic insects are not triggered.

IIA 8.3.2.3 Chronic toxicity for representative species of aquatic gastropod molluscs

As products containing the active substance iprovalicarb are not to be used directly on surface water, chronic toxicity studies with representative species of aquatic gastropods mollusc are not triggered.

IIA 8.3.3 Aquatic field testing

As products containing the active substance iprovalicarb are not to be used directly on surface water, aquatic field studies are not triggered.

IIA 8.4 Effects on algal growth and growth rate (2 species)

After Annex I listing of iprovalicarb an additional study with iprovalicarb metabolite M03 was performed. A short summary of the study is given below. Studies performed with the active substance and metabolites M10 and M15 are presented under point IIA 8.4 (EU point IIA 8.2.6) of the EU dossier submitted for Annex I listing.

Metabolite M03

Report:	**IIA 8.4 /04: [redacted] 2011**
Title:	*Pseudokirchneriella subcapitata* growth inhibition test with SZX 0722 carboxylic acid (tech.) – limit test
Document No:	M-411009-01-1 (Rep. No: E323 4074-3)
Guidelines:	OECD Guideline 201: "Freshwater Alga and Cyanobacteria, Growth Inhibition Test" (March 23, 2006)
GLP	Yes (certified laboratory)

Objective: The objective of this 72 hour growth inhibition test is to verify the assumption that the test item will cause no adverse effects on the growth of the green algae *Pseudokirchneriella subcapitata*.

Material and methods: SZX 0722 carboxylic-acid analyzed purity: 98.9% was tested, specified by origin batch no.: BCOO 6249-10-3, customer order no.: TOX09087-00 and LIMS no.: 1100544.
Pseudokirchneriella subcapitata (freshwater microalgae, formerly known as *Selenastrum capricornutum*) were exposed in a chronic multigeneration test for 3 days under static exposure conditions to the nominal concentration of 10.0 mg pure metabolite (p.m.)/L in comparison to controls. The pH values ranged from 7.8 to 7.9 in the controls and the incubation temperature ranged from 21.3°C to 22.1°C (measured in an additional incubated glass vessel) over the whole period of testing at a continuous illumination of 8336 lux.
Quantitative amounts of SZX 0722 carboxylic-acid were measured in the treatment group and in the controls on day 0 and day 3 of the exposure period.

Findings: Test conditions met all validity criteria, given by the mentioned guideline.
The analytical findings of SZX 0722 carboxylic-acid in the treatment level found on day 0 was 111% of nominal. On day 3 analytical findings of 103% of nominal was found. All results are based on nominal test concentrations of the metabolite.

The static 72 hour algae growth inhibition test provided the following effects:

Nominal concentration [mg p.m./L]	Cell number after 72 h (means) per mL	(0-72h)-average specific growth rates [days^{-1}]	Inhibition of average specific growth rate [%]
Control	707 000	1.419	--
Solvent control	722 000	1.426	--
Pooled controls	714 000	1.423	--
10.0	740 000	1.435	-0.9

Conclusions: The (0 - 72h)-E_rC_{50} for SZX 0722 carboxylic-acid is > 10.0 mg p.m./L and the (0 - 72h) - NOE_rC is ≥ 10.0 mg p.m./L.

IIA 8.5 Effects on sediment dwelling organisms

IIA 8.5.1 Acute test

A test is not required for a fungicide.

IIA 8.5.2 Chronic test

After Annex I listing of iprovalicarb additional studies with iprovalicarb and metabolite M10 were performed. Short summaries of the studies are given below.

Report:	**IIA 8.5.2 /01; [redacted].; 2010**
Title:	*Chironomus riparius* 28-day chronic toxicity test with iprovalicarb (tech.) in a water-sediment system using spiked sediment
Document No:	M-398870-01-1 (Rep. No.: EBSZL026)
Guidelines:	OECD Guideline 218: "Sediment-Water Chironomid Toxicity Test Using Spiked Sediment" (adopted 13 April 2004)
GLP	Yes (certified laboratory)

Objective: The aim of the study was to determine the influence of iprovalicarb (tech.) on emergence and development of *Chironomus riparius* for 28-days in a static water-sediment system (spiked sediment exposure), expressed as NOEC, LOEC and EC_x for emergence rate and development rate, if possible.

Material and methods: Iprovalicarb (tech.); content: 97.5% was tested, specified by batch-no.: PF90187411, TOX08831-00 and specification No.: 102000006810).
First instar of *Chironomus riparius* larvae, 4 beakers per test concentration, control and solvent control with 20 animals each) were exposed in a static test system for 28 days to initial nominal concentrations of 7.81, 15.6, 31.3, 62.5, 125 and 250 mg a.s./ kg dw sed (dry weight sediment) of a water-sediment system.
Dissolved oxygen concentrations ranged in the water phase from 7.4 to 8.5 mg O_2/L (7.4 mg O_2/L= 83% O_2 - saturation), the water pH values ranged from 8.2 to 8.5 and the water temperature ranged from 20.2°C to 20.7°C measured from parallel beakers of each test concentration over the whole period of testing.
The concentrations of iprovalicarb (SZX 0722) were analysed in the freshly prepared spiked sediments of all test concentrations and the controls on day -2. The concentrations were analyzed at day 0 (directly before inserting of the larvae), day 7 and day 28 (after insertion of the larvae) in the overlying water, the

pore water and the sediment. Accompanying chemical analyses were performed using additionally separate test vessels for all test concentrations and controls.

Findings: Test conditions met all validity criteria, given by the mentioned guideline.

Analytical findings: Chemical analyses of iprovalicarb were performed for sediment, overlying water and pore water samples.
Sediment analysis on day -2 (directly after spiking) reflect high recoveries of iprovalicarb with 92 to 107% (mean of 96.2%) of nominal concentrations in all test levels, thus all results are based on initial nominal concentrations of iprovalicarb in the sediment, expressed in mg a.s./kg dw sed.
Chemical analyses of the sediment, overlying water and pore water over time reflect the aquatic fate profile of iprovalicarb demonstrating a steady partitioning out of the sediment into the water column overtime.
Analyses of the sediment over time showed recoveries of 71.8% to 94.8% (mean = 80.5%) of nominal for all test concentrations on day 0. On day 7, 51.9% to 79.0% (mean = 61.1%) and on day 28, 31.9% to 58.5% (mean = 37.9%) of nominal were found, respectively.
Analyses of the overlying water over time showed recoveries of 13.0% to 23.4% (mean = 19.9%) of nominal applied amount of a.s. per test concentration on day 0. On day 7, 27.5% to 42.4% (mean = 37.4%) and on day 28, 33.5% to 45.4% (mean = 39.3%) of nominal were found, respectively.
Analyses of the pore water over time showed low recoveries of 2.9% to 6.8% (mean = 5.3%) of nominal concentrations on day 0 for all test concentrations. On day 7, 2.8% to 5.8% (mean = 4.0%) and on day 28, 2.3% to 3.2% (mean = 2.7%) of nominal were found, respectively.

Biological findings: Start of emergence was at day 14 and 15 for the controls and all test concentrations from 7.81 to 250 mg a.s./kg dw sed.
94.4% of the inserted (n= 160) larvae maturated to adults in the pooled controls after 28 days, fulfilling the guideline requirements.

Influence on the emergence and development after 28 days (based on nominal concentrations initial concentrations of the test item in the sediment):

Concentration initial nominal mg a.s./kg dw sed	Number of introduced larvae	Number of emerged midges	Emergence of inserted larvae			Development pooled sex rate (1/d)
			total (%)	male (%)	female (%)	
Controls [1]	160	151	94.4	51.9	42.5	0.060
7.81	80	75	93.8	38.8	55.0	0.058
15.6	80	74	92.5	46.3	46.3	0.058
31.3	80	72	90.0	48.8	41.3	0.062
62.5	80	68	85.0	522.5	32.5	0.059
125	80	73	91.3	45.0	46.3	0.059
250	80	49 [2]	61.3	36.3	25.0	0.059

[1] control and solvent-control pooled
[2] statistical significant difference

Summary of results, based on nominal initial concentrations of iprovalicarb in mg a.s./kg dw sed

Endpoints	NOEC	LOEC	EC_{15}	EC_{50}
Emergence ratio (pooled sex) (95 % confidence limits)	125	250	128 (n.d.)	> 250
Development rate (pooled sex)	≥ 250	> 250	> 250	> 250

n.d. not determined

The Chi^2-Test indicates no statistically different distribution between sexes compared to the assumption of 50% females and 50% males. Therefore male and female results were pooled for further statistical analyses to increase the statistical power.
A statistical significant difference in emergence was only estimated at the highest test concentrations of 250 mg a.s./kg dw sed as compared to the pooled controls, resulting in a NOEC of 125 mg a.s./kg dw sed.
For the development rate (pooled sex) there was no statistical significant difference up to the highest test concentration of 250 mg a.s./kg dw sed as compared to the controls, resulting in a NOEC of ≥ 250 mg a.s./kg dw sed.

Conclusion: The EC_{15} for iprovalicarb in the 28 day study with *Chironomus riparius* was determined to be 128 mg a.s./kg dw sed for emergence ratio and > 250 mg a.s./kg dw sed for development rate. The NOEC was determined to be 125 mg a.s./kg dw sed for emergence ratio and ≥ 250 mg a.s./kg dw sed.

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Metabolite M10

Report:	**IIA 8.5.2 /02; [redacted] 2010**
Title:	*Chironomus riparius* 28-day chronic toxicity test with SZX 0722-p-methylphenethylamine in a water-sediment system using spiked sediment – limit test
Document No:	M-368933-01-1 (Rep. No.: EBSZL022)
Guidelines:	OECD Guideline 218: "Sediment-Water Chironomid Toxicity Test Using Spiked Sediment" (adopted 13 April 2004)
GLP	Yes (certified laboratory)

Objective: The aim of the study was to demonstrate, that the limit test concentration of 100 mg SZX 0722-p-methylphenethylamine/kg sediment (dry weight) had no influence on growth and development of larvae of *Chironomus riparius* as compared to control findings at the 5% level of significance.

Material and methods: SZX 0722-p-methylphenethylamine, purity: 94.6% was tested, specified by batch no.: 960229ELB03, AZ: 16068 and Batch code.: AE C624117-01-01).
First instar of *Chironomus riparius* larvae, 6 beakers per test concentration, control and solvent control with 20 animals each) were exposed in a static test system for 28 days to initial nominal limit concentration of 100 mg pure metabolite (p.m.)/ kg dw sed (dry weight sediment) of a water-sediment system.
Dissolved oxygen concentrations ranged in the water phase from 7.2 to 8.4 mg O_2/L (7.2 mg O_2/L= 81.2% O_2 - saturation), the water pH values ranged from 8.0 to 8.6 and the water temperature ranged from 20.4°C to 20.8°C measured from parallel beakers of each test concentration over the whole period of testing.
The concentration of the active substance was analysed in the freshly prepared spiked sediment of the limit test concentration 100 mg p.m./kg dw sed and the controls on day -2. Its concentration was analyzed at day 0 (directly before inserting of the larvae), day 7 and day 28 (after insertion of the larvae) in the

overlying water, the pore water of the sediment and the sediment in separate test vessels of the limit test concentration and controls.

Findings: Test conditions met all validity criteria, given by the mentioned guideline.

Analytical findings: Chemical analysis was performed for SZX 0722-p-methylphenethylamine for sediment-, overlying water- and pore water -samples.
Sediment analysis on day -2 (directly after spiking) reflect a recovery of 81.3% of SZX 0722-p-methylphenethylamine of the nominal concentration, thus all results are based on the nominal initial concentration of SZX 0722-p-methylphenethylamine in the sediment.
Analyses of the sediment over time showed a recovery of 65.2% of the nominal limit concentration of 100 mg/kg dw sediment on day 0. On day 7, 51.1% and on day 28, 40.1% of nominal were found.
Chemical analysis of the overlying water over time yield 13.2% of the nominal test concentration on day 0, 19.3% on day 7 and 11.2% on day 28.
Chemical analysis of the pore water over time yield 2.37% of nominal concentration on day 0, 2.17% on day 7 and 1.0%, on day 28.

Biological findings: Start of emergence was at day 14 for the controls and the limit test concentration of 100 mg p.m./kg dw sed.
85.0% of the inserted (n= 120) larvae maturated to adults in the controls after 28 days, fulfilling the guideline requirements.

Influence on the emergence and development after 28 days (based on nominal concentrations):

Concentration initial nominal mg p.m./kg dw sed	Number of introduced larvae	Number of emerged midges	Emergence of inserted larvae total (%)	male (%)	female (%)	Development pooled sex rate (1/d)
Control	120	102	85.0	47.5	37.5	0.058
Solvent control	120	103	85.8	40.8	45.0	0.059
100	120	108	90.0	47.5	42.5	0.058

Summary of results, based on nominal initial concentration of SZX 0722-p-methylphenethylamine in mg p.m./kg dw sed

Endpoints	EC_{15}	NOEC	LOEC
Emergence ratio (pooled sex)	> 100	≥ 100	> 100
Development rate (pooled sex)	> 100	≥ 100	> 100

The Chi²-Test indicates no statistically different distribution between sexes compared to the assumption of 50% females and 50% males. Therefore male and female results were pooled for further statistical analyses to increase the statistical power. There was no statistical significant difference in emergence between the control and solvent control and at the limit test concentrations of 100 mg p.m./kg dw sed as compared to the control findings, resulting in a NOEC of ≥ 100 mg p.m./kg dw sed.
For the development rate (pooled sex) there was no statistical significant difference as compared to the control for the limit test concentration, resulting in a NOEC of > 100 mg p.m./kg dw sed.

Conclusion: The NOEC for SZX 0722-p-methylphenethylamine in the 28 day study with *Chironomus riparius* was ≥ 100 mg p.m./kg dry weight sed. The LOEC was > 100 mg p.m./kg dry weight sed. The EC_{15} was > 100 mg p.m./kg dry weight sed.

IIA 8.6 Effects on aquatic plants

A test on aquatic plants is not required for a fungicide.

IIA 8.7 Effect on bees

No further studies with bees were required or conducted to address safety of iprovalicarb.

IIA 8.7.1 Acute oral toxicity

Please refer to points IIA 8.7.1 / IIA 8.7.2 (EU point IIA 8.3.1.1) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.7.2 Acute contact toxicity

Please refer to points IIA 8.7.1 / IIA 8.7.2 (EU point IIA 8.3.1.1) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.7.3 Toxicity of residues on foliage to honey bees

Due to the findings of the acute and oral toxicity tests with the active substance iprovalicarb, further bee residue toxicity test is not necessary.

IIA 8.7.4 Bee brood feeding test

Iprovalicarb does not act as an insect growth regulator. Therefore, a bee brood feeding test is not required.

IIA 8.8 Effects on non-target terrestrial arthropods

IIA 8.8.1 Effects on non-target terrestrial arthropods using artificial substrates

IIA 8.8.1.1 Parasitoid

Please refer to point IIA 8.8.1.1 (EU point IIA 8.3.2) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.8.1.2 Predatory mites

Please refer to point IIA 8.8.1.2 (EU point IIA 8.3.2) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.8.1.3 Ground dwelling predators

Please refer to point IIA 8.8.1.3 (EU point IIA 8.3.2) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.8.1.4 Foliage dwelling predators

Please refer to point IIA 8.8.1.4 (EU point IIA 8.3.2) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.8.2 Effects on non-target terrestrial arthropods in extended laboratory/semi-field tests

Based on the results of the studies reported under points IIA 8.8.1.1 to IIA 8.8.1.4 extended laboratory/semi-field studies on predatory mites, parasitoids and further non-target arthropod species are not triggered.

IIA 8.8.2.1 Parasitoid

See point IIA 8.8.2.

IIA 8.8.2.2 Predatory mites

See point IIA 8.8.2.

IIA 8.8.2.3 Ground dwelling predatory species

See point IIA 8.8.2.

IIA 8.8.2.4 Foliage dwelling predatory species

See point IIA 8.8.2.

IIA 8.8.2.5 Other terrestrial invertebrates

See point IIA 8.8.2.

IIA 8.9 Effects on earthworms

IIA 8.9.1 Acute toxicity to earthworms

After Annex I listing of iprovalicarb an additional study with the metabolite M10 was performed. A short summary of the study is given below. A former study performed with the active substance iprovalicarb is given under point IIA 8.9.1 (EU point IIA 8.4.1) of the EU dossier submitted for Annex I listing.

Metabolite M10

Report:	**IIA 8.9.1 /02; [redacted];1999**
Title:	Toxicity of KUX 2365 (tech.) to Earthworms (*Eisenia fetida*)
Document No:	M-016516-01-1 (HBF/Rg 302)
Guidelines:	OECD 207 "OECD-Guideline for Testing Chemicals," "Earthworm, Acute Toxicity Tests" (1984)
GLP	Yes (certified laboratory)

Objective: The purpose of this study was to investigate the effects of Iprovalicarb-PMPA (KUX 2365) on the mortality of adult *Eisenia fetida*.

Material and methods: KUX 2365 (tech.), Batch No.: 130499, TOX No.: 5031-00, purity: 98.7 %. Adult *Eisenia fetida* (4 x 10 animals per concentration) were exposed in an artificial soil (with 10%

peat) for 14 days to the concentrations of 3.2, 10, 32, 100, 316 and 1000 mg test substance / kg dry weight soil (nominal concentrations).

Findings: Toxicity to earthworms after 14 days

Test substance	KUX 2365 (tech.)
Test object	*Eisenia fetida*
Exposure	14 d
LC_{50} (mg/kg)	> 1000
Lowest tested concentration with observed effects (LOEC) (mg/kg)	1000
Highest tested concentration without observed effects (NOEC) (mg/kg)	316
Threshold effect concentration, TEC (geometric mean of LOEC and NOEC) (mg/kg)	562

Observations: No mortality could be observed in the treatment groups up to 316 mg/kg dry soil. Abnormalities, e.g. changes in behaviour, were not observed. Based on weight alterations and symptoms, the NOEC has been determined as 316 mg/kg d.wt. soil. The LC_{50} was calculated as > 1000 mg/kg d.wt.soil.

Conclusions: KUX 2365 is not acutely toxic to earthworms.

IIA 8.9.2 Sublethal effects

After Annex I listing of iprovalicarb additional studies with the formulation Iprovalicarb WG 50, the active substance and metabolites M03, M10 and M15 were performed. Short summaries of the studies are given below. A former study, performed with the formulation Iprovalicarb WG50, is given under point IIA 8.9.2 (EU point IIA 8.4.2) of the EU dossier submitted for Annex I listing.

Iprovalicarb WG50

Report:	**IIA 8.9.2 /02; [redacted] 2001**
Title:	Influence of Iprovalicarb WG 50 on the Reproduction of Earthworms (*Eisenia fetida*)
Document No:	M-053073-01-1 (MPE/Rg 370/01)
Guidelines:	ISO/DIS 11268-2 (1996) BBA, Guidelines for the Testing of Plant Protection Products Within Registration, Part VI, 2 - 2, January 1994
GLP	Yes (certified laboratory)

Objective: The purpose of this study was to investigate the effects of Iprovalicarb WG 50 on the mortality, body weight, feeding activity and reproduction of adult *Eisenia fetida*.

Material and methods: Iprovalicarb WG 50, (a.i.-content: 50.6 %; specification: Batch-No.: 05250/0136(0125), Development-No.: 3000167897, TOX-No.: 5692-00) was used in this study. Adult *Eisenia fetida* (4 x 10 animals per application rate) were exposed in an artificial soil (with 10% peat) to the application rates of 1, 2 and 5 kg formulation/ha. After 28 days the number of surviving animals and their weight alteration was determined. They were then removed from the artificial soil. After further 28 days, the number of offsprings was determined.

Findings: Effects on earthworm reproduction after 56 days

Test substance	IPROVALICARB WG 50			
Test object	*Eisenia fetida*			
Exposure	56 d			
Application rates (g a. i./ha)	Control	1 kg/ha	2 kg/ha	5 kg/ha
Mortality of adult earthworms (%) after 28 days	0	0	0	0
Weight increase of adult earthworms (%)	75.25	79.49	68.26	69.68
Number of offsprings per surviving adult	15.20	17.48	16.80	15.90

The results of the most recent reference test item indicated that the test system was sensitive to the reference test item. A dose response study was carried out with the reference substance Derosal (active ingredient: 36% Carbendazim) at application rates of 0.10, 0.25 and 0.50 kg /ha. Mortality of adult earthworms as compared to control organisms was not observed at any dosage. The body weight reduction was significant at 0.25 and 0.5 kg/ha. Only the highest dosage of 0.5 kg/ha reduced the numbers of juvenile earthworms by 46 %. The no-observed-effect-level (NOEL) was 0.10 kg/ha (= 0.036 kg active ingredient/ha) and the lowest-observed-effect-level (LOEL) 0.25 kg/ha (= 0.09 kg active ingredient/ha).

Observations: Mortality or a significant body weight reduction of adult earthworms was not observed at any application rate in this study. Also the number of offsprings was not reduced at any application rate.

Conclusion: NOEL >5 kg formulation/ha (equivalent to 2.5 kg a.s./ha)
(This endpoint is equivalent to a NOEC of 10 mg a.i./kg dry weight soil considering the actual test conditions: (surface of the test vessels of approximately 200 cm^2 and the actual soil dry weight of 500 g in the test containers.).

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Iprovalicarb

Report:	**IIA 8.9.2 /03; [redacted] 2011**
Title:	Iprovalicarb tech.: Effects on survival, growth and reproduction on the earthworm *Eisenia fetida* tested in artificial soil with 5% peat
Document No:	M-405822-01-1 (LRT-Rg-R-85/11)
Guidelines:	OECD, Guideline for the testing of chemicals Nr. 222 "Earthworm, Reproduction Test" (adopted April 13, 2004) - ISO-Guideline 11268-2, "Soil quality – Effects of pollutants on earthworm (*Eisenia fetida*) – Part 2: „Determination of effects on reproduction", International Organization for Standardization, 1998
GLP	Yes (certified laboratory)

Objective: The purpose of this study was to investigate the effects of iprovalicarb on the mortality, body weight, feeding activity and reproduction of adult *Eisenia fetida*.

Materials and Methods: Test item: Iprovalicarb tech.; (TOX-No.: 08831-00; Specification No.: 102000006810; Batch code: AE 0540058-01-01; Origin Batch No.: PF90187411; LIMS No.: 0935319; Article-No.: 05448417; content of a.s. (analysed): 97.5% w/w.
Principles of the testing procedure: First run of the study: Adult *Eisenia fetida* (approx. 8 months old, 8 x 10 animals for the control group and 4 x 10 animals per test concentration of the treatment group) were exposed in an artificial soil (peat content: 5%) to the nominal test concentrations of 4 – 8 – 16 – 32

– 64 mg a.s./kg dry weight artificial soil. Second run of the study: Adult *Eisenia fetida* (approx. 6 months old, 8 x 10 animals for the control group and 8 x 10 animals for the single test concentration of the treatment group (limit test)) were exposed in an artificial soil to the nominal test concentration of 1000 mg a.s./kg dry weight artificial soil.
The test item was mixed into the soil. After 28 days the number of surviving animals and their weight alteration was determined. They were then removed from the artificial soil. After further 28 days, the number of offspring was determined.

Findings: Validity criteria were all met (see table below)

Validity criteria	Recommended	Obtained (1st run of the study)	Obtained (2nd run of the study)
Mortality of adults in the control:	≤ 10%	0%	1.25%
Mean change in growth of the adult earthworms in the control during the exposure period of four weeks	should not exceed - 20%	+ 64.4%	+ 84.0%
Reproduction per replicate in the control:	≥ 30	170 to 265	127 to 246
Coefficient of variation of reproduction in control:	≤ 30%	16.1%	21.4%

First run of the study:
The exposure of adult earthworms to the test item up to and including the highest test concentration of 64 mg a.s./kg dry weight artificial soil did not affect mortality of *Eisenia fetida*.
No statistically significant different values for the growth relative to the control were observed at the test concentrations of 4, 8, 16, 32 and 64 mg a.s./kg dry weight artificial soil.
No statistically significant different values for the number of juveniles per test vessel relative to the control were observed at the test concentrations of 4, 8, 16, 32 and 64 mg a.s./kg dry weight artificial soil.

First run of the study: Results

Test object	*Eisenia fetida*					
Test item	Control	Iprovalicarb tech.				
Test concentration [mg a.s./kg dws*]	---	4	8	16	32	64
Mortality of adult earthworms [%] after 28 days	0	0	0	0	0	0
Mean change of body weight of the adults from day 0 to day 28 [%]	+ 64.4	+ 69.2	+ 71.2	+ 70.2	+ 66.9	+ 64.1
Standard Deviation	± 8.4	± 18.8	± 8.5	± 2.9	± 8.6	± 7.9
Statistical comparison to the control **	---	n.s.	n.s.	n.s.	n.s.	n.s.
Mean number of offspring per test vessel after 56 days	222.5	236.3	240.5	224.8	217.8	256.0
Standard Deviation	± 35.7	± 15.9	± 44.6	± 21.8	± 38.2	± 19.9
Statistical comparison to the control ***	---	n.s.	n.s.	n.s.	n.s.	n.s.

* dws = dry weight artificial soil
** Result of a multiple sequentially rejective U-test after Bonferroni-Holm, two-sided, $\alpha = 0.05$
*** Result of a Williams multiple sequential t-test, one-sided smaller, $\alpha = 0.05$
n.s.: mean value not statistically significant different compared to the control ($p \geq 0.05$)

Second run of the study:
The exposure of adult earthworms to the test item concentration of 1000 mg a.s./kg dry weight artificial soil did not affect mortality of *Eisenia fetida*. A mortality rate of 1.25% was observed after 28 days of exposure at the control group.
A statistically significant different value for the growth relative to the control was observed at the test concentration of 1000 mg a.s./kg dry weight artificial soil.
No statistically significant different value for the number of juveniles per test vessel relative to the control was observed at the test concentration of 1000 mg a.s./kg dry weight artificial soil.

Overall, based on the biological and statistical significance of the effects observed on growth and reproduction, it is concluded, that the NOEC for the first and second run of this study is 64 mg a.s./kg dry weight artificial soil. Thus, the overall LOEC for the first and second run is determined to be 1000 mg a.s./kg dry weight artificial soil.

Second run of the study: Results

Test object	*Eisenia fetida*	
Test item	Control	Iprovalicarb tech.
Test concentration (mg a.s./kg dws*)	-	1000
Mortality of adult earthworms [%] after 28 days	1.25	0
Mean change of body weight of the adults from day 0 to day 28 [%]	+ 84.0	+ 58.2
Standard Deviation	± 11.7	± 7.8
Statistical comparison to the control **	-	-
Mean number of offspring per test vessel after 56 days	186.3	165.3
Standard Deviation	± 39.9	± 26.2
Statistical comparison to the control ***	-	n.s.

* dws = dry weight artificial soil
** Result of a pair-wise Mann-Whitney U-test, two-sided, $\alpha = 0.05$
*** Result of a pair-wise Student t-test, one-sided smaller, $\alpha = 0.05$
s.: mean value statistically significantly different compared to the control ($p < 0.05$)
n.s.: mean value not statistically significant different compared to the control ($p \geq 0.05$)

Overall, based on the biological and statistical significance of the effects observed on growth and reproduction, it is concluded, that the NOEC for the first and second run of this study is 64 mg a.s./kg dry weight artificial soil. Thus, the overall LOEC for the first and second run is determined to be 1000 mg a.s./kg dry weight artificial soil.

Overall endpoints [mg/kg artificial soil dry weight]

NOEC related to growth	64
LOEC related to growth	1000
NOEC related to growth	≥ 1000
LOEC related to growth	> 1000

Reference test: The results of the most recent reference test item indicated that the test system was sensitive to the reference test item.
No mortality of the adult earthworms was observed 28 days after application.
The change of body weight of the adult earthworms of the test concentrations of 1.25 and 5.0 mg a.s./kg dry weight soil was statistically significant reduced in comparison to the control (results of a Williams multiple sequential t-test, two-sided, $\alpha = 0.05$). No statistically significant different value for the

biomass relative to the control was observed at the test concentration of 2.5 mg a.s./kg dry weight artificial soil.
No statistically significant different values for the number of juveniles per test vessel relative to the control were observed at the lowest test concentration of 1.25 mg a.s./kg dry weight artificial soil. The number of juveniles per test vessel of the test concentrations of 2.5 and 5.0 mg a.s./kg dry weight soil were statistically significant reduced to the control (results of a Williams multiple sequential t-test, one-sided smaller, $\alpha = 0.05$.

Conclusions: In an earthworm reproduction and growth study with iprovalicarb the overall no-observed-effect-concentration (NOEC) was determined to be 64 mg a.s./kg soil dry weight based on the biological and statistical significance of the effects observed on growth and reproduction.

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Metabolite M03

Report:	**IIA.8.9.2 /04; [redacted] 2011**
Title:	Iprovalicarb-carboxylic acid: Effects on Reproduction and Growth of Earthworms *Eisenia fetida* in Artificial Soil with 5 % Peat.
Document No:	M-406133-01-1 (Rep. No: 59691022)
Guidelines:	OECD, Guideline for the testing of chemicals No. 222 "Earthworm, Reproduction Test" (adopted April 13, 2004) - ISO-Guideline 11268-2, "Soil quality – Effects of pollutants on earthworm (*Eisenia fetida*) – Part 2: „Determination of effects on reproduction", International Organization for Standardization, 1998
GLP	Yes (certified laboratory)

Objective: The purpose of this study was to investigate the effects of Iprovalicarb-carboxylic acid on mortality, body weight, feeding activity and reproduction of adult *Eisenia fetida*.

Materials and Methods: Iprovalicarb-carboxylic acid; origin batch no. BCOO 6249-10-3; batch code: BCS-CR79590-01-01, customer order no. TOX 09087-00; purity: 98.9% w/w.
Reference item: Luxan Carbendazim 500 FC (active ingredient carbendazim, 500 g/L nominal), tested at least once a year in a dose response study.
Control: untreated.
Iprovalicarb-carboxylic acid was mixed into the soil at 100 mg test item/kg artificial soil (dry weight) to which earthworms *Eisenia fetida* (80 worms per treatment group) were exposed at temperatures within the range of 18 to 22 °C, light within the range of 400 to 800 lux, 16 h light : 8 h dark, fed weekly with dried cattle manure. The initial soil water content was 22.5% to 22.7% (56.4% to 56.8% of the maximum water holding capacity), water content at experimental termination 25.9% to 27.3% (64.8% to 68.3% of the maximum water holding capacity); initial pH 6.3, pH 6.5 at experimental termination. The water content of the soil at experimental end was > 60% of the total water holding capacity (maximum 68.3%). This deviation to the study plan was considered minor because the guideline recommendation of no standing or free water appearing when the soil is compressed was fulfilled.
Endpoints were mortality, body weight change, feeding activity and reproduction.

Findings: All validity criteria for the study were met (see table below).

Criteria	Recommended	Obtained
Mortality of adults in the control:	≤ 10%	0%
Reproduction per replicate in the control:	≥ 30	235 to 390
Coefficient of variation of reproduction in control:	≤ 30%	14.5%

No significant effects on mortality, weight changes or reproduction were observed at the concentration of 100 mg test item/kg artificial soil (Student t-test, α =0.05). No behavioural abnormalities were observed in any of the treatment groups and the feeding activity in the single test item treated group was comparable to the control (see table below).

Iprovalicarb-carboxylic acid [mg test item/kg artificial soil dry weight]	**Control**	**100**
Mortality (day 28) [%]	0	0
Weight change (day 28) [%]	48.4	46.1 n.s. 1
No. of juveniles (day 56)	318	322 n.s. 1
Reproduction in [%] of control (day 56)	-	101.3
Food consumption [g]	25.0	25.0
Endpoints [mg/kg artificial soil dry weight]		
NOEC (day 28 mortality and weight)	≥ 100	
NOEC (day 56 reproduction)	≥ 100	

n.s. = not significantly different compared to the control
[1] Student t-test, α = 0.05, two-sided for weight and one-sided smaller for reproduction

Reference test: In the most recent test with the reference item Luxan Carbendazim 500 FC there were statistically significant effects on reproduction at a concentration of 1.0 mg carbendazim/kg artificial soil and higher; the EC_{50} for reproduction was calculated as 1.21 mg carbendazim/kg artificial soil.

Conclusions: In this study the no-observed-effect-concentration (NOEC) of Iprovalicarb-carboxylic acid for mortality, growth, reproduction and feeding activity of the earthworm *Eisenia fetida* was ≥100 mg test item/kg artificial soil dry weight.

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Metabolite M10

Report:	**IIA 8.9.2 /05; [redacted];2001**
Title:	Influence of SZX 0722-P-Methyl-Phenethylamine on the Reproduction of Earthworms (*Eisenia fetida*)
Document No:	M-043357-01-1 (MPE/Rg 369/01)
Guidelines:	ISO/DIS 11268-2 (1996) BBA, Guidelines for the Testing of Plant Protection Products Within Registration, Part VI, 2 - 2, January 1994
GLP	Yes (certified laboratory)

Objective: The purpose of this study was to investigate the effects of Iprovalicarb-PMPA on the mortality, body weight, feeding activity and reproduction of adult *Eisenia fetida*.

Material and methods: SZX 0722-P-Methyl-Phenethylamine, (a.i.-content: 97.0 % a. i., specification: Development-No.: 3000183485, Batch-No.: 130499; TOX-No.: 05676-00) was used in this study. Adult *Eisenia fetida* (4 x 10 animals per application rate) were exposed in an artificial soil (with 10% peat) to the test concentrations of 10, 32, 100, 316 and 1000 mg test substance/kg dry weight soil. After 28 days the number of surviving animals and their weight alteration was determined. They were then removed from the artificial soil. After further 28 days, the number of offsprings was determined.

Findings: Effects on earthworm reproduction after 56 days

Test substance	SZX 0722-P-Methyl-Phenethylamine					
Test object	*Eisenia fetida*					
Exposure	56 d					
Application rates (mg/kg dry weight soil)	control	10	32	100	316	1000
Mortality of adult earthworms (%) after 28 days	0	0	0	0	0	0
Weight increase of adult earthworms (%)	73.9	64.8	63.9	55.1*	60.9	47.9*
Number of offsprings per surviving adult	19.0	19.5	19.9	20.2	17.3	7.0*

* significant difference in comparison to the control

Reference test: The results of the most recent reference test item indicated that the test system was sensitive to the reference test item. A dose-response study was carried out with the reference substance Derosal (active ingredient: 36% Carbendazim) at application rates of 0.10, 0.25 and 0.50 kg /ha. Mortality of adult earthworms as compared to control organisms was not observed at any dosage. The body weight reduction was significant at 0.25 and 0.5 kg/ha. Only the highest dosage of 0.5 kg/ha reduced the numbers of juvenile earthworms by 46 %. The no-observed-effect-level (NOEL) was 0.10 kg/ha (= 0.036 kg active ingredient/ha) and the lowest-observed-effect-level (LOEL) 0.25 kg/ha (= 0.09 kg active ingredient/ha).

Observations: No mortality was observed at any concentration. At 100 mg/kg the weight increase of adult earthworms was lower than in the control. This was not considered as an effect caused by the test substance because there was no effect at 316 mg/kg. A body weight reduction was observed 1000 mg/kg. Also the number of offsprings in this study was significantly reduced at 1000 mg/kg.

Conclusion: NOEC (56 d) = 316 mg/kg dry weight soil.
LOEC (56 d) = 1000 mg/kg dry weigh soil.

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Metabolite M15

Report:	**IIA 8.9.2 /06; [redacted] 2010**
Title:	Iprovalicarb-N-acetyl-PMPA: Effects on Reproduction and Growth of Earthworms *Eisenia fetida* in Artificial Soil with 5% Peat.
Document No:	M-368040-01-1 (Rep. No: 52291022)
Guidelines:	OECD, Guideline for the testing of chemicals Nr. 222 "Earthworm, Reproduction Test" (adopted April 13, 2004) - ISO-Guideline 11268-2, "Soil quality – Effects of pollutants on earthworm (*Eisenia fetida*) – Part 2: „Determination of effects on reproduction", International Organization for Standardization, 1998
GLP	Yes (certified laboratory)

Objective: The purpose of this study was to investigate the effects of Iprovalicarb-N-acetyl-PMPA on the mortality, body weight, feeding activity and reproduction of adult *Eisenia fetida*.

Materials and Methods: Iprovalicarb-N-acetyl-PMPA: 1st experiment: Sample Description: TOX 08717-00; Batch No.: AE 1371462-01-01; Purity: AE 1371462: 97.2% w/w; 2nd experiment: Sample Description: AZ 16150; Batch No.: AE 1371462-01-01; Purity: AE 1371462: 95.5% w/w.

Reference Item: Luxan Carbendazim 500 FC (active ingredient carbendazim, 500 g/L nominal) is tested at least once a year in a dose response study; control: untreated
Iprovalicarb-N-acetyl-PMPA was mixed into the soil in a 1st experiment at concentrations of 64.3, 129, 257, 514 and 1029 mg test item/kg artificial soil dry weight (equivalent to 62.5, 125, 250, 500 and 1000 mg a.s./kg dry artificial soil) and in a 2nd experiment with lower concentrations of 10, 16, 25, 40 and 63 mg test item/kg artificial soil dry weight (equivalent to 9.55, 15.3, 23.9, 38.2 and 60.2 mg a.s./kg dry artificial soil) to which earthworms *Eisenia fetida* (80 worms per control, 40 worms per test item group) were exposed.
The test conditions at the 1st experiment were 18 to 20 °C, light 400 to 760 lux, 16 h light : 8 h dark, fed weekly with dried cattle manure, initial soil water content 20.3% to 21.1% (52.1% to 54.1% of the maximum water holding capacity), water content at experimental termination 22.0% to 24.2% (56.4% to 62.1% of the maximum water holding capacity); initial pH 6.0 to 6.2, pH 6.2 to 6.4 at experimental termination.
The test conditions at the 2nd experiment were 18 to 22°C, light 400 to 800 lux, 16 h light : 8 h dark, fed weekly with dried cattle manure, initial soil water content 22.4% to 22.9% (50.1% to 51.2% of the maximum water holding capacity), water content at experimental termination 23.8% to 27.7% (53.2% to 62.0% of the maximum water holding capacity); initial pH 6.2 to 6.4, pH 6.4 to 6.5 at experimental termination; Endpoints were mortality, body weight change, feeding activity and reproduction.

Findings: All validity criteria for the study were met (see table below).

Validity criteria	Recommended	Obtained (1st experiment)	Obtained (2nd experiment)
Mortality of adults in the control:	≤ 10%	0%	0%
Reproduction per replicate in the control:	≥ 30	297 to 403	181 to 346
Coefficient of variation of reproduction in control:	≤ 30%	11.2%	22.0%

Mortality: In the 1st experiment no mortality was observed at the concentrations up to and including 257 mg test item/kg soil. At the concentrations of 514 and 1029 mg test item/kg soil mortalities of 80% and 100% were observed, which were significantly different compared to the control (Fisher´s Exact Test, α=0.05). In the 2nd experiment no mortality was observed in any treatment group.
Body weight: In the 1st experiment the body weight changes of the earthworms after 4 weeks exposure to Iprovalicarb-N-acetyl-PMPA were statistically significantly different compared to the control except the lowest test concentration of 64.3 mg test item/kg soil dry weight (Bonferroni Welch-t test, α=0.05). In the 2nd experiment body weight changes were not statistically significantly different compared to the control at the concentrations up to and including 63.0 mg test item/kg soil dry weight (Dunnett´s t-test, α=0.05).
Reproduction: The reproduction rates in the 1st experiment of the earthworms after 8 weeks exposure to Iprovalicarb-N-acetyl-PMPA were significantly different compared to the control in all test concentrations (Dunnett´s t-test, α=0.05). The reproduction in the 2nd experiment was not significantly different compared to the control at the concentrations up to and including 63.0 mg test item/kg soil dry weight (Dunnett's test, α=0.05).
In the 1st experiment worms were found on top of the soil after 1 day of exposure in the highest concentrations of 514 and 1029 mg test item/kg soil. No further behaviour abnormalities were observed. In the 2nd experiment no behavioural abnormalities were observed. The feeding activity was comparable to the control up to and including the concentration of 257 mg test item/kg soil dry weight and appeared to be reduced at 514 mg test item/kg soil dry weight and above.

Effect of Iprovalicarb-N-acetyl-PMPA on *Eisenia fetida* in a 56-day reproduction study (1st experiment)

Iprovalicarb-N-acetyl-PMPA						
[mg test item/kg artificial soil dry weight]	**Control**	**64.3**	**129**	**257**	**514**	**1029**
[mg a.s./kg artificial soil dry weight]		**62.5**	**125**	**250**	**500**	**1000**
Mortality (day 28) [%] [1)]	0.0	0.0	0.0	0.0	80.0	100.0
Weight change (day 28) [%] [2)]	32.5	32.9 n.s.	22.8 *	19.8 *	-3.4 *	--
No. of juveniles (day 56) [3)]	331	277 *	230 *	152 *	1 *	0 *
Reproduction in [%] of control (day 56)	-	83.5	69.5	45.8	0.2	0.0
Food consumption [g]	25.0	25.0	25.0	25.0	22.4	20.0

n.s. = not significantly different compared to the control
* = significantly different compared to the control
- = not relevant
-- = all worms were dead after 4 weeks
1) Fisher´s Exact Test, α = 0.05, one-sided greater
2) Bonferroni-Welch t-test, α = 0.05, one-sided smaller
3) Dunnett's t-test, α = 0.05, one-sided smaller

Effect of Iprovalicarb-N-acetyl-PMPA on *Eisenia fetida* in a 56-day reproduction study (2nd experiment)

Iprovalicarb-N-acetyl-PMPA						
[mg test item/kg artificial soil dry weight]	Control	10.0	16.0	25.0	40.0	63.0
[mg a.s./kg artificial soil dry weight]		9.55	15.3	23.9	38.2	60.2
Mortality (day 28) [%]	0.0	0.0	0.0	0.0	0.0	0.0
Weight change (day 28) [%]	18.2	19.1 n.s.	16.0 n.s.	18.4 n.s.	20.0 n.s.	18.3 n.s.
No. of juveniles (day 56) [1)]	264	289 n.s.	258 n.s.	228 n.s.	244 n.s.	269 n.s.
Reproduction in [%] of control (day 56)	-	109.6	97.7	86.3	92.4	101.8
Food consumption [g]	25.0	25.0	25.0	25.0	25.0	25.0

n.s. = not significantly different compared to the control
1) Dunnett's t-test, α = 0.05, two-sided for weight and one-sided smaller for reproduction

Overall endpoints [mg/kg artificial soil dry weight]

NOEC (day 28 mortality and weight)	257 (equivalent to 250 mg a.s./kg soil dry weight)
NOEC (day 28 weight change)	64.3 (equivalent to 62.5 mg a.s./kg soil dry weight)
NOEC (day 56 reproduction)	63.0 (equivalent to 60.2 mg a.s./kg soil dry weight)

Reference test: In the most recent test with the reference item Luxan Carbendazim 500 FC there were statistically significant effects on reproduction at a concentration of 1.5 mg carbendazim/kg artificial soil and higher; the EC_{50} for reproduction was calculated as 1.47 mg carbendazim/kg artificial soil.

Conclusions: In an earthworm reproduction and growth study with Iprovalicarb-N-acetyl-PMPA the no-observed-effect-concentration (NOEC) was determined to be 250 mg a.s./kg soil dry weight for mortality, 62.5 mg a.s./kg soil dry weight for growth and 60.2 mg a.s./kg soil dry weight for reproduction.

IIA 8.10 Effects on soil microbial activity

IIA 8.10.1 Nitrogen transformation

After Annex I listing of iprovalicarb additional studies with the metabolites M03, M10 and M15 were performed. Short summaries of the studies are given below. A former study, performed with the active substance, is given under point IIA 8.10.1 (EU point IIA 8.5) of the EU dossier submitted for Annex I listing.

Metabolite M03

Report:	**IIA 8.10.1 /02; [redacted] 2011**
Title:	Iprovalicarb-carboxylic acid: Effects on the activity of soil microflora (Nitrogen transformation test)
Document No:	M-404388-01-1 (Rep. No: 10 10 48 055 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 purpose of this study was to determine the effects of the test item on the activity of soil microflora with regard to nitrogen transformation in a laboratory test.

Material and Methods: Iprovalicarb-carboxylic-acid, (analytical findings: 98.9% w/w (BCS-CR79590), Batch ID: BCS-CR79590-01-01, Origin Batch No.: BC000624-10-3, customer order no.:TOX 09087-00), was used in the test. A silty sand soil (DIN 4220) was exposed for 28 days to 13.33 mg test item/kg soil dry weight. Application rate was equivalent to 10 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).

Findings: The validity criteria for the study was met as the coefficients of variation in the control (NO_3-N) were maximum 3.1% and thus fulfilled the demanded range (≤ 15%).

Effects on nitrogen transformation in soil after treatment with Iprovalicarb-carboxylic acid

Time Interval (days)	Test concentration						
				Iprovalicarb-carboxylic acid			
	Control			13.33 mg/kg dry weight soil			
	Nitrate-N [1)]			Nitrate-N [1)]			% difference to control
0-7	2.34	±	0.07	1.92	±	0.14	**- 17.9***
7-14	0.46	±	0.22	0.97	±	0.05	**+ 111.5***
14-28	0.84	±	0.12	1.01	±	0.05	**+ 20.1[n.s.]**

[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 homogenous variances, 2-sided, $p \leq 0.05$).

* = statistically significant difference to control (Student-t-test for homogenous variances, 2-sided, $p \leq 0.05$).

Observations: At time interval 7-14 days after application, Iprovalicarb-carboxylic acid caused a temporary stimulation of the daily nitrate rate at the tested concentration of 13.33 mg/kg dry soil. However, no adverse effects of Iprovalicarb-carboxylic acid on nitrogen transformation in soil could be observed 28 days after application.

Only a negligible difference to control of +20.1% (test concentration 13.33 mg/kg dry soil) was measured at the end of the 28-day incubation period (time interval 14-28).

Conclusion: Iprovalicarb-carboxylic acid caused no adverse effects (difference to control < 25%, OECD 216) on the soil nitrogen transformation (measured as NO3-N production) at the end of the 28-day incubation period (time interval 14-28). The study was performed in a field soil at a concentration of 13.33 mg test item/kg soil, which was equivalent to an application rate of 10 kg test item/ha.

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Metabolite M10

Report:	**IIA 8.10.1 /03; [redacted] 2010**
Title:	Metabolite Iprovalicarb-p-methyl-phenetylamine: Determination of effects on nitrogen transformation in soil
Document No:	M-366832-01-1 (Rep. No: FRM-N-139/10)
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 0.09 mg and 0.93 mg of metabolite Iprovalicarb-p-methyl-phenetylamine/kg dry weight soil on nitrogen transformation in an agricultural soil.

Materials and Methods: Metabolite Iprovalicarb-p-methyl-phenetylamine (analytical findings: 94.6% w/w, batch code: AE C624117-01-01, origin batch No.: 960229ELB03, LIMS No.: 0923041, certificate No.: AZ 16068) was used in the test.
A loamy sand soil was exposed for 28 d to 0.09 mg and 0.93 mg test item/kg dry weight soil, which is equivalent to 0.07 kg and 0.7 kg test item/ha. This quantities were determined by taking the one-fold and the 10-fold rate of the parent compound (0.165 and 1.65 kg a.s./ha), and converting the resulting quantities into the molecular weight equivalent of metabolite. The molecular weight of iprovalicarb is 320.4 g/mol; the molecular weight of the metabolite is 135.21 g/mol. Lucerne-grass-green meal was added to the soil (5 g/kg dry weight soil) to stimulate nitrogen transformation.

Findings: The validity criteria for the study was met as the highest coefficient of variation (CV) between nitrate-N concentration in replicate control samples was 9% (14 days after treatment) and thus did not exceed the recommended limit ≤ 15%.

Effects on nitrogen transformation in soil after treatment with Iprovalicarb-p-methyl-phenetylamine

Time Interval (days)	Application rates				
	Metabolite Iprovalicarb-p-methyl-phenetylamine				
	Control	0.09 mg/kg dry weight soil		0.93 mg/kg dry weight soil	
	Nitrate-N [1)]	Nitrate-N [1)]	% difference to control	Nitrate-N [1)]	% difference to control
0-7	-0.22 ± 0.08	-0.33 ± 0.04	**45** n.s.	-0.36 ± 0.16	**60** n.s.
7-14	1.22 ± 0.20	1.29 ± 0.14	**6** n.s.	1.30 ± 0.19	**7** n.s.
14-28	0.90 ± 0.01	0.87 ± 0.09	**3** n.s.	0.90 ± 0.09	**1** n.s.

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, 2-sided, $\alpha = 0.05$).

The most recent non-GLP-test with the reference item Sodium chloride was performed at a test concentration of 16 g Sodium chloride/kg soil dry weight. In the test (non-GLP) with an agricultural soil 16 g Sodium chloride/kg dry weight soil had a distinct and long-term (> 28 days) influence on microbial mineralization of nitrogen. This shows that the test organisms are sufficiently sensitive.

Observations: During the 28-day test, 0.09 mg Metabolite Iprovalicarb-p-methylphenetylamine/kg dry weight and the 10-fold dose of the test item caused a temporary stimulation of the daily nitrate rates at the time interval 0-7 days after treatment in a loamy sand soil amended with Luzerne-grass-green meal. At the end of the test (14-28 day interval), differences in the nitrate-N rates between control soil samples and treated soil samples are < 25% and meet the trigger values of above mentioned guideline for a termination of the study.

Conclusion: After 28 days, at the end of the test, no effects ≥ 25% on nitrogen transformation were observed for the tested application rates of 0.09 mg and 0.93 mg of metabolite Iprovalicarb-p-methyl-phenetylamine/kg dry weight soil.

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Metabolite M15

Report:	**IIA 8.10.1 /04; [redacted] 2010**
Title:	Metabolite Iprovalicarb-N-acetyl-PMPA: Determination of effects on nitrogen transformation in soil
Document No:	M-366828-01-1 (Rep. No: FRM-N-138/10)
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 0.12 mg and 1.21 mg of metabolite Iprovalicarb-N-acetyl-PMPA/kg dry weight soil on nitrogen transformation in an agricultural soil.

Materials and Methods: Metabolite Iprovalicarb-N-acetyl-PMPA (analytical findings: 95.5% w/w, batch code: AE 1371462-01-01, origin batch No.: SES 10727-1-1, LIMS No.: 0927819, certificate No.: AZ 16150) was used in the test.

A loamy sand soil was exposed for 28 d to 0.12 mg and 1.21 mg test item/kg dry weight soil, which is equivalent to 0.091 kg and 0.913 kg test item/ha. This quantities were determined by taking the one-fold and the 10-fold rate of the parent compound (0.165 and 1.65 kg a.s./ha), and converting the resulting quantities into the molecular weight equivalent of metabolite. The molecular weight of iprovalicarb is 320.4 g/mol; the molecular weight of the metabolite is 177.25 g/mol. Lucerne-grass-green meal was added to the soil (5 g/kg dry weight soil) to stimulate nitrogen transformation.

Findings: The validity criteria for the study was met as the highest coefficient of variation (CV) between nitrate-N concentration in replicate control samples was 12% (7 days after treatment) and thus did not exceed the recommended limit ≤ 15%.

Effects on nitrogen transformation in soil after treatment with Iprovalicarb-N-acetyl-PMPA

Time Interval (days)	Application rates										
	Metabolite Iprovalicarb-N-acetyl-PMPA										
	Control			0.12 mg/kg dry weight soil				1.21 mg/kg dry weight soil			
	Nitrate-N [1]			Nitrate-N [1]			% difference to control	Nitrate-N [1]			% difference to control
0-7	0.02	±	0.19	-0.07	±	0.09	**462** n.s.	-0.37	±	0.15	**2129***
7-14	1.29	±	0.24	1.36	±	0.18	**5** n.s.	1.22	±	0.08	**6** n.s.
14-28	1.03	±	0.09	1.02	±	0.02	**1** n.s.	0.81	±	0.08	**22***

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, 2-sided, $p \leq 0.05$).
* = statistically significantly different to control (Student *t*-test, 2-sided, $p \leq 0.05$)

The most recent non-GLP-test with the reference item Sodium chloride was performed at a test concentration of 16 g Sodium chloride/kg soil dry weight. In the test (non-GLP) with an agricultural soil 16 g Sodium chloride/kg dry weight soil had a distinct and long-term (> 28 days) influence on microbial mineralization of nitrogen. This shows that the test organisms are sufficiently sensitive.

Observations: During the 28-day test, 0.12 mg metabolite Iprovalicarb-N-acetyl-PMPA/kg dry weight soil and the 10-fold dose of the test item caused a temporary stimulation of the daily nitrate rates at the time interval 0-7 days after treatment in a loamy sand soil amended with Luzerne-grass-green meal. Even though the 10-fold dose revealed a statistically significant difference to the control at the end of the study, the deviation from the control was still below the threshold value recommended by the guideline. At the end of the test (14-28 day interval), differences in the nitrate-N rates between control soil samples and treated soil samples are < 25% and meet the trigger values of above mentioned guideline for a termination of the study.

Conclusion: After 28 days, at the end of the test, no effects > 25% on nitrogen transformation were observed for the tested application rates of 0.12 mg and 1.21 mg of metabolite Iprovalicarb-N-acetyl-PMPA/kg dry weight soil.

IIA 8.10.2 Carbon mineralization

Please refer to IIA 8.10.2 (EU point IIA 8.5) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.10.3 Rates of recovery following treatment

Iprovalicarb shows no long term effects and is not used as a soil sterilant.

IIA 8.11 Effects on marine and estuarine organisms

No EC data requirement according to Regulation 1107/2009/EEC or Directive 414/1991/EEC.

IIA 8.11.1 Marine or estuarine organisms acute toxicity LC50/EC50

See above (IIA 8.11).

IIA 8.11.2 Marine/Estuarine fish – salinity challenge

See above (IIA 8.11).

IIA 8.12 Effects on terrestrial vascular plants

After Annex I listing of iprovalicarb, a screening study on non-target terrestrial plants with the former lead formulation Iprovalicarb WG 50 was conducted. A short summary is presented below.

Report:	**IIA 8.12 /01; [redacted] 2000**
Title:	Herbicidal Screening Data for SZX 0722 WG 50
Document No:	M-020520-01-1 (Rep. No: MPE 02/00)
Guidelines:	Procedures as recommended by OECD for non-herbicidal crop protection products (CPP's)
GLP	No

Objectives: In this test, screening data are used to show whether the product causes phytotoxic effects on non-target plants under procedures.

Material and Methods: Test item: SZX 0722 WG 50 (content: 51.0% a.s.; batch-No.: 0127) was applied at rates of 180, 250, 500, 540, 900, 1000, 2000 and 2700 g a.s./ha:
1. pre- emergent to the soil surface in which plants were subsequently grown and
2. post emergent to the foliage of emerged plants.

5 monocotyledonous and 6 dicotyledonous plant species out of 7 plant families were tested.

Findings: In the pre-emergence test no phytotoxic effect was observed on all tested plant species up to a concentration of 540 g a.i./ha. At the highest proposed yearly use rate of 900 g a.i./ha only slight phytotoxic effects (< 50%) occurred on *Beta vulgaris* (sugarbeet, BEAVA, Chenopodiaceae, dicotyledonae), *Alopecurus myosuroides* (black twitch, ALOMY, Gramineae, monocotyledonae), *Setaria viridis* (green bristlegrass, SETVI, Gramineae, monocotyledonae), *Galium aparine* (cleavers, GALAP, Rubiaceae, dicotyledonae) and *Ipomoea hederacea* (ivyleaf morningglory, IPOHE, Convolvulaceae, dicotyledonae).
At a concentration of 2700 g a.s./ha (15 times higher than the highest proposed single use rate) *Beta vulgaris* (sugarbeet, BEAVA, Chenopodiaceae, dicotyledonae), *Setaria viridis* (green bristlegrass, SETVI, Gramineae, monocotyledonae), *Galium aparine* (cleavers, GALAP, Rubiaceae, dicotyledonae) and *Ipomoea hederacea* (ivyleaf morningglory, IPOHE, Convolvulaceae, dicotyledonae) showed effects of 50 - 70%.

When applied to foliage (post-emergence) none of the 5 monocotyledonous and 6 dicotyledonous plant species out of 7 plant families showed any phytotoxic effect up to the highest tested concentration of 2700 g a.s./ha.

	Pre-emergent test					Post-emergent test
	% effects at different application rates					% effects at different application rates
Application rate [g a.s./ha)	180 to 540	900	1000	2000	2700	180 to 2700
Zea mays	0	0	0	0	0	0
Beta vulgaris	0	20	0	20	70	0
Alopecurus myosuroides	0	30	20	50	40	0
Avena fatua	0	0	0	0	20	0
Echinochloa crus-galli	0	0	0	0	0	0
Setaria viridis	0	20	0	20	50	0
Abutilon theophrasti	0	0	0	0	0	0
Amaranthus retroflexus	0	0	0	20	20	0
Galium aparine	0	30	30	50	70	0
Ipomoea hederacea	0	20	20	50	50	0
Sinapis alba	0	0	0	30	30	0

Conclusions: When applied to soil (pre-emergence) no or only weak phytotoxicity (< 50%) occurred up to a concentration of 1000 g a.s./ha. At a concentration of 2700 g a.s./ha 36% of the species showed relevant (> 50%) phytotoxic effects at SZX 0722 WG 50.
In the post-emergence test none of the tested plants showed any phytotoxic effect up to the highest tested concentration of 2700 g a.s./ha.

IIA 8.13 Effects on terrestrial vertebrates other than birds/wild mammal toxicity

No EC data requirement.

IIA 8.14 Effects on other non-target organisms (flora and fauna) believed to be at risk

After Annex I listing of iprovalicarb additional studies with the active substance and metabolites M03, M10 and M15 were performed on the collembolan species *Folsomia candida* and the soil mite species *Hypoaspis aculeifer*. Short summaries of the studies are given below.

Collembola: *Folsomia candida*

Report:	**IIA 8.14 /01; [redacted] 2010**
Title:	Iprovalicarb a.s.: Influence on the reproduction of the Collembolan species *Folsomia candida* tested in artificial soil.
Document No:	M-368058-01-1 (Rep. No: FRM-COLL-80/10)
Guidelines:	OECD-Guideline for testing chemicals No. 232 "Collembolan Reproduction Test in Soil" (adopted September 07, 2009) ISO 11267 Soil Quality – Inhibition of reproduction of Collembola (*Folsomia candida*) by soil pollutants, 1999.
GLP	Yes (certified laboratory)

Objectives: The purpose of this study was to assess the effect of iprovalicarb a.s on survival and reproduction of the collembolan species *Folsomia candida* during an exposure of 28 days in an artificial soil comparing control and treatment.

Material and Methods: Test item: Iprovalicarb a.s. analysed content: 97.5% w/w, Origin Batch No.: PF90187411, Customer Order No.: TOX 08831-00, specification No.: 102000006810, article No.: 05448417, LIMS NO.: 0935319.
10 Collembola (10-12 days old) per replicate (8 replicates for the control group and 4 replicates for each treatment group) were exposed to control (water treated), 100, 177, 316, 562 and 1000 mg test item/kg artificial soil dry weight at 20 ± 2°C, 400 - 800 Lux, 16h light : 8h dark. During the study, they were fed with granulated dry yeast.
Mortality and reproduction were determined after 28 days.

Findings: All validity criteria for the study were met (see table below).

Validity Criteria	**Recommended**	**Obtained**
Mean adult mortality	≤ 20%	8.8%
Mean number of juveniles per replicate (with 10 colembolan introduced)	≥ 100	1155
Coefficient of variation calculated for the number of juveniles per replicate	≤ 30%	15.1%

Mortality: In the control group 8.8% of the adult *Folsomia candida* died which is below the allowed maximum of ≤ 20% mortality. An LC_{50} could not be calculated and is considered to be > 1000 mg test item/kg artificial soil dry weight.
Reproduction: Concerning the number of juveniles statistical analysis (William's-t test, one-sided smaller, $\alpha = 0.05$) revealed no significant difference between control and any treatment group.
Therefore the No-Observed-Effect-Concentration (NOEC) for reproduction is ≥ 1000 mg test item/kg artificial soil dry weight. The Lowest-Observed-Effect-Concentration (LOEC) for reproduction is > 1000 mg test item/kg artificial soil dry weight. An EC_{50} could not be calculated and is considered to be > 1000 mg test item/kg artificial soil dry weight.

Effect of iprovalicarb on Collembola (*Folsomia candida*) in a 28-day reproduction study

Test item Test object Exposure	Iprovalicarb *Folsomia candida* Artificial soil		
mg test item/kg soil dry weight nominal concentration	Adult mortality (%)	Mean number of juveniles ± SD	Reproduction (% of control)
Control	8.8	1155 ± 174	-
100	17.5	1103 ± 159	95 n.s.
177	12.5	1217 ± 110	105 n.s.
316	7.5	1216 ± 179	105 n.s.
562	15.0	1321 ± 181	114 n.s.
1000	17.5	1381 ± 81	120 n.s.
$NOEC_{reproduction}$ (mg test item/kg soil dry weight) $LOEC_{reproduction}$ (mg test item/kg soil dry weight)			≥ 1000 > 1000

The calculations were performed with unrounded values
n.s. = statistically not significant (William's t-test one-sided-smaller, $\alpha = 0.05$)

Reference test: The most recent non-GLP-test with the reference item Boric acid was performed at test concentrations 44, 67, 100, 150 and 225 mg Boric acid/kg artificial soil dry weight.
Boric acid showed an EC_{50} of 96 mg test item/kg artificial soil dry weight (95% confidence limits from 87 mg to 105 mg Boric acid/kg artificial soil dry weight) for reproduction according Probit analysis using maximum likelihood regression. The result is in the recommended range of the guideline (about 100 mg Boric acid/kg artificial soil dry weight).
The $NOEC_{reproduction}$ was calculated to be 44 mg Boric acid/kg artificial soil dry weight and accordingly the $LOEC_{reproduction}$ is 67 mg Boric acid/kg artificial soil dry weight according Williams-Test multiple t-test procedure, $\alpha = 0.05$, one-sided smaller. This shows that the test organisms are sufficiently sensitive.

Conclusions:
$NOEC_{reproduction}$: ≥ 1000 mg test item/kg artificial soil dry weight.
$LOEC_{reproduction}$: > 1000 mg test item/kg artificial soil dry weight.

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Metabolite M03

Report:	**IIA 8.14 /02; [redacted] 2011**
Title:	Iprovalicarb-carboxylic acid: Effects on Reproduction of the Collembola *Folsomia candida* in Artificial Soil
Document No:	M-405347-01-1 (Rep. No: 59692016)
Guidelines:	OECD-Guideline for testing chemicals No. 232 "Collembolan Reproduction Test in Soil" (adopted September 07, 2009) ISO 11267 Soil Quality – Inhibition of reproduction of Collembola (*Folsomia candida*) by soil pollutants, 1999.
GLP	Yes (certified laboratory)

Objectives: The purpose of the study was to determine the effects of iprovalicarb-carboxylic acid on mortality and reproduction of the Collembola *Folsomia candida* in artificial soil.

Material and Methods:

Test item:	Iprovalicarb-carboxylic acid; batch code: BCS-CR79590-01-01; origin batch no. BCOO 6249-10-3; customer order no.: TOX 09087-00; purity: 98.9% w/w.
Test species:	Collembola *Folsomia candida*, 10-12 days old, from cultures held at the laboratory.
Test design:	28-d exposure in treated artificial soil. One concentration of the test item was mixed homogeneously into the soil which was placed into glass vessels before the Collembola were introduced on top of the soil; one concentration and one control; 8 replicates/concentration and control with 10 Collembola each. Feeding of Collembola with approximately 2 mg dry yeast for each test vessel at the beginning of the test and on day 14. Assessment of adult mortality, behavioural effects and reproduction was performed after 28 d.
Endpoints:	Mortality of adult Collembola, behavioural effects, number of juveniles
Reference item:	Boric acid (The effects of the reference item were investigated in a separate study.)
Test Concentration:	Control, 100 mg iprovalicarb-carboxylic acid/kg artificial soil (dry weight).
Test Conditions:	Artificial soil according to OECD 232; pH at experimental start 6.4, pH at experimental end 6.3 to 6.4; water content at experimental start 23.2 % to 23.4 % (49.4 % to 49.8 % of the maximum water holding capacity); at experimental end 21.3 % to 21.5 % (45.4 % to 45.8 % of the maximum water holding capacity); temperature: within the range of 18°C to 22°C; illumination: 16 h light : 8 h dark, light intensity within the range of 400 to 800 lux.
Statistics:	Standard procedures, Fisher's Exact Test (mortality), Student t-test (reproduction)

Findings: All validity criteria for the study were met (see table below).

Validity Criteria	**Recommended**	**Obtained**
Mortality of adults in the control:	≤ 20%	13%
Reproduction per replicate in the control	≥ 100	316 to 474
Coefficient of variation of reproduction in control	≤ 30%	14.3%

Mortality of *Folsomia candida* in the test item treated group and in the control was 13% The values were not significantly different (Fisher's Exact Test, $\alpha = 0.05$, one-sided greater).
Reproduction of the collembola exposed to iprovalicarb-carboxylic acid at the concentration of 100 mg test item/kg artificial soil represented 98% of the control reproduction, which was not statistically significantly different compared to the control (Student t-test, $\alpha = 0.05$, one-sided smaller).

Effect of iprovalicarb-carboxylic acid on Collembola (*Folsomia candida*) in a 28-day reproduction study

Iprovalicarb-carboxylic acid [mg/kg artificial soil]	Control	100
Mortality (day 28) [%]	13	13
Statistical significance[1)]	-	n.s.
No. of juveniles (day 28)	412	404
Reproduction in [%] of control (day 28)	-	98
Statistical significance[2)]	-	n.s.
Endpoints [mg/kg artificial soil]		
NOEC (mortality)	≥ 100	
NOEC (reproduction)	≥ 100	

n.s. = not significantly different compared to the control
[1)] Fisher's Exact Test, α = 0.05, one-sided greater [2)] Student t-test, α = 0.05, one-sided smaller

Reference test: In a separate study the reference item Boric acid showed statistically significant effects on reproduction at concentrations of ≥ 59.3 mg/kg artificial soil, the EC_{50} for reproduction was calculated to be 70.7 mg/kg artificial soil. Mortality was statistically significantly higher compared to the control at 88.9 mg/kg artificial soil and above.

Conclusion: Iprovalicarb-carboxylic acid caused no significant effects on mortality or reproduction of *Folsomia candida* at the single test concentration of 100 mg test item/kg artificial soil.
Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be ≥ 100 mg test item/kg artificial soil. The overall Lowest Observed Effect Concentration (LOEC) was estimated to be greater than 100 mg test item/kg artificial soil.

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Metabolite M10

Report:	**IIA 8.14 /03; [redacted] 2010**
Title:	Metabolite Iprovalicarb-p-methyl-phenethylamine: Influence on the Reproduction of the Collembola Species *Folsomia candida* tested in Artificial Soil with 5 % Peat
Document No:	M-361572-01-1 (Rep. No. FRM-COLL-78/10)
Guidelines:	OECD-Guideline for testing chemicals No. 232 "Collembolan Reproduction Test in Soil" (adopted September 07, 2009) ISO 11267 Soil Quality – Inhibition of reproduction of Collembola (*Folsomia candida*) by soil pollutants, 1999.
GLP	Yes (certified laboratory)

Objectives: The purpose of the study was to provide data for the registration of plant protection products on the lethal and sub lethal effects of the pure metabolite on the Collembola species *Folsomia candida* as a representative of the soil fauna.

Material and Methods: Metabolite Iprovalicarb-p-methyl-phenethylamine, analysed content: 94.6% w/w, Origin Batch No.: 960229ELB03, LIMS No.: 0923041, Batch Code: AE C624117-01- 01, AZ: 16068.

Toxic standard: Betosip, active ingredient: Phenmedipham (153 g/L), test concentrations 50 to 200 mg Betosip/kg artificial soil dry weight (corresponding to 7.6, 15.2 and 30.4 mg Phenmedipham/kg), tested once a year.
10 Collembola (10-12 days old) per replicate (5 replicates per treatment group) were exposed to control (water treated), 63, 125, 250, 500 and 1000 mg pure metabolite/kg artificial soil dry weight at 18 – 22°C, 400 – 800 Lux, 16h light : 8h dark, 5% peat in the artificial soil. During the study, they were fed with granulated dry yeast.
Mortality and reproduction were determined after 28 days.
The validity criteria of the test according to the guideline were fulfilled (mortality of the adults, mean rate of reproduction of juveniles and the coefficient of variation of reproduction in the control).

Findings: All validity criteria for the study were met (see table below).

Validity Criteria	**Recommended**	**Obtained**
Adult mortality	≤ 20%	6%
Reproduction of juveniles	≥ 100	956
Coefficient of variation	≤ 30%	16.8%

<u>Mortality:</u> In the control group 6% of the adult Collembola died which is within the tolerated range of ≤ 20% mortality recommended by the guideline. The highest mortality rate of 20 % was found in the test with 250 mg pure metabolite/kg artificial soil dry weight.
<u>Reproduction:</u> Concerning the number of juveniles statistical analysis (William's Test, one sided smaller, α = 0.05) reveals no significant differences between the control group and any treatment group tested with the metabolite iprovalicarb-p-methylphenethylamine.

Effect of iprovalicarb-p-methylphenethylamine on Collembola (*Folsomia candida*) in a 28-day reproduction study

Pure metabolite Test object Exposure	Metabolite iprovalicarb-p-methylphenethylamine *Folsomia candida* Artificial soil		
mg pure metabolite/kg soil dry weight nominal concentration	Adult mortality (%)	Mean number of Juveniles ± SD	Reproduction (% of control)
Control	6	956 ± 161	-
63	8	1036 ± 142	108 n.s.
125	16	933 ± 144	98 n.s.
250	20	1028 ± 226	107 n.s.
500	10	853 ± 86	89 n.s.
1000	14	1019 ± 158	107 n.s.
$NOEC_{reproduction}$ (mg pure metabolite/kg soil dry weight)			≥ 1000
$LOEC_{reproduction}$ (mg pure metabolite/kg soil dry weight)			> 1000

The calculations were performed with unrounded values
n.s. = statistically not significant (William's Test one-sided-smaller, α = 0.05)

Reference test: In the most recent test the mortality rate of adult Collembola was 4%, 6% and 60% at 50, 100 and 200 mg Betosip/kg artificial soil dry weight. In all treatment groups the number of juveniles

were statistically significant reduced (Williams-test, one-sided-smaller, α= 0.05) in comparison to the control.
$NOEC_{reproduction}$: < 50 mg Betosip (7.6 mg a.s.)/kg artificial soil dry weight.
$LOEC_{reproduction}$: 50 mg Betosip (7.6 mg a.s.)/kg artificial soil dry weight.

Conclusions:
$NOEC_{reproduction}$: ≥1000 mg pure metabolite/kg artificial soil dry weight.
$LOEC_{reproduction}$: >1000 mg pure metabolite/kg artificial soil dry weight.

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Metabolite M15

Report:	**IIA 8.14 /04; [redacted] 2010**
Title:	Metabolite Iprovalicarb-N-acetyl-PMPA: Influence on the Reproduction of the Collembola Species *Folsomia candida* tested in Artificial Soil with 5 % Peat
Document No:	M-366743-01-1 (Rep. No: ERM-COLL-81/10)
Guidelines:	OECD-Guideline for testing chemicals No. 232 "Collembolan Reproduction Test in Soil" (adopted September 07, 2009) ISO 11267 Soil Quality – Inhibition of reproduction of Collembola (*Folsomia candida*) by soil pollutants, 1999.
GLP	Yes (certified laboratory)

Objectives: The purpose of the study was to assess the effect of the metabolite iprovalicarb-N-acetyl-PMPA on survival and reproduction of the Collembola species *Folsomia candida* during an exposure of 28 days in an artificial soil with two different application rates (control and treatment).

Material and Methods:
Metabolite Iprovalicarb-N-acetyl-PMPA, Origin Batch No.: SES 10727-1-1, LIMS No.: 0927819, Batch Code: AE 1371462-01-01, analysed content: of Iprovalicarb-N-acetyl-PMPA 95.5% w/w.
Toxic standard: Betosip, active ingredient: Phenmedipham (153 g/L), test concentrations 50 to 200 mg Betosip/kg artificial soil dry weight (corresponding to 7.6 to 30.4 mg a.s./kg), tested once a year.
10 Collembola (10-12 days old) per replicate (5 replicates per treatment group) were exposed to control (water treated) and 100 mg pure metabolite/kg artificial soil dry weight at 18 – 22°C, 400 – 800 Lux, 16h light, 8h dark, 5% peat in the artificial soil. During the study, they were fed with granulated dry yeast.
Mortality and reproduction were determined after 28 days.
The validity criteria of the test according to the guideline were fulfilled (mortality of the adults, mean rate of reproduction of juveniles and the coefficient of variation of reproduction in the control).

Findings: All validity criteria for the study were met (see table below).

Validity Criteria	**Recommended**	**Obtained**
Adult mortality	≤ 20%	4%
Reproduction of juveniles in the control	≥ 100	939
Coefficient of variation in the control	≤ 30%	8.2%

Mortality: In the control group 4% of the adult Collembola died which is within the tolerated range of ≤ 20% mortality recommended by the guideline. The same mortality rate was found in the treatment group.
Reproduction: Concerning the number of juveniles statistical analysis (Student's t-test, one-sided smaller, α = 0.05) reveals no significant difference between the control group and the treatment group.

Effect of iprovalicarb-N-acetyl-PMPA on Collembola (*Folsomia candida*) in a 28-day reproduction study

Test item Test object Exposure	Metabolite iprovalicarb-N-acetyl-PMPA *Folsomia candida* Artificial soil		
mg pure metabolite/kg soil dry weight	Adult mortality (%)	Mean number of juveniles ± SD	Reproduction (% of control)
Control	4	939 ± 77	-
100	4	1177 ± 243	125 n.s.
$NOEC_{reproduction}$ (mg pure metabolite/kg soil dry weight)			≥ 100
$LOEC_{reproduction}$ (mg pure metabolite/kg soil dry weight)			> 100

The calculations were performed with unrounded values
n.s. = statistically not significant (Student's t-test one-sided-smaller, α = 0.05)

Reference test: In the most recent test the mortality rate of adult Collembola was 4%, 6% and 60% at 50, 100 and 200 mg Betosip/kg artificial soil dry weight. In all treatment groups the number of juveniles were statistically significant reduced (Williams-test, one-sided-smaller, α= 0.05) in comparison to the control.
$NOEC_{reproduction}$: < 50 mg Betosip (7.6 mg a.s.)/kg artificial soil dry weight.
$LOEC_{reproduction}$: 50 mg Betosip (7.6 mg a.s.)/kg artificial soil dry weight.

Conclusions:
$NOEC_{reproduction}$: ≥100 mg pure metabolite/kg artificial soil dry weight.
$LOEC_{reproduction}$: >100 mg pure metabolite/kg artificial soil dry weight.

Soil mite: *Hypoaspis aculeifer*

Report:	**IIA 8.14/05; [redacted] 2010**
Title:	Iprovalicarb: Influence on mortality and reproduction on the soil mite species *Hypoaspis aculeifer* tested in artificial soil with 5 % peat
Document No:	M-366603-01-1 (Rep. No: kra-HR-25/10)
Guidelines:	OECD 226: Predatory mite (*Hypoaspis* (*Geolaelaps*) *aculeifer*) reproduction test in soil, 16 Oct 2008
GLP	Yes (certified laboratory)

Objectives: The purpose of the study was to assess the effects of iprovalicarb on mortality and reproduction on the soil mite species *Hypoaspis aculeifer* tested during an exposure of 14 days in artificial soil with 5 % peat comparing control and treatment.

Material and Methods: Test item: Iprovalicarb; (TOX08831-00; Specification No.: 102000006810; Batch Code: AE 0540058-01-01; Origin Batch No. PF90187411, CAS No. 140923-17-7; Chemical names: SZX0722, AE 0540058; Article No. 05448417, purity 97.5%).
Toxic standard: Dimethoate, test concentrations 1.0, 1.8, 3.2, 5.6 and 10.0 mg dimethoate/kg dry weight artificial soil
Ten adult, fertilized, female *Hypoaspis aculeife*r per replicate (8 control replicates and 4 replicates for each test item concentration) were exposed to control and treatments. In each test vessel 20 g dry weight artificial soil were weighed in. The *Hypoaspis aculeifer* were of a uniform age not differing more than three days (31 days after start of egg laying). During the test, they were fed with cheese mites bred on brewer's yeast and with nematodes bred on watered oat flakes. During the study a temperature of 20 ± 2°C and light regime of 400 – 800 Lux, 16 h light : 8 h dark was applied. The artificial soil was prepared according to the guideline with the following constituents (percentage distribution on dry weight basis): 74.8% fine quartz sand, 5% *Sphagnum* peat, air dried and finely ground, 20% Kaolin clay and approximately 0.2% Calcium carbonate ($CaCO_3$).
After a period of 14 days, the surviving adults and the living juveniles were extracted by applying a temperature gradient using a MacFadyen-apparatus. Extracted mites were collected in a fixing solution (20% ethylene glycol, 80% deionised water, 2 g detergent/L fixing solution were added). All *Hypoaspis aculeifer* were counted under a binocular.

Findings: All validity criteria for the study were met (see table below).

Validity Criteria	Recommended	Obtained
Mean adult female mortality	≤ 20%	10.0%
Mean number of juveniles per replicate (with 10 adult females introduced)	≥ 50	227.9
Coefficient of variation calculated for the number of juvenile mites per replicate	≤ 30%	15.7%

Mortality: In the control group 10% of the adult *Hypoaspis aculeifer* died which is below the allowed maximum of ≤ 20% mortality. A LC_{50} cannot be calculated and is considered to be > 1000 mg test item/kg dry weight artificial soil.

Reproduction: Concerning the number of juveniles statistical analysis (Williams test, one-sided smaller, $\alpha = 0.05$) revealed no significant difference between control and treatment.
Therefore the No-Observed-Effect-Concentration (NOEC) for reproduction is ≥ 1000 mg test item/kg dry weight artificial soil. The Lowest-Observed-Effect-Concentration (LOEC) for reproduction is > 1000 mg test item/kg dry weight artificial soil. An EC_{50} could not be calculated and is considered to be > 1000 mg test item/kg dry weight artificial soil.

Effect of iprovalicarb on the Predatory Mite *Hypoaspis aculeifer* in a 14-day reproduction study

Test item Test object Exposure	Iprovalicarb *Hypoaspis aculeifer* Artificial soil		
mg test item/kg dry weight artificial soil	% mortality (Adults)	Mean number of juveniles per test vessel ± standard dev.	Reproduction (% of control)
Control	10.0	227.9 ± 35.7	
100	20.0	307.3 ± 44.8	134.8
178	5.0	348.3 ± 50.2	152.8
316	15.0	327.0 ± 21.5	143.5
562	10.0	313.0 ± 39.1	137.4
1000	17.5	281.8 ± 16.1	123.6
			Reproduction
NOEC (mg test item/kg dry weight artificial soil)			1000
LOEC (mg test item/kg dry weight artificial soil)			> 1000

No statistical significance (Williams test one-sided smaller $\alpha = 0.05$)

Reference test: In the most recent test, dimethoate showed an LC_{50} of 4.2 mg a.s./kg (95% confidence limits from 3.6 to 5.0 mg a.s./kg dry weight artificial soil) for mortality of the adult mites according Probit analysis using maximum likelihood regression.
The $NOEC_{reproduction}$ was calculated to be 3.2 mg a.s./kg dry weight artificial soil and accordingly the $LOEC_{reproduction}$ is 5.6 mg a.s./kg dry weight artificial soil according Williams-Test multiple t-test procedure, $\alpha = 0.05$, one-sided. Dimethoate showed a EC_{50} of 5.7 mg a.s./kg dry weight artificial soil (95 % confidence limits from 5.7 to 5.8 mg a.s./kg dry weight artificial soil) for reproduction according Probit analysis using maximum likelihood regression.
This is in the recommended range of the guideline of 3.0 – 7.0 mg a.s./kg dry weight artificial soil showing that the test organisms are sufficiently sensitive.

Conclusions:
NOEC: ≥ 1000 mg test item/kg dry weight artificial soil.
LOEC: > 1000 mg test item/kg dry weight artificial soil.

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Metabolite M03

Report:	**IIA 8.14 /06: [redacted] 2011**
Title:	Iprovalicarb-carboxylic acid: Effects on Reproduction of the Predatory Mite *Hypoaspis aculeifer* in Artificial Soil
Document No:	M-405048-01-1 (Rep. No: 59693089)
Guidelines:	OECD 226: Predatory mite (*Hypoaspis* (*Geolaelaps*) *aculeifer*) reproduction test in soil, 16 Oct 2008
GLP	Yes (certified laboratory)

Objectives: The purpose of the study was to determine the effects of iprovalicarb-carboxylic acid on mortality and reproduction of the Predatory Mite *Hypoaspis aculeifer*.

Material and Methods:

Test item: Iprovalicarb-carboxylic acid; batch code: BCS-CR79590-01-01; origin batch no. BCOO 6249-10-3; customer order no.: TOX 09087-00; purity: 98.9% w/w.

Test species: Predatory mite *Hypoaspis aculeifer*, adult females, approximately 10 days after reaching the adult stage (31 days after placing adult females in clean rearing vessel), source: [redacted], Germany.

Test design: 14-d exposure in treated artificial soil. One concentration of the test item was mixed homogeneously into the soil which was filled in glass vessels before the predatory mites were introduced on top of the soil; 1 concentration and 1 control; 8 replicates per concentration and control, with 10 female predatory mites each. Feeding of the mites with cheese mite (*Tyrophagus putrescentiae) ad libitum* at test start and two to three times a week. Assessment of adult mortality and reproduction after 14 d.

Endpoints: Mortality of adult mites, number of juveniles

Reference item: Perfekthion (a.s. dimethoate, 400 g/L, nominal). The effects of the reference item are investigated at least once a year in a separate study.

Test Rate: Control, 100 mg iprovalicarb-carboxylic acid/kg artificial soil (dry weight).

Test Conditions: Artificial soil based on OECD 226; pH at experimental start 6.4, pH at experimental end 6.2 to 6.3; water content at experimental start 23.2 % to 23.4 % (49.4% to 49.8%) of the maximum water holding capacity); at experimental end 22.8% to 23.3% (48.5% to 49.5%) of the maximum water holding capacity); temperature: within the range of 18°C to 22°C; illumination: 16 h light : 8 h dark (within the range of 400 to 800 lux).

Statistics: Standard procedures, Fisher's Exact Test (mortality), Student t-test (reproduction)

Findings: All validity criteria for the study were met (see table below).

Validity Criteria	**Recommended**	**Obtained**
Mortality of adults in the control	≤ 20%	6%
Reproduction per replicate in the control	≥ 50	90 to 164
Coefficient of variation of reproduction in control	≤ 30%	19.5%

Mortality of *Hypoaspis aculeifer* in the test item treated group was 11% while in the control 6% of the adults died. The value was not significantly different compared to the control (Fisher's Exact Test, α = 0.05, one-sided greater).
Reproduction of the predatory mites exposed to iprovalicarb-carboxylic acid at the concentration of 100 mg test item/kg artificial soil represented 87% of the control reproduction, which was not statistically significantly different compared to the control (Student t-test, α = 0.05, one-sided smaller).

Effect of iprovalicarb-carboxylic acid on the Predatory Mite *Hypoaspis aculeifer* in a 14-day reproduction study

Iprovalicarb-carboxylic acid [mg/kg artificial soil]	**Control**	**100**
Mortality (day 14) [%]	6	11

Statistical significance[1)]	-	n.s.
No. of juveniles (day 14)	119	103
Reproduction in [%] of control (day 14)	-	87
Statistical significance[2)]	-	n.s.
Endpoints [mg/kg artificial soil]		
NOEC (mortality)	≥ 100	
NOEC (reproduction)	≥ 100	

n.s. = not significantly different compared to the control
[1)] Fisher's Exact Test, $\alpha = 0.05$, one-sided greater
[2)] Student t-test, $\alpha = 0.05$, one-sided smaller

Reference test: The reference item dimethoate showed statistically significant effects on reproduction at a concentration of 4.0 mg dimethoate/kg artificial soil. The EC_{50} for reproduction was 3.24 mg dimethoate/kg artificial soil.

Conclusion: Iprovalicarb-carboxylic acid caused no significant effects on mortality or reproduction of *Hypoaspis aculeifer* at the single test concentration of 100 mg test item/kg artificial soil.
Therefore, the overall No Observed Effect Concentration (NOEC) was determined to be ≥ 100 mg test item/kg artificial soil. The overall Lowest Observed Effect Concentration (LOEC) was estimated to be greater than 100 mg test item/kg artificial soil.

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Metabolite M10

Report:	**IIA 8.14/07; [redacted] 2009**
Title:	Iprovalicarb-p-methylphenethylamine: Influence on mortality and reproduction on the soil mite species *Hypoaspis aculeifer* tested in artificial soil with 5 % peat
Document No:	M-358751-01-1 (Rep. No: KRA-HR-18/09)
Guidelines:	OECD 226: Predatory mite (*Hypoaspis* (*Geolaelaps*) *aculeifer*) reproduction test in soil, 16 Oct 2008
GLP	Yes (certified laboratory)

Objectives: The purpose of the study was to assess the effects of iprovalicarb-p-methylphenethylamine on mortality and reproduction on the soil mite species *Hypoaspis aculeifer* tested during an exposure of 14 days in artificial soil with 5% peat at 6 different application rates including control.

Material and Methods: Test item: Iprovalicarb-p-methylphenethylamine, Batch Code AE C624117-01-01, Origin Batch No. 060229ELB03, Certificate No. AZ 16068, analysed content of 94.6% Iprovalicarb-p-methylphenethylamine.
Toxic standard: Dimethoate, test concentrations 0.98, 1.61, 2.85, 4.99 and 8.92 mg dimethoate/kg dry weight (dw) artificial soil.
Ten adult, fertilized, female *Hypoaspis aculifer* per replicate (8 control replicates and 4 replicates for each application rate) were exposed to control (water treated), 63, 125, 250, 500 and 1000 mg test item/kg dry weight artificial soil. The test item was applied by mixing into the artificial soil. The *Hypoaspis aculeifer* were of a uniform age not differing more than three days (28 days after start of egg laying). During the test, they were fed with cheese mites bred on brewer's yeast. During the study a temperature of 20 ± 2°C and light regime of 400 – 800 Lux, 16 h light : 8 h dark was applied. The

artificial soil was prepared according to the guideline with the following constituents (percentage distribution on dry weight basis): 74.8% fine quartz sand, 5% *Sphagnum* peat, air dried and finely ground, 20% Kaolin clay and approximately 0.2% Calcium carbonate ($CaCO_3$).
After a period of 14 days, the surviving adults and the living juveniles were extracted by applying a temperature gradient using a MacFadyen-apparatus. Extracted mites were collected in a fixing solution (20% ethylene glycol, 80% deionised water; 2 g detergent/L fixing solution were added). All *Hypoaspis aculeifer* were counted under a binocular.

Findings: All validity criteria for the study were met (see table below).

Validity Criteria	Recommended	Obtained
Mean adult female mortality	≤ 20%	5.0%
Mean number of juveniles per replicate (with 10 adult females introduced)	≥ 50	413.6
Coefficient of variation calculated for the number of juvenile mites per replicate	≤ 30%	7.2%

Mortality: In the control group 5.0% of the adult *Hypoaspis aculeifer* died which is within the recommended range of ≤ 20% mortality. A LC_{50} cannot be calculated and is considered to be > 1000 mg test item/kg dry artificial soil.
Reproduction: Concerning the number of juveniles statistical analysis (U-test after Bonferroni-Holm, one-sided smaller, $\alpha = 0.05$) revealed no significant differences between the control and all treatment groups.
Therefore the No-Observed-Effect-Concentration (NOEC) for reproduction is ≥ 1000 mg test item/ kg dry weight artificial soil. The Lowest-Observed-Effect-Concentration (LOEC) for reproduction is > 1000 mg test item/ kg dry weight artificial soil. An EC_{50} could not be calculated and is considered to be > 1000 mg test item/kg dry artificial soil.

Effect of iprovalicarb-p-methylphenethylamine on the Predatory Mite *Hypoaspis aculeifer* in a 14-day reproduction study

Test item Test object Exposure	Iprovalicarb-p-methylphenethylamine *Hypoaspis aculeifer* Artificial soil		
mg test item/kg dry weight artificial soil	% mortality (Adults)	Mean number of juveniles per test vessel ± standard dev.	Reproduction (% of control)
Control	5.0	413.6 ± 29.9	-
63	10.0	366.3 ± 22.9	88.5
125	12.5	369.5 ± 62.1	89.3
250	10.0	375.3 ± 27.3	90.7
500	0.0	395.5 ± 34.1	95.6
1000	2.5	391.8 ± 28.6	94.7
			Reproduction
NOEC (mg test item/kg dry weight artificial soil) LOEC (mg test item/kg dry weight artificial soil)			≥ 1000 > 1000

Reference test: In the most recent test, dimethoate showed an LC_{50} of 3.86 mg a.s./kg (95% confidence limits from 3.34 mg a.s./kg to 4.45 mg a.s./kg artificial soil dw) for mortality of the adult mites according Probit analysis using maximum likelihood regression.
The $NOEC_{reproduction}$ was calculated to be 1.61 mg a. s./kg dw and accordingly the $LOEC_{reproduction}$ is 2.85 mg a.s./kg dw according Williams-Test multiple t-test procedure, α = 0.05, one-sided. Dimethoate showed a EC_{50} of 5.45 mg a.s./kg dw (95% confidence limits from 4.59 mg a.s./kg dw to 6.53 mg a.s./kg dw) for reproduction according Probit analysis using maximum likelihood regression.
This is in the recommended range of the guideline of 3.0 – 7.0 mg a.s./kg dry weight artificial soil showing that the test organisms are sufficiently sensitive.

Conclusions:
NOEC: ≥ 1000 mg test item/kg dry weight artificial soil.
LOEC: > 1000 mg test item/kg dry weight artificial soil.

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Metabolite M15

Report:	**IIA 8.14 /08; [redacted] 2010**
Title:	Iprovalicarb-N-acetyl-PMPA: Influence on mortality and reproduction on the soil mite species *Hypoaspis aculeifer* tested in artificial soil with 5 % peat
Document No:	M-364283-01-1 (Rep. No: KRA-HR-24/10)
Guidelines:	OECD 226: Predatory mite (*Hypoaspis* (*Geolaelaps*) *aculeifer*) reproduction test in soil, 16 Oct 2008
GLP	Yes (certified laboratory)

Objectives: The purpose of the study was to assess the effects of Iprovalicarb-N-acetyl-PMPA on mortality and reproduction on the soil mite species *Hypoaspis aculeifer* tested during an exposure of 14 days in artificial soil with 5% peat comparing control and treatment.

Material and Methods: Test item: Iprovalicarb-N-acetyl-PMPA, Batch Code AE 1371462-01-01, Origin Batch No. SES 10727-1-1, Certificate No. AZ 16150, analysed content of 95.5% iprovalicarb-N-acetyl-PMPA.
Toxic standard: Dimethoate, test concentrations 1.0, 1.8, 3.2, 5.6 and 10.0 mg dimethoate/kg dry weight artificial soi.
Ten adult, fertilized, female *Hypoaspis aculeife*r per replicate (8 control replicates and 8 treatment replicates) were exposed to control (water treated) and 100 mg pure metabolite/kg dry weight artificial soil. The test item was applied by mixing a test item-quartz sand-mixture into the artificial soil. The *Hypoaspis aculeifer* were of a uniform age not differing more than three days (31 days after start of egg laying). During the test, they were fed with cheese mites bred on brewer's yeast. During the study a temperature of 20 ± 2°C and light regime of 400 – 800 Lux, 16 h light : 8 h dark was applied. The artificial soil was prepared according to the guideline with the following constituents (percentage distribution on dry weight basis): 74.8% fine quartz sand, 5% *Sphagnum* peat, air dried and finely ground, 20% Kaolin clay and approximately 0.2% Calcium carbonate ($CaCO_3$).
After a period of 14 days, the surviving adults and the living juveniles were extracted by applying a temperature gradient using a MacFadyen-apparatus. Extracted mites were collected in a fixing solution (20% ethylene glycol, 80% deionised water; 2 g detergent/L fixing solution were added). All *Hypoaspis aculeifer* were counted under a binocular.

Findings: All validity criteria for the study were met (see table below).

Validity Criteria	Recommended	Obtained
Mean adult female mortality	≤ 20%	5.0%
Mean number of juveniles per replicate (with 10 adult females introduced)	≥ 50	351.8
Coefficient of variation calculated for the number of juvenile mites per replicate	≤ 30%	25.4%

Mortality: In the control group 5.0% of the adult *Hypoaspis aculeifer* died which is below the allowed maximum of ≤ 20% mortality. An LC_{50} cannot be calculated and is considered to be > 100 mg pure metabolite/kg dry artificial soil.
Reproduction: Concerning the number of juveniles statistical analysis (Student-t test, one-sided smaller, α = 0.05) revealed no significant differences between the control and all treatment groups.
Therefore the No-Observed-Effect-Concentration (NOEC) for reproduction is ≥ 100 mg pure metabolite/ kg dry weight artificial soil. The Lowest-Observed-Effect-Concentration (LOEC) for reproduction is > 100 mg pure metabolite/ kg dry weight artificial soil. An EC_{50} could not be calculated and is considered to be > 100 mg pure metabolite/kg dry artificial soil.

Effect of iprovalicarb-N-acetyl-PMPA on the Predatory Mite *Hypoaspis aculeifer* in a 14-day reproduction study

Test item Test object Exposure	Iprovalicarb-N-acetyl-PMPA *Hypoaspis aculeifer* Artificial soil		
mg pure metabolite/kg dry weight artificial soil	% mortality (Adults)	Mean number of juveniles per test vessel ± standard dev.	Reproduction (% of control)
Control	5.0	351.8 ± 89.5	-
100	10.0	332.8 ± 89.2	94.6
			Reproduction
NOEC (mg pure metabolite/kg dry weight artificial soil)			≥ 100
LOEC (mg pure metabolite/kg dry weight artificial soil)			> 100

Reference test: In the most recent test dimethoate showed an LC_{50} of 4.2 mg a.s./kg (95% confidence limits from 3.6 to 5.0 mg a.s./kg dry weight artificial soil) for mortality of the adult mites according Probit analysis using maximum likelihood regression.
The $NOEC_{reproduction}$ was calculated to be 3.2 mg a.s./kg dry weight artificial soil and accordingly the $LOEC_{reproduction}$ is 5.6 mg a.s./kg dry weight artificial soil according Williams-Test multiple t-test procedure, $\alpha = 0.05$, one-sided. Dimethoate showed a EC_{50} of 5.7 mg a.s./kg dry weight artificial soil (95 % confidence limits from 5.7 to 5.8 mg a.s./kg dry weight artificial soil) for reproduction according Probit analysis using maximum likelihood regression.
This is in the recommended range of the guideline of 3.0 – 7.0 mg a.s./kg dry weight artificial soil showing that the test organisms are sufficiently sensitive.

Conclusions:
NOEC: ≥ 100 mg pure metabolite/kg dry weight artificial soil.
LOEC: > 100 mg pure metabolite/kg dry weight artificial soil.

IIA 8.14.1 Summary of preliminary data: biological activity & dose range finding

Herbicidal activity
Screening data concerning herbicidal activity are not presented.
The relevant information is covered by the guideline studies on representative species, which are presented under point 8.12 of this section 6.

Insecticidal activity
Screening data concerning insecticidal activity are not presented.
The relevant information is covered by the guideline studies on representative species, which are presented under the points 8.7 and 8.8 of this section 6.

Further information
Further information on the biological activity of iprovalicarb is given in the respective chapters (IIA, point 3 and IIIA, point 6).

IIA 8.14.2 A critical assessment as to the relevance of the preliminary test data to potential impact on non-target species

Risk assessments for all non-target species are performed in product specific Annex III dossiers.

IIA 8.15 Effects on biological methods for sewage treatment

Please refer to point IIA 8.15 (EU point IIA 8.7) of the EU dossier submitted in the context of Annex I listing and the relevant data submitted during the EU evaluation process according to the "Review Report for Iprovalicarb (SANCO/2034/2000-FINAL, from July, 2002)".

IIA 8.16 Other/special studies

No other/special studies were considered necessary.

IIA 8.16.1 Other/special studies – laboratory studies

No other/special studies were considered necessary.

IIA 8.16.2 Other/special studies – field studies

No other/special studies were considered necessary.

IIA 8.17 Summary and evaluation of points IIA 7 and IIA 8.1 to 8.16

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 *(M30)* 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.

The calculated DT_{50} values of iprovalicarb determined in the laboratory studies (rate and route) under aerobic conditions were in the range of 2 - 29.6 days for the experiments performed at 20°C and 21.5 days for the experiment at 10°C. For major iprovalicarb soil metabolites the calculated DT_{50} values determined in laboratory studies were in the range of 1 - 2 days (SZX 0722-carboxylic acid *(M03)*), 44 - 239 days (PMPA *(M10)*) and below 1 day (N-acetyl-PMPA *(M15)*).
Iprovalicarb did degrade appreciably under anaerobic conditions in soil and would not be expected to persist in this type of environment (DT_{50} value 0f 24.4 days based on DFOP kinetics.
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.

In the field, DT_{50} values for iprovalicarb itself and the total residue of iprovalicarb and its metabolite PMPA *(M10)* ranged from 1 - 17 and 2 - 22 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 [redacted] *(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 ≥ 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. The DT_{50} values of iprovalicarb were calculated to be in the range of 19 - 56 days, referring to the entire system. 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.

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.

Effects on non-target organisms

In the following, the endpoints are given for iprovalicarb, for iprovalicarb metabolites and for the former lead formulation Iprovalicarb WG 50 resulting from ecotoxicological studies. An assessment of ecotoxicological data is only possible in connection with the label recommendations and the environmental exposure resulting from the use according to good agricultural practice. Therefore the risk assessment is performed in the Annex III dossier of the current lead formulation Iprovalicarb + Folpet WG 65.3.

Summary of effects of iprovalicarb on birds

Test Species	Test substance	Test System	Exposure duration	Results (mg a.s./kg bw/d)	Reference
Bobwhite quail	a.s.	acute oral	single application	LD_{50} > 2000	[redacted], 1995 VB-034 M-000077-01-1 IIA 8.1.1 /01 (EU: IIA 8.1.1/01)
Bobwhite quail	a.s.	dietary test	5 d	LDD_{50} > 1351 (LC_{50} = > 5000 mg/kg feed)	[redacted], 1997 SXR/VB 059 M-000066-01-1 IIA 8.1.2 /01 (EU: IIA 8.1.2/01)
Mallard duck	a.s.	dietary test	5 d	LDD_{50} > 2414 (LC_{50} = >5000 mg/kg feed)	[redacted], 1997 SXR/VE 009 M-000326-01-1 IIA 8.1.3 /01 (EU: IIA 8.1.2/02)
Bobwhite quail	a.s.	dietary test, reproduction	22 w	NOAEL 161 (NOEC 2000 mg/kg feed)	[redacted]; [redacted], 1997 177738 M-000124-01-1 IIA 8.1.4 /01 (EU: IIA 8.1.3/01)

Summary of effects of iprovalicarb and metabolites on aquatic organisms

Test species	Test substance	Test system	Exposure duration	Results (mg a.s./L)	Reference
Rainbow trout	a.s.	acute, flow through	96 h	LC_{50}: >22.7	[redacted], 1995 DOM 95060 M-000056-01-1 IIA 8.2.1.1 /01 (EU: IIA 8.2.1/01)
Bluegill sunfish	a.s.	acute, flow through	96 h	LC_{50}: 20.7	[redacted], 1995 DOM 95059 M-000050-01-1 IIA 8.2.1.2 /01 (EU: IIA 8.2.1/02)
Rainbow trout	M03	Acute, static	96 h	LC_{50}: > 10 mg p.m./L	[redacted], 2011 EBSZX156 M-409113-01-1 IIA 8.2.1.3 /03
Rainbow trout	M10	Acute, static	96 h	LC_{50}: > 100 mg p.m./L	[redacted], 1997 DOM 96063 M-000114-01-1 IIA 8.2.1.3 /01 (EU point IIA, 8.2.1/03)
Rainbow trout	M15	Acute, static	96 h	LC_{50}: > 100 mg p.m./L	[redacted], 1997 DOM 97048 M-000751-01-1 IIA 8.2.1.3 /02 (EU point IIA, 8.2.1/04)
Rainbow trout	a.s.	Chronic, semi-static	28 d	NOEC: ≥ 9.89	[redacted], 1997 DOM 96053 M-000032-01-1 IIA 8.2.3 /01 (EU point IIA, 8.2.2.1/01)
Rainbow trout	a.s.	ELS, flow-through	88 d	NOEC: 5	[redacted], 2000 443A-105 M-030681-01-1 IIA 8.2.4 /01
Bluegill sunfish	[14]C-a.s.	Bioconcentration, chronic	28 d	mean-whole fish BCF: 10 based on parent compound: BCF 1.4	[redacted], 1997 DOM 96003 M-000030-01-1 IIA 8.2.6.1 /01 (EU: IIA 8.2.3/01) [redacted], 2001 MR-066/01 M-064491-01-1 IIA 8.2.6.1 /02
Daphnia magna	a.s.	acute, static	48 h	EC_{50}: > 19.8	[redacted], 1996 HBF/DM 157 M-000039-01-1 IIA 8.3.1.1 /01 (EU: IIA 8.2.4/01)
Daphnia magna	M03	Static	48 h	EC_{50}: > 10 mg p.m./L	[redacted], 2011 EBSZX157 M-409052-01-1 IIA 8.3.1.1 /04

Test species	Test substance	Test system	Exposure duration	Results (mg a.s./L)	Reference
Daphnia magna	M10	Static	48 h	EC_{50}: 36.5 mg p.m./L	[redacted], 1997 HBF/DM 170 M-000119-01-1 IIA 8.3.1.1/02 (EU point IIA, 8.2.4/02)
Daphnia magna	M15	Static	48 h	EC_{50}: > 100 mg p.m./L	[redacted], 1997 HBF/DM 185 M-000601-01-1 IIA 8.3.1.1/03 (EU point IIA, 8.2.4/03)
Daphnia magna	a.s.	Reproduction test semi static	21 d	NOEC: 1.89	[redacted], 1996 HBF/RDM 57 M-000036-01-1 IIA 8.3.2.1 /01 (EU point IIA, 8.2.5/01)
Pseudokirchneriella subcapitata (formerly *Selenastrum capricornutum*)	a.s.	growth rate, static	72 h	$E_{r/b}C_{50}$: > 10	[redacted], 1996 AJO/141195 M-000034-01-1 IIA 8.4 /01 (EU: IIA 8.2.6/01)
Pseudokirchneriella subcapitata	M03	growth rate, static	72 h	E_rC_{50}: > 100 mg p.m./L	[redacted], 2011 EBSZX 158 M-411009-01-1 IIA 8.4 /04
Pseudokirchneriella subcapitata	M10	growth rate, static	72 h	E_rC_{50}: 15.09 mg p.m./L E_bC_{50}: 7.18 mg p.m./L	[redacted], 1997 AJO/151796 M-000079-01-1 IIA 8.4 /02 (EU point IIA, 8.2.6/02)
Pseudokirchneriella subcapitata	M15	growth rate, static	72 h	E_rC_{50}: > 100 mg p.m./L	[redacted], 1997 AJO/167297 M-000624-01-1 IIA 8.4 /03 (EU point IIA, 8.2.6/03)
Chironomus riparius	a.s.	Static, spiked sediment	28 d	$EC_{15\ emerg.}$: 128 mg a.s./kg dw sed	[redacted], 2010 EBSZL026 M-398870-01-1 AII 8.5.2 /01
Chironomus riparius	M10	Static, spiked sediment	28 d	EC_{15}: > 100 mg p.m./ kg dw sed	[redacted], 2010 EBSZL022 M-368933-01-1 AII 8.5.2 /02

Summary of effects on honey bees

Species	Test substance	Results LD_{50} (µg a.s./bee)	Reference
Apis mellifera foraging bees	a.s.	oral 48h > 199 contact 48h > 200	[redacted], 1995 95 10 48 061 M-000086-01-1 IIA 8.7.1 /01, IIA 8.7.2 /01 (EU point IIA, 8.3.1.1/01)

Impacts of Iprovalicarb WG 50 on Non-Target Arthropods in laboratory studies

Test organisms	Test substance / exposure	Results	Reference
Aphidius rhopalosiphi	WG 50 Spray deposits on glass plates, 48 h	no significant effects on mortality or reproduction up to 0.9 kg product/ha (corresponding to 0.45 kg a.s./ha)	[redacted], 1995 BAY-95-6 M-000098-01-1 IIA 8.8.1.1 /01 (EU point IIA 8.3.2/02)
Typhlodromus pyri	WG 50 Spray deposits on glass plates, 14d	no negative effects on mortality or reproduction at 0.9 kg product/ha (corresponding to 0.45 kg a.s./ha)	[redacted], 1997 SXR/TP 01 M-000112-01-1 IIA 8.8.1.2/01 (EU point IIA 8.3.2/04)
Poecilus cupreus	50 WG laboratory	no mortality or effects on feeding rate at 2x 0.9 kg product/ha	[redacted], 1996 SXR/CA 148 M-000102-01-1 IIA 8.8.1.3 /01 (EU point IIA 8.3.2/03)
Coccinella septempunctata	WG 50 Spray deposits on glass plates, 77 d	no negative effects on metamorphosis or reproduction at 1.074 kg product/ha (corresponding to 0.55 kg a.s./ha)	[redacted], 1997 HGP/LA C001 M-006377-01-1 IIA 8.8.1.4 /01 (EU point IIA, 8.3.2/01)

Summary of effects of iprovalicarb on earthworms and other soil macro-organisms

Test species	Test substance	Exposure duration	Results	Reference
Eisenia fetida	a.s.	14 d	LC_{50} > 1000 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	M10	14 d	LC_{50} > 1000 mg a.s./kg dws	[redacted] (1999) HBF/Rg 302 M-016516-01-1 IIA 8.9.1 /02
Eisenia fetida	WG 50	56 d	NOEL ≥ 0.75 kg a.s./ha equivalent to NOEC ≥ 1.0 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	WG 50	56 d	NOEL ≥ 2.5 kg a.s./ha equivalent to NOEC > 10 mg a.s./kg dws [2)]	[redacted] (2001) MPE/Rg 370/01 M-033073-01-1 IIA 8.9.2/02
Eisenia fetida	a.s.	56 d	NOEC ≥ 64 mg a.s./kg dws	[redacted], 2011 LRT-Rg-R-85/11 M-405822-01-1 IIA 8.9.2 /03
Eisenia fetida	M03	56 d	NOEC ≥ 100 mg p.m./kg dws	[redacted], 2011 59691022 M-406133-01-1 IIA 8.9.2 /04
Eisenia fetida	M10	56 d	NOEC 316 mg p.m./kg dws	[redacted], 2001 MPE/Rg 369/01 M-043357-01-1 IIA 8.9.2/05
Eisenia fetida	M15	56 d	NOEC 60.2 mg p.m./kg dws	[redacted], 2010 52291022 M-368040-01-1 IIA 8.9.2 /06
Folsomia candida	a.s.	28 d	NOEC ≥ 1000 mg a.s./kg dws	[redacted], 2010 FRM-COLL-80/10 M-368058-01-1 IIA 8.14 /01
Folsomia candida	M03	28 d	NOEC ≥ 100 mg p.m./kg dws	[redacted], 2011 59692016 M-405347-01-1 IIA 8.14 /02
Folsomia candida	M10	28 d	NOEC ≥ 1000 mg p.m./kg dws	[redacted], 2010 FRM-COLL-78/10 M-361572-01-1 IIA 8.14 /03
Folsomia candida	M15	28 d	NOEC ≥ 100 mg p.m./kg dws	[redacted], 2010 M-366743-01-1 FRM-COLL-81/10 IIA 8.14 /04
Hypoaspis aculeifer	a.s.	14 d	NOEC ≥ 1000 mg a.s./kg dws	[redacted], 2010 KRA-HR-25/10

				M-366603-01-1 IIA 8.14 /05
Hypoaspis aculeifer	M03	14 d	NOEC ≥ 100 mg p.m./kg dws	[redacted], 2011 5969089 405048-01-1 IIA 8.14 /06
Hypoaspis aculeifer	M10	14 d	NOEC ≥ 1000 mg p.m./kg dws	[redacted], 2009 KRA-HR-18/09 M-358751-01-1 IIA 8.14 /07
Hypoaspis aculeifer	M15	14 d	NOEC ≥ 1000mg p.m./kg dws	[redacted], 2010 KRA-HR-24/10 M-364283-01-1 IIA 8.14 /08

[1] Calculated considering a soil depth of 5 cm and a bulk density of the soil of 1.5 g/cm³ (standard conversion)

[2] 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.

dws. = dry weight artificial soil

Summary of effects of iprovalicarb on soil micro-organisms and sewage treatment plants

Test system	Test substance	Exposure duration	Results	Reference
C-cycle	a.s.	91 d	No influence at 6.6 mg a.s./kg dws equivalent to 4.95 kg a.s./ha	[redacted], 1996 AJO/142896 M-000096-01-1 IIA 8.10.2 /01 (EU point IIA, 8.5/01)
N-cycle	a.s.	91 d	No influence at 6.6 mg a.s./kg dws equivalent to 4.95 kg a.s./ha	[redacted] 1996 M-000094-01-1 AJO/142996 IIA 8.10.1 /01 (EU point IIA, 8.5/02)
N-cycle	M03	28 d	No influence at 13.33 mg p.m./kg dws equivalent to 10 kg p.m./ha	[redacted], 2011 M-404388-01-1 10 10 48 055 N IIA 8.10.1 /02
N-cycle	M10	28 d	No influence at 0.93 mg p.m./kg dws equivalent to 0.7 kg p.m./ha	[redacted], 2010 M-366832-01-1 FRM-N-139/10 IIA 8.10.1 /03
N-cycle	M15	28 d	No influence at 1.21 mg p.m./kg dws equivalent to 0.913 kg p.m./ha	[redacted], 2010 M-366828-01-1 FRM-N-138/10 IIA 8.10.1 /04
Activated sludge	a.s.	3 h	EC_{50} > 10 000 mg a.s./L	[redacted], 1991 BA-918269 M-000108-02-1 IIA 8.15 /01 (EU point IIA, 8.7/01)
Activated sludge	M10	30 min.	EC_{50} 1290 mg p.m./L	[redacted], 1996 587 A/96 M-000121-01-2 IIA 8.15 /02 (EU point IIA, 8.7/02)

Summary of effects of iprovalicarb to non-target terrestrial higher plants

Test	Test species	Ecotoxicological endpoint	Reference
Iprovalicarb WG 50 screening study	*Zea mays* *Beta vulgaris* *Alopecurus myosuroides* *Avena fatua* *Echinochloa crus-galli* *Setaria viridis* *Abutilon theophrasti* *Amaranthus retroflexus* *Galium aparine* *Ipomoea hederacea* *Sinapis alba*	applied at rates from 180 to 2700 g a.s./ha application pre-emergent no effects > 50% up to 1000 g a.s./ha application post-emergent no effects > 50% up to 2700 g a.s./ha	[redacted], 2000 MPE 02/00 M-020520-01-1 IIA 8.12/01

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
dws	Dry weight artificial soil	
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	

Abbreviation	Explanation	Definition
MAF	Multiple application factor	
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	