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Document Title

Tier 2 Summary

KIIA 7: Fate and behaviour in the environment

for

Iprovalicarb

(Annex I Renewal)

Specification No.

102000006810-05

Data Requirements

EU Commission Regulation No. 1141/2010
on the renewal of the inclusion of AIR2 active substances
in conjunction with Directive 91/414/EEC and Regulation EC/1107/2009

Annex II
Document M
Section 5, Point 7

Date

2012-05-07

Author(s)

[redacted]

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OWNERSHIP STATEMENT

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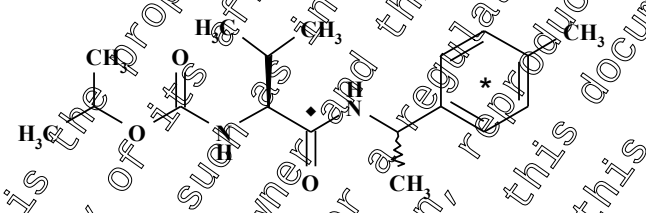
KIIA 7 Fate and behaviour in the environment

Information on the updated dossier for the Annex I renewal

Data on the fate and behaviour of iprovalicarb (SZX 0722) in soil, water and air were submitted within the EU Basic Dossier in 1998. In this Annex I Renewal only those environmental fate studies are described in sections 7.1 – 7.13 which were **not** submitted within in the EU Basic Dossier of 1998. The numbering and the headlines correspond to the new OECD guidelines. For a better overview short summaries including the results of all environmental fate studies are given in addition in this summary at the end of the corresponding chapters.

The additional environmental fate studies of iprovalicarb were performed with the following ^{14}C-labelling positions and the non-labelled compound:

** and ◆ indicate positions of ^{14}C-labels*



* = [phenyl-UL-^{14}C]iprovalicarb
(short form used in this chapter: "phenyl-label")

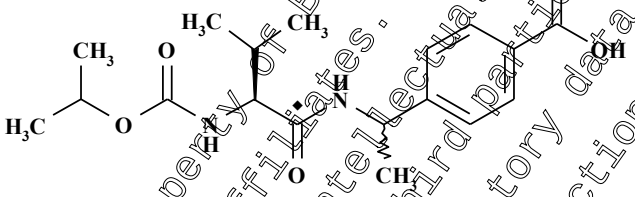
◆= [valine-1-^{14}C]iprovalicarb
sometimes also referred as [valyl-1-^{14}C]iprovalicarb
(short form used in this chapter: "valine-label")

In addition, studies with the metabolites SZX 0722-carboxylic acid *(M03)*, PMPA *(M10)* and N-acetyl-PMPA *(M15)* were performed:

- **SZX 0722-carboxylic acid *(M03)***

Studies were conducted using [valine-1-^{14}C]SZX 0722-carboxylic acid *(M03)*, and the non-labelled compound

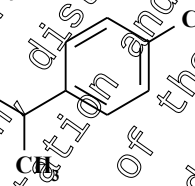
- *indicate positions of ^{14}C-label*



- = [valine-1-^{14}C]SZX 0722-carboxylic acid *(M03)*
  (short form used in this chapter: "valine-label")

- **PMPA *(M10)***

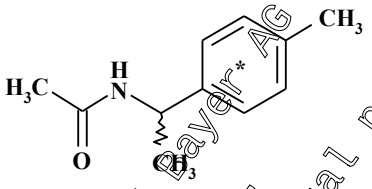
Studies were conducted using the non-labelled compound.



- **N-acetyl-PMPA *(M15)***

Studies were conducted using [phenyl-UL-^{14}C]N-acetyl-PMPA *(M15)* and the non-labelled compound.

** indicate positions of ^{14}C-label*



* = [phenyl-UL-^{14}C]N-acetyl-PMPA *(M15)*
(short form used in this chapter: "phenyl-label")

General information:
The expression "applied radioactivity" was often abbreviated as AR, e.g. as % AR in tables.

In this summary, a single name and a single code number for each metabolite are always used. A list of metabolites contains the structures, various names, short forms and code numbers attributed to the metabolites (Borchers, 2012). The matrices in which the metabolites were identified are also included in this list. This list is provided in Document N.

KIIA 7.1 Route of degradation in soil - laboratory studies

KIIA 7.1.1 Aerobic degradation

The route of iprovalicarb in soil under aerobic conditions was evaluated during the Annex I Inclusion using the phenyl-labelled parent compound ([redacted], 1997; [redacted] 1997a and 1997b (submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.1.1 /01, IIA, 7.1.1.1.1 /02 and IIA, 7.1.1.1.1 /03, respectively) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)). In addition a new soil metabolism study was performed using the valine radiolabel of iprovalicarb to complete the data according to current requirement practice ([redacted] (2011), submitted in this Dossier, KIIA 7.1.1 /04). For a better overview a short summary of the results of both radiolabels concerning the route of degradation of iprovalicarb in soil under aerobic condition is given at the end of this chapter at page 46.

New study submitted for Annex I renewal
Justification for including this study in the Annex I Renewal Dossier: The new soil metabolism and degradation study was conducted with the valine radiolabel to complement the former dossier according to current requirement practices. With the Basic EU Dossier submitted in 1998 only studies with the phenyl radiolabel were provided.

Report:	**KIIA 7.1.1 /04, [redacted] 2011**
Title:	[Valine-1-^{14}C]iprovalicarb: Aerobic metabolism/degradation in four European soils
Report No:	MEF-10/660
Document No:	M-414387-01-1
Guidelines:	- OECD Guideline for Testing of Chemicals, No. 307, Aerobic and Anaerobic Transformation in Soil, 2002 - US EPA Fate, Transport and Transformation Test Guidelines, OPPTS 835.4100 and OPPTS 835.4200, Aerobic and Anaerobic Soil Metabolism, 2008 - Commission Directive 95/36/EC amending Council Directive 91/414/EEC (Annexes II and III, Fate and Behaviour in the Environment), 1995 - Regulation (EC) No 1107/2009 of the European Parliament and of the council of 21 October 2009
GLP:	Yes

Executive Summary

The biotransformation of valine-labelled iprovalicarb was studied in four soils (a sandy loam ([redacted] AXXa), a loam ([redacted] II), a sandy loam ([redacted]), and a silt loam ([redacted] 4a)) under aerobic conditions in the dark at 20°C and 55% WHC_{max} (maximum water holding capacity). Details of the soil properties are given in Table 7.1.1- 1. Because of the fast degradation and high mineralisation rate of valine-labelled iprovalicarb the study was performed for only 21 days. Iprovalicarb was applied in the test system at a rate of 720 µg a.s./kg soil dry weight, corresponding to the intended maximum single use rate of 270 g iprovalicarb/ha. Samples were analysed after 0, 1, 2, 4, 7, 14 and 21 days of incubation.

In the following those parts of the study are summarised which were performed to elucidate the route of degradation in soil. Parts concerning evaluation of rate of degradation are reported in section KIIA 7.2.1 (study KIIA 7.2.1 /05) of this document.

The soil extracts were analysed and quantified by HPLC and TLC and identification of the transformation products was achieved by comparison with authentic reference substances with both independent chromatographic systems.

Mean material balances accounted for 97.4, 96.0, 97.2, and 98.0% of the applied radioactivity (AR) for soils [redacted] AXXa, [redacted] II, [redacted] [redacted], and [redacted] 4a, respectively. The test item was declining from 103.1, 101.9, 100.8, and 100.7% of AR at day 0 to 7.4, 3.6, 8.7 and 4.2% of AR at the end of the study (day 21) in soils [redacted] AXXa, [redacted] II, [redacted] [redacted], and [redacted] 4a, respectively. The half-lives of iprovalicarb were calculated to be 6.7, 5.1, 5.9 and 5.5 days under aerobic conditions in the tested soils [redacted] AXXa, [redacted] II, [redacted] [redacted] and [redacted] 4a, respectively.

Extractable ^{14}C-residues decreased from 103.1, 101.9, 100.8, and 100.7% of AR at day 0 to 7.5, 3.6, 8.7, and 4.2% at the study end (day 21) in soils [redacted] AXXa, [redacted] II, [redacted] [redacted], and [redacted] 4a, respectively. Non-extractable ^{14}C-residues (NER) increased from 0.1 - 0.3% of AR at day 0 to 29.5 - 33.9% of AR at study end (day 21). A further characterization (fractionation into humin, humic acids and fulvic acids) was done for all four soils for the day 14 samples. The maximum amount of $^{14}CO_2$ was 61.3% of AR recovered at study termination (soil [redacted] 4a, day 21). Volatile organic compounds were not formed in the course of the study (< 0.1% of AR at all sampling intervals).

Besides high amounts of carbon dioxide SZX 0722-carboxylic acid *(M03)* was detected as sole metabolite in the course of the study in all four soils. It was detected as major metabolite in three soils with a maximum value (sum of diastereomers) of 10.0% of AR at day 7 in soil [redacted] AXXa, with a maximum value of 7.0% of AR at day 7 in [redacted] [redacted], and with a maximum value of 5.6% of AR at day 4 in [redacted] 4a. The metabolite declined below the limit of detection until the end of the study (day 21).

The results received within this valine-labelled iprovalicarb degradation / metabolism study were in good agreement with the proposed aerobic soil degradation pathway of iprovalicarb known from studies using the phenyl-label. No new metabolite specific for the valine-label was found. The test item is rapidly degraded to SZX 0722-carboxylic acid *(M03)* and CO_2. Enantiomers of the diastereomers of the test item were not formed during the study. The high amount of formed carbon dioxide as the final product indicates a rapid and complete mineralisation of iprovalicarb in soil.

I. Material and Methods

A. Materials

1. Test Material: [valine-1-^{14}C]iprovalicarb (diastereomeric mixture SR : SS = 1:1)
CAS #: 140923-17-7 (diastereomeric mixture SR : SS = 1:1)

specific radioactivity:	SR: 3.85 MBq/mg
	SS: 3.81 MBq/mg
radiochemical purity:	SR: > 98% (HPLC, UV-detector, 210 nm)
	SS: > 99 (HPLC, UV-detector, 210 nm)

2. Soil: The soil samples (Table 7.1.1- 1) were collected freshly from the field. A few days before starting the test, the soil was carefully dried in the lab at room temperature and sieved to a particle size of ≤ 2 mm. The soil was representative of an agricultural use area as required by the guidelines.

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Table 7.1.1- 1: Soil characteristics

Parameter	Soil			
	[redacted] AXXa	[redacted] II	[redacted]	[redacted] 4a
Geographic location - city - state - country	[redacted] NRW Germany	[redacted] NRW Germany	[redacted] NRW Germany	[redacted] NRW Germany
Side description	grassland			
Soil taxonomic classification (USDA)	sandy, mixed, mesic Typic Cambudolls	N/A	loamy, mixed, mesic Typic Argudalfs	loamy, mixed, mesic Typic Argudalfs
Soil series	N/A	N/A	N/A	N/A
Soil mapping unit (GPS coordinates)	[redacted]	[redacted]	[redacted]	[redacted]
Texture class (USDA) - sand (50 µm – 2 mm) [%] - silt (2 µm – 50 µm) [%] - clay (< 2 µm) [%]	sandy loam 75 19 6	loam 35 41 24	sandy loam 55 29 16	silt loam 25 61 14
pH - in $CaCl_2$ (soil/$CaCl_2$ 1/2) - in water (soil/water 1/1) - in water (saturated paste) - in KCl	 6.1 6.4 6.4 6.1	 7.1 7.2 7.2 6.9	 5.2 5.4 5.5 5.0	 6.3 6.5 6.6 6.1
Organic matter[a)] [%]	3.6	8.1	3.4	4.0
Organic carbon [%]	2.1	4.7	2.0	2.3
Microbial biomass [mg microbial carbon/kg dry soil] - day 0 - day 21 - day 21 (acetonitrile/water 1/1[b)])	 589 510 752	 3133 3064 3328	 708 521 858	 1078 950 1199
CEC [meq/100 g]	9.6	21.2	10.7	14.5
Water holding capacity 0.33 bar (pF 2.5) [g H_2O *ad*/100 g dry soil]	12.0	32.5	16.9	21.8
MWHC [g H_2O *ad*/100 g dry soil]	52.3	87.8	56.5	61.4
Bulk density (disturbed) [g/cm³]	1.21	0.96	1.15	1.06

a) calculated: %organic matter = % organic carbon × 1.724
b) samples applied with acetonitrile/water 1/1 (solvent of application solution)
CEC cation exchange capacity
MWHC maximum water holding capacity
N/A not applicable
NRW North Rhine-Westphalia

B. Study design

1. Experimental conditions: The test systems were static systems and consisted of Erlenmeyer flasks equipped with traps to collect CO_2 and volatile organic compounds. The test item is defined as a 1:1 mixture of the valine-labelled iprovalicarb-SS- and SR-diastereomers and was applied at a target rate of 720 µg a.s./kg soil dry weight. This concentration corresponded to a field rate of 270 g iprovalicarb/ha. The target rate was calculated based on an anticipated field rate of 270 g

a.s./ha, a soil depth of 2.5 cm and a bulk density of 1.5 g/cm³ which is equivalent to a concentration of 720 µg/kg soil calculated as dry matter. Aliquots of the soils, each corresponding to 100 g dry weight were used and the water content of the soil was adjusted to 55% of the maximum water holding capacity. The soil samples were incubated under aerobic conditions in the dark at 20°C. Because of the fast degradation and high mineralisation rate of valine-labelled iprovalicarb the study was performed for only 21 days. The temperature was maintained at an average of 19.9°C (19.7 - 20.1°C) throughout the study. Water loss due to evaporation from the soil was determined by weighing the flasks without the traps on each processing day. Within the short study duration replenishment was not necessary. Determination of the soil microbial viability (microbial biomass) was performed at the start and at the end (day 21) of the study.

2. **Sampling of incubated soil:** Samples were taken for analysis at 0, 1, 2, 4, 7, 14 and 21 days of incubation. At each sampling interval two samples were analysed.

3. **Analytical procedures:** The soil samples were extracted four times with acetonitrile/water (80/20, v/v) at ambient temperature, and 1 time by hot extraction. The extracts were analysed by HPLC and TLC. The identity of the transformation products was achieved by comparison with authentic reference substances with both independent chromatographic systems (HPLC and TLC).

II. Results and Discussion

A. Extraction and quantitation of radioactivity in soil samples

Table 7.1.1- 2 summarises the total extraction of soil samples and the quantitation of identified compounds indicating the degradation of iprovalicarb as a function of time. Mean material balances accounted for 97.4% (94.8 – 103.2%), 96.0% (92.8 – 102.2%), 97.2% (93.3 - 101.0%), and 98.0% (94.9 -100.9%) of AR for soils [redacted] AXXa, [redacted] II, [redacted] [redacted], and [redacted] 4a, respectively. The amount of unchanged iprovalicarb at day 0 corresponded to 103.1, 101.9, 100.8, and 100.7% of AR and decreased to 7.4, 3.6, 8.7 and 4.2% of AR at the end of the study in soils [redacted] AXXa, [redacted] II, [redacted] [redacted], and [redacted] 4a, respectively. The half-life of iprovalicarb was calculated as 6.7, 5.1, 5.9 and 5.5 days under aerobic conditions in the tested soils [redacted] AXXa, [redacted] II, [redacted] [redacted] and [redacted] 4a, respectively.

High amounts of carbon dioxide were detected with 57.6, 56.4, 57.2 and 61.3% of AR at study end in the soils [redacted] AXXa, [redacted] II, [redacted] [redacted] and [redacted] 4a, respectively. SZX 0722-carboxylic acid *(M03)* was detected as sole metabolite in the course of the study in all four soils. It was detected as major metabolite only in soils [redacted] AXXa with a maximum value of 10.0% of AR at day 7 (sum of diastereomers), in [redacted] with a maximum value of 7.0% of AR at day 7 (sum of diastereomers) and in [redacted] 4a with a maximum value of 5.6% of AR at day 4 (sum of diastereomers). The amount declined below the limit of detection up to the end of the study (day 21).

Extractable ^{14}C-residues decreased from 103.1, 101.9, 100.8, and 100.7% of AR at day 0 to 7.5, 3.6, 8.7, and 4.2% at the study end (day 21) in soils [redacted] AXXa, [redacted] II, [redacted], and [redacted] 4a, respectively. Non-extractable ^{14}C-residues increased from 0.1 - 0.3% of AR at day 0 to 29.5 - 33.9% of AR at study end (day 21). A further characterisation (fractionation into humin, humic acids and fulvic acids) was shown for all four soils for the day 14 interval.

Volatile organic compounds were not detected (< 0.1% of the applied radioactivity at all sampling intervals).

Table 7.1.1- 2: Degradation product distribution (expressed as % of applied radioactivity) over 21 days aerobic incubation of treated soil
(results after analysis by HPLC, mean of two samples)

Soil	Compound	Days after application						
		0	1	2	4	7	14	21
[redacted]	Iprovalicarb	103.1	91.4	88.4	71.9	54.9	21.0	7.4
Hof	SZX 0722-carboxylic acid *(M03)*	n.d.	3.3	5.6	9.5	10.0	0.6	< LOD
AXXa	Unidentified radioactivity	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Total extracted radioactivity	103.1	94.6	94.0	81.4	64.9	21.6	7.5
	$^{14}CO_2$	n.a.	1.0	2.5	6.5	16.2	44.9	57.6
	Volatile organics	n.a.	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
	Non-extractable residues	0.1	1.6	3.3	6.9	14.6	28.6	30.8
	Total recovery	103.2	97.3	99.8	94.8	95.7	95.0	95.9
[redacted]	Iprovalicarb	101.9	89.3	80.2	64.7	39.3	13.1	3.6
II	SZX 0722-carboxylic acid *(M03)*	n.d.	3.2	4.3	4.5	2.6	n.d.	n.d.
	Unidentified radioactivity	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Total extracted radioactivity	101.9	92.5	84.5	69.2	41.9	13.1	3.6
	$^{14}CO_2$	n.a.	1.6	4.6	12.9	27.7	49.6	56.4
	Volatile organics	n.a.	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
	Non-extractable residues	0.3	3.3	6.5	12.9	23.2	32.4	33.9
	Total recovery	102.2	97.4	95.6	95.0	92.8	95.1	93.9
[redacted]	Iprovalicarb	100.8	91.3	84.8	69.2	46.6	13.8	8.7
Hof	SZX 0722-carboxylic acid *(M03)*	n.d.	2.3	3.5	5.6	7.0	0.3	n.d
[redacted]	Unidentified radioactivity	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	Total extracted radioactivity	100.8	93.6	88.3	74.7	53.7	14.1	8.7
	$^{14}CO_2$	n.a.	2.4	4.7	11.8	23.5	46.9	57.2
	Volatile organics	n.a.	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
	Non-extractable residues	0.2	2.4	4.5	11.0	19.7	32.2	30.0
	Total recovery	101.0	98.5	97.4	97.5	96.9	93.3	95.9
[redacted]	Iprovalicarb	100.7	91.1	83.1	66.0	44.4	13.0	4.2
	SZX 0722-carboxylic acid *(M03)*	n.d.	3.3	4.9	5.6	2.1	n.d.	n.d.
	Unidentified radioactivity	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
4a	Total extracted radioactivity	100.7	94.4	87.9	71.7	46.5	13.0	4.2
	$^{14}CO_2$	n.a.	2.0	4.8	13.5	31.5	54.3	61.3
	Volatile organics	n.a.	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
	Non-extractable residues	0.2	2.7	5.4	11.5	21.1	29.7	29.5
	Total recovery	100.9	99.0	98.1	96.6	99.1	97.1	94.9

n.d. not detected
n.a. not analysed
LOD (limit of detection) = 0.25% AR

B. Mass balance:

The total applied radioactivity at day 0 was taken as 100% for the calculation of material balances. The total radioactive material balance is shown in Table 7.1.1- 3. No time-dependent tendency was observed for the total recovery throughout all incubation periods of the study demonstrating that no significant radioactivity dissipated from the flasks or was lost during processing.

Table 7.1.1- 3: Material balance of radioactivity in soil samples (in percent of applied radioactivity)

	Soil			
	[redacted] AXXa	[redacted] II	[redacted]	[redacted] 4a
Minimum [%]	94.8	92.8	93.3	94.9
Maximum [%]	103.2	102.2	101.0	100.9
Mean [%]	97.4	96.0	97.2	98.0
Rel. standard deviation [%]	0.03	3.2	2.4	0.02

C. Bound and extractable residues:

The formation of bound residues increased with the overall metabolism of valine-labelled iprovalicarb. Non-extractable ^{14}C-residues increased from 0.1 - 0.3% of AR at day 0 to 29.5 - 33.9% of AR at the end of the study (Table 7.1.1- 4). Extractable ^{14}C-residues decreased from 100.7 - 103.1% of AR at day 0 to 3.6 – 8.7% of AR at the end of the study (Table 7.1.1- 4).

Table 7.1.1- 4: Bound and extractable residues in soil samples (in percent of applied radioactivity)

	Day	[redacted] AXXa	[redacted] II	[redacted]	[redacted] 4a
Bound residues [%]	0	0.1	0.3	0.2	0.2
	21	30.8	33.9	30.0	29.5
Extractable residue [%]	0	103.1	101.9	100.8	100.7
	21	7.5	3.6	8.7	4.2

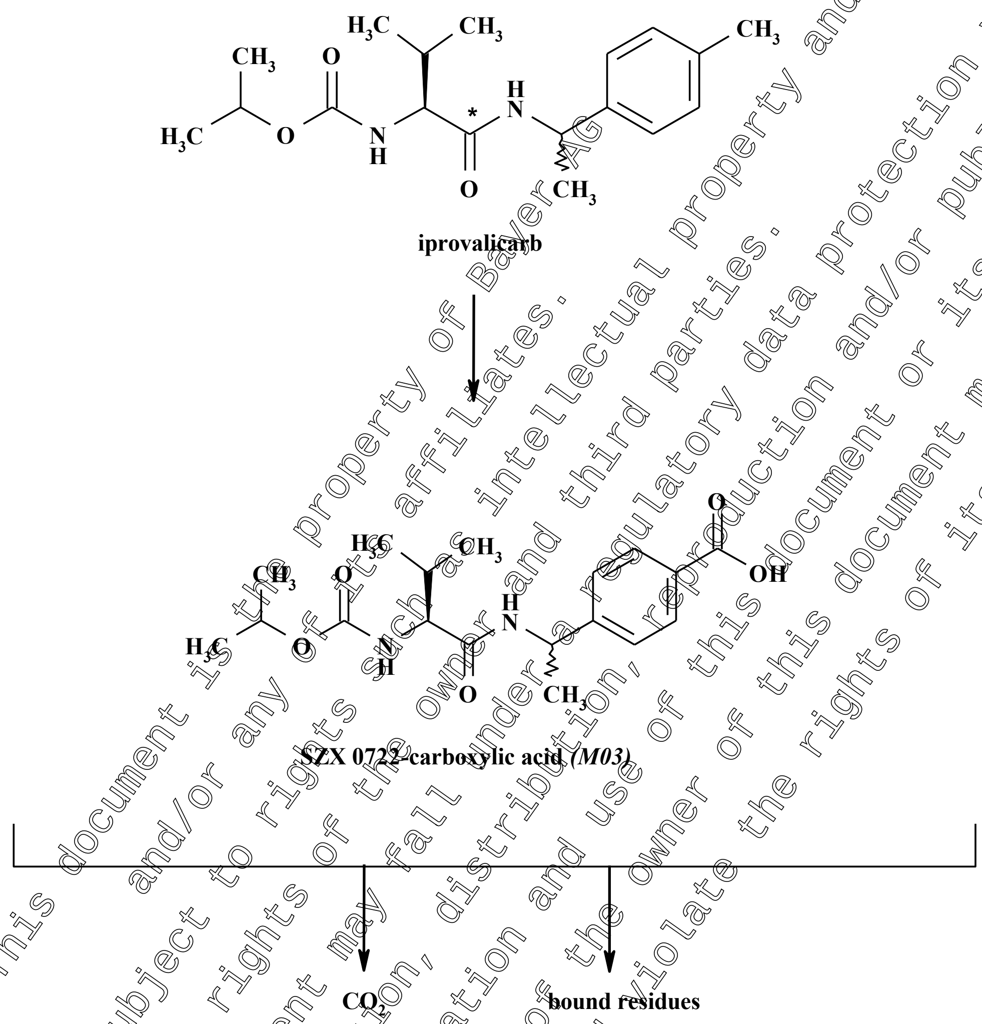
D. Volatilisation:

A high amount of valine-labelled iprovalicarb was mineralised to $^{14}CO_2$ under laboratory conditions within 21 days (56.4 - 61.3% AR at study end) (Table 7.1.1- 2). Volatile organic compounds were not detected (< 0.1% of the applied radioactivity at all sampling intervals) (Table 7.1.1- 2).

E. Transformation of parent compound:

The data gathered in the current investigation demonstrated that iprovalicarb was well degraded in a typical soil environment under standardised aerobic laboratory conditions. The main degradation product was CO_2. Besides a high amount of carbon dioxide SZX 0722-carboxylic acid *(M03)* was detected as sole metabolite in the course of the study in all four soils. This metabolite was formed by oxidation of the 4-methyl group of the parent compound under aerobic conditions (Figure 7.1.1- 1). No other metabolites were detected.

Figure 7.1.1- 1: Proposed metabolic pathway of valine-labelled iprovalicarb in soil under aerobic conditions



III. Conclusions

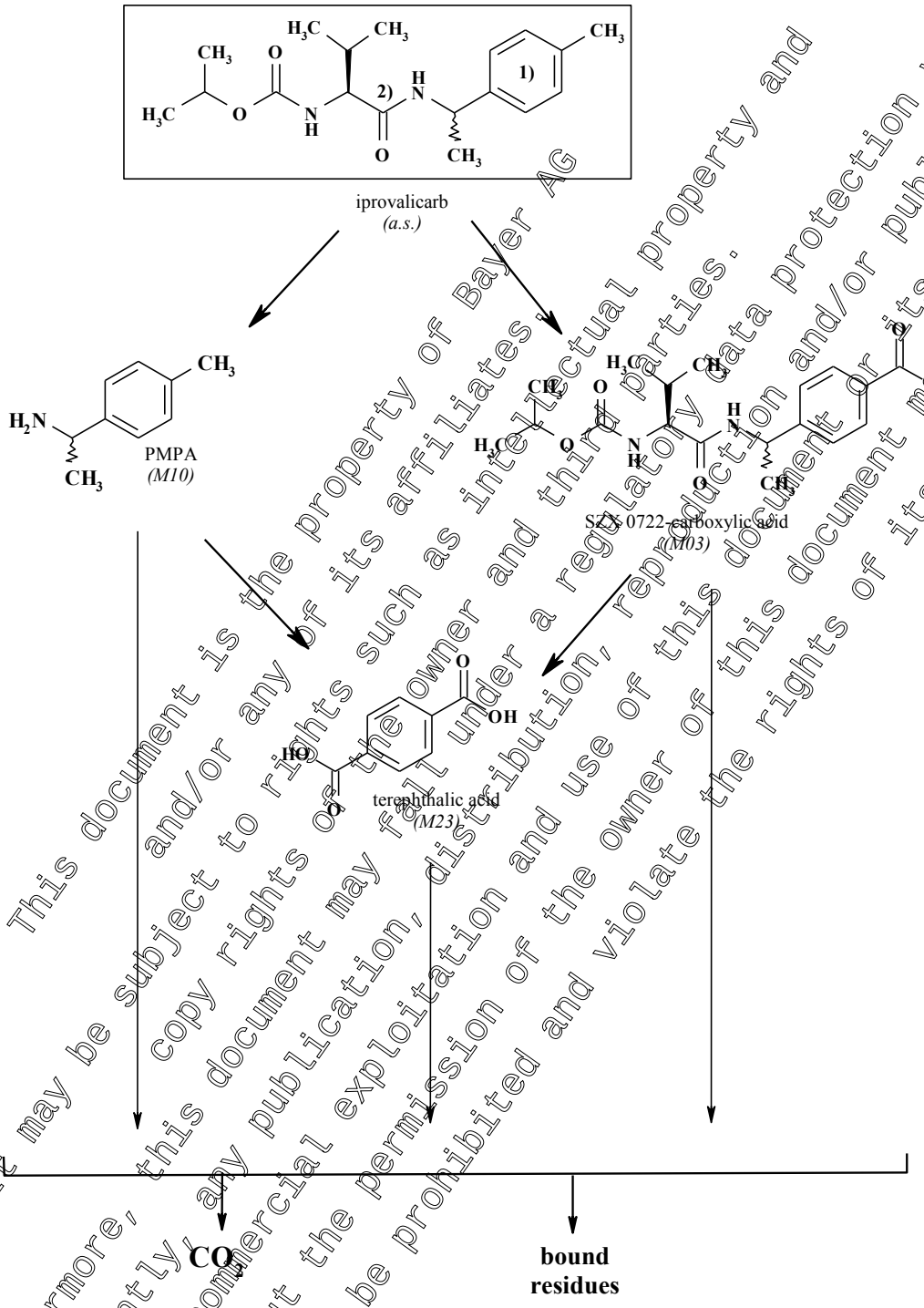
Valine-labelled iprovalicarb was well degradable in soil under aerobic conditions. The main degradation product was carbon dioxide (56.4 - 61.3% AR at study end). Besides carbon dioxide SZX 0722-carboxylic acid *(M03)* was detected as sole metabolite in the course of the study in all four soils. It was detected as major metabolite only in soils [redacted] AXXa with a maximum value of 10.0% of AR at day 7 (sum of diastereomers), in [redacted] with a maximum value of 7.0% of AR at day 7 (sum of diastereomers) and in [redacted] 4a with a maximum value of 5.6% of AR at day 4 (sum of diastereomers). The amount declined below the limit of detection up to the end of the study (day 21). Bound residues increased to 29.5 - 33.9% of AR at study end (day 21). The formation of significant amounts of CO_2 and bound residues indicates complete mineralisation of iprovalicarb and incorporation into the natural carbon cycle of soil. There is no potential for persistence and accumulation in aerobic soil.

The results received were in good agreement with the proposed aerobic soil degradation pathway of iprovalicarb known from studies using the phenyl-label. No new metabolite specific for the valine-label was found.

Summary: Route of degradation in soil under aerobic conditions - laboratory studies

The metabolism of iprovalicarb in soil under aerobic conditions has been studied using the phenyl- and the valine-labelled parent substance. The investigations were performed in the dark, in a number of soils at temperatures of 20°C and with one soil at a temperature of 10°C.
Under aerobic conditions in the dark iprovalicarb degraded to the final degradation product carbon dioxide. In parallel to mineralisation, bound residues were formed. Three metabolites were identified in the soil along with the parent compound and $^{14}CO_2$. The major metabolites (> 10% of the applied radioactivity) were SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)*, which were both degradable under aerobic conditions. 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.
The proposed metabolic pathway of iprovalicarb in soil under aerobic conditions is given in Figure 7.1.1- 2.

Figure 7.1.1- 2: Proposed metabolic pathway of iprovalicarb in soil under aerobic conditions



KIIA 7.1.2 Anaerobic degradation

Due to the proposed use patterns of iprovalicarb as a fungicide applied to vine, an anaerobic soil degradation study was not considered to be required. Therefore, no studies on the route and rate of degradation of iprovalicarb in soil under anaerobic conditions were submitted within the EU Basic Dossier in 1998. [redacted]ver, an anaerobic soil metabolism and degradation study of iprovalicarb was performed in 2011 and submitted in this Dossier ([redacted] (2011, rev. 2012), KIIA 7.1.2 /01).

New study submitted for Annex I renewal

Justification for including this study in the Annex I Renewal Dossier: This study was conducted to cover metabolism and degradation of iprovalicarb in soil under anaerobic conditions.

Report:	**KIIA 7.1.2 /01, [redacted].; 2011, revised 2012**
Title:	[Phenyl-UL ^{14}C]iprovalicarb: Anaerobic soil metabolism
Report No:	MESZL004-1
Document No:	M-399285-02-1
Guidelines:	- OECD Guideline for Testing of Chemicals, No. 307, Aerobic and Anaerobic Transformation in Soil, 2002 - Regulation (EC) No.1107/2009 of the European Parliament and of the council of 21 October 2009 - US EPA Fate, Transport and Transformation Test Guidelines, OPPTS 835.4100 and OPPTS 835.4200, Aerobic and Anaerobic Soil Metabolism, 2008
GLP:	Yes

Executive Summary

The anaerobic biotransformation of phenyl-labelled iprovalicarb was studied in a silt soil ([redacted]; organic carbon (OC) 2.2%, pH 6.5, [redacted]; Germany). During the first phase of the study, the soil was maintained under aerobic conditions for three days in the dark at 20 ± 1°C and at soil moisture of 55% maximum water holding capacity (62.2%). Following the aerobic phase, the samples were flooded with water (water:soil ratio 3:1, w/w) and maintained in the dark under anaerobic conditions for 122 days at 20 ± 1°C. Details of the soil properties are given in Table 7.1.2- 1. Iprovalicarb was applied at a rate of 1.43 µg a.s./g, equivalent to 500 g a.s./ha. The test system consisted of 250-mL Erlenmeyer flasks attached with a trap for the collection of CO_2 and volatile organic compounds during the aerobic phase. Samples were analysed at 0, 2 and 3 days of aerobic incubation, and at 0, 3, 10, 18, 25, 32, 59, 87 and 122 days of incubation following flooding of the samples (anaerobic phase).

In the following those parts of the study are summarised which were performed to elucidate the route of degradation in soil. Parts concerning evaluation of rate of degradation are reported in section KIIA 7.2.4 (study KIIA 7.2.4 /01) of this document.

The soil extracts were analysed by HPLC. Identification of the parent compound and major degradates was achieved by mass spectrometry (LC/ESI/MS) and co-chromatography using an authentic standard.

The average total material balance in the soil/water system for iprovalicarb was 100.4% ± 2.1% of the applied radioactivity (AR). In the aerobic phase, extractable [^{14}C] residues in soil decreased from

99.8% at day 0 to 82.3% by day 3. Non-extractable (bound) residues in soil increased from 0.2% at day 0 to 12.4% at day 3. At the end of the aerobic phase, 3.0% or less of the applied radioactivity was present as CO_2. No volatile organic compounds were present. The concentration of iprovalicarb in the aerobic phase decreased from 99.4% of the applied amount at day 0 to 70.1% at day 3. Soil was flooded at this point to ensure the presence of parent during the anaerobic phase. The concentration of PMPA *(M10)* increased from 5.2% at day 2 to 6.5% at day 3 of the aerobic phase. In the anaerobic phase, radioactivity in the combined water and ambient extract decreased from 81.8% at day 0 to 47.9% by the end of the study. Ag[redacted]sively extractable [^{14}C]residues ranged from 5.8% to 8.4% of the applied radioactivity in the study. Non-extractable residues in soil increased from 12.3% at day 0 to 39.8% of the applied amount at day 122. Additionally CO_2 and volatile organic compounds were produced at low levels throughout the anaerobic phase of the study (≤ 4.1%). Non-extractable residues were further characterized on a sample from day 122 which had 41.7% non-extractable residues (NER). Through fractionation into the fulvic acid, humic acid and humin components, 13.6, 26.6, and 59.8% of this NER were found to be associated with these fractions, respectively. During the anaerobic phase, the concentration of iprovalicarb in soil decreased from 75.7% at day 0 to 5.7% of the applied amount at study termination. The two major metabolites detected during the anaerobic phase of the study were PMPA *(M10)* and N-acetyl-PMPA *(M15)*. The concentration of PMPA increased from 9.5% at day 0 to a maximum of 27.9% at day 25 and decreased to 13.4% at day 122. N-acetyl-PMPA increased from 2.4% at day 3 to 29.1% at day 122. One minor metabolite was formed with a maximum of 4.1% at day 122 and was identified as SZX 0722-aminoacetonitrile *(M30)*.

I. Material and Methods

A. Materials

1. Test Material: [phenyl-UL-^{14}C]iprovalicarb
CAS #: 140923-17-7
specific radioactivity: 44.3 mCi/mMole (corresponding to 5.1 MBq/mg)
radiochemical purity: > 98%

2. Soil: The soil (Table 7.1.2- 1) was transported from Germany to [redacted], KS, by air cargo at ambient temperature. The time from collection to receipt was 8 days. The soil was sieved through a 2-mm sieve at the collection facility. Prior to treatment with the test substance, the soil was maintained in a biologically active state at an average temperature of 4°C at the testing facility for 11 days. Three days before the pre-equilibration the soil was brought to room temperature. The soil moisture was determined at Bayer CropScience, [redacted], KS, before use, and the soil was then weighed on a dry-weight basis for individual test systems. An acclimation period of 5 days at a temperature of 20°C (25.9% moisture) was carried out before treatment. HPLC grade water was deoxygenated by bubbling with nitrogen for approximately 20 minutes prior to flooding test systems.

Table 7.1.2- 1: Soil characteristic

Parameter	[redacted]
Geographic location - city - state - country	 [redacted] NRW[a)] Germany
Soil mapping unit (GPS coordinates)	[redacted]
Texture class (USDA) - sand (50 µm – 2 mm) [%] - silt (2 µm – 50 µm) [%] - clay (< 2 µm) [%]	silt loam 27 57 16
pH - in $CaCl_2$ (soil/$CaCl_2$ 1/2) - in water (soil/water 1/1)	 6.5 6.8
Organic matter [%]	3.8
Organic carbon[a)] [%]	2.2
Soil biomass [mg microbial carbon/kg dry soil] - initial (day 0 aerobic) - flooding day (day 0 anaerobic) - untreated control soil [mg microbial C/kg soil] - solvent-treated control soil [mg microbial C/kg soil] - study end (anaerobic) - untreated control soil [cells/g] - solvent-treated control soil [cells/g] - untreated control water [cells/mL] - solvent-treated control water [cells/mL]	 829 759 814 3.43×10^8 1.26×10^8 9.19×10^6 1.29×10^7
CEC [meq/100 g]	12.8
MWHC [g/100 g dry soil]	62.2
Bulk density [g/cm³]	1.13

a) % organic carbon = % organic matter / 1.724
CEC cation exchange capacity
MWHC maximum water holding capacity
NRW North Rhine-Westphalia

B. Study design

1. Experimental conditions: The test system consisted of 250-mL Erlenmeyer flasks with either a soda-lime trap or an adapter with side arms for attachment to traps for the collection of CO_2 and volatile organic compounds. The target application rate was 1.33 µg iprovalicarb/g. This concentration corresponds to a field rate of 500 g iprovalicarb/ha (soil depth of 2.5 cm, soil density of 1.5 g/cm^3). The maximum water-holding capacity of the soil was 62.2%. The moisture content was adjusted to 55% of the maximum water holding capacity (34.2%) using HPLC grade water. No further adjustments of the water were necessary.

During the aerobic phase, test systems were kept in an environmental chamber at 20 ± 1°C. During the anaerobic (flooded) phase, they were kept in a temperature-controlled incubator with a nitrogen-filled atmosphere at 20 ± 1°C. During incubations, aluminium foil was wrapped around flasks to prevent exposure to light. The microbial biomass was determined on control samples from day 0 treatment, control samples from the day of flooding (day 0 of anaerobic phase) and day 122 (post-flooding).

2. **Sampling of soil, water and volatiles:** Duplicate test systems at day 0 and a single test system at day 2 and 3 were analysed under aerobic conditions. After the 3 day aerobic incubation, duplicate anaerobic test systems were analysed at 0, 3, 10, 18, 25, 32, 59, 87 and 122 days post-flooding intervals. During the anaerobic phase of the study, both test systems were measured for pH, redox potential, and dissolved oxygen. Radioactive CO_2 and volatile organics were measured at each interval. During the anaerobic phase, the test systems were measured for pH, redox potential, and dissolved oxygen at each interval. The water was separated from the soil by decanting.

3. **Analytical procedures:** The water was decanted from each test system and the soil was extracted by a shaking method using acetonitrile/water (70:30, v/v) (ambient extract), and an ag[redacted]sive extraction using microwave with acetonitrile/water (70:30, v/v) at 70°C. The water and ambient extract were combined from each test system. The residues of ^{14}C-iprovalicarb from the combined extract and the microwave extract were analysed by HPLC using a flow-through ^{14}C-detector. Identification of the parent compound and major degradates was achieved by mass spectrometry (LC/ESI/MS) and co-chromatography using an authentic standard.

II. Results and Discussion

A. Extraction and quantitation of radioactivity in soil samples

Table 7.1.2- 2 summarises the total extraction of soil samples and the quantitation of identified compounds. The average material balance for the study was 100.4% (97.7% - 103.6%) of AR.
In the aerobic phase, extractable ^{14}C-residues in soil decreased from 99.8% at day 0 to 82.3% by day 3. Non-extractable (bound) residues in the soil increased from 0.2% at day 0 to 12.4% at day 3. At the end of the aerobic phase, 3.0% of the applied radioactivity was present as CO_2, and no organic volatile compounds were formed.
In the anaerobic phase, ^{14}C-residues in water and extracts combined decreased from 87.7% at day 0 to 54.9% at day 122. Non-extractable residues in soil increased from 12.3% at day 0 to 39.8% at day 122. At the end of the anaerobic phase, 3.9% and 0.1% of the applied radioactivity was present as CO_2 and organic volatile compounds, respectively.
During the aerobic phase, the concentration of iprovalicarb in the soil decreased from 99.4% at day 0 to 70.1% of the applied amount at day 3. The major metabolite PMPA *(M10)* increased from 0% at day 0 to 6.5% at day 3 of the aerobic phase.
During the anaerobic phase, the concentration of iprovalicarb in the water and extracts decreased from 75.7% at day 0 to 5.7% at day 122. Two major transformation products were detected during the anaerobic phase of the study. They are PMPA *(M10)* and N-acetyl-PMPA *(M15)*. PMPA increased from 9.5% at day 0 to 27.9% on day 25 and decreased to 13.4% by the end of the study. The other major metabolite N-acetyl-PMPA increased to 29.1% by the end of the study. The minor metabolite identified as SZX 0722-aminoacetonitrile *(M30)* was first observed on day 87 and reached a maximum of 4.1% on day 122.

Table 7.1.2- 2: Biotransformation of phenyl-labelled iprovalicarb in silt loam under anaerobic conditions (expressed as percentage of applied radioactivity)

Compound	Sampling time											
	aerobic phase			anaerobic phase								
	-3	-1	0	0	3	10	18	25	32	59	87	122
Iprovalicarb	99.4	80.0	70.1	75.7	58.3	47.7	50.2	33.0	33.6	18.7	9.4	5.7
PMPA *(M10)*	0.0	5.2	6.5	9.5	15.0	18.0	13.0	27.9	27.9	23.5	24.3	13.4
N-acetyl-PMPA *(M15)*	0.0	0.0	2.0	0.0	2.4	5.4	10.1	10.6	13.6	21.6	23.0	29.1
SZX 0722-aminoacetonitrile *(M30)*	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	4.1
Unidentified radioactivity	0.4	5.5	3.6	2.5	2.7	5.2	3.2	2.1	0.0	3.3	2.4	2.6
Total extracted radioactivity	99.8	90.7	82.3	87.7	78.4	76.2	76.5	73.6	75.1	67.1	60.2	54.9
$^{14}CO_2$	0.0	1.1	3.0	3.6	3.5	3.6	3.9	3.6	3.4	3.2	3.6	3.9
Volatile organics	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.1	0.2	0.2	0.2	0.1
Non-extractable residues	0.2	6.6	12.4	12.3	16.9	19.2	22.2	24.7	24.9	31.4	34.7	39.8
Total recovery	100.0	98.4	97.7	103.6	98.8	99.2	102.8	102.0	103.6	101.9	98.8	98.7

B. Mass balance:

The material balance was based on the average amount of radioactivity recovered from two replicates of the aerobic day 0 sampling interval. The total radioactive material balance is show in Table 7.1.2- 3. No time-dependent tendency was observed for the total recovery throughout all incubation periods of the study demonstrating that no significant radioactivity dissipated from the flasks or was lost during processing.

Table 7.1.2- 3: Material balance of radioactivity in soil samples (in percent of applied radioactivity)

	Soil [redacted] 4a
Minimum [%]	97.7
Maximum [%]	103.6
Mean [%]	100.4
Rel. standard deviation [%]	2.1

C. Bound and extractable residues:

In the aerobic phase the formation of bound residues increased from 0.2% at day 0 to 12.4% at day 3. Extractable residues decreased from 99.8% at day 0 to 82.3% by day 3. In the anaerobic phase the non-extractable residues in soil increased from 12.3% at day 0 to 39.8% at day 122. Extractable residues decreased from 87.7% at day 0 to 54.9% at day 122 (Table 7.1.2- 4).

Table 7.1.2- 4: Bound and extractable residues in soil samples (in percent of applied radioactivity)

	Sampling date Phase	Day	Soil [redacted]
Bound residues [%]	aerobic phase	0	0.2
		3	12.4
	anaerobic phase	0	12.3
		122	39.8
Extractable residues [%]	aerobic phase	0	99.8
		3	82.3
	anaerobic phase	0	87.7
		122	54.9

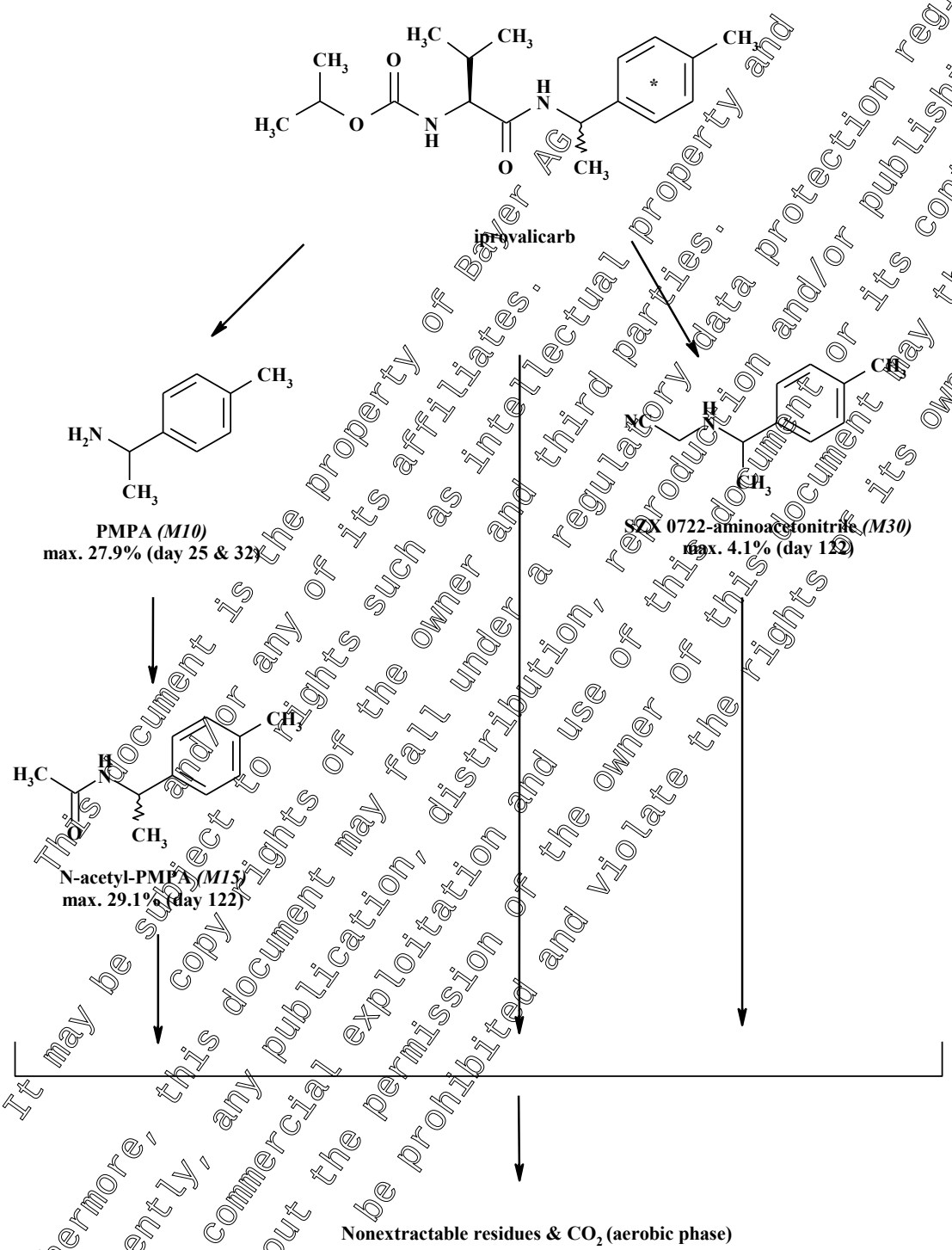
D. Volatilisation:

At the end of the aerobic phase, 3.0% of the applied radioactivity was present as CO2, and no organic volatile compounds were formed. At the end of the anaerobic phase, 3.9% and 0.1% of the applied radioactivity was present as CO2 and organic volatile compounds, respectively.

E. Transformation of the parent compound:

Iprovalicarb degraded to two major degradates. One major degradate, PMPA *(M19)*, was formed under aerobic conditions and increased under anaerobic conditions. The other major degradate N-acetyl-PMPA *(M15)* was formed during the anaerobic phase. A minor degradate, SZX 0722-aminoacetonitrile *(M30)*, was formed later in the study under anaerobic conditions and reached a maximum of 4.1% at day 122. Unextractable residues reached 39.8% by the end of the study. A proposed metabolic pathway is shown in Figure 7.1.2- 1.

Figure 7.1.2- 1: Proposed metabolic pathway of phenyl-labelled iprovalicarb in soil under anaerobic conditions



III. Conclusions

Iprovalicarb was degraded appreciably under anaerobic conditions in soil and would not be expected to persist in this type of environment. During the aerobic phase, PMPA *(M10)* was formed and increased after flooding to a max of 27.9% at 25 and 32 days. At the end of the study, PMPA reached

13.4% of the applied radioactivity. During the anaerobic phase, N-acetyl-PMPA *(M15)* was formed, reaching a maximum of 29.1% at day 122. A minor degradate, which occurred at the last two intervals (day 87 and day 122), with a maximum of 4.1% of the applied radioactivity, was identified as SZX 0722-aminoacetonitrile *(M30)*.

KIIA 7.1.3 Soil photolysis

The photodegradation of iprovalicarb in soil was evaluated during the Annex I inclusion. No additional studies have been performed for the parent compound. A short summary of the data is given below.

The photodegradation of iprovalicarb was studied under artificial light conditions considered equivalent to midday midsummer sunlight at 40° latitude ([redacted], 1997; submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.1.2 /01 & IIA, 7.1.1.2.1 /03) and accepted by the European Commission (SANCO/2034/2000-final, 2 July 2002)).

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% AR following the irradiation period. The breakdown of iprovalicarb proceeded via 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 DT_{50} values in the irradiated and dark samples were 62 and 53 days, respectively. It is evident that photodegradation on soil surface will not significantly contribute to the degradation of the parent compound.

KIIA 7.2 Rate of degradation in soil(s) – laboratory studies

KIIA 7.2.1 Aerobic degradation of the active substance in soils at 20°C

The route and rate of iprovalicarb in soil under aerobic conditions was evaluated during the Annex I Inclusion using the phenyl-labelled parent compound ([redacted], 1997, [redacted] 1997a and 1997b (submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.2.1 /01, IIA, 7.1.1.2.1 /02 and IIA, 7.1.1.2.1 /04, respectively) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)). In addition a new soil metabolism study was performed using the valine radiolabel of iprovalicarb to complete the data according to current requirement practice ([redacted] (2011), submitted in this Dossier, KIIA 7.2.1 /05).
Furthermore, a kinetic evaluation of all available studies was conducted according to FOCUS kinetics (FOCUS, 2006) to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments ([redacted] (2012), submitted in this Dossier, KIIA 7.2.1 /06, KIIA 7.2.3 /02). For a better overview of these evaluated laboratory soil degradation data of a short summary is given at the end of this chapter at page 33.

New study, not submitted for first Annex I inclusion
Justification for including this new study in the Annex I Renewal Dossier: The new soil metabolism and degradation study was conducted with the valine radiolabel to complement the former dossier according to current requirement practices. With the first dossier only studies with the phenyl radiolabel were provided.

Report:	**KIIA 7.2.1 /05, [redacted] 2011**
Title:	[Valine-1-^{14}C]iprovalicarb: Aerobic metabolism/degradation in four European soils
Report No:	MEF-10/660
Document No	M-414387-01-1
Guidelines:	- OECD Guideline for Testing of Chemicals, No. 307, Aerobic and Anaerobic Transformation in Soil, 2002 - US EPA Fate, Transport and Transformation Test Guidelines, OPPTS 835.4100 and OPPTS 835.4200, Aerobic and Anaerobic Soil Metabolism, 2008 - Commission Directive 95/36/EC amending Council Directive 91/414/EEC (Annexes II and III, Fate and Behaviour in the Environment), 1995 - Regulation (EC) No.1107/2009 of the European Parliament and of the council of 21 October 2009
GLP:	Yes

Executive Summary

The degradation data as reported in study KIIA 7.1.1 /04 were kinetically evaluated according to FOCUS (2006)[1] as part of the study to derive best fits for trigger endpoint determination. The calculated half-lives of iprovalicarb were 6.7, 5.1, 5.9 and 5.5 days under aerobic conditions in the tested soils [redacted] AXXa, [redacted] II, [redacted] [redacted] and [redacted] 4a, respectively. The results are summarised in Table 7.2.1- 1.

[1] FOCUS, 2006: Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration
Report of the FOCUS Work Group on Degradation Kinetics, EC Doc. Ref. SANCO/10058/2005, version 2.0, 2006

Table 7.2.1- 1: Calculated DT_{50} and DT_{90} values for valine-labelled iprovalicarb

Soil	Best fit kinetic model	DT_{50} [days]	DT_{90} [days]	Chi² error [%]	Visual assessment[a]
[redacted] AXXa	SFO[b]	6.7	22.2	4.3	+
[redacted] II	SFO[b]	5.1	17.0	3.3	+
[redacted]	SFO[b]	5.9	19.6	4.4	+
[redacted] 4a	SFO[b]	5.5	18.2	4.1	+

a) visual assessment: + good o medium - bad
SFO single first order

I. Material and Methods

Details on the study conduct and its results are summarised under KIIA 7.1.1 /04. The degradation rate and the DT_{50} of iprovalicarb and its single diastereomers were calculated with three different kinetic models: single first order (SFO), first order multi compartment (FOMC), and double first order in parallel (DFOP) according to FOCUS (2006) and using the software KinGUI v1.1. The most suitable kinetic model was chosen based on the chi² criterion and visual inspection of the model fit. Model input datasets were the residual amounts found in each replicate test system at each sampling interval. At day 0, the initial total recovery was included in the parameter optimisation procedure, but for optimal goodness of fit, the day 0 value was allowed to be estimated by the model.
The best-fit kinetic model was selected on the basis of the chi² scaled-error criterion and on the basis of a visual assessment of the goodness of the fits (diagrams of measured and calculated values vs. time, diagrams of residuals vs. time).

II. Results and Discussion

The data for iprovalicarb were evaluated according to FOCUS (2006). For calculation of DT_{50} values that trigger additional studies, the best available model should be used. The best fit kinetic model was chosen based on the chi² confidence criterion and visual assessment. The results are summarised in Table 7.2.1- 2. The degradation of iprovalicarb followed SFO kinetics according to the best-fit chi² criterion. In all cases, the chi² error values of the fits were 4.4 or lower, and in all cases the visual assessment of the re[redacted]sion curves gave good results. The half-live of iprovalicarb accounts for 6.7, 5.1, 5.9 and 5.5 days under aerobic conditions in the tested soils [redacted] AXXa, [redacted] II, [redacted] and [redacted] 4a, respectively.
Furthermore the degradation kinetics of the single diastereomers of iprovalicarb were evaluated separately. The degradation of the iprovalicarb diastereomers also followed SFO kinetics according the best-fit chi² criterion (chi² values 5.1 or lower). The half-lives of the SR- and SS-diastereomers are very similar with 7.3 and 5.7 days for soil [redacted] AXXA, 5.4 and 4.4 days for soil [redacted] II, 6.4 and 5.2 days for soil [redacted] and 6.0 and 4.9 days for soil [redacted] 4a. Therefore, the DT_{50} values of the sum of the diastereomers are used for risk assessment purposes.

Table 7.2.1- 2: Calculated DT_{50} and DT_{90} values for valine-labelled iprovalicarb

Soil	Kinetic model	DT_{50} [days]	DT_{90} [days]	Chi² error [%]	Visual assessment[a]
[redacted] AXXa	**SFO**	**6.7**	**22.2**	**4.3**	+
	FOMC	6.7	22.4	4.8	+
	DFOP	6.7	22.2	5.1	+
[redacted] II	**SFO**	**5.1**	**17.0**	**3.3**	+
	FOMC	5.1	17.2	3.7	+
	DFOP	5.1	17.0	3.9	+
[redacted]	**SFO**	**5.9**	**19.6**	**4.4**	+
	FOMC	5.9	19.8	4.8	+
	DFOP	5.9	19.6	5.2	+
[redacted] 4a	**SFO**	**5.5**	**18.2**	**4.1**	+
	FOMC	5.5	18.3	4.5	+
	DFOP	5.5	18.2	4.8	+

a) visual assessment: + good o medium - bad

SFO single first order
FOMC first order multiple compartment
DFOP double first order in parallel

III. Conclusion

The data gathered in the current investigation demonstrated that iprovalicarb was well degraded in a typical soil environment under standardised aerobic laboratory conditions with DT_{50} values between 5.1 and 6.7 days.

New kinetic evaluation submitted for Annex I renewal

Justification for including this study in the Annex I Renewal Dossier: The objective of this study is a kinetic evaluation of the degradation behaviour of iprovalicarb in agricultural soils under standard laboratory conditions. The modelling analysis is based on residue data from three standard aerobic laboratory studies (20°C) with two different radio-labels and one aerobic study at 10°C. The evaluation was conducted according to FOCUS kinetics (FOCUS, 2006) to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments. The kinetic parameters which lead to the best fit between measured and calculated values (as defined by FOCUS (2006) for trigger and modelling evaluations) were identified based on a mathematical optimisation algorithm and a statistical analysis.

Report:	**KIIA 7.2.1 /06, [redacted] 2012**
Title:	Kinetic evaluation of aerobic laboratory soil degradation studies after application of iprovalicarb according to FOCUS using KinGui 2 Iprovalicarb (SZX 0722) p-Methylphenethylamine (PMPA, M10) SZX 0722-carboxylic acid (M03)
Report No:	MEF-11/629
Document No:	M-428977-01-1
Guidelines:	FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference SANCO/10058/2005, v.2.0, June 2006
GLP:	No (calculation)

Executive Summary

The soil degradation of iprovalicarb has been investigated in four aerobic laboratory degradation studies, applying the parent substance on nine soils with two different radioactive labels at 10°C or 20°C and 40 - 55% of maximum water holding capacity. The evaluation was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments according to FOCUS kinetics (FOCUS, 2006).

A kinetic modelling analysis of residue data of iprovalicarb and the metabolites SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)* was conducted using the software tool KinGUI 2 (successor of KinGUI 1.1), in order to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments.

In the following those parts of the evaluation which are related to the parent compound iprovalicarb are summarised. The parts concerning the major metabolites SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)* are reported in section KIIA 7.2.3 (KIIA 7.2.3 /02) of this document.

In general, a good overall model fit was reached with the proposed metabolic pathway. The selection of the kinetic model was based on a detailed statistical analysis including visual assessment, chi^2 statistic, significance t-test and correlation analysis. For the active substance iprovalicarb, the best description could be given using a SFO fit for 7 out of 9 soils, while in one soil a FOMC fit and in one soil a DFOP fit was more appropriate. The not-normalised as well as temperature and moisture normalised $DegT_{50}$ values for modelling purpose (= $DT_{50\ mod}$) are summarised in Table 7.2.1- 3. The results for persistence trigger evaluation (not normalised) are listed in Table 7.2.1- 4.

Table 7.2.1- 3: Laboratory soil DegT$_{50}$ of iprovalicarb for modelling purpose (non-normalised & normalised to 20°C, 100% field capacity, Q10: 2.58)

Temp. [°C]	Soil	Texture	Kinetic model	f_{corr} (moisture+ temp. f. DT_{50})	$DT_{50\ mod}$ [days] non-normalised	normalised
20	[redacted] AXXa, GER	sandy loam	SFO	1	6.595	6.59
	[redacted] II. GER	loam	SFO	1	5.045	5.05
	[redacted], GER	sandy loam	SFO	1	5.831	5.83
	[redacted], GER	silt loam	SFO	1	5.379	5.38
	[redacted], GER	loamy sand	DFOP	1	68.56	68.56
	[redacted], GER	sandy loam	SFO	0.8075	6.011	4.85
	[redacted], GER	silt loam	SFO	0.8896	1.992	1.77
	[redacted], USA	sandy loam	FOMC	0.7708	13.45	10.37
10	[redacted], GER	sandy loam	SFO	0.3129	15.07	4.72
geometric mean						*6.78*

$DT_{50\ mod}$ half-lives for modelling: FOMC: $DT_{50,\ recalc}$ recalculated from $DT_{90,\ FOMC}$;
DFOP: $DT_{50,\ recalc}$ of slow phase

Table 7.2.1- 4: Laboratory soil DT$_{50\ initial}$ of iprovalicarb for trigger evaluation

Temp. [°C]	Soil	Texture	Kinetic model	$DT_{50\ initial}$ [days] non normalised	$DT_{90\ initial}$ [days]
20	[redacted] AXXa, GER	sandy loam	SFO	6.595	21.91
	[redacted] II. GER	loam	SFO	5.045	16.76
	[redacted], GER	sandy loam	SFO	5.831	19.37
	[redacted], GER	silt loam	SFO	5.379	17.87
	[redacted], GER	loamy sand	FOMC	18.00	252.12
	[redacted], GER	sandy loam	DFOP	5.995	26.56
	[redacted], GER	silt loam	SFO	1.992	6.62
	[redacted], USA	sandy loam	DFOP	8.864	45.06
10	[redacted], GER	sandy loam	SFO	15.07	50.07

I. Material and Methods

The soil degradation of iprovalicarb has been investigated in four aerobic laboratory degradation studies, applying the parent compound on nine soils with two different radioactive labels at 10 or 20°C and 40 - 55% of maximum water holding capacity. ([redacted], 1997, [redacted] 1997a and 1997b (submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.2.1 /01, IIA, 7.1.1.2.1 /02 and IIA, 7.1.1.2.1 /04, respectively) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)) and [redacted], 2011 (submitted in this Dossier, KIIA 7.2.1 /05). The evaluation was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments according to FOCUS kinetics (FOCUS, 2006).

A kinetic modelling analysis of residue data of iprovalicarb and the metabolites SZX 0722-

carboxylic acid *(M03)* and PMPA *(M10)* was conducted using the software tool KinGUI 2 (successor of KinGUI 1.1). In this evaluation, the initial soil concentration was free fitted together with all degradation rates and formation fractions, based on the IRLS error model (Iteratively reweighted least square).
The kinetic models used in this evaluation are: single first order (SFO), first order multiple compartment (FOMC), double first order in parallel (DFOP) and Hockey-stick (HS, DFOS).

II. Results and Discussion

The kinetic evaluation was started by assuming a single first-order (SFO) degradation for iprovalicarb in soil. The fitted values for the degradation rate k, the initial total soil concentration at day 0 $C_{t\,0}$ and some statistical parameters are summarised in Table 7.2.1- 5.
In most soils, 7 out of 9, the degradation of iprovalicarb for modelling purpose according FOCUS kinetics is well described assuming single first-order decay. The statistically assessment shows good results with relative errors ε of the chi² test far below < 15%. All parameters are significantly different from 0, based on a single-sided t-test. Also, the visual inspection of the fit shows a good acceptability.
Two exceptions with a low to moderate visual acceptability of the SFO-fit were obtained for soils [redacted] and [redacted]. Therefore, for both trials biphasic models were considered in addition.
For soil [redacted] due to residues > 10% of initial amount at study end, the DFOP model is considered to be most appropriate for modelling purpose. A significant decrease of the chi² value and the visual acceptability could be reached, compared to the SFO fit.
For soil [redacted], due to residues < 10% of initial amount at study end, the FOMC model is considered to be most appropriate for modelling purpose. A significant decrease of the chi² value and the visual acceptability could be reached, compared to the SFO fit.
The $DT_{50\,mod}$ values below are reported for <u>modelling purposes</u>. Therefore, where needed, recalculated SFO $DT_{50\,mod}$ are mentioned as follows: for FOMC, $DT_{50\,recalc}$ recalculated from $DT_{90,\,FOMC}$ by a factor of 3.32; for DFOP, $DT_{50\,2nd\,phase}$ of slow phase. The $DT_{50\,initial}$ values below are the initial half-lives for <u>trigger evaluation</u>. The $DT_{50\,mod}$ and $DT_{50\,initial}$ values based on the kinetic models SFO, FOMC and DFOP are summarised in Table 7.2.1- 5. A summary of the laboratory soil DT_{50} values (non-normalised and normalised) of iprovalicarb for modelling purposes in comparison to the DT_{50} and DT_{90} values for trigger evaluation (non-normalised) is given in Table 7.2.1- 6.

Table 7.2.1- 5: Results of SFO and bi-phasic fits of laboratory soil degradation trials of iprovalicarb for modelling or trigger evaluation, not normalised, fit with metabolites (results for most appropriate kinetic model marked in bold)

Kinetic model	$C_{t\,0}$ [%]	k_{fast} [1/d]	k_{slow} [1/d]	t-test, k_{slow}	t_b [days]	g_{fast}	$DT_{50\ mod}$ [days]	$DT_{50\ initial}$ [days]	χ^2-test error [%]	visual fit[a]
[redacted] **AXXa**										
SFO [m, p]	105.34		0.1051	< 0.001			**6.595**	**6.595**	4.561	+
FOMC	105.5			0.479			6.543	6.538	4.758	+
DFOP	105.3	0.1051	~0.03664	0.5		1	6.595	6.595	4.918	+
[redacted] **II**										
SFO[m, p]	104.0		0.1374	< 0.001			**5.045**	**5.045**	3.487	+
FOMC	104.2			na			5.014	5.010	3.654	+
DFOP	104.0	0.1374	~0.01866	0.5		1	5.045	5.045	3.761	+
[redacted] [redacted]										
SFO[m, p]	104.2		0.1189	< 0.001			**5.831**	**5.831**	4.638	+
FOMC	104.4			na			5.786	5.781	4.836	+
DFOP	104.2	0.1189	~0.02459	0.5		1	5.831	5.831	5.001	+
[redacted] **4a**										
SFO[m, p]	104.3		0.1289	< 0.001			**5.379**	**5.379**	4.336	+
FOMC	104.7			na			5.307	5.304	4.579	+
DFOP	104.3	0.1288	~0.04291	0.5		1	5.379	5.379	4.676	+
[redacted]										
SFO	92.48		0.03178	na			21.81	21.81	11.66	-
FOMC[p]	96.19		< 0.01				75.94	**18.00**	6.248	+
DFOP[m]	95.15	0.1047	0.04011	0.005		0.4840	**68.56**	18.31	6.693	+
[redacted]										
SFO[m]	96.996		0.1153	< 0.001			**6.011**	6.011	7.46	o
FOMC	99.04		0.015				8.955	5.451	7.173	+
DFOP[p]	96.98	0.1311	~0.00817	0.1796		0.9105	84.84	**5.995**	4.450	+
[redacted]										
SFO[m, p]	95.90		0.34799	< 0.001			**1.992**	**1.992**	5.929	o +
FOMC	96.39			0.26			2.078	1.933	7.193	o +
DFOP	95.70	0.3568	~0.002627	0.418		0.979	263.9	2.005	5.152	+
[redacted]										
SFO	100.72		0.07832	< 0.001			8.850	8.850	8.417	o
FOMC[m]	101.36			0.008			**13.45**	8.810	5.752	+
DFOP [p]	100.76	0.0947	0.01069	0.062		0.8576	64.86	**8.864**	4.553	+
[redacted] **10°C**										
SFO [m, p]	98.05		0.04598	< 0.001			**15.07**	**15.07**	4.673	+
FOMC	98.13			na			15.10	15.01	4.797	+
DFOP	99.55	~0.4887	0.04233	< 0.001		0.0573	16.38	14.98	4.245	+

$DT_{50\ mod}$ half-lives for modelling: FOMC: $DT_{50\ recalc}$ recalculated from $DT_{90,\ FOMC}$; DFOP: DT_{50} of slow phase
$DT_{50\ initial}$ initial half-life, for trigger evaluation
a) visual assessment: + good o medium - bad
SFO single first order
FOMC first-order multiple-compartment
DFOP double first-order in parallel
m best approach for modelling purpose
na not available, not appropriate
p best fit model for persistence endpoints, trigger evaluation
~ not significantly different from 0, t-test > 5 %

Table 7.2.1- 6: Laboratory soil DT_{50} and DT_{90} values of iprovalicarb for modelling purposes and trigger evaluation

Soil	for **modelling** purpose: $DT_{50\ mod}$ [days] non normalised	for **modelling** purpose: $DT_{50\ mod}$ [days] normalised	Kinetic model	for **trigger** evaluation: $DT_{50\ initial}$ [days] non normalised	for **trigger** evaluation: $DT_{90\ initial}$ [days] non normalised	Kinetic model
[redacted] AXXa	6.595	6.59	SFO	6.595	21.91	SFO
[redacted] II	5.045	5.05	SFO	5.045	16.76	SFO
[redacted]	5.831	5.83	SFO	5.831	19.37	SFO
[redacted]	5.379	5.38	SFO	5.379	17.87	SFO
[redacted]	68.56	68.56	DFOP	18.00	252.12	FOMC
[redacted]	6.011	4.85	SFO	5.995	26.56	DFOP
[redacted] im [redacted]	1.992	1.77	SFO	1.992	6.62	SFO
[redacted]	13.45	10.37	FOMC	8.864	45.06	DFOP
[redacted], 10°C	15.07	4.72	SFO	15.07	50.07	SFO
geometric mean		*6.78*				

III. Conclusions

For modelling purposes the non-normalised $DT_{50\ mod}$ of iprovalicarb were in the range of 2 to 68.6 days and the normalised $DT_{50\ mod}$ in the range of 1.8 to 68.6 days (geom. mean 6.78 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 2 to 18 days and the $DT_{90\ initial}$ in the range of 7 to 252 days.

Summary: Rate of degradation of iprovalicarb in soil under aerobic conditions - laboratory studies

The degradation of iprovalicarb in soil under aerobic conditions was evaluated during the Annex I Inclusion using the phenyl-labelled parent compound ([redacted], 1997, [redacted] 1997a and 1997b (submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.2.1 /01, IIA, 7.1.1.2.1 /02 and IIA, 7.1.1.2.1 /04, respectively) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)). In addition a new soil metabolism study was performed using the valine radiolabel of iprovalicarb to complete the data according to current requirement practice ([redacted] (2011), submitted in this Dossier, KIIA 7.2.1 /05).

To derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments a kinetic evaluation of these data was performed according to FOCUS kinetics (FOCUS, 2006) ([redacted] (2012), submitted in this Dossier, KIIA 7.2.1 /06). For modelling purpose the non-normalised $DT_{50\ mod}$ were in the range of 1.99 to 68.56 days and the normalised $DT_{50\ mod}$ in the range of 1.77 to 68.56 days (geom. mean 6.78 days). For trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 1.99 to 18.00 days and the $DT_{90\ initial}$ in the range of 6.62 to 252.12 days. (Table 7.2.1- 7).

Table 7.2.1- 7: Laboratory soil DT_{50} values of iprovalicarb for modelling purpose and persistence trigger evaluation according to FOCUS (2006)[a)]

Soil	Kinetic evaluation according to FOCUS[a)] for **modelling** purpose: $DT_{50\ mod}$ [days] non-normalised	for **modelling** purpose: $DT_{50\ mod}$ [days] normalised	for **modelling** purpose: Kinetic model	for **trigger** evaluation: $DT_{50\ initial}$ [days] non-normalised	for **trigger** evaluation: $DT_{90\ initial}$ [days] non-normalised	for **trigger** evaluation: Kinetic model
[redacted] AXXa	6.595	6.59	SFO	6.595	21.91	SFO
[redacted] II	5.045	5.05	SFO	5.045	16.76	SFO
[redacted]	5.831	5.83	SFO	5.831	19.37	SFO
[redacted]	5.379	5.38	SFO	5.379	17.87	SFO
[redacted]	68.56	68.56	DFOP	18.00	252.12	FOMC
[redacted]	6.011	4.85	SFO	5.995	26.56	DFOP
[redacted]im z/E	1.992	1.77	SFO	1.992	6.62	SFO
[redacted]	13.45	10.37	FOMC	8.864	45.06	DFOP
[redacted], 10°C	(15.07[b)])	4.72	SFO	(15.07[b)])	(50.07[b)])	SFO
range	*1.992-68.56*	*1.77-68.56*		*1.992-18.00*	*6.62-252.12*	
geometric mean		*6.78*				

a) Kinetic calculation by [redacted] (2012), submitted within this dossier (KIIA 7.2.1 /06) according to 'FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. The Final Report of the Work Group on Degradation Kinetics of FOCUS. SANCO/10058/2005, v.2.0, June 2006

b) at 10°C

KIIA 7.2.2 Aerobic degradation of the active substance in soils at 10°C

The aerobic degradation of iprovalicarb in soil at 10°C was evaluated during the Annex I Inclusion. No additional studies at 10°C have been performed for the parent compound. [redacted]ver, a kinetic evaluation of these data was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments according to FOCUS kinetics (FOCUS, 2006) ([redacted] (2012), submitted in this Dossier, KIIA 7.2.1 /06, KIIA 7.2.3 /02).

A short summary of the aerobic degradation of iprovalicarb in soil <u>at 10°C</u> submitted within the EU Basic Dossier 1998 is given below.

The degradation of iprovalicarb in soil at 10°C was performed in the laboratory under aerobic conditions ([redacted], 1997b; submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.1.1 /03) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)). PMPA *(M10)* was found as major metabolite, reaching the maximum of 32.7% of the applied radioactivity (AR) at day 59. The values of the other metabolites were below 5.9% AR. The breakdown of the molecule proceeded to the ultimate degradation product carbon dioxide which accounted for 45.1% AR after the incubation period (120 days).

For a better overview of the kinetic evaluation data for the degradation of iprovalicarb at 10°C a short summary is given below.

For <u>modelling purpose</u> the non-normalised $DT_{50\ mod}$ was calculated to be 15.07 days and the

normalised (20°C, pF2) $DT_{50\ mod}$ 4.72 days (n = 1). For trigger evaluation the (non-normalised) $DT_{50\ initial}$ was 15.07 days and the $DT_{90\ initial}$ 50.07 days. (Table 7.2.1- 7 above).

KIIA 7.2.3 Aerobic degradation of relevant metabolites in soils at 20°C

SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)* were found as major metabolites in soil metabolism studies of iprovalicarb under aerobic conditions. For these metabolites a kinetic evaluation of the data of the parent metabolism studies in which the metabolites had been detected ([redacted], 1997, [redacted] 1997a and 1997b (submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.1.1 /01, IIA, 7.1.1.1.1 /02 and IIA, 7.1.1.1.1 /03, respectively) and [redacted], 2011 (submitted in this dossier KIIA 7.1.1 /04) was conducted to derive parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessment according to FOCUS kinetics (FOCUS, 2006) ([redacted] (2012), submitted in this Dossier, KIIA 7.2.1 /06, KIIA 7.2.3 /02).

In addition, N-acetyl-PMPA *(M15)* was found as major metabolite in an anaerobic soil metabolism study with iprovalicarb. The degradation behaviour of this metabolite was investigated in a soil degradation study ([redacted] (2011), submitted in this dossier KIIA 7.2.3 /03) in soil under aerobic conditions is summarised below.

For a better overview of these laboratory soil degradation data of a short summary is given at the end of this chapter at page 51.

- **SZX 0722-carboxylic acid *(M03)***

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The new study was performed because SZX 0722-carboxylic acid *(M03)* had been found as a major metabolite in the new aerobic soil metabolism study conducted with the valine label (KIIA 7.1.1 /04).

The objective of this study is a kinetic evaluation of the degradation behaviour of iprovalicarb and its major metabolites in agricultural soils under standard laboratory conditions. The modelling analysis for the major metabolites is based on residue data from three standard aerobic laboratory studies at different temperatures. The evaluation was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments according to FOCUS kinetics (FOCUS, 2006).

Report:	**KIIA 7.2.3 /02, [redacted] 2012**
Title:	Kinetic evaluation of aerobic laboratory soil degradation studies after application of iprovalicarb according to FOCUS using KinGui 2 Iprovalicarb (SZX 0722) p-Methylphenethylamine (PMPA, M10) SZX 0722-carboxylic acid (M03)
Report No:	MEF-11/629
Document No:	M-428977-01-1
Guidelines:	FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005, v.2.0, June 2006
GLP:	No (calculation)

Executive Summary

The soil degradation of iprovalicarb has been investigated in four aerobic laboratory degradation studies, applying the parent compound on nine soils with two different radioactive labels at 10 or 20°C and 40 - 55% of maximum water holding capacity. ([redacted], 1997, [redacted] 1997a and 1997b, (submitted within the EU Basic Dossier 1998 IIA, 7.1.1.2.1 /01, IIA, 7.1.1.2.1 /02 and IIA, 7.1.1.2.1/04, respectively) and [redacted], 2011 (submitted in this Dossier, KIIA 7.2.1 /05). The evaluation was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments according to FOCUS kinetics (FOCUS, 2006).

A kinetic modelling analysis of residue data of iprovalicarb and the metabolites SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)* was conducted using the software tool KinGUI 2 (successor of KinGUI 1.1), in order to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments. In this evaluation, the initial soil concentration was free fitted together with all degradation rates and formation fractions, based on the IRLS error model (Iteratively reweighted least square).

The kinetic models used in this evaluation are: single first order (SFO), first order multiple compartment (FOMC), double first order in parallel (DFOP) and Hockey-stick (HS, DFOS).

In the following those parts of the evaluation which are related to the major metabolite SZX 0722-carboxylic acid *(M03)* are summarised. The parts concerning the parent compound iprovalicarb and

major metabolite PMPA *(M10)* are reported in section KIIA 7.2.1 (KIIA 7.2.1 /06) and KIIA 7.2.3 (KIIA 7.2.3 /02), respectively.

The best fit model of the parent for trigger and modelling purposes was chosen (Table 7.2.1- 5), and the corresponding SFO degradation rates for the metabolite SZX 0722-carboxylic acid *(M03)* were considered appropriate for modelling purposes and trigger evaluation (Table 7.2.3- 1 and Table 7.2.3- 2, respectively).

Table 7.2.3- 1: Laboratory soil DegT50 of SZX 0722-carboxylic acid *(M03)* for <u>modelling purpose</u> (normalised: 20°C, 100% field capacity, Q10: 2.58)

Soil	Texture	Kinetic model of parent/ metabolite	f_{corr} (moisture + temp. f. DT_{50})	$DT_{50\,mod}$ [days] non-normalised	$DT_{50\,mod}$ [days] normalised	formation fraction $f_{a,s\text{-}M03}$
[redacted] AXXa	sandy loam	SFO/SFO	1	1.624	1.62	0.5073
[redacted] II	loam	SFO/SFO	1	0.777	0.78	0.3831
[redacted]	sandy loam	SFO/SFO	1	1.852	1.85	0.2817
[redacted]	silt loam	SFO/SFO	1	0.742	0.74	0.4581
[redacted]	loamy sand	DFOP/SFO	1	1.730	1.73	0.1859
[redacted]	sandy loam	SFO/SFO	0.8075	0.560	0.45	0.2958
[redacted] im [redacted]	silt loam	SFO/SFO	0.8896	0.583	0.52	0.1829
[redacted]	sandy loam	FOMC/SFO	0.7708	1.498	1.15	0.2985
geometric mean					*0.97*	
arithm. mean						*0.3242*

Table 7.2.3- 2: Estimated simple first-order degradation rates of SZX 0722-carboxylic acid *(M03)* in aerobic lab studies for <u>trigger evaluation</u>, based on best fit model of parent

Soil	Texture	Kinetic model of parent/ metabolite	DT_{50} [days] non normalised	DT_{90} [days] non normalised
[redacted] AXXa	sandy loam	SFO/SFO	1.624	5.394
[redacted] II	loam	SFO/SFO	0.777	2.581
[redacted]	sandy loam	SFO/SFO	1.852	6.152
[redacted]	silt loam	SFO/SFO	0.742	2.466
[redacted]	loamy sand	FOMC/SFO	1.966	6.530
[redacted]	sandy loam	DFOP/SFO	0.617	2.049
[redacted] im [redacted]	silt loam	SFO/SFO	0.583	1.935
[redacted]	sandy loam	DFOP/SFO	1.310	4.351

I. Material and Methods

Detailed information is given in the corresponding chapter of the parent compound in section KIIA 7.2.1 (KIIA 7.2.1 /06).

II. Results and Discussion

The best and reasonable model for <u>modelling purpose</u> for the parent was chosen (section KIIA 7.2.1;

KIIA 7.2.1 /06), and the corresponding SFO degradation rates and formation fractions for the metabolite SZX 0722-carboxylic acid *(M03)* were determined (Table 7.2.3- 3). Estimated single first-order degradation rates of SZX 0722-carboxylic acid for trigger evaluation based on the best fit model of the parent (non-normalised) are summarised in Table 7.2.3- 4. The metabolite shows very good to reasonable fits in all cases. A summary of the laboratory soil DT_{50} values (non-normalised and normalised) of SZX 0722-carboxylic acid for modelling purposes in comparison to the DT_{50} and DT_{90} values for trigger evaluation (non-normalised) is given in Table 7.2.3- 5.

Table 7.2.3- 3: Estimated simple first-order degradation rates of SZX 0722-carboxylic acid *(M03)* in aerobic lab studies for modelling purpose; 20°C, not moisture normalised

Soil	Kinetic model of parent/ metabolite	k_{M03} [1/day]	DT_{50} [days]	DT_{90} [days]	t-test	ε of χ^2-test [%]	visual fit[a]	formation fraction $f_{a.s.\text{-}M03}$
[redacted] AXXa	SFO/SFO	0.4269	1.624	5.394	0.0028	35.4	o	0.5073
[redacted] II	SFO/SFO	0.8921	0.777	2.581	< 0.001	16.5	+	0.3831
[redacted]	SFO/SFO	0.3743	1.852	6.152	0.0026	36.6	o	0.2817
[redacted]	SFO/SFO	0.9338	0.742	2.466	0.0011	26.8	o	0.4581
[redacted]	DFOP/SFO	0.4007	1.730	5.746	< 0.001	10.3	+	0.1859
[redacted]	SFO/SFO	1.2376	0.560	1.861	0.0013	16.6	o +	0.2958
[redacted] im [redacted]	SFO/SFO	1.1898	0.583	1.935	< 0.001	4.58	+	0.1829
[redacted]	FOMC/SFO	0.4628	1.498	4.976	0.0135	34.15	o	0.2985
[redacted], 10°C[b)]			-					

a) visual assessment: + good o medium - bad
b) metabolite not observed

Table 7.2.3- 4: Estimated simple first-order degradation rates of SZX 0722-carboxylic acid *(M03)* in aerobic lab studies for trigger evaluation, based on best fit model of parent 20°C, not moisture normalised

Soil	Kinetic model of parent/metabolite	DT_{50} [days]	DT_{90} [days]	t-test	ε of χ^2-test [%]	visual fit[a)]
[redacted] AXXa	SFO/SFO	1.624	5.394	0.0028	35.4	o
[redacted] II	SFO/SFO	0.777	2.581	< 0.001	16.5	+
[redacted]	SFO/SFO	1.852	6.152	0.0026	36.6	o
[redacted]	SFO/SFO	0.742	2.466	0.0011	26.8	o
[redacted]	FOMC/SFO	1.966	6.530	< 0.001	12.5	o +
[redacted]	DFOP/SFO	0.617	2.049	< 0.001	13.9	o +
[redacted] im [redacted]	SFO/SFO	0.583	1.935	< 0.001	4.58	+
[redacted]	DFOP/SFO	1.310	4.351	0.0198	35.2	o
[redacted], 10°C[b)]		-				

a) visual assessment: + good o medium - bad
b) metabolite not observed

Table 7.2.3- 5: Laboratory soil DT_{50} and DT_{90} values of SZX 0722-carboxylic acid *(M03)* for modelling purpose and trigger evaluation

Soil	for **modelling** purpose			for **trigger** evaluation		
	$DT_{50\ mod}$ [days]		Kinetic model of parent/ metabolite	$DT_{50\ initial}$ [days]	$DT_{90\ initial}$ [days]	Kinetic model of parent/ metabolite
	non-normalised	normalised		non-normalised		
[redacted] AXXa	1.624	1.62	SFO/SFO	1.624	5.394	SFO/SFO
[redacted] II	0.777	0.78	SFO/SFO	0.777	2.581	SFO/SFO
[redacted]	1.852	1.85	SFO/SFO	1.852	6.152	SFO/SFO
[redacted]	0.742	0.74	SFO/SFO	0.742	2.466	SFO/SFO
[redacted]	1.730	1.73	DFOP/SFO	1.966	6.530	FOMC/SFO
[redacted]	0.560	0.45	SFO/SFO	0.617	2.049	DFOP/SFO
[redacted] im	0.583	0.52	SFO/SFO	0.583	1.935	SFO/SFO
[redacted]	1.498	1.15	FOMC/SFO	1.310	4.351	DFOP/SFO
range	*0.560-1.852*	*0.45-1.85*		*0.583-1.966*	*1.935-6.530*	
geometric mean		*0.97*				

III. Conclusions

For modelling purpose the non-normalised $DT_{50\ mod}$ of SZX 0722-carboxylic acid *(M03)* were in the range of 0.56 to 1.85 days and the normalised $DT_{50\ mod}$ in the range of 0.45 to 1.85 days (geom. mean 0.97 days). For the trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 0.58 to 1.97 days and the corresponding $DT_{90\ initial}$ values in the range of 1.94 to 6.53 days.

- **PMPA *(M10)***

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier:

PMPA *(M10)* has been found as a major metabolite in the aerobic soil metabolism studies using the phenyl labelled parent compound ([redacted], 1997, [redacted] 1997a and 1997b (submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.1.1 /01, IIA, 7.1.1.1.1 /02 and IIA, 7.1.1.1.1 /03, respectively).

The objective of this study is a kinetic evaluation of the degradation behaviour of iprovalicarb and its major metabolites in agricultural soils under standard laboratory conditions. The modelling analysis for the major metabolites is based on residue data from three standard aerobic laboratory studies at different temperatures. The evaluation was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purposes and environmental risk assessments according to FOCUS kinetics (FOCUS, 2006).

Report:	**KIIA 7.2.3 /02, [redacted].; 2012**
Title:	Kinetic evaluation of aerobic laboratory soil degradation studies after application of iprovalicarb according to FOCUS using KinGui 2 Iprovalicarb (SZX 0722) p-Methylphenethylamine (PMPA, M10) SZX 0722-carboxylic acid (M03)
Report No:	MEF-11/629
Document No:	M-428977-01-1
Guidelines:	FOCUS (2006). Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005, v 2.0, June 2006
GLP:	No (calculation)

Executive Summary

The soil degradation of iprovalicarb has been investigated in four aerobic laboratory degradation studies, applying the parent compound on nine soils with two different radioactive labels at 10 or 20°C and 40-55% of maximum water holding capacity ([redacted], 1997, [redacted] 1997a and 1997b, (submitted within the EU Basic Dossier 1998 IIA, 7.1.1.2.1 /01, IIA, 7.1.1.2.1 /02 and IIA, 7.1.1.2.1 /04, respectively) and [redacted], 2011 (submitted in this Dossier, KIIA 7.2.1 /05). The evaluation was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments according to FOCUS kinetics (FOCUS, 2006).

A kinetic modelling analysis of residue data of iprovalicarb and the metabolites SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)* was conducted using the software tool KinGUI 2 (successor of KinGUI 1.1), in order to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling and environmental risk assessments. In this evaluation, the initial soil concentration was free fitted together with all degradation rates and formation fractions, based on the IRLS error model (Iteratively reweighted least square).

The kinetic models used in this evaluation are: single first order (SFO), first order multiple compartment (FOMC), double first order in parallel (DFOP) and Hockey-stick (HS, DFOS).

In the following those parts of the evaluation which are related to the major metabolite PMPA *(M10)* are summarised. The parts concerning the parent compound iprovalicarb and major metabolite SZX 0722-carboxylic acid *(M03)* are reported in section KIIA 7.2.1 (KIIA 7.2.1 /06) and KIIA 7.2.3 (KIIA 7.2.3 /0), respectively.

The best fit model for trigger purpose of the parent was chosen (Table 7.2.1- 5), and the corresponding SFO degradation rates for the metabolite PMPA *(M10)* were considered appropriate for modelling purposes and trigger evaluation (Table 7.2.3- 6 and Table 7.2.3- 7, respectively).

Table 7.2.3- 6: Laboratory soil DegT$_{50}$ of PMPA *(M10)* for <u>modelling purpose</u> (normalised: 20°C, 100% field capacity, Q10: 2.58)

Soil	Texture	Kinetic model of parent/ metabolite	f_{corr} (moisture + temp. f. DT_{50})	$DT_{50\ mod}$ [days] non-normalised	normalised	formation fraction $f_{a.s.\text{-}M10}$
[redacted]	loamy sand	DFOP/SFO	1	187.33	187.3	0.8141
[redacted]	sandy loam	SFO/SFO	0.8075	79.44	64.15	0.3764
[redacted]im [redacted]	silt loam	SFO/SFO	0.8896	44.28	39.39	0.5644
[redacted]	sandy loam	FOMC/SFO	0.7708	74.00	57.04	0.4071
[redacted], 10°C	sandy loam	SFO/SFO	0.3129	414.59	129.8	0.3683
geometric mean					*81.08*	
arithm. mean						*0.5061*

Table 7.2.3- 7: Estimated simple first-order degradation rates of PMPA *(M10)* in aerobic lab studies for <u>trigger evaluation</u>, based on best fit model of parent

Soil	Texture	Kinetic model of parent/metabolite	DT_{50} [days] non normalised	DT_{90} [days]
[redacted]	loamy sand	FOMC/SFO	239.32	795.0
[redacted]	sandy loam	DFOP/SFO	82.17	273.0
[redacted]im Tal	silt loam	SFO/SFO	44.28	147.1
[redacted]	sandy loam	DFOP/SFO	77.83	285.5
[redacted], 10°C	sandy loam	SFO/SFO	414.6	1377.2

I. Material and Methods

Detailed information is given in the corresponding chapter of the parent compound in section KIIA 7.2.1 (KIIA 7.2.1 /06).

II. Results and Discussion

The best and reasonable model for modelling purpose for the parent was chosen (section KIIA 7.2.1; KIIA 7.2.1 /06), and the corresponding SFO degradation rates and formation fractions for the metabolite PMPA *(M10)* were selected (Table 7.2.3- 8). Estimated simple first-order degradation rates of SZX 0722-carboxylic acid for <u>trigger evaluation</u> based on best fit model of parent (non-normalised) are summarised in Table 7.2.3- 9. The metabolite shows very good to reasonable fits, assuming a simple first-order decay. A summary of the laboratory soil DT$_{50}$ values (non-normalised and normalised) of PMPA for modelling purposes in comparison to the DT$_{50}$ and DT$_{90}$ values for

trigger evaluation (non-normalised) is given in Table 7.2.3- 10.

Table 7.2.3- 8: Estimated simple first-order degradation rates of PMPA *(M10)* in aerobic lab studies for modelling purpose; 20°C, not moisture normalised

Soil	Kinetic model of parent/ metabolite	k_{M03} [1/day]	DT_{50} [days]	DT_{90} [days]	t-test	ε of χ^2-test [%]	visual fit[a)]	formation fraction $f_{a.s.\text{-}M10}$
[redacted] AXXa[b)]			-					
[redacted] II[b)]			-					
[redacted] [b)]			-					
[redacted] [b)]			-					
[redacted]	DFOP/SFO	0.00370	187.33	622.3	0.0474	9.05	+	0.8141
[redacted]	SFO/SFO	0.00873	79.44	263.9	< 0.001	11.07	+	0.3764
[redacted] im [redacted]	SFO/SFO	0.01565	44.28	147.1	< 0.001	11.98	+	0.5644
[redacted]	FOMC/SFO	0.00937	74.00	245.8	< 0.001	9.77	+	0.4071
[redacted], 10°C	SFO/SFO	0.00167	414.6	1377.2	0.0013	4.85	+	0.3683

a) visual assessment: + good o medium - bad
b) metabolite not observed due to position of radiolabel

Table 7.2.3- 9: Estimated simple first-order degradation rates of PMPA *(M10)* in aerobic lab studies for trigger evaluation, based on best fit model of parent 20°C, not moisture normalised

Soil	Kinetic model of parent/metabolite	DT_{50} [days]	DT_{90} [days]	t-test	ε of χ^2-test [%]	visual fit[a)]
[redacted] AXXa[b)]		-				
[redacted] II[b)]		-				
[redacted] [b)]		-				
[redacted] [b)]		-				
[redacted]	FOMC/SFO	239.32	795.0	0.0827	9.58	+
[redacted]	DFOP/SFO	82.17	273.0	< 0.001	10.72	+
[redacted] im [redacted]	SFO/SFO	44.28	147.1	< 0.001	11.98	+
[redacted]	DFOP/SFO	77.83	285.5	< 0.001	8.74	+
[redacted], 10°C	SFO/SFO	414.6	1377.2	0.0013	4.85	+

a) visual assessment: + good o medium - bad
b) metabolite not observed due to position of radiolabel

Table 7.2.3- 10: Laboratory soil DT_{50} and DT_{90} values of PMPA *(M10)* for modelling purpose and trigger evaluation

Soil	for **modelling** purpose			for **trigger** evaluation		
	$DT_{50\ mod}$ [days] non-normalised	$DT_{50\ mod}$ [days] normalised	Kinetic model of parent / metabolite	$DT_{50\ initial}$ [days] non-normalised	$DT_{90\ initial}$ [days] non-normalised	Kinetic model of parent / metabolite
[redacted]	187.33	187.3	DFOP/SFO	239.32	795.0	FOMC/SFO
[redacted]	79.44	64.15	SFO/SFO	82.17	273.0	DFOP/SFO
[redacted]im [redacted]	44.28	39.39	SFO/SFO	44.28	147.1	SFO/SFO
[redacted]	74.00	57.04	FOMC/SFO	72.83	285.5	DFOP/SFO
[redacted], 10°C	(414.6)	129.8	SFO/SFO	(414.6)	(1377.2)	SFO/SFO
range	*44.28-187.33*	*39.39-187.3*		*44.28-239.32*	*147.1-795.0*	
geometric mean		*81.08*				

III. Conclusions

For modelling purpose the non-normalised $DT_{50\ mod}$ of PMPA *(M15)* at 20°C were in the range of 44.3 to 187.3 days and the normalised $DT_{50\ mod}$ in the range of 39.4 to 187.3 days (geom. mean 81.1 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ at 20°C were in the range of 44.3 to 239.3 days and the corresponding $DT_{90\ initial}$ values in the range of 147.1 to 795 days.

- **N-acetyl-PMPA *(M15)***

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The new study was performed because N-acetyl-PMPA *(M15)* was found a major metabolite in the new anaerobic soil metabolism study (KIIA 7.1.2/01).

Report:	**KIIA 7.2.3 /03, [redacted] 2011**
Title:	SZX0722-N-acetyl-PMPA: Aerobic degradation in four European soils
Testing laboratory	Eurofins Agroscience Services GmbH, Germany
Report No:	S11-01623
Document No:	M-427063-01-1
Guidelines:	OECD-Guideline for Testing of Chemicals No.: 307: "Aerobic and Anaerobic Transformation in Soil", Adopted: 24th April 2002
GLP:	Yes

Executive Summary

The aim of this study was to determine the degradation rate of the iprovalicarb metabolite N-acetyl-PMPA *(M15)* in four soils ([redacted], [redacted] II, [redacted] 4a and [redacted] AXXa) under aerobic conditions at 20°C in the dark. The study was performed with non-labelled N-acetyl-PMPA, over a period of 72 hours.

The average soil moisture content was 55% of the maximum water holding capacity over the entire period of the study. The biological activity was checked directly after treatment and seven days after application.
The application rate of N-acetyl-PMPA was 6.0 µg per vessel and 50 g air dried soil, which is equivalent to 0.12 mg N-acetyl-PMPA/kg soil (dry weight).
N-acetyl-PMPA was degraded in 72 hours from initially 96.7% to 8.8% in soil [redacted]. In soil [redacted] II the amount of N-acetyl-PMPA decreased from 95.8% to 4.2% during the incubation period. In soil [redacted] 4a N-acetyl-PMPA decreased from 89.6% directly after application to 5.0% after 72 hours of incubation and in soil [redacted] AXXa from 101.3% to 6.3% after 72 hours.
The extraction efficiency during the study was demonstrated by concurrent recovery samples. Therefore untreated soil [redacted] AXXa samples were fortified at each sampling interval with N-acetyl-PMPA at the LOQ level and with the 20 x LOQ level (application rate). The mean recoveries of all concurrent recoveries were between 100.9 – 109.7%.
The degradation time (DT_{50} and DT_{90}) of N-acetyl-PMPA was calculated for each soil, whereas the results of the single first order calculation (SFO) s[redacted]d the best fit for soils [redacted]. [redacted] 4a and [redacted] AXXa. For the soil [redacted] II the first order multiple compartment calculation (FOMC) shows the best fit. The data are represented in the following table (Table 7.2.3- 11).

Table 7.2.3- 11: Best fit DT_{50} and DT_{90} values of N-acetyl-PMPA *(M15)*

Soil	DT_{50} [hours]	DT_{90} [hours]	Chi² error	Visual fit	Kinetic model
[redacted]	22.3	74.1	2.87	+	SFO
[redacted] II	9.0	39.0	2.53	+	FOMC
[redacted] 4a	20.8	69.2	7.59	+	SFO
[redacted] AXXa	18.8	62.9	4.18	+	SFO

+ = good visual fit

I. Material and Methods

A. Materials

1. Test Material: unlabelled N-acetyl-PMPA *(M15)*

description: white powder
batch: AE 1371462-01-01
chemical purity: 95.5%
CAS: 92520-13-3

2. Soils: Four test soils for European origin were used, considered representative for agricultural soils. The soils are different in physico-chemical characteristics. A summary of the soil characteristics is given in Table 7.2.3- 12. The soils were collected freshly from the field by sampling the A horizons (approx. 0 – 20 cm) of the respective sites. Stones and plant parts were removed before the soil samples were gently air-dried until they could be stepwise sieved down to 2 mm mesh size. For the acclimatization process the soil samples were adjusted with water to 55% of the MWHC

(maximum water holding capacity). The soil samples were pre-incubated under aerobic conditions for 4 days at 20°C.

Table 7.2.3- 12: Soil characteristics

	Soil			
	[redacted]	[redacted] II	[redacted] 4a	[redacted] AXXa
Geographic location (city / state / country)	[redacted]/ North Rhine-Westphalia / Germany	[redacted]/ North Rhine-Westphalia / Germany	[redacted]/ North Rhine-Westphalia / Germany	[redacted]/ North Rhine-Westphalia / Germany
Site description	grass land	grass land	grass land	grass land
Texture class[a)]	sandy loam	clay loam	silt loam	sandy loam
Soil taxonomic classification[a)]	loamy, mixed, mesic typic Argudalfs	N/A	loamy, mixed, mesic typic Argudalfs	N/A
Sand [%][a)]	53	27	15	73
Silt [%][a)]	30	42	70	20
Clay [%][a)]	17	31	15	7
pH - water	5.4	7.5	6.7	6.2
- saturated paste	5.5	7.4	6.8	6.3
- 0.01 M $CaCl_2$	5.1	7.3	6.5	6.0
- 1 N KCl	4.7	7.0	6.1	5.8
Organic matter [%][b)]	2.92	8.26	2.75	3.10
Organic carbon [%]	1.7	4.8	1.6	1.8
Microbial biomass [mg C / 100 g]				
- day 0	226.2	227.4	595.3	61.6
- day 7	212.8	112.8	460.6	48.4
Cation exchange capacity [meq/100 g]	9.9	20.9	11.6	9.1
Maximum water holding capacity [g H_2O *ad* 100 g DW]	61.9	79.3	55.9	49.4
Water holding capacity				
- at 0.33 bar (pF 2.5) [%]	16.5	34.4	21.9	11.7
- at 0.1 bar (pF 2.0) [%]	20.1	40.8	31.7	13.8
Bulk density (disturbed) [g/cm³]	1.08	0.95	1.11	1.19

N/A not analysed
a) according to USDA classification
b) % organic matter = % organic carbon x 1.724

B. Study design

1. Experimental conditions

Each soil system included 32 flasks – 22 flasks treated with test item and 10 additional untreated flasks for determination of the biomass. The glass flasks (300 mL) contained about 50 g soil (dry weight basis) except for the flasks for biomass control (250 mL) which contained 100 g soil (dry weight basis). Each flask was closed by cotton wool.

The maximum field application rate of the parent iprovalicarb is 0.27 kg a.s./ha. The corresponding field application rate for the metabolite N-acetyl-PMPA *(M15)* is 0.079 kg/ha assuming a metabolite formation of 29.1%. The expected application amount of N-acetyl-PMPA should be in the range of 0.12 mg/kg dry soil which corresponds to 5.8 µg per 50 g dry soil. The actual applied amount of

N-acetyl-PMPA was 6.0 µg/50 g air dried soil. The test item was applied with a concentration of 6 µg in 200 µL methanol/water 1/1 (v/v) to each flask containing 50 g soil. The test item solution was added drop by drop to the soil and subsequently mixed by shaking the flask.
The test systems were placed in a dark, temperature controlled climatic cabinet set to 20 ± 2°C target test temperature.
Concentrations of N-acetyl-PMPA in extracts and application solutions were determined by HPLC-MS/MS within 3 days after sampling.

2. Sampling and storage of the soil samples

Two treated flasks per soil were taken for analysis 0, 2, 6, 24, 48 and 72 hours after treatment. The soil samples were worked up and analysed immediately. Thereafter the extracted samples were stored in a freezer below -18°C.

3. Analytical procedure

Ambient extraction: Soil samples were extracted twice with 80 mL acetonitrile/water (1/1, v/v). The suspension was shaken for at least 30 minutes each. The dispersed soil was transferred in a glass centrifuge tube. The extract was separated from the sediment by centrifugation at 1295 x g for 5 minutes and decantation.
Soxhlet extraction: An additional extraction of the samples was done using a soxhlet extractor. For this the complete soil samples were transferred to soxhlet hulls and extracted with 120 mL acetonitrile/water (1/1, v/v) for 3 hours. The dispersed soil was transferred in a glass centrifuge tube. The extract was separated from the sediment by centrifugation at 1295 x *g* for 5 minutes.
After this aliquots of the ambient and the soxhlet extracts were combined and weighted. About 1 - 2 mL of the supernatant water was filtered over 0.45 µm single-use RC filters and transferred into a glass vial for HPLC-MS/MS analysis.

II. Results and Discussion

A. Measurement of Biomass

The microbial biomass of the soils was determined after arrival of the soils at the testing facility, at the start of the study and at the end of incubation. Table 7.2.3- 13 shows the results of the biomass determination by short term respiration.

Table 7.2.3- 13: Biomass of untreated soils

Days after application	Biomass of untreated samples [mg C/ 100 dry soil]			
	[redacted]	[redacted] II	[redacted] 4a	[redacted] AXXa
-17	250.6	187.9	348.6	213.6
0	226.2	227.4	595.3	61.6
7	212.8	112.8	460.6	48.4

B. Method Validation (Recoveries)

Method development and validation was performed successfully within this study prior to soil sample analyses. In addition, recovery tests concurrent to all sample analyses were performed.

The method used for analysis was linear in a range of 0.2 ng/mL (0.9% of AR, limit of detection (LOD)) to 40.0 ng/mL (186.9% of AR). The limit of quantification (LOQ) was set to 1.0 ng/mL. The accuracy and repeatability was assessed on the basis of a set of recovery samples. For this purpose, 50 g untreated soil (calculated as dry matter) was adjusted with water to 55% MWHC and fortified at LOQ level (0.27 µg /50 g soil dry weight = 5.4 µg/kg) and at 22 x LOQ level (5.8 µg/50 g soil dry weight = 0.12 mg/kg) with test item solution.

The sample work up was performed as defined under point B (Study design), subitem 3 (Analytical **procedure**).

During method validation, recoveries of N-acetyl-PMPA *(M15)* in soil [redacted] [redacted] were between 95.2 – 100.9%, with mean values of 96.5% at LOQ level and 100.1% at 22 x LOQ level (Table 7.2.3- 14).

The recoveries of N-acetyl-PMPA in soil [redacted] II were between 93.3 – 101.1% with mean values of 96.5% at LOQ level and 96.1% at 22 x LOQ level (Table 7.2.3- 15).

The recoveries of N-acetyl-PMPA in soil [redacted] 4a were between 95.6 – 101.0%, with mean values of 98.6% at LOQ level and 98.2% at 22 x LOQ level (Table 7.2.3- 16).

The recoveries of N-acetyl-PMPA in soil [redacted] AXXa were between 96.7 – 101.8%, with mean values of 97.0% at LOQ level and 100.0% at 22 x LOQ level (Table 7.2.3- 17).

The determined values of the blank samples were less than 20% of the assigned LOQ of the test item in all four soils.

Table 7.2.3- 14: Recovery of N-acetyl-PMPA *(M15)* in soil [redacted] [redacted]

Fortification level [mg/kg]	Recovery [%]	Mean recovery ± RSD [%]	Overall mean recovery ± RSD [%]
0.0054	95.2 97.8 98.5 95.6 95.6	96.5 ± 2.6	98.3 ± 2.3
0.1166	99.9 100.9 100.5 100.8 98.4	100.1 ± 2.8	

Table 7.2.3- 15: Recovery of N-acetyl-PMPA *(M15)* in soil [redacted] II

Fortification level [mg/kg]	Recovery [%]	Mean recovery ± RSD [%]	Overall mean recovery ± RSD [%]
0.0054	94.1 96.7 101.1 97.4 93.3	96.5 ± 2.2	96.3 ± 2.2
0.1166	96.7 96.1 96.2 95.8 95.8	96.1 ± 1.5	

Table 7.2.3- 16: Recovery of N-acetyl-PMPA *(M15)* in soil [redacted] 4a

Fortification level [mg/kg]	Recovery [%]	Mean recovery ± RSD [%]	Overall mean recovery ± RSD [%]
0.0054	98.5 99.6 98.1 98.1 98.1	98.6 ± 1.6	98.4 ± 1.6
0.1166	95.6 96.4 101.0 98.1 99.7	98.2 ± 2.3	

Table 7.2.3- 17: Recovery of N-acetyl-PMPA *(M15)* in soil [redacted] AXXa

Fortification level [mg/kg]	Recovery [%]	Mean recovery ± RSD [%]	Overall mean recovery ± RSD [%]
0.0054	96.7 97.8 96.7 96.7 97.0	97.0 ± 2.1	98.5 ± 1.9
0.1166	100.4 101.8 98.8 100.1 99.1	100.0 ± 2.2	

C. Degradation of N-acetyl-PMPA *(M15)* in soil

At each sampling interval two treated soil samples were analysed for their test item content. The results of the sample analysis of N-acetyl-PMPA *(M15)* in mg/kg and in % are shown in Table 7.2.3- 18 to Table 7.2.3- 21.

N-acetyl-PMPA was degraded in 72 hours from initially 96.7% to 8.8% in soil [redacted]. [redacted] (Table 7.2.3- 18). In soil [redacted] II the amount of N-acetyl-PMPA decreased from 95.8% to 4.2% during the incubation period (Table 7.2.3- 19). In soil [redacted] 4a N-acetyl-PMPA decreased from 89.6% directly after application to 5.0% after 72 hours incubation (Table 7.2.3- 20) and in soil [redacted] AXXa from 102% to 7% after 72 hours (Table 7.2.3- 21).

Table 7.2.3- 18: Degradation of N-acetyl-PMPA *(M15)* in soil [redacted]

Sampling interval [hours]	Single values [mg/kg]	Mean values [mg/kg]	Single values [%]	Mean values ± RSD [%]
0	0.117 0.115	0.116	97.5 95.8	96.7 ± 1.2
2	0.114 0.116	0.115	95.0 96.7	95.9 ± 1.3
6	0.103 0.103	0.103	85.8 85.8	85.8 ± 0
24	0.059 0.057	0.058	49.2 47.5	48.4 ± 2.5
48	0.025 0.027	0.026	20.8 22.5	21.7 ± 5.6
72	0.010 0.011	0.011	8.3 9.2	8.8 ± 7.3

Table 7.2.3- 19: Degradation of N-acetyl-PMPA *(M15)* in soil [redacted] II

Sampling interval [hours]	Single values [mg/kg]	Mean values [mg/kg]	Single values [%]	Mean values ± RSD [%]
0	0.115 0.115	0.115	95.8 95.8	95.8 ± 0
2	0.099 0.103	0.101	82.5 85.8	84.2 ± 2.8
6	0.070 0.071	0.071	58.3 59.2	58.8 ± 1.1
24	0.024 0.024	0.024	20.0 20.0	20 ± 0
48	0.005[a)] 0.009	0.007	4.2[a)] 7.5	5.9 ± 39.9
72	0.005[a)] 0.005[a)]	0.005	4.2[a)] 4.2[a)]	4.2 ± 0

a) < LOQ

Table 7.2.3- 20: Degradation of N-acetyl-PMPA *(M15)* in soil [redacted] 4a

Sampling interval [hours]	Single values [mg/kg]	Mean values [mg/kg]	Single values [%]	Mean values ± RSD [%]
0	0.118 0.097	0.108	98.3 80.8	89.6 ± 13.8
2	0.117 0.117	0.117	97.5 97.5	97.5 ± 0
6	0.106 0.105	0.106	88.3 87.5	87.9 ± 0.6
24	0.056 0.051	0.054	46.7 42.5	44.6 ± 6.7
48	0.023 0.021	0.022	19.9 17.5	18.4 ± 6.6
72	0.007 0.005[a)]	0.007	5.8 4.2[a)]	5.0 ± 22.6

a) < LOQ

Table 7.2.3- 21: Degradation of N-acetyl-PMPA *(M15)* in soil [redacted] AXXa

Sampling interval [hours]	Single values [mg/kg]	Mean values [mg/kg]	Single values [%]	Mean values ± RSD [%]
0	0.123 0.120	0.122	102.5 100.0	101.3 ±1.7
2	0.120 0.120	0.120	100.0 100.0	100 ± 0
6	0.107 0.110	0.109	89.2 91.7	90.5 ± 2.0
24	0.052 0.051	0.052	43.3 42.5	42.9 ± 1.3
48	0.020 0.020	0.020	16.7 16.7	16.7 ± 0
72	0.008 0.007	0.008	6.7 5.8	6.3 ± 10.2

The analytical results were analysed according to FOCUS Guidelines by three kinetic models (single first order (SFO), double first order in parallel (DFOP) and first order multiple compartment (FOMC)) using single values. The degradation time (DT_{50} and DT_{90}) of the test item was calculated for each soil, whereas the results of the single first order calculation s[redacted]d the best fit for the soils [redacted], [redacted] and [redacted] AXXa. For the soil [redacted] II the first order multiple compartment calculation s[redacted]d the best fit. A summary of the complete results of the degradations kinetics is given in Table 7.2.3- 22.

Table 7.2.3- 22: DT_{50} and DT_{90} values of N-acetyl-PMPA *(M15)*

Kinetic model	Soil	DT_{50} [hours]	DT_{90} [hours]	Chi^2 error [%]	Visual fit[a)]
Single First Order	[redacted]	22.3	74.1	2.87	+
(SFO)	[redacted] II	10.1	33.2	4.62	+
	[redacted] 4a	20.8	69.2	7.59	+
	[redacted] AXXa	18.8	62.6	4.18	+
Double First Order	[redacted]	22.3	74.1	3.61	+
in Parallel	[redacted] II	9.0	39.3	2.84	+
(DFOP)	[redacted] 4a	20.8	69.2	9.55	+
	[redacted] AXXa	18.8	62.6	5.26	+
First Order Multiple	[redacted]	22.1	75.2	3.34	+
Compartment	[redacted] II	9.0	39.0	2.53	+
(FOMC)	[redacted] 4a	20.6	70.2	8.56	+
	[redacted] AXXa	18.7	63.0	4.71	+

+ = good visual fit

III. Conclusions

N-acetyl-PMPA *(M15)* was found to rapidly degradate in soils under aerobic laboratory conditions, with typical half-lives ≤ 1 day for all soils. The corresponding DT_{90} values are in the range of 1.6 to 3.1 days. Therefore, the compound is unlikely to accumulate in a soil environment turning from anaerobic to viable aerobic conditions again.

Summary: Rate of degradation of iprovalicarb metabolites in soil under aerobic conditions - laboratory studies

The metabolism of iprovalicarb in soil under aerobic conditions has been studied using the phenyl- and the valine-labelled parent substance. The investigations were performed in the dark, in a number of soils at temperatures of 20°C and with one soil at a temperature of 10°C.
Under these conditions three metabolites were identified in the soil along with the parent compound and $^{14}CO_2$. The major metabolites (> 10% of the applied radioactivity) were SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)*, which were both degradable under aerobic conditions. Terephthalic acid *(M23)* was found as minor metabolite. For the two major metabolites were SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)* degradation data are reported in section KIIA 7.2.3 ([redacted] (2012), KIIA 7.2.3 /02). In addition a soil degradation study was performed with N-acetyl-PMPA *(M15)* which formed a major metabolite in the anaerobic soil metabolism study. These degradation data are also reported in section KIIA 7.2.3 ([redacted](2011), KIIA 7.2.3 /03). For a better overview of all laboratory soil degradation data of the major iprovalicarb metabolites under aerobic conditions a short summary is given below.

<u>SZX 0722-carboxylic acid *(M03)*:</u> To derive kinetic parameters for comparison with trigger values as

well as kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation based on the data of iprovalicarb soil metabolism studies was performed according to FOCUS kinetics (FOCUS, 2006). For modelling purpose the non-normalised $DT_{50\ mod}$ were in the range of 0.56 to 1.85 days and the normalised $DT_{50\ mod}$ in the range of 0.45 to 1.85 days (geom. mean 0.97 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 0.58 to 1.97 days and the corresponding $DT_{90\ initial}$ values in the range of 1.94 to 6.53 days (Table 7.2.3- 23).

Table 7.2.3- 23: Laboratory soil DT_{50} and DT_{90} values of SZX 0722-carboxylic acid *(M03)*

Soil	Kinetic evaluation according to FOCUS					
	for **modelling** purpose			for **trigger** evaluation		
	$DT_{50\ mod}$ [days] non-normalised	$DT_{50\ mod}$ [days] normalised	Kinetic model of parent/ metabolite	$DT_{50\ initial}$ [days] non-normalised	$DT_{90\ initial}$ [days] non-normalised	Kinetic model of parent/ metabolite
[redacted] AXXa	1.624	1.62	SFO/SFO	1.624	5.394	SFO/SFO
[redacted] II	0.777	0.78	SFO/SFO	0.777	2.581	SFO/SFO
[redacted]	1.852	1.85	SFO/SFO	1.852	6.152	SFO/SFO
[redacted]	0.742	0.74	SFO/SFO	0.742	2.466	SFO/SFO
[redacted]	1.730	1.73	DFOP/SFO	1.966	6.530	FOMC/SFO
[redacted]	0.560	0.45	SFO/SFO	0.617	2.049	DFOP/SFO
[redacted] im Tal	0.583	0.52	SFO/SFO	0.583	1.935	SFO/SFO
[redacted]	1.498	1.16	FOMC/SFO	1.310	4.351	DFOP/SFO
range	*0.560-1.852*	*0.45-1.85*		*0.583-1.966*	*1.935-6.530*	
geometric mean		*0.97*				

a) Kinetic calculation by [redacted] (2012), submitted within this dossier (KIIA 7.2.1 /06) according to 'FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. The Final Report of the Work Group on Degradation Kinetics of FOCUS. SANCO/10058/2005, v.2.0, June 2006'

PMPA *(M10)*: To derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation based on the data of iprovalicarb soil metabolism studies was performed according to FOCUS kinetics (FOCUS, 2006). For modelling purpose the non-normalised $DT_{50\ mod}$ at 20°C were in the range of 44.3 to 187.3 days and the normalised $DT_{50\ mod}$ in the range of 39.4 to 187.3 days (geom. mean 81.1 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ at 20°C were in the range of 44.3 to 239.3 days and the corresponding $DT_{90\ initial}$ values in the range of 147.1 to 795 days (Table 7.2.3- 24).

Table 7.2.3- 24: Laboratory soil DT_{50} and DT_{90} values of PMPA *(M10)*

Soil	Kinetic evaluation according to FOCUS[a)]					
	for **modelling** purpose			for **trigger** evaluation		
	$DT_{50\ mod}$ [days] non-normalised	$DT_{50\ mod}$ [days] normalised	Kinetic model of parent / metabolite	$DT_{50\ initial}$ [days] non-normalised	$DT_{90\ initial}$ [days] non-normalised	Kinetic model of parent / metabolite
[redacted]	187.33	187.3	DFOP/SFO	239.32	795.0	FOMC/SFO
[redacted]	79.44	64.15	SFO/SFO	82.17	273.0	DFOP/SFO
[redacted]im [redacted]	44.28	39.39	SFO/SFO	44.28	147.1	SFO/SFO
[redacted]	74.00	57.04	FOMC/SFO	77.83	285.5	DFOP/SFO
[redacted], 10°C	(414.6[b)])	129.8	SFO/SFO	(414.6[b)])	(1377.2[b)])	SFO/SFO
range	*44.28-187.33*	*39.39-187.3*		*44.28-239.32*	*147.1-795.0*	
geometric mean		*81.08*				

a) Kinetic calculation by [redacted] (2012), submitted within this dossier (KIIA 7.2.1 /06) according to 'FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. The Final Report of the Work Group on Degradation Kinetics of FOCUS. SANCO/10058/2005, v.2.0, June 2006'

b) at 10°C

N-acetyl-PMPA *(M15)*: Based on the results of a soil degradation study with N-acetyl-PMPA *(M15)* the metabolite was found to rapidly degrade in soil under aerobic conditions, with half-lives in a range of 9 to 22 hours. The corresponding DT_{90} values are in the range of 39 to 74 hours. For modelling purpose (reported in the Annex III Dossier, section IIIA 9.6) the non-normalised $DT_{50\ mod}$ were in the range of 0.42 to 0.93 days10 (10.1 to 22.3 hours) and the normalised $DT_{50\ mod}$ in the range of 0.42 to 0.93 days (geom. mean 0.72 days) (Table 7.2.3- 25).

Table 7.2.3- 25: Laboratory soil DT_{50} and DT_{90} values of N-acetyl-PMPA *(M15)*

Soil	Kinetic evaluation according to FOCUS[a)]					
	for **modelling** purpose[b)]			for **trigger** evaluation[c)]		
	$DT_{50\ mod}$ [days] non-normalised	$DT_{50\ mod}$ [days] normalised	Kinetic model	$DT_{50\ initial}$ [hours] non-normalised	$DT_{90\ initial}$ [hours] non-normalised	Kinetic model
[redacted] [redacted]	0.929	0.93	SFO	22.3	74.1	SFO
[redacted] II	0.422	0.42	SFO	9.0	39.0	FOMC
[redacted] 4a	0.868	0.85	SFO	20.8	69.2	SFO
[redacted] AXXa	0.785	0.79	SFO	18.8	62.9	SFO
range	*0.422-0.929*	*0.42-0.93*		*9.0-22.3*	*39.0-74.1*	
geometric mean		*0.72*				

a) Kinetic calculation according to 'FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. The Final Report of the Work Group on Degradation Kinetics of FOCUS. SANCO/10058/2005, v.2.0, June 2006'

b) reported in the Annex III Dossier, section IIIA 9.6

c) [redacted] (2011), submitted in this Dossier (KIIA 7.2.3 /03)

KIIA 7.2.4 Anaerobic degradation of the active substance in soil

Due to the proposed use patterns of iprovalicarb as a fungicide applied to vine, an anaerobic soil degradation study was not considered to be required. Therefore, no studies on the route and rate of degradation of iprovalicarb in soil under anaerobic conditions were submitted within the EU Basic Dossier in 1998. [redacted]ver, an anaerobic soil metabolism and degradation study of iprovalicarb was performed in 2011 and submitted in this Dossier ([redacted](2011, rev. 2012), KIIA 7.2.4 /01). In addition a kinetic evaluation was conducted to derive kinetic parameters according to FOCUS kinetics (FOCUS, 2006) ([redacted] (2012), submitted in this Dossier, KIIA 7.2.4 /02). For a better overview of this evaluated laboratory soil degradation data of a short summary is given at the end of this chapter at page 58.

New study submitted for Annex I renewal
Justification for including this study in the Annex I Renewal Dossier: This study was conducted and included to over metabolism and degradation of iprovalicarb in soil under anaerobic conditions.

Report:	**KIIA 7.2.4/01, [redacted]2011, revised 2012**
Title:	[Phenyl-UL-^{14}C]iprovalicarb: Anaerobic soil metabolism
Report No:	MESZL004-1
Document No:	M-399285-02-1
Guidelines:	- OECD Guideline for Testing of Chemicals, No. 307, Aerobic and Anaerobic Transformation in Soil, 2002 - Regulation (EC) No.1107/2009 of the European Parliament and of the council of 21 October 2009 - US EPA Fate, Transport and Transformation Test Guidelines, OPPTS 835.4100 and OPPTS 835.4200, Aerobic and Anaerobic Soil Metabolism, 2008
GLP:	Yes

Executive Summary

The degradation data as reported in study KIIA 7.1.2 /01 were kinetically evaluated. The DT_{50} values for iprovalicarb in the anaerobic soil/water system, determined using single first-order kinetics (SFO), first-order multiple compartmental (FOMC) and double first-order in parallel (DFOP) were 29.5 days (r^2 = 0.94, χ^2 = 9.9), 26.7 days (r^2 = 0.95, χ^2 = 9.9) and 24.4 days (r^2 = 0.97, χ^2 = 7.4), respectively.

I. Material and Methods

Details on the study conduct and its results are summarised under KIIA 7.1.2 /01. A kinetics modelling tool (KinGUI 1.1), which was built within the frame-work of MATLAB (Ver.7.0.4) was used to calculate the dissipation rate and half-life of iprovalicarb in the total system (soil + water) of this study. The tool uses internal routines (Levenberg-Marquardt) of MATLAB to optimise the model parameters to fit a chosen kinetics model to the observed data from this study. The objective function used for the optimisation of the parameters was to minimise the sum of squares between the calculated and observed time series data. The kinetic models used in this study are: simple first order kinetics (SFO), first order multiple compartment (FOMC), and double first order in parallel kinetics

(DFOP).

II. Results and Discussion

The SFO, FOMC and DFOP models were used to fit the observed degradation of iprovalicarb in the anaerobic soil metabolism study. The χ^2 scaled error statistic and the coefficient of determination (r^2) for the SFO model were 9.9% and 0.94, with calculated DT_{50} and DT_{90} values of 29.5 and 98.0 days, respectively. The χ^2 scaled error statistic and the coefficient of determination (r^2) for the FOMC model were 9.9% and 0.95, with calculated DT_{50} and DT_{90} values of 26.7 and > 116.6 days, respectively. The χ^2 scaled error statistic and the coefficient of determination (r^2) for the DFOP model were 7.4% and 0.97, with calculated DT_{50} and DT_{90} values of 24.4 and 103.9 days, respectively. The SFO, FOMC and DFOP kinetic end points are summarised in Table 7.2.4- 1.

Table 7.2.4- 1: Calculated DT_{50} and DT_{90} values for iprovalicarb in silt loam under anaerobic conditions (total system)

Kinetic model	DT_{50} [days]	DT_{90} [days]	χ^2 [%]	r^2
SFO	29.5	98.0	9.9	0.94
FOMC	26.7	116.6	9.9	0.95
DFOP	24.4	103.9	7.4	0.97

SFO = single first order
FOMC = first order multiple compartment
DFOP = double first order in parallel

III. Conclusion

Iprovalicarb did degrade appreciably under anaerobic conditions in soil and would not be expected to persist in this type of environment.

New kinetic evaluation submitted for Annex I renewal

Justification for including this study in the Annex I Renewal Dossier: The objective of this study is a kinetic evaluation of the anaerobic soil metabolism study of iprovalicarb (KIIA 7.1.2 /01). The evaluation was conducted to derive kinetic parameters according to FOCUS kinetics (FOCUS, 2006). The kinetic parameters which lead to the best fit between measured and calculated values were identified based on a mathematical optimisation algorithm and a statistical analysis.

Report:	**KIIA 7.2.4 /02, [redacted] 2012**
Title:	Kinetic evaluation of anaerobic laboratory soil degradation study after application of iprovalicarb according to FOCUS using KinGui 2
Report No:	MEF-11/1001
Document No:	M-429037-01-1
Guidelines:	FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005, v.2.0, June 2006
GLP:	No (calculation)

Executive Summary

The degradation data of iprovalicarb as reported in study KIIA 7.1.2 /01 were kinetically evaluated according to FOCUS kinetics (FOCUS, 2006). A kinetic modelling analysis of residue data of iprovalicarb and the metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* was conducted using the software tool KinGui II (successor of KinGui 1.1). The kinetic models used in this evaluation are: simple first order (SFO), first order multiple compartment (FOMC), double first order in parallel (DFOP) and Hockey-stick (HS, DFOS).

In the following those parts of the report are summarised which address the kinetic evaluation of the parent compound iprovalicarb. Parts concerning the kinetic evaluation of the metabolites are reported in section KIIA 7.2.5 (KIIA 7.2.5 /01) of this document.

In general, a good overall model fit was reached with the proposed metabolic pathway. The selection of the kinetic model is based on a detailed statistical analysis including visual assessment, χ^2 statistic, significance t-test and correlation analysis. In Table 7.2.4- 2 anaerobic $DegT_{50}$ for iprovalicarb are summarised, proposed for the best or appropriate fit for persistence or modelling purpose according FOCUS kinetics.

Table 7.2.4- 2: Laboratory anaerobic soil $DegT_{50}$ of iprovalicarb for modelling or persistence purpose

Kinetic model	$C_{t\,0}$ [%]	k_{fast} [1/d]	k_{slow} [1/d]	t-test, k_{slow}	g_{fast}	DT_{50} modelling [days]	DT_{50} initial [days]	DT_{90} initial [days]	χ^2-test error [%]	visual fit[a)]
SFO	67.41		0.0225	< 0.01		30.80^m	30.80	102.3	10.82	+
DFOP	74.02	13.165	0.02119	na	0.1427	32.71	25.44^p	101.4	7.81	+

a) visual assessment: + good o medium - bad
SFO single first order
DFOP double first-order in parallel
na not available, not appropriate
m best approach for modelling purpose
p best fit model for persistence endpoints

I. Material and Methods

The soil degradation of the phenyl-labelled iprovalicarb has been investigated under anaerobic laboratory conditions in one German soil (KIIA 7.1.2 /01). A kinetic modelling analysis of residue data of iprovalicarb and the metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* was conducted using the software tool KinGui II (successor of KinGui 1.1). The kinetic models used in this evaluation are: simple first order (SFO), first order multiple compartment (FOMC), double first order in parallel (DFOP) and Hockey-stick (HS, DFOS).

Due to the intention to evaluate the kinetic behaviour under anaerobic conditions, the kinetic fit was started at time, when anaerobic conditions have been available. Thus, residue data of the first 3 days under aerobic conditions, when already metabolite residues have been measured, were not taken into account for the fit. Therefore in this evaluation, the initial soil concentration of all three compounds was free fitted together with all degradation rates and formation fractions, based on the IRLS error model (Iteratively reweighted least square).

II. Results and Discussion

The degradation of the parent substance iprovalicarb in anaerobic soil was evaluated assuming different kinetic models. Best fit of the parent for persistence purpose could be reached using a DFOP model (Table 7.2.4- 3). For modelling purpose according to FOCUS kinetics, the degradation of iprovalicarb is well described assuming simple first-order decay (Table 7.2.4- 3). The statistically assessment shows good results with a relative error ε of the χ^2 test < 15%. All parameters are significantly different from 0, based on a single-sided t-test. Also, the visual inspection of the fit shows a good acceptability.

Table 7.2.4- 3: SFO and bi-phasic fits of anaerobic lab degradation of iprovalicarb

Kinetic model	C_0 [%]	k_{fast} [1/d]	k_{slow} [1/d]	t-test, k_{slow}	g_{fast}	DT_{50} modelling [days]	DT_{50} initial [days]	DT_{90} initial [days]	χ^2-test error [%]	visual fit a)
SFO	67.41		0.0225	< 0.01		**30.80**^{m}	30.80	102.3	10.82	+
FOMC	68.56			<0.23		33.91	28.91	112.6	10.66	+
DFOP	74.02	13.165	0.02119	na	0.1427	32.71	**25.44**^{p}	101.4	7.81	+

a) visual assessment: + good, o medium, - bad
SFO single first order
FOMC first-order multiple-compartment
DFOP double first-order in parallel
na not available, not appropriate
m best approach for modelling purpose
p best fit model for persistence endpoints

III. Conclusion

The degradation of iprovalicarb and two major metabolites in anaerobic soil was evaluated assuming different kinetic models. Best fit of the parent for the persistence purpose could be reached using a DFOP model ($DT_{50\ initial}$ = 25.4 days). For modelling purpose according to FOCUS kinetics, the degradation of iprovalicarb is well described assuming SFO decay ($DT_{50\ modelling}$ = 30.8 days).

Summary: Rate of degradation of iprovalicarb in soil under anaerobic conditions

The degradation of iprovalicarb in soil under anaerobic conditions was performed in 2011 and submitted in this Dossier ([redacted] (2011, rev. 2012), KIIA 7.2.4 /01).

To derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation of these data was performed according to FOCUS kinetics (FOCUS, 2006) ([redacted] (2012), submitted in this Dossier, KIIA 7.2.4 /02). The degradation of iprovalicarb and two major metabolites in anaerobic soil was evaluated assuming different kinetic models. Best fit of the parent for the persistence purpose could be reached using a DFOP model ($DT_{50\ initial}$ = 25.4 days). For modelling purpose according to FOCUS kinetics, the degradation of iprovalicarb is well described assuming SFO decay ($DT_{50\ modelling}$ = 30.8 days). (Table 7.2.4- 4)

Table 7.2.4- 4: SFO and bi-phasic fits of anaerobic lab degradation of iprovalicarb for modelling purpose and persistence trigger evaluation according to FOCUS (2006)

Kinetic model	$DT_{50\ modelling}$ [days]	$DT_{50\ initial}$ [days]	$DT_{90\ initial}$ [days]
SFO	**30.80**[m]	30.80	102.3
FOMC	33.91	28.91	112.6
DFOP	32.71	**25.44**[p]	101.4

SFO single first order
FOMC first-order multiple-compartment
DFOP double first-order in parallel
na not available, not appropriate
m best approach for modelling purpose
p best fit model for persistence endpoints

KIIA 7.2.5 Anaerobic degradation of relevant metabolites in soil

PMPA *(M10)* and N-acetyl-PMPA *(M15)* were found as major metabolites in a soil metabolism study with iprovalicarb under anaerobic conditions.

Based on the results of the anaerobic soil metabolism study of the parent compound a kinetic evaluation was conducted based to derive kinetic parameters according to FOCUS kinetics (FOCUS, 2006) ([redacted] (2012), submitted in this Dossier, KIIA 7.2.3 /02). The degradation behaviour of these metabolites in soil under anaerobic conditions is summarised below.

For a better overview of this evaluated laboratory soil degradation data of a short summary is given at the end of this chapter at page 62.

- **PMPA *(M10)***

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The new study was performed because PMPA *(M10)* was found as a major metabolite in the new anaerobic soil metabolism study (KIIA 7.1.2 /01).

Report:	**KIIA 7.2.5 /01, [redacted] 2012**
Title:	Kinetic evaluation of anaerobic laboratory soil degradation study after application of iprovalicarb according to FOCUS using KinGui 2
Report No:	MEF-11/1001
Document No:	M-429037-01-1
Guidelines:	FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005, v.2.0, June 2006
GLP:	No (calculation)

Executive Summary

The degradation data as reported in study KIIA 7.1.2 /01 were kinetically evaluated according to FOCUS kinetics (FOCUS, 2006). A kinetic modelling analysis of residue data of iprovalicarb and the metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* was conducted using the software tool KinGui II (successor of KinGui 1.1). The kinetic models used in this evaluation are: simple first order (SFO), first order multiple compartment (FOMC), double first order in parallel (DFOP) and Hockey-stick (HS, DFOS).

In the following those parts of the report are summarised which address the kinetic evaluation of the iprovalicarb metabolite PMPA *(M10)*. Parts concerning the kinetic evaluation of the parent compound and the major metabolite N-acetyl-PMPA *(M15)* are reported in section KIIA 7.2.4 (KIIA 7.2.4 /02) and KIIA 7.2.5 (KIIA 7.2.5 /0), respectively.

In general, a good overall model fit was reached with the proposed metabolic pathway. The selection of the kinetic model is based on a detailed statistical analysis including visual assessment, χ^2 statistic, significance t-test and correlation analysis. The anaerobic $DegT_{50}$ and formation fractions for the metabolite PMPA *(M10)*, proposed for the best or appropriate fit for persistence or modelling purpose according FOCUS kinetics are summarised in Table 7.2.5- 3.

Table 7.2.5- 1: Estimated simple first order degradation rates of PMPA *(M10)* in laboratory anaerobic soil study

Kinetic model for parent	$C_{t\,0}$ [%]	k_{PMPA} [1/d]	DT_{50} [days]	DT_{90} [days]	t-test	ε of χ^2-test [%]	visual accept-ability$^{a)}$	formation fraction $f_{a.s.\text{-}M10}$
SFO	11.3	0.01797	38.58^{m}	128.1^{m}	< 0.001	16.66	+	0.7620
DFO	6.93	0.01608	43.11^{p}	143.2^{p}	na	17.70	+	0.6707

a) visual assessment: + good o medium - bad
SFO single first order
DFOP double first-order in parallel
na not available, not appropriate
m best approach for modelling purpose
p best fit model for persistence endpoints

I. Material and Methods

A detailed description for iprovalicarb and the metabolites in given in section of the parent compound (KIIA 7.2.4, KIIA 7.2.4 /02) of this document.

II. Results and Discussion

The metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* were fitted together with the parent compound, to describe best its total degradation pathways. As during the first 3 days of aerobic degradation already a certain amount of metabolite was formed, the initial mass at day 0 ($C_{t\,0}$) of the anaerobic degradation was free fitted together with the further parameters and was not fixed to 0. The best and reasonable model for modelling (SFO) or for persistence purpose (DFOP) for the parent was chosen, and the corresponding degradation rates and formation fractions for the metabolite PMPA *(M10)* were selected (Table 7.2.5- 2). PMPA shows very good to reasonable fits, assuming a simple first-order decay.

Table 7.2.5- 2: Estimated simple first order degradation rates of PMPA *(M10)* in laboratory anaerobic soil study

Kinetic model for parent	$C_{t\,0}$ [%]	k_{PMPA} [1/d]	DT_{50} [days]	DT_{90} [days]	t-test	ε of χ^2-test [%]	visual accept-ability a)	formation fraction $f_{a.s.\text{-}M10}$
SFO	11.3	0.01797	38.58^{m}	128.1^{m}	< 0.001	16.66	+	0.7620
DFOP	6.93	0.01608	43.11^{p}	143.2^{p}	na	17.70	+	0.6707

a) visual assessment: + good o medium - bad
SFO single first order
DFO double first-order in parallel
m best approach for modelling purpose
p best fit model for persistence endpoints
na not available, not appropriate

III. Conclusion

The degradation of iprovalicarb and two major metabolites in anaerobic soil was evaluated assuming different kinetic models. The metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* were fitted together with the parent compound, to describe best its total degradation pathways. PMPA *(M10)* shows very good to reasonable fits, assuming SFO decay (DT_{50} for modelling purpose: 38.6 days) and DFOP decay (DT_{50} for persistence endpoints: 43.1 days).

- **N-acetyl-PMPA *(M15)***

New kinetic evaluation submitted for Annex I renewal

Justification for including this new study in the Annex I Renewal Dossier: The new study was performed because N-acetyl-PMPA *(M15)* was found a major metabolite in the new anaerobic soil metabolism study (KIIA 7.1.2 /01).

Report:	**KIIA 7.2.5 /01, [redacted] 2012**
Title:	Kinetic evaluation of anaerobic laboratory soil degradation study after application of iprovalicarb according to FOCUS using KinGui 2
Report No:	MEF-11/1001
Document No:	M-429037-01-1
Guidelines:	FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005, v.2.0, June 2006
GLP:	No (calculation)

Executive Summary

The degradation data as reported in study KIIA 7.1.2 /01 were kinetically evaluated according to FOCUS kinetics (FOCUS, 2006). A kinetic modelling analysis of residue data of iprovalicarb and the metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* was conducted using the software tool KinGui II (successor of KinGui 1.1). The kinetic models used in this evaluation are: simple first order (SFO), first order multiple compartment (FOMC), double first order in parallel (DFOP) and Hockey-stick (HS, DFOS).

In the following those parts of the report are summarised which address the kinetic evaluation of the iprovalicarb metabolites. Parts concerning the kinetic evaluation of the parent compound and the major metabolite PMPA *(M10)* are reported in section KIIA 7.2.4 (KIIA 7.2.5 /01) and KIIA 7.2.5 (KIIA 7.2.5 /01), respectively.

In general, a good overall model fit was reached with the proposed metabolic pathway. The selection of the kinetic model is based on a detailed statistical analysis including visual assessment, χ^2 statistic, significance t-test and correlation analysis. The anaerobic $DegT_{50}$ and formation fractions for the metabolite N-acetyl-PMPA *(M15)*, proposed for the best or appropriate fit for persistence or modelling purpose according FOCUS kinetics are summarised in Table 7.2.5- 3.

Table 7.2.5- 3: Estimated simple first order degradation rates of N-acetyl-PMPA *(M15)* in laboratory anaerobic soil study

Kinetic model for parent	C_{t0} [%]	k_{PMPA} [1/d]	DT_{50} [days]	DT_{90} [days]	t-test	ε of χ^2-test [%]	visual accept-ability[a)]	formation fraction $f_{M10\text{-}M15}$
SFO	2.72	0.00909	76.23[m]	253.2[m]	< 0.001	10.57	+	1 [fix b)]
DFOP	3.37	0.00656	105.7[p]	351.3[p]	na	10.69	+	1 [fix b)]

a) visual assessment: + good o medium - bad
b) fixed to 1, after check
na not available, not appropriate

SFO single first order
DFOP double first-order in parallel
m best approach for modelling purpose
p best fit model for persistence endpoints

I. Material and Methods

A detailed description for iprovalicarb and the metabolites in given in section of the parent compound (KIIA 7.2.4, KIIA 7.2.4 /02) of this document.

II. Results and Discussion

The metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* were fitted together with the parent compound, to describe best its total degradation pathways. As during the first 3 days of aerobic degradation already a certain amount of metabolite was formed, the initial mass at day 0 ($C_{t\,0}$) of the anaerobic degradation was free fitted together with the further parameters and was not fixed to 0. The best and reasonable model for modelling (SFO) or for persistence purpose (DFOP) for the parent was chosen, and the corresponding degradation rates and formation fractions for the metabolite N-acetyl-PMPA *(M15)* were selected (Table 7.2.5-4). N-acetyl-PMPA shows very good to reasonable fits, assuming a simple first-order decay.

Table 7.2.5- 4: Estimated simple first order degradation rates of N-acetyl-PMPA *(M15)* in laboratory anaerobic soil study

Kinetic model for parent	$C_{t\,0}$ [%]	k_{PMPA} [1/d]	DT_{50} [days]	DT_{90} [days]	t-test	ε of χ^2-test [%]	visual accept-ability[a)]	formation fraction $f_{M10\text{-}M15}$
SFO	2.72	0.00909	76.23[m]	253.2[m]	< 0.001	10.57	+	1 [fix b)]
DFOP	3.37	0.00656	105.7[p]	351.3[p]	na	10.69		1 [fix b)]

a) visual assessment: + good o medium - bad
b) fixed to 1, after check
SFO single first order
DFOP double first-order in parallel
m best approach for modelling purpose
p best fit model for persistence endpoints
na not available, not appropriate

III. Conclusion

The degradation of iprovalicarb and two major metabolites in anaerobic soil was evaluated assuming different kinetic models. The metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* were fitted together with the parent compound, to describe best its total degradation pathways. N-acetyl-PMPA *(M15)* shows very good to reasonable fits, assuming SFO decay (DT_{50} for modelling purpose: 76.2 days) and DFOP (DT_{50} for persistence endpoints: 105.7 days).

Summary: Rate of degradation of iprovalicarb metabolites in soil under anaerobic conditions

PMPA *(M10)* and N-acetyl-PMPA *(M15)* were found as major metabolites in a soil metabolism study with iprovalicarb under anaerobic conditions. Based on the results of the anaerobic soil metabolism study of the parent compound a kinetic evaluation was conducted based to derive kinetic parameters according to FOCUS kinetics (FOCUS, 2006) which are summarized below.

To derive kinetic parameters for comparison with trigger values as well as kinetic parameters

suitable for modelling purpose and environmental risk assessments a kinetic evaluation of these data was performed according to FOCUS kinetics (FOCUS, 2006) ([redacted] (2012), submitted in this Dossier, KIIA 7.2.3 /0 and KIIA 7.2.3 /02). The degradation of iprovalicarb and two major metabolites in anaerobic soil was evaluated assuming different kinetic models. The metabolites PMPA *(M10)* and N-acetyl-PMPA *(M15)* were fitted together with the parent compound, to describe best its total degradation pathways. PMPA *(M10)* shows very good to reasonable fits, assuming SFO decay (DT_{50} for modelling purpose: 38.6 days) and DFOP decay (DT_{50} for persistence endpoints: 43.1 days). N-acetyl-PMPA *(M15)* shows very good to reasonable fits, assuming SFO decay (DT_{50} for modelling purpose: 76.2 days) and DFOP decay (DT_{50} for persistence endpoints: 105.7 days). (Table 7.2.5- 5)

Table 7.2.5- 5: SFO and bi-phasic fits of anaerobic lab degradation of iprovalicarb metabolites for modelling purpose and persistence trigger evaluation according to FOCUS (2006)

Compound	Kinetic model	DT_{50} [days]	DT_{90} [days]
PMPA *(M10)*	SFO	38.58[m]	128.1[m]
	DFOP	43.10[p]	143.2[p]
N-acetyl-PMPA *(M15)*	SFO	76.23[m]	253.2[m]
	DFOP	105.7[p]	351.3[p]

SFO	single first order
FOMC	first-order multiple-compartment
DFOP	double first-order in parallel
m	best approach for modelling purpose
p	best fit model for persistence endpoints

KIIA 7.3 Field studies

KIIA 7.3.1 Soil dissipation testing in a range of representative soils

The soil degradation and dissipation of iprovalicarb has been investigated at six field dissipation sites in Europe as reported in the EU Basic Dossier in 1998 ([redacted], 1997; submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.2.2 /01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)). A kinetic evaluation of these data for persistence or trigger purpose according to FOCUS kinetics (FOCUS, 2006) was performed ([redacted] (2012), submitted in this Dossier, KIIA 7.3.1 /02). A short summary of these evaluated data is given at the end of this chapter at page 74.
In addition a study to determine the storage stability of iprovalicarb and its metabolite PMPA *(M10)* in soil ([redacted] (2000) submitted in this Dossier, KIIA 7.3.1 /03) was performed.

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The objective of this study is a kinetic evaluation of the dissipation behaviour of iprovalicarb and its metabolite PMPA *(M10)* in agricultural soils under representative field conditions in Europe. The analysis is based on residue data from a terrestrial field dissipation study ([redacted], 1997, submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.2.2 /01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)). The evaluation was conducted to derive kinetic parameters suitable for persistence purpose according to FOCUS kinetics, intended for comparison with appropriate ecotoxicological endpoints and studies. The kinetic parameters which lead to the best fit between measured and calculated values were identified based on a mathematical optimisation algorithm and a statistical analysis (KinGui 2).

Report: **KIIA 7.3.1 /02, [redacted] 2012**
Title: Kinetic evaluation of a field dissipation study with iprovalicarb according to FOCUS for trigger purpose using KinGui 2
Report No: MEF-11/926
Document No: M-429030-01-1
Guidelines: FOCUS: Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005, v.2.0, June 2006
GLP: No (calculation)

Executive Summary

The soil degradation and dissipation of iprovalicarb has been investigated at six field dissipation sites in Europe as reported in the EU Basic Dossier in 1998. A kinetic modelling analysis of these residue data of iprovalicarb and the metabolite PMPA *(M10)* was conducted using the software tool KinGui 2 (successor of KinGui 1.1). In this evaluation, the initial soil concentration was free fitted together with all degradation rates and formation fractions, based on the IRLS error model (Iteratively reweighted least square). The selection of the kinetic model was based on a detailed statistical analysis including visual assessment, χ^2 statistic and significance of a t-test.

In most soils, 5 out of 6, the best fit for dissipation of iprovalicarb in the field could be described assuming a DFOP model (based on SFO, FOMC, DFOP). The best fit model of the parent was chosen then, and the corresponding SFO degradation rates for the metabolite were considered here appropriate for trigger purpose. The non-normalised $DisT_{50}$ values proposed for persistence or trigger purpose are summarised in Table 7.3.1- 1 and Table 7.3.1- 2, for iprovalicarb and its metabolite PMPA *(M10)*, respectively.

Table 7.3.1- 1: Results of SFO and bi-phasic fits at field dissipation trials of iprovalicarb, for trigger purpose (not temperature or moisture normalised)

Site	Country	Model	$DisT_{50,\ initial}$ [days]	$DisT_{90,\ initial}$ [days]	χ^2 error [%]	p > t	visual acceptability[a)]
[redacted]	Germany	SFO	12.72	42.25	5.291	< 0.001	+ + o
		FOMC	12.14	45.33	4.072	< 0.015	+
		DFOP[b)]	**12.45**	**43.45**	1.502	< 0.001	+
[redacted]	Germany	**SFO[b)]**	**8.29**	**27.53**	6.727	< 0.001	+
		FOMC	8.28	27.56	7.732	0.4	+
		DFOP	8.29	27.53	9.594	na[c)]	+
[redacted]	Great Britain	SFO	12.71	42.23	12.18	< 0.001	+ o
		FOMC	10.77	52.28	4.888	< 0.001	+
		DFOP[b)]	**10.33**	**54.93**	4.485	0.0011	+
[redacted]	France	SFO	10.10	33.56	21.11	< 0.001	o
		FOMC	8.08	57.91	11.68	< 0.013	+
		DFOP[b)]	**9.05**	**61.67**	9.808	< 0.005	+
[redacted]	France	SFO	7.79	25.87	17.57	< 0.001	o
		FOMC	5.62	36.90	7.442	< 0.003	+
		DFOP[b)]	**6.40**	**37.45**	6.467	< 0.002	+
[redacted]	Italy	SFO	3.89	12.92	2.575	< 0.001	+ o
		FOMC	2.99	12.45	2.326	< 0.132	+
		DFOP[b)]	**3.73**	**12.78**	1.560	< 0.01	+

a) visual acceptability: + = good, o = medium, - = bad
b) best fit model for persistence or trigger endpoints
c) na = not available, not appropriate

Table 7.3.1- 2: Results of SFO and bi-phasic fits at field dissipation trials of PMPA *(M10)*, for trigger purpose (not temperature or moisture normalised)

Site	Country	Model for parent	$DisT_{50,\ initial}$ PMPA [days]	$DisT_{90,\ initial}$ PMPA [days]	t-test	ε of χ^2 [%]	visual acceptability[a)]
[redacted]	Germany	DFOP	187.4	622.6	< 0.001	19.15	+ o
[redacted]	Germany	SFO	34.36	114.2	< 0.001	21.23	o
[redacted]	Great Britain	DFOP	160.7	533.8	0.0276	28.39	o +
[redacted]	France	DFOP	228.4	758.9	< 0.001	15.61	+ o
[redacted] Du[redacted]s	France	DFOP	58.50	194.3	0.006	25.62	o
Ca[redacted]	Italy	DFOP	22.15	73.58	0.0174	25.35	+

a) visual acceptability: + = good, o = medium, - = bad

I. Material and Methods

The soil degradation and dissipation of iprovalicarb has been investigated at six field dissipation sites in Europe ([redacted], 1997; submitted within the EU Basic Dossier 1998 (IIA, 7.1.1.2.2 /01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)).
A kinetic modelling analysis of residue data of iprovalicarb and the metabolite PMPA *(M10)* was conducted using the software tool KinGui 2 (successor of KinGui 1.1), in order to derive half-lives suitable for trigger evaluation in environmental risk assessments. In this evaluation, the initial soil concentration was free fitted together with all degradation rates and formation fractions, based on the IRLS error model (Iteratively reweighted least square). The selection of the kinetic model was based on a detailed statistical analysis including visual assessment, χ^2-statistic and significance of a t-test.

II. Results and Discussion

Results of the simple first-order or bi-phasic kinetic evaluation of six field dissipation trials according to FOCUS kinetics (FOCUS, 2006) including the parent iprovalicarb and the metabolite PMPA *(M10)* are given in Table 7.3.1- 3 and Table 7.3.1- 4, respectively.). The dissipation rates are evaluated for the corresponding study conditions at the field site (not temperature or moisture normalised). For trigger purpose the best fit model is required (SFO, FOMC, DFOP), based on the error of the χ^2 test and visual acceptability.

Iprovalicarb: The kinetic evaluation was started by assuming a simple first-order (SFO) degradation for iprovalicarb in soil. The fitted values for the initial $DisT_{50}$ and $DisT_{90}$, the initial total soil concentration at day 0 ($C_{t=0}$) and some statistical parameters are summarised in Table 7.3.1- 3.
In most soils, 5 out of 6, the best fit for dissipation of iprovalicarb for trigger or persistence purpose could be described assuming a DFOP model (based on SFO, FOMC, DFOP). The statistical assessment shows good results with relative errors ε of the χ^2 test far < 15%. All parameters are significantly different from 0, based on a single-sided t-test. Also, the visual inspection of the fit shows a good acceptability.

Table 7.3.1- 3: Results of SFO and bi-phasic fits at field dissipation trials of iprovalicarb, for trigger purpose (not temperature or moisture normalised)

Site, Country	Model	$C_{t\,0}$ [g/ha]	$DisT_{50,\,initial}$ [days]	$DisT_{90,\,initial}$ [days]	χ^2 error [%]	p > t	visual acceptability[a)]
[redacted], Germany	SFO	485.1	12.72	42.25	5.291	< 0.001	+ o
	FOMC	486.9	12.14	45.33	4.072	< 0.015	+
	DFOP[b)]	486.1	**12.45**	**43.45**	1.502	< 0.001	+
[redacted], Germany	**SFO[b)]**	512.7	**8.29**	**27.53**	6.727	< 0.001	+
	FOMC	512.7	8.28	27.56	7.732	0.4	+
	DFOP	512.7	8.29	27.53	9.594	na[c)]	+
[redacted], Great Britain	SFO	500.1	12.71	42.23	12.18	< 0.001	+ o
	FOMC	506.9	10.77	52.28	4.888	< 0.001	+
	DFOP[b)]	507.7	**10.33**	**54.93**	4.485	0.0011	+
[redacted], France	SFO	486.5	10.10	33.56	21.11	< 0.001	o
	FOMC	486.7	8.08	57.91	11.68	< 0.013	+
	DFOP[b)]	486.6	**9.05**	**61.67**	9.808	< 0.005	+
[redacted] Du [redacted], France	SFO	348.8	7.79	25.87	17.57	< 0.001	o
	FOMC	351.0	5.62	36.90	7.442	< 0.003	+
	DFOP[b)]	351.1	**6.40**	**37.45**	6.467	< 0.002	+
Ca [redacted], Italy	SFO	312.1	3.89	12.92	2.575	< 0.001	+ o
	FOMC	312.1	2.99	12.45	2.326	< 0.132	+
	DFOP[b)]	312.1	**3.73**	**12.78**	1.560	< 0.01	+

a) visual acceptability: + = good, o = medium, – = bad
b) best fit model for persistence or trigger endpoints
c) na = not available, not appropriate

PMPA *(M10)*: The metabolite PMPA was fitted together with the parent compound, to describe best its total dissipation pathway. The best fit model for trigger purpose of the parent was chosen (Table 7.3.1- 3), and the corresponding SFO dissipation rates for the metabolite were considered here (Table 7.3.1- 4). The metabolite s[redacted]d good to reasonable and acceptable fits, assuming a simple first-order decay. Therefore, the SFO dissipation rates of PMPA were considered here appropriate for trigger purpose.

In general, the 15% threshold value for the scaled error ε of the chi-square χ^2 test should not be employed as absolute cut-off criteria. Especially for metabolites, the mean value of the experimental data is much lower (far below 100 %) than for the parent substance. As the calculated error reflects to this experimental mean value and the deviation between measured and simulated data, much higher errors are calculated for low metabolites as for the parent, although a similar optical fit is reached. Therefore, the errors ε of the metabolites should be considered case by case. Additionally, it should be noted, that several residue data of PMPA already range below the limit of quantification (LOQ > 16 g a.s. eq./ha for PMPA), which will not allow to interpret an exact time curve. Thus, the SFO dissipation rates of PMPA were considered here appropriate for trigger purpose.

Table 7.3.1- 4: Results of SFO and bi-phasic fits at field dissipation trials of PMPA *(M10)*, for trigger purpose (not temperature or moisture normalised)

Site	Model for parent	$DisT_{50, initial}$ PMPA [days]	$DisT_{90, initial}$ PMPA [days]	t-test	ε of χ^2 [%]	visual acceptability[a)]	Formation fraction $f_{ipro-PMPA}$
[redacted], Germany	DFOP	187.4	622.6	< 0.001	19.15	+ o	0.1565
[redacted], Germany	SFO	34.36	114.2	< 0.001	21.23	o	0.4065
[redacted], Great Britain	DFOP	160.7	533.8	0.0276	28.39	o +	0.0966
[redacted], France	DFOP	228.4	758.9	< 0.001	15.61	+ o	0.2453
Du [redacted]s, France	DFOP	58.50	194.3	0.006	25.62	o	0.0748
Ca [redacted], Italy	DFOP	22.15	73.58	0.0174	25.35	+	0.1607

a) visual acceptability: + = good, o = medium, - = bad

III. Conclusion

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

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: As the evaluation of the data on the determination of the stability of iprovalicarb and its metabolite PMPA *(M10)* in soil under storage conditions was not finalised at that time no storage stability study was submitted within the EU Basic Dossier in 1998. This study was finalised in 2000 and is summarised below.

Report: **KIIA 7.3.1/03, [redacted], 2000**
Title: Storage stability of SZX 0722 and the metabolite p-methylphenethylamine in soil
Report No: MR-779/97
Document No: M-023590-01-1
Guidelines: not applicable
GLP: Yes

Executive Summary

The purpose of this study was to determine the stability of iprovalicarb 0722 and its metabolite PMPA *(M10)* in soil under the storage conditions.

Untreated soil samples were fortified with iprovalicarb or with PMPA *(M10)*. The fortified concentration for iprovalicarb and PMPA was 203 µg/kg and 187 µg/kg, respectively.

Soil samples were analysed at day 0 and after 63, 103, 162, 278, 370, 481, 601 and 740 days of storage between -18°C and -25°C.

Soil samples were analysed for iprovalicarb and the metabolite PMPA according to the liquid chromatographic method of [redacted], 1997 (submitted within the EU Basic Dossier in 1998 (IIA, IIA, 4.2.2 /01): Soil samples were extracted with boiling methanol/water/ammonia solution (25%) (800/200/10; v/v/v). After solvent evaporation to the aqueous remainder of about 5 mL, the volume is adjusted to 10 mL and the sample is centrifuged. Quantitative determination of the active ingredient and the metabolite is done by high performance liquid chromatography using MS/MS detection. For quantification, internal standards (iprovalicarb-ethyl-homologue and p-ethylphenethyl-amine) are added post-column by a second HPLC-system, to compensate possible matrix effects in the MS-detector. The mean recoveries of the method, which were determined in the range of 5 to 400 µg/kg were 100% for iprovalicarb and 84.6% for PMPA with relative standard deviations of 9.2% for iprovalicarb and 9.1% for PMPA.

The limit of quantification of the method is 5 µg/kg for iprovalicarb and PMPA. The limit of detection of the method is 2 µg/kg for iprovalicarb and PMPA.

The mean recoveries of the method validations conducted before and during the study, were 98.4% for iprovalicarb and 89.2% for PMPA with relative standard deviations of 6.9% for iprovalicarb and 10.0% for PMPA.

The mean concurrent recoveries during analyses of the samples were 96.2% for iprovalicarb with a relative standard deviation of 4.0% and 84.5% for PMPA with a relative standard deviation of 8.3%. The recovered amounts of iprovalicarb and PMPA after storage for 740 days were 91.5% and 84.5%, respectively. These values are very close to the concurrent recoveries fortified at the day of analysis. It is apparent that there is no significant degradation of iprovalicarb or the metabolite PMPA in soil during storage of samples up to 740 days between -18°C and -25°C.

I. Material and Methods

A. Materials

1. Test Material: unlabelled iprovalicarb (diastereomeric mixture SR : SS = 48.8 : 50.1)
description: white powder
purity: 99.0% (isomer SR. 48.9%; isomer SS: 50.1%)
unlabelled PMPA *(M19)*
description: colourless liquid
purity: 99.9%

2. Internal standards: The iprovalicarb-ethyl homologue is used as internal standard for the quantification of iprovalicarb and the compound p-ethylphenethylamine is used as internal standard for the quantification of PMPA *(M10)*.

2. Soil: Soil samples of soils 2.1, 2.2 and 2.3 of [redacted] were mixed (1/1/1; w/w/w [w = parts by weight]) and used for this storage stability study. The mixture was used instead of one single soil 2.1, 2.2 or 2.3 to register a possible influence of all three different soil types. Soil parameters as well as the textural classifications are summarised in Table 7.3.1- 5.

Table 7.3.1- 5: Soil characteristics

Parameter	Soil [redacted] soil 2.1	[redacted] soil 2.2	[redacted] soil 2.3
Texture class (USDA)	sand	loamy sand	sandy loam
- sand (50 µm – 2 mm) [%]	89.4	86.2	66.8
- silt (2 µm – 50 µm) [%]	10.5	7.7	22.4
- clay (< 2 µm) [%]	0.1	6.1	10.8
pH in $CaCl_2$	5.3	6.2	6.6
Organic matter[a)] [%]	0.98	4.44	2.48
Organic carbon [%]	0.7	2.58	1.44
CEC [meq/100 g]	5.0	9.7	12.5
40% of max. moisture capacity [g/100 g dry soil]	11.95	44.3	20
Nitrogen content [g/100 g dry soil]	130	220	100

B. Study design

1. Preparation of the soil samples: To determine the storage stability of iprovalicarb and PMPA *(M10)*, untreated soil samples of 25 g (mixture of soils 2.1, 2.2 and 2.3 of [redacted]) were weighed into 168 extraction thimbles each, which could be taken for extraction during analysis. 84 soil samples were fortified with 0.5 mL of a solution of 10.15 µg/mL iprovalicarb in water/acetonitrile/ammonia solution (25%) (500/500/1; v/v/v) resulting in a concentration of 203 µg/kg soil. 84 soil samples were fortified with 0.5 mL of a solution of 9.34 µg/mL PMPA in water/acetonitrile/ammonia solution (25%) (500/500/1; v/v/v) resulting in a concentration of 187 µg/kg soil. Iprovalicarb was spiked into a special set of samples because a transformation of iprovalicarb to the metabolite PMPA is possible.
The remaining soil samples were used as control samples and samples to be spiked for determination of concurrent recoveries.

2. Storage: Samples prepared at day 0 were transported to the cold storage depot immediately and were stored between -18°C and -25°C. After 63, 103, 162, 278, 370, 481, 601 and 740 days the samples were taken out of the cold storage depot for analysis. One control sample and four treated soil samples were analysed. A second control sample was used for determination of the concurrent recovery.

3. Residue analysis: Soil samples were analysed for the active substance iprovalicarb and the metabolite PMPA *(M10)* via the liquid chromatographic method 00394 ([redacted] (1997); submitted within the EU Basic Dossier 1998 (IIA, 4.2.2 /01)) using internal standards.

II. Results and Discussion

A. Recoveries during method validation

Before and during the analyses of the storage stability study the method was validated with a mixture of soils 2.1, 2.2 and 2.3 of [redacted] (1/1/1; w/w/w). Fortification levels of iprovalicarb and

PMPA *(M10)*, recoveries and relative standard deviations for the validations are presented in Table 7.3.1- 6.

Table 7.3.1- 6: Recoveries of iprovalicarb and PMPA *(M10)* during method validation

Compound	Fortification level [µg/kg]	Soil	Single values [%]	Mean value [%]	RSD [%]
Iprovalicarb	3.662	2.1, 2.2, 2.3	97.4 / 98.3 / 104.3 / 106.4 / 105.5	102	4.2
	3.662	2.1, 2.2, 2.3	97.0 / 113.3 / 102.6 / 104.0 / 100.8	104	6.1
	4.133	2.1, 2.2, 2.3	103.1 / 106.0 / 107.2 / 103.7	105	1.9
	4.348	2.1, 2.2, 2.3	106.0 / 104.9 /98.2 / 105.8 / 101.2	103	3.4
	36.62	2.1, 2.2, 2.3	103.7 / 98.9 / 102.7 / 102.2 / 93.6	100	4.1
	36.62	2.1, 2.2, 2.3	101.8 / 101.6 / 99.4 / 100.3 / 102.3	101	1.2
	41.33	2.1, 2.2, 2.3	103.4 / 106.0 / 103.4 / 103.0 / 106.3	104	1.6
	43.48	2.1, 2.2, 2.3	96.4 / 102.4 / 105.3 / 100.0 / 96.6	100	3.8
	366.2	2.1, 2.2, 2.3	83.8 / 90.2 / 92.3 / 90.2 / 84.2	88.1	3.9
	366.2	2.1, 2.2, 2.3	88.2 / 83.8 / 85.3 / 87.2 / 91.5	87.2	3.0
	413.3	2.1, 2.2, 2.3	93.0 / 91.7 / 92.1 / 91.9 / 93.0	92.3	0.6
	434.8	2.1, 2.2, 2.3	95.4 / 89.0 / 91.7 / 97.0 / 96.1	93.9	3.4
			over all single values	*98.4*	*6.9*
PMPA *(M10)*	3.793	2.1, 2.2, 2.3	81.4 / 76.4 / 80.1 / 81.5	79.9	2.4
	4.152	2.1, 2.2, 2.3	91.5 / 104.6 / 98.7 / 95.3 / 97.6	97.5	4.8
	4.152	2.1, 2.2, 2.3	101.0 / 99.6 / 106.1 / 100.7 / 101.8	102	2.5
	4.308	2.1, 2.2, 2.3	88.7 / 88.7 / 86.1 / 93.3 / 74.3	86.2	7.2
	37.93	2.1, 2.2, 2.3	90.8 / 91.9 / 92.8 / 91.7 / 89.3	91.3	1.4
	41.52	2.1, 2.2, 2.3	94.2 / 97.1 / 100.8 / 87.4 / 96.3	95.1	4.9
	41.52	2.1, 2.2, 2.3	101.3 / 97.9 / 104.9 / 99.8 / 104.1	102	2.9
	43.08	2.1, 2.2, 2.3	82.9 / 82.3 / 80.0 / 74.1 / 75.1	78.8	4.1
	379.3	2.1, 2.2, 2.3	89.2 / 88.1 / 85.3 / 87.4 / 90.8	88.2	2.1
	415.2	2.1, 2.2, 2.3	97.0 / 93.6 / 94.2 / 94.0 / 99.7	95.7	2.6
	415.2	2.1, 2.2, 2.3	88.2 / 81.1 / 76.4 / 75.4 / 79.1	80.1	5.1
	430.8	2.1, 2.2, 2.3	70.1 / 76.0 / 70.1 / 70.2 / 74.5	72.2	2.9
			over all single values	*98.4*	*6.9*

RSD = relative standard deviation

B. concurrent recoveries during storage stability study

In addition to the validations of the analytical method, recoveries were conducted concurrently with each analytical run of the study. They were performed to verify the integrity of the analysed residues found in sets of samples analysed on respective days. The single values, mean recoveries and standard deviations for each study are reported in Table 7.3.1- 7.

Table 7.3.1- 7: Current recoveries of iprovalicarb and PMPA *(M10)* during storage stability study

Compound	Fortification level [µg/kg]	Single values [%]	Mean value [%]	RSD [%]
Iprovalicarb	183.1 to 217.4	87.07	96.2	4.0
		97.49		
		100.2		
		96.98		
		95.50		
		93.93		
		97.77		
		98.77		
		98.32		
PMPA *(M10)*	186.7 to 215.4	78.42	84.5	8.3
		87.66		
		95.94		
		85.26		
		94.63		
		81.73		
		78.88		
		76.66		
		81.04		

RSD = relative standard deviation

C. Results of the storage stability experiment

The results of the storage stability samples for iprovalicarb and PMPA *(M10)* are summarised in Table 7.3.1- 8.

Table 7.3.1- 8: Current recoveries of iprovalicarb and PMPA *(M10)* during storage stability study

Compound	Day	Recovered amounts, single values [%]				Recovered amounts, mean values [%]	RSD [%]
Iprovalicarb	0	94.62	93.51	92.17	91.96	93.1	1.3
	63	90.38	94.98	94.32	98.17	94.5	3.4
	103	94.51	99.56	96.41	98.18	97.2	2.3
	162	93.68	96.58	94.21	103.7	97.0	4.8
	278	96.93	92.69	90.91	91.52	93.0	2.9
	370	94.74	95.55	93.83	95.83	95.0	0.9
	481	98.66	96.82	95.23	92.87	95.9	2.6
	601	89.05	99.11	92.63	93.88	93.7	4.4
	740	93.30	89.86	92.54	90.18	91.5	1.9
	overall single values					*94.5*	*3.3*
PMPA *(M10)*	0	85.66	80.25	79.42	82.63	82.0	3.4
	63	81.80	85.77	87.76	87.82	85.8	3.3
	103	80.19	79.32	81.31	80.17	80.2	1.0
	162	86.63	84.16	88.35	89.53	87.2	2.7
	278	83.91	93.93	93.82	96.34	92.0	6.0
	370	84.36	81.50	84.24	88.15	84.6	3.2
	481	74.24	79.11	82.61	77.00	78.2	4.5
	601	76.72	82.56	83.24	86.34	82.2	4.9
	740	82.87	86.03	84.23	85.00	84.5	1.6
	overall single values					*84.1*	*5.7*

RSD = relative standard deviation

The recovered amounts of iprovalicarb and PMPA *(M10)* at day 0 and after a storage period of 740 days compared to the concurrent recoveries fortified at the day of analysis are listed in Table 7.3.1- 9. The recovered amounts of 91.5% (iprovalicarb) and 84.5% (PMPA *(M10)*) at day 740 are very close to the concurrent recoveries fortified at the day of analysis (Table 7.3.1- 7). These results show that there is no significant degradation of iprovalicarb and PMPA in soil after a storage period of 24 months between -18°C and -25°C.

Table 7.3.1- 9: Recovered amounts after storage of iprovalicarb and PMPA *(M10)* for 0 days and 740 days compared to the concurrent recoveries fortified at the day of analysis

	Iprovalicarb [%]	PMPA *(M10)* [%]
Recovered amount after storage of 0 days	93.1	82.0
Concurrent recoveries fortified at the day of analysis (day 0)	87.1	78.4
Recovered amount after storage of 740 days	91.5	84.5
Concurrent recoveries fortified at the day of analysis (day 740)	98.3	81.0

III. Conclusions

The recovered amounts of iprovalicarb and PMPA *(M10)* after storage for 740 days were 91.5% and 84.5%, respectively. These values are very close to the concurrent recoveries fortified at the day of analysis. It is apparent that there is no significant degradation of iprovalicarb or the metabolite PMPA in soil during storage of samples up to 740 days between -18°C and -25°C.

Summary: Soil dissipation testing in a range of representative soils

The dissipation of iprovalicarb under field conditions has been investigated a number of sites in England, France and Germany. The kinetic evaluation of six field dissipation trials for persistence or trigger purpose according to FOCUS kinetics (FOCUS, 2006) resulted in non-normalised half-lives of 3.7 to12.5 days for iprovalicarb and 22.2 to 228.4 days for the metabolite PMPA *(M10)*. The corresponding DT_{90} values were in the range of 12.8 to 61.7 days and 73.6 to 758.9 days, respectively (Table 7.3.1- 10).

Table 7.3.1- 10: Results of SFO or bi-phasic fits (best fit model) at field dissipation trials of iprovalicarb and PMPA *(M10)*, for trigger purpose (not temperature or moisture normalised)

Compound	Site	Kinetic model	DT_{50} [days]	DT_{90} [days]
Iprovalicarb	[redacted], GER	DFOP	12.45	43.45
	[redacted], GER	SFO	8.29	27.53
	[redacted], UK	DFOP	10.33	54.93
	[redacted], FRA	DFOP	9.05	61.67
	[redacted] Du [redacted] FRA	DFOP	6.40	37.45
	[redacted] [redacted], ITA	DFOP	3.73	12.78
	range		*3.73-12.45*	*12.78-61.67*
PMPA *(M10)*	[redacted], GER	DFOP[a)]	187.4	622.6
	[redacted], GER	SFO[a)]	34.36	114.2
	[redacted], UK	DFOP[a)]	160.7	533.8
	[redacted], FRA	DFOP[a)]	228.4	758.9
	[redacted] Du [redacted], FRA	DFOP[a)]	58.50	194.3
	[redacted] [redacted], ITA	DFOP[a)]	22.15	73.58
	range		*22.15-228.4*	*73.58-758.9*

SFO single first order
DFOP double first-order in parallel
a) kinetic model for parent

KIIA 7.3.2 Soil residue testing

The behaviour of iprovalicarb in laboratory soil is described in section KIIA 7.1. The uptake of residues by the roots and the metabolism in confined rotational crops was described in section KIIA 6.6.2. The behaviour of iprovalicarb in field soil was investigated and described in the soil dissipation section KIIA 7.3.1.

KIIA 7.3.3 Soil accumulation testing on relevant soils

Due to the rapid degradation of iprovalicarb, no soil accumulation study was conducted.

KIIA 7.4 Mobility studies

KIIA 7.4.1 Adsorption and desorption of the active substance

The adsorption/desorption behaviour of iprovalicarb investigated in a batch equilibrium study was evaluated during the Annex I Inclusion using the phenyl-labelled parent compound ([redacted] (1996), submitted within the EU Basic Dossier 1998; IIA, 7.1.2 /01). A new soil adsorption/desorption study was performed according the Brazilian Guidelines ([redacted] (2000), submitted in this Dossier, KIIA 7.4.1 /02). The study was included since it enlarged the data set on the leaching behaviour of iprovalicarb. For a better overview of the results of both adsorption/desorption studies a short summary is given at the end of this chapter at page 84.

In addition an estimation of the adsorption coefficient of iprovalicarb on soil using high performance liquid chromatography was performed to show whether there could be a difference in the adsorption behaviour of the two diastereomers on soil or not ([redacted] (2012), submitted in this Dossier, KIIA 7.4.1 /03).

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The study was not available at Annex I submission. The new study was included since it enlarged the data set on adsorption data.

Report:	**KIIA 7.4.1 /02, [redacted].; 2000**
Title:	Soil adsorption/desorption of SZX 0722 TÈCNICO
Report No:	M10222
Document No:	M-033366-01-1
Guidelines:	IBAMA, Manual de testes para avaliação da ecotoxicidade de agentes químicos, Brasília, 1990, Part E3, Teste para avaliação da adsorção/dessorção, review/1996
GLP:	Yes

Executive Summary

The adsorption/desorption of phenyl-labelled iprovalicarb was investigated in three Brazilian soils with different textures (fine clayley, very fine clayley and fine loamy soil).
Iprovalicarb was applied to soil samples at four different concentrations: 0.0724, 0.2, 1.0 and 6.7 µg/mL.
The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.76 to 4.64 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 44 and 221 mL/g with an arithmetic mean of 132 mL/g.

I. Material and Methods

A. Materials

1. Test Material: [phenyl-UL-^{14}C]iprovalicarb
CAS #: 140923-17-7
Specific radioactivity: 138 µCi/mg (corresponding to 5.1 MBq/mg)
Radiochemical purity: 99%

2. Soil: Three Brazilian soils with different textures were used were collected freshly from the field. The soils were collected at 0 – 20 cm depth in the soil profile. Soil samples were air-dried and sieved through a 2.0 mm screen. The soil characteristics are summarised in Table 7.4.1- 1.

Table 7.4.1- 1: Soil characteristics

Parameter	Soil GH	Soil LR	Soil LE
Brazilian taxonomy	Gleissolo Melânico Alumínico incéptico	Latossolo Vermelho Distroferríco típico e	Latossolo Vermelho Distrofico psamítico
American taxonomy	Gley humic, high aluminum, low clay activity (Cumulic Humaquept)	Dusky red latosol distrofic, ochrid epipedon (Rhodic Hapludox)	dark red latosol, high aluminium, ochrid epipedon (Typic Hapludox)
American texture	fine clay	very fine clay	fine loam
Texture			
- sand [%]	9	51	68
- silt [%]	25	10	8
- clay [%]	66	39	24
pH in $CaCl_2$	6.4	5.7	6.4
Organic matter [%]	6.1	3.02	0.6
Organic carbon [%]	3.54	1.74	0.35
CEC$^{a)}$ [mmol/kg]	2875.0	151.5	111.7

a) CEC = cation exchange capacity

B. Study design

1. Experimental conditions: The tests of adsorption and desorption were carried out with four concentrations of a.s. (0.0724, 0.2, 1.0 and 6.7 mg/L).
For the application solution A phenyl-labelled iprovalicarb was dissolved in 1000 µL acetone, resulting in a solution containing 100 µCi/mL of radioactivity (725 µg iprovalicarb/mL). For the solution B 27.8 µL of solution A was dissolved in 5.0 mL of $CaCl_2$ 0.01mol/L, resulting in a concentration of 0.56 µCi/mL of radioactivity (4.03 µg iprovalicarb/mL). For solution C 10.78 mg of non radiolabelled iprovalicarb was dissolved in 10 mL acetone using a volumetric flask, resulting in a concentration of 1.04 mg iprovalicarb/mL. The preparation of the treatment solutions is given in Table 7.4.1- 2.

Table 7.4.1- 2: Preparation of the treatment solutions

Concentration [µg/mL]	Volume solution B [µL]	Volume solution C [µL]	Final volume [mL]
0.0724	900	-	50
0.2	900	6.1	50
1.0	900	44.7	50
6.7	900	319.2	50

- **Adsorption phase:** The test was carried out in duplicate using centrifuge tubes containing 1.0 g soil and 2 mL treatment solutions. Immediately after the solutions were added to the soils, the tubes were agitated vigorously for 1 minute with a vortex mixer. The tubes were then shaken for 48 hours in the dark at24 - 26°C, and then centrifuged for 20 minutes. From the supernatant, 1.0 mL was removed, in duplicates, and placed into scintillation vials for LS analysis.

- **Desorption phase:** From the above test, the remaining solution in the centrifuge tubes was pipetted into a disposable bottle for radiochemical analysis. After complete drainage of solution, tubes were filled with 5.0 mL of 0.01 mol/L $CaCl_2$, placed on a shaker for 48 hours. The samples were then centrifuged for 20 minutes. 1.0 mL was pipetted and radioassayed as described above.

2. **Analytical procedures:** The samples were centrifuged and aliquots of the supernatant were removed for LS-measurement to quantify the amount of iprovalicarb remaining in the solution. The amount of adsorbed product was then calculated.

II. Results and Discussion

The ^{14}C-concentrations measured in the adsorption- and desorption solutions after equilibration were used to calculate adsorption- and desorption-isotherms as well as distribution coefficients (K_{oc} values).

- **Adsorption**

The proportion of iprovalicarb being adsorbed on soil GH ranged from 68.0% to 74.8%. Adsorption rate on soil LR ranged from 21.4% to 38.6%, and that of soil LE ranged from 22.1% to 36.5%. The values are not mentioned in the report but calculated for this summary (see Table 7.4.1- 3).

Table 7.4.1- 3: Proportions of iprovalicarb being adsorbed in three Brazilian soils

Test concentration [µg/mL]	Proportions iprovalicarb adsorbed[a)] [%] Soil		
	GH	LR	LE
0.0724	74.6	38.6	36.5
0.2	74.8	35.6	34.8
1.0	72.6	30.6	31.3
6.7	68.0	21.4	22.1

a) values are not mentioned in the report, they were calculated for this summary

The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.77 to 4.64 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 44 and 221 mL/g with an arithmetic mean of 132 mL/g

(Table 7.4.1- 4).

Table 7.4.1- 4: Adsorption of phenyl-labelled iprovalicarb to three Brazilian soils

Soil	1/n	K_f [mL/g]	K_{oc} [mL/g]	r^2
GH	0.93	4.64	131	0.9994
LR	0.83	0.76	44	0.9988
LE	0.85	0.77	221	0.9979
arith. mean			*132*	

- **Desorption**

After the adsorption step it was tested to which extent the initially adsorbed iprovalicarb could be desorbed from the test soils. On the basis of these data the determined K_f values were in the range of 0.76 to 1.43 mL/g. The corresponding K_{oc} values were in the range of 40 to 224 mL/g (Table 7.4.1- 5).

Table 7.4.1- 5: Desorption of phenyl-labelled iprovalicarb in three Brazilian soils

Soil	1/n	K_f [mL/g]	K_{oc} [mL/g]	r^2
GH	1.04	1.43	40	0.9964
LR	1.06	0.76	44	0.9997
LE	1.03	0.78	224	0.9999
arith. mean			*103*	

III. Conclusions

The adsorption constants K_f that were calculated from the FREUNDLICH-isotherms for iprovalicarb range from 0.76 mL/g to 4.64 mL/g. The respective K_{oc} values range from 44 mL/g to 221 mL/g.

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The new study was included to show whether there could be a difference in the adsorption behaviour of the two diastereomers of iprovalicarb on soil or not.

Report: **KIIA 7.4.1 /03, [redacted] 2012**
Title: Iprovalicarb: Estimation of the adsorption coefficient (K_{oc}) on soil using high performance liquid chromatography
Report No: MEF-11/981
Document No: M-427058-01-1
Guidelines: OECD-Guideline for Testing of Chemicals No.: 121. Estimation of the Adsorption Coefficient (K_{oc}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC), adopted 22nd January 2001
GLP: Yes

Executive Summary

The HPLC-K_{oc} values for the two diastereomers of iprovalicarb (S,R- and S,S-configuration) were

determined by investigation of their retention behaviour on a cyanopropyl HPLC column run in reverse phase mode. Based on these results an estimation regarding the adsorption behaviour of the two diastereomers on soil was made. A citrate buffered test system (pH 6) was used to investigate the retention behaviour of the two test items on a cyanopropyl column run in reverse phase mode. Six reference items for which K_{oc} values are known from the literature were chromatographed in duplicate on a cyanopropyl HPLC column, covering a K_{oc} range from 18 mL/g to 389 mL/g. Sodium nitrate was used for determination of the void volume of the chromatographic system. Thus, average capacity factors (k') were derived for each reference item in the test system, and a linear calibration plot was established for measured log k' values vs. literature log K_{oc} values:

Calibration function slope = 2.47, intercept = 2.28, R^2 = 0.90

The capacity factors of the test items and their equimolar mixture were determined by replicate analysis within the same autosampler worklist as used for the analysis of the reference items.
The two test items eluted with an identical retention time of 7.2 min from the cyanopropyl HPLC column run in reverse phase mode (separate injection of the test items). The analysis of the equimolar mixture of the test items resulted in one, symmetric peak, eluting with the retention time of the single test items.
The K_{oc} values of the single diastereomers and their equimolar mixture were deduced from the established calibration plot (Table 7.4.1- 6).

Table 7.4.1- 6: Iprovalicarb: log K_{oc} and K_{oc} values for the single diastereomers and their equimolar mixture

Compound	log K_{oc}	K_{oc} [mL/g]
S,R-configured isomer	2.34	220
S,S-configured isomer	2.34	220
equimolar mixture	2.34	220

Since the K_{oc} values determined according to the OECD Test Guideline No. 121 were identical for the two diastereomers, it was concluded that also the adsorption behaviour on soil is identical for both diastereomers.

I. Material and Methods

A. Materials

1. Test material: Test item: iprovalicarb: single diastereomers (S,R- and S,S configured) and equimolar mixture of both diastereomers

Reference items: acetanilide, carbaryl, carbofuran, isoproturon, linuron, phenol, sodium nitrate

2. Test system: A high pressure liquid chromatography system was used as test system, fitted with a pulse-free binary pump and a flow-through radioactivity as well as UV absorbance detector. A commercially available cyanopropyl-bonded column was used. Peak integration was done manually by selecting the peak start and stop times for each analysis. The peak areas were evaluated as "regions of interest". The test system for estimation of the soil adsorption coefficient of iprovalicarb was based on an isocratic chromatographic method using a pre-mixed eluent consisting of 45% aqueous citrate buffer (0.01 M, pH 6) and 55% methanol (v/v) according to the OECD Test

Guideline No. 121. Special effort was made to develop a chromatographic method, which allows the separation of the two diastereomers of iprovalicarb to determine the diasteromeric ratio of the stock solution. Therefore, a special cross-linked trifunctional C18-stationary phase, developed for challenging separations, combined with gradient elution (buffered, acidic eluent system (pH 2.75)) was used.

B. Study design

1. Test item:

Stock solutions: To yield a nominal concentration of 2 mg/mL for the stock solution 1.12 mg of the S,R-configured diastereomer of iprovalicarb and 1.09 mg of the S,S-configured diastereomer were dissolved in 56 µL and 545 µL MeOH, respectively. For preparation of a stock solution containing an equimolar mixture of both diastereomers, 86 µL of the stock solution of the S,R-configured diastereomer were mixed with 100.0 µL of stock solution of the S,R-diastereomer. The diasteromeric ratio of the resulting stock solution was determined by HPLC/UV detection to be approximately 1:1.

Test solutions: For analysis with the chromatographic method mentioned above the stock solutions were diluted 1:20 (*v:v*) with the eluent of this chromatographic method.

1. Reference items:

Stock solutions:

Acetanilide:	1.65 mg of acetanilide was dissolved in 825 µL MeOH to yield a nominal concentration of 2 mg/mL. Following, 100 µL of this solution were diluted with 900 µL MeOH (1:10, v/v) to yield a final stock solution with a nominal concentration of 0.2 mg/mL.
Carbaryl:	1.32 mg of carbaryl was dissolved in 660 µL MeOH to yield a nominal concentration of 2 mg/mL. Following, 250 µL of this solution were diluted with 750 µL MeOH (1:4, v/v) to yield a final stock solution with a nominal concentration of 0,5 mg/mL.
Carbofuran:	1.23 mg of carbofuran was dissolved in 615 µL MeOH to yield a nominal concentration of 2 mg/mL.
Isoproturon:	1.07 mg of isoproturon was dissolved in 535 µL MeOH to yield a nominal concentration of 2 mg/mL. Following, 100 µL of this solution were diluted with 900 µL MeOH (1:10, v/v) to yield a final stock solution with a nominal concentration of 0.2 mg/mL.
Linuron:	1.49 mg of linuron was dissolved in 745 µL MeOH to yield a nominal concentration of 2 mg/mL. Following, 100 µL of this solution were diluted with 900 µL MeOH (1:10, v/v) to yield a final stock solution with a nominal concentration of 0.2 mg/mL.
Phenol:	1.21 mg of phenol was dissolved in 605 µL MeOH to yield a nominal concentration of 2 mg/mL.
Sodium nitrate:	no stock solution was prepared for sodium nitrate.

Test solutions: For analysis with the chromatographic method mentioned above the stock solutions of the reference items were diluted 1:20 (*v:v*) with the eluent of this chromatographic method. The

test solution concentration for each reference item was chosen to yield an UV-signal (peak height) between 50 to 200 mV at 263 nm. The following test solutions of reference items were prepared (Table 7.4.1- 7):

Table 7.4.1- 7: Test solutions: Nominal concentrations of the reference items

Compound	Nominal concentration [µg/mL]
Acetanilid	10
Carbaryl	50
Carbofuran	100
Isoproturon	10
Linuron	10
Phenol	100
Sodium nitrate[a)]	2000

a) the test solution of sodium nitrate was prepared by dissolving 2 mg of sodium nitrate directly in 1000 µL of the eluent of the chromatographic method mentioned above, yielding a nominal concentration of 2 mg/mL

3. Retention parameters: For determination of the retention times (t_R) of the test and reference items in the chromatographic systems the test solutions were injected individually and in replicate, together within the same autosampler worklist. Each reference item was run once before and once after the single diastereomers of iprovalicarb and the equimolar mixture of the test items, to minimise influence of possible retention time drift. Injection of sodium nitrate was carried out at the beginning and at the end of the analytical series. Since sodium nitrate is unretained on reversed phase columns, its retention time is equal to the void volume (t_0) of the chromatography system.

4. Evaluation:

Calculation of capacity factors: The capacity factors (k') of the test and reference items were calculated from the system void volume (t_0, mean of all replicates) and the retention times (t_R, single measurements) of the test and reference items according to the following formula

$$k' = \frac{t_R - t_0}{t_0}$$

Following, the average capacity factors were calculated (arithmetic mean) for the test and reference items.

Determination of log K_{oc} of the test items: Using the HPLC estimation method, the adsorption coefficients (K_{oc}) of the test items are deduced from their capacity factors (single and mean values), by means of a linear calibration plot established for measured log k' versus known log K_{oc} of the reference items. Therefore, measured mean log k' data of the reference items were plotted versus their literature log K_{oc} data. Linear re[redacted]sion was used for statistical evaluation, and the log K_{oc} data of the test items were calculated as follows

$$\log K_{oc} = \text{slope} \cdot \log k' + \text{intercept}$$

Statistical methods:

- Linear re[redacted]sion analysis was used for the reference item calibration plot to determine the log K_{oc} data of the test items (Microsoft® Excel).
- Arithmetic means of the capacity factors (k') of the reference and test items were used for the plot of the log k' data vs the log K_{oc} data.

- Standard deviation was calculated for the capacity factors k' by the following formula:

$$\sqrt{\frac{\sum(x-\bar{x})^2}{n}}$$

- Outlier rejection criteria were not used

II. Results and Discussion

A. Calibration plots

The chromatographic systems were calibrated using the six reference items, which covers a K_{oc} range from 18 mL/g to 389 mL/g. The employed reference items were heterogeneous in chemical nature, including compounds with structural relationship to the test item (aromatic ring systems, peptide bonds). No trend for irregular behaviour was observed for any specific structural elements.
Sodium nitrate was used for determination of the void volume of the chromatographic systems.
The void volume of the chromatographic system was determined to be t_0 = 3.5 min and the following linear calibration function was established for the plot of measured log k' values of the reference items vs. their literature log K_{oc} values (correlation coefficient R^2 = 0.90)

$$\log K_{oc} = 2.47 \cdot \log k' + 2.28$$

HPLC retention data and calculation of capacity factors (k') for the reference items are provided in Table 7.4.1- 8.

Table 7.4.1- 8: Synopsis of retention times and capacity factors of calibration curve and final test

Compound	R_t [min]	k'	log k'	log K_{oc} a)	K_{oc} b) [mL/g]
Reference items					
Sodium nitrate	3.5				0
Acetanilid	4.9 4.9	0.400 0.400	- 0.40	1.25	18
Phenol	4.9 4.9	0.400 0.400	- 0.40	1.32	21
Carbofuran	5.5 5.4	0.571 0.543	- 0.25	1.66	46
Isoproturon	6.5 6.5	0.857 0.857	- 0.07	1.86	72
Carbaryl	6.3 6.3	0.800 0.800	- 0.10	2.32	211
Linuron	8.2 8.1	1.343 1.314	0.12	2.59	389
Test item					
S,R-configured diastereomer of iprovalicarb	7.2 7.2	1.057 1.057	0.02	2.34	220
S,S-configured diastereomer of iprovalicarb	7.2 7.2	1.057 1.057	0.02	2.34	220
equimolar mixture of the S,R- and S,S-configured diastereomers of iprovalicarb	7.2 7.2	1.057 1.057	0.02	2.34	220

a) reference items: literature values
test item: values calculated from calibration function
b) reference items: values calculated by antilog-transformation from literature log K_{oc} values
test item: values calculated by antilog-transformation from calculated log K_{oc} values

B. Test results

Iprovalicarb was retained on the cyanopropyl column run in reversed phase mode. Its single diastereomers eluted with identical retention times (separate injection of the test items). The analysis of the equimolar mixture of the two diastereomers resulted in one, symmetric peak, eluting with the retention time of the single test items.

The average capacity factors (k') and log k' values determined for the single diastereomers of iprovalicarb and their equimolar mixture are summarised in Table 7.4.1- 9. Based on these results, the K_{oc} values were calculated and also summarised in Table 7.4.1- 9. The measured capacity factors of the test items fell within the range covered by the calibration series, thus at least the capacity factor of one of the reference items was above and one was below the capacity factors of the test items.

Table 7.4.1- 9: Iprovalicarb: k', log k' and K_{oc} values for the single diastereomers and their equimolar mixture

Compound	k'	log k'	K_{oc} [mL/g]
S,R-configured diastereomer	1.057	0.02	220
S,S-configured diastereomer	1.057	0.02	220
equimolar mixture of the S,R- and S,S-configured diastereomers	1.057	0.02	220

The results indicate an identical adsorption behaviour of the two diastereomers of iprovalicarb. Therefore, all higher tier tests investigating the adsorption behaviour of iprovalicarb can be carried out with the equimolar mixture of the two diastereomers of iprovalicarb. Moreover, these results allow for a combined leaching assessment of the S,R- and S,S-configured diastereomers of iprovalicarb.

III. Conclusions

The K_{oc} values determined for the single diastereomers of iprovalicarb using the HPLC method according to OECD Test Guideline No. 121 were identical, and were calculated to be 220 mL/g. These K_{oc} values are in agreement with the soil adsorption coefficients determined for iprovalicarb by the batch equilibrium method ([redacted], 1996; submitted within the EU Basic Dossier 1998, (IIA, 7.1.2/ 01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)) and Bonetti, 2000 (submitted in this Dossier, KIIA 7.4.1 /02)).
Since the K_{oc} values determined according to OECD Test Guideline No. 121 were identical for the single diastereomers of iprovalicarb, it was concluded that also the adsorption behaviour on soil is identical for both diastereomers.
The results indicate an identical adsorption behaviour of the two diastereomers of iprovalicarb. Therefore, all higher tier tests investigating the adsorption behaviour of iprovalicarb can be carried out with the equimolar mixture of the two diastereomers of iprovalicarb. Moreover, these results allow for a combined leaching assessment of the S,R- and S,S-configured diastereomers of iprovalicarb.

Summary: Adsorption/desorption data of iprovalicarb

The adsorption/desorption behaviour of iprovalicarb was investigated in two batch equilibrium studies. One study was submitted within the EU Basic Dossier in 1998 ([redacted](1996), IIA, 7.1.2/01). A second study is summarised in this Dossier (Bonetti (2000), KIIA 7.4.1 /02). In addition HPLC-K_{oc}-values for the two diastereomers of iprovalicarb (S,R- and S,S-configuration) were determined to show whether there could be a difference in the adsorption behaviour of the two diastereomers of iprovalicarb ([redacted], 2012, summarised in this Dossier, KIIA 7.4.1 /03).
For a better overview of the results of these adsorption/desorption studies a short summary is given below.

The adsorption/desorption of iprovalicarb was investigated in three US, one German and three Brazilian soils. The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.60 to 4.64 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 44 and 221 mL/g with an arithmetic mean of 114 mL/g. The desorption constants K_f were in the range of 0.76 to 3.61 mL/g and the corresponding K_{oc} values ranged from 40 to 372 mL/g. A summary of the adsorption/desorption data of iprovalicarb based on batch equilibrium studies is given in Table 7.4.1- 10.

Table 7.4.1- 10: Summary of the adsorption/desorption data of iprovalicarb

Soil	Adsorption				Desorption			
	1/n	K_f [mL/g]	K_{oc} [mL/g]	r^2	1/n	K_f [mL/g]	K_{oc} [mL/g]	r^2
[redacted], Germany[a)]	0.9150	0.8360	121	0.9999	0.9346	1.8881	274	0.9998
[redacted], USA[a)]	0.8595	1.0037	90	0.9988	0.9123	2.4939	223	0.9997
[redacted], USA[a)]	0.8410	1.2682	131	1.0000	0.8139	3.6051	372	0.9990
[redacted], USA[a)]	0.8821	0.6003	61	0.9999	0.7809	1.7453	176	0.9941
[redacted], Brazil[b)]	0.93	4.64	131	0.9994	1.04	1.43	40	0.9964
[redacted], Brazil[b)]	0.83	0.76	44	0.9988	1.06	0.76	44	0.9997
[redacted], Brazil[b)]	0.85	0.77	221	0.9979	1.03	0.78	224	0.9999
arith. mean			*114*				*103*	

a) [redacted] (1998), submitted within the EU Basic Dossier in 1998, IIA, 7.1.2/01
(One soil ([redacted]) was decided not to be used for further assessments, as it is considered as an extreme sandy soil with an organic carbon content < 0.3 % (0.2%).)
b) [redacted] (2000), submitted in this Dossier, KIIA 7.4.1 /02

Since the K_{oc} values determined for the single diastereomers of iprovalicarb using the HPLC method were identical for the two diastereomers it was concluded that also the adsorption behaviour on soil is identical for both diastereomers. Therefore, all higher tier tests investigating the adsorption behaviour of iprovalicarb can be carried out with the equimolar mixture of the two diastereomers of iprovalicarb. Moreover, these results allow for a combined leaching assessment of the S,R- and S,S-configured diastereomers of iprovalicarb.

KIIA 7.4.2 Adsorption & desorption of rel. metabolites, degr. & react. Products

In soil metabolism studies with iprovalicarb under aerobic conditions two major metabolites (> 10% of the applied radioactivity) were identified: SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)*. Under anaerobic conditions N-acetyl-PMPA *(M15)* was formed a major metabolite in the anaerobic soil metabolism study. For the metabolite PMPA *(M10)* an adsorption/desorption study was submitted within the EU Basic Dossier in 1998 ([redacted] (1996), IIA, 7.1.2 /02). Nevertheless, a short summary of these data is given at page 101. For the two other major metabolites SZX 0722-carboxylic acid *(M03)* and N-acetyl-PMPA *(M15)* additional adsorption studies were performed and summarised in this dossier (KIIA 7.4.2 /02, KIIA 7.4.2 /03 and KIIA 7.4.2 /04).
For a better over view of the adsorption/desorption data of the major iprovalicarb a short summary is given at the end of this section at page 105.

- **SZX 0722-carboxylic acid *(M03)***

SZX 0722-carboxylic acid *(M03)* was found a major metabolite in the new aerobic soil metabolism study conducted with the valine labelled parent compound. Therefore, the adsorption/desorption behaviour of SZX 0722-carboxylic acid *(M03)* was performed based on batch equilibrium procedure ([redacted] (2012), submitted in this Dossier, KIIA 7.4.2 /02). In addition an estimation of the adsorption coefficient of SZX 0722-carboxylic acid *(M03)* on soil using high performance liquid chromatography was performed to show whether there could be a difference in the adsorption behaviour of the two diastereomers on soil or not ([redacted] (2012), submitted in this Dossier, KIIA 7.4.2 /03).

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The new study was performed because SZX 0722-carboxylic acid *(M03)* was found a major metabolite in the new aerobic soil metabolism study conducted with the valine label (KIIA 7.1.1 /04).

Report:	**KIIA 7.4.2 /02, [redacted] 2012**
Title:	[Valine-1-^{14}C]SZX 0722-carboxylic acid: Adsorption/Desorption on five soils
Report No:	MEF-11/986
Document No:	M-428013-01-1
Guidelines:	- SANCO/11802/2010 Rev. 00, Draft Commission Regulation laying down the requirements for the dossier to be submitted for the approval of active substances contained in plant protection products, 2010 - SANCO/11844/2010 Rev. 00, Draft Commission Communication in the framework of the implementation of Commission Regulation (EU) No [SANCO/11802/2010]/2010 as regards the requirements for the dossier to be submitted for the approval of an active substance, 2010 - OECD Guideline for the Testing of Chemicals No. 106, Adsorption/Desorption, January 21st, 2000 - US EPA Fate, Transport and Transformation Test Guidelines, OPPTS 835.1230, Adsorption/Desorption (Batch Equilibrium), October 2008 - Canada PMRA, Environmental Chemistry and Fate, Guidelines for registration of Pesticides in Canada, PMRA DACO No. 8.2.4.2, 1987
GLP:	Yes

Executive Summary

In batch equilibrium experiments the adsorption/desorption behaviour of valine-labelled SZX 0722-carboxylic acid *(M03)* was investigated in five German soils originating from the sites [redacted] (AXXa), [redacted], [redacted], [redacted] II and [redacted] ([redacted]).

The adsorption phase of the study was carried out using air-dried soils pre-equilibrated in aqueous $CaCl_2$ solution containing $HgCl_2$ with a soil-to-solution ratio of 1:1.3 for the soils [redacted] (AXXa) and [redacted] II and a soil-to-solution ratio of 1:1 for the soils [redacted], [redacted] and [redacted] ([redacted]). SZX 0722-carboxylic acid was applied at nominal concentrations of 1.0, 0.3, 0.1, 0.03 and 0.01 mg/L in aqueous $CaCl_2$ solution. The adsorption phase was carried out for 48 hours followed by one desorption phase of 24 hours in the

dark at 20°C.
The calculated adsorption constants $K_{F(ads)}$ of the Freundlich isotherms ranged from 0.012 to 0.354 mL/g (mean: 0.118 mL/g). These values were normalised to the organic carbon content and corresponded to K_{oc} values ranged between 0.6 and 13.1 mL/g (mean: 5.2 mL/g). The Freundlich exponents 1/n were in the range of 0.9232 to 1.1069 (mean: 1.0250).
Due to low adsorption (<5% AR) in three soils the desorption experiments were not evaluated for these soils. The desorption constants $K_{f(des)}$ in the two other soils were in the range of 1.23 to 2.06 mL/g and the corresponding K_{oc} values ranged from 72.2 to 76.2 mL/g. The desorption $K_{f(des)}$ and the normalised $K_{oc(des)}$ values were significantly higher (5.8 to 8.6 times higher) than those obtained for the adsorption phase, indicating that the amount of test item once adsorbed to soil is not readily desorbed.

I. Material and Methods

A. Materials

1. Test material: [valine-1-^{14}C]SZX 0722-carboxylic acid
(equimolare mixture of S,R and S,S diastereomers)
Specific radioactivity: S,R: 3.39 MBq/mg (91.72 µCi/mg)
S,S: 3.33 MBq/mg (89.92 µCi/mg)
Radiochemical purity: S,R: > 98% (HPLC, radioactivity detector)
S,S: > 99% (HPLC, radioactivity detector)

2. Soil: The soil samples were collected freshly from the field. The soils were sieved to a particle size of ≤ 2 mm and stored refrigerated at ≤ 8°C for 1 to 6 months. Details of the soil samples are given in Table 7.4.2.1.

Table 7.4.2- 1: Soil characteristics

Parameter	Soil				
	[redacted] AXXa	[redacted] 4a	[redacted]	[redacted] II	[redacted]
Geographic location - city - state - country	[redacted] NRW[a)] Germany	[redacted] NRW[a)] Germany	[redacted] NRW[a)] Germany	[redacted] NRW[a)] Germany	[redacted] NRW[a)] Germany
Soil taxonomic classification (USDA)	sandy, mixed, mesic, Typic Cambudolls	loamy, mixed, mesic, Typic Argudalfs	N/A[b)]	N/A[b)]	loamy, mixed, mesic, Typic Argudalfs
Soil series	N/A[b)]	N/A[b)]	N/A[b)]	N/A[b)]	N/A[b)]
Soil mapping unit (GPS coordinates)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Texture class (USDA) - sand (50 µm – 2 mm) [%] - silt (2 µm – 50 µm) [%] - clay (< 2 µm) [%]	sandy loam 73 20 7	silt loam 15 70 15	silt loam 31 54 15	loam 37 40 23	sandy loam 53 30 17
pH (soil:solution) in: - 0.01 M $CaCl_2$ (1:2) - water (1:1) - saturated paste - 1 N KCl (1:1)	 6.0 6.2 6.3 5.8	 6.5 6.7 6.8 6.1	 5.3 5.7 5.8 4.9	 7.3 7.5 7.4 7.0	 5.1 5.4 5.5 4.7
Organic matter[c)] [%]	3.1	2.8	4.7	7.6	2.9
Organic carbon [%]	1.8	1.6	2.7	4.4	1.7
CEC[d)] [meq/100 g]	9.1	11.6	9.6	19.2	9.9
Water holding capacity at: - 0.1 bar (pF 2.0) [%] - 0.33 bar (pF 2.5) [%]	 13.8 11.7	 31.7 21.9	 36.7 25.6	 41.1 34.7	 20.1 16.5
Bulk density [g/cm³]	1.19	1.11	1.04	0.98	1.08

a) NRW = North Rhine-Westphalia
b) N/A = not applicable
c) calculated: %organic matter = % organic carbon × 1.724
d) CEC = cation exchange capacity

B. Study design

1. Experimental conditions: The adsorption phase of the study was carried out using air-dried soils pre-equilibrated in aqueous 0.01 M $CaCl_2$ solution containing $HgCl_2$ (approx. 50 mg/L) with a soil-to-solution ratio of 1:1.3 for the soils [redacted] AXXa and [redacted] II and a soil-to-solution ratio of 1:1 for the soils [redacted], [redacted] and [redacted]. SZX 0722-carboxylic acid *(M03)* was applied at nominal concentrations of 1.0, 0.3, 0.1, 0.03 and 0.01 mg/L in aqueous 0.01 M $CaCl_2$ solution. The desorption phase was performed by supplying pre-adsorbed soil samples with fresh aqueous 0.01 M $CaCl_2$ solution containing $HgCl_2$ (approx. 50 mg/L) for one desorption cycle. The adsorption phase was carried out for 48 hours followed by one desorption phase of 24 hours in the dark at 20°C.

2. Analytical procedures: The aqueous supernatant after adsorption and desorption was

separated by centrifugation and the amount of SZX 0722-carboxylic acid in the supernatants were analysed by liquid scintillation counting (LSC). After desorption the soils were extracted, dried and combusted. The trapped $^{14}CO_2$ after combustion was measured by LSC.

II. Results and Discussion

The test item was sufficient stable throughout the study. The parental mass balance for all soils was in the range of 91.6 to 99.4% of the applied radioactivity (AR) (mean: 96.6% AR) for at least 72 hours.

Overall mass balances were established during the definitive test by determination of the radioactivity content of the $CaCl_2$ supernatants of the adsorption and desorption phases as well as of the remaining soils using LSC measurements and combustion/LSC, respectively. The recovery of the applied radioactivity for all concentrations and soils was in the range of 96.2 to 110.0% AR (mean: 100.8% AR). The recovery of radioactivity after adsorption and desorption is summarised in Table 7.4.2- 2.

Table 7.4.2- 2: Overall material balance for soils after adsorption, desorption and combustion expressed as percentage of applied radioactivity (measured in duplicates)

Test concentration [mg/L]	Soil				
	[redacted] AXXa	[redacted] 4a	[redacted]	[redacted] II	[redacted]
1.0	100.0 101.0	99.2 99.5	99.4 99.5	99.2 99.2	101.7 99.5
0.3	102.1 101.6	100.4 100.6	99.2 100.8	100.5 97.3	99.7 99.5
0.1	101.6 102.7	102.5 102.3	101.2 102.1	100.9 101.7	100.7 100.8
0.03	102.5 101.9	102.3 101.7	99.2 101.2	101.5 100.9	100.9 100.2
0.01	110.0 106.5	100.7 102.0	100.1 99.5	99.4 99.9	98.6 96.2
mean	*103.0*	*101.4*	*100.2*	*100.1*	*99.8*
for all soils:					
mean:	*100.8*				
min:	*96.2*				
max:	*110.0*				

- **Adsorption**

In the definitive adsorption test 2.5 - 4.0% AR, 0.1 - 2.4% AR, 13.6 – 25.6% AR, 1.2 - 4.6% AR and 12.7 – 16.9% AR were adsorbed in soils [redacted] AXXa, [redacted], [redacted], [redacted] II and [redacted], respectively (see Table 7.4.2- 3).

Table 7.4.2- 3: Percentage of SZX 0722-carboxylic acid *(M03)* at the end of adsorption equilibrium in five German soils (in percent of the applied radioactivity)

Test concentration [mg/L]	Portions of SZX 0722-carboxylic acid *(M03)* adsorbed [%] Soil				
	[redacted] AXXa	[redacted] 4a	[redacted]	[redacted] II	[redacted]
1.0	4.0	1.8	23.7	2.7	12.7
0.3	3.1	1.0	21.5	3.5	14.1
0.1	3.3	n.e.	25.6	1.2	13.6
0.03	3.1	0.1	23.4	2.7	14.4
0.01	2.5	2.4	13.6	4.6	16.9

n.e. = not evaluated

The calculated adsorption constants $K_{f(ads)}$ of the Freundlich isotherms for the five test soils ranged from 0.012 to 0.354 mL/g (mean: 0.118 mL/g). These values were normalised to the organic carbon content and corresponded to K_{oc} values ranged between 0.6 and 13.1 mL/g (mean: 5.2 mL/g). The Freundlich exponents 1/n were in the range of 0.9232 to 1.1069 (mean: 1.0250) (Table 7.4.2- 4).

Table 7.4.2- 4: Adsorption constants of SZX 0722-carboxylic acid *(M03)* in five German soils

Soil	$K_{f(ads)}$ [mL/g]	1/n	$K_{oc(ads)}$ [mL/g]	r^2
[redacted] AXXa	0.054	1.1007	3.0	0.9817
[redacted] 4a	0.012	1.0551	0.7	0.7494
[redacted]	0.354	1.1069	13.1	0.9831
[redacted] II	0.028	0.9232	0.6	0.7781
[redacted]	0.143	0.9393	8.4	0.9984
arith. mean	*0.118*	*1.0250*	*5.2*	*0.8981*

- **Desorption**

After the end of adsorption and first desorption phase, 31.5 – 34.8%, and 31.6 – 42.4% of the initially adsorbed amount were desorbed in soils [redacted] and [redacted], respectively. Due to low adsorption (<5% AR) in the soils [redacted] AXXa, [redacted] and [redacted] II the desorption experiments were not evaluated for these soils (Table 7.4.2- 5).

Table 7.4.2- 5: Percentage of SZX 0722-carboxylic acid *(M03)* at the end of desorption equilibrium in five German soils (expressed as percentage of the initially adsorbed material, one desorption step for all concentrations)

Test concentration [mg/L]	Portions of SZX 0722-carboxylic acid *(M03)* desorbed [% of the initial adsorbed material] Soil				
	[redacted] AXXa	[redacted] 4a	[redacted]	[redacted] II	[redacted]
1.0	60.5	40.1	31.5	12.1	37.6
0.3	70.5	60.4	33.9	n.e	40.3
0.1	77.2	n.e.	34.5	20.2	42.4
0.03	80.7	n.e.	34.8	14.6	40.0
0.01	46.7	47.9	32.3	5.8	31.6

n.e. = not evaluated

The desorption $K_{f(des)}$ and the normalised $K_{oc(des)}$ values were significantly higher (5.8 to 8.6 times higher) than those obtained for the adsorption phase, indicating that the amount of test item once adsorbed to soil is not readily desorbed (Table 7.4.2- 6).

Table 7.4.2- 6: Desorption constants of SZX 0722-carboxylic acid *(M03)* in German soils

Soil	$K_{f(des)}$ [mL/g]	1/n	$K_{oc(des)}$ [mL/g]	r^2
[redacted] AXXa	n.e. [a]			
[redacted] 4a	n.e. [a]			
[redacted] II	2.057	1.0062	76.2	0.9980
[redacted]	n.e. [a]			
[redacted]	1.227	0.9480	72.2	0.9893
arith. mean	*1.642*	*0.9771*	*74.2*	*0.9936*

a) due to low adsorption (K_{oc} < 1 mL/g) the desorption experiment was not evaluated for these soils

III. Conclusions

The adsorption constants $K_{f(ads)}$ of SZX 0722-carboxylic acid *(M03)* for the five test soils calculated based on the Freundlich isotherms ranged from 0.012 to 0.354 mL/g (mean: 0.118 mL/g). The respective $K_{oc(ads)}$ values were in the range of 0.6 and 13.1 mL/g (mean: 5.2 mL/g).
The desorption constants $K_{f(des)}$ of SZX 0722-carboxylic acid were significantly higher (up to 8.6 times) than the respective adsorption constants, indicating a strengthened binding of the test item once adsorbed to the soils representing conditions relevant for the environment.

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The new study was included to show whether there could be a difference in the adsorption behaviour of the two diastereomers of iprovalicarb on soil or not.

Report:	**KIIA 7.4.2 /03, [redacted] 2012**
Title:	[Valine-1-^{14}C]SZX 0722-carboxylic acid: Estimation of the adsorption coefficient (K_{oc}) on soil using high performance liquid chromatography
Report No:	MEF-11/958
Document No:	M-427055-01-1
Guidelines:	OECD-Guideline for Testing of Chemicals No.: 121. Estimation of the Adsorption Coefficient (K_{oc}) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC), adopted 22nd January 2001
GLP:	Yes

Executive Summary

The adsorption behaviour of the two diastereomers of SZX 0722-carboxylic acid *(M03)* (S,R- and S,S-configuration) on soil was estimated using the HPLC method according to OECD Guideline for Testing of Chemicals No. 121. Therefore, the retention behaviour of the test items on a cyanopropyl HPLC-column run in reverse phase mode was investigated. Based on these results the K_{oc} values of the two diastereomers of SZX 0722-carboxylic acid on soil were calculated.

Two test systems were used to investigate the retention behaviour of the two test items on a cyanoproyl column run in reversed phase mode. The first test system was an isocratic, citrate buffered chromatographic system (pH 6), which is a standard system recommended by the OECD Test Guideline No. 121. Using this test system most of the test item molecules were present in their dissociated (ionic) form, due to their acidic nature, as it would possibly happen under environmental conditions. The second test system was an isocratic, formate buffered chromatographic system (pH 2.75), which enabled the investigation of the non-dissociated (neutral) form of the test items, as only a minor part of the test item molecules would be dissociate at pH 2.75.

For each test system the same six reference items for which K_{oc} values are known from the literature were chromatographed in duplicate on a cyanopropyl-HPLC column, covering a K_{oc} range from 18 mL/g to 72 mL/g and up to 389 mL/g. Sodium nitrate was used for determination of the void volume of the chromatographic systems. Thus, average capacity factors (k') were derived for each reference item in each test system, and a linear calibration plot was established for measured log k' values vs. literature log K_{oc} values.

Calibration function of citrate buffered test system (pH 6): slope= 2.83, intercept = 2.19, R^2=0.96

Calibration function of formate buffered system (pH 2.75): slope= 2.63, intercept = 2.38, R^2=0.96

The capacity factors of the test items and their equimolar mixture were determined for each test system by replicate analysis within the same autosampler worklist as used for the analysis of the respective reference items.

No retention of the test items was observed in the citrate buffered test system (pH 6) indicating only weak adsorption of the test item on soil under environmental conditions. Using the formate buffered

test system (pH 2.75), the test items were retained on the column and eluted with an identical retention time of 5.1 min (separate injection of the test items). The analysis of the equimolar mixture of the test items resulted in one, symmetric peak, eluting with the retention time of the single test items. The K_{oc} values of the single diastereomers and their equimolar mixture were deduced from the established calibration plot using the formate buffered test system (Table 7.4.2- 7).

Table 7.4.2- 7: SZX 0722-carboxylic acid *(M03)*: log K_{oc} and K_{oc} values for the single diastereomers and their equimolar mixture (formate buffered test system)

Compound	log K_{oc}	K_{oc} [mL/g]
S,R-configured isomer	1.58	38
S,S-configured isomer	1.58	38
equimolar mixture	1.58	38

Since the K_{oc} values determined according to the OECD Test Guideline No. 121 were identical for the two diastereomers, it was concluded that also the adsorption behaviour on soil is identical for both diastereomers.

I. Material and Methods

A. Materials

1. Test material: Test item: [valine-1-^{14}C]SZX 0722-carboxylic acid
single diastereomers (S,R- and S,S configured) and equimolar mixture of both diastereomers

Specific radioactivity: S,R: 3.39 MBq/mg (91.72 µCi/mg)
S,S: 3.33 MBq/mg (89.92 µCi/mg)

Radiochemical purity: S,R: > 99%
S,S: > 99%

Reference items: acetanilid, atrazine, carbofuran, isoproturon, linuron, phenol, sodium nitrate

2. Test system: For both test systems a high pressure liquid chromatography system was used, fitted with a pulse-free binary pump and a flow-through radioactivity as well as UV absorbance detector. A commercially available cyanopropyl-bonded column was used. Peak integration was done manually by selecting the peak start and stop times for each analysis. The peak areas were evaluated as “regions of interest”.

Test system #1 was based on an isocratic chromatographic method using a pre-mixed eluent consisting of 45% aqueous citrate buffer and 55% methanol at pH 6 according to the OECD Test Guideline No. 121. According to the Henderson-Hasselbach equation about 98% of the test items molecules would be dissociated in an aqueous system with pH 2.75. Thus, it can be also concluded that most of the test item molecules were present in their dissociated (ionic) form under the chromatographic conditions of test system #1.

Test system #2 was based on a slightly modified chromatographic method, according to test system #1:The citrate buffer was substituted by a formate buffer (pH 2.75) to gain more acidic conditions and prevent the dissociation of the test item. All other parameters were kept constant.

The theoretically degree of dissociation of the test items in an aqueous system with pH 2.75 is approx. 2% when calculation is performed according to the Henderson-Hasselbach equation. Thus, it can be also concluded that most of the test item molecules were present in their non-dissociated (neutral) form under the chromatographic conditions of test system #2.
Special effort was made to develop a chromatographic method, which allows the separation of the two diastereomers of SZX 0722-carboxylic acid *(M03)* to determine the diasteromeric ratio of the stock solution. Therefore, a special cross-linked trifunctional C18-stationary phase, developed for challenging separations, combined with gradient elution (buffered, acidic eluent system (pH 2.75)) was used.

B. Study design

1. Test item:

Stock solutions: The total delivered amount of the S,R-configured diastereomer of valine-labelled SZX 0722-carboxylic acid was dissolved in 5 mL ACN/H2O (1:1, v:v) to yield a nominal concentration of 1.48 MBq/mL (equivalent to 0.44 mg/mL). For determination of the radioactivity content by liquid scintillation counting (LSC) 50 µL of this stock solution were diluted with 950 µL ACN. The concentration of this stock solution was determined to be 1422.99 kBq/mL (equivalent to 0.42 mg/mL).
The total delivered amount of the S,S-configured diastereomer of valine-labelled SZX 0722-carboxylic acid, was also dissolved in 5 mL ACN/H2O (1:1, v:v) to yield a nominal concentration of 1.48 MBq/mL (equivalent to 0.44 mg/mL). For determination of the radioactivity content by LSC 50 µL of this stock solution were diluted with 950 µL ACN. The concentration of this stock solution was determined to be 1474.62 kBq/mL (equivalent to 0.44 mg/mL).
For preparation of a stock solution containing an equimolar mixture of both diastereomers, 105.5 µL of stock solution of the S,R-configured diastereomer were mixed with 100.0 µL of stock solution of the S,S-configured diastereomer to yield a nominal concentration of approx. 0.22 mg/mL (equivalent to 0.74 MBq/mL) of each diastereomer. The diasteromeric ratio and the radiochemical purity of the resulting stock solution was determined by HPLC/radio detection. The diastereomeric ratio was approximately 1:1 (are/area) and the radiochemical purity was 99.5%.

Test solution: For analysis with the chromatographic methods the stock solutions were diluted 1:100 (v:v) with the eluent of the respective chromatographic system.

2. Reference items:

Stock solutions:

Acetanilide: Citrate buffered solution: 1.32 mg of acetanilide were dissolved in 1.32 mL MeOH/citrate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL.. Following, 40 µL of this solution were diluted (1:25, v:v) with 960 µL MeOH/citrate buffer (55/45, v:v) to yield a final stock solution labelled with a nominal concentration of 0.04 mg/mL.
Ammonium formate buffered solution: 1.20 mg of acetanilide were dissolved in 1.20 mL MeOH/ammonium formate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL.

Atrazin: Citrate buffered solution: 1.31 mg of atrazine were dissolved in 1.31 mL MeOH/citrate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL.

Ammonium formate buffered solution: 1.15 mg of atrazine were dissolved in 1.15 mL MeOH/ammonium formate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL.

Carbofuran: Citrate buffered solution: 1.23 mg of carbofuran were dissolved in 1.23 mL MeOH/citrate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL. Ammonium formate buffered solution: 1.61 mg of carbofuran were dissolved in 1.61 mL MeOH/ammonium formate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL.

Isoproturon: Citrate buffered solution: 1.00 mg of isoproturon were dissolved in 1.00 mL MeOH/citrate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL. Following, 100 µL of this solution were diluted (1:10, v:v) with 900 µL MeOH/citrate buffer (55/45, v:v) to yield a final stock solution with a nominal concentration of 0.1 mg/mL.
Ammonium formate buffered solution: 1.15 mg of isoproturon were dissolved in 1.15 mL MeOH/ammonium formate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL.

Linuron: Citrate buffered solution: 1.40 mg of linuron were dissolved in 1.40 mL MeOH/citrate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL. Following, 50 µL of this solution were diluted (1:20, v:v) with 950 µL MeOH/citrate buffer (55/45, v:v) to yield a final stock solution with a nominal concentration of 0.05 mg/mL.
Ammonium formate buffered solution: 1.26 mg of linuron were dissolved in 1.26 mL MeOH/ammonium formate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL.

Phenol: Citrate buffered solution: 1.53 mg of phenol were dissolved in 1.53 mL MeOH/citrate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL. Ammonium formate buffered solution: 1.16 mg of phenol were dissolved in 1.16 mL MeOH/ammonium formate buffer (55/45, v:v) to yield a nominal concentration of 1 mg/mL.

Sodium nitrate: no stock solution was prepared for sodium nitrate.

Test solutions: The concentration of each reference item was chosen to yield an UV-signal (peak height) between 50 to 150 mV at 254 nm. The test solutions of the respective reference items were prepared yielding the following nominal concentrations (Table 7.4.2- 8):

Table 7.4.2- 8: Test solutions: Nominal concentrations of the reference items

Compound	Nominal concentration [mg/mL]
Acetanilid	0.02
Atrazine	0.05
Carbofuran	0.10
Isoproturon	0.05
Linuron	0.025
Phenol	0.10
Sodium nitrate	2

3. Retention parameters: For determination of the retention times (t_R) of the test and reference items in the chromatographic systems the test solutions were injected individually and in replicate, together within the same autosampler worklist. One autosampler worklist was established for each chromatographic system. Each reference item was run once before and once after the single diastereomers of SZX 0722-carboxylic acid *(M03)* and the equimolar mixture of the test items, to minimise influence of possible retention time drift. Injection of sodium nitrate was carried out at the beginning and at the end of the analytical series. Since sodium nitrate is unretained on reversed phase columns, its retention time is equal to the void volume (t_0) of the chromatography system.

4. Evaluation:

Calculation of the degree of dissociation: The degree of dissociation of a substance with a known pK_a value at a given pH in an aqueous system can be calculated according to the Henderson-Hasselbach equation as follows:

$$pH = pK_a + \log \frac{c(A^-)}{c(HA)}$$

$$\Leftrightarrow \log \frac{c(A^-)}{c(HA)} = pH - pK_a$$

$$\Leftrightarrow \frac{c(A^-)}{c(HA)} = 10^{pH - pK_a}$$

Calculation of capacity factors: The capacity factors (k') of the test and reference items were calculated from the system void volume (t_0, mean of all replicates) and the retention times (t_R, single measurements) of the test and reference items according to the following formula

$$k' = \frac{t_R - t_0}{t_0}$$

Following, the average capacity factors were calculated (arithmetic mean) for the test and reference items.

Determination of log K_{oc} of the test items: Using the HPLC estimation method, the adsorption coefficients (K_{oc}) of the test items are deduced from their capacity factors (single and mean values), by means of a linear calibration plot established for measured log k' versus known log K_{oc} of the reference items. Therefore, measured mean log k' data of the reference items were plotted versus their literature log K_{oc} data. Linear re[redacted]sion was used for statistical evaluation, and the log K_{oc} data of the test items were calculated as follows

$$\log K_{oc} = \text{slope} \cdot \log k' + \text{intercept}$$

Statistical methods:

- Linear re[redacted]sion analysis was used for the reference item calibration plot to determine the log K_{oc} data of the test items (Microsoft® Excel).
- Arithmetic means of the capacity factors (k') of the reference and test items were used for the plot of the log k' data vs the log K_{oc} data.
- Standard deviation was calculated for the capacity factors k' by the following formula:

$$\sqrt{\frac{\sum(x-\bar{x})^2}{n}}$$

- Outlier rejection criteria were not used

II. Results and Discussion

A. Calibration plots

The chromatographic systems were calibrated using the six reference items, which covers a K_{oc} range from 18 mL/g to 72 mL/g and up to 389 mL/g. The employed reference items were heterogeneous in chemical nature, including compounds with structural relationship to the test item (aromatic ring systems, peptide bonds). No trend for irregular behaviour was observed for any specific structural elements. Sodium nitrate was used for determination of the void volume of the chromatographic systems.

For the citrate buffered chromatographic system (Test system #1) the void volume of the chromatographic system was determined to be t_0 = 3.2 min and the following linear calibration function was established for the plot of measured log k' values of the reference items vs. their literature log K_{oc} values (correlation coefficient R^2 = 0.96)

$$\log K_{oc} = 2.83 \cdot \log k' + 2.19$$

HPLC retention data and calculation of capacity factors (k') for the reference items are provided in Table 7.4.2- 9.

Table 7.4.2- 9: Synopsis of retention times and capacity factors of calibration curve and final test using the chromatographic test system #1 (MeOH/citrate buffer, pH 6)

Compound	R_t [min]	k'	log k'	log K_{oc} a)	K_{oc} b) [mL/g]
Reference items					
Sodium nitrate	3.2				0
Acetanilid	4.8 4.8	0.500 0.500	- 0.30	1.25	18
Phenol	4.7 4.7	0.469 0.469	- 0.33	1.32	21
Carbofuran	5.2 5.1	0.625 0.594	- 0.22	1.66	46
Atrazine	5.5 5.5	0.719 0.719	- 0.14	1.81	65
Isoproturon	6.0 6.0	0.875 0.875	- 0.06	1.86	72
Linuron	7.4 7.4	1.313	0.12	2.50	389
Test item					
S,R-configured diastereomer of SZX 0722-carboxylic acid *(M03)*	3.2 3.2	0.000 0.000	-	-	-
S,S-configured diastereomer of SZX 0722-carboxylic acid *(M03)*	3.2 3.2	0.000 0.000	-	-	-
equimolar mixture of the S,R- and S,S-configured diastereomers of SZX 0722-carboxylic acid *(M03)*	3.2 3.2	0.000 0.000	-	-	-

a) reference items: literature values
test item: values calculated from calibration function
b) reference items: values calculated by antilog-transformation from literature log K_{oc} values
test item: values calculated by antilog-transformation from calculated log K_{oc} values

For the formate buffered chromatographic system (Test system #2) the void volume was determined to be t_0 = 3.4 min and the following linear calibration function was established for the plot of measured log k' values of the reference items vs. their literature log K_{oc} values (correlation coefficient R^2 = 0.96):

$$\log K_{oc} = 2.63 \cdot \log k' + 2.38$$

HPLC retention data and calculation of capacity factors (k') for the reference items are provided in Table 7.4.2- 10.

Table 7.4.2- 10: Synopsis of retention times and capacity factors of calibration curve and final test using the chromatographic test system #2 (MeOH/ammoniumformate buffer, pH 2.75)

Compound	R_t [min]	k'	log k'	log K_{oc} a)	K_{oc} b) [mL/g]
Reference items					
Sodium nitrate	3.4				0
Acetanilid	4.7 4.7	0.382 0.382	- 0.42	1.25	18
Phenol	4.7 4.7	0.382 0.382	- 0.42	1.32	21
Carbofuran	5.1 5.1	0.500 0.500	- 0.30	1.66	46
Atrazine	5.5 5.5	0.618 0.618	- 0.21	1.81	65
Isoproturon	5.9 5.9	0.735 0.735	- 0.13	1.86	72
Linuron	7.2 7.2	1.118 1.118	0.05	2.59	389
Test item					
S,R-configured diastereomer of SZX 0722-carboxylic acid *(M03)*	5.1 5.1	0.500 0.500	- 0.30	1.5837	38
S,S-configured diastereomer of SZX 0722-carboxylic acid *(M03)*	5.1 5.1	0.500 0.500	- 0.30	1.5837	38
equimolar mixture of the S,R- and S,S-configured diastereomers of SZX 0722-carboxylic acid *(M03)*	5.1 5.1	0.500 0.500	- 0.30	1.5837	38

a) reference items: literature values
test item: values calculated from calibration function
b) reference items: values calculated by antilog-transformation from literature log K_{oc} values
test item: values calculated by antilog-transformation from calculated log K_{oc} values

B. Test results

SZX 0722-carboxylic acid *(M03)* showed no retention on the cyanopropyl column run in reversed phase mode using the citrate buffered test system (pH 6) (Test system #1). The test items eluted within the void volume of the chromatographic system. These results are consistent with theoretical considerations of the degree of dissociation of SZX 0722-carboxylic acid at pH 6. According to the Henderson-Hasselbach equation (see Section 4) approximately 98% of the test item molecules are dissociated in an aqueous system with pH 6. Hence, none to low retention of SZX 0722-carboxylic acid is to be expected under reversed phase conditions when using test system #1, as in general ionic molecules will not be retarded in reverse phase mode.

For a reliable evaluation of the similarity of the adsorption behaviour of the two diastereomers of SZX 0722-carboxylic acid an interaction of the test items with the stationary phase of the chromatographic system is required, thus considering not only the ionic nature of the test items at a given pH value, but also further structural elements like aromatic ring systems and peptide bonds. Therefore, the retention of the test items on a cyanopropyl column run in reverse phase mode was investigated in a second test system (Test system #2). This test system was based on a formate buffered chromatographic system (pH 2.75). The more acidic pH was chosen to move the ratio of dissociated and non-dissociated test item molecules towards the non-deprotonated form. According

to the Henderson-Hasselbach equation (see Section 4) the theoretical degree of dissociation of SZX 0722-carboxylic acid is approximately 2% in an aqueous system with pH 2.75.
Using this modified test system the test items were retained on the cyanopropyl column and eluted after the void volume of the chromatographic system with identical retention times (separate injection of the test items). The analysis of the equimolare mixture of the test items resulted in one symmetric peak, eluting with the retention time of the single test items.
The average capacity factors (k') and log k' values determined for the single diastereomers of SZX 0722-carboxylic acid and their equimolar mixture are summarised in Table 7.4.2- 11. Based on these results, the K_{oc} values were calculated and also summarised in Table 7.4.2- 11. The measured capacity factors of the test items fell within the range covered by the calibration series, thus at least the capacity factor of one of the reference items was above and one was below the capacity factors of the test items.

Table 7.4.2- 11: SZX 0722-carboxylic acid *(M03)*: k', log k' and K_{oc} values for the single diastereomers and their equimolar mixture

Compound	k'	log k'	K_{oc} [mL/g]
S,R-configured diastereomer	0.500	- 0.30	38
S,S-configured diastereomer	0.500	- 0.30	38
equimolar mixture of the S,R- and S,S-configured diastereomers	0.500	- 0.30	38

The results indicate an identical adsorption behaviour of the two diastereomers of SZX 0722-carboxylic acid *(M03)*. Therefore, all higher tier tests investigating the adsorption behaviour of SZX 0722-carboxylic acid can be carried out with the equimolar mixture of the two diastereomers of SZX 0722-carboxylic acid. Moreover, these results allow for a combined leaching assessment of the S,R- and S,S-configured diastereomers of SZX 0722-carboxylic acid.

III. Conclusions

The adsorption behaviour of the test items on soil under environmental conditions was estimated to be weak. The K_{oc} values determined according to OECD Test Guideline No. 121 for the single diastereomers of the non-dissociated SZX 0722-carboxylic acid *(M03)* under acidic conditions were identical, and were calculated to be 38 mL/g.
Since the K_{oc} values determined according to OECD Test Guideline No. 121 were identical for the single diastereomers of SZX 0722-carboxylic acid, it was concluded that also the adsorption behaviour on soil is identical for both diastereomers, whether they are deprotonated or not.
The results indicate an identical adsorption behaviour of the two diastereomers of SZX 0722-carboxylic acid *(M03)*. Therefore, all higher tier tests investigating the adsorption behaviour of SZX 0722-carboxylic acid can be carried out with the equimolar mixture of the two diastereomers of SZX 0722-carboxylic acid. Moreover, these results allow for a combined leaching assessment of the S,R- and S,S-configured diastereomers of SZX 0722-carboxylic acid.

- **PMPA *(M10)***

PMPA *(M10)* was found as major metabolite in the aerobic soil metabolism studies conducted with the phenyl-labelled parent compound and evaluated during the Annex I inclusion. The adsorption/desorption behaviour of PMPA *(M10)* in soil was also evaluated during the Annex I Inclusion. No additional studies have been performed for PMPA. A short summary of the data is given below.

A batch equilibrium procedure was used to determine the K_f and K_{oc} values of phenyl-labelled PMPA *(M10)* in four soils ([redacted] (1996), submitted within the EU Basic Dossier 1998; IIA, 7.1.2 /02). The adsorption constants K_f calculated from the Freundlich isotherms for the four soils ranged from 0.67 to 11.09 mL/g. When recalculating the K_f values with the organic C content of the soils, K_{oc} values of 117.9 to 574.6 mL/g were obtained. The percentage of adsorption of the compound varied between 24.8 and 74.0% of the applied compound depending on soil type and concentration.

Running a desorption experiment with 0.01 M $CaCl_2$ solution, 32.1 to 58.3% of adsorbed PMPA was desorbed again. This gives calculated desorption K_f values from 1.43 to 13.0 mL/g, and corresponding K_{oc} values from 250.6 to 673.2 mL/g.

The results of the adsorption/desorption experiments are summarised in Table 7.4.2- 12.

Table 7.4.2- 12: Adsorption and desorption of phenyl-labelled PMPA *(M10)* in four different soils

Soil designation	Soil type	Adsorption 1/n	Adsorption K_f [mL/g]	Adsorption K_{oc} [mL/g]	Desorption 1/n	Desorption K_f [mL/g]	Desorption K_{oc} [mL/g]
[redacted]	silt loam	0.8637	1.5935	177.1	0.8838	2.5784	286.5
[redacted]	sand	0.9110	0.6720	117.9	0.9363	1.4282	250.6
[redacted]	silty clay loam	0.8721	11.0906	574.6	0.8951	12.9933	673.2
[redacted]	loamy sand	0.8048	3.2624	291.3	0.8482	4.8362	431.8

- **N-acetyl-PMPA *(M15)***

N-acetyl-PMPA *(M15)* was found a major metabolite in the new anaerobic soil metabolism study. Therefore, a study on the adsorption/desorption behaviour of N-acetyl-PMPA *(M15)* was performed ([redacted] (1998), submitted in this Dossier, KIIA 7.4.2 /04).

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The study was not available at Annex I submission. It will be submitted now to meet the requirement for a major soil metabolite as N-acetyl-PMPA was found as a major metabolite in the anaerobic soil metabolism study (KIIA 7.1.2 /01).

Report:	**KIIA 7.4.2 /04, [redacted].; 1998**
Title:	Adsorption/desorption of [phenyl-UL-^{14}C]WAK 7312 on four different soils
Report No:	FM769
Document No:	M-077024-01-1
Guidelines:	- EPA, Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate § 163-1, Leaching and Adsorption/Desorption Studies of October 18, 1982 - EC, Commission Directive 95/36/EC amending Council Directive 91/414/EEC (Annexes I and II, Fate and Behaviour in the Environment), July 14, 1995 - OECD – Guideline for Testing of Chemicals No.: 106 Adsorption/Desorption, May 12, 1981
GLP:	Yes

Executive Summary

The adsorption of phenyl-labelled N-acetyl-PMPA *(M15)* was investigated in four soils sandy loam ([redacted] AXXa, Germany), loam ([redacted], CA, USA), silty clay loam ([redacted], KS, USA), and sandy loam ([redacted], IN, USA). N-acetyl-PMPA was applied to soil samples at four different concentrations corresponding to 5.00 mg, 1.0 mg, 0.19 mg and 0.04 mg test substance/Liter $CaCl_2$ solution.

The percentage of N-acetyl-PMPA adsorbed to soil varied between 15% and 39%. The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.34 to 0.65 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 32.2 and 53.4 mL/g with an arithmetic mean of 39.7 mL/g.

Desorption tests s[redacted]d that between 18% and 66% of the adsorbed test substance was desorbed again from the soils. For desorption, the K_f was determined to be in the range of 1.15 to 1.56 mL/g, corresponding to K_{oc} values for desorption between 71.5 and 123.3 mL/g, with an arithmetic mean of 97.1 mL/g.

I. Material and Methods

A. Materials

1. Test Material: [phenyl-UL-^{14}C]N-acetyl-PMPA
Specific radioactivity: 3.5 MBq/mg
Radiochemical purity: 98.0%

2. Soil: The soils were air-dried and sieved to a particle size of ≤ 2 mm. Details of the soil samples are given in Table 7.4.2- 13.

Table 7.4.2- 13: Soil characteristics

Parameter	Soil			
	[redacted] AXXa	[redacted]	[redacted]	[redacted]
Geographic location - city - state - country	[redacted] NRW[a)] Germany	[redacted] California USA	[redacted] Kansas USA	[redacted] Indiana USA
Texture class (USDA)	sandy loam	loam	silty clay loam	sandy loam
Particle distribution (USDA) - sand [%] - silt [%] - clay [%]	 72.4 22.6 5.0	 27.8 48.1 24.1	 12.4 48.0 39.6	 65.7 26.4 7.9
pH (H_2O)	7.2	7.7	5.9	6.7
Organic matter[cb] [%]	3.47	1.7	2.86	1.93
Organic carbon [%]	2.02	0.99	1.66	1.12
CEC[c)] [meq/100 g]	8	22	18.5	10
Bulk density [g/mL]	-	1.16	1.14	-

a) NRW = North Rhine-Westphalia
b) calculated: % organic matter = % organic carbon × 1.72
c) CEC = cation exchange capacity

B. Study design

1. Experimental conditions: Four different test concentrations of the application solution were prepared (5.00, 1.00, 0.19, and 0.04 mg/L phenyl-labelled N-acetyl-PMPA). The time to achieve the equilibrium for adsorption and the ratio of soil/water was determined in pre-tests using a mixture of unlabelled and labelled N-acetyl-PMPA. The main test for the determination of the adsorption/desorption data was carried out using an $CaCl_2$-solution and a shaking period of 24 hours.

2. Analytical procedures: The samples were centrifuged and aliquots of the supernatant were removed for LS-measurement. The supernatant was decanted, the volume of the supernatant was determined and aliquots of the highest test concentration were chromatographed by HPLC equipped with a radiodetector to quantify the test substance.

II. Results and Discussion

The adsorption of phenyl-labelled N-acetyl-PMPA was investigated in four soils. N-acetyl-PMPA was applied to soil samples at four different concentrations corresponding to 5.00, 1.00, 0.19, and 0.04 mg test substance/L $CaCl_2$ solution.

- **Adsorption**

The proportion of N-acetyl-PMPA being adsorbed on soil [redacted] AXXa ranged from 23.2% to 39.4%. Adsorption rate on soil [redacted] ranged from 14.7% to 20.4%, that of soil [redacted] ranged from 24.8% to 33.8%, and that of soil [redacted] ranged from 24.6% to 36.6% (Table 7.4.2- 14).

Table 7.4.2- 14: Proportions of N-acetyl-PMPA *(M15)* being adsorbed in four different soils

Test concentration [mg/L]	Proportions N-acetyl-PMPA *(M15)* adsorbed [%] Soil			
	[redacted] AXXa	[redacted]	[redacted]	[redacted]
5.00	23.2	14.7	24.8	24.6
1.00	31.4	20.4	29.2	25.3
0.19	34.1	17.3	31.5	31.3
0.04	39.4	19.0	33.8	36.6

The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.34 to 0.65 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 32.2 and 53.4 mL/g with an arithmetic mean of 39.7 mL/g (Table 7.4.2- 15).

Table 7.4.2- 15: Adsorption of N-acetyl-PMPA *(M15)* to four different soils

Soil	1/n	K_f [mL/g]	K_{oc} [mL/g]	R^2
[redacted] AXXa	0.86	0.65	32.2	0.9992
[redacted]	0.96	0.34	34.7	0.9974
[redacted]	0.91	0.64	38.4	0.9998
[redacted]	0.88	0.60	53.4	0.9994
arith. mean			39.7	

- **Desorption**

Desorption tests showed that between 18% and 66% of the adsorbed test substance was desorbed again from the soils (Table 7.4.2- 16). For desorption, the K_f value was determined to be 1.56 mL/g for soil [redacted], 1.15 mL/g for soil [redacted], 1.19 mL/g for soil [redacted], and 1.38 mL/g for soil [redacted]. The K_{oc} value for desorption was calculated to be 77 mL/g for soil [redacted], 116 mL/g for soil [redacted], 72 mL/g for soil [redacted], and 123 mL/g for soil [redacted] (Table 7.4.2- 17).

Table 7.4.2- 16: Proportions of N-acetyl-PMPA *(M15)* being desorbed in four different soils

Test concentration [mg/L]	Proportions N-acetyl-PMPA *(M15)* desorbed [%] Soil			
	[redacted] AXXa	[redacted]	[redacted]	[redacted]
5.00	49.4	61.2	64.2	65.7
1.00	46.5	61.9	60.0	51.0
0.19	27.5	42.4	46.3	46.2
0.04	18.1	44.1	36.1	45.2

Table 7.4.2- 17: Desorption of N-acetyl-PMPA *(M15)* to four different soils

Soil	1/n	K_f [mL/g]	K_{oc} [mL/g]	R^2
[redacted] AXXa	0.77	1.56	77.2	0.9998
[redacted]	0.92	1.15	116.2	0.9998
[redacted]	0.72	1.19	71.5	0.9981
[redacted]	0.87	1.38	123.3	0.9983
arith. mean			97.1	

III. Conclusions

The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.34 to 0.65 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 32.2 and 53.4 mL/g with an arithmetic mean of 39.7 mL/g.

Summary: Adsorption/desorption data of iprovalicarb metabolites

SZX 0722-carboxylic acid *(M03)* and PMPA *(M10)* were identified as major metabolites in soil metabolism studies with iprovalicarb under anaerobic conditions In addition N-acetyl-PMPA *(M15)* was formed a major metabolite in an anaerobic soil metabolism study. For all these major metabolites adsorption/desorption studies were performed (batch equilibrium procedure).
In addition HPLC-K_{oc}-values for the two diastereomers of SZX 0722-carboxylic acid *(M03)* (S,R- and S,S-configuration) were determined to show whether there could be a difference in the adsorption behaviour of the two diastereomers of SZX 0722-carboxylic acid. For a better overview of a short summary is given below.

<u>SZX 0722-carboxylic acid *(M03)*:</u> The adsorption/desorption of SZX 0722-carboxylic acid was investigated in batch equilibrium experiments in five German soils. The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.012 to 0.354 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 0.6 and 13.1 mL/g with an arithmetic mean of 5.2 mL/g. Due to low adsorption (<5% AR) in three soils the desorption experiments were not evaluated for these soils. The desorption constants $K_{f(des)}$ in the two other soils were in the range of 1.23 to 2.06 mL/g and the corresponding K_{oc} values ranged from 72.2 to 76.2 mL/g. The desorption $K_{f(des)}$ and the normalised $K_{oc(des)}$ values were significantly higher (5.8 to 8.6 times higher) than those obtained for the adsorption phase, indicating that the amount of test item once adsorbed to soil is not readily desorbed.
A summary of the adsorption/desorption data of SZX 0722-carboxylic acid based on batch equilibrium studies is given in Table 7.4.2- 18.

Table 7.4.2- 18: Summary of the adsorption/desorption data of SXZ 0722-carboxylic acid *(M03)*

Soil	Adsorption				Desorption			
	1/n	K_f [mL/g]	K_{oc} [mL/g]	r²	1/n	K_f [mL/g]	K_{oc} [mL/g]	r²
[redacted]	1.1007	0.054	3.0	0.9817	a)			
[redacted]	1.0551	0.012	0.7	0.7494	a)			
[redacted]	1.1069	0.354	13.1	0.9831	1.0062	2.057	76.2	0.9980
[redacted] II	0.9232	0.028	0.6	0.7781	a)			
[redacted]	0.9393	0.143	8.4	0.9984	0.9480	1.227	72.2	0.9893
arith. mean			*5.2*				*74.2*	

a) due to low adsorption (K_{oc} < 1 mL/g), the desorption experiment was not evaluated for these soils

Since the K_{oc} values determined for the single diastereomers of SZX 0722-carboxylic acid using the HPLC method were identical for the two diastereomers it was concluded that also the adsorption behaviour on soil is identical for both diastereomers. Therefore, all higher tier tests investigating the adsorption behaviour of SZX 0722-carboxylic acid can be carried out with the equimolar mixture of the two diastereomers of SZX 0722-carboxylic acid. Moreover, these results allow for a combined leaching assessment of the S,R- and S,S-configured diastereomers of SZX 0722-carboxylic acid.

<u>PMPA *(M10)*:</u> The adsorption/desorption of PMPA was investigated in batch equilibrium experiments in two German and two US soils. The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.67 to 11.09 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 117.9 and 574.6 mL/g with an arithmetic mean of 290.2 mL/g. The desorption constants K_f were in the range of 1.43 to 13.0 mL/g and the corresponding K_{oc} values ranged from 250.6 to 673.2 mL/g. A summary of the adsorption/desorption data of PMPA based on batch equilibrium studies is given in Table 7.4.2- 19.

Table 7.4.2- 19: Summary of the adsorption/desorption data of PMPA *(M10)*

Soil	Adsorption				Desorption			
	1/n	K_f [mL/g]	K_{oc} [mL/g]	r²	1/n	K_f [mL/g]	K_{oc} [mL/g]	r²
[redacted]	0.8637	1.5935	177.1	0.9999	0.8838	2.5784	286.5	1.0000
[redacted]	0.9110	0.6720	117.9	0.9981	0.9363	1.4282	250.6	0.9995
[redacted]	0.8721	11.0906	574.6	0.9996	0.8951	12.9933	673.2	0.9995
[redacted]	0.8048	3.2624	291.3	0.9991	0.8482	4.8362	431.8	0.9998
arith. mean			*290.2*				*410.5*	

<u>N-acetyl-PMPA *(M15)*:</u> The adsorption/desorption of N-acetyl-PMPA was investigated in batch equilibrium experiments in one German and three US soils. The adsorption constants K_f were calculated by means of the Freundlich adsorption isotherm and ranged from 0.34 to 0.65 mL/g. These values were normalised to the organic carbon content and corresponded to K_{oc} values between 32.2 and 53.4 mL/g with an arithmetic mean of 39.7 mL/g. The desorption constants K_f were in the

range of 1.15 to 1.56 mL/g and the corresponding K_{oc} values ranged from 71.5.6 to 123.3 mL/g. A summary of the adsorption/desorption data of N-acetyl-PMPA based on batch equilibrium studies is given in Table 7.4.2- 20.

Table 7.4.2- 20: Summary of the adsorption/desorption data of N-acetyl-PMPA *(M15)*

Soil	Adsorption				Desorption			
	1/n	K_f [mL/g]	K_{oc} [mL/g]	r^2	1/n	K_f [mL/g]	K_{oc} [mL/g]	r^2
[redacted]	0.86	0.65	32.2	0.9992	0.77	1.56	77.2	0.9998
[redacted]	0.96	0.34	34.7	0.9974	0.92	1.15	116.2	0.9998
[redacted]	0.91	0.64	38.4	0.9998	0.72	1.19	71.5	0.9981
[redacted]	0.88	0.60	53.4	0.9994	0.87	1.38	123.3	0.9983
arith. mean			*39.7*				*97.1*	

KIIA 7.4.3 Column leaching studies with the active substance

No column leaching studies were performed with iprovalicarb. However, this requirement is covered by adsorption studies with the parent compound. The results are described in section KIIA 7.4.1.

KIIA 7.4.4 Column leaching studies rel. metabolites, degr. & react. Products

No column leaching studies were performed with the quantitatively relevant metabolites of iprovalicarb. However, this requirement is covered by adsorption studies with these metabolites. The results are described in section KIIA 7.4.2.

KIIA 7.4.5 Aged residue column leaching

No aged residue column leaching studies were performed. However this requirement is covered by adsorption studies and degradation studies with the active ingredient and the quantitatively relevant metabolites.

KIIA 7.4.6 Leaching (TLC)

Not required by Directive 91/414/EEC.

KIIA 7.4.7 Lysimeter studies

New study submitted for Annex I renewal
Justification for including this new study in the Annex I Renewal Dossier: The study was not available at ‘Annex I submission. The study was included since it enlarged the data set on the leaching behaviour of iprovalicarb.

Report:	**KIIA 7.4.7 /01, [redacted] 2001**
Title:	Degradation and translocation behaviour of iprovalicarb (SZX0722) under field conditions (Lysimeter experiment)
Report No:	MR-097/00
Document No:	M-042379-01-1
Guidelines:	BBA Assessment Guideline Part IV, 4-3, February 1990 (including its modification dated August 1991)
GLP:	Yes

Executive Summary

Over a period of 3 years the leaching behaviour of phenyl-labelled iprovalicarb, formulated as WG 50 (51% a.s.) and its degradation products was investigated under practice-relevant field conditions.
Two grape vines, cultivated on two undisturbed soil cores (1m^2 surface area, 1.3 m soil depth) of a sandy loam, were sprayed three times in 1994 as well as 1995 with each nominal 0.5kg a.s./ha (1.5 kg a.s./ha/year). The first application in each year was just before flowering.
The results of the two lysimeters were in very good accordance. The total amount of applied radioactivity detected in the bunches of grapes amounted to 0.4% of the total applied radioactivity.
The loss of radioactivity during the study was attributed to mineralisation of the active ingredient and amounted to 86% of the total applied radioactivity.
The majority of the recovered radioactivity (8.3% of the applied radioactivity) remained in the top 0 - 10 cm soil layer of the lysimeters.
A total of 0.04% of the applied radioactivity leached through the soil cores during the study. In each year the amount of iprovalicarb was ≤ 0.02 µg/L, and the amount of the metabolites SZX 0722-carboxylic acid *(M03)* and terephthalic acid *(M23)* were ≤ 0.03 µg/L each.
There was no single radioactive zone with a concentration of > 0.09 µg/L. The residue might also be composed of substances into which liberated $^{14}CO_2$ has been incorporated by micro-organisms.
It can be concluded that iprovalicarb and its metabolites will not contaminate deeper soil layers or ground water at concentrations ≥ 0.1 µg/L.

I. Material and Methods

A. Materials

1. Test Material: [phenyl-UL-^{14}C]iprovalicarb (diastereomeric mixture SR : SS = 1 : 1)
CAS #: 140923-25-7
Specific radioactivity: 138 µCi/mg (corresponding to 5.1 MBq/mg)
Radiochemical purity: > 98%

2. Lysimeter:

Kind of soil: sandy loam (layers of 10 cm; 0 - 120 cm), loamy sand (120 - 130 cm). A detailed soil characteristic of each layer is given in Table 7.4.7- 1.

Size of the area: 1 m² (1 m x 1 m) A band of 5 cm on the margin remained untreated in order to largely preclude marginal effects, so that 0.81 m² (0.9 x 0.9) was actually treated.

Depth of soil packing: 1.3 m

Location: The lysimeter was removed from the field plot [redacted] AXXa in [redacted] (Germany)

Installation of the lysimeter: the two lysimeters (lysimeter 13 and lysimeter 14) were installed in the open unit of the Institute for Metabolism Research, BCS AG, [redacted], Germany. Each lysimeter was standing in the middle of an area of about 9 m^2 (3 x 3 m), planted with grape vines. The outlet of the leachate was each connected to two 20 L stainless steel. One lysimeter had a ground water simulation at a depth of 129 ± 2 cm. The other lysimeter has a normal outlet for the leachates at the bottom of the tray.

Kind of vegetation: grape vine, one plant per 1 m² lysimeter. The age of grape vines was about 3 years when first being treated.

Table 7.4.7- 1: [redacted] AXXa: soil characteristics

Depth [cm]	Classification[a)]	Texture[a)] sand [%]	silt [%]	clay [%]	pH H_2O	$CaCl_2$ (0.01 M)	org. C [%]
0 - 10	sandy loam	70.8	20.7	8.6	7.2	6.6	1.8
10 - 20	sandy loam	69.4	22.2	8.5	7.2	6.4	1.1
20 - 30	sandy loam	68..3	21.1	10.6	7.2	6.3	0.7
30 - 40	sandy loam	67.5	20.7	11.8	7.3	6.5	0.5
40 - 50	sandy loam	70.3	18.0	11.8	7.5	6.5	0.3
50 - 60	sandy loam	71.7	15.7	12.6	7.5	6.5	0.2
60 - 70	sandy loam	75.5	15.1	9.4	7.6	6.5	0.2
70 - 80	sandy loam	73.2	13.0	13.8	7.7	6.5	0.2
80 - 90	sandy loam	68.7	12.8	18.5	7.7	6.6	0.2
90 - 100	sandy loam	70.2	12.2	17.6	7.7	6.6	0.2
100 - 110	sandy loam	78.0	10.4	11.6	7.7	6.6	0.1
110 - 120	sandy loam	77.3	8.8	13.9	7.7	6.6	0.1
120 - 130	loamy sand	81.5	10.2	8.3	7.7	6.7	0.1

a) according to USDA

B. Study design

1. Experimental conditions: The long-term leaching behaviour of iprovalicarb was investigated in two undisturbed soil cores under practice-relevant field conditions. The test was laid out for a period of 3 years. The test substance was applied three times per year in two following years to grape vine. The application rates for each lysimeter are summarised in Table 7.4.7- 2.

Table 7.4.7- 2: Application rates in mg iprovalicarb per lysimeter

		mg a.s./lysimeter	
		lysimeter 13	lysimeter 14
1st year	1. application	38.39	37.46
	2. application	37.04	37.40
	3. application	46.94	50.10
	total	122.37	124.99
mean (total/lysimeter)		123.67	
2nd year	1. application	42.60	43.20
	2. application	43.17	42.55
	3. application	36.69	35.81
	total	122.46	121.58
mean (total/lysimeter)		122.02	

The size of the surface area of the lysimeter was 1 m². A band of 5 cm on the margin remained untreated in order to largely preclude marginal effects, so that 0.81 m² of the lysimeter was actually treated. The application rates per hectare related to this area of 0.81 m² are summarised in Table 7.4.7- 3. Nevertheless, the leachates were collected from the area of 1.0 m². Therefore, the application rates per hectare related to 1.0 m² are summarised also in this table (not given in the report). Both calculations show that the application rate used in this study is an overdose compared to the actual application rate of iprovalicarb used in agricultural practice.

Table 7.4.7- 3: Application rates in kg iprovalicarb per hectare

		Application rate [kg a.s./ha]			
		related to the application area (0.81 m²)[a)]		related to the collection areaof the leachate (1.0 m²)[b)]	
		lysimeter 13	lysimeter 14	lysimeter 13	lysimeter 14
1st year	1. application	0.474	0.463	0.384	0.375
	2. application	0.457	0.462	0.370	0.374
	3. application	0.580	0.619	0.469	0.501
	total	1.511	1.543	1.224	1.250
mean (total/lysimeter)		1.527		1.237	
2nd year	1. application	0.526	0.534	0.426	0.432
	2. application	0.533	0.525	0.432	0.426
	3. application	0.453	0.442	0.367	0.358
	total	1.512	1.501	1.225	1.216
mean (total/lysimeter)		1.506		1.220	

a) The size of the surface area of the lysimeter was 1 m². But a band of 5 cm on the margin remained untreated in order to largely preclude marginal effects, so that 0.81 m² of the lysimeter was actually treated.
b) As the leachates were collected from the area of 1.0 m² the application rates per hectare were also related to 1.0 m² (not given in the report)

2. Handling of the leachates: In steps of about 2 weeks the leachates obtained were collected and the radioactivity was determined under native (pH about 8) and acidified conditions

(1 mL 1 N HCl to 10 mL leachate). The acidified leachates were sonicated. The radioactivity was determined. Sub-samples (3% of each leachate of the same annual period) were combined for the annual mixed sample. The water samples were deep-frozen at -20°C until processing. The water with a total radioactivity 0.01 µg/L was discarded. Storage stability tests were not performed because the annual leachates were analysed directly and there was no individual substance in the annual leachates with > 0.1 µg/L.

3. Handling of the soil:

Depth of sampling: 130 cm depth (entire lysimeter), 13 layers of 10 cm each, gravel layer 5 cm

Extraction method: The first 10 cm layer was mixed by turning with a s[redacted]100 times. One mixed sample of about 1000 g (50 individual samples of about 20 g each) was taken, and homogenised. An aliquot of the mixed sample (about 100 g dry weight) was extracted 3 times with acetonitrile, centrifuged and the extracts were combined. The volume and radioactivity of the combined extracts were measured. The extracted soil was combusted to determine the non-extracted part. The 6 soil cores of one and the same 10 cm layer (10 to 110 cm) and the soil samples 110 - 120 cm and 120 - 130 cm were mixed and then aliquots were combusted to determine TRR. The average values were related to the weight of dry soil (104°C). The gravel samples (about 400 g each) were washed with 400 mL methanol.

II. Results and Discussion

A. Leachates

The total amount of leachate water collected for each year is summarised in Table 7.4.7- 4.

Table 7.4.7- 4: Total amount of leachate water after each year

	Leachate [L]	
	lysimeter 13	lysimeter 14
1. year[a)]	314.951	296.591
2. year[b)]	159.211	142.291
3. year[c)]	318.361	332.481

a) 1994-06-28 to 1995-06-30
b) 1995-07-01 to 1996-06-30
c) 1996 -07-01 to 1997-07-31

Each individual leachate sample was analysed for TRR and the annual leachate samples for parent, metabolites and non-identified radioactivity.

The total radioactive residue (TRR) expressed as µg/L was very similar in the annual leachates of both lysimeter 13 and 14 and amounted to 0.1 - 0.2 µg/L. The analyses of the leachates s[redacted]d that the parent compound was not translocated into the annual leachates with > 0.02 µg/L. Two metabolites with < 0.1 µg/L were identified by thin layer co-chromatography: SZX 0722-carboxylic acid *(M03)* (< 0.02 µg/L) and terephthalic acid *(M23)* (< 0.03 µg/L single annual values). The concentration of each individual unknown radioactive zone was < 0.09 µg a.s. equivalent/L leachate. It is probable that the unknown radioactive compounds occurring in the leachates consisted of humic substances and/or endogenous substances of micro-organisms into which liberated $^{14}CO_2$ and/or radioactive iprovalicarb fragments have been incorporated. The radiochemical impurities of the

active ingredient accounting for less than 1% could also be a reason for this low radioactivity in the leachates.

The concentrations of iprovalicarb, the metabolites and the non-identified radioactivity relative to the leachates (Table 7.4.7- 4) are given in Table 7.4.7- 5.

Table 7.4.7- 5: Concentrations of iprovalicarb, metabolites and non-identified radioactivity in the annual leachate samples (µg/L, relative to leachate water in Table 7.4.7- 4)

Year	Compound	Lysimeter 13	Lysimeter 14	mean
1. year[a)]	Iprovalicarb	0.01	0.02	0.02
	SZX 0722-carboxylic acid *(M03)*	0.01	0.01	0.01
	Non identified radioactivity[e)]	0.08	0.09	0.08
2. year[b)]	Iprovalicarb	0.02	< 0.01	0.01
	SZX 0722-carboxylic acid *(M03)*	0.02	0.01	0.02
	Non identified radioactivity[e)]	0.17	0.13	0.15
3. year[c)]	Iprovalicarb	< 0.01	< 0.01	< 0.01
	SZX 0722-carboxylic acid *(M03)*	0.02	0.02	0.02
	Terephthalic acid *(M23)*	0.03	0.02	0.03
	Non identified radioactivity[e)]	0.10	0.11	0.10
Mean of three years[d)]	Iprovalicarb	0.01	0.01	0.01
	SZX 0722-carboxylic acid *(M03)*	0.02	0.01	0.02
	Terephthalic acid *(M23)*	0.01	0.01	0.01
	Non identified radioactivity[e)]	0.12	0.11	0.11

a) 1994-06-28 to 1995-06-30
b) 1995-07-01 to 1996-06-30
c) 1996 -07-01 to 1997-07-31
d) 1994-06-28 to 1997-07-31
e) non identified radioactivity consisted of 4-8 zones. Each single concentration was < 0.1 µg/l.

B. Soil

Total radioactive residues (TRR): The main radioactivity was in the first 0 - 10 cm layer with 8.3%. A total of 0.2% of the applied radioactivity was translocated below the 60 cm layer. (Mean values, Table 7.4.7- 6, Table 7.4.7- 7).

Extracted radioactivity: The soil layer 0 - 10 cm contained 8.3% of the applied radioactivity (mean value). The extracted part of this radioactivity was 8.4%, corresponding to 0.7% of the applied radioactivity; 35% of the extracted part was attributed to iprovalicarb. Thus 0.2% of the applied radioactivity was attributed to iprovalicarb in the soil layer 0 - 10 cm.

Non-extracted radioactivity: The non-extracted radioactivity of the soil layer 0 - 10 cm (with 7.6% of applied radioactivity = 91.6% of the radioactivity of soil layer 0 - 10 cm) was relatively high in comparison to the extracted part (0.7% of applied radioactivity = 8.4% of the radioactivity of soil layer 0 - 10 cm). Probably ^{14}C-fragments were incorporated into the soil matrix to produce bound residue. Thus this radioactivity is more or less not extractable.

Table 7.4.7- 6: Balance of the soil layers

Lysimeter	Layer [cm]	Amount of dry soil		Values per layer (TRR)						Results corresp. to 0.81 m² a)	
				extraction		combustion		total			
		per 1 m² layer	per 0.81 m² layer	[MBq]	[% of applied] b)	[MBq]	[% of applied] b)	[MBq]	[% of applied]	[kBq/kg dry soil]	[µg/kg dry soil]
Lysimeter 13	0 - 10	149.88	121.40	3.442	0.68	44.388	9.46	47.830	9.5	393.98	190.70
	10 - 20	150.00	121.50			15.645	3.1	15.645	3.1	128.77	62.33
	20 - 30	150.00	121.50			6.629	1.3	6.629	1.3	54.56	26.41
	30 - 40	150.00	121.50			1.905	0.4	1.905	0.4	15.68	7.59
	40 - 50	150.00	121.50			0.875	0.2	0.875	0.2	7.20	3.49
	50 - 60	150.00	121.50			0.294	0.1	0.294	0.1	2.42	1.17
	60 - 70	150.00	121.50			0.140	< 0.1	0.140	< 0.1	1.15	0.56
	70 - 80	150.00	121.50			0.094	< 0.1	0.094	< 0.1	0.77	0.37
	80 - 90	150.00	121.50			0.074	< 0.1	0.074	< 0.1	0.61	0.29
	90 - 100	150.00	121.50			0.057	< 0.1	0.057	< 0.1	0.47	0.23
	100 - 110	150.00	121.50			0.065	< 0.1	0.065	< 0.1	0.53	0.26
	110 - 120	150.00	121.50			0.110	< 0.1	0.110	< 0.1	0.91	0.44
	120 - 130	150.00	121.50			0.092	< 0.1	0.092	< 0.1	0.76	0.37
	gravel 130 - 135	75.00	60.75	0.011	< 0.1			0.011	< 0.1	0.18	0.09
	total	2024.88	1640.15						14.6		
Lysimeter 14	0 - 10	148.07	119.94	3.474	0.7	32.862	6.45	36.336	7.1	302.96	146.64
	10 - 20	150.00	121.50			16.458	3.2		3.2	135.46	65.56
	20 - 30	150.00	121.50			5.735	1.1		1.1	47.20	22.85
	30 - 40	150.00	121.50			3.957	0.8		0.8	32.57	15.76
	40 - 50	150.00	121.50			1.909	0.4		0.4	15.71	7.61
	50 - 60	150.00	121.50			0.304	0.1		0.1	2.50	1.21
	60 - 70	150.00	121.50			0.143	< 0.1		< 0.1	1.18	0.57
	70 - 80	150.00	121.50			0.126	< 0.1		< 0.1	1.04	0.50
	80 - 90	150.00	121.50			0.316	0.1		0.1	2.60	1.26
	90 - 100	150.00	121.50			0.569	0.1		0.1	4.68	2.27
	100 - 110	150.00	121.50			0.489	0.1		0.1	4.02	1.95
	110 - 120	150.00	121.50			0.032	< 0.1		< 0.1	0.26	0.13
	120 - 130	150.00	121.50			0.021	< 0.1		< 0.1	0.17	0.08
	gravel 130 - 135	75.00	60.75	0.006	< 0.1		< 0.1	0.006	< 0.1	0.10	0.05
	total	2023.07	1638.69						13.0		

a) corresponding to the applied area of 0.81 m²
b) not given in the report

Table 7.4.7- 7: Mean TRR of both lysimeter (in % of applied radioactivity)

Lysimeter	Layer [cm]	Mean TRR value per layer [% of applied]
Mean lysimeter 13 & lysimeter 14	0 - 10	8.3
	10 - 20	3.2
	20 - 30	1.2
	30 - 40	0.6
	40 - 50	0.3
	50 - 60	0.1
	60 - 70	0.1
	70 - 80	< 0.1
	80 - 90	0.1
	90 - 100	0.1
	100 - 110	0.1
	110 - 120	< 0.1
	120 - 130	0.1
	gravel 130 - 135	0.1
	total	13.8

C. Plants

A total of 0.4% (mean value) was taken up by the bunches of grapes (Table 7.4.7- 8). The values of 1994 and 1995 correspond to the annual application rates. Leaves and pruning offal were left on the lysimeter for composting. Aliquots of the leaves were analysed occasionally for radioactivity. Since the leaves do not belong to the eatable crop part, the corresponding values were not validated and consequently not reported.

Table 7.4.7- 8: Total radioactivity in the bunches of the grapes

Year	Lysimeter 13		Lysimeter 14	
	MBq		MBq	
1994 bunches of grapes	0.814	0.3% = 0.4 mg TRR/kg	1.233	0.5% = 0.5 mg TRR/kg
1995 bunches of grapes	0.464	0.2% = 0.2 mg TRR/kg	1.253	0.5% = 0.4 mg TRR/kg
1996 bunches of grapes	0.005	= 0.001 mg TRR/kg	0.005	= 0.002 mg TRR/kg
total radioactivity	1.283	0.25%	2.491	0.49%

D. Total balance (sum of radioactivity from leachate, soil, brunches of grapes)

The recovery of the applied radioactivity is given in Table 7.4.7- 9. The loss of radioactivity of 86% within 3 years was attributed to the mineralisation of iprovalicarb.

Table 7.4.7- 9: Recovery of the applied radioactivity

	Lysimeter 13		Lysimeter 14	
	MBq	%	MBq	%
Application	505.863	100.00	509.410	100.00
Leachate	0.207	0.04	0.182	0.04
Soil	73.821	14.59	66.401	13.03
Brunches of grapes	1.283	0.25	2.491	0.49
Total	75.311	14.88	69.074	13.56

III. Conclusions

The total radioactive residue (TRR) expressed as µg/L was very similar in the annual leachates of both lysimeter 13 and 14 and amounted to 0.1-0.2 µg/L. The analyses of the leachates s[redacted]d that the parent compound was not translocated into the annual leachates with > 0.02 µg/L. Two metabolites with < 0.1 µg/L were identified: SZX 0722-carboxylic acid *(M03)* (< 0.02 µg/L) and terephthalic acid *(M23)* (< 0.03 µg/L single annual values). The concentration of each individual unknown radioactive zone was < 0.09 µg a.s. equivalent/L leachate. It is probable that the unknown radioactive compounds occurring in the leachates consisted of humic substances and/or endogenous substances of micro-organisms into which liberated $^{14}CO_2$ and/or radioactive iprovalicarb fragments have been incorporated. The radiochemical impurities of the active ingredient accounting for less than 1% could also be a reason for this low radioactivity in the leachates. The majority of the recovered radioactivity remained in the top (0 - 10 cm) soil layer accounting for 8.3% of the total applied radioactivity.

A total of 0.4% (mean value) was taken up by the bunches of grapes. The loss of radioactivity within 3 years was attributed to mineralisation of iprovalicarb and amounted to 86% of the applied radioactivity.

KIIA 7.4.8 Field leaching studies

No problems concerning the groundwater contamination will be expected, which was also confirmed by a lysimeter study (KIIA 7.4.7) and by the PEC_{gw} computer simulation (see Annex III / IIIA 9.6). Therefore, field leaching studies with iprovalicarb are not necessary.

KIIA 7.4.9 Volatility - laboratory study

No laboratory volatility studies were performed with iprovalicarb. The volatilisation of iprovalicarb was determined in a field trial ([redacted] (1996); submitted within the EU Basic Dossier of 1998; IIA 7.2.2.2/01).

KIIA 7.5 Hydrolysis rate of relevant metabolites at pH values 4, 7 and 9

Hydrolysis studies with metabolites were not conducted as no hydrolysis products were detected in the study with parent compound.

In addition to section 1, point KIIA, 2.9.1, a short summary of the hydrolysis of the parent substance at different pH values is presented here to provide a complete and comprehensive overview on the fate and behaviour of iprovalicarb in the environmental fate section IIA 7.

The hydrolysis of iprovalicarb in sterile aqueous buffer solutions was evaluated during the Annex I Inclusion. No additional studies have been performed for the parent compound. A short summary of

the data is given below.

The hydrolysis of iprovalicarb was studied in sterile aqueous buffer solutions adjusted to pH 5, 7 and 9 ([redacted], (1996), submitted in the EU Basic Dossier in 1998; IIA, 2.9.1 /01 and IIA, 7.2.1.1 /01).

Iprovalicarb was stable at pH 5, 7 and 9 and no formation of hydrolysis products was observed. Iprovalicarb accounted for approximately 100% of the radioactivity recovered in the solutions at termination of the experiment. 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.

As no hydrolysis products were detected in the studies with the parent compound, no further studies are necessary.

KIIA 7.6 Direct phototransformation of relevant metabolites in water

As no direct photodegradation of iprovalicarb in the aqueous environment is to be expected, no photodegradation products could be formed. Therefore no further studies concerning metabolites are necessary.

In addition to section 1, point KIIA, 2.9.2, a short summary of the aqueous photolysis of the parent substance is presented here to give a complete and comprehensive overview on the fate and behaviour of iprovalicarb in the environmental fate section IIA 7.

The UV-VIS absorption data in the environmentally relevant pH range (buffers at pH 5, 7 and 9) ([redacted], (1994), submitted in the EU Basic Dossier in 1998; IIA 2.9.2 /01 and IIA, 7.2.1.2 /01) s[redacted]d 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.

KIIA 7.7 Ready biodegradability of the active substance

A study on the "Ready Biodegradability" of iprovalicarb was not performed. [redacted]ver, this requirement is covered by water-sediment studies, which are described in section KIIA 7.8.3.

KIIA 7.8 Degradation in aquatic systems

KIIA 7.8.1 Aerobic biodegradation in aquatic systems

Studies on the aerobic biodegradation in aquatic systems are not required by Directive 91/414/EEC. [redacted]ver, water-sediment studies with iprovalicarb provide a comprehensive overview of the fate and behaviour in aqueous aquatic systems (section KIIA 7.8.3).

KIIA 7.8.2 Anaerobic biodegradation in aquatic systems

This type of study is not required by Directive 91/414/EEC.

KIIA 7.8.3 Water/sediment studies

The degradation and dissipation behaviour of iprovalicarb in water-sediment systems under aerobic conditions was evaluated during Annex I inclusion using the phenyl-labelled parent compound ([redacted], 1997c; submitted within the EU Basic Dossier 1998 (IIA, 7.2.1.3.2/01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)). In addition a new water-sediment study under aerobic condition was performed using the valine radiolabel of iprovalicarb to complete the data according to current requirement practice ([redacted] (2011), submitted in this Dossier, KIIA 7.8.3 /02). For a better overview a short summary of both studies is given at the end of this chapter at page 139.

Furthermore, a kinetic evaluation of these data was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessment according to FOCUS kinetics (FOCUS, 2006) ([redacted] (2012), submitted in this Dossier, KIIA 7.8.3 /03). For a better overview of these evaluated data of a short summary is also given at the end of this chapter at page 139.

New study, not included for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The new aquatic (water/sediment) metabolism study was conducted with the valine radiolabel to complement the former dossier according to current requirement practices. With the first dossier only studies with the phenyl radiolabel were provided.

Report:	**KIIA 7.8.3 /02, [redacted].; 2011**
Title:	[Valine-1-^{14}C]Iprovalicarb (SZX0722): Aerobic aquatic metabolism
Report No:	MEF-11/650
Document No:	M-419466-01-1
Guidelines:	- OECD Guideline for the Testing of Chemicals 308, Aerobic and Anaerobic Transformation in Aquatic Sediment Systems, Adopted April 24, 2002 - Official Journal of the European Communities, No. L 172 (EN), July 14, 1995, Commission Directive, 95/36/EC, amending Council Directive 91/414/EEC concerning the placing of plant protection products on the market: Annexes II+III, Fate and Behavior in the Environment 7171/VI/94-EN - US EPA Fate, Transport and Transformation Test Guidelines, OPPTS 835.4300 and OPPTS 835.4400, Aerobic and Anaerobic Aquatic Metabolism, October 2008
GLP:	Yes

Executive Summary

The aerobic biotransformation of iprovalicarb was studied in two different water/sediment systems ([redacted], water: pH 8.1, total organic carbon ≤ 3.3 mg/L; sediment: sand, pH 7.1, organic carbon 0.3% from [redacted], and [redacted], water: pH 7.0, total organic carbon ≤ 8.5 mg/L; sediment: sandy loam, pH 5.4, organic carbon 3.8% from a location near [redacted], Germany) for a maximum of 120 days in the dark at 20°C.

The test item valine-labelled iprovalicarb (equimolar mixture of S,R- and S,S-configured isomers) was applied to the test systems with an average rate of approx. 50 µg/batch, corresponding to approx. 95 µg/L. This application rate correspond to 350% (3.5-fold) of the recommended maximum single field use rate of iprovalicarb, which is 270 g/ha. The over dosage was chosen due to processing, stability and analytical reasons. The test system consisted of laboratory microcosm flasks attached to traps for collection of CO_2 and volatile organic compounds. The water/sediment ratio was 3/1 (v/v). Duplicate samples of both water/sediment systems were analysed after 0, 1, 3, 7, 14, 30, 60, 91 and 120 days of incubation.

Before any processing aliquots of the water layers were subjected to liquid scintillation counting (LSC) to determine their radioactivity content. Afterwards, the water layers were decanted, centrifuged and concentrated after addition of a solubilizer. These concentrates were analysed by high performance liquid chromatography/radiodetection (HPLC/radiodetection) to quantify the test item as well as possible transformation products. The sediment samples were extracted twice with acetonitrile/water, followed by two extraction steps with pure acetonitrile (all at ambient temperature). Afterwards, the sediments were extracted once more, using a microwave-accelerated solvent extraction with acetonitrile/water. The ambient extracts were combined, concentrated after addition of a solubilizer and analysed by LSC and HPLC/radiodetection. The microwave extracts, which contained more than 1% AR were separately analysed using the same methods. The identity

of the test item and its transformation products was exemplarily elucidated by high performance liquid chromatography hyphenated to tandem mass spectrometry (HPLC-MS/MS) and/or by co-chromatography with an reference item in water layers and extracts of selected processing intervals.

The average material balance of the two water/sediment systems was 100.2% of the applied radioactivity (AR) for the system [redacted] and 96.8% AR for the system [redacted]. The material balance indicated no significant losses of radioactivity.

The radioactivity content in the water layer of the system [redacted] decreased steadily from 104.8% AR (2 hours after application) to 3.0% AR at study termination, day 120 (Table 7.8.3- 5). The total radioactivity in the water layer of the [redacted] decreased steadily from 92.2% AR (day 0) to 0.4% AR at day 120 (Table 7.8.3- 6).

The total extractable radioactivity from sediments increased in the [redacted] water/sediment system from 1.5% AR at day 0 to a maximum of 11.2% AR at day 14 and decreased again to 1.3% AR at study termination (day 120) (Table 7.8.3- 5). Total radioactive sediment extractables in the [redacted] water/sediment system increased from 2.5% AR at day 0 to a maximum of 37.8% AR at day 14 and decreased to 4.2% AR at study termination (day 120) (Table 7.8.3- 6).

The maximum of radioactive non-extractable residues (NERs) was 25.1% AR at day 60 for the system [redacted] and 23.3% AR at study termination (day 120) for the system [redacted]. At the end of the study 79.9% AR ([redacted]) and 65.3% AR ([redacted]) was mineralised to $^{14}CO_2$. Organic volatile compounds accounted for less than 0.1% AR in both systems (Table 7.8.3- 5 and Table 7.8.3- 6).

The amount of iprovalicarb in the water layer of the system [redacted] decreased rapidly from 104.8% AR (day 0) to non-detectable amounts at study termination (day 120). The amount of iprovalicarb in the water layer of the system [redacted] decreased from 92.2% AR (day 0) to non-detectable amounts at day 120. The amount of iprovalicarb in the sediment of the system [redacted] increased from 1.4% AR (day 0) to 10.9% AR at day 14 and declined to 1.2% AR at day 120. The amount of iprovalicarb in the sediment of the system [redacted] increased from 2.4% AR (day 0) to 35.5% AR at day 14 and then declined to 3.8% AR at study termination (Table 7.8.3- 5 and Table 7.8.3- 6).

SXZ 0722-carboxylic acid *(M03)* was observed as minor degradation product of iprovalicarb in the water layer of the system [redacted] with a maximum amount of 0.8% AR at day 60, as well as in the water layer and in the sediment extracts of the system [redacted] with a maximum amount of 3.8% AR and 1.4% AR at day 14, respectively (Table 7.8.3- 7 and Table 7.8.3- 8). No other transformation products, except CO_2 and NERs were detected during the study.

The dissipation time (DT_{50}) of iprovalicarb from the water layer (sum of degradation processes and translocation into the sediment) was calculated to be 14.8 days for the system [redacted] and 16.1 days for the system [redacted]. The degradation half-lives (DT_{50}) of iprovalicarb in the

entire water-sediment systems were calculated to be 19.2 days for the system [redacted] and 43.5 days for the system [redacted], respectively (Table 7.8.3- 1).

Table 7.8.3- 1: Dissipation kinetics of iprovalicarb

Compartment	Test system	Best fit kinetic model	DT_{50} [days]	DT_{90} [days]	χ^2 error [%]	Visual assessment[a)]
Water layer	[redacted]	DFOP[b)]	14.8	58.2	3.5	+
	[redacted]	DFOP[b)]	16.1	72.5	3.0	+
Entire system	[redacted]	DFOP[b)]	19.2	66.9	3.7	+
	[redacted]	SFO[c)]	43.5	144.4	4.9	+

a) visual assessment: + good o medium - bad
DFOP double first order in parallel
SFO single first order

I. Material and Methods

A. Materials

1. Test Material: [valine-1-^{14}C]iprovalicarb (equimolar mixture of the S,R- and S,S-configured diastereomers)
CAS #: 140923-17-7 (unlabelled iprovalicarb, without specification of stereochemistry)
single isomers:
- S,R-configured isomer:
  [valine-1-^{14}C]SZX 0932, sample ID: KATH6410
  specific radioactivity: 3.85 MBq/mg, 104 µCi/mg
  radiochemical purity: > 99%
- S,S-configured isomer:
  [valine-1-^{14}C]SZX 6045, sample ID: KATH6411
  specific radioactivity: 3.81 MBq/mg, 103 µCi/mg
  radiochemical purity: > 99%

2. Test system: Two natural aquatic sediment systems were collected, one from a site in [redacted], Germany ([redacted]), and one from a site close to [redacted], Germany ([redacted]). The system [redacted] is a small lake (reclaimed gravel-pit) used only for fishing and the system [redacted] is an artificially dammed pond in the course of the "[redacted]" and has a strong water current. Details of both systems are provided in Table 7.8.3- 2. Water and sediment were freshly sampled prior to the start of the study.

Table 7.8.3- 2: Physico-chemical characteristics of the water and sediment of the test systems [redacted] and [redacted]

	[redacted]	[redacted]
Geographic location	[redacted], North Rhine-Westphalia, Germany	[redacted] close to [redacted], North Rhine-Westphalia, Germany
Collection date	2010-03-03	2010-03-03
Water		
Temperature at collection [°C]	6.9	9.7
pH at collection	7.2	7.1
Hardness [°dh]	9.8	2.8
Total organic carbon (TOC) [mg/L] - at start of acclimation - at day 0 (application) - at day 120 (study termination)	 < 2 3 5	 < 2 4 20
Dissolved organic carbon (DOC) [mg/L] - at start of acclimation acclimation	 < 2	 < 2
Redox potential E_h [mV] at collection	+ 412	+ 386
Oxygen content at collection [mg/L]	9.2	9.8
Oxygen content at collection [%]	101	107
Sediment		
Soil taxonomic classification (USDA) - sand (2000-50 µm) [%] - silt (2-50 µm) [%] - clay (< 2 µm) [%]	Sand 95 3 2	Sandy loam 58 35 7
pH - water - $CaCl_2$	 7.3 7.1	 5.4 5.3
Organic matter [%][a)] - at start of acclimation - at day 0 (application) - at day 120 (study termination)	 0.55 0.50 0.43	 6.29 6.71 6.76
Organic carbon [%] - at start of acclimation - at day 0 (application) - at day 120 (study termination)	 0.32 0.29 0.25	 3.65 3.89 3.92
Soil microbial activity [mg CO_2/h/kg sediment (dry wt)] - at start of acclimation - at day 0 (application) - at day 120 (study termination)	 7.92 5.42 1.25	 25.83 22.50 15.00
Cation exchange capacity [meq/100g] - at start of acclimation	 2.7	 7.6
Total nitrogen [weight-%] - at start of acclimation	 0.005	 0.31
Total phosphorus [mg/kg] - at start of acclimation	 150	 560
atro dry matter content [% AD] - at start of acclimation	 123.4	 210.8
Redox potential E_h [mV] at collection	+ 370	+ 116

a) = % organic matter = % organic carbon x 1.724

B. Study design

1. Experimental conditions: The water to sediment ratio was 3/1 (v/v). Sediment volumes of 175 mL (height about 2 cm) were transferred to the incubation vessels, and water volumes of 520 mL (height about 6 cm) were added. The vessels were fitted with solid trap attachments permeable for oxygen but absorbing volatile compounds formed in the test systems to soda lime (CO_2) and polyurethane foam (organic volatiles). For acclimatisation of the test systems and for establishment of phase separation, the test systems were placed in the climatic chamber for 13 days prior to application under the intended study incubation conditions.

The test item valine-labelled iprovalicarb (equimolar mixture of S,R and S,S-configured isomers) was applied to the test systems with an average rate of approx. 50 µg/batch, corresponding to approx. 95 µg/L (Table 7.8.3- 3). These application rates (ca. 950 g/ha) correspond to 350% (3.5-fold) of the recommended maximum single field use rate of iprovalicarb, which is 270 g/ha. Aerobic conditions were maintained by the solid trap which was permeable for air. The flasks were incubated in the dark at 20°C. The pH values of the water and sediment phases, the redox potentials and the amount of dissolved oxygen were measured at each sampling date. Duplicate samples of both test systems were processes and analysed 0, 1, 3, 7, 14, 30, 60, 91 and 120 days after application of the test item.

Table 7.8.3- 3: Test concentrations

Test system	Samples	Test concentrations test vessel	
		[kBq]	[µg]
[redacted]	DAT-0 to DAT-14 DAT-14 to DAT-120	189.3 175.3	49.8 46.1
[redacted]	DAT-0 to DAT-14 DAT-14 to DAT-120	185.2 202.3	48.7 53.2

2. Extraction and analytical procedures: For the sampling dates day 0 to day 3 the supernatant water was decanted from the sediment, centrifuged and decanted again. Aliquots of the processed water were taken for LSC measurements and further characterisation by a chromatographic method. As strong mineralisation of the test item was observed, for the sampling dates from day 7 forward the processing procedure was adjusted to prevent inaccurate LSC measurements, due to losses of dissolved $^{14}CO_2$, which could possibly occur during processing of the water layer. Therefore, the aliquots for LSC measurements were also taken from the undisturbed water layer before any measurements or processing. Additionally, the scintillation cocktail was made alkaline by addition of sodium hydroxide, to prevent volatilisation of the dissolved carbon dioxide. The further processing of the water layer followed the processing procedure like for the sampling dates day 0 to day 3.
For a exhaustive extraction the moist sediment was extracted four times at ambient conditions and once using a microwave-accelerated extraction procedure. For the ambient extraction procedure the sediment was extracted twice with acetonitrile/water, followed by two extractions with pure acetonitrile. Each time the samples were extracted on a horizontal shaker and were centrifuged afterwards. The supernatants were decanted each time and all extracts from ambient conditions were combined and the volume was determined. Finally, the sediment was extracted by microwave-accelerated solvent extraction. After extraction and centrifugation the supernatant was decanted and the volume was determined. Aliquots of ambient and microwave extracts were taken for LSC measurements and further characterisation by a chromatographic method, if necessary. The

exhaustive extracted sediment was dried and at a later time point it was. Aliquots of these homogenised, exhaustive extracted sediment were subjected to combustion/LSC to determine the non-extractable residues (NER).
Characterisation of NERs was performed at the end of the study using the exhaustive extracted sediments of day 120. The NERs of one sediment sample of [redacted] and [redacted], respectively, were investigated for humin, humic acid and fulvic acid.
The radioactivity absorbed by the soda lime ($^{14}CO_2$) was liberated by 18% aqueous HCl and purged with nitrogen into cooled LSC cocktails. The absorbed radioactivity in the scintillation cocktails was measured by LSC.
The subsamples of the water layers and the sediments were treated likewise to determine the amount of dissolved $^{14}CO_2$and bounded ^{14}C-carbonates, respectively.
Volatile organic compounds possibly contained in the PU foam plugs were extracted with ethyl acetate and aliquots were radio-assayed by LSC. Due to the low amount (< 0.1% AR) they were not further analysed.

Iprovalicarb and SZX 0722-carboxylic acid *(M03)* were identified by co-chromatography with reference compounds as well as by HPLC-MS/MS and HPLC-^{1}H-NMR.

C. Degradation kinetics

DT_{50} and DT_{90} values were calculated for the degradation of iprovalicarb. The data for the test item iprovalicarb as well as for its single diastereomers were evaluated following the recommendations of FOCUS rules according to the FOCUS guidance document on degradation kinetics (SANCO/10058/2005, version 2.0). Kinetic evaluations were conducted with the software KinGUI (version 1.1). The Single First Order (SFO), First Order Multi-Compartment (FOMC), and Double First Order in Parallel (DFOP) models were used to find the best fitting kinetics.

II. Results and Discussion

The degradation and metabolism of iprovalicarb was studied in two water/sediment systems at 20°C. The pH values of the [redacted] water (pH between 7.8 and 8.4) and of [redacted] (pH between 5.9 and 7.6) remained stable during the test period. The redox potential in the supernatant water of both test systems after acclimation remained at high positive mV-values (342 to 498 mV). The redox potential in the sediment was between 85 mV and 540 mV. Some variations between different vessels were observed. The relative oxygen content (dissolved oxygen) in the supernatant water was also determined and varied approx. between 57 - 88% in the individual test vessels. In general, the pro[redacted]s of both parameters indicates aerobic conditions of both water/sediment systems during the entire incubation period.
The microbial activity indicated that the systems were biologically active during the entire period of the test. For test systems of both water/sediment systems a reduction of the microbial activity during the study course was observed. This is characteristic for a laboratory experiment due to the gradual depletion of nutrients in the sediment and lacking supply of organic matter as a source of energy. During the study the total organic carbon (TOC) of the water layer was in a range of < 2 to 20 mg/L in both systems.

A. Extraction and quantification of radioactivity in water/sediment systems

The extraction efficiency of the method was tested for sediment samples of day 0 (approximately 2 hours post-application). A total of 106.3% and 94.8% AR was extracted for sediment of [redacted] and [redacted], respectively (Table 7.8.3- 5 and Table 7.8.3- 6). The portions of non-extractable radioactivity of day 0 were 0.1% of the AR for the two sediments.

The radioactivity content in the water layer of the [redacted] test systems decreased steadily from 104.8% AR at day 0 (approx. 2 hours after application) to 3.0% AR at study termination (day 120). The radioactivity content in the water layer of [redacted] test systems decreased steadily from 92.2% AR at day 0 to 0.4% AR at study termination (Table 7.8.3- 5 and Table 7.8.3- 6).

After the application of the test item onto the water surface, the total extractable radioactivity from sediment increased in the [redacted] water/sediment system from 1.5% AR at day 0 to a maximum of 11.2% AR at day 14 and decreased again to 1.3% AR at study termination. Total radioactive sediment extractable in the [redacted] water/sediment system increased from 2.5% AR at day 0 to a maximum of 37.8% AR at day 14 and decreased to 4.2% AR at study termination (Table 7.8.3- 5 and Table 7.8.3- 6).

B. Mass balance

For the determination of the amount of dosed test item, the total recovery of radioactivity at day 0 was determined and set as 100%. The total recovery of radioactivity of all sampling intervals of the system [redacted] ranged from 94.9% to 109.3% (overall mean 100.2%, RSD 4.8%) during the study course (Table 7.8.3- 5). The material balance for eight sampling intervals of the test system [redacted] ranged from 93.2% to 104.1% (overall mean 96.8%, RSD 5.5%) (Table 7.8.3- 6). The complete material balance found at all regarded sampling intervals demonstrated that no significant portion of radioactivity dissipated from the vessels or was lost during processing of theses samples.

C. Bound and extracted residue

The residues for [redacted] test systems were 0.1% AR at day 0. They increased to a maximum of 25.1% AR at day 60 and decreased again to 15.2% AR at study termination. For [redacted] test systems, the residues were 0.1% AR at day 0 and increased to a maximum of 23.3% AR at study termination.

Since the formation of non-extractable residues exceeded 15% AR in both water/sediment systems, further characterization of the non-extractable residues was conducted exemplarily for DAT-120 samples (one replicate of each sediment). Recoveries were 88.6% for [redacted] and 99.2% for [redacted] water/sediment system.

The distribution of the non-extractable residues in different humic substance fractions was found to be of heterogeneous nature in case of both water/sediment systems the results are shown in the table below:

Table 7.8.3- 4: Non-extractable residues in different humic substance fractions at day 120

Water-sediment system	Fractions						
	Humin		Fulvic		Humic acid		Total
	[% NER]	[% AR]	[% NER]	[% AR]	[% NER]	[% AR]	[% AR]
[redacted]	44.3	7.7	34.9	6.0	9.5	1.6	15.3
[redacted]	34.3	8.0	14.8	3.5	50.1	11.7	23.1

D. Volatilisation

The amount of liberated ^{14}C-carbon dioxide formed in both water/sediment systems is presented in Table 7.8.3- 5 and Table 7.8.3- 6 as sum of the ^{14}C-carbon dioxide determined in the soda lime of the trap attachments and the amount of ^{14}C-carbon dioxide determined in the water layers as well as in the exhaustive extracted sediments. Both water/sediment systems showed a strong mineralisation of iprovalicarb with a maximum of 79.9% AR in [redacted] and 65.3% AR in [redacted] water/sediment system at study termination.

Table 7.8.3- 5: Material balance of radioactivity after application of valine-labelled iprovalicarb from aerobic aquatic metabolism in [redacted], expressed as percent of applied radioactivity

	Days after treatment								
	0	1	3	7	14	30	60	91	120
Volatile radioactivity									
$^{14}CO_2$	n.a.	1.3	4.1	9.9	18.0	38.1	68.7	73.8	79.9
Organic volatiles	n.a.	< 0.1	0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
Total volatiles	n.a.	1.3	4.1	9.9	18.0	38.1	68.7	73.8	79.9
Extractable radioactivity									
Water layer[a)]	104.8	92.2	83.3	66.7	57.4	30.2	12.2	5.0	3.0
Sediment:									
- ambient extract	1.4	7.7	8.8	10.2	10.9	7.3	2.9	1.2	1.2
- microwave extract	< 0.1	0.2	0.2	0.3	0.4	0.4	0.3	0.2	0.2
- total sediment extractables	1.5	7.9	9.1	10.6	11.2	7.7	3.2	1.3	1.3
Total water layer and sediment	106.3	100.2	92.4	77.2	68.6	37.9	15.5	6.4	4.3
Non-extractable residue[b)]	0.1	1.5	4.5	8.6	10.0	18.9	25.1	15.9	15.2
Material balance	106.3	102.9	101.0	95.8	96.6	94.9	109.3	96.1	99.4

n.a. not analysed
a) values corrected by CO_2-content of water layer
b) values corrected by CO_2-content of sediment

Table 7.8.3- 6: Material balance of radioactivity after application of valine-labelled iprovalicarb from aerobic aquatic metabolism in [redacted], expressed as percent of applied radioactivity

	Days after treatment[a)]							
	0	1	3	7	14	30	60	120
Volatile radioactivity								
$^{14}CO_2$	n.a.	0.3	1.0	2.7	6.5	15.0	34.2	65.3
Organic volatiles	n.a.	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1
Total volatiles	n.a.	0.3	1.0	2.7	6.5	15.0	34.2	65.3
Extractable radioactivity								
Water layer[b)]	92.2	85.7	72.3	65.8	49.9	34.1	18.0	0.4
Sediment: - ambient extract	2.4	13.7	21.1	30.4	36.9	32.9	26.1	3.8
- microwave extract	0.1	0.3	0.5	0.8	0.9	1.0	1.1	0.4
- total sediment extractables	2.5	14.0	21.6	31.2	37.8	33.8	27.2	4.2
Total water layer and sediment	94.7	99.6	93.9	97.0	87.7	68.0	45.1	4.6
Non-extractable residue[c)]	0.1	0.8	2.1	4.4	8.7	13.4	17.7	23.3
Material balance	94.8	100.7	97.0	104.1	102.9	96.4	97.0	93.2

n.a. not analysed
a) samples of sampling day 91 have to be evalulated as invalid
b) values corrected by CO_2-content of water layer
c) values corrected by CO_2-content of sediment

E. Iprovalicarb and transformation products

The metabolism of iprovalicarb and its metabolites including $^{14}CO_2$ in the entire test system can be tracked in Table 7.8.3- 7 to Table 7.8.3- 8 (values in % AR). The amount of iprovalicarb in the entire [redacted] water-sediment system declined to 1.2% AR at study termination. In the [redacted] system 3.8% AR was found as unchanged test item at study termination in the entire system. The metabolite SZX 0722-carboxylic acid *(M03)* amounted to a maximum of 0.8% AR (day 60) in [redacted] water-sediment system and 5.2% AR (day 14) in [redacted] water-sediment system.

The maximum amount of minor radioactivity zones in the entire system was 5.0% [redacted] water-sediment systems. All minor radioactivity zones detected in the entire system of [redacted] were beneath the limit of detection (LOD). Both water-sediment systems s[redacted]d a continuous degradation of iprovalicarb and a strong mineralisation until study termination (79.9% AR in [redacted] and 65.3% AR in [redacted] water-sediment system).

The iprovalicarb content in the water layer of the [redacted] water-sediment system decreased from 104.8% AR at day 0 to non-detectable amounts at study termination. The amount of iprovalicarb in the water layer of the [redacted] water-sediment system decreased from 92.2% AR at day 0 to non-detectable amounts at study termination (see Table 7.8.3- 7 to Table 7.8.3- 8). No major degradation product of iprovalicarb was detected in the water layer of both water-sediment systems. Only dissolved $^{14}CO_2$ was detected temporarily in the water layer of the [redacted] water-sediment system. SZX 0722-carboxylic acid *(M03)* was detected as minor degradation product of iprovalicarb in the water layer of both test systems, with a maximum of 0.8% AR (day 60) in [redacted] water-

sediment system and of 3.8% AR (day 14) in [redacted] water-sediment system. Additional, minor radioactive zones were detected temporarily in the water layer of [redacted], but their amounts expressed in percent of applied radioactivity were beneath the LOD. In the day 91 and day 120 samples of the [redacted] water layer no further metabolites were detected except dissolved CO_2. Hence, the radioactivity content of these samples was evaluated as diffuse radioactivity with an one-time maximum of 5% AR. It can be concluded that there is no potential for accumulation of iprovalicarb in the supernatant water.

The iprovalicarb content in the sediment of the [redacted] test system increased from 1.4% AR at day 0 to 10.9% AR at day 14 and declined then to 1.2% AR at study termination. The amount of iprovalicarb in the sediment of the [redacted] test system increased from 2.4% AR at day 0 to 35.5% AR at day 14 and declined then to 3.8% AR at study termination (see Table 7.8.3- 7 to Table 7.8.3- 8). SZX 0722-carboxylic acid *(M03)* was also observed as minor degradation product of iprovalicarb in the sediment extracts of [redacted] water-sediment systems. The maximum detected amount of SZX 0722-carboxylic acid was 1.4% AR at day 14. The major amount of iprovalicarb (> 95% AR) was degraded in both water-sediment systems after 120 days and a strong mineralisation was observed. The results show that Iprovalicarb is translocated into the sediment and then rapidly degraded.

Table 7.8.3- 7: Biotransformation of iprovalicarb in [redacted] test system under aerobic conditions (expressed as percent of applied radioactivity)

Compound	Compartment	Days after treatment								
		0	1	3	7	14	30	60	91	120
Iprovalicarb	water layer	104.8	91.6	82.3	65.9	56.4	28.9	11.0	n.d.	n.d.
	sediment	1.4	7.7	8.8	10.2	10.9	7.2	2.9	0.7	1.2
	entire system	106.3	99.3	91.1	76.1	67.3	36.1	14.0	0.7	1.2
SZX 0722-carboxylic acid *(M03)*	water layer	n.d.	< LOD	< LOD	0.6	< LOD	< LOD	0.8	n.d.	n.d.
	sediment	n.d.	n.d.	n.d.	0.6	n.d.	n.d.	n.d.	n.d.	n.d.
	entire system	n.d.	< LOD	< LOD	0.6	< LOD	< LOD	0.8	n.d.	n.d.
Unidentified/diffuse radioactivity	water layer	n.d.	n.d.	< LOD	n.d.	n.d.	< LOD	< LOD	5.0	2.6
	sediment	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	entire system	n.d.	n.d.	< LOD	n.d.	n.d.	< LOD	< LOD	5.0	2.6

n.d. not detected

Table 7.8.3- 8: Biotransformation of iprovalicarb in [redacted] test system under aerobic conditions (expressed as percent of applied radioactivity)

Compound	Compartment	Days after treatment							
		0	1	3	7	14	30	60	120
Iprovalicarb	water layer	92.2	85.0	70.1	62.9	46.1	31.3	14.7	n.d.
	sediment	2.4	13.7	21.1	30.4	35.5	32.3	24.8	3.8
	entire system	94.6	98.6	91.2	93.4	81.6	63.7	39.5	3.8
SZX 0722-carboxylic acid *(M03)*	water layer	n.d.	0.7	2.2	2.8	3.8	2.8	3.3	n.d.
	sediment	n.d.	n.d.	n.d.	n.d.	1.4	0.5	1.3	n.d.
	entire system	n.d.	0.7	2.2	2.8	5.2	3.3	4.6	n.d.
Unidentified/diffuse radioactivity	water layer	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.3
	sediment	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	entire system	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	0.3

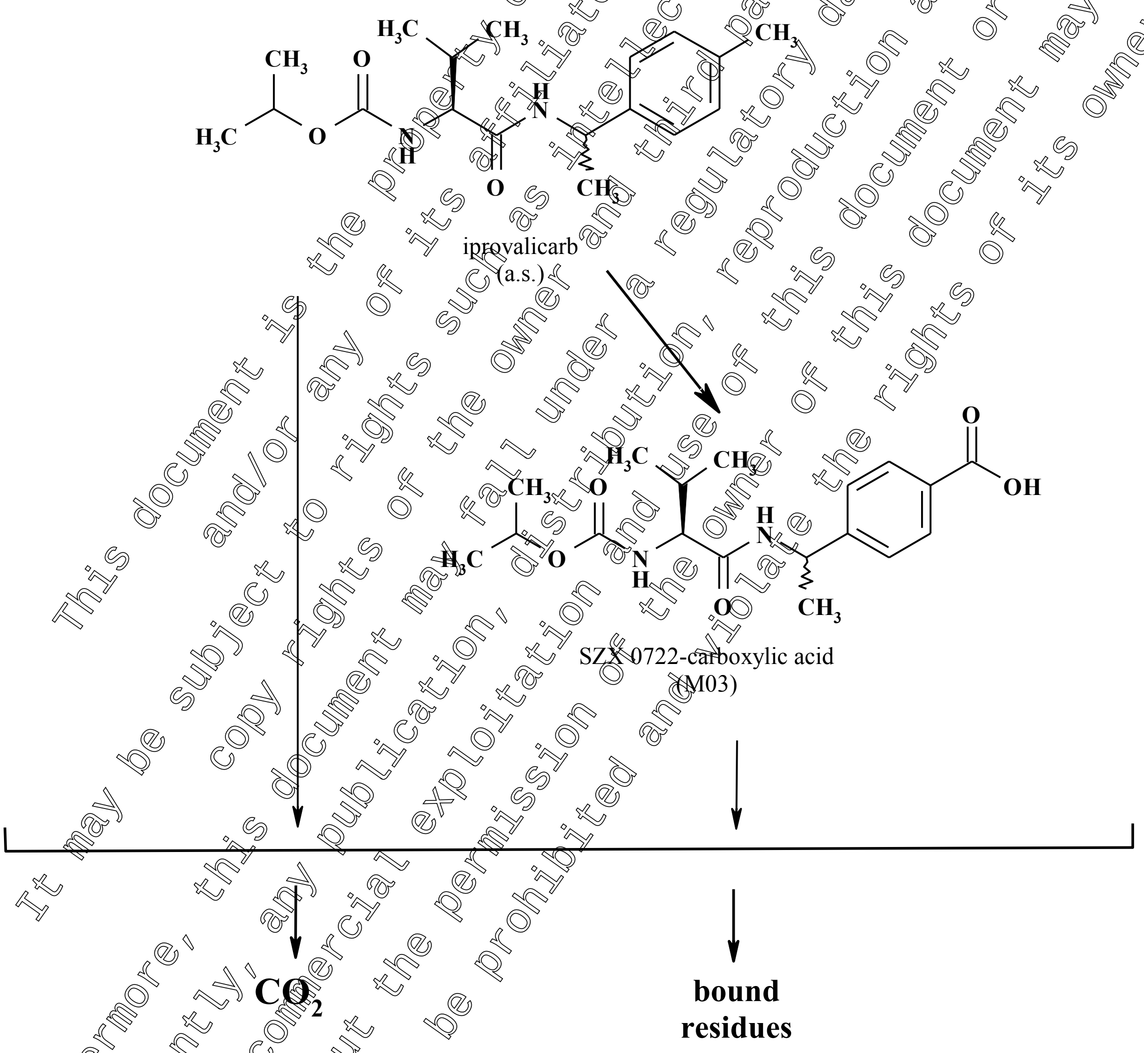
n.d. not detected

F. Degradation pathway

Based on the results obtained within this study a metabolic pathway for the aerobic degradation of valine-labelled iprovalicarb in water-sediment systems is proposed (see Figure 7.8.3- 1). The test item was degraded by the following main degradation reactions:

- Oxidation of the methyl group of the aromatic system yielding the SZX 0722-carboxylic acid *(M03)*
- Mineralisation (CO_2 formation)
- Formation of non-extractable residues (NERs)

Figure 7.8.3- 1: Proposed metabolic pathway of valine-labelled iprovalicarb in aerobic aquatic systems



G. Dissipation kinetics

Water layer: The kinetic calculations, describing the dissipation of iprovalicarb (sum of diastereomers) from the supernatant water layer are summarized in Table 7.8.3- 9. The best fit kinetic calculations followed DFOP kinetics in the water layer of both water sediment systems according to the lowest chi^2 values. The amount of iprovalicarb in the supernatant water was

declining during the test period of 120 days. The half-lives in the supernatant water under aerobic laboratory conditions for iprovalicarb (sum of diastereomers) were 14.8 days in [redacted] test system and 16.1 days in [redacted] test system. The degradation kinetics of the single diastereomers followed also DFOP kinetics according the lowest chi² value. The half-lives in the supernatant water for the SR- and SS-diastereomers were 12.8 and 17.1 days for the system [redacted] and 13.6 and 18.9 days for system [redacted], respectively. It is likely, that iprovalicarb is eliminated from the supernatant water via translocation into the sediment as well as via degradation.

Entire system: The best fit kinetic calculations, describing the dissipation of iprovalicarb (sum of diastereomers) from the entire water-sediment system are also summarised in Table 7.8.3- 9. In the entire [redacted] system the best fit calculation followed DFOP and in the entire test system [redacted] SFO kinetics. The amount of iprovalicarb in the entire water-sediment systems was declining during the test period of 120 days. The half-lives in the entire system under aerobic laboratory conditions for iprovalicarb (sum of diastereomers) were 19.2 days in [redacted] test system and 43.5 days in [redacted] test system.
The degradation of the single diastereomers of iprovalicarb were also evaluated. In the test system [redacted] the best fit calculation for the SR-isomer followed DFOP kinetic and for the SS-diastereomer SFO kinetics, in the test system [redacted] the best fit calculation followed SFO kinetics for both diastereomers. The half-lives for the SR- and SS-diastereomers in the entire systems were 15.9 and 23.7 days in the test system [redacted] and 33.8 and 54.3 days in the test system [redacted]. It is likely, that iprovalicarb is eliminated from the entire system by degradation as well as by irreversible translocation into the sediment (formation of non-extractable residues).

Table 7.8.3- 9: Dissipation kinetics of iprovalicarb

compartment	Test system	Kinetic model	DT_{50} [days]	DT_{90} [days]	Chi² error [%]	Visual assessment[a)]
Water layer	[redacted]	SFO	16.6	55.3	6.2	+
		FOMC	15.6	59.8	6.1	+
		DFOP	**14.8**	**58.2**	**3.5**	**+**
	[redacted]	SFO	18.4	61.2	6.3	o
		FOMC	14.9	96.2	5.1	+
		DFOP	**16.1**	**72.5**	**3.0**	**+**
Entire system	[redacted]	SFO	19.9	66.2	3.9	+
		FOMC	19.6	67.3	4.2	+
		DFOP	**19.2**	**66.9**	**3.7**	**+**
	[redacted]	**SFO**	**43.5**	**144.4**	**4.9**	**+**
		FOMC	43.1	150.3	5.7	+
		DFOP	43.5	144.4	5.7	+

a) visual assessment: + good o medium - bad
SFO single first order
FOMC first order multiple compartment
DFOP double first order in parallel

III. Conclusions

Iprovalicarb is well degradable in aerobic water-sediment systems under formation of SZX 0722-carboxylic acid *(M03)* as minor metabolite and strong mineralisation to carbon dioxide. The DT_{50} values for iprovalicarb in the entire water-sediment systems were calculated to be 19.2 days for [redacted] and 43.5 days for [redacted] water-sediment system, thus indicating that the test item is not persistent in a natural aquatic environment.

New study, not submitted for first Annex I inclusion

Justification for including this new study in the Annex I Renewal Dossier: The new study was included due to recent FOCUS kinetics requirements.

Report:	**KIIA 7.8.3 /03, [redacted] 2012**
Title:	Kinetic evaluation of aerobic aquatic metabolism of iprovalicarb in water / sediment systems according to FOCUS kinetics using KinGUI 2
Report No:	MEF-11/630
Document No:	M-429017-01-1
Guidelines:	FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005, v.2.0, June 2006
GLP:	No (calculation)

Executive Summary

The degradation and dissipation behaviour of iprovalicarb and metabolites was investigated by kinetic evaluation of two aerobic water-sediment studies conducted with two different radioactive labels in four different test systems at 20°C and darkness ([redacted], 1997c; submitted within the EU Basic Dossier 1998 (IIA, 7.2.1.3.2 /01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)) and [redacted], 2011 (submitted in this Dossier, KIIA 7.8.3 /02).
Aquatic risk assessment requires the determination of the exposure to an active substance and its major metabolites in a typical surface water environment. For this purpose, the distribution of the parent substance between the water and sediment phase, and their dissipation and degradation in each of the two phases was determined in water-sediment systems under laboratory conditions.
The kinetic evaluation was conducted to obtain kinetic parameters for the use in environmental fate models (modelling endpoints) and as persistence endpoints describing the disappearance behaviour of a compound in the water or sediment phase as well as in the total system of water-sediment systems. Data were processed and evaluated according to the recommendation of the FOCUS kinetics (FOCUS, 2006).
A kinetic evaluation of two water-sediment studies with iprovalicarb has been conducted using the computer program KinGUI 2 according to FOCUS Kinetics guidance (FOCUS, 2006).
According to recommendations of FOCUS kinetics, (Level P-I) dissipation and degradation DT_{50} values of iprovalicarb for water, sediment and total systems were derived, separately, for modelling (Table 7.8.3- 10) and persistence endpoints (Table 7.8.3- 11).
Further on, a 2-compartmental approach was taken into account to estimate the degradation of

iprovalicarb in water and sediment compartment, in parallel, including partitioning processes via reaction rates (Level P-II). [redacted]ver, as the degradation rates in water as well as sediment were not significantly different from 0 (t-test), the total system $DegT_{50}$ might be used for water, sediment or total system, at FOCUS surface water Step 2 level.

Table 7.8.3- 10: Modelling endpoints for degradation and dissipation of iprovalicarb in water, sediment and total system

Compartment	System	Kinetic level	Kinetic model	$DT50_{mod}$ [days]
Water	[redacted] I[a]	P-I: water $DisT_{50}$	SFO	57.28
	[redacted] I[a]	P-I: water $DisT_{50}$	SFO	20.88
	[redacted] II[b]	P-I: water $DisT_{50}$	SFO	16.65
	[redacted] II[b]	P-I: water $DisT_{50}$	SFO	18.42
	geo mean	*P-I: water $DisT_{50}$*		*24.61*
water	all	P-II: water $DegT_{50}$	SFO	n.s.[c]
Sediment	[redacted] I[a]	P-I: sediment $DisT_{50}$	SFO	78.99
	[redacted] I[a]	P-I: sediment $DisT_{50}$	SFO	48.96
	[redacted] II[b]	P-I: sediment $DisT_{50}$	SFO	24.20
	[redacted] II[b]	P-I: sediment $DisT_{50}$	SFO	51.18
	geo mean	*P-I: sediment $DisT_{50}$*		*46.78*
sediment	all	P-II: sediment $DegT_{50}$	SFO	n.s.[c]
Total system	[redacted] I[a]	P-I: system $DegT_{50}$	SFO	58.67
	[redacted] I[a]	P-I: system $DegT_{50}$	SFO	28.39
	[redacted] II[b]	P-I: system $DegT_{50}$	SFO	19.93
	[redacted] II[b]	P-I: system $DegT_{50}$	SFO	43.86
	geo mean	*P-I: system $DegT_{50}$*		*34.73*

a) [redacted] (1997), submitted within the EU Basic Dossier 1998 (IIA, 7.2.1.3.2 /01)
b) [redacted] (2011), new submission (see KIIA 7.8.3 /02)
c) n.s. = not significant (t-test), not reliable

Table 7.8.3- 11: Persistence endpoints, best fit model, for degradation and dissipation of iprovalicarb in water, sediment and total water-sediment system

Compartment	System	Kinetic level	Kinetic model	$DT_{50,\ initial}$ [days]	$DT_{90,\ initial}$ [days]
Water	[redacted] I[a]	P-I: water $DisT_{50}$	SFO	**57.28**	190.28
	[redacted] I[a]	P-I: water $DisT_{50}$	DFOP	19.46	73.00
	[redacted] II[b]	P-I: water $DisT_{50}$	DFOP	14.84	58.23
	[redacted] II[b]	P-I: water $DisT_{50}$	DFOP	16.08	72.53
Sediment	[redacted] I[a]	P-I: sediment $DisT_{50}$	SFO	**78.99**	262.4
	[redacted] I[a]	P-I: sediment $DisT_{50}$	SFO	48.96	162.7
	[redacted] II[b]	P-I: sediment $DisT_{50}$	SFO	24.20	80.4
	[redacted] II[b]	P-I: sediment $DisT_{50}$	SFO	51.18	170.0
Total system	[redacted] I[a]	P-I: system $DegT_{50}$	SFO	**58.67**	194.90
	[redacted] I[a]	P-I: system $DegT_{50}$	SFO	28.39	94.31
	[redacted] II[b]	P-I: system $DegT_{50}$	DFOP	19.17	66.93
	[redacted] II[b]	P-I: system $DegT_{50}$	SFO	43.47	144.39

a) [redacted] (1997), submitted within the EU Basic Dossier 1998 (IIA, 7.2.1.3.2 /01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)
b) [redacted] (2011), new submission (see KIIA 7.8.3 /02)

Additionally, Level M-I degradation DT_{50} in total systems of the metabolites SZX 0722-carboxylic acid (*M03)*, PMPA *(M10*) and N-acetyl-PMPA *(M15*) were evaluated (Table 7.8.3- 12 and Table 7.8.3- 13). All evaluations for metabolites in total systems were carried out together with the appropriate fit of parent for modelling purpose and all evaluable metabolites. [redacted]ver, especially for metabolites, in some systems no fully reliable or significant degradation rates (t-test, visual fit) could be reached.

In case of PMPA *(M10)*, system [redacted] I (Table 7.8.3- 13), a $DegT_{50}$ of 66 days might be true with a similar probability as a $DegT_{50}$ of about 870 days, based on visual and statistical fit assessment. Obviously showing this very high uncertainty, it is considered appropriate to exclude the [redacted] fit for PMPA from any further assessment, to avoid a shift of $DegT_{50}$ to any uncertain direction. So, for further assessments, the $DegT_{50}$ total system of 66.34 days is considered appropriate and reliable for PMPA in total water-sediment systems.

In case of N-acetyl-PMPA *(M15)*, no reliable and statistically significant degradation parameters could be evaluated. The estimation resulted in unsignificant $DegT_{50}$ total system of 8 to > 1000 days. So, for predictive modelling, a conservative default DT_{50} of 1000 days might be assumed in a total water-sediment system for N-acetyl-PMPA (FOCUS, 2003[1], 2006).

Table 7.8.3- 12: Estimated parameter for the degradation of SZX 0722-carboxylic acid *(M03)* in total water-sediment system (level M-1), evaluation for persistence and modelling endpoints

System	Kinetic model of parent	Formation fraction $f_{f.s\text{-}M03}$	$DegT_{50,\ total\ system}$ [days]	$DegT_{90,\ total\ system}$ [days]
[redacted] I[a)]		-	-	-
[redacted] I[a)]		-	-	-
[redacted] II[b)]	SFO	0.0194	26.15	86.85
[redacted] II[b)]	SFO	0.4716	5.642	18.74
geo mean			*12.15*	

a) [redacted] (1997), submitted within the EU Basic Dossier 1998 (IIA, 7.2.1.3.2 /01)
b) [redacted] (2011), new submission (see KIIA 7.8.3 /02)
- metabolite not observed

Table 7.8.3- 13: Estimated parameter for the degradation of PMPA *(M10)* in total water-sediment system (level M-1), evaluation for persistence and modelling endpoints

System	Kinetic model of parent	Formation fraction $f_{f.s\text{-}M10}$	$DegT_{50,\ total\ system}$ [days]	$DegT_{90,\ total\ system}$ [days]
[redacted] I[a)]	SFO	0.4709	66.34	220.38
[redacted] I[a)]	SFO	0.1914	870[nr]	> 1000[nr]
[redacted] II[b)]		-	-	-
[redacted] II[b)]		-	-	-

a) [redacted] (1997), submitted within the EU Basic Dossier 1998 (IIA, 7.2.1.3.2 /01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)
b) [redacted] (2011), new submission (see KIIA 7.8.3 /02)
nr not fully reliable, mathematically not significantly different from 0, not usable
- metabolite not observed

[1] FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC
Report prepared by the FOCUS Working Group on Surface Water Scenarios
EC Document Reference: SANCO/4802/2001-rev. 2, 245 pp.; May 2003

I. Material and Methods

The behaviour of iprovalicarb in aquatic systems has been investigated in two aerobic water-sediment studies, conducted with two different radioactive labels in four different test systems at 20°C and darkness ([redacted], 1997c; submitted within the EU Basic Dossier 1998 (IIA, 7.2.1.3.2 /01) and accepted by the European Commission (SANCO/2034/2000-Final, 2 July 2002)) and [redacted], 2011 (submitted in this Dossier, KIIA 7.8.3 /02).

The evaluation was conducted to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments according to FOCUS kinetics (FOCUS, 2006).

A kinetic modelling analysis of residue data of iprovalicarb and the metabolites SZX 0722-carboxylic acid *(M03)*, PMPA *(M10)* and N-acetyl-PMPA *(M15)* was conducted using the software tool KinGui II (successor of KinGui 1.1), in order to derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling and environmental risk assessments.

For the kinetic evaluation of water-sediment studies FOCUS (FOCUS, 2006) distinguishes two levels of kinetics:

Level I: One compartmental approach to estimate the dissipation from the water column, the sediment (from maximum onwards) or the degradation from the total system, as a single compartment.

Level II: Multi-compartmental approach to estimate the degradation in the water column and sediment compartments, in parallel, inclusive partitioning processes via reaction rates or sorption isotherms.

For the aquatic exposure assessment, a Level II evaluation is not mandatory. FOCUS recommends e.g. for parent compound to use the Level I total-system degradation half-life for both compartments at STEP 2 level, or in combination with the conservative worst-case default degradation half-life of 1000 days for the respective other compartment at STEP 3 level. For lower tier calculations or the comparison with persistence trigger values often a Level I evaluation of the dissipation is appropriate.

The kinetic models used in this evaluation are: simple first order (SFO), first order multiple compartment (FOMC), double first order in parallel (DFOP) and Hockey-stick (HS, DFOS).

II. Results and Discussion

The dissipation of the parent substance iprovalicarb in the water phase of a water-sediment system was evaluated assuming different kinetic models.

Persistence endpoints: Best fit for the dissipation of iprovalicarb in water and estimation of persistence endpoints could be reached using SFO or DFOP models (Table 7.8.3- 14). [redacted]ver, evaluated $DisT_{50}$, water, initial values are very narrow for all model evaluations. The evaluation for the systems [redacted] II and [redacted] II was originally carried out by [redacted], 2011 (submitted in this Dossier, KIIA 7.8.3 /02) and just repeated here.

The dissipation of iprovalicarb in the sediment phase was evaluated starting from the observed maximum onwards until end of the study. Best and appropriate fit for the dissipation of iprovalicarb

in sediment could be described using SFO model, for persistence endpoints (Table 7.8.3- 14) as well as modelling endpoints.

The degradation (= dissipation) of the parent substance iprovalicarb in the total water-sediment system was evaluated assuming different kinetic models. Best fit for the degradation of iprovalicarb in the total water / sediment system and evaluation of persistence endpoints could be reached using SFO or DFOP models (Table 7.8.3- 15). [redacted]ver, evaluated $DegT_{50,\ water,\ intital}$ values are very narrow for all model evaluations. The evaluation for the systems [redacted] II and [redacted] II was originally carried out by [redacted], 2011 (submitted in this Dossier, KIIA 7.8.3 /02) (evaluation without metabolites) and just reported here.

Table 7.8.3- 14: Estimated parameters for dissipation of iprovalicarb from water and sediment phase (Level P-I) best fit model for persistence endpoints in bold

Compartment / System	Kinetic model	C_0 [% appl.]	$DisT_{50,\ initial}$ [days]	$DisT_{90,\ initial}$ [days]	χ^2 error [%]	p > t	visual fit[a]
Water phase							
[redacted] I	**SFO[p]**	92.94	**57.28**	190.28	2.359	< 0.001	+
	FOMC	92.94	57.27	190.50	2.521	0.498	+
	DFOP	92.94	57.28	190.26	2.718	na	+
[redacted] I	SFO	86.57	20.88	69.36	3.681	< 0.001	+
	FOMC	87.42	19.84	75.07	3.635	< 0.217	+
	DFOP[p]	90.71	**19.46**	73.00	2.035	< 0.1031	+
[redacted] II	SFO	97.83	16.65	55.31	6.158	< 0.001	+
	FOMC	98.88	15.64	59.75	6.103	< 0.16	+
	DFOP[p]	104.70	**14.84**	58.23	3.459	< 0.04	+
[redacted]	SFO	85.97	18.42	61.20	6.329	< 0.001	+
	FOMC	89.51	14.90	96.20	5.076	< 0.074	+
	DFOP[p]	92.68	**16.08**	72.53	2.968	< 0.091	+
Sediment phase							
[redacted] I	**SFO[p]**	6.35	**78.99**	262.4	2.238	< 0.001	+ o
	FOMC	6.35	78.99	262.6	2.420	0.471	+ o
[redacted] I	**SFO[p]**	20.58	**48.96**	162.7	6.15	0.003	+ o
	FOMC	20.58	48.93	163.1	7.048	0.498	+ o
[redacted] II	**SFO[p]**	10.97	**24.20**	80.4	5.498	< 0.001	+
	FOMC	10.97	24.18	80.5	5.825	0.495	+
[redacted]	**SFO[p]**	38.55	**51.18**	170.0	10.63	0.0176	+ o
	FOMC	38.55	51.18	170.2	12.15	0.4997	+ o

a) visual acceptability: + good, o medium, - bad
p best fit model for persistence endpoints
na not available

Table 7.8.3- 15: Estimated parameters for degradation of iprovalicarb in total system (Level P-1), best fit model for persistence endpoints in bold

Entire system	Kinetic model	C_0 [% appl.]	**DegT**$_{50,\ initial}$ [days]	**DegT**$_{90,\ initial}$ [days]	χ^2 error [%]	p > t	visual fit[a)]
[redacted] I	**SFO**[p]	99.14	**58.67**	194.90	2.331	< 0.001	+
	FOMC	99.28	58.37	203.64	2.632	< 0.21	+
	DFOP	99.13	58.67	194.9	2.686	< 0.001	+
[redacted] I	**SFO**[p]	101.5	**28.39**	94.31	1.860	< 0.001	+
	FOMC	101.5	28.42	94.39	1.983	na	+
	DFOP	101.5	28.41	94.36	2.142	0.004	+
[redacted] II	SFO	103.6	19.92	66.17	3.865	< 0.001	+
	FOMC	103.9	19.65	67.30	4.161	< 0.37	+
	DFOP[p]	106.3	**19.17**	66.93	3.741	< 0.001	+
[redacted]	**SFO**[p]	99.0	**43.47**	144.39	4.92	< 0.001	+
	FOMC	99.2	43.08	150.32	5.568	< 0.44	+
	DFOP	99.0	43.47	144.39	5.668	< 0.001	+

a) visual acceptability: + good, o medium, - bad
p best fit model for persistence endpoints
na not available

Modelling endpoints: The SFO model resulted in an appropriate fit for the dissipation of iprovalicarb in the water phase of all systems and provided an excellent visual fit and a low χ^2 error (Table 7.8.3- 16) for estimation of modelling endpoints. The evaluation for the systems [redacted] II and [redacted] II was originally carried out by [redacted], 2011 (submitted in this Dossier, KIIA 7.8.3 /02) and just repeated here.

The dissipation of iprovalicarb in the sediment phase was evaluated starting from the observed maximum onwards until end of the study. Best and appropriate fit for the dissipation of iprovalicarb in sediment could be described using SFO model, for persistence endpoints as well as modelling endpoints (Table 7.8.3- 16).

The SFO model resulted in an appropriate fit for the degradation of iprovalicarb in all total water-sediment systems and provided an excellent visual fit and a low χ^2 error (Table 7.8.3- 17) for estimation of modelling endpoints.

All evaluations for modelling purpose were carried out including residue data and fits of metabolites.

Table 7.8.3- 16: Estimated parameters for dissipation of iprovalicarb from water and sediment phase (Level P-I) best fit model for <u>modelling</u> endpoints in bold

Compartment / System	Kinetic model	C_0 [% appl.]	$k_{slow\ phase}$ [1/d]	**$DisT_{50,\ modelling}$** [days]	χ^2 error [%]	p > t	visual fit[a)]
Water phase							
[redacted] I	**SFO^m**	92.94	0.0121	**57.28**	2.359	< 0.001	+
[redacted] I	**SFO^m**	86.57	0.033198	**20.88**	3.681	< 0.001	+
[redacted] II	**SFO^m**	97.83	0.0416	**16.65**	6.158	< 0.001	+
[redacted] I[b)]	**SFO^m**	85.97	0.0376	**18.42**	6.329	< 0.001	+
geo. mean				*24.61*			
Sediment phase							
[redacted] I	**SFO^m**	6.35	0.008775	**78.99**	2.238	< 0.001	+ o
[redacted] I	**SFO^m**	20.58	0.014156	**48.96**	6.15	0.003	+ o
[redacted] II	**SFO^m**	10.97	0.028641	**24.20**	5.498	< 0.001	+
[redacted] II	**SFO^m**	38.55	0.013542	**51.18**	10.63	0.0176	+ o
geo. mean				*46.78*			

a) visual acceptability: + good, o medium, - bad
m appropriate approach for modelling purpose

Table 7.8.3- 17: Estimated parameters for degradation of iprovalicarb in total system (Level P-1) best fit model for <u>modelling</u> endpoints in bold

Total system	Kinetic model	C_0 [% appl.]	$k_{slow\ phase}$ [1/d]	**$DegT_{50,\ modelling}$** [days]	χ^2 error [%]	p > t	visual fit[a)]
[redacted] I	**SFO^m**	99.14	0.01181	**58.67**	2.331	< 0.001	+
[redacted] I	**SFO^m**	101.5	0.02441	**28.39**	1.860	< 0.001	+
[redacted] II	**SFO^m**	103.6	0.03478	**19.93**	3.865	< 0.001	+
[redacted] II	**SFO^m**	99.0	0.013806	**43.86**	4.92	< 0.001	+
geo. mean				*34.73*			

a) visual acceptability: + good, o medium, - bad
m appropriate approach for modelling purpose

For metabolites all evaluations in total systems were carried out together with the appropriate fit of parent for modelling purpose and all evaluable metabolites.

SZX 0722-carboxylic acid *(M03)*: The data of the test systems [redacted] II and [redacted] II were used for the kinetic evaluation as SXZ 0722-carboxyliacid was observed only in these systems. In both systems, statistical reliable degradation rates could be evaluated for SZX 0722-carboxylic acid, which can be used for further modelling (Table 7.8.3- 18). The moderately high error of χ^2test is considered to be acceptable together with a significant t-test, as it just reflects slightly scattering and partly very low absolute residue data of the metabolite. Additionally, the visual fit is considered to be sufficiently conservative.

Table 7.8.3- 18: Estimated parameters for degradation of SZX 0722-carboxylic acid *(M03)* in total system (Level M-1), evaluation for persistence and modelling endpoints

Total system	Kinetic model of parent	$f_{a.s.\text{-}M03}$	k_1 [1/d]	**$DegT_{50,}$ total system [days]**	**$DegT_{90,}$ total system [days]**	χ^2 error [%]	p > t	visual fit[a]
[redacted] II	SFO	0.0194	0.0265	**26.15**	86.85	38.15	0.0236	o
[redacted] II	SFO	0.4716	0.1229	**5.642**	18.74	26.89	0.0073	+ o
geo. mean				*12.15*				
arith. mean				*15.89*				

a) visual acceptability: + good, o medium, - bad
$f_{a.s.\text{-}M03}$ formation fraction from iprovalicarb to SZX 0722-carboxylic acid *(M03)*

PMPA *(M10)*: The data of the test systems [redacted] I and [redacted] I were used for the kinetic evaluation as PMPA was only observed in these systems. Only in the system [redacted] I, statistical reliable degradation rates could be evaluated for PMPA, which can be used for further modelling or trigger purpose (Table 7.8.3- 20). The slightly higher error of χ^2 test is considered to be acceptable together with a significant t-test, as it just reflects the low absolute residue data of a metabolite.

For [redacted] I, in case of free fitting all parameters, no reliable and statistically significant degradation parameters could be evaluated (Table 7.8.3- 20). The estimation resulted in an unsignificant $DegT_{50\ total\ system}$ of 870 days, which usually should not be used for any further assessment. [redacted]ver, to check for the uncertainty of the long DT_{50} an additional comparison was carried out (comparison 1). It was found, that a reasonable visual fit of the residue data of PMPA at [redacted] I could also be reached assuming a $DegT_{50}$ of 66.3 days, as evaluated reliably at [redacted] I (Table 7.8.3- 20). So, a comparable fit, visually and χ^2 test, could be reached with 66 days as well as 870 days DT_{50} (Table 7.8.3- 20). This clearly shows that the evaluation of this metabolite is very uncertain. Thus, a half-life of 66 days might be true with a similar probability as a half-life of 870 days for PMPA, in the system [redacted] I. Finally, it is considered appropriate to exclude the [redacted] fit for PMPA from any further assessment, to avoid a shift of DT_{50} to any uncertain direction. So, for further assessments, modelling and trigger, the $DegT_{50\ total\ system}$ of 66.34 days is considered appropriate and reliable for PMPA in total water-sediment systems.

Table 7.8.3- 19: Estimated parameters for degradation of PMPA *(M10)* in total system (Level M-1), evaluation for <u>persistence</u> and <u>modelling</u> endpoints

Total system	Kinetic model of parent	$f_{a.s.-M10}$	k_1 [1/d]	**DegT$_{50,}$** total system [days]	**DegT$_{90,}$** total system [days]	χ^2 error [%]	p > t	visual fit[a)]
[redacted] I	SFO	0.4709	0.01045	**66.34**	220.38	17.92	0.067	+ o
[redacted] I	SFO	0.1914	0.0008 ^{nr}	870^{nr}	> 1000^{nr}	28.00	0.385	+ o
Comparison 1 [redacted] I	SFO	0.2749	0.01045	66.3	220.3	31.88	fix	+ o

a) visual acceptability: + good, o medium, - bad
$f_{a.s.-M10}$ formation fraction from iprovalicarb to PMPA *(M10)*
nr not fully reliable, mathematically not significantly different from 0, not usable

<u>N-acetyl-PMPA *(M15)*:</u> The data of the test systems [redacted] I and [redacted] I were used for the kinetic evaluation as N-acetyl-PMPA was observed only in these systems. In both systems, no reliable and statistically significant degradation parameters could be evaluated for N-acetyl-PMPA (Table 7.8.3- 20). The estimation resulted in unsignificant DegT$_{50\ total\ system}$ of 8 to > 1000 days. Although at [redacted] I the visual fit and the error of χ^2 test might be acceptable, the degradation parameters are not significantly different form 0 (t-test 0.5). So, for predictive modelling, a conservative default DT$_{50}$ of 1000 days might be assumed in a total water-sediment system for N-acetyl-PMPA (FOCUS, 2003, 2006).

Table 7.8.3- 20: Estimated parameters for degradation of N-acetyl-PMPA *(M15)* in total system (Level M-1), evaluation for <u>persistence</u> and <u>modelling</u> endpoints

Total system	Kinetic model of parent	$f_{M10-M15}$	k_1 [1/d]	**DegT$_{50,}$** total system [days]	**DegT$_{90,}$** total system [days]	χ^2 error [%]	p > t	visual fit[a)]
[redacted] I	SFO	0.7662^{nr}	< 0.0001^{nr}	>1000^{nr}	>1000^{nr}	4.334	0.5	+
[redacted] I	SFO	0.5212^{nr}	0.0805^{nr}	8.6 ^{nr}	28.58	112.3	0.368	-

a) visual acceptability: + good, o medium, - bad
$f_{M10-M15}$ formation fraction from PMPA *(M10)* to N-acetyl-PMPA *(M15)*
nr not fully reliable, mathematically not significantly different from 0

III. Conclusions

The behaviour of iprovalicarb was investigated in two aerobic water-sediment studies conducted with two different radioactive labels in four different test systems at 20°C and darkness. To derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation of these data was performed according to FOCUS kinetics (FOCUS, 2006) for the parent compound the major metabolites.

For **iprovalicarb** the DisT$_{50}$ for <u>modelling purpose</u> in the water phase were in the range of 16.65 to 57.28 days (geom. mean 24.61 days) and in the range of 24.20 to 78.99 days (geom. mean 46.78 days) for the sediment phase. In the total system the DegT$_{50}$ for modelling purpose were in the range of 19.93 to 58.67 days (geom. mean 34.73 days).

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

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

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

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

Summary: water-sediment studies - aerobic conditions

Studies with iprovalicarb in four different natural water/sediment systems under aerobic conditions s[redacted]d that the compound was thoroughly degraded leading to CO_2 as the end product of the mineralisation process. In parallel to mineralisation, bound residues were formed. 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. The proposed pathway of iprovalicarb in water-sediment systems under aerobic conditions is given in Figure 7.8.3-2.

To derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation of the data from the two water-sediment studies was performed according to FOCUS kinetics (FOCUS, 2006) for the parent compound the major metabolites.

For iprovalicarb the $DisT_{50}$ for modelling purpose in the water phase were in the range of 16.65 to 57.28 days (geom. mean 24.61 days) and in the range of 24.20 to 78.99 days (geom. mean 46.78 days) for the sediment phase. In the total system the $DegT_{50}$ for modelling purpose were in the

range of 19.93 to 58.67 days (geom. mean 34.73 days). For persistence trigger evaluation the $DisT_{50}$ in the water phase were in the range of 14.84 to 57.28 days and in the range of 24.20 to 78.99 days for the sediment phase. In the total system the $DegT_{50}$ for persistence trigger evaluation were in the range of 19.17 to 58.67 days. The corresponding $DisT_{90}$ in the water phase were in the range of 58.2 to 190.3 days and in the range of 80.4 to 262.4 days for the sediment phase. In the total system the $DegT_{90}$ were in the range of 66.9 to 194.9 days. (see Table 7.8.3- 21).

Table 7.8.3- 21: DT_{50} (and DT_{90}) values of iprovalicarb metabolites in the total water sediment system for modelling purpose and trigger evaluation

Compartment	Kinetic evaluation according to FOCUS[a)] for **modelling** purpose DT_{50}[b)] [days]		for **trigger** evaluation DT_{50}[b)] [days]	DT_{90}[b)] [days]
	range	geo. mean		
Water phase	16.65-57.28	24.64	14.84-57.28	58.2-190.3
Sediment	24.20-78.99	46.78	24.20-78.99	80.4-262.4
Total system	19.93-58.67	34.73	19.17-58.67	66.9-194.9

a) Kinetic calculation by [redacted] (2012), submitted within this dossier (KIIA 7.8.3 /03) according to FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. The Final Report of the Work Group on Degradation Kinetics of FOCUS. SANCO/10058/2005, v.2.0, June 2006
b) water and sediment phase: $DisT_{50}$, total system: $DegT_{50}$

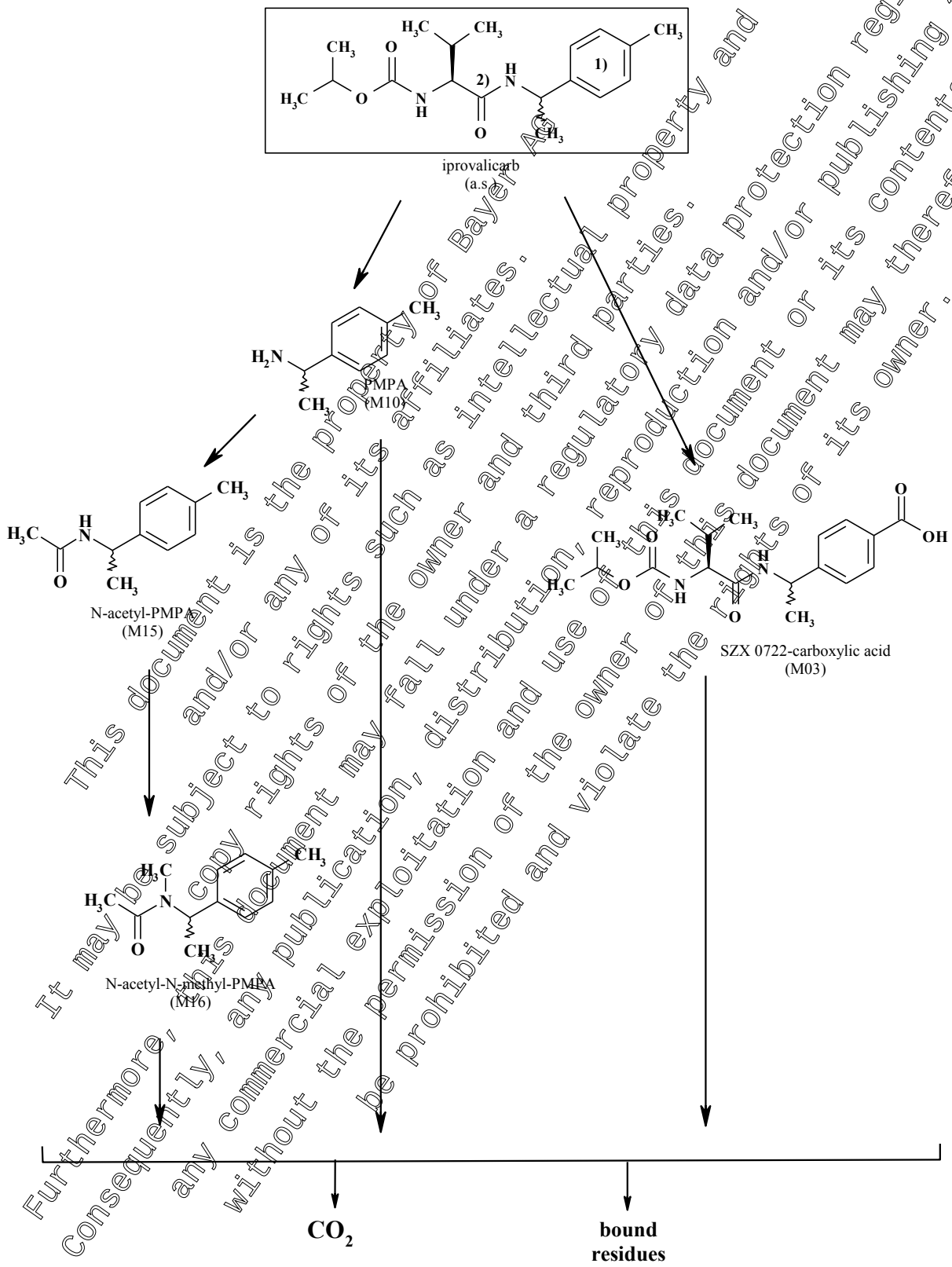
For SZX 0722-carboxylic acid *(M03)* the $DegT_{50}$ in the total systems for modelling purpose and trigger evaluation were in the range of 5.64 to 25.15 days (geom. mean 12.15 days, arith. mean 15.89 days). The corresponding $DegT_{90}$ were in the range of 18.74 to 86.85 days.
For PMPA *(M10)* a $DegT_{50}$ in the total systems for modelling purpose and trigger evaluation of 66.34 days is considered appropriate. The corresponding $DegT_{90}$ is 220.4 days.
For N-acetyl-PMPA *(M15)* no reliable and statistically significant degradation parameters could be evaluated. So, for predictive modelling, a conservative default DT_{50} of 1000 days might be assumed in a total water-sediment system for N-acetyl-PMPA. (Summary of the data these metabolites see Table 7.8.3- 22.)

Table 7.8.3- 22: Evaluation for <u>persistence</u> and <u>modelling</u> endpoints of iprovalicarb metabolites in water sediment systems

Compartment	Compound	Kinetic evaluation according to FOCUS[a)] for modelling purpose and trigger evaluation $DegT_{50}$ [days]		$DegT_{90}$ [days]
		range	geo. mean/ arith. mean	
Total system	SZX 0722-carboxylic acid *(M03)*	5.64-25.15	12.15/15.89	18.74-86.85
	PMPA *(M10)*	66.34	-	220.4
	N-acetyl-PMPA *(M15)*	1000[b)]	-	-

a) Kinetic calculation by [redacted] (2012), submitted within this dossier (KIIA 7.8.3 /03) according to FOCUS (2006): Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. The Final Report of the Work Group on Degradation Kinetics of FOCUS. SANCO/10058/2005, v.2.0, June 2006
b) default value

Figure 7.8.3- 2: Proposed metabolic pathway of iprovalicarb in water-sediment systems under aerobic conditions



KIIA 7.9 Degradation in the saturated zone

The results of field degradation along with the calculations for the risk assessment in groundwater demonstrated that there is no risk of a contamination of sub-soils by iprovalicarb or metabolites, when applied according to good agricultural practice. Therefore, the degradation in the saturated zone was not investigated.

KIIA 7.10 Rate and route of degradation in air

The rate and route of degradation of iprovalicarb in air was evaluated during the Annex I inclusion. No additional studies have been performed for the parent compound. A short summary of the data is given below.

Estimates of the chemical lifetime in the troposphere resulted in half-lives < 1 day ([redacted] (1995), submitted within the EU Basic Dossier 1998; IIA, 7.2.2.3 /01). In addition, based on the results concerning vapour pressure, Henry Law Constant (both [redacted] (1995, rev. 1996), submitted within the EU Basic Dossier 1998; IIA, 7.2.2.1 /01) and volatilisation in a field experiment ([redacted] (1996), submitted within the EU Basic Dossier 1998; IIA, 7.2.2.2 /01) it can be concluded that significant volatilisation of iprovalicarb is not to be expected. According to these results an accumulation of iprovalicarb in the air and a contamination by wet or dry deposition are not to be expected.

KIIA 7.11 Definition of the residue

SZX 0722-carboxylic acid *(M03)*, PMPA *(M10)* and N-acetyl-PMPA *(M15)* were found as major metabolites in environmental studies with iprovalicarb. Due to limited formation and fast degradation of SZX 0722-carboxylic acid *(M03)* and N-acetyl-PMPA *(M15)* only few levels of these metabolites are expected in soil, water and air under relevant environmental conditions. Potential higher but transient amounts of PMPA *(M10)* could be found. [redacted]ver this metabolite is neither of pesticidal nor of toxicological relevant. Therefore, the residue definition for monitoring in soil, water and air is parent compound only.

KIIA 7.12 Monitoring data concerning fate and behaviour

No monitoring data for iprovalicarb are available.

KIIA 7.13 Other/special studies

No additional special studies for iprovalicarb were performed.

KIIA 7.14 Overall sumary on the fate and behaviour in the environment for iprovalicarb

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, 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. To derive kinetic parameters for comparison with trigger values as well as kinetic

parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation of these data was performed according to FOCUS kinetics (FOCUS, 2006) for the parent compound the major soil metabolites.
For iprovalicarb the non-normalised $DT_{50\ mod}$ for modelling purpose were in the range of 1.99 to 68.56 days and the normalised $DT_{50\ mod}$ in the range of 1.77 to 68.56 days (geom. mean 6.78 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 1.99 to 18.00 days and the $DT_{90\ initial}$ in the range of 6.62 to 252.12 days.
For SZX 072-carboxylic acid *(M03)* the non-normalised $DT_{50\ mod}$ for modelling purpose were in the range of 0.56 to 1.852 days and the normalised $DT_{50\ mod}$ in the range of 0.45 to 1.85 days (geom. mean 0.97 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 0.58 to 1.97 days and the $DT_{90\ initial}$ in the range of 1.94 to 6.53 days.
For PMPA *(M10)* the non-normalised $DT_{50\ mod}$ for modelling purpose were in the range of 44.28 to 187.33 days and the normalised $DT_{50\ mod}$ in the range of 39.39 to 187.4 days (geom. mean 81.08 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 44.28 to 239.32 days and the $DT_{90\ initial}$ in the range of 147.1 to 759.0 days.
For N-acetyl-PMPA *(M10)* the non-normalised $DT_{50\ mod}$ for modelling purpose were in the range of 0.422 to 0.929 days and the normalised $DT_{50\ mod}$ in the range of 0.42 to 0.93 days (geom. mean 0.72 days). For persistence trigger evaluation (non-normalised) the $DT_{50\ initial}$ were in the range of 9.0 to 22.3 hours (0.4 to 0.9 days) and the $DT_{90\ initial}$ in the range of 39.0 to 74.1 hours (1.6 to 3.1 days).

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

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

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

The adsorption constants K_f for iprovalicarb calculated by means of the Freundlich adsorption isotherm ranged from 0.60 - 4.64 mL/g. The corresponding K_{oc} were in the range of 44 - 221 mL/g with an arithmetic mean of 114 mL/g. For the major soil metabolites SZX 0722-carboxylic acid *(M03)*, PMPA *(M10)* and N-acetyl-PMPA *(M15)* the K_f 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 s[redacted]d 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.

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 s[redacted]d 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 s[redacted]d that the compound was thoroughly degraded leading to CO_2 as the end product of the mineralisation process. PMPA *(M10)* was identified as major metabolite (> 10% of the applied radioactivity) in the water and sediment layers and N-acetyl-PMPA *(M15)* as major metabolite in the water layer. SZX 0722-carboxylic acid *(M03)* was found in amounts of 5.2% of the applied radioactivity in one entire system and N acetyl-N-methyl-PMPA *(M16)* was found in very small amounts (< 0.5% of the applied radioactivity). Iprovalicarb was metabolised to the endpoint CO_2 via several routes. In one route iprovalicarb was degraded via oxidation of the methyl group of the aromatic system yielding the SZX 0722-carboxylic acid *(M03)*. In the other route the breakdown of the molecule started with cleavage in one of the amide bonds which led to the main metabolite PMPA *(M10)*. Subsequently PMPA reacted with an activated acidic acid derivative yielding N-acetyl-PMPA *(M15)*. This metabolite was methylated in very small amounts to form N-acetyl-N-methyl-PMPA *(M16)*. Ultimately the breakdown of iprovalicarb led to total mineralisation of the aromatic nucleus in the form of carbon dioxide.
To derive kinetic parameters for comparison with trigger values as well as kinetic parameters suitable for modelling purpose and environmental risk assessments a kinetic evaluation of the data from the two water-sediment studies was performed according to FOCUS kinetics (FOCUS, 2006) for the parent compound the major metabolites.

For iprovalicarb the $DisT_{50}$ for modelling purpose in the water phase were in the range of 16.65 to 57.28 days (geom. mean 24.61 days) and in the range of 24.20 to 78.99 days (geom. mean 46.78 days) for the sediment phase. In the total system the $DegT_{50}$ for modelling purpose were in the range of 19.93 to 58.67 days (geom. mean 34.73 days). For persistence trigger evaluation the $DisT_{50}$ in the water phase were in the range of 14.84 to 57.28 days and in the range of 24.20 to 78.99 days for the sediment phase. In the total system the $DegT_{50}$ for persistence trigger evaluation were in the range of 19.17 to 58.67 days. The corresponding $DisT_{90}$ in the water phase were in the range of 58.2 to 190.3 days and in the range of 80.4 to 262.4 days for the sediment phase. In the total system the $DegT_{90}$ were in the range of 66.9 to 194.9 days.
For SZX 0722-carboxylic acid *(M03)* the $DegT_{50}$ in the total systems for modelling purpose and trigger evaluation were in the range of 5.64 to 25.15 days (geom. mean 12.15 days, arith. mean 15.89 days). The corresponding $DegT_{90}$ were in the range of 18.74 to 86.85 days.
For PMPA *(M10)* a $DegT_{50}$ in the total systems for modelling purpose and trigger evaluation of 66.34 days is considered appropriate. The corresponding $DegT_{90}$ is 220.4 days.
For N-acetyl-PMPA *(M15)* no reliable and statistically significant degradation parameters could be evaluated. So, for predictive modelling, a conservative default DT_{50} of 1000 days might be assumed in a total water-sediment system for N-acetyl-PMPA.

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.