Annex I Fate to the CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2

International Chemical Identification:

Captan (ISO) 1,2,3,6-tetrahydro-N-(trichloromethylthio)phthalimide

EC Number: **205-087-0**
CAS Number: **133-06-2**
Index Number: **613-044-00-6**

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Version number: 01 **Date: 15.01.2022**

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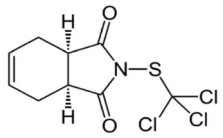
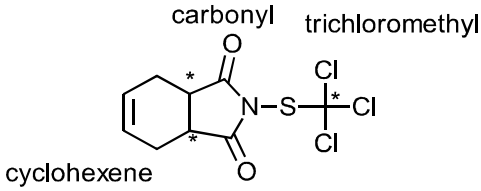
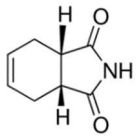
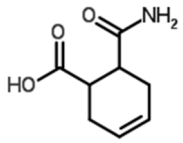
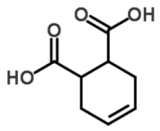
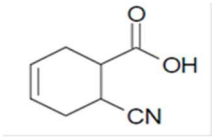
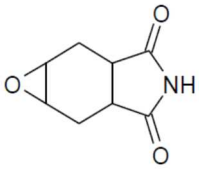
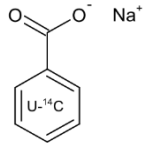
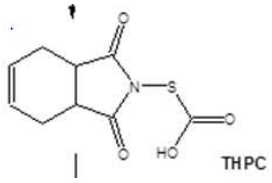
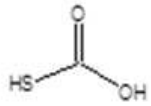
B.8. ENVIRONMENTAL FATE AND BEHAVIOUR

Environmental fate studies on captan were conducted using cyclohexene-radiolabelled captan, carbonyl-radiolabelled captan or trichloromethyl-radiolabelled captan (Table B.8-1) as well as the non-labelled parent compound.

Common names, codes, chemical name, structure and molecular mass of parent and metabolites which were observed in environmental compartments or which were used as reference substances are given in Table B.8.1.

Table B.8-1: Substances and metabolites (codes, names, structures, synonyms)

Common name (codes and synonyms)	**Description (Chemical name, CAS number)**	**Molecular weight** [g/mol]	**Structure**
Captan (Parent compound)	N-(trichloromethylthio)cyclohex-4-ene-(1,2 ^{14}C)-1,2-dicarboxyimide 133-06-2 $C_9H_8Cl_3NO_2S$	300.59	
Captan (Parent compound) – labelling positions		300.59	
THPI 1.2.3.6-Tetrahydrophthalimide	cis-4-cyclohexane-1.2-dicarboximide 1469-48-3 $C_8H_9NO_2$	151.2	
THPAM 1.2.3.6-Tetrahydrophthalamic acid	3-cyclohexene-1-carboxylic acid-6-(aminocarbonyl) 2028-12-8 $C_8H_{11}NO_3$	169.18	
THPAI 1.2.3.6-Tetrahydrophthalic acid	4-cyclohexene-1,2-dicarboxylic acid 88-92-2 $C_8H_{10}O_4$	170.17	
THCY	4-Cyanocyclohex-3-ene-1-carboxylic acid 6-cyanocyclohex-3-ene-1-carboxylic acid 1115747-07-4 $C_8H_9NO_2$	151	
THPI-Epoxide	Tetrahydro-1a*H*-oxireno[*f*]isoindole-3,5(2*H*,4*H*)-dione		

[ring-U-^{14}C] Benzoic acid, sodium salt		146.7	
THPC Tetrahydrophthalimido-thiocarbonate			
Thiocarbonic acid			

B.8.1. FATE AND BEHAVIOUR IN SOIL

B.8.1.1. Route and rate of degradation in soil

B.8.1.1.1. Route of degradation in soil

B.8.1.1.1.1. Aerobic degradation

Study 1 (1992)

Reference:	**Aerobic metabolism of [trichloromethyl -^{14}C] captan in soil**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1992
Report/Doc. number:	PMS-320 / R-9280/TMN-0323
Guideline(s):	USEPA 162-1
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

The aerobic metabolism of [trichloromethyl - ^{14}C] captan (radiochemical purity 99.0%, specific activity 40.4 mCi/mmole) was investigated in a sandy loam soil in the dark in accordance with USEPA Guidelines in a 1992 study. The soil characteristics are summarised in Table B. 8.1.1.1.1 1. Radiolabelled Captan was mixed with non-radiolabelled Captan and added to biometer test systems containing 100 g of sandy loam soil (non-sterile). The concentration of the test substance in soil was equivalent to 8.76 mg/kg. The incubation conditions were 75% of field capacity at a temperature of 25 ± 2°C, for periods of 4 hours to 28 days under O_2 atmosphere. A further experiment was performed with a sterile soil sample under similar conditions. Duplicate samples were taken for each sample point.

The study met the essential criteria of USEPA 162-1. It was conducted according to Good Laboratory Practice.

Table B. 8.1.1.1.1-1: Soil characteristics for aerobic metabolism study of [trichloromethyl - 14C] captan

Characteristic	**Soil**
Soil name	Visalia
Location	California, USA
pH	7.70
Sand (%)[1]	54.8[1]
Silt (%)	33.4
Clay (%)	11.8
Texture[2]	Sandy loam
Organic matter (%)	0.70
Organic carbon (%)[3]	0.41
Cation exchange capacity meq/100 g)	9.1
Half saturation (approximate field capacity) (%)	16.0

[1] Combination of very coarse sand (1.4%), coarse sand (3.8%), and medium to fine sand (49.6%).
[2] USDA classification.
[3] Organic carbon = organic matter/1.72

The results obtained, in terms of distribution of radioactivity and metabolites at different sampling dates in the non-sterile soil are summarised in table B.8.1.1.1.1-2. Average total recoveries were in the range 84-96 % applied radioactivity (AR). The amount of $^{14}CO_2$ evolved increased during the study to 80.8% AR after the incubation period of 28 days. The level of bound residue increased to 13.3% during that period, reaching a maximum of 14.8% after 14 days. Low levels of other volatiles of about 0.2% AR were detected between 3 and 28 days.

Levels of captan declined from 86% to 0.1 % AR during the 28 days of the study, and thiocarbonic acid was detected between 7 and 28 days at levels of 0.6 - 1.1% AR. Three minor unknowns (unk-0, unk-1 and unk-2) were detected, each individually at a level of <1% AR, and these appeared to be declining towards the end of the study.

Table B. 8.1.1.1.1-2: Distribution of radioactivity in non-sterile aerobic soil (mean of duplicates)

Time	(% of applied radiolabel)[1]								
	Captan	$^{14}CO_2$	Volatiles	Bound residues	Thio-carbonic acid	Unk-0	Unk-1	Unk-2	Total
0 hour	86.07	0	-	0.15	0	0	0.46	0	92.53
4 hours	45.05	25.27	-	7.96	0	0.29	0.45	0.89	83.99
8 hours	49.85	30.62[2]	-	10.71	0	0.19	0.47	0.49	96.67
1 day	35.74	37.51	-	8.36	0	0.15	0.39	0.47	89.89
3 days	14.13	58.66	0.17	13.97	0	0	0.16	0.12	92.77
7 days	9.57	65.27	0.21	11.90	0.82	0	0	0.11	90.23
14 days	1.15	76.73	0.18	14.81	1.12	0	0	0.13	95.80
28 days	0.1	80.82	0.19	13.33	0.63	0	0.02	0.04	95.38

[1]Levels at origins of TLC systems used to separate metabolites were 0.03 - 1.21% (aqueous extracts) and 0.16 - 2.24% (organic extracts).
[2]Value from one sample only.

Results were obtained for the sterile soil at 3 days and 24 days. Total recoveries were 79.5 - 85.6% AR. $^{14}CO_2$ evolution was increased from 25.9 to 39.1% AR, while other volatiles were detected at slightly higher levels than for non-sterile soil, at 1.7-1.9% AR. Bound residues increased from 15.2 - 22.4%.

In non-sterile soils**,** captan was rapidly degraded under aerobic conditions. The experimentally observed DT_{50} was less than 4 hours, although the calculated DT_{50} using linear regression was 2.5 days if eight data points through 28 days were utilised, or 1.0 days if five earlier data points up to 7 days were utilised. The experimental mineralisation half life was less than 3 days.

The [trichloromethyl - ^{14}C] label indicated conversion to thiocarbonic acid and then to CO_2. Three minor unknown degradates were detected at low levels (less than 1% of the applied radioactivity). During the course of the study, the radioactive residues bound to soil reached up to 14.8 % of the applied dose.

In sterile soil, some mineralisation to CO_2 was observed at a lower rate.

Captan degraded very rapidly in non-sterile soil under aerobic conditions. The experimentally observed DT_{50} was less than 4 hours, although the calculated DT_{50} using linear regression was 2.5 days if eight data points through 28 days were utilised, or 1.0 days if five earlier data points up to 7 days were utilised.

Captan was rapidly degraded in soil under aerobic conditions.

Comments RMS

The study shows some minor deviations to the current OECD 307; however these are considered to be not relevant for the derivation of reliable DT_{50} values:

- The incubation temperature was 25 °C instead of 20 °C, which is considered not critical and could be even seen as representing a more conservative approach. Compared to lower 20 °C, a potential increased chemical hydrolysis and increased microbial activity might result in a potential increased metabolite formation.
- The study duration of 28 d instead of 120 is considered not relevant since at end of the study less than 10 % of captan was present and 80 % of AR was detected to be CO_2 and 13 % AR was found to be bound residues.
- The recovery was below 90 % at one sampling point (84 %, 4 h). However, no important formation of metabolites was observed at any stage of the study.
- The reporting of the soil biomass is missing. Assuming that the rapid degradation of captan is mainly due to the known rapid hydrolysis, soil microbial activity is of lower importance in this case.

- The LOD/LOQ is not given.
- It is not stated which medium was used for pH measurement.
- No single value per time point is available but only the average value of two flasks is given.
- No soil history, no information concerning collection, storage, previous treatment is given; it is only mentioned that the soil was received from Visalia Experimental Station.

Although there are some deviations from the relevant OECD 307 guidance, the study is considered acceptable for the derivation of a reliable DT_{50} value. The absence of this information is not considered an impediment to continue using this study to investigate the degradation rate in soil. The study provides a reliable DT_{50} value and thus addresses the rate of degradation sufficiently since the points mentioned above do not have an impact on the half-life value.
Moreover, the study provides insight into the fate of the thio(trichloromethyl) sidechain under aerobic conditions. Based on this study, it can be concluded that the main route of degradation of the thio(trichloromethyl) side chain most likely is rapid conversion to thiocarbonic acid and then to CO_2.

Study 2 (1988)

Reference:	**Aerobic soil metabolism of [trichloromethyl -^{14}C] captan**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1988
Report/Doc. number:	MEF 0060/8809887 / R-4994/ TMN-0324
Guideline(s):	USEPA 162-1
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

The aerobic metabolism of [trichloromethyl - ^{14}C] captan (radiochemical purity 99.9 %, specific activity 40.4 mCi/mmoles) was investigated in a sandy loam soil in the dark in accordance with USEPA Guidelines. The soil characteristics are summarised in Table B.8.1.1.1.1-3. The concentration of the test substance in soil was 4.6 to 6.1 mg/kg, equivalent to an exaggerated field application rate of 23.2 to 30.7 kg a.s./ha, assuming 50% captan reaches the soil, and that it penetrates the top 15 cm of soil. The soil samples were incubated at 80% of field capacity and a temperature of 25 ± 0.1°C, for a period of 30 days maximum under oxygen atmosphere.

The study met the essential criteria of USEPA 162-1. It was conducted according to Good Laboratory Practice.

Table B. 8.1.1.1.1-3: Soil characteristics aerobic metabolism study of [trichloromethyl - ^{14}C] captan

Characteristic	**Soil**
Soil name	Greenville
Location	Mississippi, USA
pH	7.2
Sand (%)	58
Silt (%)	30
Clay (%)	12
Texture[1]	Sandy loam
Organic matter (%)	1.2
Organic carbon (%)[2]	0.7
Cation exchange capacity (meq/100 g)	7.7
Capacity at 1/3 bar (%)	14.8

[1]USDA classification.
[2]Organic carbon = organic matter/1.72.

The results obtained, in terms of distribution of radioactivity and metabolites at different sampling dates are summarised in table B.8.1.1.1.1-4. Average total recoveries were in the range 83-113% AR. The amount of $^{14}CO_2$ evolved increased during the study to 77.4 - 91.6 % AR after the incubation period of 30 days and low levels of

other volatiles of about 0.7 - 1.2% AR were detected between 1 and 30 days. The level of bound residue increased to 16.7% AR after 1 day, and remained at a similar level during the rest of the study (14.3% AR at day 30). No non-volatile metabolites were detected during this study.

Table B. 8.1.1.1.1-4: Distribution of radioactivity in soil (mean of duplicates at 1, 3, 14 and 30 days, and quadruplicates at 0 and 7 days)

Days	(% of applied radiolabel)			
	Captan	$^{14}CO_2$/volatiles[1]	Bound residues	Total
0	105.3	0	0.5	105.8
1	19.4	47.2	16.7	83.2
3	9.7	60.3	18.7	88.7
7	9.6	69.7	14.8	94.1
14	5.5	81.8	14.4	101.7
30	7.6	90.8	14.3	112.7

[1] $^{14}CO_2$ and volatile results recorded separately at 1, 2, 4, 5, 7, 12, 14, 22 and 30 days.

Captan was rapidly degraded in soil under aerobic conditions with an estimated DT_{50} of less than 1 day. The estimated mineralisation half-life was less than 3 days. Bound residues levels plateaued after four days at about 14% AR. The [trichloromethyl - ^{14}C] label indicated extensive mineralisation to CO_2.

Captan degraded very rapidly under aerobic conditions, with an estimated DT_{50} of less than 1 day.

Comments RMS

The study shows some minor deviations to the current OECD 307; however these are considered to be not relevant for the derivation of reliable DT_{50} values:

- The study temperature was 25°C instead of 20°C, which is considered not critical and could be even seen as representing a more conservative approach. Compared to lower 20 °C, a potential increased chemical hydrolysis and increased microbial activity might result in a potential increased metabolite formation.
- The samples were incubated for only 30 days instead of 120 days, which is considered not relevant since at the end of the study less than 10 % of captan was present and 90 % of AR was detected to be CO2 and 14 % AR was found to be bound residues.
- The recovery was below 90% at day 1 and 3. Thereafter, the recoveries were between 94 and 113% AR. No important formation of metabolites was observed at any stage of the study.
- For pH measurement it is not stated which medium was used.
- The microbial activity was not determined. Only a microbial analysis was performed by counting bacteria, fungi and actinomycetes. The counts were found to be “normal” to “above average”. However, the rapid degradation observed is likely caused by the rapid hydrolysis of Captan and the lack of information on soil microbial activity is of lower importance in this case.
- No information about soil history and no information concerning collection, storage or previous treatment was given.
- The treatment rate of 4.6 ppm and 6.1 ppm corresponds to 23.2 and 30.7 kg/ha if a soil depth of 15 cm is assumed. For the permanent cultures pome fruit, peaches and cherry a soil depth of 5 cm should be used. Therefore, the treatment rate does not correspond to the highest application rate applied for if degradation between applications is not considered. If degradation between applications is considered the highest application rate applied for will be covered by treatment rate.
- The LOQ is not specified but the LOD is < 1 % AR.

The study using captan labelled at the trichloromethyl side chain could be used to describe the degradation of this part of the molecule. But due to the low recovery at day 1 and day 3 (83% and 88.7 % AR) the metabolism pathway is not deemed to be fully described. It cannot be excluded that other relevant metabolites (e.g. thiocarbonic acid, thiophosgene) would occur. Therefore, the study is not considered acceptable for investigating the potential formation of thiophosgen in soil.

The study shows some deficiencies and deviations from the OECD 307; however these are considered not relevant for the derivation of reliable DT_{50} values. The points mentioned above are not expected to have an impact on the half-life value and therefore, the study could address the rate of degradation sufficiently.

Study 3 (2016a)

Reference:	**[^{14}C] Captan Aerobic Degradation and Metabolism in One Soil at 20°C in the Dark**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, (2016a)
Report/Doc. number:	R-35448/S14-05275
Guideline(s):	OECD Guideline 307 (2002)
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	New study submitted for renewal

Executive summary

The route and rate of degradation of Captan was studied in one soil, Lufa 2.3, in the dark under aerobic conditions at 20°C and a soil moisture content of 50% MWHC. The study was performed with radio-labelled [cyclohexene-^{14}C] over a period of 33 days.

The test substance was mixed into 50 g soil (dry weight) at an application rate of 302 µg per vessel, which corresponds to 6.039 mg/kg dry soil and approximately 4 × 3 kg a.s./ha. Triplicate samples were taken for analysis at 0, 1, 3, 5, 7, 10, 14, 19, 25 and 33 days after treatment. The entire soil per flask was extracted one time under ambient conditions using acetonitrile/water (4:1, v/v), followed by three times under ambient conditions using acetonitrile/water (4:1, v/v) amended with 0.1% formic acid. A fourth extraction was done for samples from day 3 onwards at 60°C supported by a microwave using the same solvent as before. The last extraction was performed at ambient conditions again with acetone. The combined extracts were analysed for [^{14}C] Captan and possible transformation products with high performance liquid chromatography (HPLC) with automated fraction collection. The fractions were measured by LSC. As confirmatory method served high performance liquid chromatography/mass spectrometry (HPLC-MS/MS).

Mean recoveries were between 94.4 - 104.4% of applied radioactivity (AR).

Under aerobic conditions at 20°C in the dark Captan degraded in soil Lufa 2.3 with a DT_{50} of 5.63 days and a DT_{90} of 18.7 days following first-order kinetics. Two major transformation products (THPI and THPAM) and several minor transformation products were observed. THPI reached maximum values of 25.1% AR at day 7 and THPAM had a maximum of 14.5% AR at day 10. All minor metabolites did not exceed 5% AR. The mineralization was 61.5% AR at the end of the study. Non-extractable residues contributed to the decline of the test item, accounting for 32.1% AR at day 33.

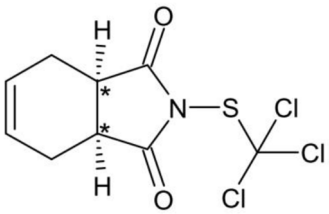
I. MATERIALS AND METHODS

MATERIALS

Test and reference items:

1. Labelled test item:	**[cyclohexene-^{14}C] Captan**
Chemical name:	*N*-(trichloromethylthio)cyclohex-4-ene-1,2-dicarboximide
Molecular weight:	300.6

Chemical structure:

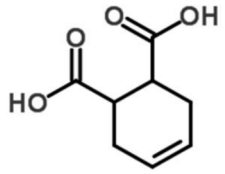


* = position of ^{14}C-label

Batch no.:	150320
CAS no.:	133-06-2
Radiochemical purity:	100%
Specific activity:	55 mCi/mmol
Expiry date:	2016-02

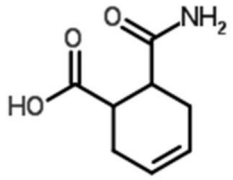
2. Unlabelled test item: **Captan**
Batch no.: SZBD242XV
CAS no.: 133-06-2
Active ingredient: Captan
Purity (analysed): 99.4%
Molecular weight: 300.6 g/mol
Appearance: solid (colourless)
Expiry date: 2018-08

3. Reference item: **THPAI (1.2.3.6-Tetrahydrophthalic acid)**
Chemical name: 4-cyclohexene-1,2-dicarboxylic acid
Batch no.: 516-143-00
CAS no.: 88-92-2
Purity (analysed): 96.8% w/w
Molecular weight: 170.2 g/mol
Chemical structure:



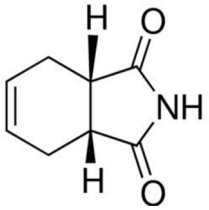
Appearance: solid (white)
Expiry date: 2020-01

THPAM (1.2.3.6-Tetrahydrophthalamic acid)
Chemical name: 3-cyclohexene-1-carboxylic acid-6-(aminocarbonyl)
Batch no.: 516-156-00
CAS no.: 2028-12-8
Purity (analysed): 98.1% w/w
Molecular weight: 169.18 g/mol
Chemical structure:



Appearance: solid (white)
Expiry date: 2017-02

THPI (1.2.3.6-Tetrahydrophthalimide)
Chemical name: cis-4-cyclohexane-1.2-dicarboximide
Batch no.: 279-071-02
CAS no.: 1469-48-3
Purity (analysed): 98.5% w/w
Molecular weight: 151.2 g/mol
Chemical structure:



Appearance: solid (white)
Expiry date: 2017-02

Soil:
The aerobic degradation of Captan was performed in the European soil Lufa 2.3 (sandy loam, Offenbach, Germany). Pesticide history is known for at least 5 years. The supplied field fresh soil samples were already passed through a 2 mm sieve. The samples were pre-incubated under aerobic conditions for 6 days at 20 ± 2°C in the dark. The intended soil water content after application was ca. 50% of the MWHC.
Soil characteristics are given in Table B.8.1.1.1.1-8 and soil microbial biomass is presented in Table B.8.1.1.1.1-9.

Table B. 8.1.1.1.1-5: Characterization of the test soil Lufa 2.3

Soil parameter	Value
Soil type (USDA)	Sandy loam
Sand [%]	60.8
Silt [%]	33.5
Clay [%]	5.7
Organic Matter [%]	1.14
Organic Carbon [%]	0.66
pH [$CaCl_2$]	5.78
Cation Exchange Capacity [meq/100 g]	6.0
Maximum Water Holding Capacity [%]	34.82
Bulk density (disturbed) [g/L]	1370

Table B. 8.1.1.1.1-6: Soil microbial biomass

Sample	Soil microbial biomass [mg C/100 g TS]		
	Untreated	Treated with solvent	Treated with solvent and non-labelled test item
After arrival	124.7	-	-
At incubation start	92.8	121.4	132.7
At incubation end (32 days)	54.1	103.4	108.7

STUDY DESIGN
Experimental conditions:
For the study a flow-through system was used. Each test vessel (300 mL flasks) was filled with 50 g soil (dry weight). The samples were pre-incubated under aerobic conditions for 6 days at 20 ± 2°C in the dark and moisturized to 50% WHC. The storage of the soil including pre-incubation did not exceed 3 months. In order to keep the moisture content, samples were weighed and the soil water content was adjusted by adding deionised water weekly.
The dose rate was 6.243 mg/kg dry soil (equals 312 µg/test vessel) which corresponds to an application rate of approximately 4 × 3 kg a.s./ha, assuming a 5 cm layer and a soil bulk density of 1.5 g/cm^3. A worst case DT_{50} of 7 days (worst case field) was considered for these calculations together with no interception. The resulting PEC_{soil} represents the worst case compared to the PEC_{soil} of other intended uses (e.g. 10 x 1.6 kg/ha, pome fruit). 50 flasks were treated with the test item at which 30 were analysed and 20 were kept in reserve. 10 flasks treated with solvent only were used for the determination of the biomass at the start and at the end of the study. A further 10 flasks were left untreated for comparable biomass determination at the start, in the middle and at the end of the study. All flasks were equipped with two sodium hydroxide traps to capture the carbon dioxide, and one Tenax® trap to capture the organic volatiles. The application solution was applied drop by drop to the soil and subsequently mixed by shaking the flasks. After treatment, samples were incubated up to a maximum of 33 days under aerobic condition at 20°C in the dark.
Sampling
Triplicate samples were taken at 0, 1, 3, 5, 7, 10, 14, 19, 25 and 33 days after treatment. The samples were worked up immediately and analysed a maximum of three days later.
Description of analytical procedures:
The entire soil per flask was extracted one time under ambient conditions using acetonitrile/water (4:1, v/v), followed by three times under ambient conditions using acetonitrile/water (4:1, v/v) amended with 0.1% formic

acid. A fourth extraction was done for samples from day 3 onwards at 60°C supported by a microwave using the same solvent as before. The last extraction was performed at ambient conditions again with acetone. The combined extracts were analysed for [^{14}C]Captan and possible transformation products with high performance liquid chromatography (HPLC) with automated fraction collection. The fractions were measured by LSC. As confirmatory method served high performance liquid chromatography/mass spectrometry (HPLC-MS/MS). The amount of non-extractable radioactivity was determined by combustion and LSC. LSC: LOQ < 1 % AR

II. RESULTS AND DISCUSSION

Method validation (recoveries):
Mean recoveries were between 94.4 - 104.4% of applied radioactivity (AR).

VOLATILIZATION
The amount of organic volatiles was < 1% of applied radioactivity (AR) for all samples.

TRANSFORMATION
The extractable radioactivity decreased from 100.9 % at day 0 to 6.5 % AR after 33 days. [^{14}C]Captan was degraded from maximum 98.1% AR directly after application to 1.7% AR within 33 days. Two major metabolites were formed during this time, tetrahydrophthalimide (THPI) and tetrahydrophthalamic acid (THPAM). THPI accounted for a maximum 25.1% AR 7 days after treatment, decreasing to 1.1% AR at the end of the study. THPAM increased until day 10 with a maximum 14.5% AR and then decreased to 3.8% AR at day 25. At the end of the study (33 days) THPAM was not detectable. Additionally, numerous minor metabolites were formed not exceeding 5% AR. One of them was tetrahydrophthalic acid (THPAI) with a maximum of 1.8% AR at day 10.
The amount of non-extractable radioactive residues in soil increased from 0.4% AR at day 0 to maximum 32.1% AR at the end of the study. Total mineralisation to CO_2 was observed from sampling interval day 3 onwards. The obtained values increased from 3.8 to 61.5% AR at the end of the study.
The distribution of radioactivity is shown in table B.8.1.1.1.1-10 and the characterisation of the extractable radioactivity is presented in table B.8.1.1.1.1-11.

Table B. 8.1.1.1.1-7: Distribution of radioactivity in % of applied radioactivity (AR)

Sampling interval	Radioactivity in extracts	Captan	THPAM	THPAI	THPI	Bound residues	Carbon dioxide	Organic volatiles	Recovery
0	100.9	98.1	0	0	2.4	0.4	n.p.	n.p.	101.3
1	97.6	81.6	1.6	0	14.2	2.5	0.1	<0.1	100.2
3	88.6	58.9	6.6	0.8	22.1	5.9	3.8	<0.1	98.4
5	86.2	67.8	4.1	0.3	11.9	4.9	4.4	<0.1	95.5
7	78.5	44.1	7.4	1.4	25.1	11.2	14.7	<0.1	104.4
10	56.6	15.6	14.5	1.8	23.9	18.5	19.3	<0.1	94.4
14	36.1	14.5	7.0	0.6	13.8	25.9	33.9	0.5	96.2
19	27.2	12.7	5.8	0	7.8	28.2	47.8	0.3	103.5
25	18.6	6.5	3.8	0.3	5.7	32.1	51.4	0.5	102.4
33	6.5	1.7	0	0	1.1	32.1	61.5	<0.1	100.2

n.p. not performed

Table B. 8.1.1.1.1-8: Characterisation of the extractable radioactivity in % of the applied radioactivity (AR) of [^{14}C]Captan in soil 2.3

sampling interval	0	1	3	5	7	10	14	19	25	33
Captan	101.6 98.2 94.6	88.1 87.2 69.5	31.1 74.0 71.6	63.5 73.5 66.3	68.1 21.1 43.2	17.8 28.3 0.8	9.8 20.1 13.7	11.2 4.1 22.7	4.9 10.8 3.7	2.2 1.6 1.4
THPAM	0.0 0.0 0.0	1.2 1.1 2.5	15.7 1.9 2.2	5.2 3.8 3.1	2.5 15.3 3.6	9.7 14.3 19.5	6.6 3.6 10.9	1.0 15.0 1.5	0.0 4.2 7.1	0.0 0.0 0.0
THPAI	0.0 0.0 0.0	0.0 0.0 0.0	2.1 0.3 0.0	0.3 0.7 0.0	0.0 3.1 0.9	0.7 2.5 2.2	0.6 0.0 1.3	0.0 0.0 0.0	0.0 1.0 0.0	0.0 0.0 0.0

THPI	0.4 1.5 5.2	7.6 6.8 28.3	40.0 11.8 14.6	10.9 9.4 15.6	11.6 32.4 31.2	24.9 11.3 35.4	16.4 15.0 10.0	18.6 0.0 4.8	4.7 12.3 0.0	3.4 0.0 0.0

The degradation residues were evaluated according to FOCUS Kinetics Guidelines using single first order, double first order in parallel, first order multi compartment and hockey stick kinetic models, whereat the results of the single first order calculations showed the best fit. The calculations were performed using the software CAKE 3.1. The calculated DT_{50} and DT_{90} values are presented in table B.8.1.1.1.1-12.

Table B. 8.1.1.1.1-9: Calculated half-lives for Captan

Soil	Kinetic model	DT_{50} [days]	DT_{90} [days]	Chi^2 error ($\chi 2$)	Visual fit
Lufa 2.3	SFO	5.63	18.7	14.3	moderate

Based on the results, the following metabolic pathway could be proposed:

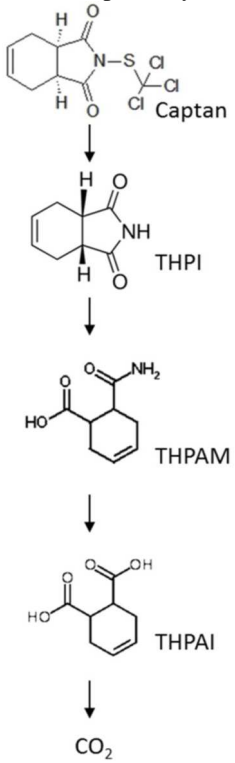


Figure B.8.1.1.1.1-1: Proposed metabolic pathway of Captan in soil under aerobic conditions

III. CONCLUSIONS

Degradation of Captan under aerobic conditions at 20°C in the dark was observed in soil Lufa 2.3 (DT_{50} = 5.63 days, DT_{90} = 18.7 days) following first-order kinetics. Two major transformation products (THPI and THPAM) and several minor transformation products were observed. THPI reached maximum values of 25.1% AR at day 7 and THPAM had a maximum of 14.5% AR at day 10. All minor metabolites did not exceed 5% AR. The mineralization was 61.5% AR at the end of the study. Non-extractable residues contributed to the decline of the test item, accounting for 32.1% AR at day 33.

Comments RMS

The study is performed according to the current OECD 307 Guideline; though the following information is missing:

- Information concerning the conditions during storage of the soil (temperature, moisture, darkness) was not provided. It is just mentioned that the soil was fresh samples, biologically active and the storage did not exceed 3 months (including pre-incubation). But the determination of biomass indicates sufficient viability of the soil.
- Details concerning the history of the field site were not provided. It is just mentioned that the pesticide history is known for at least 5 years.

The study shows some minor deviations to the current OECD 307; however, the absence of this information is not considered an impediment to use this study to investigate the route and rate of degradation of captan in soil. Therefore, the study is considered acceptable by the RMS.

After the peer review details concerning the pesticide use history and concerning the storage conditions were provided as study amendment und are presented below:

Reference:	**Report Amendment 3 - [^{14}C] Captan Aerobic Degradation and Metabolism in at 20°C in the Dark**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2018
Report/Doc. number:	R-35632/S14-05275
Guideline(s):	OECD Guideline 307 (2002)
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	New study submitted for renewal

The following additional information was provided:

- Information concerning pesticide use history: No pesticides used for previous five years.
- Information concerning soil conditions during storage: Soil was stored at 4°C in the dark for 2 months.

The kinetic evaluation is replaced by a new kinetic re-evaluation (study 5 and 6, 2016 and 2017) which is presented under point B.8.1.1.2.1.1.

B.8.1.1.2. Rate of degradation

B.8.1.1.2.1. Laboratory studies

B.8.1.1.2.1.1. Aerobic degradation of the active substance

Study 1 (1992)

Reference:	**Aerobic metabolism of [trichloromethyl -^{14}C] captan in soil**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1992
Report/Doc. number:	PMS-320 / R-9280/TMN-0323
Guideline(s):	USEPA 162-1
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Study 2 (1988)

Reference:	**Aerobic soil metabolism of [trichloromethyl -^{14}C] captan**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1988
Report/Doc. number:	MEF 0060/8809887 / R-4994/ TMN-0324
Guideline(s):	USEPA 162-1
GLP:	Yes

Deviations:	Minor
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Study 3 (2016a)

Reference:	**[^{14}C] Captan Aerobic Degradation and Metabolism in One Soil at 20°C in the Dark**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, (2016a)
Report/Doc. number:	R-35448/S14-05275
Guideline(s):	OECD Guideline 307 (2002)
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	New study submitted for renewal

The studies are described above in point B.8.1.1.1.1. on the route of degradation in soil.

Study 4 (2014)

Reference:	**Captan Aerobic Degradation in One European Soil**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, (2014)
Report/Doc. number:	R-35039/S14-00502
Guideline(s):	OECD Guideline 307 (2002)
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	New study submitted for renewal

Executive summary

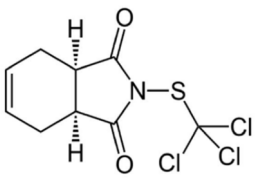
The aerobic degradation of Captan was studied in one soil in the dark under aerobic conditions at 20 ± 2°C and soil moisture content of 45% MWHC. The study was performed with non-labelled Captan over a period of 28 days. The test substance was applied at a rate of 1.07 mg/50 g dry soil, which was equivalent to 21.40 mg Captan/kg soil. Duplicate samples were worked-up at each sampling interval. Soil extracts were analysed for Captan residues by reversed phase high performance liquid chromatography/mass spectrometry (HPLC-MS/MS). The limit of quantification (LOQ) of the method was 1.07 mg/kg. The limit of detection (LOD) was defined as 1% of applied dose and equals 0.214 mg/kg. The extraction efficiency during the study was demonstrated by concurrent recovery samples. All the single values of the concurrent recoveries were between 80 - 109%.

Captan was degraded in the tested soil from 112% of applied amount to values below 1% of applied amount within 28 days. Captan dissipated from the investigated soil with a half-live of 136 hours (5.67 d).

I. MATERIALS AND METHODS

MATERIALS

Test material: Captan
Batch No.: 93138112
Purity: 94.3%
Molecular weight: 300.59
Chemical structure:



Soil:

One test soil of European origin was used. The standard soil was freshly obtained from LUFA Speyer, Germany. The soil pesticide history is known for at least 5 years. Soil samples were already sieved using a 2 mm sieve. Soils water content was adjusted with deionised water to 45% of the MWHC and samples were pre-incubated under aerobic conditions for 6 days at 20 ± 2°C in the dark. The biological activity of the soil was checked by short term respiration immediately after arrival and before the application. Soil characteristics are given in table B.8.1.1.2.1.1-1and soil microbial biomass presented in table B.8.1.1.2.1.1-2**.**

Table B. 8.1.1.2.1.1-1: Characterization of soil LUFA 2.1

Soil parameter	Value
Soil type (USDA)	Sand
Sand [%]	86.4
Silt [%]	12.6
Clay [%]	1.0
Organic Matter [%]	1.26
Organic Carbon [%]	0.73
Bulk Density Disturbed [kg/dm^3]	1.397
pH [$CaCl_2$]	4.72
Cation Exchange Capacity [meq/100 g]	5.0
Maximum Water Holding Capacity [g H_2O/100 g dry soil]	32.8

Table B. 8.1.1.2.1.1-2: Soil microbial biomass

Days after application	Soil microbial biomass [mg C/100 g soil]	
	Untreated (acetonitrile/H_2O)	Treated (captan and acetonitril/H_2O)
-2	34.7	-
0	33.2	32.5
14	57.3	70.6
36	51.7	57.9

STUDY DESIGN

Experimental conditions:

Each test system included 50 g soil (dry weight). Samples were pre acclimatised by adjusting the soil water content to 45% MWHC and pre-incubated under aerobic conditions for 6 days at 20 ± 2°C in the dark. Captan was applied at a nominal application rate of 21.40 mg/kg soil which corresponds to 1.07 mg/50g dry soil. This corresponds to maximum annual field application rate of 16 kg/ha when assuming 5 cm soil layer in the field and a soil bulk density of 1.5 g/cm^3. The test item solution was added drop wise to the soil and subsequently mixed by shaking the flask. After treatment, samples were incubated for a period of 28 days under aerobic condition at 20 ± 2°C in the dark.

Sampling

Duplicate samples were taken at 0, 2, 4, 8, 24, 48, 72, 120, 336 and 672 hours (28 days) after treatment.

Description of analytical procedures:

Captan was extracted from the soil with 100 mL acetonitrile/water (80/20; v/v). The extraction was performed three times. The ambient extracted soil samples were further extracted using a Microwave. The samples were treated with 100 mL acetonitrile/water (80/20; v/v) and extracted at 65°C for 20 min. For each test system, all soil extracts were combined and further processed for HPLC-MS/MS analysis.

II. RESULTS AND DISCUSSION

Method validation (recoveries):

Untreated soil samples (50 g dry weight) were adjusted with water to 45% MWHC and fortified with test item solution at LOQ level and at 110% of application level. The test item and concurrent recoveries were extracted from the treated soil with 100 mL acetonitrile/water (80/20, v/v). Soil different extracts were combined and further processed for HPLC-MS/MS analysis. Mean recovery of Captan was 92% ± 2% RSD at LOQ level and 94% ± 3% RSD at 110% of application level. The overall mean recovery was 93% ± 3% RSD. All the single values of the concurrent recoveries were between 80 - 109%.

VOLATILIZATION

Volatile components were not recovered in this study.

TRANSFORMATION

Captan was degraded from 112% of applied amount to values below 1% of applied amount within 28 days (672 h). The results of the sample analysis are shown in table B.8.1.1.2.1.1-3. The degradation residues were evaluated according to FOCUS Kinetics Guidelines using single first order (SFO), double first order in parallel (DFOP) and first order multi compartment (FOMC) kinetic models using the software KinGui 2. Best fits were obtained when applying SFO. The calculated DT_{50} and DT_{90} value are presented in table B.8.1.1.2.1.1-4.

Table B. 8.1.1.2.1.1-3: Results of sample analysis in mg/kg and in % of applied

Sampling interval [h]	Single values [mg/kg]	Mean values (mg/kg)	Single values [%]	Mean values [%]
0	23.829	24.040	111.4	112.3 ± 1.2
0	24.251		113.3	
2	22.672	22.544	105.9	105.3 ± 0.7
2	22.417		104.8	
4	22.146	21.836	103.5	102 ± 2
4	21.527		100.6	
8	22.741	22.693	106.3	106 ± 0.3
8	22.645		105.8	
24	19.670	20.657	91.9	96.5 ± 6.7
24	21.644		101.1	
48	19.804	20.311	92.5	94.9 ± 3.6
48	20.818		97.3	
72	16.358	15.677	76.4	73.3 ± 6.1
72	14.996		70.1	
120	10.360	11.247	48.4	52.6 ± 11.2
120	12.135		56.7	
336	6.694	5.149	31.3	24.1 ± 42.6

336	3.604		16.8	
672	<LOD	<LOD	<LOD	<LOD
672	<LOD		<LOD	

LOD…Limit of detection corresponds to 1 % of applied dose

Table B. 8.1.1.2.1.1-4: Calculated half-lives for Captan

Soil	Kinetic model	DT_{50} [days]	DT_{90} [days]	Chi^2 error ($\chi 2$)
LUFA 2.1	SFO	5.67	18.79	4.80
	FOMC	5.63	19.00	5.33
	DFOP	5.00	16.71	5.52

III. CONCLUSIONS

The result of kinetic evaluation of Captan residues showed that under aerobic conditions at 20°C in the dark Captan dissipated from the investigated soil following first-order kinetics with a half-live (DT_{50}) of 5.67 days. The corresponding DT_{90} value was 18.79 days.

Comments RMS

The study is performed according to the current OECD 307 Guideline; though the following information is missing:

- Details concerning the history of the field site were not provided. It is just mentioned that the pesticide history is known for at least 5 years.

The study shows some minor deviations to the current OECD 307; however, the absence of this information is not considered an impediment to use this study to investigate the rate of degradation of captan in soil. Therefore, the study is considered acceptable by the RMS.

The kinetic evaluation is replaced by a new kinetic re-evaluation (study 5, 2016) which is presented below.

The kinetic re-evaluation of all four above mentioned studies is summarised in the following report.

Study 5 (2016)

Reference:	**Calculation of soil degradation values for Captan and major metabolites according to the recommendations of FOCUS Degradation Kinetics workgroup**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2016
Report/Doc. number:	562961-CA-070102-01
Guideline(s):	FOCUS (2006, 2014)
GLP:	Not applicaple
Deviations:	None
Validity:	Yes
Status:	New calculation submitted for renewal

Executive summary

Soil degradation rates for Captan and metabolites THPI and THPAM were derived from soil residue data obtained in four different soils (in total) from different laboratory studies. Degradation rates were calculated according to the recommendations of the FOCUS workgroup on degradation kinetics (2006) and the FOCUS kinetics generic guidance (2014) based on that document for use as modelling and persistence endpoints.
Soil residue data obtained from each study were processed according to the recommendations of FOCUS kinetics before fitting a curve to the data set. Curve fitting was performed using the latest version of KinGUI software (version 2.1) in a stepwise approach as recommended in the FOCUS kinetics in order to derive modelling and persistent endpoints for Captan and its metabolites THPI and THPAM.
The calculated modelling DT_{50} values for Captan ranged from 1.8 to 5.7 days. For Captan metabolites the modelling DT_{50} value ranged from 3.1 to 15 for THPI and from 2.1 to 11.2 for THPAM.
Normalised DT50 value for Captan for use in modelling was found to be 3.8 days (geometric mean, n = 4). For THPI and THPAM, the normalised DT_{50} value was found to be 6.8 and 5.5 days (geometric mean, n = 4), respectively.
A summary of modelling endpoints for Captan and metabolites THPI and THPAM are presented table B.8.1.1.2.1.1-5 to table B.8.1.1.2.1.1-7, respectively. The corresponding persistent endpoints are summarised in table B.8.1.1.2.1.1-8 to table B.8.1.1.2.1.1-10, respectively.

Table B. 8.1.1.2.1.1-5: Summary of modelling endpoints obtained for Captan in four soils

Study / Soil	Calculated DT_{50} [d]	Study temp [°C]	Study moisture	Ref. temp. [°C]	Ref. moisture at 10 kPa	Moist corr. factor	Temp. corr. factor	Normalised DT_{50} at [20°C & pF2]
Study 3 (2016) / LUFA 2.3 Sandy loam	5.528 [a**]	20	50% MWHC	20	19	0.941	1	**5.205** [d**]
Study 4 (2014) / LUFA 2.1 Sand	5.666 [a]	20	45% MWHC	20	12	1.156	1	**5.666** [e]
Study 1 (1992) /. Visalia (USA) Sandy loam	1.756 [b]	25	75% FC	20	19	0.779***	1.606	**2.306** [f]
Study 2 (1988) / Greenville Sandy loam	2.206 [c]	25	80% FC	20	19	0.855	1.606	**3.031** [f]
Geometric mean (n = 4)								**3.789**

a SFO kinetics
b back-calculated from DT_{90} FOMC ($DT_{50} = DT_{90}/3.32$)
c SFO modified fit
d moisture correction only
e no correction was needed since moisture correction factor is above 1 and temperature correction factor = 1
f temperature and moisture correction was performed
/* see comments RMS

Comments RMS
**Soil Lufa 2.3: the DT_{50} determined was 5.533 d which would result in a normalised DT_{50} of 5.207 d
***Soil Visalia:
The value of 0.779 for moisture correction is not reproducible.
According to the study the soil moisture during the study accounted for 11.25 % (75 % FC), which would result in a fmc of 0.693 ($(11.25/19)^{0.7} = 0.693$) and a normalized DT_{50} of 1.954 days.

According to the study the soil moisture approximate FC accounted for 16 %, 75 % FC would correlate to 12% and a fmc of 0.725 ($(12/19)^{0.7}$=0.725) and a normalized DT_{50} of 2.045 days.
The normalization presented by the notifier is based on the reference soil moisture of FC of 19 %, which correlates to a soil moisture of 14.25 % at 75 % FC. This assumption results in a fmc of 0.8176 ($(14.25/19)^{0.7}$=0.8176) and a normalized DT_{50} of 2.306 d which is presented in the table. The fmc of 0.779 presented in the table is not reproducible and would not result in a normalised DT_{50} of 2.306 d.
The normalized DT_{50} based on reference soil moisture of FC = 19 % and 75 % FC = 14.25 % and fmc = 0.8176 ($(14.25/19)^{0.7}$) is the worst case/highest DT_{50} compared to the DT_{50} values based on soil moisture mentioned in the study (FC of 16 % and 75 % FC of 11.25 %) and therefore this assumption is acceptable.

During the peer review the notifier provided the following equation which was used to determine the moisture correction factor:

$$f_{moisture} = \left(\frac{8.438 \left(= \frac{75\% \, FC \times 11.25}{100} \right)}{11.25} \right)^{0.7}$$

Table B. 8.1.1.2.1.1-6: Summary of modelling endpoints obtained for metabolite THPI in four soils

Study / Soil	Calculated DT_{50} [d]	Study temp [°C]	Study moisture	Ref. temp. [°C]	Ref. moisture at 10 kPa	Moist corr. factor	Temp. corr. factor	Normalised DT_{50} at [20°C & pF2]
Study 3 (2016) / LUFA 2.3 Sandy loam*	3.268 [a]	20	50% MWHC	20	19	0.941	1	**3.085** [c]
Study 7 (1993) / Hyde Farm Sandy loam[e] **	5.845 [b]	20	40% MWHC	20	19	1.122	1	**5.845** [d]
Study 7 (1993) / Speyer 2.1 Sand [e] **	15.000 [b]	20	40% MWHC	20	12	1.023	1	**15.000** [d]
Study 7 (1993) / Speyer 2.2 Loamy sand[e] **	7.894 [b]	20	40% MWHC	20	14	1.441	1	**7.894** [d]
Geometric mean (n = 4)								**6.798**

a SFO kinetics (pathway fit)
b SFO kinetics (metabolite applied as parent)
c moisture correction only
d temperature and moisture corrections were not needed
e summary of the study on rate of degradation of the metabolite can be found in point B.8.1.1.2.1.2.

Comments RMS
*study 3: the DT_{50} determined was 3.280 d which would result in a normalised DT_{50} of 3.086 days.

**Study 7: Residues of day 0 were processed according to FOCUS kinetic by RMS (2 values of the same extract were averaged). The kinetic re-calculation resulted in the following endpoints:

Hyde Farm: DT_{50}= 6.107 days, DT_{90}=20.286 days
Speyer 2.1: DT_{50}= 15.583 days, DT_{90}=51.764 days
Speyer 2.2: DT_{50}= 7.9708 days, DT_{90}=26.478 days

The resulting geometric mean DT_{50} would be 6.96 days (n=4).

Table B. 8.1.1.2.1.1-7: Summary of modelling endpoints obtained for metabolite THPAM in four soils

Study / Soil	Calculated DT_{50} [d]	Study temp [°C]	Study moisture	Ref. temp. [°C]	Ref. moisture at 10 kPa	Moist corr. factor	Temp. corr. factor	Normalised DT_{50} at [20°C & pF2]
Study 3 (2016) / LUFA 2.3 Sandy loam*	2.237 [a*]	20	50% MWHC	20	19	0.941	1	**2.111** [c*]
Study 8 (1993) / Hyde Farm Sandy loam [e]	5.650 [b]	20	40% MWHC	20	19	1.122	1	**5.650** [d]
Study 8 (1993) / Speyer 2.1 Sand [e]	11.220 [b]	20	40% MWHC	20	12	1.023	1	**11.220.** [d]
Study 8 (1993) / Speyer 2.2 Loamy sand [e]	6.976 [b]	20	40% MWHC	20	14	1.441	1	**6.976** [d]
Geometric mean (n = 4)								**5.529**

a SFO kinetics (pathway fit)
b SFO kinetics (metabolite applied as parent)
c moisture correction only
d temperature and moisture corrections were not needed
e summary of the study on rate of degradation of the metabolite can be found in point B.8.1.1.2.1.2.

A formation fraction value of 0.85 for THPI (from Captan) was obtained and 0.74 for THPAM (from THPI).

Comments RMS
*study 3: The kinetic evaluation of THPAM showed that the k value was not significantly different from 0 and therefore no acceptable DT_{50} value was obtained from this study. This DT_{50} should not be used for determination of the geometric mean DT_{50}. This also applies for the formation fraction of THPAM. It is recommended using a default value of 1 for the formation fraction.
The geometric mean DT_{50} considering only the values of the study 8 would be 7.62 days (n=3).
A revised kinetic fitting using CAKE and the alternative optimizer MCMC (study 6, 2017) was provided by the applicant later. The RMS evaluated and accepted the new kinetic fitting (please see page 80). The recalculated DT50 value is 2.0 days which corresponds to a normalized DT50 of 1.9 days.

Table B. 8.1.1.2.1.1-8: Summary of persistent endpoints obtained for Captan in four soils

~~Study~~	Soil	Kinetics model	Persistent endpoints

			DT_{50} [d]	DT_{90} [d]
Study 3 (2016)	LUFA 2.3	SFO	5.533	18.379
Study 4 (2014)	LUFA 2.1	SFO	5.666	18.820
Study 1 (1992)	Visalia (USA)	DFOP*	0.408	5.142
Study 2 (1988)	Greenville	DFOP**	0.349	1.956

*FOMC: DT_{50} = 0.468 d, DT_{90} = 5.829 d should be used
**modified SFO: DT_{50} = 2.206 d , DT_{90} = 7.328 d should be used

Comments RMS
*Soil Visalia (1992): the persistent endpoint should be derived from FOMC kinetics: DT_{50} = 0.468 d, DT_{90} = 5.829 d since the FOMC kinetics provided a better visual fit.
**Soil Greenville (1988): the persistent endpoint should be derived from modified SFO kinetics: DT_{50} = 2.206 d , DT_{90} = 7.328 d since all four kinetic models provided no acceptable statistic evaluation using the full data set.

Table B. 8.1.1.2.1.9-9: Summary of persistent endpoints obtained for metabolite THPI in four soils

Study	Soil	Kinetics model	Persistent endpoints	
			DT_{50} [d]	DT_{90} [d]
Study 3 (2016)	LUFA 2.3	SFO	3.280	10.895
Study 7 (1993)	Hyde Farm	SFO	5.845*	19.420*
Study 7 (1993)	Speyer 2.1	SFO	15.0*	49.820*
Study 7 (1993)	Speyer 2.2	SFO	7.894*	26.220*

Comments RMS
*study 7: The samples of day 0 were worked up and analysed twice which resulted in 4 values at day 0. Two of the four values were taken by the notifier without further explanation concerning the selection. The residue data of day 0 used by the notifier were not accepted by RMS. Therefore, the RMS recalculated the kinetics using average values of the same extract of day 0. The following DT_{50} and DT_{90} values for the degradation of THPI were obtained.

Study	Soil	Kinetics model	Persistent endpoints	
			DT_{50} [d]	DT_{90} [d]

Study 7 (1993)	Hyde Farm	SFO	6.107	20.286
Study 7 (1993)	Speyer 2.1	SFO	15.583	51.764
Study 7 (1993)	Speyer 2.2	SFO	7.9708	26.478

Table B. 8.1.1.2.1.1-10: Summary of persistent endpoints obtained for metabolite THPAM in four soils

Study	Soil	Kinetics model	Persistent endpoints	
			DT_{50} [d]	DT_{90} [d]
Study 3 (2016)	LUFA 2.3	SFO	2.247*	7.465*
Study 8 (1993)	Hyde Farm	SFO	5.650	18.770
Study 8 (1993)	Speyer 2.1	SFO	11.220	37.280
Study 8 (1993)	Speyer 2.2	SFO	6.976	23.180

Comments RMS
*study 3: The kinetic evaluation of THPAM showed that the k value was not significantly different from 0 and therefore no acceptable DT_{50} value was obtained from this study.
A revised kinetic fitting using CAKE and the alternative optimizer MCMC (study 6, 2017) was provided by the applicant later. The RMS evaluated and accepted the new kinetic fitting (please see page 80). The recalculated DT50 value is 2.0 days and the recalculated DT90 value is 6.8 days.

MATERIALS AND METHODS

Study 3 (2016): The result of fitting the SFO kinetic model to residue data of Captan (table B.8.1.1.2.1.1-11) in soil LUFA 2.3 (parent only fit) provides acceptable visual fit to the data set (table B.8.1.1.2.1.1-12). The k-rate is significantly different from zero and the Chi^2 error value is below 15%. The SFO fit was compared with FOMC fit to determine the best-fit model to be used for the pathway fit. The FOMC model provides acceptable visual fit to the data set; however, it does not improve the fit compared to SFO. Therefore, SFO kinetics is the best-fit model and it is used for pathway fit.

The result of fitting the SFO kinetic model to residue data of Captan and metabolites (pathway fit) provides acceptable visual fit for Captan data set (table B.8.1.1.2.1.1-13). The k-rate is significantly different from zero and the Chi^2 error value is below 15%.
For the metabolites THPI and THPAM, the overall visual fit is considered acceptable since the overall pattern of formation and decline phases of metabolite is sufficiently described by the model and the estimated k-rate for both metabolites is significantly different from zero. In addition, the residuals are randomly distributed around the zero. The Chi^2 error value is above 15%. However, this might be due to large variation between replicates within samples. A formation fraction value of 0.8464 for THPI (from Captan) and 0.7355 for THPAM (from THPI) was obtained.

Table B. 8.1.1.2.1.1-11: Residue data [% AR] for Captan and metabolites obtained from aerobic soil metabolism study with [^{14}C] Captan in soil LUFA 2.3 processed according to FOCUS kinetics for kinetic evaluation

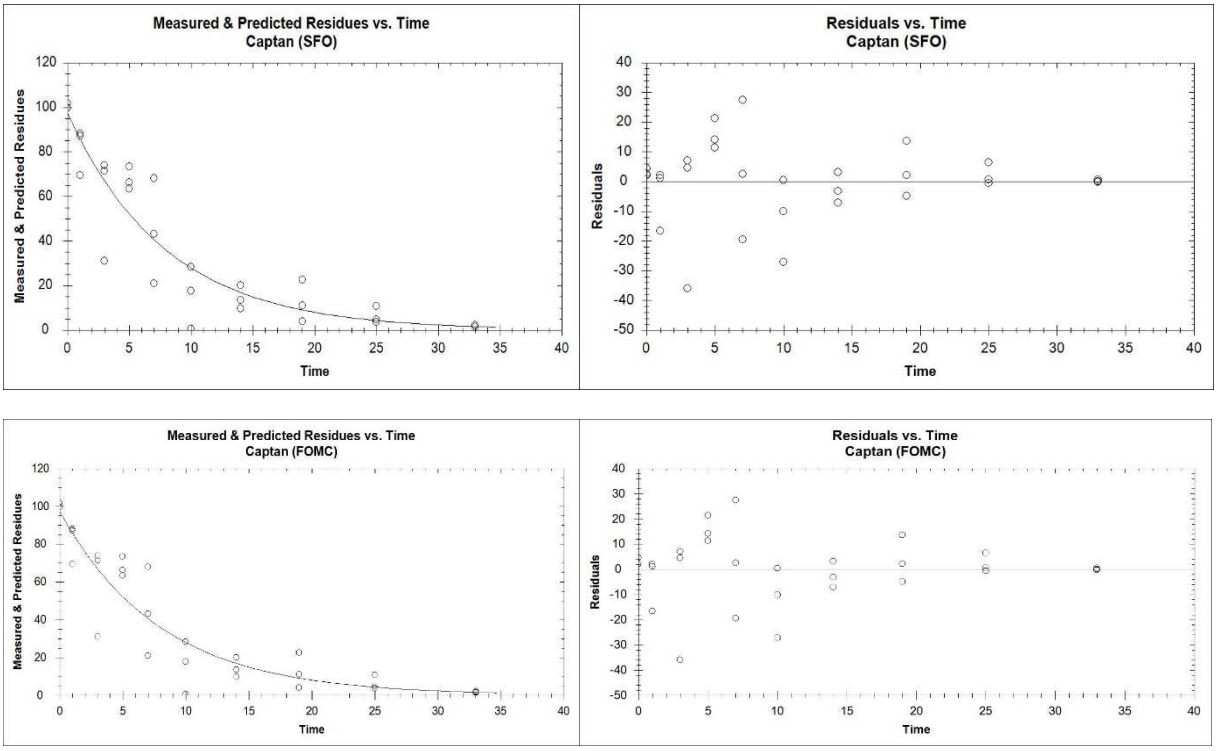
Time [d]	Captan [%AR]	THPI [%AR]	THPAM [%AR]

0	102.0 [a]	0 [b]	0
0	99.7 [a]	0 [b]	0
0	99.8 [a]	0 [b]	0
1	88.1	7.6	1.2
1	87.2	6.8	1.1
1	69.5	28.3	2.5
3	31.1	40.0	15.7
3	74.0	11.8	1.9
3	71.6	14.6	2.2
5	63.5	10.9	5.2
5	73.5	9.4	3.8
5	66.3	15.6	3.1
7	68.1	11.6	2.5
7	21.1	32.4	15.3
7	43.2	31.2	3.6
10	17.8	24.9	9.7
10	28.3	11.3	14.3
10	0.8	35.4	19.5
14	9.8	16.4	6.6
14	20.1	15.0	3.6
14	13.7	10.0	10.9
19	11.2	18.6	1.0
19	4.1	0.5 [c]	15
19	22.7	4.8	1.5
25	4.9	4.7	0.5 [c]
25	10.8	12.3	4.2
25	3.7	0.5 [c]	7.1
33	2.2	3.4	0.5 [c]
33	1.6	0.5 [c]	0.5 [c]
33	1.4	0.5 [c]	0.5 [c]

AR applied radioactivity
a sum of parent and metabolite residue concentration at day zero
b set to zero according to FOCUS kinetics
c set to ½ LOD according to FOCUS kinetics (LOD = 1% AR)

Table B. 8.1.1.2.1.1-12: Results of SFO and FOMC fits to soil residue data of Captan obtained from soil LUFA 2.3 (Parent only fit)

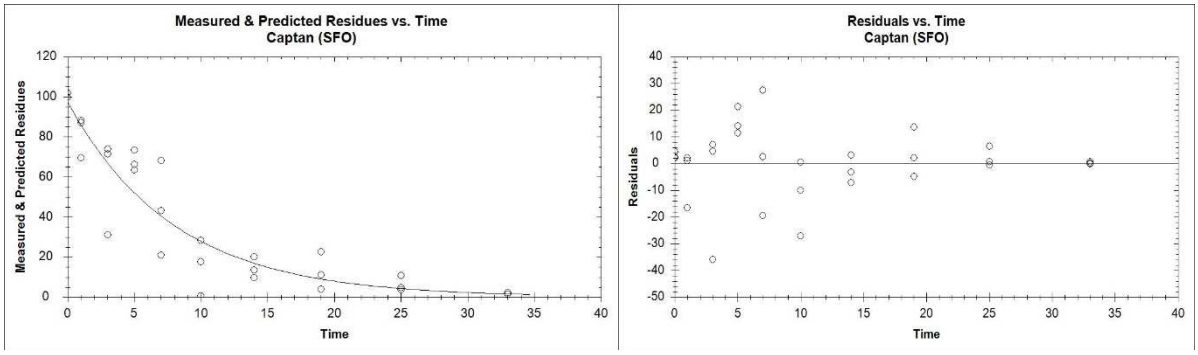
Study	**Study 3 (2016)**							
Soil	**Kinetics**	**Parameter**	**Prob > t**	**St. Dev.**	**Chi² error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**
LUFA 2.3	SFO	k0.12523	3.53e-09	n.r.	14.4	acceptable	5.535	18.39
	FOMC	α: 1.775e+03 β: 1.417e+04	**95% CI:** α: -1.9e+06 – 1.9e+06 β: -1.5e+07 – 1.5e+07	α: 9.7e+05 β: 7.8e+06	15.1	acceptable	5.534	18.39

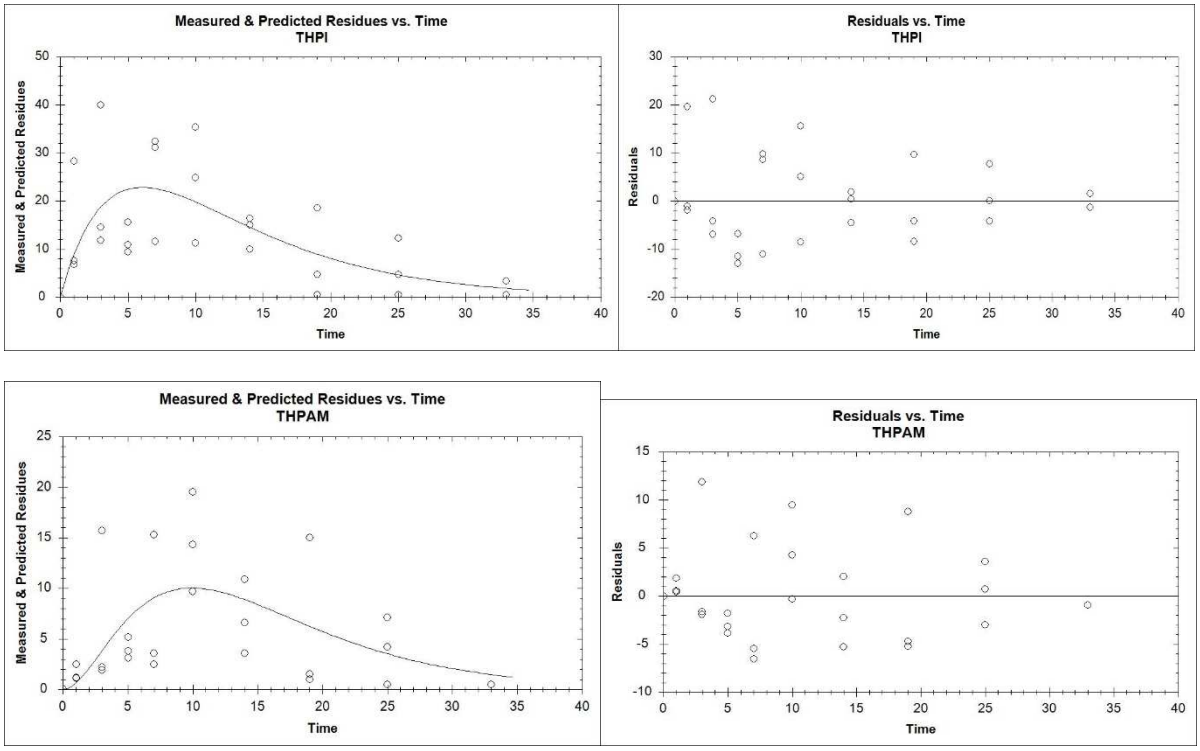


Kinetic evaluation soil LUFA 2.3 (SFO and FOMC), captan only

Table B. 8.1.1.2.1.1-13: Results of SFO fit to soil residue data of Captan and metabolites THPI and THPAM obtained from soil LUFA 2.3 (Pathway fit)

Study	**Study 3 (2016)**							
Soil	**Substance**	**Parameter**	**Prob > t**	**Chi² error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**	**Formation fraction [-]**
LUFA 2.3	Captan	k_par: 0.12529	1.21e-12	14.39	acceptable	5.533	18.379	n.r.
	THPI	k_THPI: 0.21134	0.002404	25.27	acceptable	3.280	10.895	0.8451
	THPAM	k_THPAM: 0.30846	0.054072	31.67	acceptable	2.247	7.465	0.7360





Kinetic evaluation soil LUFA 2.3 (SFO), captan and metabolites THPI and THPAM

Comments RMS

The kinetics was re-calculated by the RMS and the results presented by the notifier were confirmed.

Captan only, FOMC kinetic: Additionally, α and β were not significantly different from 0 since the probability is not smaller than 0.05 and the confidence interval contains zero. Therefore, the FOMC kinetics is not acceptable and SFO kinetics should be used for pathway fit.

Pathway fit:

THPAM: The k value is not significantly different from 0 since the probability is not smaller than 0.05 and the confidence interval contains zero. Therefore, the resulting DT_{50} and the formation fraction are not acceptable for the metabolite THPAM. It is recommended using a default worst case formation fraction of 1 for the degradation of THPI to THPAM.

A revised kinetic fitting using CAKE and the alternative optimizer MCMC (study 6, 2017) was provided by the applicant later. The RMS evaluated and accepted the new kinetic fitting (please see page 80). Additionally, the kinetic assessment was discussed during the pesticide peer review meeting 15 (please see p.83).

However, the RMS recalculated the kinetic evalution before the new kinetic fitting was available using the following approaches:

The RMS recalculated the kinetic evaluation assuming a formation fraction of 1 for the degradation of THPI to THPAM. The results are presented in the table below:

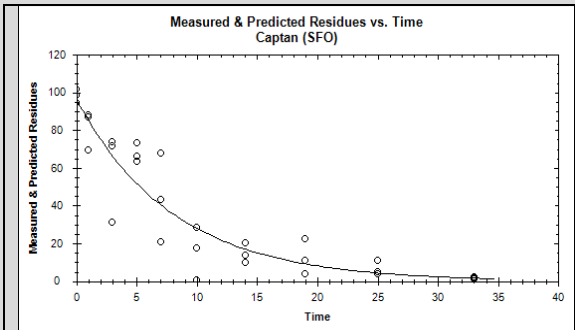
Results of SFO fit to soil residue data of Captan and metabolites THPI and THPAM obtained from soil LUFA 2.3 (Pathway fit) RMS evaluation (ff=1 for THPI to THPAM)

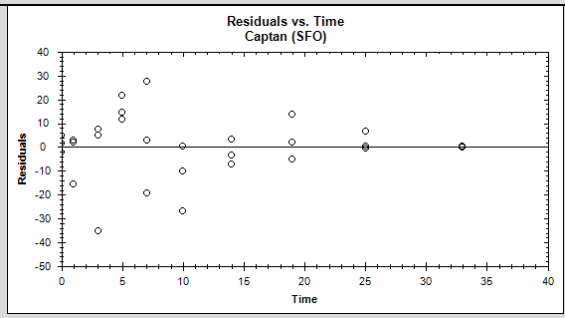
Study	**Study 3 (2016)**							
Soil	**Substance**	**Parameter**	**Prob > t**	**Chi^2 error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**	**Formation fraction [-]**
LUFA 2.3	Captan	k_par: 0.12448	4.75e-13	14.32	acceptable	5.5684	18.498	0.8014 to THPI

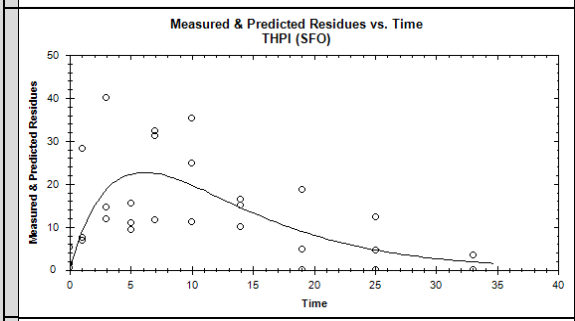
	THPI	k_THPI: 0.19395	2.35e-6	26.97	acceptable	3.5738	11.872	1 to THPAM
	THPAM	k_THPAM: 0.39756	0.00018	31.16	acceptable	1.7435	5.7918	

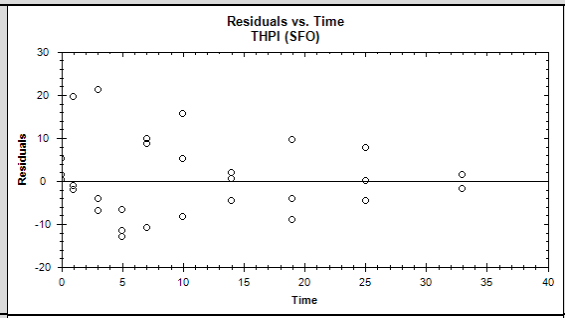
Additionally, the RMS recalculated the kinetics considering the metabolite THPAI which occurred with a maximum of 3.1 % after 7 days and which was built from THPAM. Furthermore, a formation fraction of 1 for the degradation of THPI to THPAM and from THPAM to THPAI was assumed. The results are presented in the following table:

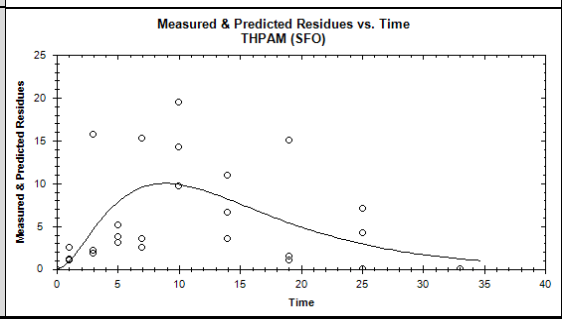
Study	**Study 3 (2016)**							
Soil	**Substance**	**Parameter**	**Prob > t**	**Chi² error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**	**Formation fraction [-]**
LUFA 2.3	Captan	k_par: 0.12452	3.77e-14	14.32	acceptable	5.567	18.492	0.8551 to THPI
	THPI	k_THPI: 0.21245	9.16e-8	26.83	acceptable	3.2626	10.838	1 to THPAM
	THPAM	k_THPAM: 0.44583	2.58e-5	31.95	acceptable	1.5547	5.1647	1 to THPAI
	THPAI	k THPAI: 3.8888	0.000238	51.88	acceptable	0.1782	0.5921	

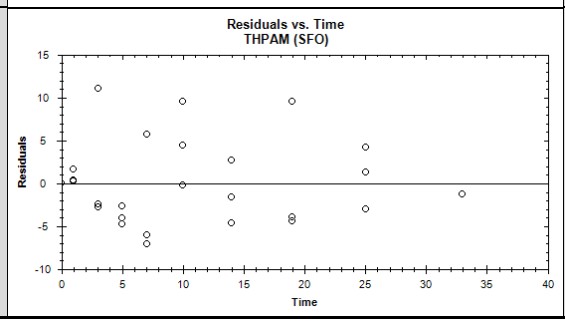


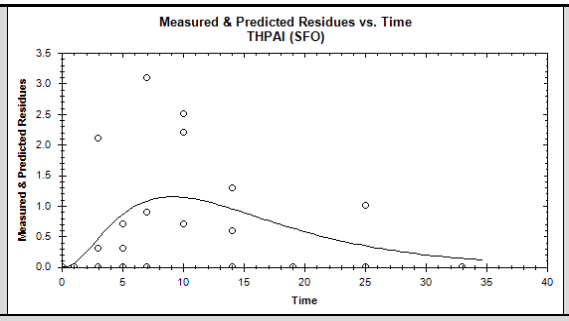


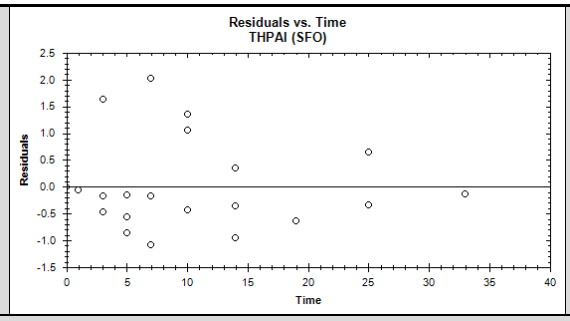








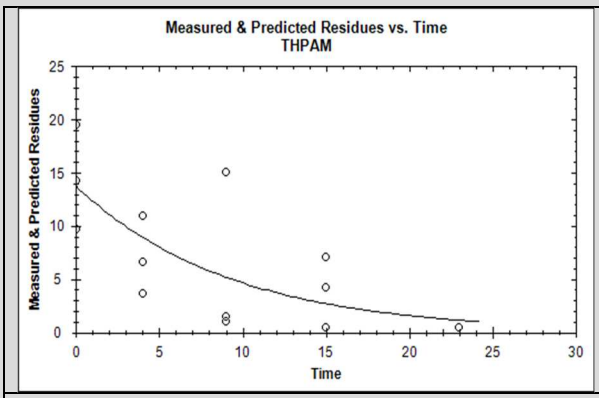


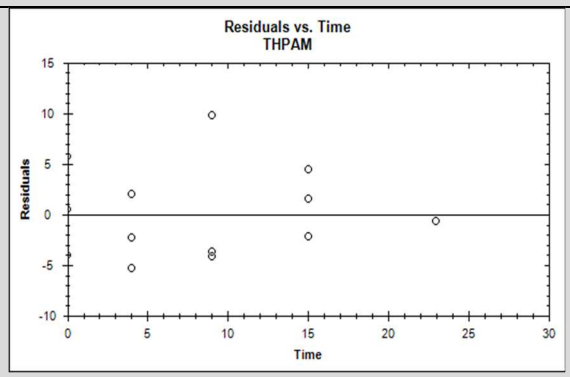


Additionally, the RMS recalculated the kinetics assuming a DT_{50} of 6.4 d for THPAM, which was calculated from the decline curve of THPAM, and a ff of 1 (FOCUS, 2014, p156).

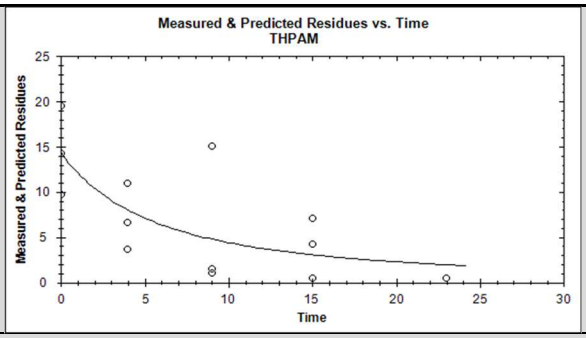
Residue data of THPAM from day 10 onwards (=Maximum) were fitted to SFO kinetics using KinGUI. The resulting decline curve showed an acceptable visual fit; the χ^2 value is below 15 % and the k-rate is significantly different from 0. The results are presented below:
The calculated DT_{50} of 6.4 days is in the range of the DT_{50} values obtained from the studies dosed with THPAM (5.65 d, 11.22 d, 6.98 d) (and is therefore deemed to be suitable for further calculation).
Additionally, the data were fitted to FOMC kinetics resulting in confidence intervals containing 0 for α and β. Therefore, the FOMC kinetics is not acceptable.

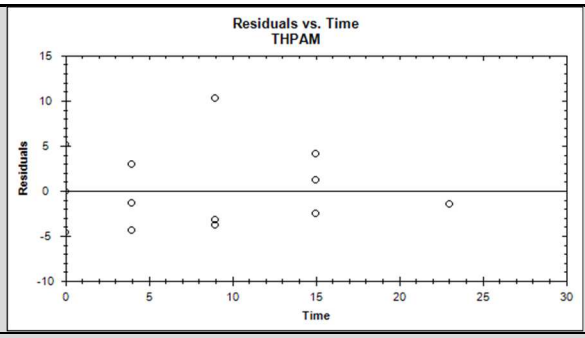
Study	**Study 3 (2016)**							
Soil	**Kinetic**	**Substance**	**Parameter**	**Prob > t**	**Chi² error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**
Lufa 2.3	SFO	THPAM	k=0.10904	0.0104	14.26	Acceptable	6.357	21.118
	FOMC	THPAM	α = 1.526 β = 8.477	CI α:-3.132-6.184 β:-33.8-50.7	14.24	Acceptable	4.874	29.853





THPAM, degradation from maximum onwards, SFO, soil Lufa 2.3

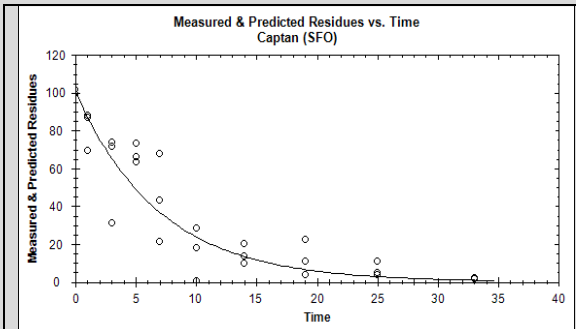


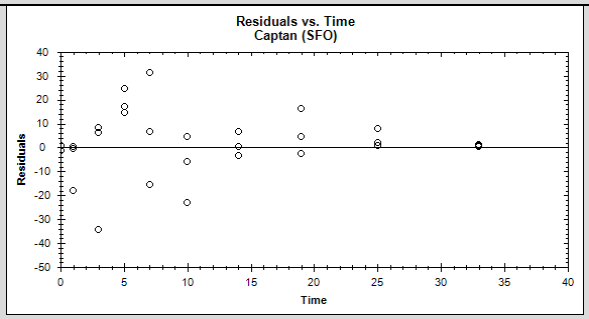


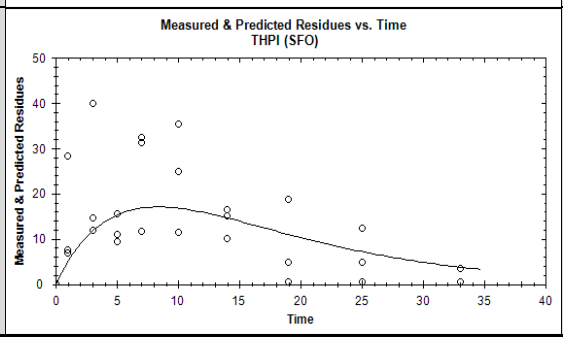
THPAM, degradation from maximum onwards, FOMC, soil Lufa 2.3

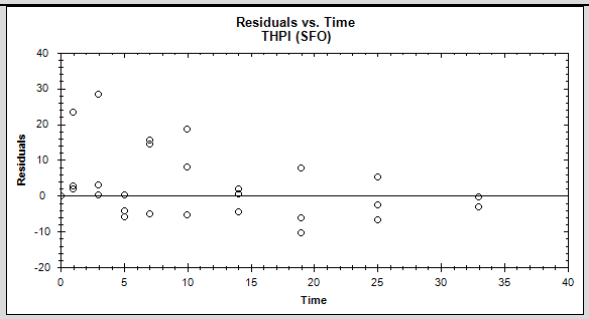
Then, the residues were refitted to SFO assuming a DT_{50} of 6.4 days for THPAM and a ff of 1 (THPI to THPAM). The visual fit was not improved and the residuals were higher for THPI and THPAM.
Due to high variance between the replicates it was not possible to achieve a better fit. Therefore, it is recommended by the RMS to exclude the DT_{50} of THPAM of this study and to use a ff of 1 for modelling.

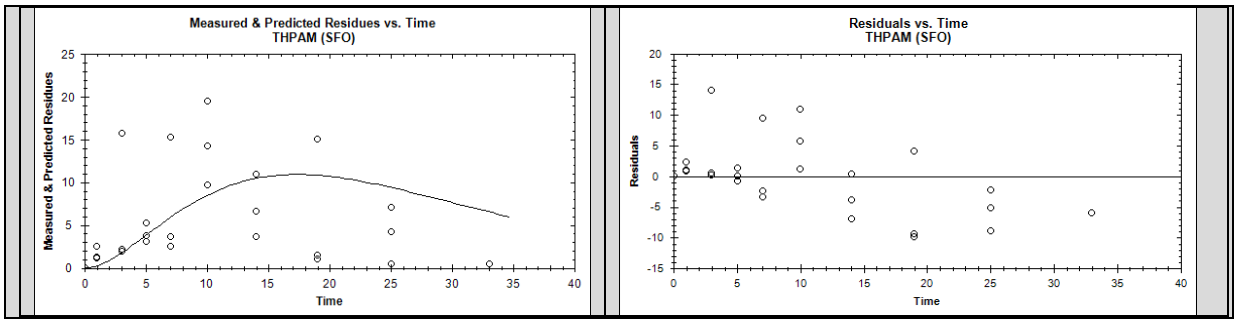
Study	**Study 3 (2016)**							
Soil	**Substance**	**Parameter**	**Prob > t**	**Chi^2 error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**	**Formation fraction [-]**
LUFA 2.3	Captan	k_par: 0.1449	<2e-16	15.49	acceptable	4.7835	15.89	0.3808 to THPI
	THPI	k_THPI: 0.09783	1.15e-13	35.15	acceptable	7.0852	23.536	1 to THPAM
	THPAM	k_THPAM: 0.10904	- (fixed)	55.06	acceptable	6.3568	21.117	-











Study 4 (2014): The result of fitting the SFO kinetic model to residue data of Captan (table B.8.1.1.2.1.1-14) obtained from soil LUFA 2.1 provides acceptable visual fit to the data set (table B.8.1.1.2.1.1-15). The k-rate is significantly different from zero and the Chi^2 error value is well below 15%. Therefore, SFO kinetics is considered appropriate to derive modelling endpoint for Captan in this soil. In order to identify the best-fit model to derive persistent endpoints, SFO fit was compared with the FOMC fit. The FOMC model does not improve the fit compared to SFO. The FOMC visual fit is acceptable. However, statistically FOMC fit is not better that SFO (table B.8.1.1.2.1.1-15). Therefore, SFO kinetics is also used to derive persistent endpoint for Captan from this soil.

Table B. 8.1.1.2.1.1-14: Residue data [% AD] for Captan obtained from aerobic soil degradation study with Captan in soil LUFA 2.1, and processed data set according to FOCUS kinetics for kinetic evaluation

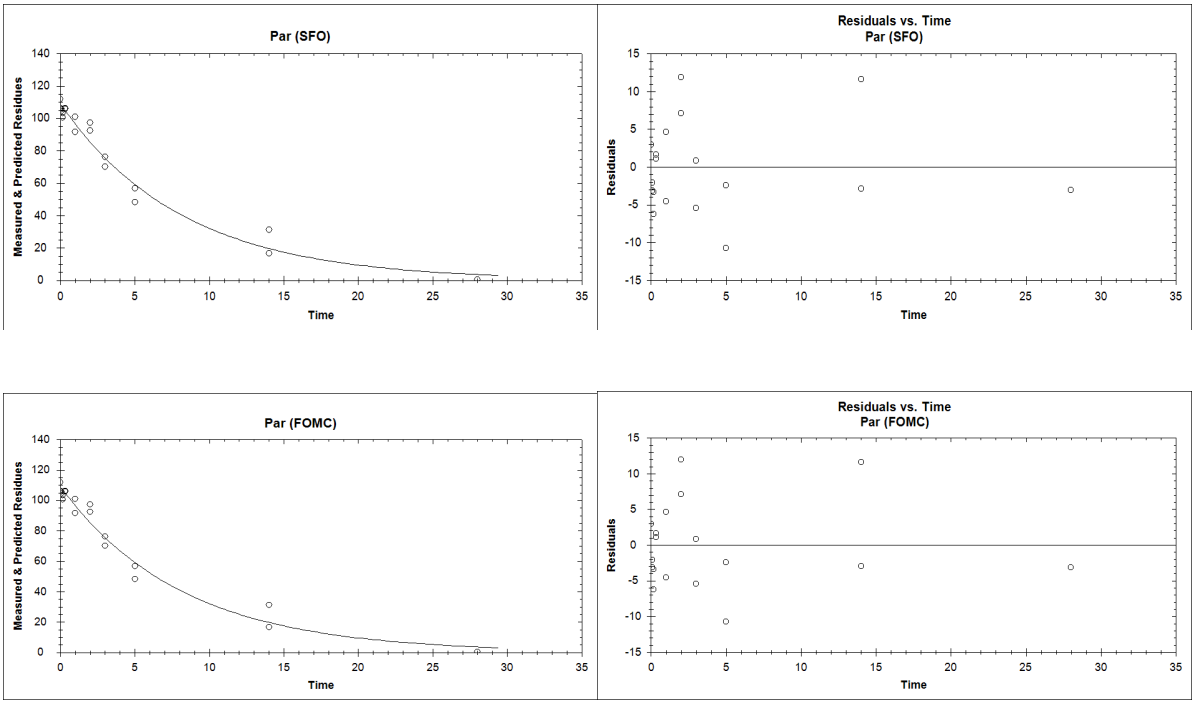
Raw residue data obtained from study		Processed residue data according to FOCUS kinetics	
Time [h]	Captan [%AD]	Time [d]	Captan [%AD]
0	111.4	0	112[a]
0	113.3	0	112[a]
2	105.9	0.083	105.9
2	104.8	0.083	104.8
4	103.5	0.167	103.5
4	100.6	0.167	100.6
8	106.3	0.333	106.3
8	105.8	0.333	105.8
24	91.9	1	91.9
24	101.1	1	101.1
48	92.5	2	92.5
48	97.3	2	97.3
72	76.4	3	76.4
72	70.1	3	70.1
120	48.4	5	48.4
120	56.7	5	56.7
336	31.3	14	31.3
336	16.8	14	16.8
672	<LOD	28	0.5[b]
672	<LOD	28	0.5[b]

AD applied dose
a set to initial applied
b set to 1/2 LOD according to FOCUS kinetics (LOD = 1% AD)

Table B. 8.1.1.2.1.1-15: Results of SFO and FOMC fits to soil residue data of Captan obtained from soil LUFA 2.1

Study	Study 4 (2014)							
Soil	Kinetics	Parameter	Prob > t	St. Dev.	Chi^2 error [%]	Visual fit	DT_{50} [d]	DT_{90} [d]

LUFA 2.1	SFO	k: 0.1223	8.12e-11	n.r.	4.8	acceptable	5.666	18.820
	FOMC	α: 2.25E+02 β: 1.84E+03	**95% CI:** α: -1.9e+04 – 1.9e+04 β: -1.6e+05 – 1.6e+05	α: 9.8e+03 β: 8.0e+04	5.0	acceptable	5.660	18.870



Comments RMS
RMS recalculated kinetics using KINGUI 2; the results presented by the notifier were confirmed.

FOMC kinetic: α and β were not significantly different from 0 since the probability was not below 0.05 and the confidence interval contained 0. Therefore, the FOMC kinetics is not deemed acceptable and SFO should be used for modelling and persistent end point.

Study 1 (1992): The result of fitting the SFO kinetic model to residue data of Captan (table B.8.1.1.2.1.1-16) obtained from soil Visalia (USA) provides an unacceptable visual fit to the data set (table B.8.1.1.2.1.1-17). The k-rate is significantly different from zero, however, the Chi^2 error value is above 15%. Since 10% of initial measured concentration was reached within the experimental period, the FOMC model was fitted to the data set. The FOMC provides acceptable visual fit and the Chi^2 error value is well below 15%. Therefore, FOMC is considered appropriate to derive modelling endpoints for Captan from this soil.
To derive endpoint for use as persistent, the FOMC fit was compared with the DFOP fit. The DFOP fit improved the fit more than the FOMC. However, since the DT50 and DT90 values obtained are longer than those obtained by DFOP, FOMC is considered also for deriving persistent endpoint for Captan in soil Visalia.

Table B. 8.1.1.2.1.1-16: Residue data [% AR] obtained from aerobic metabolism study with [^{14}C] Captan in soil Visalia (USA), and processed data set according to FOCUS kinetics used for kinetic evaluation

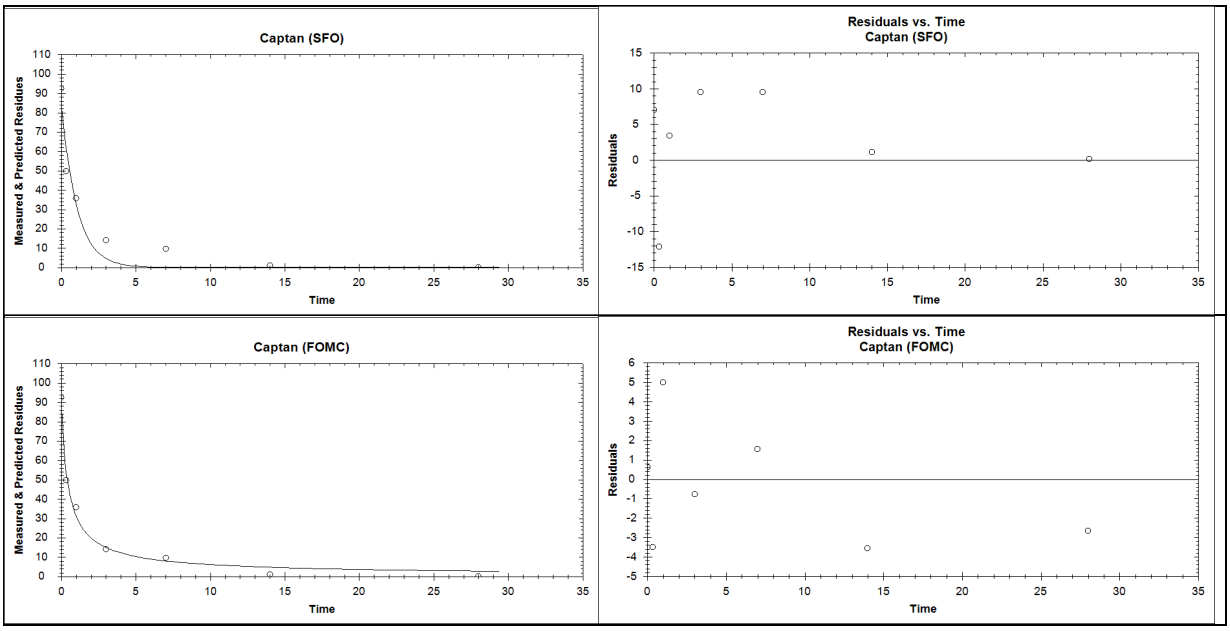
Raw residue data obtained from study (mean of duplicates)			Processed residue data according to FOCUS kinetics	
Time	**Captan [%AR]**	**Recovery [%AR]**	**Time [d]**	**Captan [%AR]**
0 h	86.07	92.53	0	92.53[a]

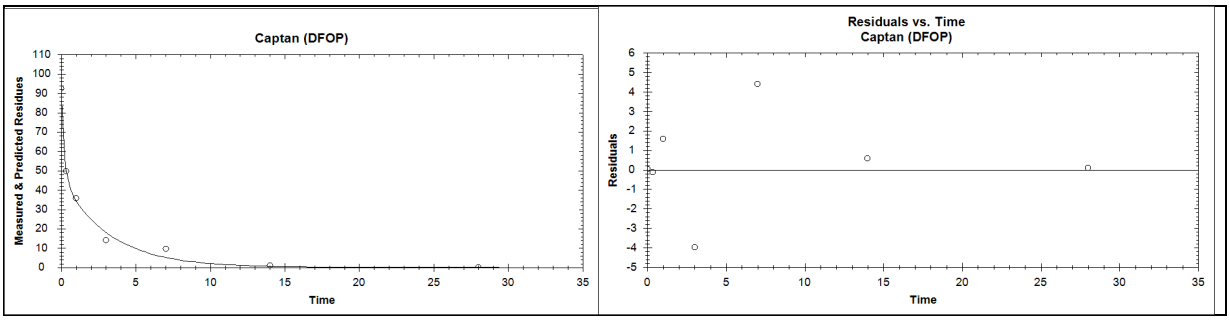
4 h	45.05	83.99	-	-[b]
8 h	49.85	96.67	0.33	49.85
1 d	35.74	89.89	1	35.74
3 d	14.13	92.77	3	14.13
7 d	9.57	90.23	7	9.57
14 d	1.15	95.80	14	1.15
28 d	0.1	95.38	28	0.1

AR applied radioactivity
a set total recovery at day 0
b data point was excluded since recovery is less than 90% AR
h hour
d day

Table B. 8.1.1.2.1.1-17: Results of SFO, FOMC and DFOP fits to soil residue data of Captan obtained from soil Visalia (USA)

Study	**Study 1(1992)**							
Soil	**Kinetics**	**Parameter**	**Prob > t**	**St. Dev.**	**Chi² error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**
Visalia (USA)	SFO	k: 0.9740	0.0063	n.r.	20.48	not acceptable	0.712	2.364
	FOMC	α: 0.7882 β: 0.3318	**95% CI:** α: 0.442 – 1.134 β: 0.043 – 0.621	α: 0.176 β: 0.148	8.70	acceptable	0.468	5.829
	DFOP	k1: 5.2445 k2: 0.3135 g: 0.4987	k1: 0.057 k2: 0.018 **95% CI:** g: 0.322 – 0.675	g: 0.090	7.61	acceptable	0.408	5.142





Comments RMS
For the kinetic evaluation the residues after 4 h were considered as outliers and not used for kinetic evaluation since the recovery was less than 90 % AR at that time point.
The RMS recalculated the DT_{50}/DT_{90} values, the results presented by the Notifier were confirmed with the following exceptions:
SFO kinetic: t-test for k (prob >1) resulted in 0.016 instead of 0.0063
FOMC kinetic: t-test (prob >1) for α was 0.00481 and for β was 0.04438
DFOP kinetic: t-test (prob>1) for k1=0.0767 instead of 0.057 and for k2=0.0351 instead of 0.018 and for g=0.0103. k1 is not significantly different from 0 since the probability is not smaller than 0.05 for k1 (0.0767). The DFOP improved the χ^2 value compared to FOMC kinetics, but the RMS is of the opinion that the FOMC kinetic provided a better visul fit. Additionally, k1 is not significantly different from 0 since the probability is not smaller than 0.05 for k1 (0.0767). Therefore, for persistent endpoint the DT_{50} and DT_{90} values derived from FOMC kinetics should be used.

Study 2 (1988): The result of fitting the SFO kinetic model to residue data of Captan obtained from soil Greenville (USA) provides an unacceptable visual fit (**Table 7.1.2.1.1-16**). The k-rate is significantly different from zero, but the Chi^2 error value is above 15%. The SFO fit was further compared with FOMC fit. FOMC improved the visual fit and provides a Chi^2 error value well below 15%. However, a wide conveyance (95%) interval was obtained for the parameter beta. Therefore, FOMC was further compared with DFOP fit. DFOP reduced the Chi^2 error value more than FOMC, however, k rate (slow phase) is not significant. Therefore, none of the three models is considered for appropriate to derive modelling and persistent endpoints.
In order to derive reliable degradation rates for Captan in this soil, a modified SFO fit was performed. Since the study was performed with radiolabelled Captan, all data points corresponding to mass balance (recovery) below 90% or above 110% were exclude from the data set. Therefore, modified SFO was performed with three data points only. The residue data are presented in (table B.8.1.1.2.1.1-18).
Modified SFO shows acceptable visual fit to data set and the Chi^2 error value is well below 15%. The k rate is significantly different from zero. Therefore, modified SFO fit is used for deriving modelling and persistent endpoints for Captan in soil Greenville (USA) (table B.8.1.1.2.1.1-19).

Table B. 8.1.1.2.1.1-18: Residue data [% AR] obtained from aerobic metabolism study with [^{14}C] Captan in soil in soil Greenville (USA), and processed data set according to FOCUS kinetics used for kinetic evaluation

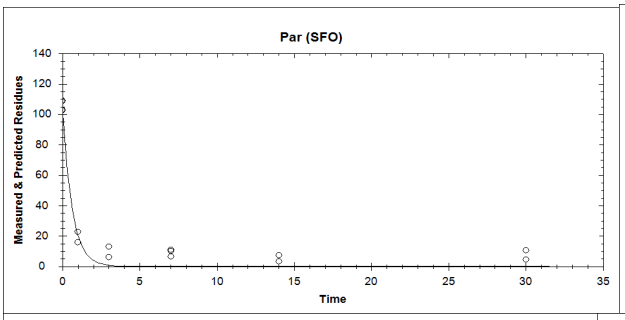
Raw residue data obtained from study			Processed residue data according to FOCUS kinetics		Processed residue data according to FOCUS kinetics (used for modified fit)	
Time [d]	**Captan [%AR]**	**Recovery [%AR]**	**Time [d]**	**Captan [%AR]**	**Time [d]**	**Captan [%AR]**
0	102.3	103.0	0	103.0[a]	0	103.0[a]
0	108.0	108.8	0	108.8[a]	0	108.8[a]
0	108.9	109.1	0	109.1[a]	0	109.1[a]
0	102.2	102.5	0	102.5[a]	0	102.5[a]
1	16.0	82.1	1	16.0	7	10.4
1	22.7	84.4	1	22.7	7	11.0
3	13.3	89.6	3	13.3	14	7.4
3	6.1	87.7	3	6.1	14	3.5
7	10.2	88.7	7	10.2		
7	6.7	83.2	7	6.7		
7	10.4	101.7	7	10.4		
7	11.0	102.5	7	11.0		
14	7.4	102.7	14	7.4		
14	3.5	100.7	14	3.5		
30	4.7	111.3	30	4.7		
30	10.5	114.2	30	10.5		

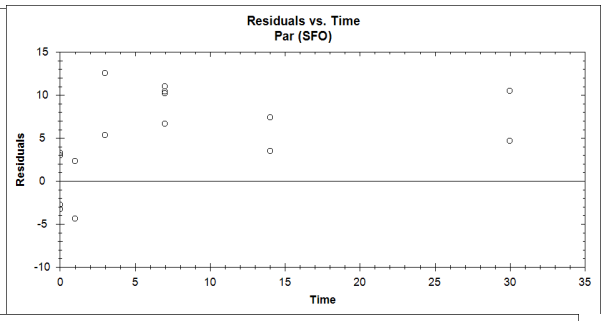
AR applied radio activity
a set to total recovery at day 0

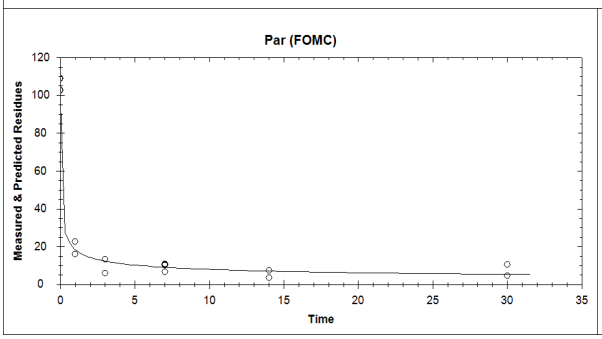
Table B. 8.1.1.2.1.1-19: Results of SFO, FOMC and DFOP fits to soil residue data of Captan obtained from soil Greenville (USA)

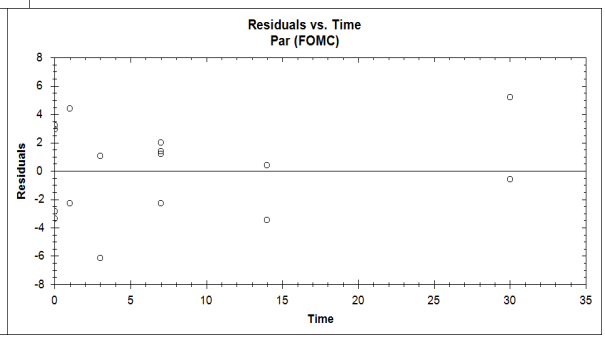
Study	**Study 2 (1988)**							
Soil	**Kinetics**	**Parameter**	**Prob > t**	**St. Dev.**	**Chi^2 error [%]**	**Visual fit**	**DT$_{50}$ [d]**	**DT$_{90}$ [d]**
Greenville (USA)	SFO	k: 1.6483	1.25e-05	n.r.	19.95	not acceptable	0.420	1.397
	FOMC	α: 0.3663 β: 0.0084	**95% CI:** α: 0.190 – 0.542 β: -0.015 – 0.032	α: 0.0898 β: 0.0120	5.40	acceptable	0.047	4.482
	DFOP	k1: 2.2888 k2: 0.0132 g: 0.91	k1: 3.63e-06 **k2: 0.209** 95% CI:	g: 0.0191	4.6	acceptable	0.349	1.956

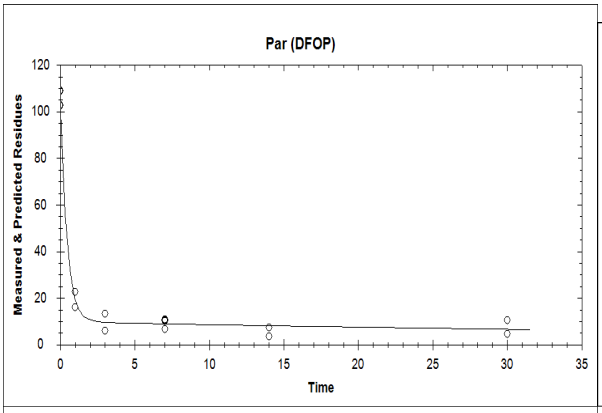
			g: 0.871 - 0.945					
	SFO modified fit	k: 0.3142	2.76e-05	n.r.	5.36	acceptable	2.206	7.328

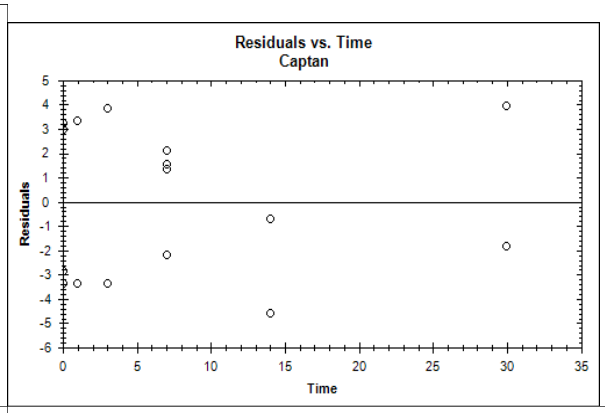


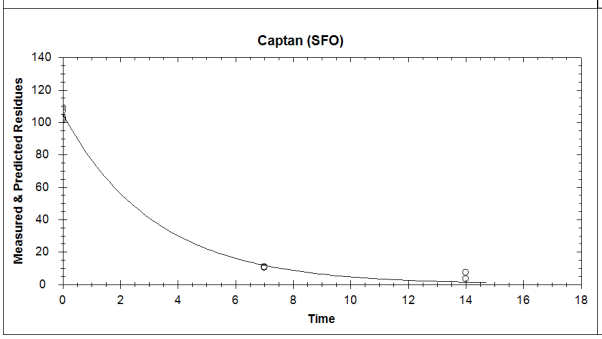


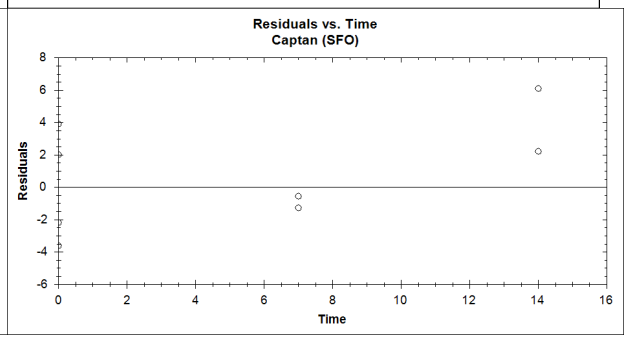








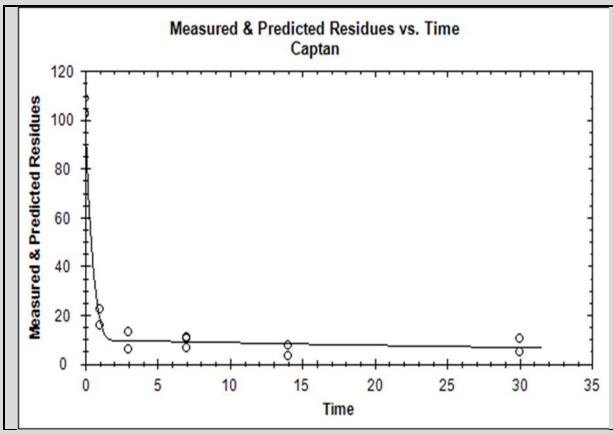


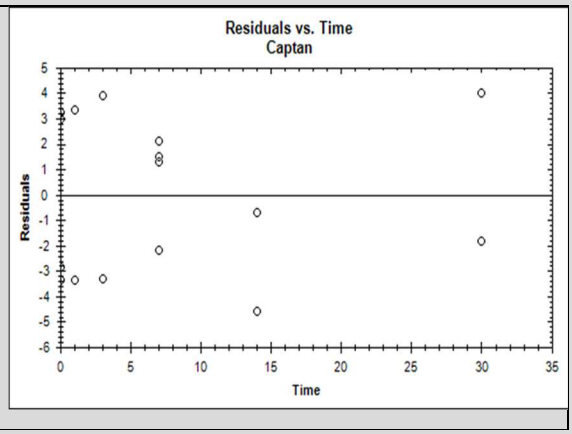


Comments RMS

The visual fit of the SFO kinetic is not deemed acceptable since later time points are not adequately described. The fit of the FOMC is deemed acceptable. But the probability (Prob > t) for α was 0.000896 and for β it was 0.261645. β is not significantly different from 0 since the probability is not smaller than 0.05 and zero is included in the confidence interval! Therefore, FOMC kinetic is not appropriate for deriving endpoints.
DFOP: The fit of the DFOP kinetic is deemed acceptable. But k2 is not significantly different from 0 since the probability is not smaller than 0.05 for k2 (0.209). Therefore, DFOP kinetic is not appropriate for deriving endpoints. The probability for g was determined to be $2.46e^{-15}$.
Additionally, the RMS fitted the data to HS kinetics. The fit is deemed acceptable. But k2 is not significantly different from 0 since the probability is not smaller than 0.05 for k2 (0.217). Therefore, the HS kinetic is not appropriate for deriving endpoints.

Soil	Kinetics	Parameter	Prob > t	Chi^2 error [%]	Visual fit	DT_{50} [d]	DT_{90} [d]
Greenville (USA)	HS	k1: 1.69933 k2: 0.01357 tb: 1.41147	k1: 6.63e-09 k2: 0.217 tb: 4.89e-07	4.599	acceptable	0.4079	1.3550





For the modified SFO only three time points were left after modification. However, the derived endpoints (DT_{50}, DT_{90} values) adequately describe the degradation of captan in soil Greenville and they appear to be conservative enough.
Due to the rapid degradation at the beginning (which might be due to hydrolysis) only 16-22 % captan were left after one day and ≤ 11 % captan could be detected from day 7 onwards. Most of the data points were available after about 90 % of captan was already degraded. The visual fit is acceptable and the residual do not indicate systematic deviation. The χ2 value of 5.36 is below the trigger of 15 and k is significantly different from 0 (t-test: 2.27e-5).

Study 7 (1993): In order to derive modelling endpoints for the metabolite THPI, the SFO kinetics was fit to residue data obtained for THPI in soils Hyde Farm, Speyer 2.1 and Speyer 2.2. The residue data used for the kinetic evaluation are presented in table B.8.1.1.2.1.1-20. For all three soils, SFO shows acceptable visual fit to residue data, the Chi^2 error below 15% (except for soil Speyer 2.2 slightly above, 15.1%) and the estimated k rate is significantly different from zero (table B.8.1.1.2.1.1-21). Therefore, SFO kinetic is appropriate to derive modelling endpoints for THPI from these soils.
To derive persistence endpoints, the SFO fits were compared with FOMC fits (table B.8.1.1.2.1.1-21). For all three soils, FOMC does not improve the visual fit or reduce the Chi^2 error. Therefore, SFO is also considered appropriate for deriving persistence endpoints for THPI from soils Hyde Farm, Speyer 2.1 and Speyer 2.2.

Table B. 8.1.1.2.1.1-20: Residue data [mg/kg] obtained for THPI from three soils in laboratory soil degradation study processed according to FOCUS kinetics for kinetic evaluation

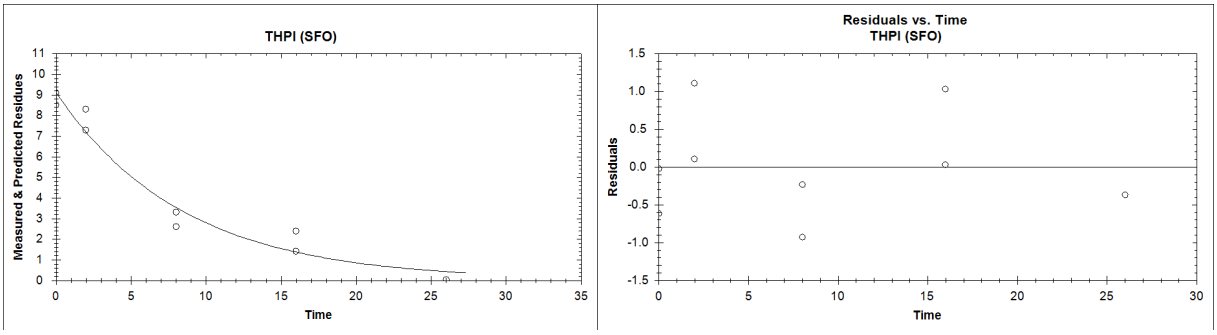
Soil Hyde Farm		Soil Speyer 2.1		Soil Speyer 2.2	
Time [d]	**THPI [mg/kg]**	**Time [d]**	**THPI [mg/kg]**	**Time [d]**	**THPI [mg/kg]**
0	8.5	0	8.7	0	8.4
0	9.1	0	9.0	0	9.3
2	8.3	2	9.9	2	9.4
2	7.3	2	9.8	2	8.9
8	3.3	8	7.6	8	6.3
8	2.6	8	7.0	8	5.5
16	1.4	16	5.7	16	2.2
16	2.4	16	6.7	16	1.0
26	0.05 [a]	26	NA	26	0.17
26	0.05 [a]	26	NA	26	0.70
		33	3.0	33	0.05[a]
		33	0.14	33	0.05 [a]
		40	0.05 [a]		
		40	0.05 [a]		

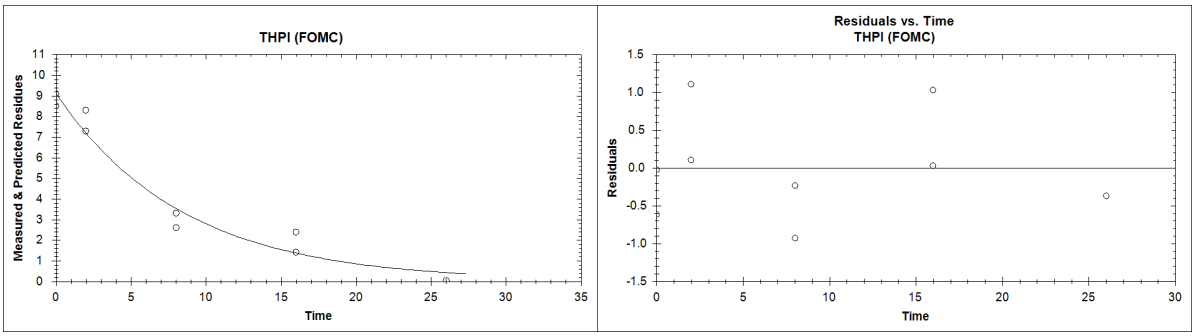
NA not available
a set to ½ LOD according to FOCUS kinetics (LOD = 0.1 mg/kg)

Table B. 8.1.1.2.1.1-21: Results of kinetics fits soil residue data of THPI obtained from three soils

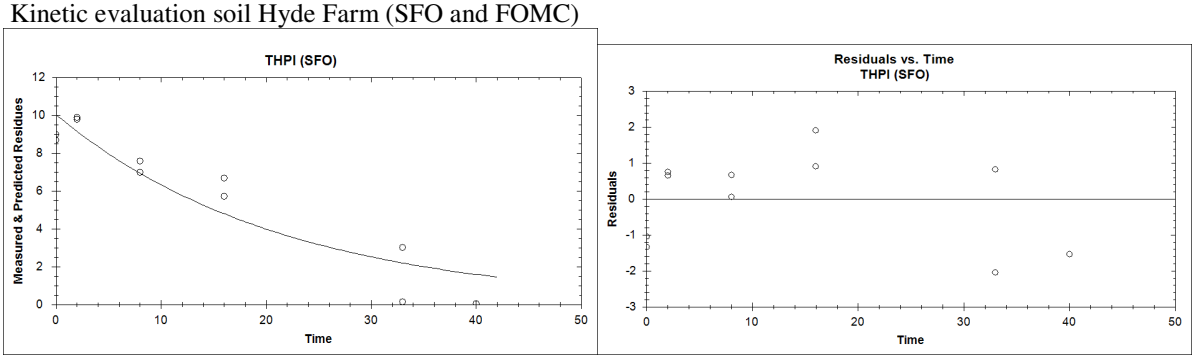
Study	**Study 7, 1993**							
Soil	**Kinetics**	**Parameter**	**Prob > t**	**St. Dev.:**	**Chi^2 error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**
Hyde Farm	SFO	k: 0.1186	1.50e-05	n.r.	9.2	acceptable	5.845	19.420
	FOMC	α: 3.532e+03 β: 2.978e+04	**95% CI:** α: 2.67e+03 – 4398.21 β: 2.97e+04– 29880.65	α: 4.419e+02 β: 5.241e+01	10.5	acceptable	5.844	19.420
Speyer 2.1	SFO	k: 0.0462	0.00012	n.r.	14.95	acceptable	15.0	49.820
	FOMC	α: 1.255e+04 β: 2.717e+05	**95% CI:** α: 7.895e+03 – 17214.37 β:	α: 2.377e+03 β: 1.099e+02	16.5	acceptable	15	49.83

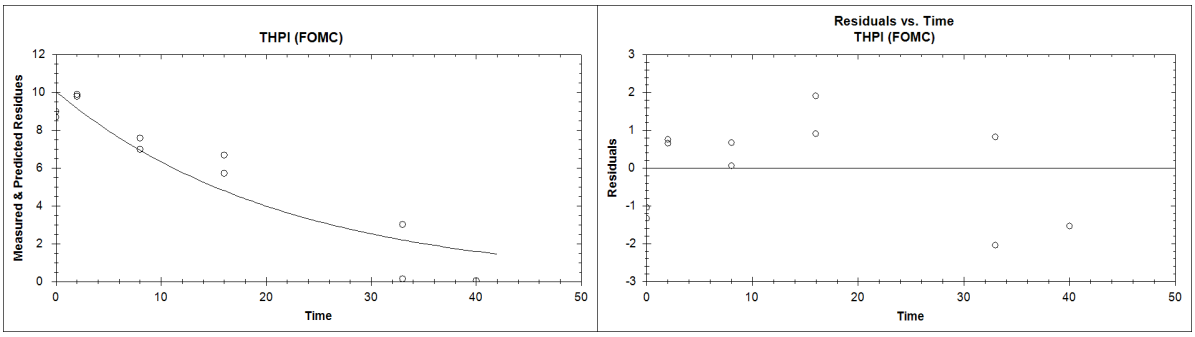
			2.714e+05 – 271867.32					
Speyer 2.2	SFO	k: 0.0878	1.63e-05	n.r.	15.1	acceptable	7.894	26.220
	FOMC	α: 8462.40 β: 96368.86	**95% CI:** α: 6021.53 – 10903.28 β: 96154.54 – 96583.18	α: 1245.37 β: 109.35	16.7	acceptable	7.894	26.230



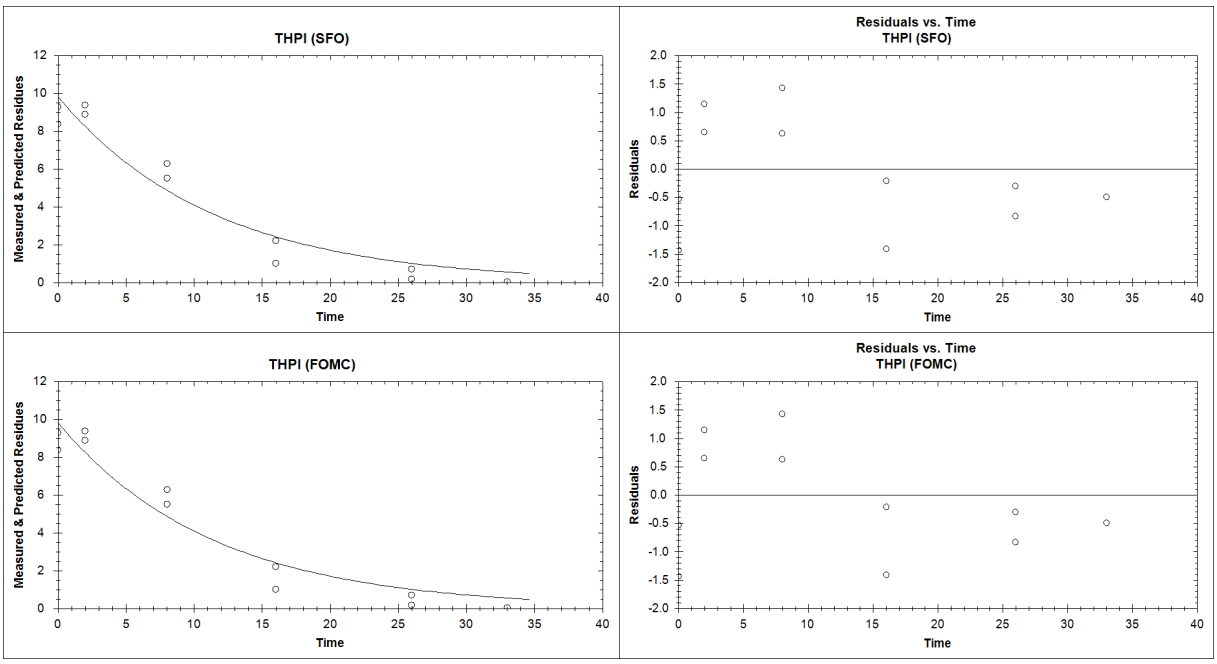


Kinetic evaluation soil Hyde Farm (SFO and FOMC)





Kinetic evaluation soil Speyer 2.1 (SFO and FOMC)



Kinetic evaluation soi Speyer 2.2 (SFO and FOMC)

Comments RMS

Study 7, 1993 (THPI):

Extracts from day 0 were worked up and analysed twice which resulted in 4 values at day 0. For the kinetic evaluation only two values were considered - no explanation was provided why only two of the four values were taken and how these values were selected.

According to FOCUS 2014 replicate analytical results from a single sample are not true independent replicates and should be average and treated as one sample. Therefore the RMS averaged the 2 values of the same extract on day 0 and recalculated the kinetic using the following residue data:

Residue data [mg/kg] obtained for THPI from three soils in laboratory soil degradation study processed according to FOCUS kinetics for kinetic evaluation (using averaged values of the same extract on day 0)

Soil Hyde Farm		**Soil Speyer 2.1**		**Soil Speyer 2.2**	
Time [d]	**THPI [mg/kg]**	**Time [d]**	**THPI [mg/kg]**	**Time [d]**	**THPI [mg/kg]**
0	8.1	0	8.1	0	8.9
0	8.6	0	8.3	0	8.5
2	8.3	2	9.9	2	9.4
2	7.3	2	9.8	2	8.9
8	3.3	8	7.6	8	6.3
8	2.6	8	7.0	8	5.5
16	1.4	16	5.7	16	2.2
16	2.4	16	6.7	16	1.0
26	0.05 [a]	26	NA	26	0.17
26	0.05 [a]	26	NA	26	0.70

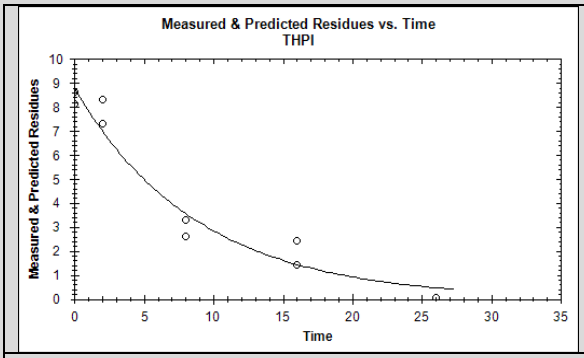
		33	3.0	33	0.05[a]
		33	0.14	33	0.05 [a]
		40	0.05 [a]		
		40	0.05 [a]		

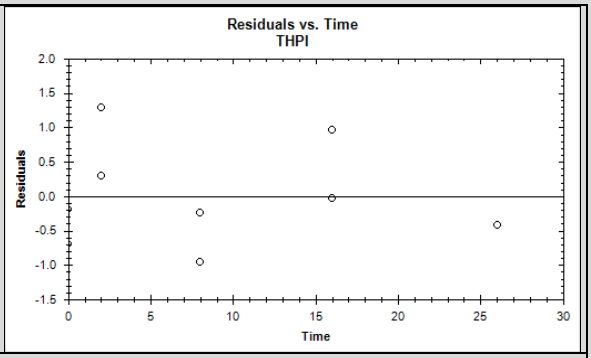
NA not available

a set to ½ LOD according to FOCUS kinetics (LOD = 0.1 mg/kg)

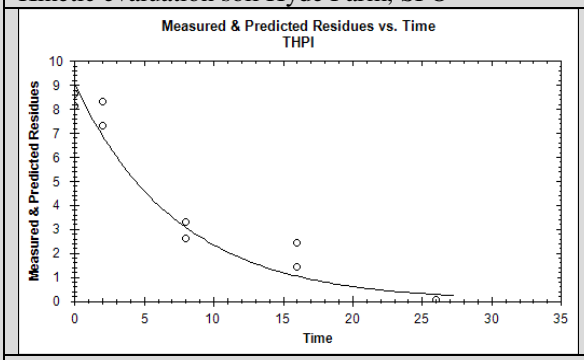
Results of kinetics fits soil residue data of THPI obtained from three soils (average values of the same extract on day 0)

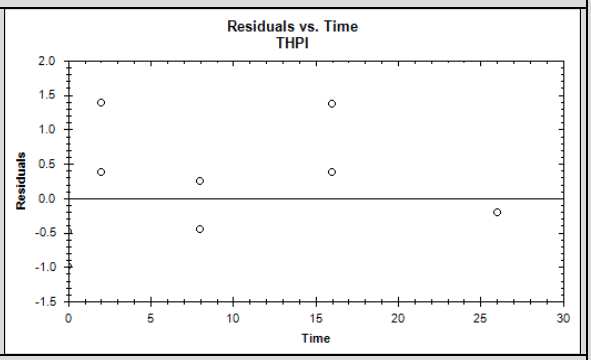
Soil	Kinetics	Parameter	Prob > t	St. Dev.:	Chi^2 error [%]	Visual fit	DT_{50} [d]	DT_{90} [d]
Hyde Farm	SFO	k: 0.11351	2.6e-5	n.r.	10.64	acceptable	6.107	20.286
	FOMC	α: 5658.522 β: 41531.383	0.0296 0.0296	2513.779 18452.995	14.18	acceptable	5.088	16.904
Speyer 2.1	SFO	k: 0.044482	0.000132	n.r.	17.11	acceptable	15.583	51.764
	FOMC	α:3.759e3 β: 6.063e4	0.234 0.234	4.961e+03 8.004e+04	22.79	?	11.182	37.155
Speyer 2.2	SFO	k: 0.08696	5.88e-6	n.r.	15.8	acceptable	7.9708	26.478
	FOMC	α: 1.585e3 β: 1.305e4	0.36 0.36	4.295e+03 3.539e+04	23.11	acceptable	5.7091	18.975



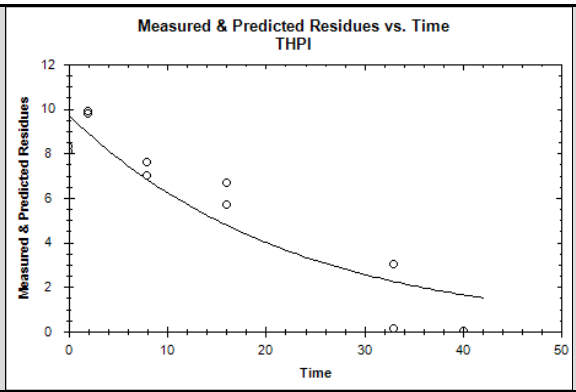


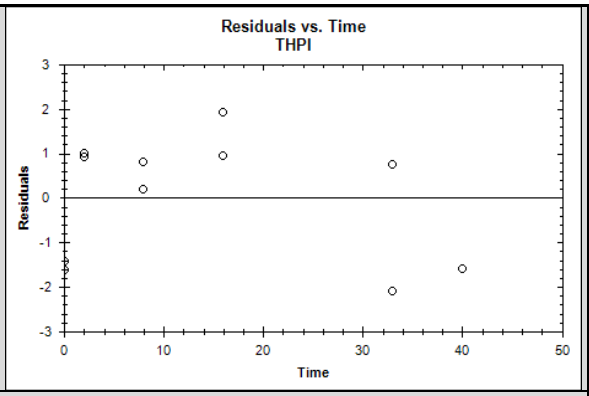
Kinetic evaluation soil Hyde Farm, SFO



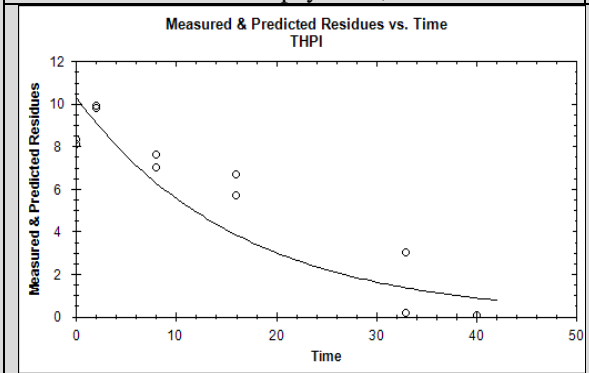


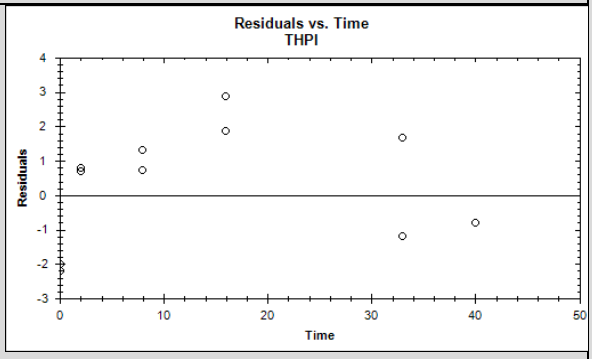
Kinetic evaluation soil Hyde Farm, FOMC



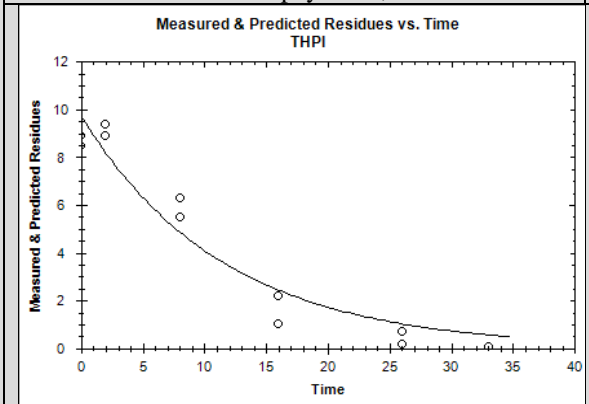


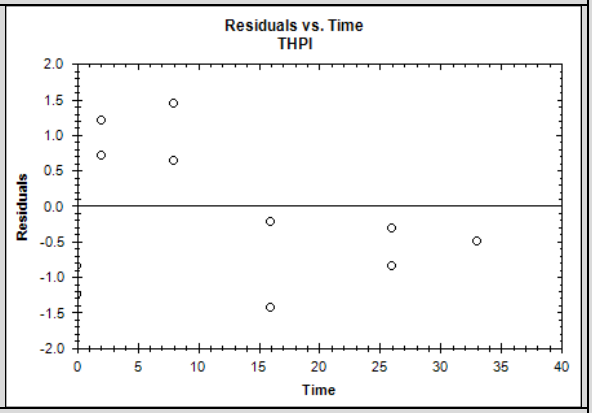
Kinetic evaluation soil Speyer 2.1, SFO



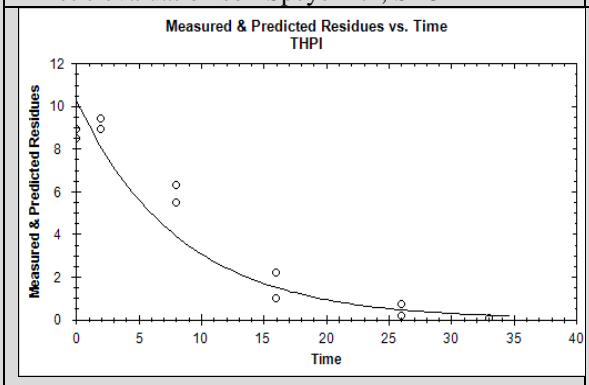


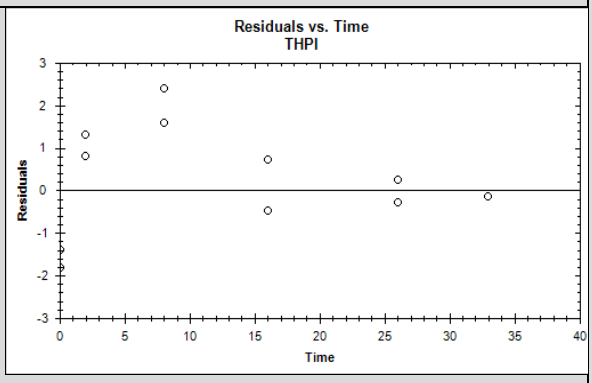
Kinetic evaluation soil Speyer 2.1, FOMC





Kinetic evaluation soil Speyer 2.2, SFO





Kinetic evaluation soil Speyer 2.2, FOMC

Additionally, the RMS recalculated the kinetic using FOMC and residue data with two values as proposed by the notifier and the two averaged values of the same extract on day 0 for all three soils. The following deviations occurred: α and β were not significantly different from 0 since the confidence interval contained 0 and the

probability was not smaller than 0.05. Only for the soil Hyde Farm α and β were significantly different from 0 when the averaged values of day 0 were used. These results support the recommendation that SFO kinetic should be used for deriving modelling and persistent endpoints for the metabolite THPI.

Study 8 (1993): In order to derive modelling endpoints for the metabolite THPAM, the SFO kinetics was fit to residue data obtained for THPAM in soils Hyde Farm, Speyer 2.1 and Speyer 2.2. The residue data used for kinetic evaluation are presented in table B.8.1.1.2.1.1-22. For all three soils, SFO kinetic shows acceptable visual fits to residue data, the Chi^2 error below 15% and the estimated k rate is significantly different from zero (table B.8.1.1.2.1.1-23). Therefore, SFO kinetic is appropriate to derive modelling endpoints for THPAM from these soils.
To derive persistence endpoints, the SFO fits were compared with FOMC fits (table B.8.1.1.2.1.1-23). For all three soils, FOMC does not improve the visual fit or reduce the Chi^2 error. Therefore, SFO is also considered appropriate for deriving persistence endpoints for THPAM from soils Hyde Farm, Speyer 2.1 and Speyer 2.2.

Table B. 8.1.1.2.1.1-22: Residue data [mg/kg] obtained for THPAM from three soils in laboratory soil degradation study processed according to FOCUS kinetics for kinetic evaluation

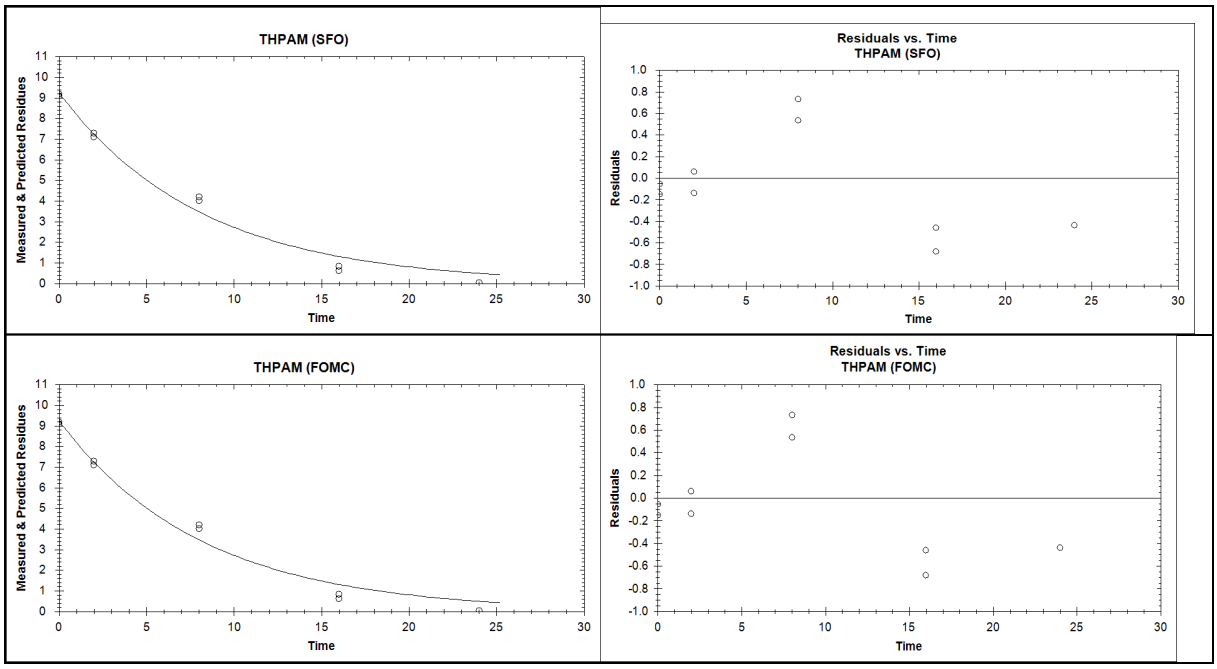
Soil Hyde Farm		Soil Speyer 2.1		Soil Speyer 2.2	
Time [d]	**THPAM [mg/kg]**	**Time [d]**	**THPAM [mg/kg]**	**Time [d]**	**THPAM [mg/kg]**
0	9.2	0	10.6	0	9.8
0	9.1	0	10.9	0	9.8
2	7.1	2	9.5	2	8.3
2	7.3	2	8.7	2	4.1
8	4.2	8	7.3	8	4.9
8	4.0	8	7.4	8	4.9
16	0.84	16	4.2	16	2.0
16	0.62	16	3.7	16	2.1
24	0.05[a]	24	NA	24	0.15
24	0.05 [a]	24	NA	24	0.25
30		30	1.6	30	
30		30	1.7	30	
41		41	0.05 [a]	41	
41		41	0.1	41	

NA not available
a set to ½ LOD according to FOCUS kinetics (LOD = 0.1 mg/kg)

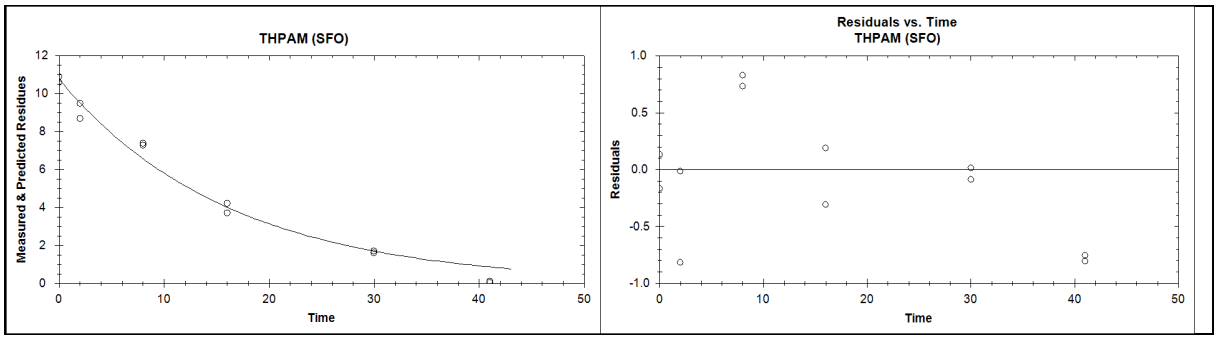
Table B. 8.1.1.2.1.1-23: Results of kinetics fits soil residue data of THPAM obtained from three soils

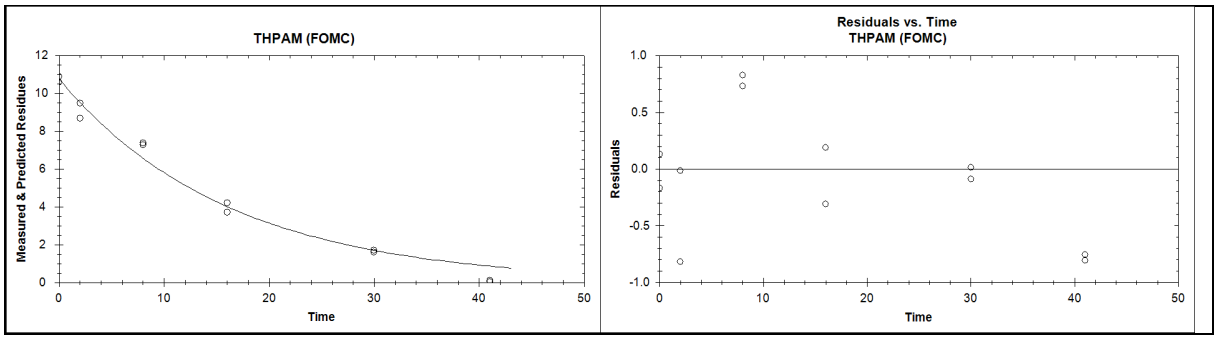
Study	**Study 8, 1993**							
Soil	**Kinetics**	**Parameter**	**Prob > t**	**St. Dev.:**	**Chi^2 error [%]**	**Visual fit**	**DT_{50} [d]**	**DT_{90} [d]**
Hyde Farm	SFO	k: 0.1227	9.46e-07	n.r.	8.1	acceptable	5.650	18.770

	FOMC	α: 1.545e+04 β: 1.260e+05	**95% CI:** α: 1.284e+04 – 1.807e+04 β: 1.256e+05 – 1.263e+05	α: 1.334e+03 β: 1.637e+02	9.3	acceptable	5.650	18.770
Speyer 2.1	SFO	k: 0.0618	4.35e-08	n.r.	7.0	acceptable	11.220	37.280
	FOMC	α: 1.540e+04 β: 2.493e+05	**95% CI:** α: 1.307e+04 – 17721.51 β: 2.491e+05 – 249431.58	α: 1.186e+03 β: 7.324e+01	7.7	acceptable	11.220	37.280
Speyer 2.2	SFO	k: 0.0994	0.000975	n.r.	13.7	acceptable	6.976	23.180
	FOMC	α: 5.085e+03 β: 5.117e+04	**95% CI:** α: 2.751e+03 – 7419.36 β: 5.094e+04 – 51404.27	α: 1.191e+03 β: 1.183e+02	15.65	acceptable	6.976	23.180

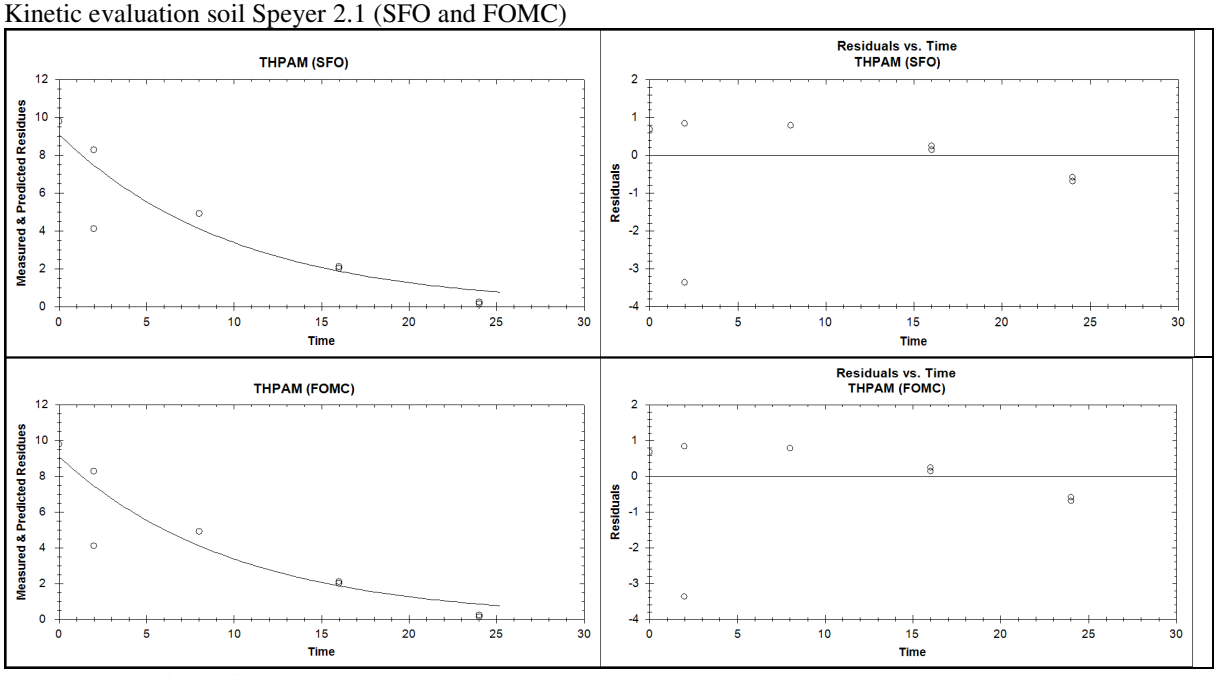


Kinetic evaluation soil Hyde Farm (SFO and FOMC)





Kinetic evaluation soil Speyer 2.1 (SFO and FOMC)



Kinetic evaluation soil Speyer 2.2 (SFO and FOMC)

Comments RMS
The kinetic was recalculated by RMS using KINGUI 2. For SFO kinetic the results provided by the applicant could be confirmed. For FOMC the following deviations occurred: α and β were not significantly different from 0 since the confidence interval contained 0 and the probability was not smaller than 0.05. These results support the recommendation that SFO kinetic should be used for deriving modelling and persistent endpoints for the metabolite THPAM.

CONCLUSIONS
Soil degradation of Captan was well described by SFO model in three soils (LUFA 2.3, LUFA 2.1 and in Greenville) and by FOMC model in one soil (Visalia (USA)). Degradation of Captan metabolites THPI and THPAM followed SFO kinetics in all four soils.

The calculated modelling DT_{50} values for Captan ranged from 1.8 to 5.7 days. For Captan metabolites the modelling DT_{50} value ranged from 3.1 to 15 for THPI and from 2.1 to 11.2 for THPAM. A formation fraction value of 0.85 for THPI (from Captan) in one soil was obtained and 0.74 for THPAM (from THPI).

Comments / Conclusions RMS

Based on the provided studies evaluated and commented above and the kinetic re-evaluation presented below (study 6, 2017) and considering the outcome of the discussion at the pesticide peer review meeting 15 (September 2019) (see study 6, 2017, comments RMS) the following modelling and persistent endpoints are proposed by RMS.

Summary of modelling endpoints obtained for Captan in four soils

Study / Soil	Calculated DT_{50} [d]	Study temp [°C]	Study moisture	Ref. temp. [°C]	Ref. moisture at 10 kPa	Moist corr. factor	Temp. corr. factor	Normalised DT_{50} at [20°C & pF2]
Study 3 (2016) / LUFA 2.3 Sandy loam	5.41	20	50% MWHC	20	19	0.941	1	**5.1**
Study 4 (2014) / LUFA 2.1 Sand	5.666 [a]	20	45% MWHC	20	12	1.156	1	**5.666** [e]
Study 1 (1992) /. Visalia (USA) Sandy loam	1.756 [b]	25	75% FC	20	19	0.8176	1.606	**2.306** [f]
Study 2 (1988) / Greenville Sandy loam	2.206 [c]	25	80% FC	20	19	0.855	1.606	**3.031** [f]
Geometric mean (n = 4)								**3.77**

a SFO kinetics
b back-calculated from DT_{90} FOMC ($DT_{50} = DT_{90}/3.32$)
c SFO modified fit
d moisture correction only
e no correction was needed since moisture correction factor is above 1 and temperature correction factor = 1
f temperature and moisture correction was performed

Summary of modelling endpoints obtained for metabolite THPI in four soils

Study / Soil	Calculated DT_{50} [d]	Study temp [°C]	Study moisture	Ref. temp. [°C]	Ref. moisture at 10 kPa	Moist corr. factor	Temp. corr. factor	Normalised DT_{50} at [20°C & pF2]
Study 3 (2016) / LUFA 2.3 Sandy loam	3.06	20	50% MWHC	20	19	0.941	1	**2.9**
Study 7 (1993) / Hyde Farm Sandy loam	6.107[b]	20	40% MWHC	20	19	1.122	1	**6.107**[d]

Study 7 (1993) / Speyer 2.1 Sand	15.583[b]	20	40% MWHC	20	12	1.023	1	**15.583[d]**
Study 7 (1993) / Speyer 2.2 Loamy sand	7.9708[b]	20	40% MWHC	20	14	1.441	1	**7.9708[d]**
Geometric mean (n = 4)								**6.85**

a SFO kinetics (pathway fit)
b SFO kinetics (metabolite applied as parent)
c moisture correction only
d temperature and moisture corrections were not needed

The calculated formation fraction value of 1 for THPI (from Captan) should be used.
The kinetic of study 7 was recalculated by RMS since the residues of day 0 used by the notifier were not accepted by RMS.

Summary of modelling endpoints obtained for metabolite THPAM in three soils

Study / Soil	**Calculated DT_{50} [d]**	**Study temp [°C]**	**Study moisture**	**Ref. temp. [°C]**	**Ref. moisture at 10 kPa**	**Moist corr. factor**	**Temp. corr. factor**	**Normalised DT_{50} at [20°C & pF2]**
Study 3 (2016)* / LUFA 2.3 Sandy loam	2.0 [a]	20	50% MWHC	20	19	0.941	1	**1.9 [c]**
Study 8 (1993) / Hyde Farm Sandy loam	5.650 [b]	20	40% MWHC	20	19	1.122	1	**5.650 [d]**
Study 8 (1993) / Speyer 2.1 Sand	11.220 [b]	20	40% MWHC	20	12	1.023	1	**11.220. [d]**
Study 8 (1993) / Speyer 2.2 Loamy sand	6.976 [b]	20	40% MWHC	20	14	1.441	1	**6.976 [d]**
Geometric mean (n = 3)								**5.38**

a SFO kinetics (pathway fit)
b SFO kinetics (metabolite applied as parent)
c moisture correction only
d temperature and moisture corrections were not needed

*From study 3 no acceptable DT_{50} value could be obtained using the model KINGUI and the optimizer IRLS. This also applies for the formation fraction of THPAM. Therefore, a new kinetic evaluation for soil Lufa 2.3

using the model CAKE and the optimizer MCMC was provided and is presented below. The re-evaluation resulted in reliable and statistically significant degradation rate and formation fraction. The calculated DT50 value of 1.9 d and the formation fraction value of 1 for THPAM (from THPI) should be used.

Summary of persistent endpoints obtained for Captan in four soils

Study	Soil	Kinetics model	Persistent endpoints	
			DT_{50} [d]	DT_{90} [d]
Study 3 (2016)	LUFA 2.3	SFO	5.533	18.379
Study 4 (2014)	LUFA 2.1	SFO	5.666	18.820
Study 1 (1992)	Visalia (USA)	FOMC	0.468	5.829
Study 2 (1988)	Greenville	SFO modified	2.206	7.328

Summary of persistent endpoints obtained for metabolite THPI in four soils

Study	Soil	Kinetics model	Persistent endpoints	
			DT_{50} [d]	DT_{90} [d]
Study 3 (2016)	LUFA 2.3	SFO	3.280	10.895
Study 7 (1993)	Hyde Farm	SFO	6.107	20.286
Study 7 (1993)	Speyer 2.1	SFO	15.583	51.764
Study 7 (1993)	Speyer 2.2	SFO	7.9708	26.478

Summary of persistent endpoints obtained for metabolite THPAM in four soils

Study	Soil	Kinetics model	Persistent endpoints	
			DT_{50} [d]	DT_{90} [d]
Study 3 (2016)*	LUFA 2.3	SFO-SFO	2.0	6.8

Study 8 (1993)	Hyde Farm	SFO	5.650	18.770
Study 8 (1993)	Speyer 2.1	SFO	11.220	37.280
Study 8 (1993)	Speyer 2.2	SFO	6.976	23.180

*From study 3 no acceptable DT_{50} value could be obtained since the k value was not significantly different from 0. Therefore, the notifier provided a kinetic re-evaluation using CAKE software which is presented below. The re-evaluation resulted in reliable and statistically significant degradation rate and formation fraction.

The kinetic evaluation of study 3 (2016) did not result in a statistically significant k value and formation fraction for THPAM using KINGUI and the Iteratively Reweighted Least Squares (IRLS) algorithm as optimiser. Therefore, a re-evaluation of the kinetic evaluation using the latest version of CAKE software (version 3.3) with Markov-Chain Monte Carlo (MCMC) method was provided and is presented below.

Study 6 (2017)

Reference:	**Calculation of soil degradation values for Captan and major metabolites THPI and THPAM according to the recommendations of FOCUS Degradation Kinetics workgroup using CAKE 3.3**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2017
Report/Doc. number:	562961-CA-070102-02
Guideline(s):	FOCUS workgroup on degradation kinetics (2006), FOCUS kinetics generic guidance (2014)
GLP:	No
Deviations:	
Validity:	valid
Status:	New calculation submitted for renewal

Executive summary

Soil degradation rates for Captan and metabolites THPI and THPAM were derived from soil residue data obtained in one soil from a laboratory study. Degradation rates were calculated according to the recommendations of the FOCUS workgroup on degradation kinetics (2006) and the FOCUS kinetics generic guidance (2014) based on that document for use as modelling and persistence endpoints.

Soil residue data obtained from the study were processed according to the recommendations of FOCUS kinetics before fitting a curve to the data set. Curve fitting was performed using the latest version of CAKE[1] software (version 3.3) with Markov-Chain Monte Carlo (MCMC) method in a stepwise approach as recommended in the FOCUS kinetics in order to derive modelling and persistent endpoints for Captan and its metabolites THPI and THPAM.

The calculated persistence and modelling DT_{50} value (both SFO) for Captan was 5.4 days. For Captan metabolites, the modelling DT_{50} values were 3.1 days for THPI and 2.0 days for THPAM.

The normalised DT_{50} value for Captan for use in modelling was 5.1 days. For THPI and THPAM, the normalised DT_{50} value was found to be 2.9 and 1.9 days, respectively.

A summary of the derived modelling and persistence endpoints for Captan and metabolites THPI and THPAM are presented in table B.8.1.1.2.1.1-24.

[1] Computer Assisted Kinetic Evaluation "CAKE", version 3.3. Copyright© 2011-2016 Syngenta Limited.

Table B. 8.1.1.2.1.1-24: Summary of modelling and persistence endpoints obtained for Captan in sandy loam soil in study 3 (2016)

Substance	Calculated DT_{50} [d]	Study temp [°C]	Study moisture	Ref. temp. [°C]	Ref. moisture at 10 kPa	Moist corr. factor	Temp. corr. factor	Normalised DT_{50} at [20°C & pF2]
Captan	5.4 [a]	20	50% MWHC	20	19	0.941	1	**5.1** [b]
THPI	3.1 [a]	20	50% MWHC	20	19	0.941	1	**2.9** [b]
THPAM	2.0 [a]	20	50% MWHC	20	19	0.941	1	**1.9** [b]

a SFO kinetics (pathway fit)
b moisture correction only

A formation fraction value of 0.84 for THPI (from Captan) was obtained and 0.73 for THPAM (from THPI).

MATERIALS AND METHODS

Previous kinetic evaluation of the aerobic soil degradation study 3 (2016) was undertaken with the KinGUI[2] software (version 2.1) as presented in the report from study 5 (2016). This evaluation used for optimisation the Iteratively Reweighted Least Squares (IRLS) algorithm. The evaluation however showed that in the t-test, the k value was not significantly different from 0 with a p-value of 0.054, i.e. slightly above 0.05. Considering the times scattered nature of some of the residue data for the metabolites (not surprising considering the rapid formation and degradation of the substances), it is plausible that the IRLS algorithm in combination with this particular residue data set does not allow for the best fitting to be found.

Therefore, this new evaluation attempted to improve the kinetic fitting to derive a better statistically acceptable fitting for the data using an alternative optimisation algorithm, i.e. Markov-Chain Monte Carlo (MCMC). This approach is supported in the FOCUS kinetics generic guidance (2014) which states that "*the peer review of substances now accepts the use of the techniques of iteratively reweighted least squares (Gao et al., 2011)*[3] *and Markov-Chain Monte Carlo (Goerlitz et al., 2011)*[4] *to estimate parameter values and confidence intervals, taking into account that the recommendations on sequential fitting still need to be followed.*" Therefore, it can be concluded that the results obtained with CAKE using MCMC method for Captan and its metabolites are robust and reliable.

Initial optimisation of the data was undertaken with KinGUI using the MCMC algorithm. However, the step-wise fitting was not possible to be completely processed in the model and an error message was returned as follows: "*Not able to estimate the covariance matrix due to non-positive definite hessian*". Therefore, the CAKE model was used in order to achieve a successful optimisation and fitting procedure.

Kinetic evaluation of the aerobic soil degradation study 3 (2016) was performed using the latest version of Computer Assisted Kinetic Evaluation (CAKE)[5] Application (version 3.3) with Markov-Chain Monte Carlo (MCMC) optimiser. CAKE uses a Simple First Order (SFO) kinetic model for each compartment. As recommended in the FOCUS kinetics, CAKE follows a stepwise procedure for curve fitting and fit sequence when more than a single compartment (i.e. parent to one or more metabolites) are to be considered. Specifically, it applies the following process:

[2] KinGUI version 2.1 Developed by Bayer Technology Services for Bayer CropScience (2006).

[3] Gao et al., (2011): Improving uncertainty analysis in kinetic evaluations using iteratively reweighted least squares. Environmental Toxicology & Chemistry 30(10) 2363-2371

[4] Goerlitz et al., (2011): Statistical analysis of chemical transformation kinetics using Markov-Chain Monte-Carlo Methods. Environmental Science & Technology 45:4429–4437

[5] Computer Assisted Kinetic Evaluation "CAKE", version 3.3. Copyright© 2011-2016 Syngenta Limited.

- The parent compartment is fitted first without any reference to the metabolites.
- The parameters of all previously fitted compartments are fixed and each of the metabolites whose immediate parents have all already been considered are fitted individually in turn.
- Everything so far is fitted simultaneously.
- The previous steps are repeated until all compartments have been fitted.

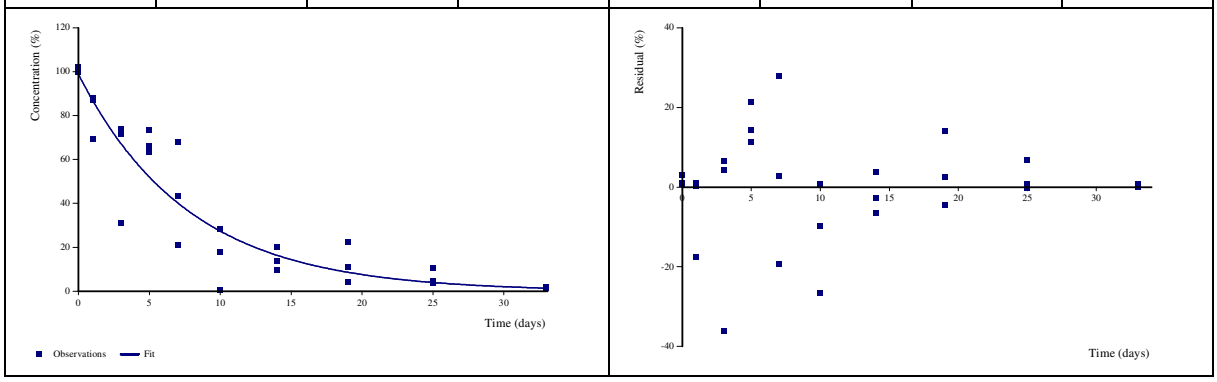
Estimated values for parameters at each step are used as initial values at the next. The higher the number of parameters being allowed to vary simultaneously is, the more complex the fitting operation. However, this approach of building up the complexity gradually allows each step to begin reasonably close to its optimum, improving the chances of convergence.

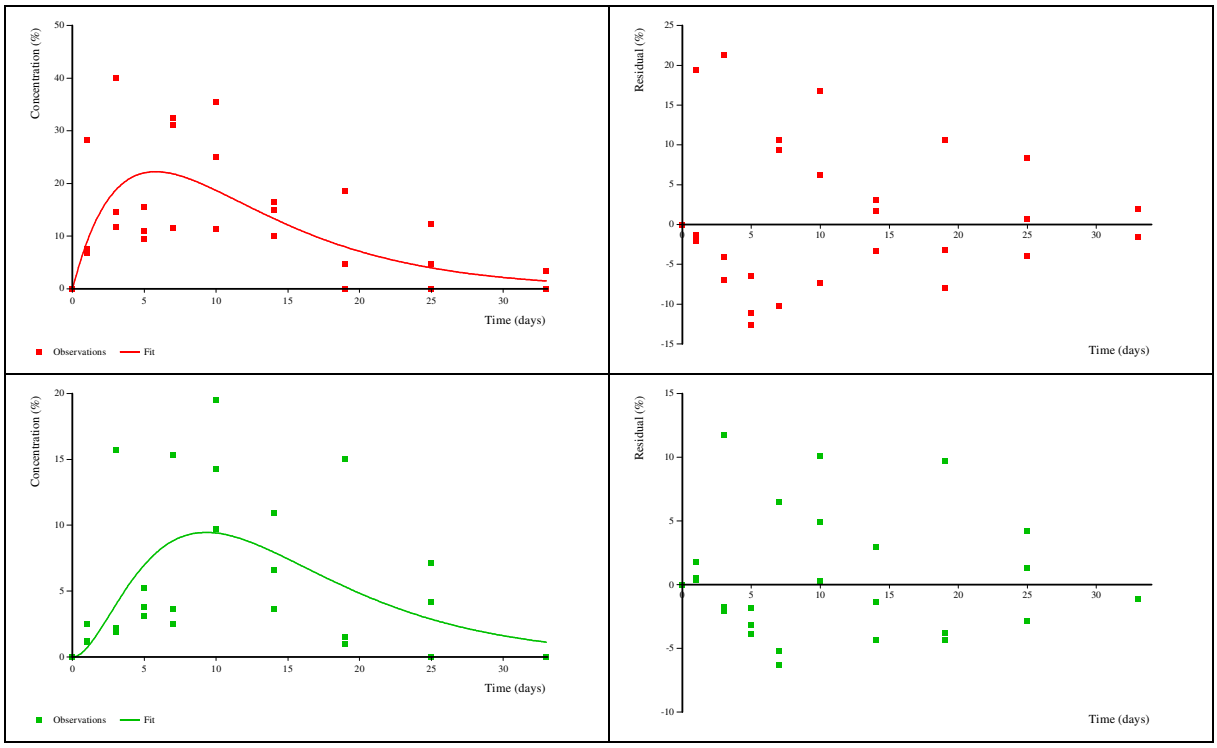
RESULTS

Fitting the SFO kinetics to soil residue data of Captan and its metabolites provides acceptable visual fit for Captan, Chi^2 error value below 15% and the k-rate is significantly different from zero (table B.8.1.1.2.1.1-25). For metabolites THPI and THPAM, moderate visual fits were obtained along with a Chi^2 error value above 15% for both metabolites. However, k-rate value was the found to be significantly different from zero for both metabolites.
The aerobic soil degradation study 3 (2016) of Captan showed that all substances (Captan and its metabolites) are degraded and nearly no mass is left at the end of the study. The study also showed that soil residue data of metabolites are highly scattered. Even though, the Chi^2 error value is high (25.8 and 33.1%), the residuals are randomly distributed around the zero line which indicates that no systematic deviation in the study has occurred. Therefore, the uncertainty (high Chi^2 error value) can be attributed to the fact that experimental data are scattered, especially for THPAM as 2nd generation metabolite.
A reliable formation fraction for THPI and THPAM was determined with high accuracy. A formation fraction value of 0.84 (stdev ± 0.11) and 0.73 (stdev ± 0.18) for THPI from parent and for THPAM from THPI were obtained, respectively.
The overall pathway fit for Captan and metabolites is considered acceptable and provides a reliable estimation of the degradation rates for all substances as well as formation fractions for metabolites.

Table B. 8.1.1.2.1.1-25: Results of SFO fit to residue data of Captan and its metabolites for soil LUFA 2.3 (Parent and metabolites fit)

Substance	Parameter	Prob > t	Chi^2 error [%]	Visual fit	DT_{50} [d]	DT_{90} [d]	Formation fraction [-]
Captan	k_par: 0.1282	< 0.05	14.5	acceptable	5.41	18.0	n.r.
THPI	k_THPI: 0.2266	< 0.05	25.8	moderate	3.06	10.20	0.835 (0.11*) from parent
THPAM	k_THPAM: 0.3394	< 0.05	33.1	moderate	2.04	6.78	0.725 (0.18*) from THPI





n.r. not relevant
* Standard deviation

CONCLUSIONS

The kinetic evaluation of Captan residue data obtained from aerobic soil degradation study 3 (2016) was performed using CAKE with MCMC optimiser. Degradation rates of Captan and its metabolites THPI and THPAM were derived according to the recommendations of the FOCUS workgroup on degradation kinetics (2006, 2014). According to the FOCUS kinetics generic guidance (2014), the peer review of substances now accept the use of the techniques of iteratively reweighted least squares (Gao et al., 2011)[6] and Markov-Chain Monte Carlo (Goerlitz et al., 2011)[7] to estimate parameter values and confidence intervals, taking into account that the recommendations on sequential fitting still need to be followed. However, according to Goerlitz et al. (2011), the MCMC approach seems to be more appropriate to determine the real probability distribution of model parameters than the standard non-linear least-squares methods.
Therefore, it can be concluded that the results obtained with CAKE using MCMC method for Captan and its metabolites are robust and reliable.

Aerobic soil degradation of Captan and its metabolites THPI and THPAM was well described by SFO kinetics.
The calculated normalised (20°C and pF2) DT_{50} and DT_{90} values for Captan in soil LUFA 2.3 were 5.1 and 16.9 days, respectively.
The normalised (20°C and pF2) DT_{50} and DT_{90} values for THPI in LUFA 2.3 were 2.9 and 9.6 days, respectively.
For THPAM, the normalised (20°C and pF2) DT_{50} and DT_{90} values in soil LUFA 2.3 were 1.9 and 6.4 days, respectively.
For both metabolites, a reliable formation fraction with high accuracy was determined. A formation fraction value of 0.84 ± 0.1 for THPI from parent was obtained. For THPAM formed from THPI, the formation fraction value was 0.73 ± 0.2.

Comments RMS

6 Gao et al., (20011): Improving uncertainty analysis in kinetic evaluations using iteratively reweighted least squares. Environmental Toxicology & Chemistry 30(10) 2363-2371
7 Goerlitz et al., (2011): Statistical analysis of chemical transformation kinetics using Markov-Chain Monte-Carlo Methods. Environmental Science & Technology 45:4429–4437

The RMS re-calculated the kinetic pathway fitting using KINGUI and the optimizer MCMC following the stepwise approach recommended by FOCUS: the results provided by the notifier could be confirmed. The DT_{50} values calculated for captan, THPI and THPAM were 5.33 d, 3.15 d and 2.09 d; for the degradation of captan to THPI a formation fraction of 0.82 was determined and for the degradation of THPI to THPAM a formation fraction of 0.73 was determined. The calculated χ^2 errors accounted for 14.46 for captan, 25.53 for THPI and 32.26 for THPAM. The confidence intervals calculated for Mo, the k-rates for captan, THPI and THPAM and the formation fractions did not contain 0, indicating that the calculated values were significantly different from 0.

During the peer review and during the **pesticide peer review meeting 15** (September 2019) the kinetic assessment of the study was discussed.
The reliability of the kinetic assessment was questioned since χ^2 values were high due to the high scattering of the data and high residuals were observed for the metabolites. In some replicates the fitted curves were far below the maximum observed amounts of the metabolites. The experts agreed that the markov chain monte carlo (MCMC) kinetic fitting might be retained as the agreed DT50 endpoints, because there was only one soil investigating the route of degradation. But for exposure modelling a kinetic formation fraction of 1 should be implemented for all the metabolites due to the scattering of the underlying data and because there is only evidence from a single soil. The formation fraction of 1 was also considered justified considering the fast hydrolysis of captan.
The experts concluded that the **DT50 values of the MCMC kinetic** should be used for the derivation of the modelling endpoint and a **formation fraction of 1** for the degradation of captan to THPI and of THPI to THPAM.

B.8.1.1.2.1.2. Aerobic degradation of metabolites, breakdown and reaction products

Study 7 (1993)

Reference:	**Tetrahydrophthalimide : laboratory soil degradation study (BBA)**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1993
Report/Doc. number:	RJ1440B / R-7219/TMN-0346
Guideline(s):	BBA Guidelines IV, 4-1
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

The rate of degradation of THPI was investigated in one sand, one loamy sand and one sandy loam soil in accordance with the BBA Guidelines in 1993. Soil metabolism studies (Point 7.1.1.1.1) had shown captan itself degrades very rapidly in soil, and that THPI is the major soil metabolite of captan. The soil characteristics are summarised in table B.8.1.1.2.1.2-1. The concentration of THPI in soil was 10 mg/kg; this was a rounded value of 11.32 mg/kg, which is the THPI equivalent of 22.56 mg/kg captan in soil, taking into account the molecular weight conversion, and quantitative conversion of captan to THPI. This concentration of 22.56 mg/kg is equivalent to a maximum total application rate of 22.56 kg a.s./ha of captan, assuming the rate/soil concentration equivalence recommended by the BBA. Fortified samples were incubated in the dark at 20 ± 2 °C, and sufficient distilled water was added to maintain 40% water holding capacity. Samples were analysed at specific intervals, up to 50 days after treatment.

The study met the essential criteria of BBA Guidelines IV, 4-1. It was conducted according to Good Laboratory Practice.

Table B. 8.1.1.2.1.2-1: Soil characteristics for rate of degradation of 1,2,3,6-tetrahydrophthalimide (THPI) in soil

Characteristic	**Soil 1**	**Soil 2**	**Soil 3**
Soil name	Speyer 2.1	Speyer 2.2	Hyde Farm

Location	East Jubilee Field, Jealotts Hill, Berks., UK[2]	East Jubilee Field, Jealotts Hill, Berks., UK[2]	Hyde Farm, Pinkneys Green, Berks., UK
pH	6.3	6.0	7.1
Sand (%)	90.0	85.0	59.0
Silt (%)	6.0	8.0	24.0
Clay (%)	4.0	7.0	17.0
Texture	Sand	Loamy sand	Sandy loam
Organic matter (%)	0.7	3.7	3.2
Organic carbon (%)[1]	0.4	2.2	1.9
Cation exchange capacity (meq/100 g)	-	-	-
100 % Moisture holding capacity (%)	31.0	59.0	56.0

[1] Organic carbon = organic matter/1.72
[2] From fallow graves at UK site - originally from Speyer, Germany

During analysis, the mean recovery of THPI was 93 ± 12 % (range 74- 113%), over the fortification range 0.5 - 10 mg/kg. THPI levels in the soils are summarised in table B.8.1.1.2.1.2-2. Extracts from the day 0 sampling interval were worked up and analysed twice.

Table B. 8.1.1.2.1.2-26: THPI residue levels (mg/kg) in soil (uncorrected values of duplicate samples A and B)

Days	Speyer 2.1	Speyer 2.2	Hyde Farm
0	7.4 - 9.0	7.7 - 9.4	7.7 - 9.1
2	9.8 - 9.9	8.9 - 9.4	7.3 - 8.3
8	7.0 - 7.6	5.5 - 6.3	2.6 - 3.3
16	5.7 - 6.7	1.0 - 2.2	1.4 - 2.4
26	NA	0.17 - 0.70	< 0.1
33	0.14 - 3.0[1]	< 0.1	< 0.1
40	< 0.1	NA	NA
50	< 0.1	NA	NA

[1] Mean of duplicate sample analysis; when mean taken data from sample B rejected, based on sample B only.
NA - not analysed at this interval

Using the Timme and Frehse model[8], THPI degraded with a DT_{50} of 6 days and 5 days in the 'Speyer 2.2' and 'Hyde Farm' soils, respectively. DT_{90} values were 19 days and 28 days, respectively.

THPI degraded with a DT_{50} of 20 days in 'Speyer 2.1' soil, using the Timme and Frehse model. However, between 33 and 40 days after treatment the residue level of THPI decayed through 5 half-lives in 7 days, indicating a DT_{50} of approximately 1 day. This observation is possibly associated with the microbial properties of Speyer 2.1 soil. The DT_{90} value was 65 days.

THPI degraded rapidly in sandy loam and loamy sand soils, with DT_{50} of 5-6 days, and DT_{90} values of 19 - 28 days. Slower initial degradation was observed in a sandy soil with DT_{50} of 20 days and DT_{90} of 65 days. However, a more rapid degradation (a DT_{50} of 1 day) was observed between days 33 and 40, which was ascribed to the microbial properties of the soil.

[8] Timme, G., Frehse, H., Laska, V. Statistical interpretation and graphic representation of the degradation behaviour of Pesticide Residues, Part II, Pflanzenschutznachrichten Bayer, 39/1986, 2.

Comments RMS

The study showed some deficiencies to the current OECD 307 guideline:

- Details concerning the history of the field site were not provided.
- Information concerning collection, storage and previous treatment of the soils was not provided. It is just mentioned that the soils were obtained from LUFA Speyer and Hyde farm. However, the determination of biomass indicates sufficient viability of the soils.
- It is not stated which medium was used for pH measurement.

The study shows some deficiencies and deviations from the OECD 307; however the absence of this information is not considered an impediment to use this study to investigate the rate of degradation in soil. The points mentioned above are not expected to have an impact on the half-life value and therefore, the study is considered acceptable by the RMS.

The test concentration of 10 mg THPI/kg covers the max. application rate of 10 x 1.6 kg Captan /ha (assuming 100 % conversion, no degradation and no interception, considering molecular weight).
The limit of detection of the method was 1 % (0.1 mg/kg).

These results of the kinetic evaluation are now superseded by the kinetic re-evaluation provided (study 5, 2016) which is presented under point B.8.1.1.2.1.1.

Study 8 (1993)

Reference:	***cis*- Tetrahydrophthalmic acid: laboratory soil degradation study (BBA)**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1993
Report/Doc. number:	RJ1441B / R-7220/TMN-0345
Guideline(s):	BBA Guidelines IV, 4-1
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

Soil metabolism studies (Point 7.1.1.1.1.) had shown captan itself degrades very rapidly in soil, and that THPI is the major soil metabolite of captan, which degrades further to produce THPAM. The rate of degradation of *cis*-tetrahydrophthalamic acid (THPAM) was investigated in one sand, one loamy sand and one sandy loam soil in accordance with the BBA Guidelines in 1993. The soil characteristics are summarised in table B.8.1.1.2.1.2-3. The concentration of THPAM in soil was 10 mg/kg; this was a rounded value of 12.67 mg/kg, which is the THPAM equivalent of 22.56 mg/kg captan in soil, taking into account the molecular weight conversion and quantitative conversion to THPAM. The concentration of 22.56 mg/kg is equivalent to a maximum total application rate of 22.56 kg a.s./ha of captan, assuming the rate/soil concentration equivalence recommended by the BBA. Fortified samples were incubated in the dark at 20 ± 2 °C, and sufficient distilled water was added to maintain 40% water holding capacity. Samples were analysed at specific intervals, up to 50 days after treatment.

The study met the essential criteria of BBA Guidelines IV, 4-1. It was conducted according to Good Laboratory Practice.

Table B. 8.1.1.2.1.2-3: Soil characteristics for rate of degradation of *cis*-tetrahydrophthalamic acid (THPAM) in soil

Characteristic	**Soil 1**	**Soil 2**	**Soil 3**
Soil name	Speyer 2.1	Speyer 2.2	Hyde Farm
Location	East Jubilee Field, Jealotts Hill, Berks., UK[2]	East Jubilee Field, Jealotts Hill, Berks., UK[2]	Hyde Farm, Pinkneys Green, Berks., UK
pH	6.3	6.0	7.1
Sand (%)	90.0	85.0	59.0

Silt (%)	6.0	8.0	24.0
Clay (%)	4.0	7.0	17.0
Texture	Sand	Loamy sand	Sandy loam
Organic matter (%)	0.7	3.7	3.2
Organic carbon (%)[1]	0.4	2.2	1.9
Cation exchange capacity (meq/100 g)	-	-	-
100 % Moisture holding capacity (%)	31.0	59.0	56.0

[1] Organic carbon = organic matter/1.72.
[2] From fallow graves at UK site - originally from Speyer, Germany.

During analysis, the mean recovery of THPAM was 88 ± 9 % (range 75- 103%), over the fortification range 0.5 - 10 mg/kg. THPAM levels in the soils are summarised in table B.8.1.1.2.1.2-4.

Table B. 8.1.1.2.1.2-4: THPAM residue levels (mg/kg) in soil (uncorrected values of duplicate samples A and B)

Days	Speyer 2.1	Speyer 2.2	Hyde Farm
0	10.6 - 10.9	9.8	9.1 - 9.2
2	8.7 - 9.5	4.1 - 8.3	7.1 - 7.3
8	7.3 - 7.4	4.9	4.0 - 4.2
16	3.7 - 4.2	2.0 - 2.1	0.62 - 0.84
24	NA	0.15 - 0.25	< 0.1
30	1.6 - 1.7	0.20 - 0.25	NA
41	< 0.1 - 0.1	NA	NA
50	< 0.1	NA	NA

NA - not analysed

Using the Timme and Frehse model, THPAM degraded with a DT_{50} of 7 days, 5 days and 4 days in the 'Speyer 2.1', 'Speyer 2.2' and 'Hyde Farm' soils, respectively. DT_{90} values were 22 days, 16 days and 12 days, respectively.

THPAM degraded rapidly in sand, sandy loam and loamy sand soils, with DT_{50} of 4 - 7 days, and DT_{90} values of 12 - 22 days.

Comments RMS

The study showed some deficiencies and deviations from OECD guideline:

- Details concerning the history of the field site were not provided.
- Information concerning collection, storage and previous treatment of the soils was not provided. It is just mentioned that the soils were obtained from LUFA Speyer and Hyde farm. The determination of biomass indicates sufficient viability of the soils.
- It is not stated which medium was used for pH measurement.

The study shows some deficiencies and deviations from the OECD 307; however the absence of this information is not considered an impediment to use this study to investigate the rate of degradation in soil. The points mentioned above are not expected to have an impact on the half-life value and therefore, the study is considered acceptable by the RMS.

The test concentration of 10 mg THPAM/kg covers the max. application rate of 10 x 1.6 kg Captan /ha (assuming 100 % conversion, no degradation and no interception, considering molecular weight).
The limit of detection of the method was 1 % (0.1 mg/kg).

These results of the kinetic evaluation are now superseded by the kinetic re-evaluation provided (study 5, 2016) which is presented under point B.8.1.1.2.1.1.

B.8.2. FATE AND BEHAVIOUR IN WATER AND SEDIMENT

B.8.2.1. Route and rate of degradation in aquatic systems (chemical and photochemical degradation)

B.8.2.1.1. Hydrolytic degradation of the active substance captan

Study 1 (1989a)

Reference:	[trichloromethyl-^{14}C] Captan - Hydrolysis at 25°C.
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1989a
Report/Doc. number:	WRC 89-44/ ENV-011
Guideline(s):	USEPA 161-1
GLP:	Yes
Deviations:	None
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

Materials and methods: The hydrolysis of [trichloromethyl-^{14}C] captan (radiochemical purity 98.0%, specific activity 40.4 mCi/mmol) and unlabelled captan (chemical purity 98.9%) was investigated in the dark at a temperature of 25°C in sterile aqueous buffer solutions at pH 5, 7 and 9.

Solutions at a concentration of 2.15 mg/L were prepared and incubated over a period of up to 25 hours. Radioactivity was measured with LSC and samples were analysed using HPLC and an UV/VIS detector and GC/MS.

Findings:

The recovery and distribution of the applied radioactivity from the aqueous buffer solutions is summarised in tables B.8.2.1.1-2, B.8.2.1.1-3 and N.8.2.1.1-4.

At all pH levels the amount of applied radioactivity recovered ranged from 90.6 to 97.5 % indicating a complete mass balance. The mean first-order hydrolysis rates were 18.8 hr, 4.9 hr and 8.3 min at pH values of 5, 7 and 9, respectively. At each pH value the hydrolysis products consisted of carbonate and two unknown components, unk 1 and unk 2. The levels of carbonate observed were more prominent at acidic pH values and the two unknown components were more prominent at alkaline pH values. The levels of the carbonate detected comprised maximum levels of 65.5, 25.1 and 1.2% of applied radioactivity at pH values of 5, 7 and 9, respectively. The unknown components unk 1 and unk 2 were detected at levels of 1.3 and 3.9, 7.6 and 28.0 and 12.2 and 38.4% of applied radioactivity at pH values of 5, 7 and 9, respectively. The degradation rates of the hydrolysis products observed were not assessed.

Table B.8.2.1.1-1: The distribution of radioactivity (% AR) in the hydrolysis of [trichloromethyl-^{14}C] captan at pH 5

Time (hours)	% of applied radioactivity (AR)				
	captan	**carbonate**	**unk 1**	**unk 2**	**total**
Run 1					
0.00	88.9	0.1	0.4	3.9	93.3
0.08	90.7	0.3	0.4	2.6	94.0
4.58	76.3	14.3	0.6	3.0	94.2
10.08	62.1	27.0	0.4	2.2	91.7
15.00	55.5	35.8	0.8	2.1	94.2
18.83	54.8	36.8	0.8	1.7	94.1
25.30	30.6	64.7	0.5	1.3	97.1
Run 2					
0.00	88.9	0.1	0.4	3.9	93.3

0.17	89.8	1.2	0.6	2.6	94.2
4.58	79.7	10.2	0.8	2.8	93.5
10.08	65.9	29.2	0.3	2.1	97.5
15.00	50.6	39.1	1.3	1.9	92.9
18.87	41.1	48.2	0.7	0.7	90.7
25.33	27.1	65.5	1.3	1.3	95.2

Table B.8.1.1.2.1: The distribution of radioactivity (% AR) in the hydrolysis of [trichloromethyl-^{14}C] captan at pH 7

Time (hours)	% of applied radioactivity (AR)				
	captan	carbonate	unk 1	unk 2	total
Run 1					
0.00	88.9	0.1	0.4	3.9	93.3
0.18	84.4	0.6	0.6	6.3	91.9
1.29	71.3	6.0	2.7	13.1	93.1
2.28	63.0	8.2	0.6	18.8	90.6
3.33	53.6	13.0	5.1	22.1	93.8
4.37	45.3	19.0	5.9	24.2	94.4
5.30	39.7	21.6	6.6	26.5	94.4
6.35	34.5	25.1	7.2	28.0	94.8
Run 2					
0.00	88.9	0.1	0.4	3.9	93.3
0.20	85.2	2.1	0.7	5.8	93.8
1.25	72.3	5.5	2.7	12.7	93.2
2.20	64.3	9.0	3.9	16.4	93.6
3.18	55.4	13.2	4.7	19.0	92.3
4.13	47.8	18.7	5.5	22.3	94.3
5.10	42.5	18.4	6.3	23.4	90.6
6.10	39.6	18.0	7.6	26.5	91.7

Table B.8.2.1.1-2: The distribution of radioactivity (% AR) in the hydrolysis of [trichloromethyl-^{14}C] captan at pH 9

Time (minutes)	% of applied radioactivity (AR)				
	captan	carbonate	unk 1	unk 2	total
Run 1					
0.0	88.9	0.1	0.4	3.9	93.3
1.0	84.1	0.2	1.0	7.6	92.9
3.0	63.4	1.2	5.3	23.0	92.9
5.0	58.0	0.4	6.9	27.7	93.0
7.0	44.9	0.9	10.2	36.5	92.5
10.0	40.3	0.5	12.2	38.4	91.4

Captan was observed to hydrolyse rapidly at all pH levels, the rate of degradation increased with pH value. The two unknown components observed were considered to be sodium thiocarbonate and sodium S-(tetrahydrophthalimido) thiocarbonate both of which are suggested to rapidly degrade to carbon dioxide.

Conclusions: Captan exhibited rapid first-order hydrolysis at all pH values in sterile water with half-lifes of 18.8 hr, 4.9 hr and 8.3 min at pH values of 5, 7 and 9, the rate of degradation increasing with pH. Two unidentified products were observed which were presumed to be sodium thiocarbonate and sodium-(tetrahydrophthalimido) thiocarbonate, both of which are suggested to rapidly degrade to carbon dioxide.

Comments RMS

Two unidentified products (Unknown 1 and 2 exceeding 10 % AR at pH 9 and unknown 2 exceeding 10 % AR at pH 7) were observed which were presumed to be sodium thiocarbonate (unknown 1) and sodium S-

(tetrahydrophthalimido) thiocarbonate (unknown 2). At pH 7 and pH 9 the two unknown products increased during the study and reached their maximum occurrence at the end of the study. Therefore, no degradation was observed during the study.

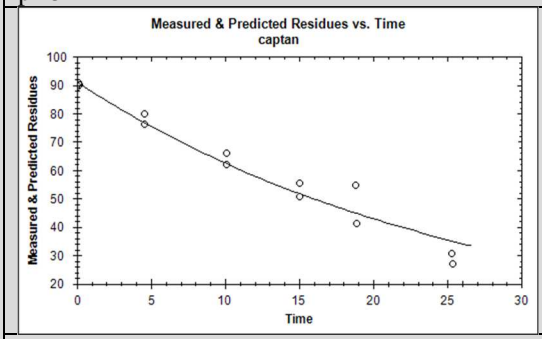
Further clarification is requested by CoRMS concerning the identification of unknown 1 and unknown 2 and concerning their rapid degradation to CO_2.
According to the study the two metabolites could not completely be identified. From experiments with an aqueous solution of unknown 1 and 2 which was stored in a freezer, melted and analysed it could be concluded that the two metabolites were unstable and degraded further to sodium carbonate.

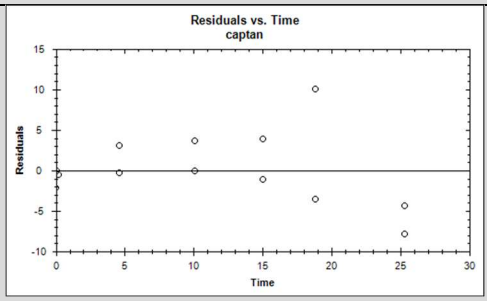
Unknown 2 was also detected in the study with ^{14}C-ring-labelled captan (where it could be identified as THPC) presented below.

The RMS re-calculated the DT_{50} values using KINGUI verion 2, the results presented by the notifier could be confirmed:

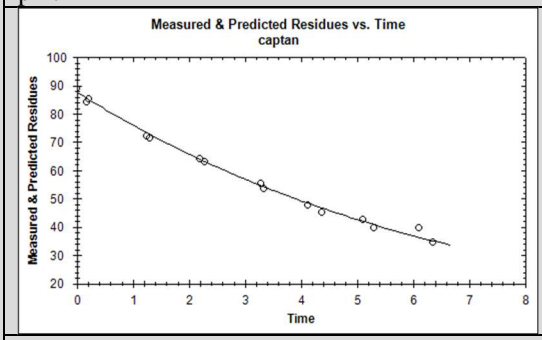
pH	Kinetics	Parameter	Prob > t	χ^2 error	DT_{50}	DT_{90}
5	SFO	k-value	$5.75e^{-10}$	5.924	18.4 h	61.0 h
7	SFO	k-value	$< 2e^{-16}$	1.645	4.8 h	15.9 h
9	SFO	k-value	0.000197	3.721	7.8 min	26.0 min

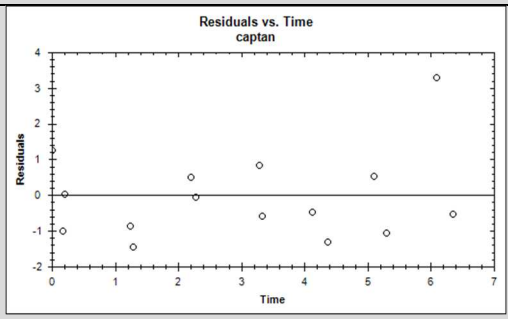
pH5



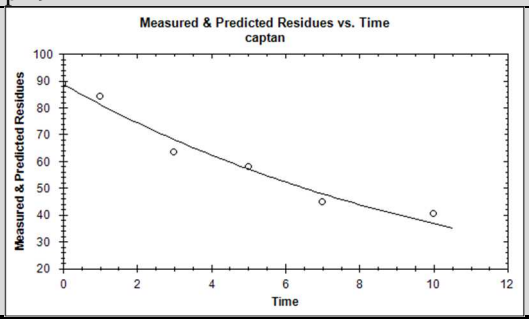


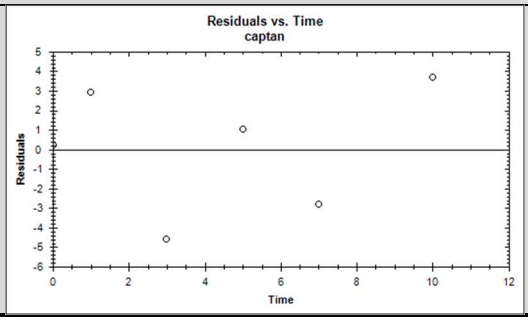
pH7





pH9





During the peer-review further data were required for identification of metabolites unknowns 1 and 2.
The applicant provided a statement concerning the metabolites unknown 1 and 2:
Anonymous, 2017: Hydrolysis of Captan
Metabolite unknown 2 was formed from both labels (^{14}C-ring & trichloromethyl-^{14}C) and was identified by HPLC/MS as THPC. Metabolites unknown 1 was formed only with the trichloromethyl-^{14}C label, it could not be identified. The analysis by GC/MS of the acidified sample showed only carbonyl sulphide and no Cl.

Comments RMS

No new information was provided:
The metabolite unknown 2 was also detected in the study with 14C-ring-labelled captan where it could be identified as THPC.
The metabolite unknown 1 could not be identified but it is concluded that it is a thiocarbonic acid or a corresponding salt.

Study 2 (1989b)

Reference:	[ring-1-^{14}C] Captan - Hydrolysis at 25°C.
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1989b
Report/Doc. number:	RR 89-068B, ENV-012
Guideline(s):	USEPA 161-1
GLP:	Yes
Deviations:	None
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

Materials and methods: The hydrolysis of [ring-1-^{14}C] captan (radiochemical purity 96.4%, specific activity 20.8 mCi/mmol) and unlabelled captan (chemical purity 98.9 %) was investigated in the dark at a temperature of 25°C in sterile aqueous buffer solutions at pH 5, 7 and 9.

Solutions at a concentration of 2.15 mg/L were prepared and incubated over a period of up to 18.8 hours. Due to the rapid degradation duplicate sets of analyses were conducted at each pH level. Samples were analysed by LSC and HPLC with UV/VIS detector and GC/MS analysis.

Findings:

The recovery and distribution of the applied radioactivity from the aqueous buffer solutions is summarised in tables B.8.2.1.1-5, B.8.2.1.1-6 and B.8.2.1.1-7.

At all pH levels the amount of applied radioactivity recovered ranged from 98.6 to 99.2% indicating a complete mass balance. The mean first-order hydrolysis rates were 11.7 hr, 4.7 hr and 8.1 min at pH values of 5, 7 and 9 respectively. At pH values of 5 and 7 the main hydrolysis product was THPI which accumulated to 62 and 46 % of applied radioactivity, respectively, by the end of the incubation period. The hydrolysis product THPC, S-(tetrahydrophthalimido) thiocarbonate was also observed in minor amounts at pH 5 (4.6% maximum) and in more significant amounts at pH 7 (26.7 % maximum). At pH 9 hydrolysis was even more rapid and the main hydrolysis product observed was THPC which comprised of a maximum level of 46.6% of the applied radioactivity. At pH 9 THPI was observed in minor amounts and comprised of 15.1% of applied radioactivity by the end of the incubation period. At all pH values an unknown component was observed, but did not exceed 9.4% of applied radioactivity. The degradation rates of the hydrolysis products observed were not assessed.

Table B.8.2.1.1-3: The distribution of radioactivity (% AR) in the hydrolysis of [ring-1-^{14}C] captan at pH 5

Time (hours)	% of applied radioactivity (AR)				
	captan	THPI	Unk 1	THPC	Total
Run 1					
0.10	91.4	2.5	0.7	4.6	99.2

3.45	74.1	18.8	1.7	4.3	98.9
7.00	60.5	32.9	2.2	3.2	98.8
10.50	49.2	44.2	2.7	2.6	98.7
13.50	41.4	51.8	3.0	2.4	98.6
18.18	30.7	62.0	3.6	2.3	98.6
Run 2					
0.12	91.0	2.8	0.8	4.5	99.1
3.73	72.9	20.6	1.5	3.8	98.8
7.03	60.5	33.0	2.0	3.2	98.7
10.50	49.3	43.9	2.8	2.6	98.6
13.50	41.2	51.8	3.2	2.4	98.6
18.08	31.4	61.5	3.6	2.2	98.7

Table B.8.2.1.1-4: The distribution of radioactivity (% AR) in the hydrolysis of [ring-1-^{14}C] captan at pH 7

Time (hours)	% of applied radioactivity (AR)				
	captan	THPI	Unk 1	THPC	Total
Run 1					
0.07	86.3	3.1	1.5	8.0	98.9
1.33	74.1	11.6	1.7	11.6	99.0
3.15	57.1	22.5	2.4	17.0	99.0
5.18	42.6	31.0	3.8	21.7	99.1
7.23	31.7	37.7	5.4	24.2	99.0
9.47	22.9	43.4	7.2	25.6	99.1
Run 2					
0.08	90.3	2.6	0.9	5.1	98.9
2.02	66.0	15.9	1.8	15.3	99.0
4.10	47.4	26.6	3.2	21.9	99.1
6.28	33.6	34.5	4.9	26.1	99.1
8.40	24.4	40.5	6.9	27.4	99.2
11.17	15.9	46.0	9.4	27.8	99.1

Table B.8.2.1.1 -5: The distribution of radioactivity (% AR) in the hydrolysis of [ring-1-^{14}C] captan at pH 9

Time (minutes)	% of applied radioactivity (AR)				
	captan	THPI	Unk 1	THPC	Total
Run 1					
0.33	79.1	5.2	1.1	13.7	99.1
1.00	73.7	6.7	1.4	17.4	99.2
3.00	61.6	9.4	1.6	26.5	99.1
5.00	52.2	11.6	1.9	33.4	99.1
7.00	43.2	13.5	2.1	40.4	99.2
10.50	35.3	15.1	2.3	46.6	99.3
Run 2					
1.7	74.2	6.2	1.6	16.9	98.9
3.5	60.0	10.0	2.4	26.5	98.9
5.0	51.6	11.8	2.5	33.1	99.0
7.5	43.4	13.7	2.7	39.3	99.1

Captan was observed to hydrolyse rapidly at all pH levels, the rate of degradation increased with pH value.

Conclusions: Captan exhibited rapid first-order hydrolysis at all pH values in sterile water with a half-life of 11.7 hours at pH 5, 4.7 hours at pH 7 and 8.1 minutes at pH 9. Two main hydrolysis products were observed: THPI and THPC. The hydrolysis product THPI was predominant at acidic and neutral pH values whereas the hydrolysis product THPC was predominant at pH 9. The metabolite THPI reached up to 62 % (ph 5), 46 % AR (pH 7) and 15.1 % AR (pH 9); the metabolite THPC reached up to 4.6 % (pH 5), 27.8 % AR (pH 7) and 46.6 % AR (pH 9).

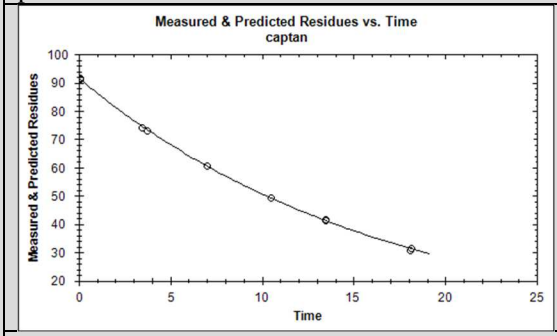
Comments RMS

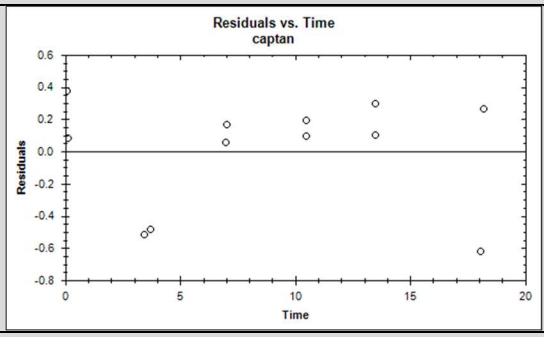
The RMS re-calculated the DT_{50} values using KINGUI version 2, the results of the notifier could be confirmed:

Captan						
pH	Kinetics	Parameter	Prob > t	Chi2 error	DT_{50}	DT_{90}
5	SFO	k-value	< 2e-16	0.460	11.7 h	33.8 h
7	SFO	k-value	1.63e-13	2.159	4.6 h	15.4 h
9	SFO	k-value	9.72e-09	2.354	8.1 min	26.8 min

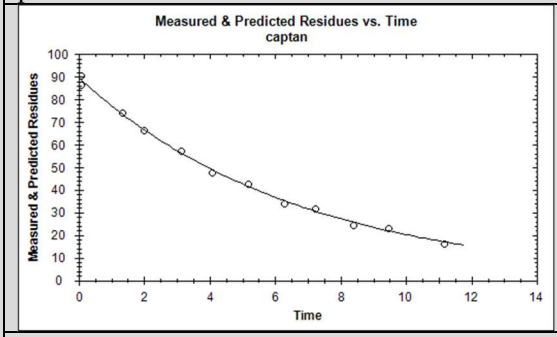
CAPTAN

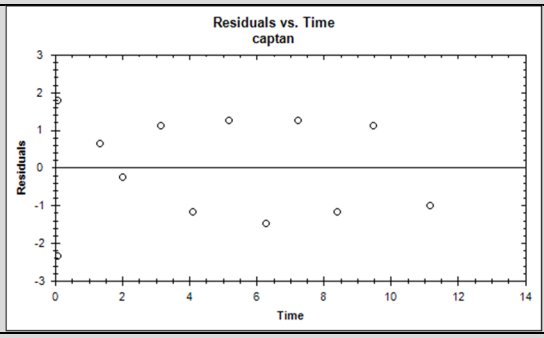
pH 5



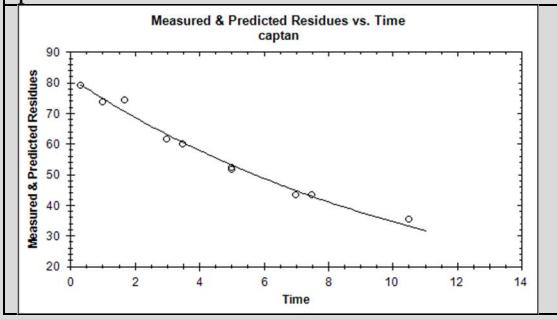


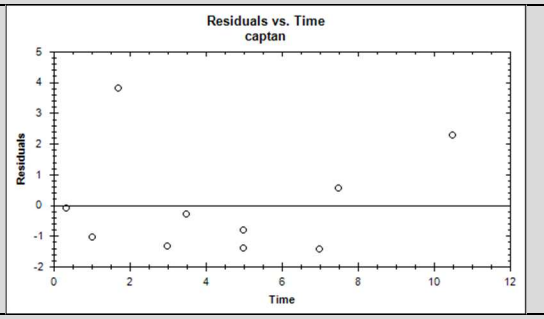
pH7





pH9





For the metabolite THPC, the DT_{50} was also re-calculated by the RMS using KINGUI version 2:

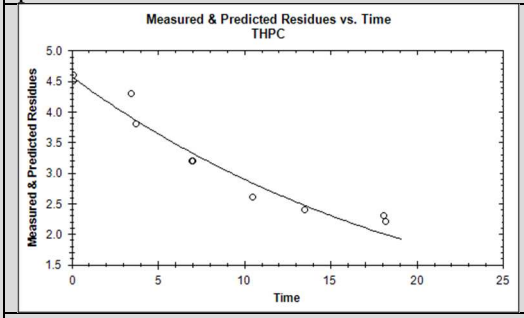
THPC							
pH	Kinetics	Parameter	Prob > t	Chi2 error	DT_{50}	DT_{90}	Remark
5	SFO	k-value	3.87e-08	4.747	15.1 h	50.3 h	From peak onwards
7	SFO	k-value THPC	0.00837	13.018	8.1 h	26.9 h	Pathway fit

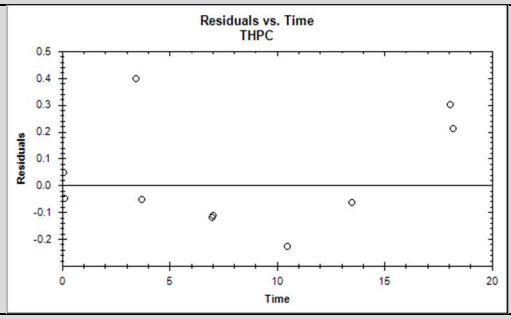
9	SFO	k-value THPC	NA	12.49	12.0 min	40.0 min	Pathway fit
9 –1st run	SFO	k-value THPC	NA	12.837	11.8 min	39.2 min	Pathway fit
9 – 2nd run	SFO	k-value THPC	0.019372	3.911	4.1 min	13.8 min	Pathway fit

NA…not analysed, was not calculated by model

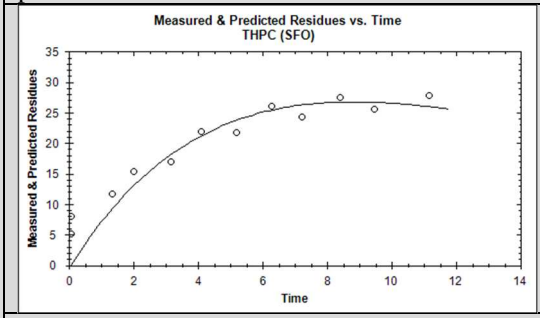
THPC

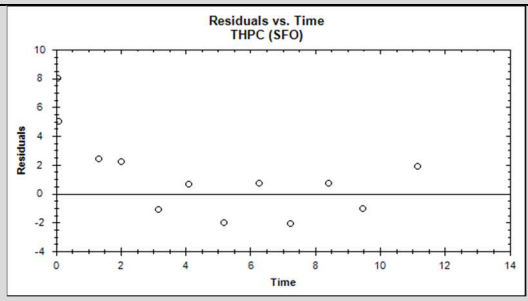
pH 5



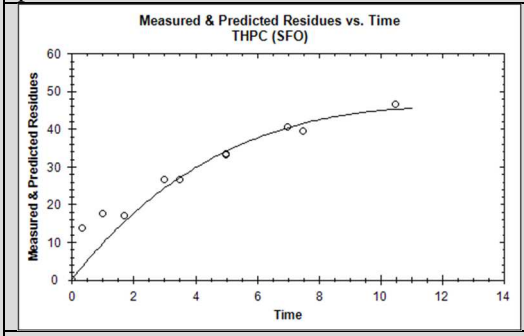


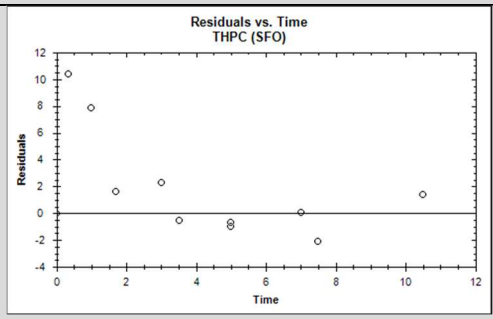
pH7



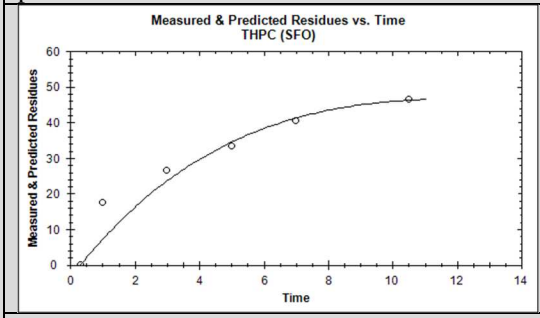


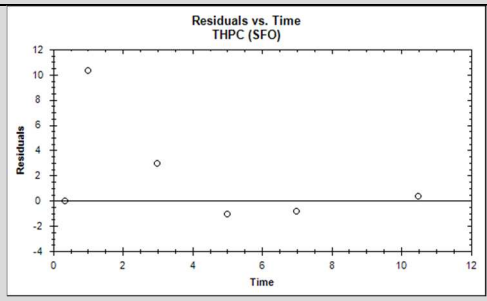
pH9



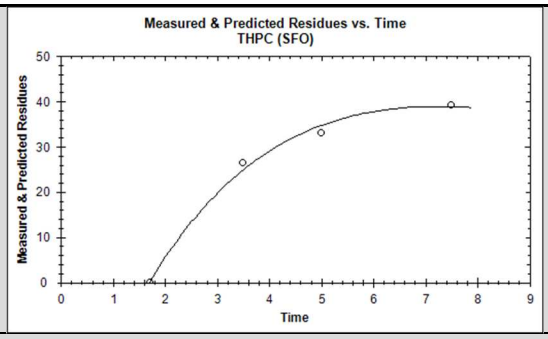


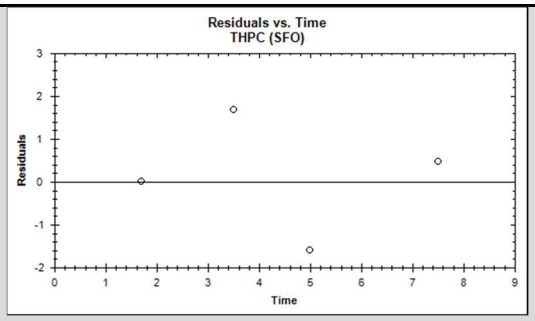
pH9 - first run





pH9 - second run





For the metabolites THPC at pH 9 no statistically acceptable DT_{50} could be calculated. Since the metabolite exceeds 10 % AR the hydrolytic degradation rate should be determined and a respective study should be provided (at least at pH9).

During the peer-review a study investigating the hydrolysis of the metabolite THPC at least at pH 9 was requested. The applicant provided a statement concerning this request (Spickermann, G., 2018).
A DT50 value was calculated by RMS for THPC at pH9, unfortunately no value for the t-test was calculated by the model. However, the chi2% is clearly < 15% and the visual fit looks good. A kinetic evaluation for Run1 and Run2 were additionally provided with chi2% values clearly < 15%, for Run1 no value for the t-test was calculated by the model, for Run2 the p-value of the t-test was clearly < 0.05, indicating together with a chi2% value of 3.911 that the fit is very good and statistical reliable. Therefore, based on the data of Run 2 a statistically reliable DT50 of 4.1 min for THPC at pH9 could be calculated.
The applicant concluded that there is no need to conduct a stand-alone hydrolysis study for THPC at pH 9 since a statistically reliable DT50 of 4.1 min for THPC at pH 9 at least for one run is available.

Comments RMS

Duplicate sets of analysis were conducted at each pH and used for the same kinetic evaluation. The kinetic evaluation of THPC at pH 9 resulted in no statistically reliable DT50. The kinetic evaluation of each single run resulted in a non reliable DT50 for run 1 and a reliable DT50 for run 2, but run 2 consists of 4 data points only, which is hardly sufficient for a robust estimation. Therefore, the RMS is still of the opinion that a hydrolysis study of the metabolite THPC at least at pH 9 should be provided.

Hydrolytic degradation of metabolites

Study 3 (2002a)

Reference:	Hydrolysis determination of THPI at different pH values.
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2002a
Report/Doc. number:	833714/ R-14370a/TMN-0357B
Guideline(s):	OECD 111, EEC 92/69, C.7, EPA OPPTS 835.2110
GLP:	Yes
Deviations:	None
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

Materials and methods: The hydrolysis of non-radiolabelled THPI (purity: 99.51 %) was investigated in sterile aqueous buffer solutions at pH values of 4.0, 7.0 and 9.0.

Initially buffer solutions were prepared with THPI concentrations of 48.138, 54.136 and 46.004 µg/mL at pH values of 4, 7 and 9 and incubated at a temperature of 50°C.

Further test were conducted at temperatures of 60 and 70°C for buffer solutions at pH values of 7 and 9.

Duplicate samples were taken after 2.4 h, 24 h and 5 d incubation and aliquots analysed with HPLC and UV-detector.

Findings:

Initial investigations conducted at 50°C are summarised in table B.8.2.1.1-8.

Table B. 8.1.1.2.1: Hydrolysis of THPI at a temperature of 50°C

Buffer pH value	Incubation period						
	0 hours	2.4 hours		24 hours		5 days	
	Initial concentration (µg/mL)	THPI (µg/mL)	Hydrolysis reaction (%)	THPI (µg/mL)	Hydrolysis reaction (%)	THPI (µg/mL)	Hydrolysis reaction (%)
pH 4.0	48.13	48.07	0	47.69	1	43.65	9
	46.69	48.14	-3	47.82	-2	45.91	2
pH 7.0	54.85	53.85	2	48.29	12	30.35	45
	55.15	54.45	1	49.24	11	33.23	40
pH 9.0	45.16	30.82	32	< 4.2	n.a	< 4.2	n.a
	45.11	32.91	27	< 4.2	n.a	< 4.2	n.a
n.a – not applicable.							

At a pH value of 4.0 no significant degradation (i.e. < 10%) was observed after 5 days, corresponding to an estimated half-life of greater than 1 year under environmental conditions (i.e. 25°C). At pH values of 7.0 and 9.0 significant degradation had occurred (i.e. > 10%) after 5 days. However as the level of degradation observed after 2.4 hours was < 50%, further testing was conducted. In addition, as the degradation of THPI at pH values of 7.0 and 9.0 followed pseudo-first order kinetics, the degradation was investigated at two additional temperatures (60 and 70°C) as summarised in tables B.8.2.1.1-9 and B.8.2.1.1-10.

Table B. 8.1.1.2.1: Hydrolysis of THPI in sterile aqueous buffer at pH value 7.0 at various temperatures

Temperature 50°C		Temperature 60°C		Temperature 70°C	
Time (hours)	THPI (µg/mL)	Time (hours)	THPI (µg/mL)	Time (hours)	THPI (µg/mL)
0.0	56.7	0.0	52.7	0.0	53.2
66.5	41.7	16.3	40.2	7.8	37.0
90.5	37.1	17.0	39.1	9.0	33.9
112.5	35.0	18.0	38.5	10.0	32.6
119.5	32.1	20.0	38.2	12.0	29.6
138.5	26.6	21.0	36.4	14.3	26.4
161.5	26.3	43.0	25.0	16.0	24.2
233.5	16.7	46.0	25.0	--	--
--	--	48.0	23.4	--	--
rate constant, k ($hours^{-1}$) = 0.00519 $T_{1/2}$ (hours) = 137		rate constant, k ($hours^{-1}$) = 0.01749 $T_{1/2}$ (hours) = 43.5		rate constant, k ($hours^{-1}$) = 0.05224 $T_{1/2}$ (hours) = 14.5	

Table B.8.2.1.1-6: Hydrolysis of THPI in sterile aqueous buffer at pH value 9.0 at various temperatures

Temperature 50°C		Temperature 60°C		Temperature 70°C	
Time (hours)	THPI (µg/mL)	Time (hours)	THPI (µg/mL)	Time (hours)	THPI (µg/mL)
0.0	50.0	0.0	44.5	0.0	58.2
2.0	38.7	0.5	37.5	0.3	48.9
2.5	36.0	0.9	34.0	0.4	44.7
3.0	34.7	1.2	30.4	0.5	40.3
3.5	32.2	1.5	27.0	0.6	37.4
4.5	28.5	1.8	24.8	0.7	34.6

5.0	26.3	2.3	20.8	0.8	31.6
5.5	24.4	2.5	19.3	0.9	30.1
6.5	21.7	2.8	17.7	1.0	26.6
7.5	19.9	3.0	15.9	1.1	25.4
--	--	--	--	1.2	23.8
rate constant, k (hours^{-1}) = 0.12529 $T_{1/2}$ (hours) = 5.5		rate constant, k (hours^{-1}) = 0.35374 $T_{1/2}$ (hours) = 2		rate constant, k (hours^{-1}) = 0.78601 $T_{1/2}$ (hours) = 1	

Hydrolysis was more rapid at pH 9 with half-lives ranging from 1 to 5.5 hours at temperatures of 70 and 50°C, respectively. At pH 7 the hydrolysis rate ranged from 14.5 to 137 hours at temperature of 70 and 50°C, respectively.

The rate constants determined at the various temperatures were used to calculate the equivalent rate constant at a temperature of 25°C, see table B.8.2.1.1-11.

Table B.8.2.1.1-7: Calculation of rate constants for hydrolysis at 25°C

Temperature	Rate constant, k (hours^{-1})	Activation energy, E (kJ/mol)	Rate constant, k at 25°C (hours^{-1})	Half-life, $T_{1/2}$ at 25°C (days)
pH 7.0				
50°C	0.00519	105.7	1.89 x 10^{-4}	152.4
60°C	0.01749			
70°C	0.05224			
pH 9.0				
50°C	0.12529	84.7	9.16 x 10^{-3}	3.2
60°C	0.35374			
70°C	0.78601			

The activation energy was determined to be 105.7 and 84.7 kJ/mol at pH values of 7 and 9 respectively. Using the Arrhenius equation the half-live at 25°C was calculated for pH 7 and 9.

Conclusions: The metabolite THPI was stable to hydrolysis at pH 4 in sterile aqueous buffer solutions at 25°C. At pH values of 7 and 9 hydrolysis proceeded with pseudo-first order half lives of 152 and 3 days, respectively.

Comments RMS

None.

Study 4 (2002b)

Reference:	Hydrolysis determination of THPAM at different pH values.
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2002b
Report/Doc. number:	833725/ R-14370b/TMN-0357C
Guideline(s):	OECD 111, EEC 92/69, C.7, EPA OPPTS 835.2110
GLP:	Yes
Deviations:	None
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

Materials and methods: The hydrolysis of non-radiolabelled THPAM (purity 94.3 %) was investigated in sterile aqueous buffer solutions at pH values of 4.0, 7.0 and 9.0.

Initially buffer solutions were prepared with THPAM concentrations of 50.36, 50.68 and 49.84 µg/mL at pH values of 4, 7 and 9 and incubated at a temperature of 50°C.

Further test were conducted at temperatures of 50, 29 and 30°C with buffer solutions at pH value of 4 and at temperatures of 50, 60 and 70°C with buffer solutions at pH value of 7.

Findings:

Initial investigations conducted at 50°C are summarised in table B.8.2.1.1-12.

Table B.8.2.1.1-8: Hydrolysis of THPAM at a temperature of 50°C

Buffer pH value	Incubation period						
	0 hours	2.4 hours		24 hours		5 days	
	Initial concentration (µg/mL)	THPAM (µg/mL)	Hydrolysis reaction (%)	THPAM (µg/mL)	Hydrolysis reaction (%)	THPAM (µg/mL)	Hydrolysis reaction (%)
pH 4.0	50.36	30.28	40	< 1.7	n.a	< 1.7	n.a
	49.78	30.36	39	< 1.7	n.a	< 1.7	n.a
pH 7.0	54.04	52.79	2	51.28	5	43.39	20
	52.98	52.85	0	50.52	5	43.64	18
pH 9.0	51.87	51.74	0	50.96	2	52.64	-1
	51.77	52.05	-1	52.13	-1	48.80	6

At a pH value of 9.0 no significant degradation (i.e. < 10%) was observed after 5 days, corresponding to an estimated half-life of greater than 1 year under environmental conditions (i.e. 25°C). At pH values of 4.0 and 7.0 significant degradation had occurred (i.e. > 10%) after 5 days, however as the level of degradation observed after 2.4 hours was < 50% further testing was conducted. In addition as the degradation of THPAM at pH values of 4.0 and 7.0 followed pseudo-first order kinetics the degradation was investigated at two additional temperatures (29 and 39°C at pH 4, 60 and 70°C at pH 7) as summarised in tables B.8.2.1.1-13 and B.8.2.1.1-14.

Table B.8.2.1.1-9: Hydrolysis of THPAM in sterile aqueous buffer at pH value 4.0 at various temperatures

Temperature 29°C		Temperature 39°C		Temperature 50°C	
Time (hours)	THPAM (µg/mL)	Time (hours)	THPAM (µg/mL)	Time (hours)	THPAM (µg/mL)
0.0	45.7	0.0	41.0	0.0	54.5
4.0	44.8	6.0	29.5	1.3	42.0
6.5	43.2	7.5	26.2	1.8	38.4
24.0	33.5	8.5	25.2	2.3	33.6
31.0	30.2	9.5	23.2	2.8	30.6
48.5	23.5	11.0	21.4	3.3	27.8
53.5	22.3	13.5	18.1	4.0	23.8
57.3	22.3	14.5	17.5	4.5	20.1
72.3	17.4	--	--	5.0	18.9
77.5	16.6	--	--	5.5	17.2
rate constant, k ($hours^{-1}$) = 0.01314 $T_{1/2}$ (hours) = 53		rate constant, k ($hours^{-1}$) = 0.06143 $T_{1/2}$ (hours) = 11.5		rate constant, k ($hours^{-1}$) = 0.21505 $T_{1/2}$ (hours) = 3	

Table B.8.2.1.1-10: Hydrolysis of THPAM in sterile aqueous buffer at pH value 7.0 at various temperatures

Temperature 50°C		Temperature 60°C		Temperature 70°C	
Time (hours)	THPAM (µg/mL)	Time (hours)	THPAM (µg/mL)	Time (hours)	THPAM (µg/mL)
0.0	57.1	0.0	53.5	0.0	56.2
124.5	46.3	67.5	35.6	22.0	38.5
172.0	42.9	95.5	31.2	30.0	36.0
260.0	38.3	115.0	28.2	46.0	29.0

333.0	34.5	139.5	27.7	54.0	26.8
436.0	29.7	235.8	18.1	70.0	21.7
484.0	28.4	238.0	18.0	78.0	21.0
604.5	23.7	--	--	94.0	20.0
675.5	21.4	--	--	--	--
rate constant, k (hours^{-1}) = 0.00137 $T_{1/2}$ (hours) = 507		rate constant, k (hours^{-1}) = 0.00393 $T_{1/2}$ (hours) = 177		rate constant, k (hours^{-1}) = 0.00992 $T_{1/2}$ (hours) = 70	

Hydrolysis was more rapid at pH 4 with half-lives ranging from 3 to 53 hours at temperatures of 50 and 29°C, respectively. At pH 7 the hydrolysis rate ranged from 70 to 507 hours at a temperature of 70 and 50°C respectively.

The rate constants determined at the various temperatures were used to calculate the equivalent rate constant at a temperature of 25°C, see table B.8.2.1.1-15.

Table B.8.2.1.1-11: Calculation of rate constants for hydrolysis at 25°C

Temperature	Rate constant, k (hours^{-1})	Activation energy, E (kJ/mol)	Rate constant, k at 25°C (hours^{-1})	Half-life, $T_{1/2}$ at 25°C (days)
pH 4.0				
29°C	0.01314	108	7.8×10^{-3}	4
39°C	0.06143			
50°C	0.21505			
pH 7.0				
50°C	0.00137	91.2	8.03×10^{-5}	360
60°C	0.00393			
70°C	0.00992			

Using this method the activation energy was determined to be 108 and 91.2 kJ/mol at pH values of 4 and 7 respectively. Using the Arrhenius equation the half-live at 25°C was calculated for pH 4 and 7.

Conclusions: The metabolite THPAM was stable to hydrolysis at pH 9 in sterile aqueous buffer solutions at 25°C. At pH values of 4 and 7, hydrolysis proceeded with pseudo-first order half lives of 4 and 360 days respectively.

Comments RMS

None.

B.8.2.1.2. Direct photochemical degradation

Photolysis studies are not considered further for classification regarding rapid degradability in the aquatic environment.

Study 5 (1986b)

Reference:	Photolysis of captan in sterile aqueous solution
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1986b
Report/Doc. number:	MEF-0001, 8702326/ R-4393*/TMN-0364*
Guideline(s):	USEPA 161-2
GLP:	Yes
Deviations:	Minor
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

*document numbers taken from original DAR could not be verified in the study

Summary based on original DAR

Materials and methods: [Trichloromethyl - ^{14}C] - captan (radiochemical purity 98.8%, specific activity 38 mCi/mmole) was dissolved in sterile aqueous buffer solution at pH 5 (the pH at which captan is most stable to chemical hydrolysis) using an aliquot of acetonitrile, to give a nominal concentration of 1 mg/L, and continuously irradiated with UV light at 25°C according to EPA guidelines. The UV source was a black light fluorescent lamp which produced radiant energy in the 320 to 380 nm range, with a maximum intensity at 363 nm. The radiation energy of the light was 2 x 10^3 µw/cm^2. The light energy was 0.5 - 1.5 times that of natural sunlight. Results were compared with those of a dark control solution at the same pH, concentration and temperature. Samples were taken after 1, 2, 3, 6, 24, and 48 hour and analysed by reversed phase HPLC.

Findings:

The results are summarised in table B.8.2.1.2-1. Analysis of the data showed that the degradation process in both the irradiated solution and controls was first order, and that the half-life in the irradiated solution was 9.9 hours, and that of the dark control almost identical at 10.1 hours, respectively. This indicated that chemical hydrolysis was the principal route of degradation under these conditions. Therefore, no photoproducts were determined.

Table B.8.2.1.2-1: The aqueous photolysis of [trichloromethyl - ^{14}C] - captan

Hours	Captan (% AR)[1]	
	Irradiated solution	Dark Control
0	100	100
1	92.8	85.6
2	84.3	82.3
3	76.9	77.2
6	60.9	63.5
24	18.3	18.3
48	2.0	3.7

[1] Identified as captan by ion-pairing reverse phase HPLC.

Conclusions: Photolysis of captan in sterile aqueous conditions is a very minor route of degradation compared to chemical hydrolysis, and is not expected to be a significant route of captan breakdown in the aquatic environment.

Comments RMS

The RMS re-calculated the DT_{50} values; the results of the notifier could be confirmed.
Metabolites were not identified since the degradation in irradiated samples and dark control samples was comparable; therefore, it was concluded that hydrolysis is the main route of degradation.

The light source used was a black light fluorescent lamp with a light intensity of 2 x 10^3 µW/cm^2 (20 W/m^2) producing UV radiant energy from 320 to 380 nm.
A Xenon lamp simulating natural sunlight from 290 nm to about 800 nm would have been more suitable. But as the most relevant wavelength for phototransformation of chemicals in the environment is expected to be in the range of 295 – 400 nm, the use of a blacklight fluorescent lamp is considered to be acceptable.

A study investigating the photolysis of ring labelled captan was not provided and is missing.

During the peer-review a study investigating the aquatic photolysis of ring labelled captan was requested. The applicant provided a statement concerning this request (Spickermann, G., 2018).
The applicant compared the aquatic degradation pathway of captan and folpet which has a very similar structure; folpet has an aromatic ring while captan has a cyclohexene ring. Both compounds hydrolyse rapidly and form the main metabolite THPI (phthalimid) using [ring-^{14}C]captan or [carbonyl-^{14}C]folpet.

The aqueous photolysis of [thrichloromethyl-^{14}C]-captan showed similar degradation of captan under irradiated and dark conditions. Therefore, it was concluded that hydrolysis is the main route of degradation of captan under aqueous conditions. But no metabolites were determined.
The aqueous photolysis of [carbonyl-^{14}C]folpet at pH 3 showed similar degradation of folpet and the same metabolites under irradiated and dark conditions after 8 hours. The metabolites were the same metabolites determined in the hydrolysis study of [carbonyl-^{14}C]folpet.
It was concluded by the applicant that the main degradation pathway of captan and folpet under aqueous conditions is hydrolysis and that an aqueous photolysis study with ring labelled captan will not provide any new information.

Comments RMS

The aquatic degradation of folpet and captan is similar but shows some differences: The hydrolytic degradation of folept is faster; and a main hydrolysis product of folpet is THPAI (phthalic acid) at pH 7 and pH 9, whereas the hydrolysis of captan resulted in the main metabolite THPC (phthalimidothiocarbonate) at pH 7 and pH 9.
It is agreed by RMS that from the studies provided it can be concluded that hydrolysis is the main route of degradation. But since no information about the photolytic degradation products of captan was provided the pathway should be confirmed with an aquatic photolysis study using ring-labelled captan.

Study 6 (2002a)

Reference:	Aqueous photolysis of THPI under laboratory conditions and determination of quantum yield
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2002a
Report/Doc. number:	833736/ R-14256a/TMN-0369
Guideline(s):	Directive 95/36/EEC and 94/37/EEC, SETAC (March 1995), OECD guidance document (97)21, EPA OPPTS 835.2210
GLP:	Yes
Deviations:	None
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

Materials and methods: The aqueous photolysis of non-radiolabelled THPI (batch no. ASW01685-01A, chemical purity 99.51 %) was investigated in sterile buffer solution at pH 7 and a temperature of 22.4°C using an artificial light source.

Solutions of THPI at a concentration of 30.5 mg/L were prepared using a phosphate buffer (0.02M) and sterilised by autoclaving. The solutions were exposed to an artificial light source (xenon lamp) using a Suntest Hanau apparatus, for a period of 15 days. Wavelenghts below 290 nm were removed and an intensity of 56 W/m^2 was reached within 300-400 nm. Control samples were incubated under identical conditions but in the dark. Samples from the exposed and dark controls were analysed by HPLC at intervals of 0, 3 hours and 1, 3, 7, 10 and 15 days.

Findings:

The levels of THPI detected in the exposed samples and the dark control is shown in table B.8.2.1.2-2. No significant degradation was observed. After 15 days of continuous exposure to the artificial light source THPI represented 101.7 and 94.1% of the initial concentration in the exposed samples and dark controls respectively.

Table B.8.2.1.2-2: The aqueous photolysis of THPI

Exposure	THPI (%)	
	Irradiated solution	Dark Control
0 hour	100.0	100.0
3 hour	99.0	100.6
1 day	107.6	103.7
3 day	100.4	91.5
7 day	100.4	93.0

10 day	96.5	97.3
15 day	101.7	94.1

The extent of degradation was similar for both the exposed samples and dark controls indicating that THPI is not significantly photo-degraded.

Due to the stability of THPI observed the quantum yield was not determined.

Conclusions: THPI is stable to photo-degradation in aqueous solutions at a pH 7.

Comments RMS

None.
THPI was shown to be stable to photolysis in aqueous solutions at a pH 7.

Study 7 (2002b)

Reference:	Aqueous photolysis of THPAM under laboratory conditions and determination of quantum yield
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2002b
Report/Doc. number:	833747/ R-14256b/TMN-0370
Guideline(s):	Directive 95/36/EEC and 94/37/EEC, SETAC (March 1995), OECD guidance document (97)21, EPA OPPTS 835.2210
GLP:	Yes
Deviations:	None
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

Materials and methods: The aqueous photolysis of non-radiolabelled THPAM (batch no. ASW1584R chemical purity 94.3 %) was investigated in sterile buffer solution at pH 7 and a temperature of 22.3°C using an artificial light source.

Solutions of THPAM at a concentration of 25.8 mg/L were prepared using a phosphate buffer (0.02M) and sterilised by autoclaving. The solutions were exposed to an artificial light source (xenon lamp) using a Suntest Hanau apparatus, for a period of 15 days. Wavelenghts below 290 nm were removed and an intensity of 56.5 W/m^2 was reached within 300-400 nm. Control samples at an initial concentration of 28.5 mg/Lwere incubated under identical conditions but in the dark. Samples from the exposed and dark controls were analysed by HPLC at intervals of 0, 3 hours and 1, 3, 7, 10 and 15 days.

Findings:

The levels of THPAM detected in the exposed samples and the dark control is shown in table B.8.2.1.2-3. No significant degradation was observed, after 15 days of continuous exposure to the artificial light source THPAM represented 96.3 and 95.9% of the initial concentration in the exposed samples and dark controls respectively.

Table B.8.2.1.2-3: The aqueous photolysis of THPAM

Exposure	**THPAM (%)**	
	Irradiated solution	**Dark Control**
0 hour	100.0	100.0
3 hour	93.5	94.3
1 day	97.6	97.6
3 day	95.4	97.3
7 day	95.2	96.1
10 day	95.1	94.2
15 day	96.3	95.9

The extent of degradation was similar for both the exposed samples and dark controls indicating that THPAM is not significantly photo-degraded.

Due to the stability of THPAM observed the quantum yield was not determined.

Conclusions: THPAM is stable to photo-degradation in aqueous solutions at a pH 7.

Comments RMS
None. THPAM was shown to be stable to photolysis in aqueous solutions at a pH 7.

B.8.2.2. **Route and rate of biological degradation in aquatic systems**

B.8.2.2.1. Ready biodegradability

Study 8 (2015)

Reference:	**CAPTAN, [carboximide-^{14}C] Ready Biodegradability Modified Sturm Test.**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2015
Report/Doc. number:	R-34731
Guideline(s):	OECD 301 B / CO_2 Evolution Test (Modified Sturm)
GLP:	Yes
Deviations:	None
Validity:	
Status:	Submitted for renewal

Executive Summary

The ready biodegradability Captan was determined with a non-adaptive activated sludge over a period of 28 days in the modified Sturm test. Captan was tested at a concentration of 738 µg/L (based on < 10 % of EC_{50} value measured in a study) composed of 113 µg/L Captan, [carboximide-^{14}C] and 625 µg/L of technical Captan with 2 replicates corresponding to an activity in the test solution of 578 kBq/L, equivalent to 1.04 MBq per test vessel. The test vessels were incubated at low light conditions and at 20 – 24 °C.

The biodegradation of Captan was followed by analysing the quantity of $^{14}CO_2$ evolved via respiration of bacteria. The biodegradation test was terminated on day 28 by acidification of the test solutions and the last determination was made on day 29 after residual of $^{14}CO_2$ has been purged from the test solutions over a period of 24 hours. Aniline was used as functional control to check the activity of the test system. The degradation of the functional control reached the pass level of 60 % after 12 days and a biodegradation of 76 % after 28 days.

Toxicity control containing both test and reference items were investigated. A biodegradation of 46% was related to the reference item was determined within 14 days and reached 72 % after 28 days. The biodegradation was not inhibited by the test item in the toxicity control.

The percentages of $^{14}CO_2$ production were calculated in relation to the theoretical production of $^{14}CO_2$ of Captan and the biodegradation was calculated for each sampling time. The biodegradation of Captan was increased only slowly within the course of the study. The 10 % level was not reached within the study duration (28 days), but after the acidification on day 28. The 60 % level was not reached. The mean biodegradation after 28 days was 13 %. The result of the study showed that Captan is not biodegradable in the 10-days window and within 28 days.

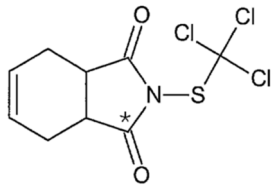
I. MATERIALS AND METHODS

A. MATERIALS

1. Labelled test item: **CAPTAN, [carboximide-^{14}C]**

Chemical name: 2-[(Trichloromethyl)sulfanyl]-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dioe

Chemical structure:



* = position of ^{14}C-label

Batch no.:	XXI/58/A//2
CAS no.:	133-06-234123-59-6
Chemical purity:	92.13%
Radiochemical purity:	93.46%
Specific activity:	5.11 MBq/mg corresponding to 41.68 mCi/mmol
2. Unlabelled test item:	**Captan Technical**
Batch no.:	93138112
CAS no.:	133-06-2
Active ingredient:	Captan
Content (certified):	94.3%
Molecular weight:	300.61 g/mol
Appearance:	Off-white powder (solid)
Water solubility:	Insoluble
Expiry date:	2015-02-16
3. Functional control test item:	**Mixture of Aniline and aniline sulphate, [^{14}C(U)]-**
Batch no.:	BCBN3667V (Aniline)
	266-170-110-A-2014024-PVA (Aniline sulphate, [^{14}C(U)]-)
CAS no.:	62-53-3 (Aniline)
Purity:	100 % (Aniline)
Radiochemical purity:	99.2% (Aniline sulphate, [^{14}C(U)]-)
Expiry date:	April 2016 (Aniline)

B. STUDY DESIGN

1. Experimental conditions

The study was performed according to the guideline OECD 301 B / CO2 Evolution Test (modified Sturm Test) over a period of 28 days with a non-adaptive activated sludge in order to check the rate of biodegradation in % by determination of evolved $^{14}CO_2$ by LSC measurements. Activated sludge system was collected from Municipal sewage treatment plant at Hildesheim – Germany. The sewage plant considered suitable because it receives predominantly municipal sewage and hardly any industrial chemical waste.

The activated sludge was washed twice with chlorine free tap water. After that, the settled sludge was resuspended in mineral salts medium and was maintained in an aerobic condition by aeration for 1 hour. Then, it was homogenised with a blender. After sedimentation the supernatant was decanted and maintained under aerobic conditions by aeration with CO_2 free air for 4 days. Ten mL/L of this mixture was used to initiate inoculation.

Test vessels used for functional controls were prepared with a mixture of Aniline and Aniline sulphate, [^{14}C(U)]- without replicates. The actual concentration in the test was 743.2 µg/L, composed of 8.2 µg/L Aniline sulphate, [^{14}C(U)]- and 735 µg/L Aniline. Duplicate test vessels were prepared for test item Captan. The actual test concentration was 738 µg/L, composed of 113 µg Captan, [carboximide-^{14}C] and 625 µg/L Captan technical. These concentrations were chosen based on the determined NOEC and EC_{50} value obtained from different study. The activity in the test solution was 578 kBq/L, equivalent to 1.04 MBq per test vessel. No pretreatment was performed on the samples used for the test item. Single test vessels were prepared for the toxicity test with the test item and reference item in test concentration. Inoculum controls were prepared in duplicates with the test medium without test and/or reference item. Brown glass test vessels were used (2000 mL) filled with 1800 mL of the test medium. Inoculation was performed once at the start of the test (~10^7 – 10^8 CFU/L).

The duration of the test was 28 days with continuous stirring and aeration at a rate of 30 -100 mL/min. The nominal test temperature was 22 ± 2 °C. The actual measured temperature was 20 – 24 °C. On day 28, test vessels were acidified by adding 1 mL of 37% HCL to each. Aeration was continued further for 24 hour and the quantity of $^{14}CO_2$ evolved was determined. The pH value for all solutions was measured prior acidification. The pH values

were 7.8 – 7.81, 8.13, 8.40 - 8.41 and 8.40 – 8.60 for inoculum control, functional control, test item and toxicity control, respectively.

2. Description of analytical methods

Determination of radioactivity was carried out by LSC method. The percentage of $^{14}CO_2$ trapped in the NaOH traps was determined for each measurement. The NaOH trap was replaced by new one after each measurement. $^{14}CO_2$ measurements were carried out three times a week during the first 10 days and twice a week thereafter. The total radioactivity in the test vessels, functional control and toxicity control was determined at test start by LSC.
The analytical method was validated with regard to accuracy and precision according to the test facility stand operating procedures. The limit of quantification of the analytical method (LOQ) for the traps was fixed to 5 Bq/3 mL. The analytical method was validated at 1× and 1000× LOQ. One blank and one replicate containing no test item were included in all validation sets to demonstrate that there were no background interferences.
In addition, the following validity criteria were considered

- The percentage of degradation of the functional control must reach the pass level of 60 % by day 14.
- The differences between replicate values at the end of the test, at the plateau or at the end of the 10-days window must be < 20 %.
- The percentage of degradation of the toxicity control must reach the pass level of 25 % by day 14. If the percentage is lower that 25 % the test item would be assumed to have inhibitory effect and the study must be repeated with lower test concentration.

The net amount of $^{14}CO_2$ produced was calculated by correcting the results of the test item and functional control for endogenous of $^{14}CO_2$ production by the control group (= background). The biodegradation was calculated from the ratio of applied radioactivity to net radioactivity determined in the $^{14}CO_2$ trap. Degradation percentage = (net radioactivity/applied radioactivity) × 100.

II. RESULTS AND CONCLUSSIONS

A. FINDINGS

1. Method validation

The validity of the analytical method was demonstrated by the results obtained for the fortification samples for the NaOH traps. The accuracies of the method were between 102 % for 1 × LOQ and 104 % for 1000 × LOQ. The mean recovery at each fortification level was between 90 and 110 % with a standard deviation lower that 10 % and coefficient of variation of 1.3 % The results of method validation are summarised in table B.8.2.2.1-1.

Table B.8.2.2.1-1: Recoveries of the analytical method at 1 × LOQ and 1000 × LOQ fortification levels

Replicate	1 × LOQ		1000 × LOQ	
	Radioactivity	Recovery rate	Radioactivity	Recovery rate
	[Bq / 3 mL]	[%]	[Bq / 3 mL]	[%]
1	5.17	103	5320.6	106
2	5.16	103	5157.3	103
3	5.08	102	5146.2	103
4	5.08	102	5158.5	103
5	4.99	100	5152.3	103
Mean	5.10	102	5187	104
SD ±	0.06	-	67	-
CV [%]	1.3	-	1.3	-

1 × LOQ = 5Bq/3mL, equivalent to 0.00048 % of applied radioactivity of the test item
1000 × LOQ = 5000 Bq/3mL, equivalent to 0.48 % of applied radioactivity of the test item
SD standard deviation
CV coefficient of variation

2. $^{14}CO_2$ production and biodegradation

The values $^{14}CO_2$ produced after 28 days incubation are shown in comparison to the ready degradable functional control and toxicity control are summarised in table B.8.2.2.1-2. The results of the net $^{14}CO_2$ production (as Total Radioactivity in kBq) and biodegradation rate of each measurement are given in table B.8.2.2.1-3 and table B.8.2.2.1-5.

Table B.8.2.2.1 -2: $^{14}CO_2$ production and biodegradation after 28 days

$^{14}CO_2$ production	Functional control	Test item	Toxicity control

		Replicate 1	Replicate 1	Test item & Reference item
Net: [kBq/1.8L] [kBq/L]	 147.9 82.2	 159.3 88.5	 116.0 64.4	 278.0 154.4
Theoretical: [kBq/1.8L] [kBq/L]	 190.0 105.6	 1040 578		 1230 683
Degradation: [%]	76	15	11	#

not applicable due to difference in the specific activity of test item and reference item, for detail see Table 7.7-4.

Table B.8.2.2.1-3: $^{14}CO_2$ production (as Total Radioactivity) and biodegradation in the inoculum control and the functional control

Incubation time	Inoculum control [kBq/1.8L]	Functional control [kBq/1.8L]		Degradation
[days]	Mean value	Gross sum	Net sum	[%]
1	0.0	0.0	0.0	0
2	0.0	0.1	0.0	0
5	0.0	1.6	1.5	1
7	0.0	42.6	42.6	22
9	0.0	90.9	90.8	47
12	0.1	119.5	119.4	61
14	0.1	128.2	128.1	66
16	0.1	133.1	133.1	69
19	0.1	138.3	138.2	71
22	0.1	142.3	142.2	73
26	0.1	144.8	144.7	75
28	0.1	145.9	145.8	75
29	0.1	148.0	147.9	76

Table B.8.2.2.1-4: $^{14}CO_2$ production (as Total Radioactivity) and biodegradation in the toxicity control related to the reference item Aniline sulphate, [^{14}C(U)]

Incubation time	Toxicity control [kBq/1.8L]			Degradation
[days]	Gross sum	Net sum	Net sum RI*	[%]
1	0.2	0.2	0.0	0
2	0.9	0.9	-0.2	0
5	6.2	6.2	0.8	0
7	44.5	44.5	32.6	17
9	81.3	81.2	64.2	33
12	104.1	104.1	82.0	42
14	114.2	114.2	89.6	46
16	121.7	121.6	94.7	49
19	133.4	133.3	100.6	52
22	150.0	149.9	110.1	57
26	190.1	190.0	132.4	68
28	210.2	210.1	136.2	70
29	278.1	278.0	140.4	72

* Values for the reference item (RI) were corrected for the mean of $^{14}CO_2$ production in the test item replicates

Table B.8.2.2.1-5: $^{14}CO_2$ production (as total radioactivity) and biodegradation in the test item vessels

Incubation time	Replicate 1 [kBq/1.8L]		Degradation	Replicate 2 [kBq/1.8L]		Degradation
[days]	Gross sum	Net sum	[%]	Gross sum	Net sum	[%]

1	0.3	0.3	0	0.3	0.3	0
2	1.1	1.0	0	1.0	1.0	0
5	5.4	5.4	1	5.6	5.5	1
7	10.2	10.2	1	13.6	13.5	1
9	16.4	16.4	2	17.7	17.6	2
12	22.6	22.5	2	21.7	21.6	2
14	25.4	25.3	2	23.9	23.8	2
16	27.9	27.9	3	25.9	25.8	2
19	32.1	32.0	3	33.4	33.3	3
22	39.4	39.3	4	40.3	40.2	4
26	62.6	62.5	6	52.8	52.7	5
28	87.5	87.4	8	60.6	60.5	6
29	159.4	159.3	15	116.1	116.0	11

B. CONCLUSIONS
Captan is not readily biodegradable in the 10-days window and within 28 days.

Comments RMS
None. Agreed.

B.8.2.2.2. Aerobic mineralisation in Surface Water

Study 9 (2016b)

Reference:	**Aerobic Mineralisation of [^{14}C] Captan in Surface Water**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2016b
Report/Doc. number:	S14-05599
Guideline(s):	OECD 309 (2004)
GLP:	Yes
Deviations:	Minor
Validity:	Yes
Status:	Submitted for renewal

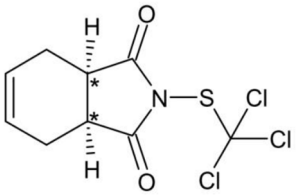
Executive Summary
The objective of the study was to determine the rate of degradation of Captan and to evaluate the major pathway of its degradation. The study was performed with [cyclohexene-^{14}C] Captan under aerobic conditions in the dark using natural aerobic surface water taken from a large water body.
The test water was sampled from Rhineland-Palatinate (67374 Hanhofen, Germany).
The experiment was conducted in accordance with the OECD Guideline for Testing of Chemicals No. 309 and in compliance with the OECD Principles of Good Laboratory Practice.
To be able to determine the degradation rate and to follow the transformation products two different application rates (9.8 µg/L and 93.3 µg/L) of radio-labelled test item were applied. Assuming a specific activity of 6.77 MBq/mg, this corresponds to a spiked radioactivity of about 0.033 MBq and 0.32 MBq per vessel, respectively.
The water system was incubated in the dark at 20 ±3°C under constant aeration. The incubation period after treatment was 60 days. Organic volatiles and carbon dioxide were trapped.
Duplicate samples were taken for analysis at specified intervals up to 60 days after application. The radioactivity was quantified by liquid scintillation counting and characterised by HPLC. LC-MS/MS was used for confirmation of active substance in selected samples.
Mean recoveries of radioactivity in the water system within 60 days of incubation with the low and high test concentrations were within the range of 97.1% to 105.2% AR and 97.6% to 104.2% AR, respectively.
The formation of organic volatiles was negligible for both tested concentrations. Only amounts <0.1% AR were detected. Carbon dioxide was detected at maximum amounts of 3.4% AR.
Five major metabolites were formed during the whole incubation period. Two could be identified as THPI and THPAM at maximal amounts of 69.2% AR (1 h) and 77.9% AR (14 d), respectively. M2, M3 and M7 were found at maximal amounts of 52.9% (2 h), 88.9% (1 d) and 35.8% AR (60 d), respectively. Additionally, five minor metabolites, M1, M4, M5, M6 and M9, occurred at maximum amounts of 1.9% AR (0 d), 1.6% AR (2 h), 2.5% AR (14 d), 6.4% AR (21 d) and 5.2 % AR (0 d), respectively.

Due to the rapid degradation of the test item the performance of kinetic calculations was not possible. The amount of the applied radioactivity of the parent substance was < LOQ after 1 hour of incubation for both concentrations. Thus, the DT_{50}-value can be assumed to be < 1 h.
After 7 days 80% AR of the reference substance were mineralised. Thus, the test system was biologically active and the test was valid.
In sterile samples, [cyclohexene-^{14}C] Captan was degraded to THPAM, M3 and M7 after 2 days of incubation. The degradation pattern shows an indication that the parent substance was (partially) degraded by hydrolysis.

I. MATERIALS AND METHODS

A. MATERIALS

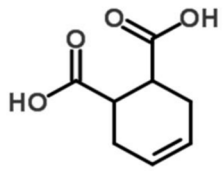
1. Labelled test item: **[cyclohexene-^{14}C] Captan**
Molecular weight: 300.6
Chemical structure:



* = position of ^{14}C-label
Batch no.: 150320
CAS no.: 133-06-2
Radiochemical purity (analysed): 100%
Specific activity: 55 mCi/mmol
Expiry date: 2016-02

2. Unlabelled test item: **Captan**
Batch no.: SZB9174XV
CAS no.: 133-06-2
Purity (analysed): 99.6%
Molecular weight: 300.6 g/mol
Appearance: solid (colourless)
Expiry date: 2016-06

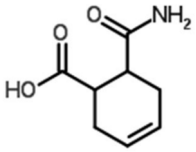
3. Reference item: **THPAI (1.2.3.6-Tetrahydrophthalic acid)**
Chemical name: 4-cyclohexene-1,2-dicarboxylic acid
Batch no.: 516-143-00
CAS no.: 88-92-2
Purity (analysed): 96.8% w/w
Molecular weight: 170.2 g/mol
Chemical structure:



Appearance: solid (white)
Expiry date: 2020-01

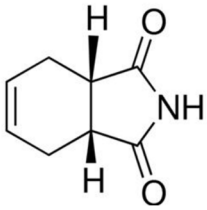
THPAM (1.2.3.6-Tetrahydrophthalamic acid)
Chemical name: 3-cyclohexene-1-carboxylic acid-6-(aminocarbonyl)
Batch no.: 516-156-00
CAS no.: 2028-12-8
Purity (analysed): 98.1% w/w
Molecular weight: 169.18 g/mol

Chemical structure:



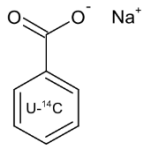
Appearance: solid (white)
Expiry date: 2017-02

THPI (1.2.3.6-Tetrahydrophthalimide)
Chemical name: cis-4-cyclohexane-1.2-dicarboximide
Batch no.: 279-071-02
CAS no.: 1469-48-3
Purity (analysed): 98.5% w/w
Molecular weight: 151.2 g/mol
Chemical structure:



Appearance: solid (white)
Expiry date: 2017-02

4. Reference substance: [ring-U-^{14}C] Benzoic acid, sodium salt
Batch no.: CFQ41756
CAS no.: not available
Radiochemical purity (analysed): 100% w/w
Specific activity: 81 mCi/mmol
Molecular weight: 146.7 g/mol
Chemical structure:



Appearance: solid
Expiry date: 2016-03

5. Water System:
Water was sampled from a natural aerobic surface water source in Rhineland-Palatinate (67374 Hanhofen, Germany). The location, date of sampling and conditions of the water at sampling time were recorded.
Water was sampled from the top 5 to 10 cm of the natural resource. The water was transported in polyethylene containers to the laboratory. Since the transport duration did not exceed 2 to 3 hours, the water samples did not have to be cooled to 4°C. Prior to use, coarse particles were removed by filtration through a filter with 100 µm mesh size. The test water was cooled to 4 °C and aerated prior to use.
The water system characteristics are summarized in table B.8.2.2.2-1.

Table B.8.2.2.2-1: Physico-chemical characteristics of the water system

at the time of sampling		at study start	
Parameter	**Results**	**Parameter**	**Results**
Temperature [°C]	21		
pH	8.18	pH	7.98

at the time of sampling		at study start	
Parameter	**Results**	**Parameter**	**Results**
Oxygen (below the water surface) [mg/L]	9.58	Total Organic Carbon (TOC) [mg/L]	8.4
Oxygen (water/sediment interface) [mg/L]	9.1	Dissolved Organic Carbon (DOC) [mg/L]	8.4
Redox [mV]	178	BOD5 [mg/L]	<1
Appearance	low turbidity	Suspended soils [mg/L]	3.0
Smell	neutral		

B. STUDY DESIGN

1. Experimental conditions

1.1. Equilibration
The test vessels were each filled with 500 mL surface water (4 days after sampling) and incubated at 20 ± 3°C in the dark for one day. Each water system was aerated by a slightly orbital movement of the test vessel on an orbital shaker and constant air flow.

1.2. Test conditions
Samples were incubated in the dark at 20 ± 3°C and aeration was performed using slightly constant orbital movement and constant air flow.
Each water system included flasks as follows:
- 20 samples, treated with 9.8 µg/L [cyclohexene-^{14}C]Captan. 18 were analysed
- 20 samples, treated with 93.3 µg/L [cyclohexene-^{14}C]Captan. 18 were analysed
- 4 sterilised samples, treated with 93.3 µg/L [cyclohexen.-e-^{14}C]Captan. 2 were analysed
- 6 reference samples, treated with 10 µg/L [ring-U-^{14}C]Benzoic acid, sodium salt, 4 were analysed
- 2 blank controls

All flasks were equipped with two sodium hydroxide traps to capture the carbon dioxide and one Tenax® trap to capture the organic volatiles.

1.3. Application
Two different test concentrations (9.8 µg/L and 93.3 µg/L) of the radio-labelled test item were used. Based on the specific activity of 6.77 MBq/mg, this corresponds to an applied radioactivity of about 0.033 MBq and 0.32 MBq per vessel, respectively.
The application solutions were prepared as follow:
- High application rate (A_HT_1): 4.0 mL radio-labelled test substance was dissolved in ethanol.
- Low application rate (A_HT_2): 0.34 mL A_HT_1 was dissolved in 3.06 mL ethanol.

The application volume was 125 µL A_HT_1 and 131 µl A_HT_2. The concentration of the application solutions was determined by LSC measurements.
The application solutions were added in small drops directly onto the surface of the water of each test flask.
The concentration of the organic solvent was below 1% of the amount of test water present in each test vessel.

The application solution of the reference item [ring-U-^{14}C] Benzoic acid, sodium salt was prepared by dissolving an aliquot in 10 mL water. The concentration of the reference item solution was determined by LSC measurements.
The application volume was 71 µL.

2. Sampling
Duplicate samples of each system were worked up at the following sampling time points:
0, 0.04 (1 h), 0.08 (2 h), 0.17 (4 h), 1, 4, 14, 21 and 60 days after treatment.
The flasks for the reference item were sampled on day 0 and 7.

3. Description of analytical procedures

3.1. Organic Volatiles
Traps for organic volatiles (Tenax®) were extracted with 5 mL acetone for one hour on a flatbed shaker and the amount of radioactivity in the extract was determined by liquid scintillation counting (LSC) of an aliquot (1 × 0.5 mL).

3.2. Carbon Dioxide
The radioactive carbon dioxide evolved from the test system was trapped by two series-connected flasks containing sodium hydroxide. They were monitored for radioactivity at the sampling date of the corresponding flask by LSC.

3.3. pH-value and Oxygen Concentration
The pH-value and the dissolved oxygen concentration of the water phase were measured in the blank controls once a week throughout the study.

3.4. Water Phase
The amount of radioactivity in the test water was determined by LSC measurement. At each sampling, four aliquots (each 2 mL) were taken from the water phase before it was poured out of the incubation flask. Two aliquots served for determination of the total radioactivity within the water phase. The other two aliquots were used for determination of the radioactivity after stripping out the dissolved $^{14}CO_2$. This was performed by adding 200 µL of acetic acid to each aliquot, shaking vigorously and measuring the remaining radioactivity by LSC an hour later. In the mass balance, the amount of stripped out $^{14}CO_2$ was added to the amount of $^{14}CO_2$ measured in the sodium hydroxide traps.
A further aliquot of the test water was analysed by HPLC.

3.5. Quantification of Radioactivity
The quantity of radioactivity in solutions was determined by LSC. Each solution (water phase, extracts of water phase and all solutions during sample preparation) containing radioactivity or expected to contain radioactivity was analysed. The total volume of each solution was determined. From every sample an aliquot was diluted and mixed with scintillation cocktail (Scintillator-Rotiscient).
The beta particles, which are caused by radioactive disintegration, initiate a photochemical excitation in the mix with liquid scintillation cocktail. The efficiency of photochemical excitation and observation of the emitted photons by photo multiplier was corrected for external standard radiation in the liquid scintillation counter. The results of these determinations were analysed on their energy spectrum (identification of ^{14}C) and quantified (as total decay of ^{14}C in measurement vial). The analytical limits were obtained from blank samples containing no radioactivity. LOQ was set to 50 dpm (decays per minute).

3.6. Characterisation of Radioactivity
HPLC method as main method and LC-MS/MS as confirmatory method were used to characterise the radioactivity.

3.7. HPLC System
The radioactivity of the application solution and the samples was separated with HPLC, whereas fractions of 0.08 min were collected and analysed by LSC (offline).
The radioactivity of [cyclohexene-^{14}C]Captan and its metabolites were received by offline LSC measurements after HPLC and the data were transferred in Excel. Only fractions > 20 dpm were used for the calculation of the peak area.

3.8. LC-MS/MS System
Selected samples were analysed for [cyclohexene-^{14}C]Captan residues by a Shimadzu HPLC system coupled with mass spectrometry.

3.9. Quantification and detection limits (LOQ and LOD)
The limit of quantification (LOQ) of radioactive fractions analysed by LSC was set to 20 dpm and therefore below 10% AR. LOD was defined as a half LOQ and therefore >1 % of the initial amount applied.

II. RESULTS AND DISCUSSION

A. MASS BALANCE
Mean recoveries of radioactivity in the water system within 60 days of incubation with the low (9.8 µg/L) and high (93.3 µg/L) test concentrations were within the range of 97.1% to 105.2% AR (table B.8.2.2.2-2) and 97.6% to 104.2% AR (table B.8.2.2.2-3), respectively.

B. DISTRIBUTION OF THE RADIOACTIVITY

Low concentration samples (9.8 µg/L):

The amount of radioactivity in the water phase ranged between 96.2% - 105.2% AR after 60 days of incubation (**Table 7.2.2.2-2**). Carbon dioxide formed in maximum amounts of 1.3% and organic volatiles were below 0.1% AR.

Table B.8.2.2.2 -2: Distribution of the radioactivity between test water, carbon dioxide and organic volatiles in % of the applied radioactivity (AR) (mean values) for the test concentration of 9.8 µg/L

Sampling interval [days]	0	0.04	0.08	0.17	1	4	14	21	60
	% AR								
Water phase	100.2	97.3	105.2	101.2	103.2	98.9	101.2	101.5	96.2
Carbon dioxide	0	0.1	0	0.1	1.0	0.3	1.0	1.3	1.0
Organic volatiles	n.a.	0	0.1	0	0	0	0	0	0
Recovery	100.2	97.5	105.2	101.4	104.2	99.3	102.2	102.8	97.1

n.a.: not analysed

High concentration samples (93.3 µg/L):

The amount of radioactivity in the water phase ranged between 96.2% - 103.4% AR after 60 days of incubation (**Table 7.2.2.2-3**). Carbon dioxide formed in maximum amounts of 3.4% AR and organic volatiles were below 0.1% AR.

Table B.8.2.2.2 -3: Distribution of the radioactivity between test water, carbon dioxide and organic volatiles in % of the applied radioactivity (AR) (mean values) for the test concentration of 93.3 µg/L

Sampling interval [days]	0	0.04	0.08	0.17	1	4	14	21	60
	% AR								
Water phase	96.9	100.8	101.7	101.5	103.4	99.6	103.4	99.4	96.2
Carbon dioxide	3.4	0.3	1.0	0.1	0.3	0.6	0.8	1.6	1.4
Organic volatiles	n.a.	0	0	0	0	0	0	0	0
Recovery	100.3	101.1	102.7	101.6	103.8	100.3	104.2	101.0	97.6

n.a.: not analysed

C. CHARACTERISED RADIOACTIVITY

Low concentration samples (9.8 µg/L):

The concentration of [cyclohexene-^{14}C]Captan was < LOQ after 1 hour of incubation from initially 95.1% AR. Five major metabolites were detected, whereat two could be identified as THPI and THPAM at maximal amounts of 69.2% AR (1 h) and 77.9% AR (14 d), respectively. The unknown major metabolites M2, M3 and M7 were detected in maximum amounts of 52.9% (2 h), 88.9% (1 d) and 35.8% AR (60 d), respectively. Additionally, two minor metabolites, M1 and M6, occurred once at amounts of 1.9% AR (0 d) and 6.4% AR (21 d), respectively. For a detailed characterisation refer to table B.8.2.2.2-4.

Table B.8.2.2.2-4: Characterisation of the water phase in % of the applied radioactivity (AR) for the test concentration of 9.8 µg/L (mean of duplicates)

Sampling interval [days]	0	0.04	0.08	0.17	1	4	14	21	60
	% AR								
Parent	95.1	0	0	0	0	0	0	0	0
M1	1.9	0	0	0	0	0	0	0	0
THPI	0	69.2	35.9	47.4	2.5	4.2	0	0	0
M2	0	28.1	52.9	37.4	0	0	0	0	0
M3	0	0	0	0	88.9	43.2	22.3	20.3	14.2
THPAM	0	0	11.8	12.3	11.8	41.8	77.9	72.1	46.2
M7	0	0	0	0	0	0	1.0	2.6	35.8
M6	0	0	0	0	0	0	0	6.4	0

High concentration samples (93.3 µg/L):

The concentration of [cyclohexene-^{14}C]Captan was < LOQ after 1 hour of incubation from initially 91.2% AR. Five major metabolites were detected, whereat two could be identified as THPI and THPAM at maximal amounts of 36.3% AR (2 h) and 72.4% AR (14 d), respectively. The unknown major metabolites M2, M3 and M7 were detected in maximum amounts of 52.7% (1 h), 87.2% (1 d) and 14.7% AR (60 d), respectively. Additionally, five minor metabolites, M1, M4, M5, M6 and M9, occurred at amounts of 0.5% AR (0 d), 1.6% AR (2 h), 2.5% AR (14 d), 5.4% AR (21 d) and 5.2 % AR (0 d), respectively. For a detailed characterisation refer to table B.8.2.2.2-5.

Table B.8.2.2.2-5: Characterisation of the water phase in % of the applied radioactivity (AR) for the test concentration of 93.3 µg/L (mean of duplicates)

Sampling interval [days]	0	0.04	0.08	0.17	1	4	14	21	60
	% AR								
Parent	91.2	0	0	0	0	0	0	0	0
M1	0.5	0	0	0	0	0	0	0	0
M9	5.2	0	0	0	0	0	0	0	0
THPI	0	29.7	36.3	0	0	0.4	0	0	0
M2	0	52.7	41.1	0	0	0	0	0	0
M3	0	0	0	86.2	87.2	47.1	25.4	18.9	16.1
THPAM	0	18.4	22.8	15.3	16.2	52.1	72.4	68.9	63.7
M4	0	0	1.6	0	0	0	0	0	0
M5	0	0	0	0	0	0	2.5	1.9	1.7
M6	0	0	0	0	0	0	0	5.4	0
M7	0	0	0	0	0	0	3.2	4.3	14.7

Sterilized Samples

The sterilized test samples were sampled and analysed at day 2. The mean recovery of radioactivity in the water system of the sterilized test samples was 105.0% AR. $^{14}CO_2$ was detected at mean amounts of 0.4% AR. No organic volatiles were detected.

No parent substance was observed after 2 days of incubation. THPAM was detected at amounts of 28.7% AR. The unknown metabolite M3 was observed at amounts of 65.9% AR. The amount of metabolite M7 observed was 1.6% AR. The degradation pattern in the sterile sample indicates that the decline of [cyclohexene-^{14}C]Captan was (partially) mediated by hydrolysis.

Table B.8.2.2.2-6: Distribution of the radioactivity between test water, carbon dioxide and organic volatiles in % of the applied radioactivity (AR) (mean values) in the sterile samples

Sampling interval [days]	2
	% AR
Water phase	104.6
Carbon dioxide	0.4
Organic volatiles	0
Recovery	105.0

Table B.8.2.2.2-7: Characterisation of the water phase in % of the applied radioactivity (AR) (mean values) in the sterile samples

Sampling interval [days]	2
	% AR
Parent	0
M3	65.9
THPAM	28.7
M7	1.6
Total	102.8

Reference Samples

The reference samples were sampled and analysed at day 0 and 7.

The mean recovery of radioactivity in the water system of the reference samples was 100% and 96.7% AR at 0 and 7 DAT, respectively. After 7 days, 80% AR of the reference substance were mineralised. This indicates that the test system was biologically active. Therefore, the test was valid.

D. pH-VALUE AND OXYGEN CONTENT

The measurement of pH-value (range: 8.29-8.52) and oxygen content (range: 8.52-12.71 mg/L) demonstrated constant experimental conditions during the test.

Based on the current results a preliminary metabolic pathway could be proposed:

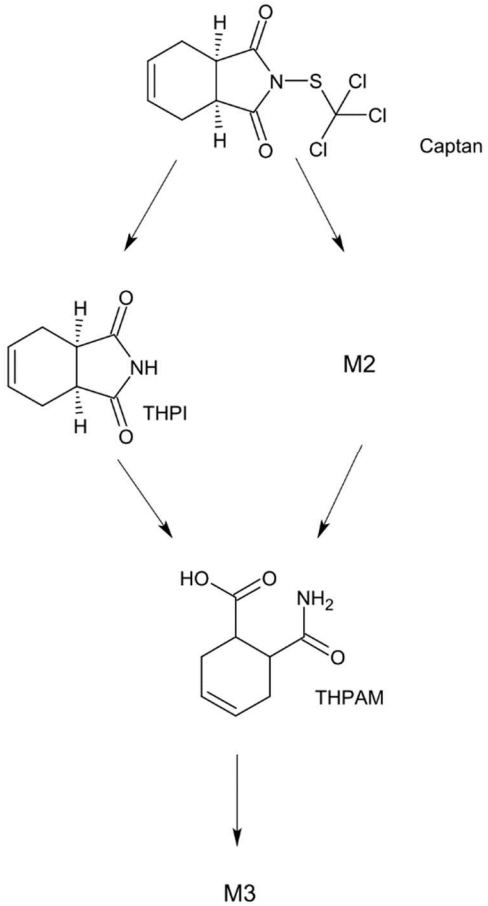


Figure B.8.2.2.2-1: Proposed metabolic pathway of captan in surface water

III. CONCLUSIONS

After 7 days 80% AR of the reference substance were mineralised. Thus, the test system was biologically active and the test was valid.

Mean recoveries of radioactivity in the water system within 60 days of incubation with the low and high test concentrations were within the range of 97.1% to 105.2% AR and 97.6% to 104.2% AR, respectively.

The amount of the applied radioactivity of the parent substance was < LOQ after 1 hour of incubation for both concentrations. Thus, the DT_{50}-value can be assumed to be < 1 h.

Five major metabolites were formed during the whole incubation period. Two could be identified as THPI and THPAM at maximal amounts of 69.2% AR (1 h) and 77.9% AR (14 d), respectively. M2, M3 and M7 were found at maximum amounts of 52.9% (2 h), 88.9% (1 d and 35.8% AR (60 d), respectively. Additionally, five minor metabolites, M1, M4, M5, M6 and M9, occurred at maximum amounts of 1.9% AR (0 d), 1.6% AR (2 h), 2.5% AR (14 d), 6.4% AR (21 d) and 5.2 % AR (0 d), respectively.

The formation of organic volatiles was negligible for both tested concentrations. Only amounts <0.1% AR were detected. Carbon dioxide was detected at maximum amounts of 3.4% AR (0 d).

In sterile samples, [cyclohexene-^{14}C]Captan was degraded to THPAM, M3 and M7 after 2 days of incubation. The degradation pattern indicates that the parent substance was (partially) degraded by hydrolysis.

Comments RMS

No description of the sampling site was given; no information concerning contamination history was presented. The amount of test substance and reference substance applied is not clearly described since the concentration in the application solution was not given.
LOQ was below 10 % AR as required but LOD was > 1 % AR (should be at least 1 % AR).

The metabolites M2, M3 and M7 exceeded 10 % of AR and should be identified.

An amendment (Study 10, 2016) to the aerobic mineralisation study 9 (2016) summarised above was provided. In this amendment the identification of the metabolites M3 and M7 is presented and discussed; it is summarised below.

Study 10 (2016)

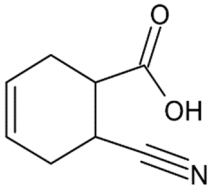
Reference:	**Amendment 1: Aerobic Mineralisation of [^{14}C] Captan in Surface Water;**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2016
Report/Doc. number:	R-35636
Guideline(s):	OECD 309 (2004)
GLP:	Yes
Deviations:	Minor
Validity:	Yes
Status:	Submitted for renewal

I. MATERIALS AND METHODS

A. MATERIALS

As summarised above in KCA 7.2.2.2/01 (study 9, 2016b).
In addition, the following reference item was also used:

Reference item: **THCY**
Chemical name: 6-cyanocyclohex-3-ene-1-carboxylic acid
Batch no.: 534-046-00
CAS no.: 115747-07-4
Purity (analysed): 100% w/w
Molecular weight: 151 g/mol
Chemical structure:



Appearance: solid (white)
Expiry date: 2017-06

Reference item: **THPI-Epoxid**
Chemical name: Octahydro-1aH-oxireno[2,3-f]isoindole-3,5-dione
Batch no.: 534-111-00
CAS no.: 6251-87-2
Purity (analysed): 98.1 % w/w
Appearance: solid (white)
Expiry date: 2017-10

B. STUDY DESIGN

As summarised above in KCA 7.2.2.2/01 (Study 9, 2016b).

Additionally, this study amendment provided information on the structural elucidation of the two metabolites M3 and M7 by LC/MS. A HPLC system was utilised along with a Raytest Mira radioactivity detector and MS-detector. Methanol was used instead of acetonitrile due to significantly better MS response of all analytes in methanol. Samples were analysed by LC-MS; the mass accuracy for all metabolites was ≤ 1 ppm.

II. RESULTS AND DISCUSSION

As summarised above in KCA 7.2.2.2/01 (Study 9, 2016b) corrected for typing errors.
Additionally, this study amendment provided information on the characterisation of the two metabolites M3 and M7 by LC/MS.

Low concentration samples (9.8 µg/L):
[Cyclohexene-^{14}C]Captan decreased from initially 95.1% AR to values < LOQ within 1 hour of incubation. The metabolites THPI and THPAM were detected at maximal amounts of 69.2% (1 h) and 77.9% (14 d) AR. The metabolites M3 and M7 were identified as THCY and THPAI. They were observed in amounts up to 88.9% (THCY, 1 d) and 35.8% (THPAI, 60 d) AR, respectively.
The unknown minor metabolites M1 and M6 were detected once at amounts of 1.9% (0 d) and 6.4% AR (21 d).
Co-chromatography failed for identification of the transient metabolite M2 nor could it be related to the mass of one of the reference compounds during LC-MS/MS experiments. Based on sponsor request, the identity of the unknown metabolite M2 (max amount 60.6% AR) was not further analytically investigated by LC/MS as this was a transient metabolite rapidly formed and equally rapidly degraded in water. Moreover, M2 was unstable in the stored samples.

Table B.8.2.2.2-8: Characterisation of the water phase in % of the applied radioactivity (AR) for the test concentration of 9.8 µg/L (mean of duplicates)

Sampling interval [days]	0	0.04 (1 h)	0.08 (2 h)	0.17 (4 h)	1	4	14	21	60
	% AR								
Parent	95.1 [a]	0	0	0	0	0	0	0	0
M1	1.9 [a]	0	0	0	0	0	0	0	0
THPI	0	69.2 [a]	36.1 [a]	52.6 [a]	2.5	0 [a]	0	0	0
M2	0	28.1 [a]	60.6 [a]	36.9 [a]	0	0	0	0	0
THCY (M3)	0	0	0	0	88.9	44.3 [a]	22.3	20.3	14.2
THPAM	0	0	13.3 [a]	12.0 [a]	11.8	54.8 [a]	77.9	72.1	46.2
THPAI (M7)	0	0	0	0	0	0	1.0	2.6	35.8
M6	0	0	0	0	0	0	0	6.4	0

[a] based on single values

High concentration samples (93.3 µg/L):
[Cyclohexene-^{14}C]Captan decreased from initially 91.2% AR to values < LOQ within 1 hour of incubation. The metabolites THPI and THPAM were detected at maximal amounts of 36.3% (2 h) and 72.4% (14 d) AR. The metabolites M3 and M7 were identified as THCY and THPAI. They were observed in amounts up to 87.2% (THCY, 1 d)) and 14.7% (THPAI, 60 d) AR, respectively.
The unknown minor metabolites M1 and M6 were detected once at amounts of 0.5% (0 d) and 5.4% (21 d) AR.
Co-chromatography failed for identification of the transient metabolite M2 nor could it be related to the mass of one of the reference compounds during LC-MS/MS experiments. Based on sponsor request, the identity of the unknown metabolite M2 (max amount 52.7% AR) was not further analytically investigated by LC/MS as this was a transient metabolite rapidly formed and equally rapidly degraded in water. Moreover, M2 was unstable in the stored samples.

Table B.8.2.2.2-9: Characterisation of the water phase in % of the applied radioactivity (AR) for the test concentration of 93.3 µg/L (mean of duplicates)

Sampling interval [days]	0	0.04 (1 h)	0.08 (2 h)	0.17 (4 h)	1	4	14	21	60
	% AR								
Parent	91.2	0	0	0	0	0	0	0	0
M1	0.5	0	0	0	0	0	0	0	0
M9	5.2	0	0	0	0	0	0	0	0
THPI	0	29.7 [a]	36.3	0	0	0.4	0	0	0
M2	0	52.7 [a]	41.1	0	0	0	0	0	0
THCY (M3)	0	0	0	86.2	87.2	47.1	25.4	18.9	16.1
THPAM	0	18.4 [a]	22.8	15.3	16.2	52.1	72.4	68.9	63.7
M4	0	0	1.6	0	0	0	0	0	0
M5	0	0	0	0	0	0	2.5	1.9	1.7
M6	0	0	0	0	0	0	0	5.4	0
THPAI (M7)	0	0	0	0	0	0	3.2	4.3	14.7

[a] based on single values

III. CONCLUSIONS

After 7 days 80% AR of the reference substance were mineralised. Thus, the test system was biologically active and the test was valid.
Mean recoveries of radioactivity in the water system within 60 days of incubation with the low and high test concentrations were within the range of 97.1% to 105.2% AR and 97.6% to 104.2% AR, respectively.
The amount of the applied radioactivity of the parent substance was < LOQ after 1 hour of incubation for both concentrations. Thus, the DT_{50}-value can be assumed to be < 1 h.
Five major metabolites were formed during the whole incubation period. Two were identified in the original report as THPI and THPAM at maximal amounts of 69.2% AR (1 h) and 77.9% AR (14 d), respectively. This report amendment provided identification of two additional metabolites THCY (M3) and THPAI (M7) which occurred at maximum amounts of 88.9% (1 d) and 35.8% AR (60 d), respectively. The fifth metabolite, M2, could not be identified. However, this was a transient metabolite rapidly formed and equally rapidly degraded in water and, furthermore, was unstable in the stored samples.
Additionally, five minor metabolites, M1, M4, M5, M6 and M9, occurred at maximum amounts of 1.9% AR (0 d), 1.6% AR (2 h), 2.5% AR (14 d), 6.4% AR (21 d) and 5.2 % AR (0 d), respectively.
The formation of organic volatiles was negligible for both tested concentrations. Only amounts <0.1% AR were detected. Carbon dioxide was detected at maximum amounts of 3.4% AR (day 0).
In sterile samples, [cyclohexene-^{14}C]Captan was degraded to THPAM (28.7 %), THCY (M3, 65.9 %) and THPAI (M7, 1.6 %) after 2 days of incubation. The degradation pattern indicates that the parent substance was (partially) degraded by hydrolysis.

Comments RMS

The following points would need further clarification:

- At some sampling time points only one value (instead of the mean of two values) was used:
  Day 0: a technical error occurred during sample processing, day 0.04 (1 h): mass balance recovery < 90 %, day 0.08 (2 h), 0.17 (4 h) and 4: no explanation was given and should be provided.
- It is not clearly explained why the identification of M7 (as metabolite THPAI) was not possible earlier. The reference substance THPAI was already used in the final report of the study.

- For the additional HPLC system combined with LC/MS presented in the amendment to the final report no RT (retention time) is given for the metabolite THPAI.
- The exact mass and elemental composition for THPI (242.0401; $C_9H_9NO_4Na_2$) should be confirmed or corrected.

The notifier provided a statement for Report Amendment 1 for clarification of the points mentioned above, the statement is summarised below.

The notifier provided a statement for Report Amendment 1 for clarification of the points mentioned above, the statement is summarised below.

Study 11 (2017)

Reference:	**Statement for Report Amendment 1: Aerobic Mineralisation of [^{14}C] Captan in Surface Water;**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2017
Report/Doc. number:	S14-05599 / R-35636
Guideline(s):	OECD 309 (2004)
GLP:	No
Deviations:	-
Validity:	Yes
Status:	Submitted for renewal

Point for clarification: At some sampling time points of the low concentration (9.8 µg/L) the value of one replicate was used (instead of the mean of two values). For the samples at day 0.08 (2 h), day 0.17 (4 h) and day 4 no explanation was given.
Clarification:
For replicates of these intervals substantial amounts of radioactivity were assigned to HPLC/radiodetection-signals which were classified as artefacts. The classification of the peaks as artefacts is based on peak characteristics in the chromatograms. The respective signals consist of one single data point. The signal at day 4 was observed only one time in one replicate. Since similar signals were not observed in other samples from the same study the signal was classified as aretefact.
Those signals classified as artefacts were excluded from further evaluation and, consequently, values from the whole respective replicate cannot be used for further evaluation. Those samples had to be excluded in total, and therefore, only single values were used at those time points.

Point for clarification: It is not clearly explained why the identification of M7 (as metabolite THPAI) was not possible earlier. The reference substance THPAI was already used in the final report of the study.
Clarification:
Due to the unexpected shift between radioactivity trace and UV trace in the HPLC analysis, further attempts had to be done for a clear identification. Consequently, analysis with LC-MS/MS was not originally scheduled but had to be performed for a clear identification. After LC-MS/MS experiments further experimental effort was made analysing the respective fraction expected to be THPAI by high resolution LC-MS. Those experiments could be run only after submission deadline due to capacity reasons.

Point for clarification: For the additional HPLC system combined with LC/MS presented in the amendment to the final report, no retention time is given for the metabolite THPAI.
Clarification:
The retention time is given in the report for all methods used. But for LC/MS there was a typing error in the tabulated list of reference compounds and retention times. The 'I' is missing for THPAI and reads now THPA. The retention time of THPAI in LC/MS analysis is 13.4 minutes. It can be seen in Figure 23, where the retention time is given for the respective signal and connected to the correct reference name.

Point for clarification: Please confirm/correct the exact mass and elemental composition for THPI (242.0401; $C_9H_9NO_4Na_2$).
Clarification:
The exact mass of THPI is given in the report as seen during MS analysis as adduct of M+Na+HCOONa. But this explanation was missing.

Comments RMS
None. No further clarification needed.

In addition, a position paper (2016) is presented here discussing the metabolism observed in the new aerobic mineralisation of Captan in surface water study summarised above (Study 9, 2016b and study 10, 2016, respectively) and proposing a structure for the unidentified metabolite M2.

Study 13 (2016)

Reference:	**Metabolism of Captan in the environment**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2016
Report/Doc. number:	R-37590/1405319.UKO-4905
Guideline(s):	Not relevant, position paper
GLP:	Not relevant, position paper
Deviations:	Not relevant, position paper
Validity:	Not relevant, position paper
Status:	Submitted for renewal

Summary

In the metabolism mineralisation study (refer above to study 9, 2016b & study 10, 2016) conducted with radioactive Captan, metabolites THPI, THCY, THPAM and THPAI were identified by co-chromatography using corresponding reference standards or by LC/MS (see metabolic pathway below in figure 7.2.2.2-2). Additionally, a significant unknown metabolite M2 was detected and represented up to 60.6% AR. M2 showed to be an intermediate metabolite which was further rapidly hydrolysed and could not be identified by LC/MS. Therefore, the data from the new mineralisation study, and from the existing hydrolysis, water sediment and anaerobic soil studies were evaluated in order to compare the metabolic pattern and propose a structure for the unknown M2 metabolite.

Aerobic mineralisation study (study 9, 2016b & study 10, 2016):

From the mineralisation study, the pattern results clearly show that M2 is directly formed from the parent. After application of Captan to the test system it is instantaneously hydrolysed to form THPI and M2 and their concentration will depend on the dissolved oxygen concentration as well as on the pH or ions present in the system. These two metabolites were further degraded to form mainly THCY.

As a first step, THPI and M2 were first degraded to only THPAM. This reaction seems to be stopped after about 2 hours of incubation. Thereafter, THPI and M2 were completely degraded to only THCY. THCY was then further slowly hydrolysed to THPAM. It seems that when most probably the water oxygen content was reduced in the system due to consumption by the oxidation of the parent to M2/THPAM and sodium carbonate, the reaction changed to lead to the formation of only THCY. This is in agreement with the results of the anaerobic soil study with [carbonyl-14C]Captan (please refer to DAR 2005) where THCY was only detected under anaerobic conditions, but not in the aerobic water sediment study. It should be noted that control flasks showed high oxygen concentrations. This is because the control flasks are not treated, and are opened before oxygen measurement and at each interval, and therefore they might show higher oxygen values.

Furthermore, for the high and low doses treated samples, there is evidence that when M2 concentration decreases, THPI concentration increases. Therefore, M2 must still have the molecular structure part of THPI.

Because the rate of degradation of Captan in the mineralisation study is very rapid, the formation of THPI and M2 can only be due to hydrolysis and not to microbial degradation. Therefore, it is to be expected that the same metabolites are formed in the mineralisation study as in the hydrolysis studies, at similar temperature and at the pH 8-9 of the water in the mineralisation study.

Hydrolysis studies (DAR 2005), refer also to 7.2.1.1

In the DAR hydrolysis study (study 2, 1989b), the hydrolysis conducted at 25°C and pH 5, 7 and 9 showed the formation of THPI and THPC (S-tetrahydrophthalimido thiocarbonate) as main metabolites formed instantaneously. THPC was the main hydrolysis product at pH 9 representing up to 46.6% AR after 10.5 minutes. As the test system was sterile, the formed amounts of THPI and THPC remained stable until the end of the incubation (ca. 10-11 hours).

These results are similar to the mineralisation study results where water with a pH of ca. 8.5 was used. The rapid degradation of these hydrolysis products in the mineralisation study is mainly due to further microbial degradation. A hydrolysis half-life of 152 and 3 days at pH 7 and 9, respectively, was estimated at 25°C for THPI. It could be estimated that this will be the same for THPC, based on DAR hydrolysis study results. Additionally THPC showed similar HPLC chromatographic behaviour and polarity when compared to M2. Although a different HPLC method was used, this showed similar chromatographic polarity conditions.

Water sediment study (DAR 2005) / aerobic conditions
In the water sediment study, THPI was the main metabolite. Additional microbially formed metabolites such as THPAM, THPAI, THPIdiol and THPIepox were detected. However, no THCY was detected.
Based on the results of the mineralisation study, THCY should have been also detected in the water phase due to its rapid formation in water. THPI was degraded in water directly and mainly to THPAM, due most probably to the higher oxygen water content in the water/sediment study. This can be confirmed by a new water sediment study (Dodd, 2016, see KCA 7.2.2.3/02 for full study summary) conducted under anaerobic conditions.

Water sediment (Dodd, 2016) / anaerobic conditions
When Captan was applied to the aquatic systems under anaerobic conditions, similar behaviour and metabolic pattern as detected in the mineralisation study was observed. Captan was instantaneously and mainly degraded to THPI in time 0 samples. THPI showed to degrade mainly to THCY under anaerobic conditions, as a first step. The study also shows that THCY degrades rapidly back to THPI by re-cyclisation under anaerobic conditions but observed only in the short time intervals. A much slower rate of degradation of THCY was observed in the longer intervals, which might be due to the consumption of any introduced oxygen during the application of the samples (see also soil anaerobic study). THPI or THCY were further degraded to THPAM. An unknown metabolite (unknown 1), which corresponds to M2 from the aerobic mineralisation study based on its chromatographic behaviour and retention time, was observed in the first intervals between 1 and 4 hours of incubation and represented up to 34% AR and highest in the water with the highest pH (pH 8) (similarly to the hydrolysis study). Therefore, the formation of the unknown is due to hydrolysis in the presence of any oxygen introduced in the system during the application. The unknown 1 (or M2) metabolite showed to further degrade to THPI.

Soil anaerobic study (DAR 2005)
In the anaerobic soil (pH 7.2 - 7.7) studies using the trichloromethyl label and following ageing under aerobic conditions, apart from CO_2, no significant metabolites were formed similarly to the aerobic conditions. This shows that trichloromethyl group is rapidly oxidised and mainly under aerobic conditions, as no anaerobic conditions will have been established in the system within the short time after flooding.
In the anaerobic soil study where anaerobic conditions were achieved before application of Captan by flooding the soil with water and flushing with nitrogen, a similar degradation as in the hydrolysis studies was observed, with the exception of the formation of THCY. The major metabolites were THPI, THCY, THPAM and THPAI. THCY represented up to 21% AR and remained practically constant during the whole incubation period of 256 days. Therefore, it can be concluded that THCY is formed in a system with low oxygen concentration (available in the opened system during the treatment) and without oxygen, THCY will not be further oxidised to THPAM.
The pattern of metabolites of Captan applied to water/soil system under anaerobic conditions is similar to the pattern observed in the mineralisation study. It should however be pointed out that the first interval was taken only after 7 days in the flooded anaerobic soil study.
Therefore, it can be concluded that THCY can only be formed in systems with low oxygen concentration. This might explain its formation in the mineralisation study once all oxygen present in water was consumed by part of Captan oxidation to THPI and the mineralisation of the trichloromethyl group to CO_2.

Conclusion

- M2 metabolite was further degraded to THPI and therefore it can only be a chemical structure between the parent and THPI due to its rapid formation by hydrolysis
- M2 was rapidly degraded and is in agreement with the results of the trichloromethyl label studies by mineralisation of the carbonyl group to form THPI
- M2 showed similar chromatographic behaviour as the hydrolysis product THPC
- M2 is formed by hydrolysis of Captan in water with low oxygen concentration

Therefore, based on the rapid formation of M2 which is only due to hydrolysis, it can be concluded that the unknown metabolite M2 formed in the mineralisation study or unknown 1 formed in the anaerobic water sediment

study is clearly THPC (S-tetrahydrophthalimido thiocarbonate) and can be considered as a non-stable intermediate as it will be extremely rapidly degraded in the environment or aquatic systems.
Based on these studies results, the metabolic pathway of Captan in water of the mineralisation study can be postulated as presented below in **Figure 8.2.2.2-2**.

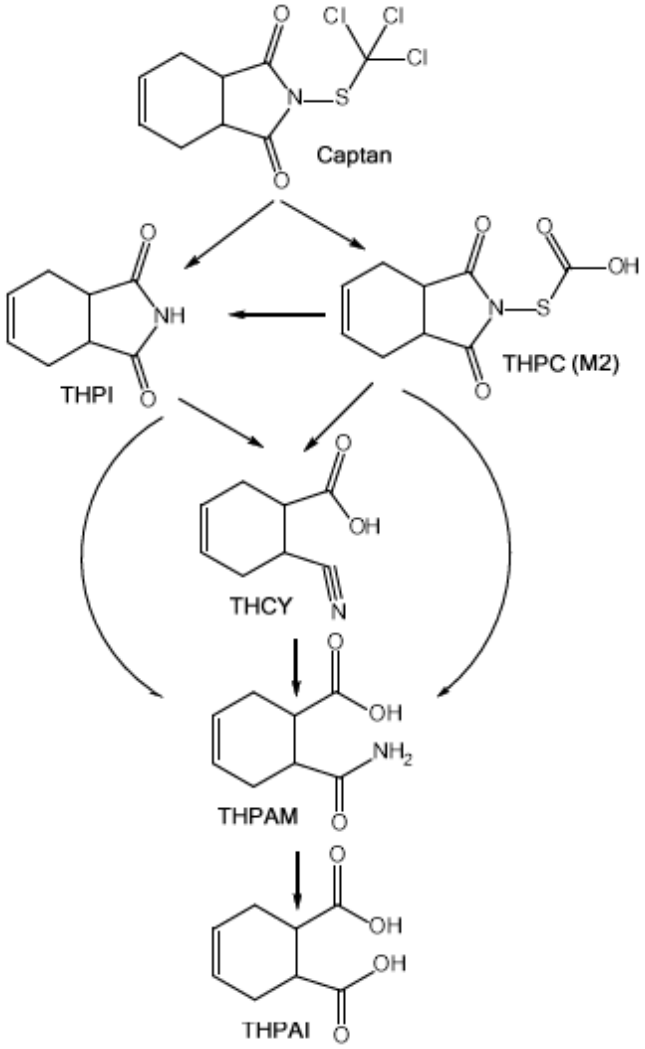


Figure 8.2.2.2-2: Proposed metabolic pathway of Captan in water of the aerobic mineralisation study

Comments RMS

Hydrolysis
The amounts of THPI and THPC were not stable during the hydrolysis study: At pH 7 and pH 9 the amounts of THPI and THPC were increasing as the amount of captan was decreasing. At pH 5 the amount of THPI was increasing as the amount of captan was decreasing; the amount of THPC was low, reached its peak at the beginning (0.1 hours) and then decreased.

Aerobic mineralisation:
Captan rapidly degraded to THPI and M2. These two metabolites were further degraded to THPAM first, and then to THCY (first detection after 4 h or 1 day), which was further degraded to THPAM. The rapid degradation of captan (no captan after 1 h detected) and of THPI (no THPI after 4 h and 2.5 % after 1 d) and of M2 (no M2 after 4 h or 1 d) indicates that the degradation is mainly caused by hydrolysis. This is confirmed by the known fast hydrolysis of captan and THPI at alkaline pH-values. Therefore, it seems to be possible that the same metabolites are formed in the mineralisation study as in the hydrolysis studies at

comparable environmental conditions. But, it could not be shown that the concentration of oxygen would decrease and that the depletion of oxygen would result in anaerobic conditions.
It is agreed that there is evidence that when M2 concentration decreases, THPI concentration increases. Therefore, it can be assumed that M2 still has the molecular structure part of THPI.

Aerobic water/sediment.
THCY was not detected in the aerobic water/sediment study and it could not be detected since it was not one of the reference substances. In the water extracts 3 -9 % AR (Old Basing) and 6 – 11 % AR (Virginia water) were not further identified, but it is stated in the study report that none of the unknown metabolites amounted to > 5 % AR in any of the water-sediment extracts.
The main metabolite THPI is further degraded to THPAM and THPAI; the impact of higher or lower oxygen content is not demonstrated.

Anaerobic water/sediment:
The amount of THPI increased from 4 h to 1 d after application although almost no captan was left. Therefore, THPI might be generated from unknown 1 or /and THCY (via re-cyclisation).
Neither unknown 1 (from the anaerobic metabolism study) nor M2 (from the aerobic mineralisation study) could be characterised and they were analysed with different HPLC systems in the two studies. Even if they showed similar chromatographic behaviour and retention times (unknown 1: retention time 18.7 min/19.05 min; M2: retention time 16.68 min) it was not demonstrated that they would be metabolite THPC.

Anaerobic soil study
An anaerobic soil metabolism study conducted with [trichloromethyl - ^{14}C] captan indicated that the only major degradation product was CO_2. An anaerobic soil metabolism study conducted with [carbonyl - ^{14}C] captan indicated that captan was rapidly degraded in soil under anaerobic conditions generating four major metabolites: THPI, THCY, THPAM and THPAI. The metabolite THCY was formed within 7 days and remained approximately constant at about 16-17% AR, indicating that it will be degraded very slowly under anaerobic conditions. Under aerobic conditions THCY was quickly degraded. THPAI should not be considered as major metabolite since it occurred with more than 5 % AR 112 d after application and it is not likely that anaerobic conditions will last for such a long period.

Conclusion:
The unknown metabolite M2:
The rapid degradation of captan in the aerobic mineralisation study indicates that the degradation is mainly caused by hydrolysis. Therefore, it seems to be possible that the same metabolites are formed in the mineralisation study as in the hydrolysis studies at comparable environmental conditions. As THPI concentration increases when M2 concentration decreases it can be assumed that M2 still has the molecular structure part of THPI. Therefore, it could be possible that the unknown metabolite M2 is the metabolite THPC (S-tetrahydrophthalimido thiocarbonate), but it could not be demonstrated.

The metabolite THCY:
The detection of the metabolite THCY in the aerobic mineralisation study was ascribed to low oxygen concentrations in the water during the study, which was caused by the oxidation of the parent to M2 and sodium carbonate and further mineralisation to CO_2. But the oxygen concentrations were only measured in blank control but not in the treated samples. In the blank control samples the oxygen content was not decreasing.
The metabolite THCY was further detected in anaerobic soil degradation studies and in an anaerobic water/sediment study.

During the peer-review a comment was received that it should be discussed that captan is not readily biodegradable but degrades very fast in aquatic systems:
Captan was hydrolysed very fast at all pH values in sterile water with a half-life of 11.7 hours at pH 5, 4.7 hours at pH 7 and 8.1 minutes at pH 9. Several degradation products with pH-dependent degradation rates were detected but no CO_2 was determined.
In order to to investigate ready biodegradability of captan in aquatic systems a CO_2 Evolution Test (Modified Sturm) according to OECD 301 B was conducted. The percentages of $^{14}CO_2$ production were calculated in relation to the theoretical production of $^{14}CO_2$ of Captan and the biodegradation was calculated. The mean biodegradation after 28 days was 13 %; the 60 % level was not reached. The result of the study showed that Captan is not biodegradable in the 10-days window and within 28 days.

In the aerobic mineralisation study (60 d) captan degraded very rapidly to several degradation products. Carbon dioxide was detected at maximum amounts of 3.4% AR.
In the water/sediment study captan degraded very rapidly to several degradation products. 30 d after incubation < 10 % CO_2 were detected, 90 d after incubation about 50 % AR were determined as CO_2.

The studies indicate that captan is rapidly hydrolysed to several hydrolysis products but total mineralisation (of the degradation products) occurres at later time points.

During the peer-review a comment was received that it should be discussed that captan is not readily biodegradable but degrades very fast in aquatic systems:
All aquatic studies (hydrolysis, aerobic mineralisation, water/sediment) showed a rapid degradation of captan in water to several degradation prroducts. Carbon dioxide was not detected or detected at low amounts; higher amounts of CO_2 (> 10 % AR) occurred only in the water/sediment study at later timepoints (60 d, 90 d).
The ready biodegradability was tested with a CO_2 Evolution Test (Modified Sturm). The percentages of $^{14}CO_2$ production were calculated in relation to the theoretical production of $^{14}CO_2$ of Captan. The 60 % level was not reached within 28 days.
The studies indicate that captan is rapidly hydrolysed to several hydrolysis products but total mineralisation (of the degradation products) occurres at later time points.

B.8.2.2.3. Water/sediment studies

Study 14 (1993)

Reference:	**Captan: degradation in sediment-water systems under laboratory conditions**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 1993
Report/Doc. number:	RJ1439B / 92JH101
Guideline(s):	Not specified, but complies with the SETAC guideline
GLP:	Yes, although some exceptions specified in the report
Deviations:	Minor
Validity:	Valid
Status:	Submitted for evaluation in the original DAR for the first Annex I inclusion

Summary based on original DAR

Materials and Methods: The degradation of [cyclohexene 1,2- ^{14}C]-captan (purity of unlabbeled captan: 98.9% and specific activity of the application solution: 349 Bq/µg) was studied in two natural water/sediment systems under laboratory conditions in the dark at 20°C up to 90 days. Before treatment, the systems were incubated until the redox potential in the water and sediment layers had reached equilibrium. Characteristics of the soil and water phases are summarised in table B.8.2.2.3-1 and table B.8.2.2.3-2, respectively. One sediment presented a high organic matter content and a fine texture ('Old Basing', 21.5% organic matter, 72 % clay and silt), and the other sediment a low organic matter content and a coarse texture ('Virginia Water', 5.4% organic matter, clay and silt 20 %). Each water/sediment test system contained 10% sediment based on dry weight. [Cyclohexene 1,2- ^{14}C]-captan was applied at an initial concentration of 1.2 mg/L, equivalent to a single application of 3.57 kg a.s./ha evenly distributed over 30 cm depth body of water. Untreated control systems and sterile water/sediment systems were also used.

Complete samples of the water plus sediment were taken in triplicate from each of the system at specific incubation times (0, 1, 3, 7, 14, 30, 59, 90 days) up to 90 days.

The samples were centrifuged and aliquots of the water phase analysed by LSC. Water phases were acidified and further extracted; aliquots of the aqueous and organic phases were analysed by LSC. Sediments were acidified and further extracted. Aliquots of the sediment extracts were analysed by LSC and extracted sediments combusted and further analysed by LSC. All extracts containing > 5 % AR were analysed by TLC using autoradiography and quantified by radiochromatogram scanning. The volumes of the trapping solutions were recorded and aliquots analysed by LSC.

Table B.8.2.2.3-1: Sediment characteristics for [cyclohexene 1,2 - ^{14}C]- captan sediment/water study

	Sediment 1	**Sediment 2**

Sediment name	Old Basing	Virginia Water
Location	Bridge Farm Trout Fishery, Basingstoke. Hampshire, UK	Stream in Windsor Great Park , Berkshire, UK
pH	8.01	6.17
Sand (%)	28	80
Silt (%)	40	9
Clay (%)	32	11
Texture[1]	Clay loam	Loamy sand
Organic matter (%)	21.5	5.4
Organic carbon[2] (%)[1]	12.5	3.1
Cation exchange capacity (meq/100 g)	47.8	12.5
Total nitrogen (%)	1.02	0.21
Available phosphorus (mg/L)	45.8	18.4
Dry matter %	19.3	51.8

[1] US Department of Agriculture (USDA) classification.
[2] Organic carbon = organic matter/1.72.

Table B.8.2.2.3 -2: Water characteristics for [cyclohexene 1,2 - ^{14}C]- captan sediment/water study

	Old Basing	**Virginia Water**
pH	8.1	7.8
Suspended solids (mg/L)	2	< 2
Total organic carbon (µg/L)	1.1	5.0
Total oxidised nitrogen (mg N/L)	5.0	1.4
Total phosphates (mg P/L)	0.02	0.02

Findings:

The distribution of radioactivity in the two sediment/water systems is shown in table B.8.2.2.3-3. The total recovery in old basing water-sediment system ranged from 86.3 % AR to 98.8 %AR. For Virginia water, the total recovery ranged from 74.6 % AR to 104.2 %AR.

The levels of evolved radiocarbon, as $^{14}CO_2$ were seen to increase throughout the 90-day incubation period. The rate of $^{14}CO_2$ evolution was similar for both systems, with approximately 50 % AR mineralised by day 90 of the incubation period. In contrast, < 0.01% AR was mineralised to $^{14}CO_2$ in the same 90 day period in the sterile systems.

Over the first seven days of incubation, the surface waters in the 'Old Basing' systems contained approximately 55 % AR, whereas surface waters in the 'Virginia Water' systems contained approximately 80 % AR. The amount of radioactivity in the surface water fell in both systems after day 7 to 2.4 and 0.9 % AR by day 59 in both non-sterile systems. In the sterile systems, the level of radioactivity in the surface water remained high (> 48 % AR) throughout the incubation period.

At day 0, the majority of the radioactivity in the surface water partitioned into ethyl acetate for both sediment phase types. With incubation of the 'Old Basing' system, levels of organosoluble material decreased from 14:1 (organic:aqueous phases) at day 0 to 1:1.5 by day 30. With the 'Virginia Water' system, the majority of the radiolabel in the surface water was organosoluble throughout the incubation, although the proportion in the ethyl acetate phase decreased to 2.3:1 on day 1, and remained about this level on day 30. By day 59, there were only negligible amounts of radioactivity in the water phases.

In the sterile systems, the majority of the radioactivity in the surface water remained organosoluble throughout the incubation, although by day 90, the ratio in the organic and aqueous phases had fallen to 1.4:1 in the sterile 'Old Basing' system and 7.9:1 in the sterile 'Virginia Water' systems.

The amount of radioactivity extracted from the sediments fell throughout the incubation period, from approximately 40 % AR at day 0, to 3 % AR at day 90, these values being the sum of the first and second sediment extracts. This trend was accompanied by an increase in the unextractable radiocarbon from the sediment from approximately 2 % AR at day 0 to a maximum of 50 % AR at day 59. In the 'Virginia Water' system, the amount of radioactivity extracted from the sediment increased from 9 % AR at day 0 to 16 % AR at day 1, and remained at 16 - 18 % AR until day 30. By day 59 the amount of radioactivity extracted from the sediment had fallen to 9.5 % AR and was similar (10.6 % AR) at day 90. The unextractable radiocarbon in the 'Virginia Water' sediments remained low (less than or equal to 9 % AR) until day 59 when levels rose to a maximum of about 30 % AR.

The amount of radiolabel extracted from the sterile sediments tended to be higher than the corresponding non-sterile sediments. In the sterile 'Old Basing' sediments, 53 % AR was extracted at day 0, and declined to 22 % AR at day 90. Correspondingly, levels of unextracted radioactivity in the sterile 'Old Basing' sediment increased to approximately 15 % AR over the 90 day incubation.

In the sterile 'Virginia Water' sediments, 24 % AR was extracted at day 0, and levels declined over 29 days to 15 % AR, remaining at this level for 90 days. Levels of untextracted radioactivity in the sterile 'Virginia Water' sediment remained below 2 % AR.

The levels of captan and its metabolites in the two systems are shown table B.8.2.2.3-4 for the 'Old Basing' system, and table B.8.2.2.3-5 for the 'Virginia Water' system. Even at day 0, directly after application, only 5.6 % AR was found to be captan in the 'Old Basing' water sediment extracts. Levels of captan extracted on day 0 from the sterile 'Old Basing' systems were also low with only 11 % AR in the extracts. In the 'Virginia Water' system, captan comprised a greater proportion of the extracted radioactivity in both sterile and non-sterile systems (61 and 54 % AR, respectively). By day 1, captan was not detected in any of the sample extracts, non-sterile or sterile, with either of the sediment types.

The major initial metabolite in both sediment/water systems was THPI. In the 'Old Basing' system, the decline of THPI followed first-order kinetics over the first 14 days of incubation, with a half-life of about 5 days. Levels of THPI in the 'Virginia Water' systems fluctuated over the first 30 days. However, THPI was reduced to undetectable levels (< 0.1 % AR) in both systems by day 60. In the 'Old Basing' systems, THPI was distributed approximately 50:50 between the surface water and sediment phases. In the 'Virginia Water' systems, THPI was largely associated with the water phase.

THPI was also found in the sterile systems. In the 'Old Basing' system, the total amount of extractable THPI was 77 % AR at day 0, which declined to 36 % AR by day 90. In the 'Virginia Water' system, the total level of THPI reached a maximum of 80 % AR at day 60, and declined to 64 % AR by day 90.

The second highest level of metabolite was that of THPAM, which was found virtually exclusively in the water extracts for all systems. In the 'Old Basing' systems, THPAM was found at maximum levels in the water/sediment extracts on day 7 and 14 (approximately 26 % AR) and declined to undetectable levels (< 0.1 % AR) by day 60. In the 'Virginia Water' system, levels of THPAM in the water extracts reached a maximum of 22.5 % AR at day 1, and declined to undetectable levels (< 0.1 % AR) by day 60.

In the sterile 'Old Basing' system, THPAM was detected at a maximum level of 25 % AR after 90 days, whilst in the sterile 'Virginia Water' systems, THPAM reached only 6.5 % AR at day 60, and declined to < 1 % AR by day 90.

THPAI reached a maximum level of 11 % AR on day 14 in the 'Old Basing' system, and 7.5 % AR on day 30 in the 'Virginia Water' system. THPAI was also detected in sterile systems but at very low levels (< 2.5 % AR).

Low levels of a fourth metabolite, THPI epoxide, were detected in both non-sterile and sterile systems. THPI epoxide reached a maximum level of 5 % AR in the Old Basing' non-sterile system on day 1 and declined to undetectable levels (< 0.1 % AR) by day 60. In the 'Virginia Water' system, THPI epoxide also reached its maximum level of 10% AR on day 1. In the sterile systems, the highest levels of THPI epoxide were observed later in the incubation period, at day 90 (10 % AR) in the 'Old Basing' system and at day 60 (10 % AR) in the 'Virginia Water' system.

No unknown metabolites amounting to > 5 % AR were found in any of the sediment/water systems.

Thus, the two metabolites THPI and THPAM are considered as major metabolites in water in addition to the two major metabolites in sediment (THPI and THPAI).

Table B.8.2.2.3-3: Distribution of radioactivity (% applied radioactivity) in water/sediment systems in [cyclohexene 1,2 - ^{14}C]- captan sediment/water study

Sediment type	Fraction	Days of incubation							
		0	**1**	**3**	**7**	**14**	**30[1]**	**59[1]**	**90**
Old Basing[2]	$^{14}CO_2$	ND	ND	0.1	0.2	2.4	8.9	38.8	52.5
	Surface water total	52.7	55.8	55.9	52.8	41.6	42.0	2.4	1.7
	Sediment extracts	41.1	31.2	29	21.2	17.8	14.5	4.6	2.9
	Bound residue	1.8	11.1	13.8	25.5	28.6	28.6	50.2	29.2
	Overall total	95.6	98.1	98.8	97.7	90.4	94.0	96.0	86.3
Virginia Water[2]	$^{14}CO_2$	ND	ND	0.3	2.0	5.4	9.8	36.5	48.9
	Surface water total	85.1	72.8	72.4	75.3	58.4	71.9	0.9	2.4
	Sediment extracts	9.2	16.1	17.9	16.1	18.2	17.3	9.5	10.6
	Bound residue	0.2	2.3	3.3	3.8	9.0	5.2	27.7	23.5
	Overall total	94.5	97.2	93.9	97.2	91.0	104.2	74.6	85.4
Old Basing sterile	$^{14}CO_2$	ND	NS	NS	NS	NS	ND	ND	ND
	Surface water total	48.3	NS	NS	NS	NS	63.1	63.0	63.3
	Sediment extracts	53.1	NS	NS	NS	NS	31.6	26.1	21.8
	Bound residue	1.4	NS	NS	NS	NS	6.7	11.1	14.8
	Overall total	102.8	NS	NS	NS	NS	101.4	100.2	99.9
Virginia Water sterile	$^{14}CO_2$	ND	NS	NS	NS	NS	ND	ND	ND
	Surface water total	70.3	NS	NS	NS	NS	80.2	79.0	75.9
	Sediment extracts	24.1	NS	NS	NS	NS	15.3	16.5	15.9
	Bound residue	0.3	NS	NS	NS	NS	1.1	1.4	0.5
	Overall total	94.7	NS	NS	NS	NS	96.6	96.9	92.3

ND = not detected.
NS = not sampled.
[1] Sterile samples were sampled on day 29 and 60.
[2] Values for non-sterile systems are an average of two samples except day 1 and Old Basing day 59, where a single measurement is reported.

Table B.8.2.2.3-4: Distribution and levels (% applied radioactivity) of captan and identified metabolites in Old Basing water/sediment systems in [cyclohexene 1,2 - ^{14}C]- captan sediment/water study

Sediment type	Days of incubation	Fraction	Compound							
			Captan	THPI	THPI diol	THPAI	THPI Epox	THPAM	Baseline	Others
Old	0	Surface water	5.6	40.0	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	3.7
Basing		Sediment extract	< 0.1	41.2	< 0.1	< 0.1	0.2	< 0.1	0.1	0.6
		Overall Total	5.6	81.2	< 0.1	< 0.1	0.2	< 0.1	0.1	4.3
	1	Surface water	< 0.1	32.5	< 0.1	0.7	4.4	11.3	1.1	5.8
		Sediment extract	< 0.1	23.9	< 0.1	2.5	0.3	0.4	0.4	3.7
		Overall Total	< 0.1	56.4	< 0.1	3.2	4.7	11.7	1.5	9.5
	3	Surface water	< 0.1	26.9	< 0.1	0.6	2.3	12.2	1.9	2.7
		Sediment extract	< 0.1	21.6	< 0.1	< 0.1	0.9	< 0.1	1.8	4.7
		Overall Total	< 0.1	48.5	< 0.1	0.6	3.2	12.2	3.7	7.4
	7	Surface water	< 0.1	11.8	0.7	1.2	1.5	25.6	3.5	2.9
		Sediment extract	< 0.1	13.0	0.2	3.6	0.8	1.4 *	1.7	0.6
		Overall Total	< 0.1	24.8	0.9	4.8	2.2	27.0	5.2	3.5
	14	Surface water	< 0.1	6.3	< 0.1	3.5	0.4	25.3	4.3	2.6
		Sediment extract	< 0.1	7.0	< 0.1	7.3	0.1	1.0	1.3	0.7
		Overall Total	< 0.1	13.3	< 0.1	10.8	0.5	26.3	5.6	3.3
	30	Surface water	< 0.1	5.3	< 0.1	3.8	0.5	17.7	5.8	1.9
		Sediment extract	< 0.1	7.9	< 0.1	3.0	0.3	< 0.1	1.6	1.5
		Overall Total	< 0.1	13.2	< 0.1	6.8	0.8	17.7	7.4	3.4
Old Basing	0	Surface water	9.5	29.0	< 0.01	< 0.1	< 0.1	< 0.1	< 0.1	1.8
sterile		Sediment extract	2.0	48.3	< 0.01	< 0.1	< 0.1	< 0.1	0.2	2.6
		Overall Total	11.5	77.3	< 0.01	< 0.1	< 0.1	< 0.1	0.2	4.4
	29	Surface water	< 0.1	39.9	< 0.1	0.5	5.5	7.7	1.0	1.0
		Sediment extract	< 0.1	26.8	< 0.1	1.2	1.7	0.3	0.4	1.2
		Overall Total	< 0.1	66.7	< 0.1	1.6	7.2	8.0	1.4	2.2
	60	Surface water	< 0.1	41.2	< 0.1	0.4	5.6	6.5	1.4	2.1
		Sediment extract	< 0.1	19.2	< 0.1	1.9	2.8	0.3	0.3	1.7
		Overall Total	< 0.1	60.4	< 0.1	2.3	8.4	6.8	1.8	3.7
	90	Surface water	< 0.1	21.0	< 0.1	< 0.1	6.9	24.4	2.5	1.0
		Sediment extract	< 0.1	14.8	0.6	2.4	2.6	0.2	0.6	1.4
		Overall Total	< 0.1	35.8	0.6	2.4	9.6	24.6	3.0	2.4

NA = not analysed. Radioactivity in extract < 5 % of applied.
*typo in table appendix Va (THPAM 12.2% AR): 21.2 % AR in sediment extract, sum of all identified metabolites 19.9 %, possible max of THPAM 1.3 % AR

Table B.8.2.2.3-5: Distribution and levels (% applied radioactivity) of captan and identified metabolites in Virginia Water water/sediment systems in [cyclohexene 1,2 - ^{14}C]- captan sediment/water study

Sediment type	Days of incubation	Fraction	Compound							
			Captan	THPI	THPI diol	THPAI	THPI Epox	THPAM	Baseline	Others
Virginia	0	Water extract	61.01	13.3	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	4.9
Water		Sediment extract	0.14	7.4	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	0.5
		Overall Total	61.1	20.6	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	5.4
	1	Surface water	< 0.1	33.7	< 0.1	1.1	8.55	19.4	3.3	5.4
		Sediment extract	< 0.1	5.7	< 0.1	1.5	0.80	3.1	2.5	2.5
		Overall Total	< 0.1	39.4	< 0.1	2.6	9.4	22.5	5.8	12.0
	3	Surface water	< 0.1	36.2	< 0.1	0.5	3.9	12.8	3.2	5.8
		Sediment extract	< 0.1	7.2	< 0.1	1.5	0.6	2.5	1.9	2.6
		Overall Total	< 0.1	43.4	< 0.1	2.6	4.5	15.3	5.1	8.4
	7	Surface water	< 0.1	50.7	< 0.1	0.7	0.9	7.8	0.8	3.2
		Sediment extract	< 0.1	9.9	< 0.1	3.1	0.3	1.2	2.1	0.5
		Overall Total	< 0.1	60.6	< 0.1	4.0	1.2	8.9	2.9	3.6
	14	Surface water	< 0.1	25.6	0.40	2.6	< 0.1	15.8	3.8	3.3
		Sediment extract	< 0.1	5.1	< 0.1	4.9	< 0.1	1.6	3.7	1.3
		Overall Total	< 0.1	30.6	0.40	7.5	< 0.1	17.3	9.2	4.6
	30	Surface water	< 0.1	42.6	< 0.1	5.2	0.5	8.2	3.6	3.6
		Sediment extract	< 0.1	8.5	< 0.1	2.3	< 0.1	0.6	3.7	2.2
		Overall Total	< 0.1	51.1	< 0.1	7.5	0.5	8.8	7.3	5.9
	59	Surface water	NA	NA	NA	NA	NA	NA	NA	NA
		Sediment extract	NA/< 0.1	NA/< 0.1	NA/< 0.1	NA/< 0.1	NA/< 0.1	NA/< 0.1	NA/5.3	NA/1.4
		Overall Total	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	5.3	1.4
	90	Surface water	NA/	NA	NA	NA	NA	NA	NA	NA
		Sediment extract	NA/< 0.1	NA/< 0.1	NA/< 0.1	NA/< 0.1	NA/< 0.1	NA/< 0.1	NA/6.7	NA/2.5
		Overall Total	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	< 0.1	6.7	2.5

NA = not analysed. Radioactivity in extract < 5 % of applied.

Table B.8.2.2.3-5: continued Distribution and levels (% applied radioactivity) of captan and identified metabolites in Virginia Water water/sediment systems in [cyclohexene 1,2 - ^{14}C]- captan sediment/water study

Sediment type	Days of incubation	Fraction	Compound							
			Captan	THPI	THPI diol	THPAI	THPI Epox	THPAM	Baseline	Others
Virginia	0	Surface water	46.5	21.2	< 0.01	< 0.1	< 0.1	< 0.1	< 0.1	0.8
Water		Sediment extract	7.6	14.7	< 0.01	< 0.1	< 0.1	< 0.1	< 0.1	0.9
sterile		Overall Total	54.2	35.9	< 0.01	< 0.1	< 0.1	< 0.1	< 0.1	1.8
	29	Surface water	< 0.1	67.5	0.2	0.3	5.7	0.5	1.2	0.6
		Sediment extract	< 0.1	11.5	<j 0.1	< 0.1	0.7	< 0.1	< 0.1	1.0
		Overall Total	< 0.1	79.0	0.2	0.3	6.5	0.5	1.2	1.6
	60	Surface water	< 0.1	69.3	0.2	0.3	9.6	6.5	0.4	2.2
		Sediment extract	< 0.1	10.6	< 0.1	< 0.1	0.4	< 0.1	< 0.1.	1.5
		Overall Total	< 0.1	79.9	0.2	0.3	10.1	6.5	0.4	3.7
	90	Surface water	< 0.1	54.7	0.3	< 0.1	5.8	0.9	1.9	2.4
		Sediment extract	< 0.1	9.0	< 0.1	< 0.1	0.8	< 0.1	< 0.1	1.0
		Overall Total	< 0.1	63.8	0.3	2.4	6.6	0.9	2.2	3.4

NA = not analysed. Radioactivity in extract < 5 % of applied.

Conclusions: Captan was hydrolysed very rapidly to THPI in both sterile and non-sterile water/sediment systems. After 24 hours incubation, captan was not detected in any of the systems, and a DT_{50} could not be determined.

In the non-sterile systems, the radioactivity in surface water decreased during the incubation period to levels lower than 2.5 % of the applied radioactivity, although the radioactivity increased in the sediment as bound residues, reaching approximately 25% AR. In the sterile systems, radioactivity remained in the surface water at levels of 63-76% AR after 90 days incubation; in the sediment bound residues were lower than 15%.

THPI was observed as main metabolite in all the systems from day 1. In Old Basing it reached its maximum of 81 % AR on day of application and in Virginia water the maximum of 60.6 % was reached on day 7. It exhibited a DT_{50} of approximately 5 days in a non-sterile system containing a high organic matter content, high pH sediment, in which it was evenly distributed between sediment and water. In a non-sterile system containing a lower organic matter, lower pH sediment, THPI was predominantly in the water phase, and a DT_{50} could not accurately be determined. However, THPI had completely degraded to undetectable levels in both non-sterile systems in 59 days.

Two other major metabolites detected were detected: THPAM and THPAI. The metabolite THPAM which was mainly detected in the surface water phase, reached its maximum of 27 % AR in Old Basing after 7 d and in Virginia water on the first day (22.5 % AR). The metabolite THPAI exceeded 5 % AR on two consecutive sampling points in both systems and reached its maximum of 10.8 % AR on day 14.
The metabolite THPI epoxide exceeded 5 % only once with 9.4 % AR on day 1 in Virginia water. Amounts then declined to undetectable levels after 59 days of incubation for these 3 metabolites.

In sterile systems, THPI was the first and main metabolite reaching up to 77. 3 % AR (old Basing, day 1) and 79.9 % AR (Virginia Water, day 60). It degraded more slowly than in non-sterile systems, suggesting that micro-organisms enhanced the degradation.
In the sterile systems, THPAM, THPAI and THPI epoxide were also observed after 30 days of incubation, suggesting that the degradation of THPI occurs in the absence of microbial activity, although more slowly.

In the non-sterile systems, approximately 50% of the captan applied had been mineralised to $^{14}CO_2$ after 90 days incubation, whereas in the sterile systems, negligible amounts of $^{14}CO_2$ were evolved throughout the incubation, implying that microbial activity is required for mineralisation.

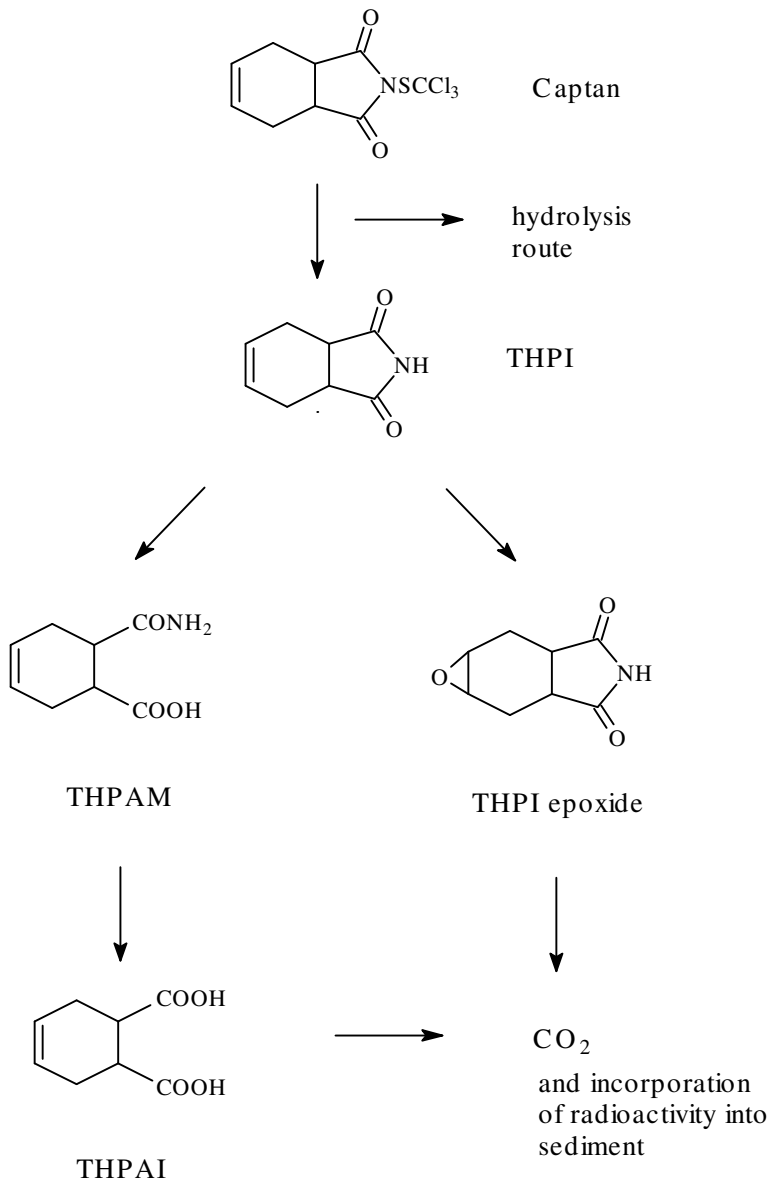


Figure B.8.2.2.3-1: Degradation of captan in sediment/water system

A new kinetic evaluation was provided for the renewal of captan and is described below.

Kinetic evaluation for study 14 (1993). Captan: degradation in water-sediment systems under laboratory conditions. ICI Agrochemicals UK, unpublished report No. RJ1439B (Company file: R-6851/TMN-0365), was performed according to FOCUS kinetic (2006, 2014) in order to derive kinetics parameters and persistence endpoints and is summarised in the following

Due to fast hydrolysis of Captan in the water phase of both water/sediment systems with few hours after incubation, it was not possible to perform kinetic evaluation for residue data of Captan since only one data point was available. Thus, the formerly agreed worst case DT50 value of 1 day is proposed.

Kinetic evaluation for residue data of Captan metabolites THPI and THPAM from the whole system, water phase or sediment phase was performed where possible based on metabolite decline from peak. Since Captan hydrolyses rapidly to THPI within few hours residue data of the parent compound Captan detected at days zero was added to residue data of the metabolite THPI at day zero because degradation of THPI is the rate determining step according to FOCUS kinetic (2006, 2014), and used for kinetic analysis. Processed residue data according to FOCUS kinetic

(2006, 2014) for metabolites THPI and THPAM used for kinetic evaluation are given in table B.8.2.2.3-6 to table B.8.2.2.3-7.
In order to estimate the persistence and modelling endpoints by dissipation at Level M-I, the decline data after the peak height for the whole system, the water column and the sediment were all entered and two of the three default kinetic models (SFO and FOMC) were run without any data modification. If FOMC kinetic model gave a better fit than the SFO model, another bi-phasic model DFOP was fit to residue data and results compared with FOMC results to select the best-fit model.

In all cases, the fit and the results of kinetic models were evaluated based on graphical and statistical evaluation (random distribution of residuals, low Chi2 error and t-test for the rate constant parameters passing at 5 % error level). The model appeared to give acceptable fits to the data was used to derive the persistence and modelling endpoints as required.
Detailed results on kinetic evaluation of residue data obtained from water/sediment systems of old basing and Virginia water are presented in Table B.8.2.2.3-6 to Table B.8.2.2.3-7.
The calculated modelling and persistence endpoints for THPI and THPAM in the water/sediment systems are summarised in Table B.8.2.2.3-8.

Table B.8.2.2.3-6: Residue data of metabolites THPI and THPAM identified in the water/sediment system of Old Basing processed according to FOCUS kinetics and used for kinetic evaluation [% of applied radioactivity]

Time [days]	Water [%AR]	Sediment [%AR]	Total system [%AR]
THPI			
0	**45.6**[a]	**41.2**[a]	**86.9**[b]
1	32.5	23.9	56.4
3	26.9	21.6	48.5
7	11.8	13.0	24.8
14	6.3	7.0	13.3
30	5.3	7.9	13.2
59	0.05[c]	0.05[c]	0.05[c]
THPAM			
0	0[e]	0[e]	0[e]
1	11.3	0.4	11.7
3	12.2	0.05[c]	12.2
7	**25.6**	**1.4**	**27.0**
14	25.3	0.05[c]	25.3
30	17.7	0.05[c]	17.7

a sum of parent (Captan) residue value and metabolite residue value (THPI) at day 0
b sum of residue values of a substance in water and sediment at the respective sampling day
c values below LOD (LOD = 0.1 AR) or not detected (n.d.) set to 1/2 LOD according to FOCUS kinetics
e value set to zero according to FOCUS kinetics
Bold indicate peak value of the substance

Table B.8.2.2.3-7: Residue data of metabolites THPI and THPAM identified in the water/sediment system of Virginia Water processed according to FOCUS kinetics and used for kinetic evaluation [% of applied radioactivity]

Time [days]	Water [%AR]	Sediment [%AR]	Total system [%AR]
THPI			
0	**74.3**[a]	7.5[a]	**81.9**[b]
1	33.7	5.7	39.4
3	36.2	7.2	43.4
7	50.7	**9.9**	60.6
14	25.6	5.1	30.7
30	42.6	8.5	51.1
59	0.05[c]	0.05[c]	0.05[c]
THPAM			
0	0[e]	0[e]	0[e]

1	**19.4**	**3.1**	**22.5**
3	12.8	2.5	15.3
7	7.8	1.2	9.0
14	15.8	1.6	17.4
30	8.2	0.6	8.8
59	0.05[c]	0.05[c]	0.05[c]

a sum of parent (Captan) residue value and metabolite residue value (THPI) at day 0
b sum of residue values of a substance in water and sediment at the respective sampling day
c values below LOD (LOD = 0.1 AR) or not detected (n.d.) set to 1/2 LOD according to FOCUS kinetics
e value set to zero according to FOCUS kinetics
Bold indicate peak value of the substance

Table B.8.2.2.3-8: Results of kinetic evaluation for residue data obtained for the metabolite THPI obtained in the water/sediment system of Old Basing

Compartment	Kinetic model	Parameter	Prob > t	Chi^2 error [%]	Visual fit evaluation	DT_{50} [days]	DT_{90} [days]
Water	**SFO**	**k: 0.16979**	**<0.01**	**12.1**	**acceptable**	**4.1**	**13.6**
	FOMC	*α: 1.40752* *β: 5.23048*	*0.0475* *0.1153 (CI contains 0)*	*9.3*	*good*	*3.3*	*21.6*
	DFOP	k1: 0.27162 k2: 0.03264 g: 0.78075	k1: 0.055 k2: >0.05	10.0	good	3.5	24.4
Sediment	**SFO**	**k: 0.14584**	**<0.05**	**21.8**	**acceptable**	**4.8**	**15.8**
	FOMC	*α: 0.5688* *β: 0.9572*	*<0.05* *>0.05 (CI contains0)*	*13.3*	*good*	*2.3*	*53.9*
	DFOP	k1: 0.06338 k2: 2.18725 g: 0.43127	k1: <0.05 k2: >0.05 (CI contains 0)	13.0	acceptable	2.2	27.4
Total system	**SFO**	**k: 0.16041**	**<0.05**	**16.5**	**acceptable**	**4.3**	**14.4**
	FOMC	*α: 0.8687* *β: 2.3704*	*<0.05* *>0.05 (CI contains0)*	*11.0*	*good*	*2.9*	*31.2*
	DFOP	k1: 0.03918 k2: 0.40042 g: 0.34726	k1: >0.05 (CI contains 0) k2: >0.05 (CI contains 0)	12.8	good	3.1	31.8

Bold selected model to derive modelling endpoints
Italic selected model to derive persistence endpoints

Table B.8.2.2.3-9: Results of kinetic evaluation for residue data obtained for the metabolites THPI and THPAM obtained in the water/sediment system of Virginia Water

Compartment	Kinetic model	Parameter	Prob > t	Chi^2 error [%]	Visual fit evaluation	DT_{50} [days]	DT_{90} [days]

THPI							
Water	SFO	k: 0.02561	not sig.	31.7	not acceptable	27.1	89.9
Sediment		k: 0.01593	not sig.	28.6	not acceptable	43.5	144.5
Total system		k: 0.02379	not sig.	30.1	not acceptable	29.1	96.8
THPAM							
Water	SFO	k: 0.02980	not sig.	27.6	not acceptable	23.3	77.3
Sediment		k: 0.06476	<0.05	18.8	acceptable	10.7	35.6
Total system		k: 0.03235	not sig.	26.2	not acceptable	21.4	71.2

Table B.8.2.2.3-10: Summary of modelling and persistence endpoints obtained for the metabolites THPI and THPAM in the water/sediment systems of Old Basing and Virginia Water

Water / Sediment system	Substance	Kinetic model	Compartment	Chi² error [%]	Modelling endpoints		Persistence endpoints	
					DT_{50} [days]	DT_{90} [days]	DT_{50} [days]	DT_{90} [days]
Old Basing	THPI	SFO[a] / FOMC[b]	Water	12.1/9.3	4.1	13.6	3.3	21.6
		SFO[a] / FOMC[b]	Sediment	21.8/13.3	4.8	15.8	2.3	53.9
		SFO[a] / FOMC[b]	Total system	16.5/11.0	4.3	14.4	2.9	31.2
Virginia Water	THPAM	SFO[c]	Sediment	18.8	10.7	35.6	10.7	35.6

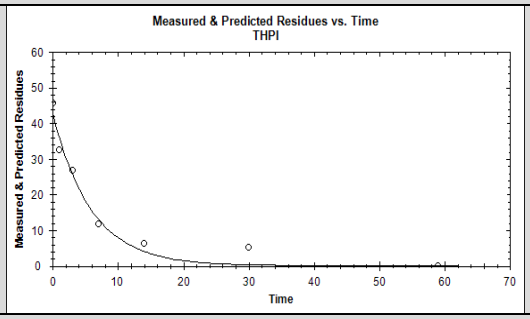
a used to derive modelling endpoints
b used to derive persistence endpoint
c used to derive both modelling and persistence endpoints

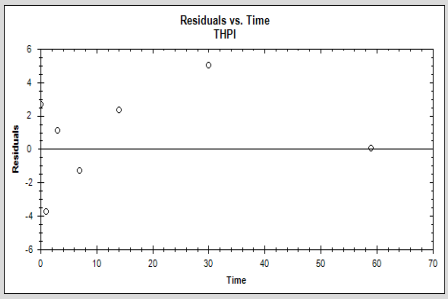
Due to few data points remained for Virginia Water test system after processing according to FOCUS kinetics (2006, 2014), it was only possible to apply SFO kinetics to residue data of metabolite THPI to derive kinetic endpoints.
The results of kinetic evaluation showed that, for THPI a DT_{50} value of 4.1, 4.8 and 4.3 days for water, sediment and total system, respectively, was obtained for Old Basing water test system. For THPAM, it was only possible to determine a DT_{50} (DT_{50} = 10.7 days) in sediment phase of Virginia water test system.

Comments RMS

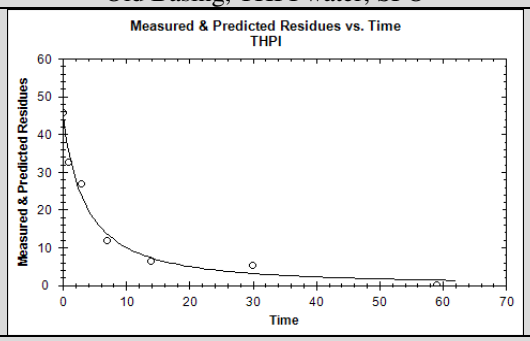
The specific activity of the application solution (349 Bq/µg) was determined, but the specific activity of [cyclohexene 1,2- ^{14}C]-captan was not given. The purity of unlabelled captan (98.9%) was given but the radiochemical purity of labelled captan was missing.
The sediment Old Basing showed a very high Corg content of 12.5 % and the sediment of Virginia Water showed a high Corg content of 3.1 %. However, the sediments differed concerning their Corg content and their texture.
The water: sediment ratio was 9:1 instead of between 3:1 and 4:1 as recommended and the amount of sediment (20 g) was below the recommended 50 g.
Duplicate samples were analysed at each time point but only mean values were presented in the tables of the study.
The recovery was below 90 % for the Old Basing system at day 90 (86.3 % AR) and for the Virginia Water system at day 59 (74.6 % AR) and day 90 (85.4 % AR). For Old Basing the recovery at day 60 was 96 % AR and the extracts of surface water and sediment contained less than 5 %AR. Therefore, it is not expected that on day 90 any metabolite would exceed 5 % AR.

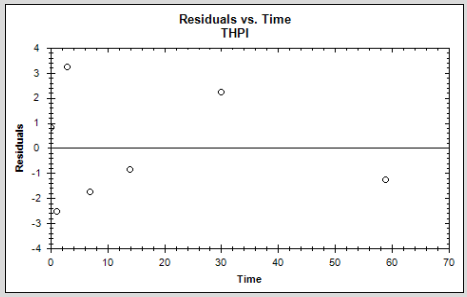
The RMS re-evaluated the kinetic study using KINGUI version 2; the results presented by notifier could be confirmed. The respective graphs of the fits are presented below.



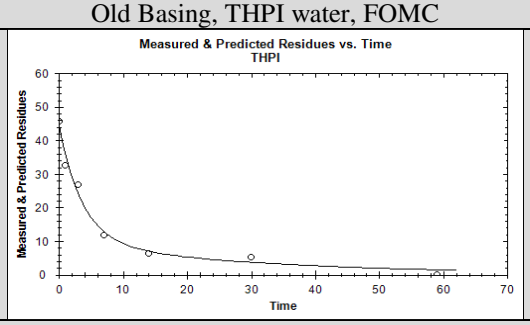


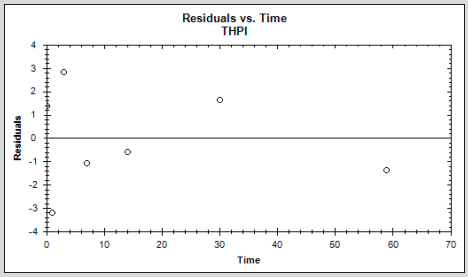
Old Basing, THPI water, SFO



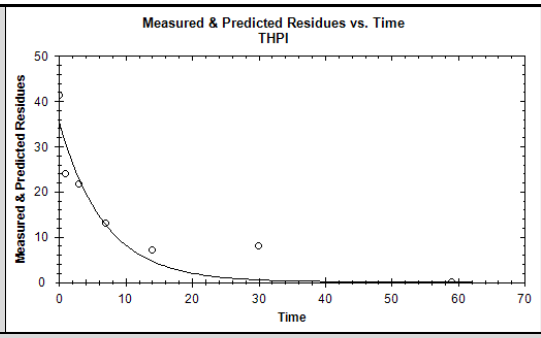


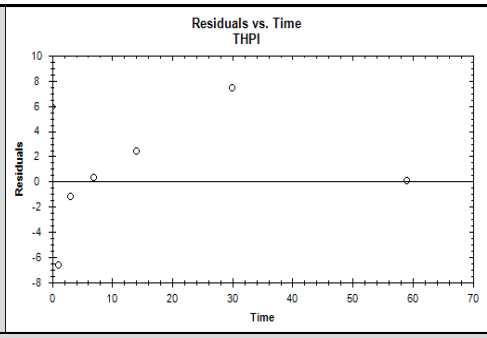
Old Basing, THPI water, FOMC



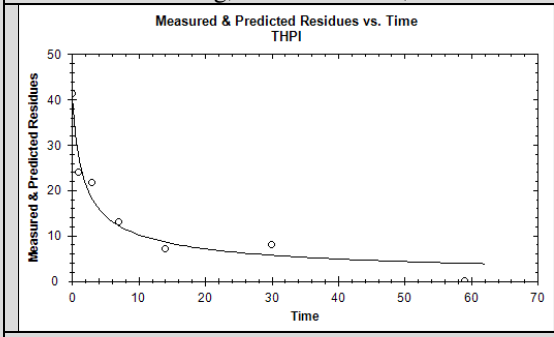


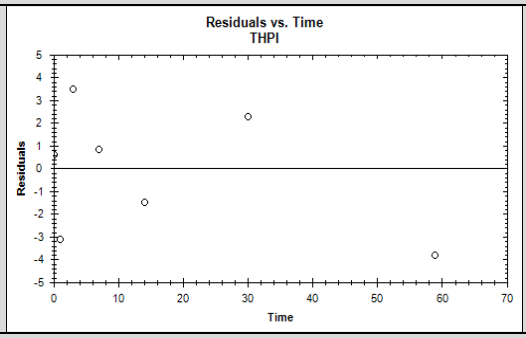
Old Basing, THPI water, DFOP



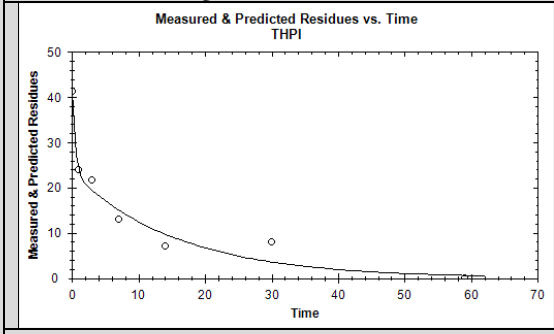


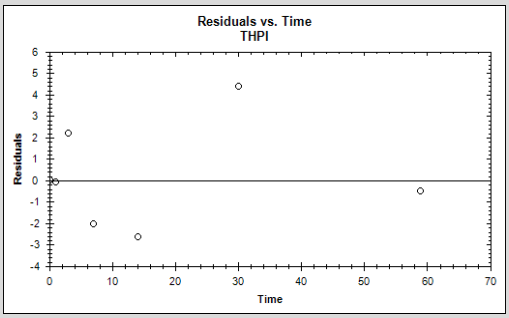
Old Basing, THPI sediment, SFO



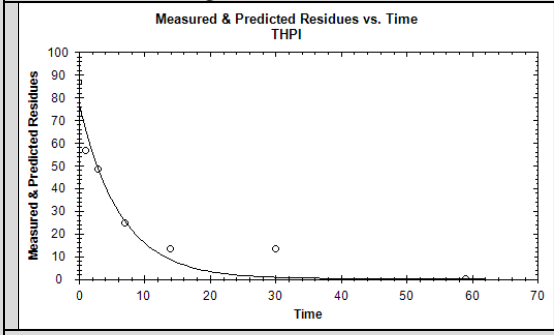


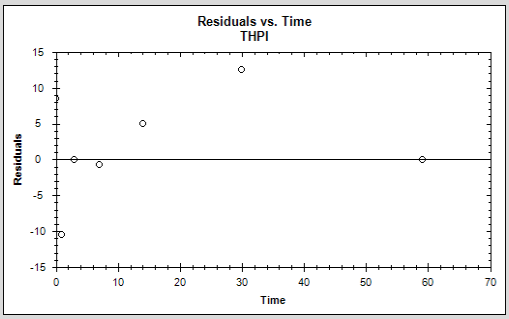
Old Basing, THPI sediment, FOMC



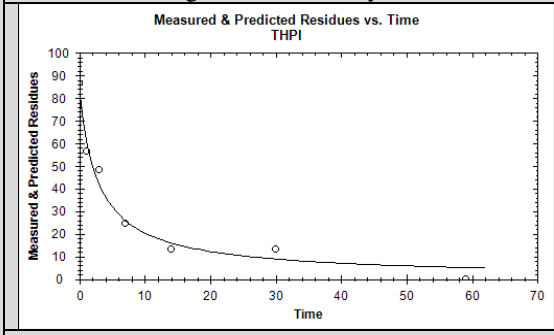


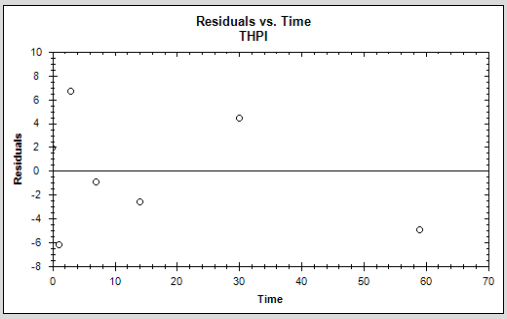
Old Basing, THPI sediment, DFOP



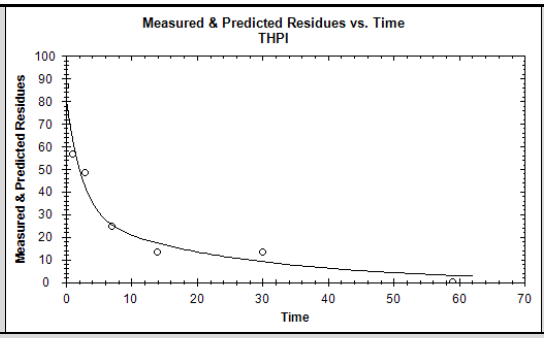


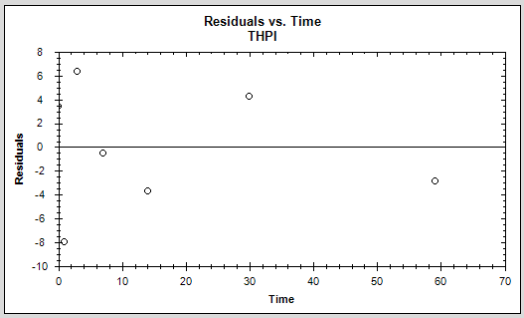
Old Basing, THPI, whole system, SFO





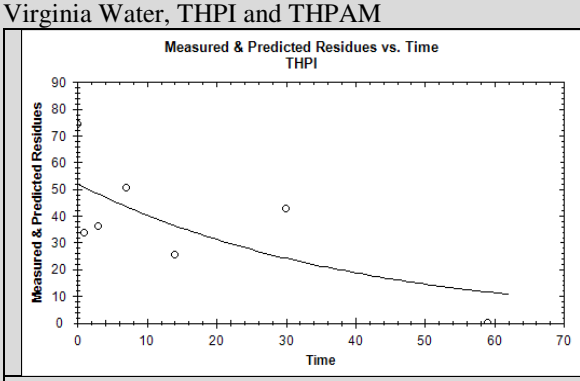
Old Basing, THPI, whole system, FOMC

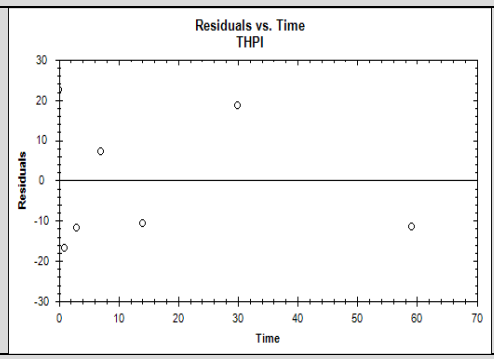




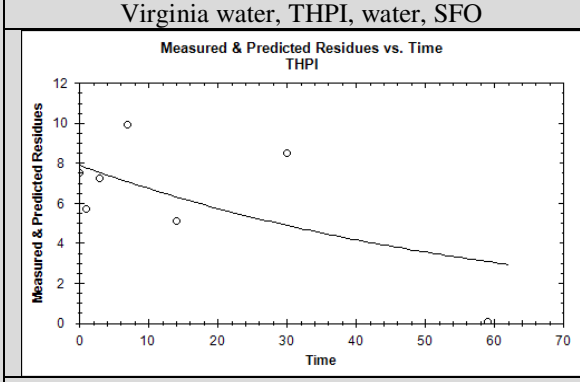
Old Basing, THPI, whole system, DFOP

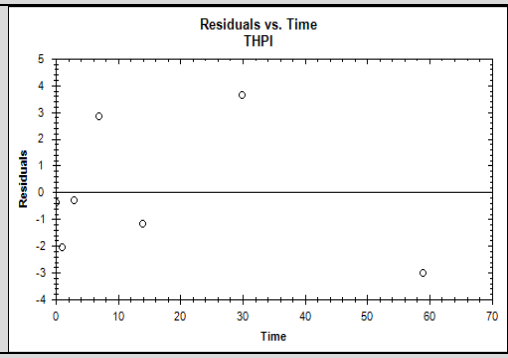
Virginia Water, THPI and THPAM



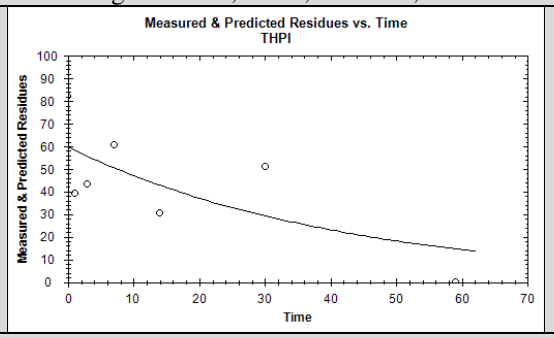


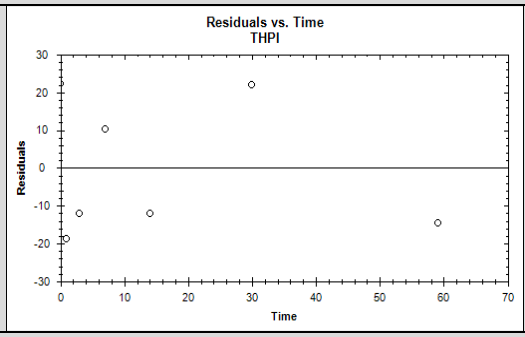
Virginia water, THPI, water, SFO



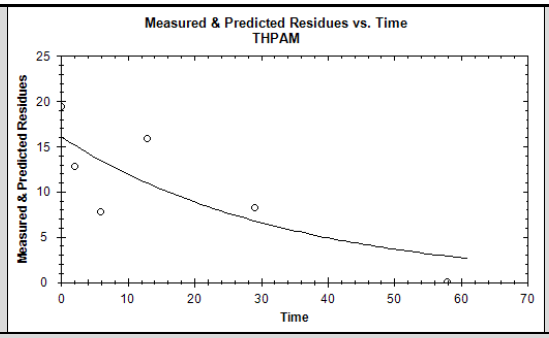


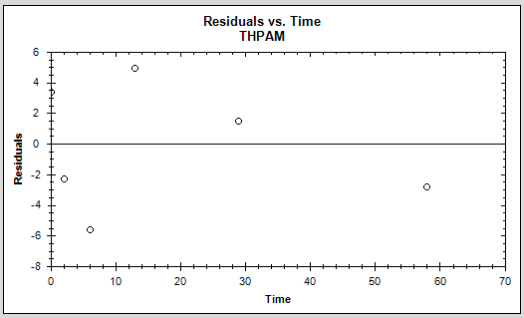
Virginia water, THPI, sediment, SFO



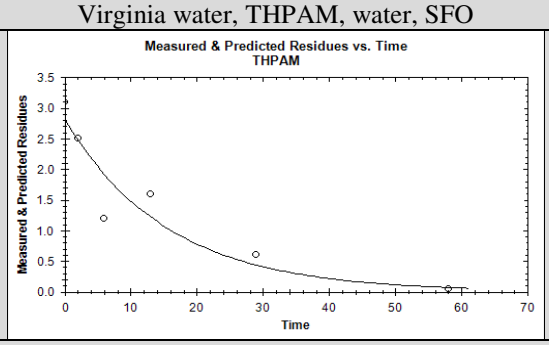


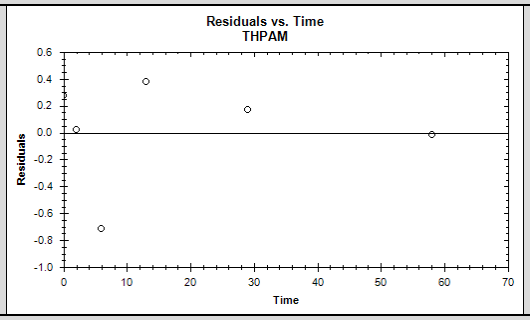
Virginia water, THPI, whole system, SFO



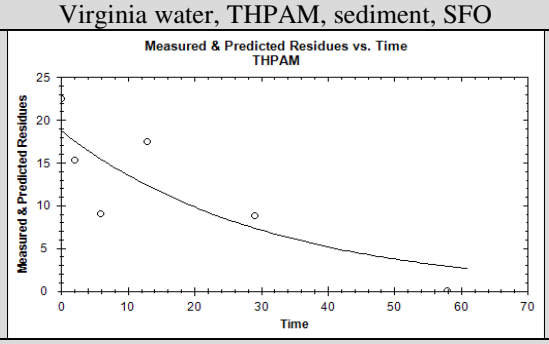


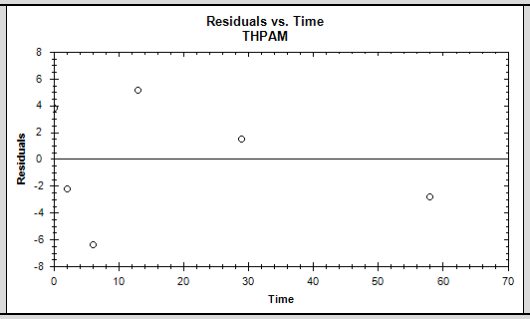
Virginia water, THPAM, water, SFO





Virginia water, THPAM, sediment, SFO





Virginia water, THPAM, whole system, SFO

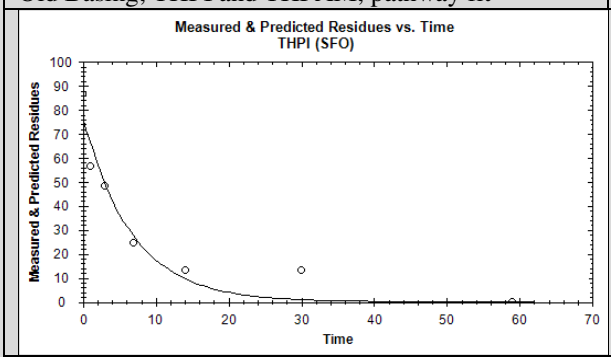
For Virginia water the RMS performed a kinetic evaluation for THPI and THPAM with FOMC and DFOP model; but this kinetic evaluation did not result in statistically significant parameters.

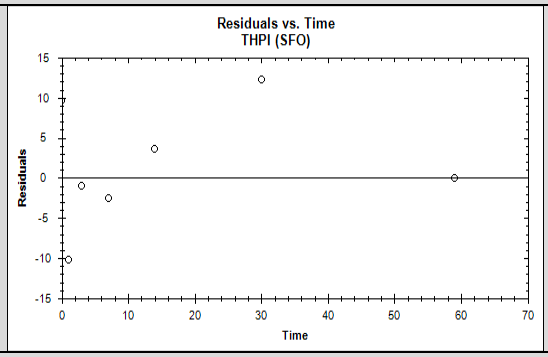
Additionally, the RMS re-evaluated the kinetic fitting for the **whole system** with simultaneous fitting of the parent THPI and of the metabolite THPAM. The results of the pathway fit are presented below.

Compartment	Kinetic model	Parameter	Prob > t	Chi² error [%]	Visual fit evaluation	DT_{50} [days]	DT_{90} [days]
Old Basing							
Whole system	THPI: SFO	k: 0.14889	k: <0.05	16.6	acceptable	4.7	15.5
	THPAM: SFO	k: 0.05106	k: <0.05	16.4	good	13.6	45.1
Whole system	THPI:FOMC	*α: 1.11233* *β:3.8938*	*α: <0.05* *β: >0.05(CI contains 0)*	11.5	Good	3.4	27.0
	THPAM: SFO	k: 0.04063	k: <0.05	20.9	acceptable	17.1	56.7
Whole system	THPI: DFOP	k1: 0.25093 k2: 0.02791 g: 0.78	k1: <0.05 k2: >0.05 *(CI contains 0)* g: <0.05	14.0	Good	3.8	28.6

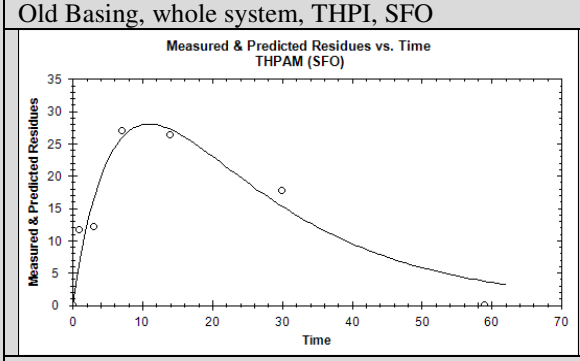
	THPAM: SFO	k: 0.04273	k: <0.05	19.8	acceptable	16.2	53.9
Virgin Water							
Whole system	THPI: SFO	k: 0.041448	k: >0.05 *(CI contains 0)*	32.6	Not acceptable	16.7	55.6
	THPAM: SFO	k: 108475	k: >0.05 *(CI contains 0)*	60.0	Not acceptable	6.4	21.2
Whole system	THPI: FOMC	*α: 5.355e-02* *β: 2.402e-06*	*α: <0.05* *β: >0.05(CI contains 0)*	32.9	Not acceptable	1.0	>1000
	THPAM: SFO	k: 3.876e-02	k: <0.05	27.3	Not acceptable	17.9	59.4
Whole system	THPI: DFOP	k1: 1.308e+01 k2: 1.936e-02 g: 3.813e-01	k1: >0.05 *(CI contains 0)* k2: >0.05 *(CI contains 0)* g: <0.05 *(CI contains 0)*	28.6	Not acceptable	11.0	94.1
	THPAM: SFO	k: 7.211e-02	k: >0.05 *(CI contains 0)*	26.8	Not acceptable	9.6	31.9

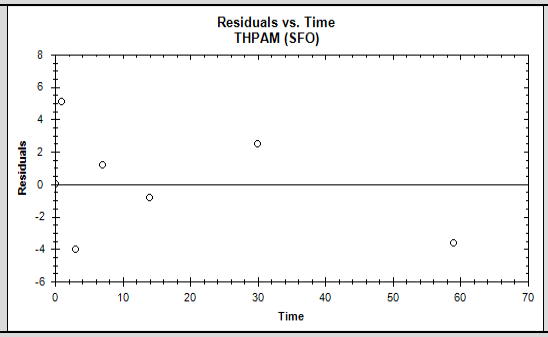
Old Basing; THPI and THPAM, pathway fit



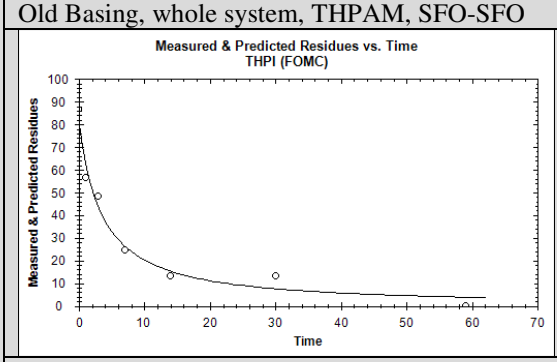


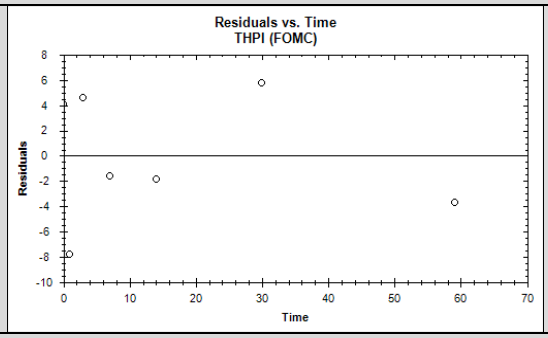
Old Basing, whole system, THPI, SFO



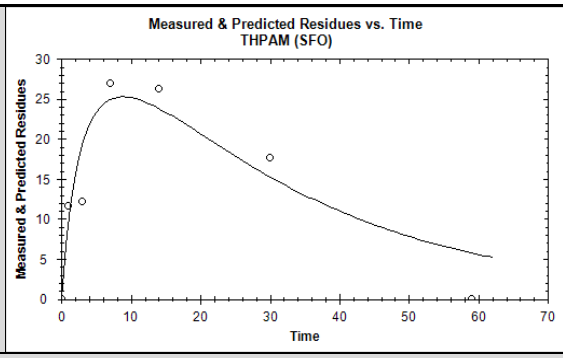


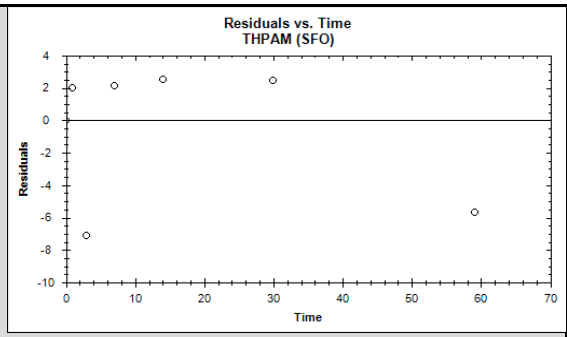
Old Basing, whole system, THPAM, SFO-SFO



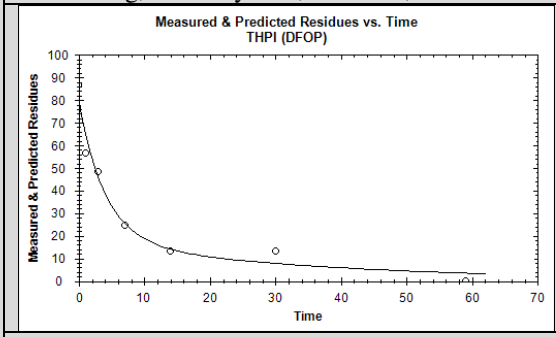


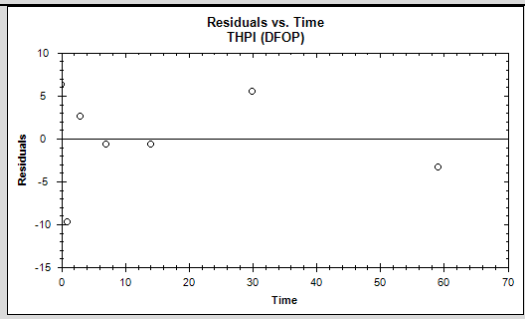
Old Basing, whole system, THPI, FOMC



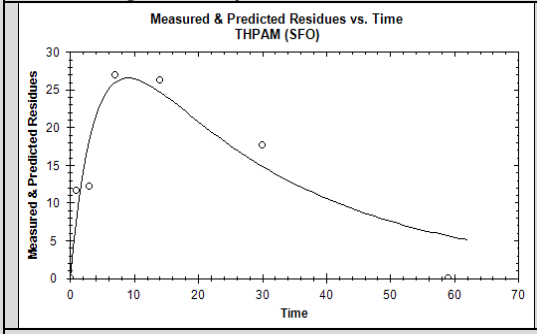


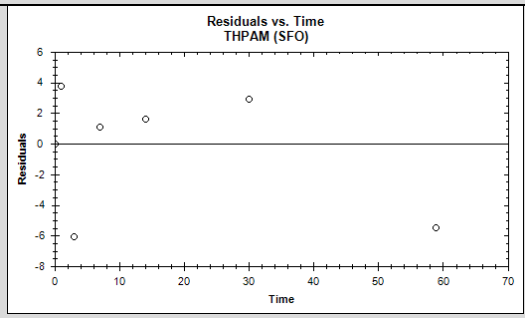
Old Basing, whole system, THPAM, FOMC-SFO





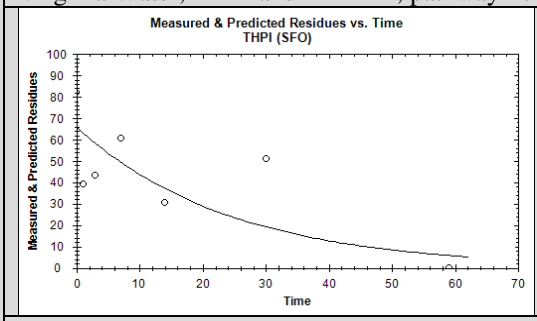
Old Basing, whole system, THPI, DFOP

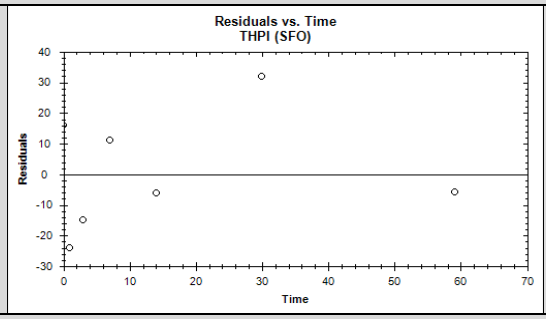




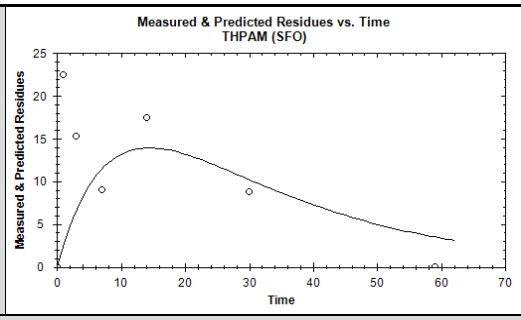
Old Basing, whole system, THPAM, DFOP-SFO

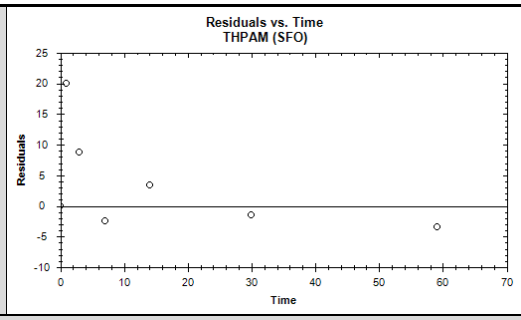
Virginia Water, THPI and THPAM, pathway fit



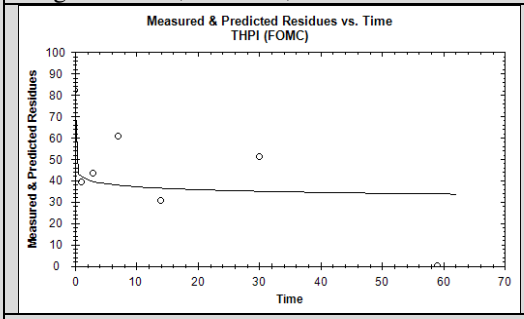


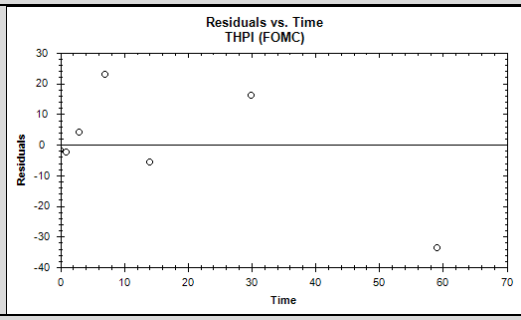
Virginia Water, THPI, SFO



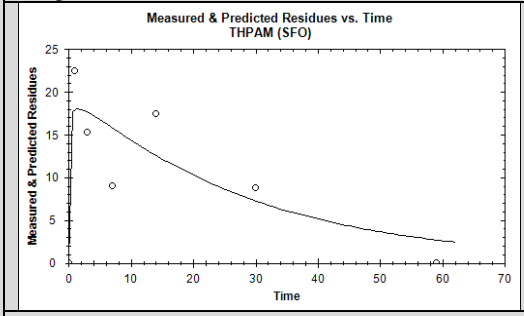


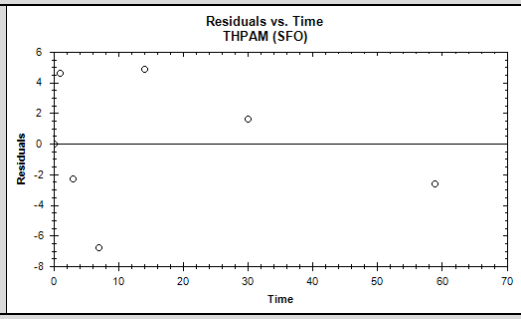
Virginia Water, THPAM, SFO-SFO



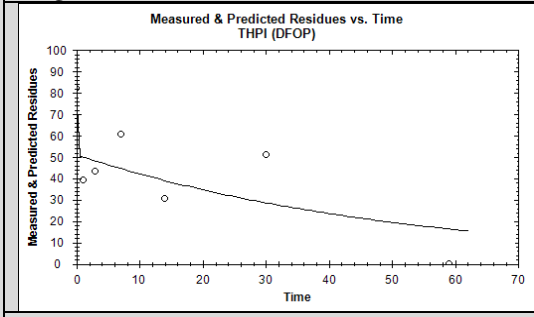


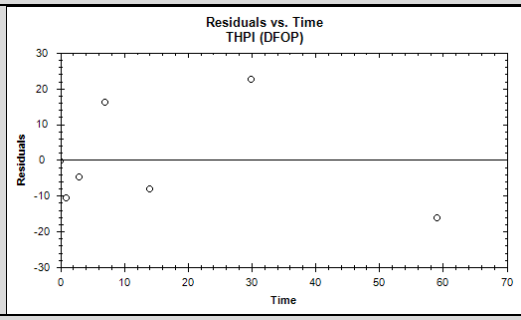
Virginia Water, THPI, FOMC



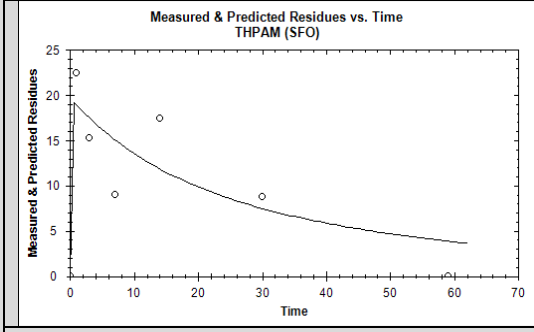


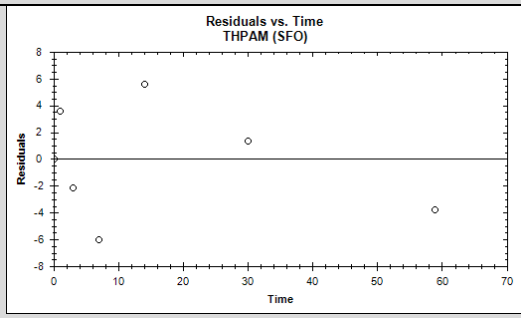
Virginia Water, THPAM, FOMC-SFO





Virginia Water, THPI, DFOP





Virginia Water, THPAM, DFOP-SFO

For Old Basing, the pathway fit resulted in visually acceptable and statistically significant fits for the SFO-model. THE FOMC and DFOP model did not provide statistically significant fits.

For Virginia Water, the pathway fit did not result in visually acceptable and statistically significant fits.

In conclusion, the study shows some deficiencies but is still considered acceptable and adequate to describe the fate and behaviour of captan and its metabolites in water/sediment systems.
Captan degraded very rapidly to THPI and was not detected one day after application.
THPI reached its maximum of 81.2 % AR in Old Basing on the day of application and in Virginia Water after 7 days with 60.6 % AR. THPI was further degraded to THPAM and THPAI. The metabolite THPAM which was mainly detected in the surface water, reached its maximum occurrences of 27 % AR (Old Basing) and 22.5 % AR (Virgin water) after 7 days and after 1 day. The metabolite THPAI exceeded 2 x 5 % AR in the whole system only and reached its maximum of 10.8 % AR 14 days after application. Those extracts which contained < 5 % AR were not further analysed; extracts > 5 % AR were analysed but no metabolites were detected 59 days after application.
Due to the rapid degradation of captan no DT_{50} could be determined for the active ingredient. The kinetic evaluation provided DT_{50} and DT_{90} values for THPI in water (4.1/13.6 d), sediment (4.8/15.8 d) and the whole system (4.3/14.4 d) for Old basing. For THPAM only $DT_{50/90}$ values in the sediment (10.7/35.6 d) for Virginia water could be determined. The pathway fitting for the whole system provided DT_{50} and DT_{90} values for THPI (4.7/15.5) and THPAM (13.6/45.1) for Old Basing. For the system Virginia water no acceptable and reliable half lifes could be determined.

To support the metabolism observed and described in the new aerobic mineralisation of Captan in surface water study presented above (study 9, 2016b and study 10, 2016) and as discussed in the position paper (study 13, 2016), a new anaerobic water/sediment study is presented and summarised here.

Study 15 (2016)

Reference:	**Captan: Anaerobic aquatic metabolism**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2016
Report/Doc. number:	LEB0133/ R-35450
Guideline(s):	US EPA OCSPP 835.4100, Anaerobic aquatic metabolism, October 2008
GLP:	Yes
Deviations:	None
Validity:	Valid
Status:	Submitted for renewal

Executive Summary

The objective of this study was to determine the route and rate of degradation of ^{14}C-Captan in two water/sediment systems under anaerobic conditions at about 20°C in the dark. Water and sediment samples from two different natural systems were acclimated for 3 weeks in the dark until equilibrium had been established. After acclimatisation the samples were treated with ^{14}C-Captan at a rate of 0.5 mg/L.
Duplicate samples were taken for analysis at specified intervals up to 182 days after application. Organic volatiles and carbon dioxide were trapped. Radioactivity in the water and sediment was quantified by LSC, while the characterisation was conducted through HPLC.
Measurements of oxygen concentration and redox potentials were conducted to confirm anaerobic conditions in the test systems.
The total recoveries from the water/sediment system were 91.5 – 105.1% AR except on four occasions where the recoveries were 84.3, 88.0% AR (both day 182 replicates from Calwich Abbey Lake), 82.2% AR (one day 0 replicate from Swiss Lake; recovery for the other replicate was 101.3% AR) and 89.9% AR (one day 182 replicate from Swiss Lake). The mineralization to CO_2 was increasing up to a maximum of 8.5 and 13.1% AR after 182 days for Calwich Abbey Lake and Swiss Lake, respectively. Non-extractable residues were low, comprising maximum 13.6 and 11.8% AR. Total residues determined in sediment were maximum 29.8 and 19.4 % AR.
Captan quickly dissipated in the water phase from a mean of 71.5 and 66.7% AR at time zero to 1.7 and 3.5% AR after 4 hours of incubation in samples from Calwich Abbey Lake and Swiss Lake systems, respectively, and was not found in the sediment phase. Four major metabolites (THPI, THPAM, THCY and THPAI) were formed all above 10% AR in water phase. In sediment phase only THPAM was detected above 5% AR in the Calwich Abbey Lake system and only THPI above 5% AR in the Swiss Lake System.
Two transient unknown degradates were identified. Unknown 1 (Rt≈19 minutes) accounted for up to maximum 36.9% AR and 23.7% AR after 4 hours in Calwich Abbey Lake and Swiss Lake system, respectively. Unknown 2

(Rt≈20.5 minutes) was present at low levels (2.5% AR) in one sample at 1 or 4 hours, respectively. Both were not detected in any later sampling dates.
A percentage of the applied radioactivity could not be resolved. This polar material was investigated further and showed that the radioactivity was comprised of multiple components, each < 10% AR.
Captan rapidly dissipated from the water and total system with DT_{50} values of 0.02 days (Calwich Abbey Lake) and 0.03 days (Swiss Lake).

I. MATERIALS AND METHODS

A. MATERIALS

1. Test Material: [carboximide-^{14}C]Captan
CAS #: 133-06-2
Lot #: XXII/15/A/2
Purity: radiochemical purity 97.9%
Specific activity: 3.214 MBq/mg, 968 MBq/mmol, 26.11 mCi/mmole

2. Test Material: Unlabelled test item, Captan
Lot/batch #: 499-170-01
Purity: 98.9%
Expiry date: - 27/04/2019

3. Further Test Material: 1,2,3,6-tetrahydrophthalamic acid (THPAM)
Purity: 98.1%
Lot #: 516-156-00
Expiry date: 02/02/2017

4. Further Test Material: 1,2,3,6-tetrahydrophthalimide (THPI)
Purity: 98.5%
Lot #: 279-071-02
Expiry date: 02/04/2017

5. Further Test Material: 1,2,3,6-tetrahydrophthalic acid (THPAI)
Purity: 96.8%
Lot #: 516-143-00
Expiry date: 20/01/2020

6. Further Test Material: 6-Cyanocyclohex-3-ene-1-carboxylic acid (THCY)
Purity: 100.0%
Lot #: 534-046-00
Expiry date: 12/06/2017

7. Further Test Material: Octahydro-1aH-oxireno[2,3-f]isoindole-3-5-dione (THPI epoxide)
Purity: 98.1%
Lot #: 534-111-00
Expiry date: 12/10/2017

8. Water/Sediment: Two test systems were used. Water and sediment were sampled from two different locations with no pesticide use in immediate vicinity within past 5 years:
1) Calwich Abbey Lake (Staffordshire, UK) and
2) Swiss Lake (Derbyshire, UK)
The sediment and water characteristics are summarized in tables B.8.2.2.3-11 and B.8.2.2.3-12.

Table B.8.2.2.3-11: Characterisation of water and sediment at time of sampling

Compartment	Parameter	Calwich Abbey lake Staffordshire, UK	Swiss lake Derbyshire, UK
Water	Temperature [°C]: - just below surface	8.8	6.9
	- 5 cm above sediment	8.8	7.0
	pH	7.99	6.47

	Oxygen saturation [%]: - just below water surface	103.7	95.1
	- at water/sediment interface	103.5	95.7
	Depth over sample area [cm]	25-35	25-30
Sediment	Depth of sediment layer [cm]	100	<5
	Depth of sampled layer [cm]	Not specified, taken from anaerobic layer	Not specified, taken from anaerobic layer

Table B.8.2.2.3-12: Characterisation of water and sediment during the study

Compartment	Parameter	Calwich Abbey lake Staffordshire	Swiss lake Derbyshire
Water	Total P [mg/L]	< 0.2	< 0.2
	Total N [mg/L]	2.6	0.6
	Total organic carbon [mg/L] Beginning of the study After 30 days	 11.0 10.9	 20.1 15.0
	Total suspended solids [mg/L]	< 10	< 10
	Redox potential [mV] (at day of application)	Vessel 1: 48 Vessel 2: -32	Vessel 1: 47 Vessel 2: -50
Sediment	pH (in $CaCl_2$)	7.4	5.6
	Total organic carbon [%] Beginning of the study After 30 days	 5.1 5.4	 0.80 0.69
	Cation exchange capacity [meq/100g]	23.5	3.5
	Total P [mg/kg]	1095	154
	Total N [%]	0.47	0.08
	$CaCO_3$ [%]	40.5	< 2
	Soil type (UK classification) Sand Silt Clay	Sandy silt loam 30 56 14	Sand 93 4 3
	Microbial biomass [colony forming units/g] [a] Beginning of the study After 30 days After 100 days	 2.34×10^6 4.34×10^6 1.95×10^6	 2.40×10^5 5.47×10^6 7.15×10^6
	Redox potential [mV] (at day of application)	Vessel 1: -285.8 Vessel 2: -284.5	Vessel 1: -281.0 Vessel 2: -274.0

a presented as sum at each sampling time of all quantified aerobic and anaerobic bacteria and spores as well as actinomycetes and fungi; aerobic and anaerobic bacteria comprised the majority.

B. STUDY DESIGN

1. Experimental conditions

Water was filtered through a 0.2 mm sieve and the sediment was sieved through a 2.0 mm sieve. The study was performed with a flow-through system using cylindrical 1 L glass bottles (9.5 cm internal diameter) containing 1 : 3 sediment (wet weight) to water ratio. Acclimatisation took place for a period of 21 days. Nitrogen was drawn through each system at a flow rate of approximately 50 mL/minute continuously until anaerobic conditions were established. Afterwards, the nitrogen was drawn through the system for three periods of 20 min each day until the end of incubation period.

The radio-labelled test substance was radiodiluted with non-radiolabelled Captan and further diluted with acetonitrile. The application rate of Captan (0.53-0.55 mg/L) resulted in an amount of application solution of 330 or 340 µL/vessel for Calwich Abbey Lake and Swiss Lake samples, respectively.

After application, the flasks were incubated at 20 ± 2°C in the dark up to 182 days. The organic volatiles were trapped by trap containing ethyl digol as adsorbent, while the carbon dioxide was trapped by a potassium hydroxide solution.

2. Sampling

Duplicate samples per test system were taken for analysis immediately after application and after 1, 4 hours and subsequently after 1, 2, 7, 15, 30, 100 and 182 days of incubation.
For monitoring of methanogenesis, a single vessel of each aquatic sediment type was taken for analysis after 15 and 30 days of incubation.
Microbiological activity was measured at the start of the test and after 30 and 100 days after incubation and additionally at 182 days of incubation.
The samples used for measurement for oxygen concentration, pH and redox potential of the water phase and the redox potential of the sediment were sampled weekly throughout the acclimatisation period and 1 and 4 days after application and further at every sampling interval after day 15.

3. Description of analytical procedures
The amount of radioactivity in the traps was measured by LSC.
The radioactivity in the water was determined directly by LSC of an aliquot (0.75 or 1.0 mL) taken from the water phase descanted into a weighed bottle where a portion (75 mL) of 1% acetic acid in methanol was added. The concentrated extract were analysed by HPLC.
The sediment was extracted with one portion of acetone by sonicating and shaking. The sediment and extract were separated by centrifugation. The extract was then weighed and duplicate aliquots (0.5 mL) taken for LSC. Concentrated extracts of samples up to Day 182 were analysed by HPLC. The sediment samples from Day 182 were extracted twice as above and analysed by TLC.
The sediment debris remaining after extraction was air-dried, weighted and duplicate (0.3 g) taken for combustion and LSC.
The quantity of radioactivity in solutions was determined by liquid scintillation counting (LSC). The TLC plates were put on a Fujifilm FLA-5000 Bio Image Analyser. The TLC Plates were read out with a TINA software.
Non-radiolabelled Captan and its reference substances were detected by their quenching of the UV fluorescent indicator on the TLC plate or by exposure to iodine vapour.
HPLC was carried out with UV and radioactivity detection employing Laura software.
The decline of Captan, THPI and THCY in the water and sediment were modelled using the NAFTA guidance. The most appropriate fit was determined.

II. RESULTS AND DISCUSSION

A. MASS BALANCE
The total recoveries from the water/sediment system were 91.5 – 105.1% AR except on four occasions where the recoveries were 84.3, 88.0% AR (both day 182 replicates from Calwich Abbey Lake), 82.2% AR (one day 0 replicate from Swiss Lake; recovery for the other replicate was 101.3% AR) and 89.9% AR (one day 182 replicate from Swiss Lake). Results are presented in tables B.8.2.2.3-13 and B.8.2.2.3-14.

B. DISTRIBUTION OF THE RADIOACTIVITY
Calwich Abbey Lake aquatic sediment:
The radioactivity in the water phase decreased from mean of 97.5% AR at time zero to 74.7% after 30 days, and then to 53.8% after 182 days. In the sediment, total radioactivity increased to a mean of 27.9% AR after 30 days and remained at similar levels to the end of the incubation period. Non-extractable radioactivity in the sediment increased to a maximum 13.6% AR at day 100. Volatile radioactivity was shown to be associated with $^{14}CO_2$ and reached its maximum with a mean value of 8.1% AR at Day 182. The course of the distribution of radioactivity is summarized on table B.8.2.2.3-13.

Table B.8.2.2.3-13: Distribution of radioactivity in Calwich Abbey Lake aquatic sediment system treated with [^{14}C]-Captan (% applied radioactivity)

Time	CO_2	Organic Volatiles	Water Phase	Sediment (total extractable)	Non-extractable	Sum
[days]	[% AR]					
0	n.a.	n.a.	96.0	3.7	1.2	100.9
0	n.a.	n.a.	98.9	1.9	0.7	101.5
0.04	-	-	92.3	4.1	1.7	98.1
0.04	-	-	95.3	2.0	0.9	98.2
0.17	-	-	93.5	3.2	1.5	98.2

Time	CO_2	Organic Volatiles	Water Phase	Sediment (total extractable)	Non-extractable	Sum
[days]	[% AR]					
0.17	-	-	93.0	4.9	2.1	100.0
1	-	-	90.6	5.2	3.6	99.4
1	-	-	89.7	5.7	3.6	99.0
2	-	-	91.7	4.9	4.9	101.5
2	-	-	87.9	7.6	6.4	101.9
7	0.1	-	82.4	9.8	8.0	100.3
7	< 0.05	-	88.1	8.2	6.4	102.7
15	0.1	-	80.4	11.7	12.4	104.6
15	0.1	-	77.4	12.2	11.5	101.2
30	0.4	-	74.1	14.2	12.8	101.5
30	0.4	-	75.3	15.7	13.1	104.5
100	2.2	-	73.3	16.0	13.6	105.1
100	1.7	-	67.8	15.5	11.3	96.3
182	8.5	-	51.9	14.7	9.1	84.3
182	7.6	-	55.6	15.2	9.6	88.0

n.a. not applicable
- not detected

Swiss Lake aquatic sediment
The radioactivity in the water phase decreased from a range of 75.4 to 92% AR at time zero to 65.7% AR after 182 days. In the sediment, total radioactivity increased to a mean of 19.4% AR after 100 days and decreased to 15.7 % at the end of the incubation period. Non-extractable radioactivity in the sediment increased to a maximum 11.8% AR (100 d) during incubation period. Volatile radioactivity was shown to be associated with $^{14}CO_2$ and reached its maximum with a mean value of 9.4% AR at Day 182. The course of the distribution of radioactivity is summarized on table B.8.2.2.3-14.

Table B.8.2.2.3-14: Distribution of radioactivity in Swiss Lake aquatic sediment system treated with [^{14}C]-Captan (% applied radioactivity)

Time	CO_2	Organic Volatiles	Water Phase	Sediment (total extractable)	Non-extractable	Sum
[days]	[% AR]					
0	n.a.	n.a.	75.4	4.7	2.0	82.1
0	n.a.	n.a.	92.0	6.4	2.9	101.3
0.04	-	-	91.6	3.0	0.9	95.5
0.04	-	-	94.3	3.5	1.3	99.1
0.17	-	-	93.6	4.3	1.9	99.8
0.17	-	-	98.5	3.1	1.2	102.8
1	< 0.05	-	87.0	2.8	1.9	91.7
1	-	-	87.8	3.7	2.4	93.9
2	< 0.05	-	90.4	6.1	4.0	100.5
2	< 0.05	-	90.9	6.6	3.7	101.2
7	< 0.05	-	87.2	7.4	5.6	100.2

Time	CO_2	Organic Volatiles	Water Phase	Sediment (total extractable)	Non-extractable	Sum
[days]	[% AR]					
7	< 0.05	-	86.9	8.3	6.0	101.2
15	0.2	-	85.2	9.5	8.5	103.4
15	0.1	-	83.6	9.7	8.4	101.8
30	0.3	-	80.7	9.1	9.3	99.4
30	0.3	-	79.0	9.1	9.3	98.0
100	4.0	-	73.0	7.6	11.8	96.4
100	2.0	-	76.2	8.4	11.0	97.6
182	5.6	-	70.3	7.4	8.2	91.5
182	13.1	-	61.0	8.6	7.2	89.9

n.a. not applicable
- not detected

There were no measurable levels of volatile radioactivity as methane or low molecular weight organic compound detected in the samples taken for methanogensis analysis from either aquatic sediment system.

C. SUM OF CHARACTERISED RADIOACTIVITY

Total system

The proportion of Captan declined rapidly from a mean of 71.5% and 66.7% AR at time zero to 1.7 and 3.5% after 4 hours of incubation in samples of Calwich Abbey Lake and Swiss Lake aquatic sediment systems, respectively. Captan was then not detected after 4 hours of incubation.

A percentage of the applied radioactivity could not be resolved. This polar material was investigated further and showed that the radioactivity was comprised of multiple components, each < 10% AR.

Two transient unknown degradates were identified. Unknown 1 (Rt≈19 minutes) accounted for up to maximum 36.9% AR and 23.7% AR after 4 hours in Calwich Abbey Lake and Swiss Lake system, respectively. Unknown 2 (Rt≈20.5 minutes) was present at low levels (2.5% AR) in one sample at 1 or 4 hours, respectively. Both were not detected in any later sampling dates.

Please refer to tables B.8.2.2.3-15 and B.8.2.2.3-16 for details.

Table B.8.2.2.3-15: Distribution of the radioactivity in the <u>total system</u> of Calwich Abbey Lake aquatic sediment system treated with ^{14}C-Captan (% applied radioactivity)

Time	Captan	THPAM	THPI	THPAI	THCY	Polar [a]	Unknown 1	Unknown 2	Others [b]
[days]	[% AR]								
0	63.6	-	18.8	-	6.6	-	-	-	6.9
0	79.4	-	12.2	-	-	-	-	-	7.3
0.04	20.1	-	9.3	-	33.7	-	28.5	-	0.6
0.04	12.4	-	14.6	-	38.5	-	25.5	2.5	1.8
0.17	-	-	16.0	-	33.0	-	36.9	-	7.6
0.17	3.3	-	11.3	-	43.6	-	31.3	-	3.3
1	-	26.8	40.7	-	23.0	-	-	-	5.3
1	-	22.8	48.4	-	23.8	-	-	-	0.4
2	-	36.4	35.1	-	20.7	-	-	-	4.2
2	-	39.3	33.3	-	16.1	-	-	-	6.7
7	-	52.8	23.6	-	10.0	-	-	-	5.8
7	-	48.2	29.8	-	12.1	-	-	-	6.2
15	-	58.7	19.7	-	5.4	-	-	-	8.3
15	-	57.9	18.3	-	7.7	0.5	-	-	5.2
30	-	59.6	11.1	2.9	7.6	1.4	-	-	5.7
30	-	52.1	20.7	2.5	9.6	1.2	-	-	4.9

Time	Captan	THPAM	THPI	THPAI	THCY	Polar [a]	Unknown 1	Unknown 2	Others [b]
[days]	[% AR]								
100	-	61.8	-	11.2	8.0	1.1	-	-	7.3
100	-	58.4	-	12.5	6.6	1.1	-	-	4.8
182	-	42.9	1.4	0.8	5.8	14.9	-	-	0.8
182	-	45.6	1.5	2.2	4.7	15.3	-	-	1.6

- not detected
a Comprised of up to four multiple components, each < 10% AR
b Radioactivity distributed throughout regions of the chromatogram other than those specified and which did not contain any discrete radioactive components

Table B.8.2.2.3-16: Distribution of the radioactivity in the total system of Swiss Lake aquatic sediment system treated with ^{14}C-Captan (% applied radioactivity)

Time	Captan	THPAM	THPI	THPAI	THCY	Polar [a]	Unknown 1	Unknown 2	Others [b]
[days]	[% AR]								
0	56.8	-	17.0	-	-	-	-	-	6.4
0	76.6	-	15.4	-	-	-	-	-	6.4
0.04	34.3	-	9.7	-	34.4	-	11.9	-	1.4
0.04	37.4	-	9.4	-	29.3	-	12.1	-	6.0
0.17	3.3	-	21.7	-	40.1	2.8	22.1	-	3.7
0.17	3.6	-	21.1	-	41.5	-	23.7	2.5	6.1
1	-	24.1	37.8	-	16.9	4.4	-	-	3.8
1	-	25.5	40.5	-	18.4	-	-	-	3.3
2	-	21.9	54.2	-	11.6	-	-	-	8.7
2	-	21.7	62.1	-	8.8	-	-	-	4.9
7	-	32.1	43.4	-	11.3	-	-	-	7.9
7	-	27.3	49.9	2.6	7.9	5.9	-	-	1.6
15	-	44.8	33.2	0.3	9.4	-	-	-	7.0
15	-	35.8	38.7	0.3	6.0	7.5	-	-	5.0
30	-	40.0	26.7	1.5	6.2	7.2	-	-	8.3
30	-	40.5	29.5	2.7	12.0	-	-	-	3.3
100	-	42.5	9.2	8.0	6.5	9.7	-	-	4.6
100	-	42.0	9.8	6.5	7.2	11.4	-	-	7.6
182	-	36.6	1.0	10.8	7.5	21.0	-	-	0.9
182	-	31.9	1.2	5.0	5.1	24.8	-	-	1.7

- not detected
a Comprised of up to three multiple components, each < 10% AR
b Radioactivity distributed throughout regions of the chromatogram other than those specified and which did not contain any discrete radioactive components

Water phase

In the water phase Captan was metabolised to THPI, THPAM, THPAI, THCY, polar material and up to two unknown degradates after 182 days of incubation. Please refer to tables B.8.2.2.3-17 and B.8.2.2.3-18 for details.

Table B.8.2.2.3-17: Distribution of the radioactivity in the water phase of Calwich Abbey Lake aquatic sediment system treated with ^{14}C-Captan (% applied radioactivity)

Time	Captan	THPAM	THPI	THPAI	THCY	Polar [a]	Unknown 1	Unknown 2	Others [b]
[days]	[% AR]								
0	63.6	-	18.8	-	6.6	-	-	-	6.9
0	79.4	-	12.2	-	-	-	-	-	7.3

Time	Captan	THPAM	THPI	THPAI	THCY	Polar [a]	Unknown 1	Unknown 2	Others [b]
[days]	[% AR]								
0.04	20.1	-	9.3	-	33.7	-	28.5	-	0.6
0.04	12.4	-	14.6	-	38.5	-	25.5	2.5	1.8
0.17	-	-	16.0	-	33.0	-	36.9	-	7.6
0.17	3.3	-	11.3	-	43.6	-	31.3	-	3.3
1	-	26.8	36.9	-	22.1	-	-	-	4.8
1	-	21.7	45.0	-	23.0	-	-	-	-
2	-	35.3	32.2	-	20.1	-	-	-	3.9
2	-	37.4	29.0	-	15.2	-	-	-	6.2
7	-	48.9	19.5	-	9.0	-	-	-	5.0
7	-	45.8	25.9	-	10.9	-	-	-	5.5
15	-	52.7	15.9	-	4.3	-	-	-	7.6
15	-	52.3	14.4	-	6.3	-	-	-	4.3
30	-	52.6	8.0	2.6	5.7	-	-	-	5.2
30	-	45.3	16.1	2.2	7.5	-	-	-	4.1
100	-	50.6	-	10.1	5.8	-	-	-	6.8
100	-	47.6	-	11.5	4.9	-	-	-	3.9
182	-	33.8	-	-	5.8	11.8	-	-	0.5
182	-	35.9	-	1.4	4.7	12.4	-	-	1.3

- not detected
a Comprised of up to four multiple components, each < 10% AR
b Radioactivity distributed throughout regions of the chromatogram other than those specified and which did not contain any discrete radioactive components

Table B.8.2.2.3-18: Distribution of the radioactivity in the water phase of Swiss Lake aquatic sediment system treated with ^{14}C-Captan (% applied radioactivity)

Time	Captan	THPAM	THPI	THPAI	THCY	Polar [a]	Unknown 1	Unknown 2	Others [b]
[days]	[% AR]								
0	56.8	-	12.4	-	-	-	-	-	6.3
0	76.6	-	9.2	-	-	-	-	-	6.2
0.04	34.3	-	9.7	-	34.4	-	11.9	-	1.4
0.04	37.4	-	9.4	-	29.3	-	12.1	-	6.0
0.17	3.3	-	21.7	-	40.1	2.8	22.1	-	3.7
0.17	3.6	-	21.1	-	41.5	-	23.7	2.5	6.1
1	-	24.1	37.8	-	16.9	4.4	-	-	3.8
1	-	25.5	40.5	-	18.4	-	-	-	3.3
2	-	21.9	49.3	-	10.9	-	-	-	8.3
2	-	21.7	56.7	-	8.1	-	-	-	4.4
7	-	30.8	38.5	-	10.5	-	-	-	7.4
7	-	25.9	44.3	2.6	7.2	5.9	-	-	1.0
15	-	42.0	28.6	-	8.4	-	-	-	6.1
15	-	33.3	33.0	-	5.3	7.5	-	-	4.5
30	-	37.5	21.9	1.1	5.4	7.2	-	-	7.6
30	-	38.2	24.9	2.4	10.6	-	-	-	2.9
100	-	39.1	7.7	7.4	5.6	9.1	-	-	4.0
100	-	38.0	8.2	5.8	6.1	11.0	-	-	7.0
182	-	33.1	-	10.3	7.5	18.9	-	-	0.6
182	-	27.8	-	4.1	5.1	22.8	-	-	1.2

- not detected
a Comprised of up to three multiple components, each < 10% AR

b Radioactivity distributed throughout regions of the chromatogram other than those specified and which did not contain any discrete radioactive components

Sediment phase:
Total radioactivity in the sediment increased to a mean 28.2% AR after 100 days in Calwich Abbey Lake system or to a mean of 19.4% AR after 100 days in Swiss Lake system and remained at similar levels to the end of the incubation period. Captan was not detected in the sediment extracts.
Please refer to tables B.8.2.2.3-19 and Table B.8.2.2.3-20 for details.

Table B.8.2.2.3-19: Distribution of the radioactivity in the sediment phase of Calwich Abbey Lake aquatic sediment system treated with ^{14}C-Captan (% applied radioactivity)*

Time	THPAM	THPI	THPAI	THCY	Polar	Others [b]
[days]	[% AR]					
1	-	3.8	-	0.9	-	0.5
1	1.1	3.4	-	0.8	-	0.4
2	1.1	2.9	-	0.6	-	0.3
2	1.9	4.3	-	0.9	-	0.5
7	3.9	4.1	-	1.0	-	0.8
7	2.4	3.9	-	1.2	-	0.7
15	6.0	3.8	-	1.1	-	0.7
15	5.6	3.9	-	1.4	0.5	0.9
30	7.0	3.1	0.3	1.9	1.4	0.5
30	6.8	4.6	0.3	2.1	1.2	0.8
100	11.2	-	1.0	2.2	1.1	0.5
100	10.8	-	1.0	1.7	1.1	0.9
182 [a]	9.1	1.4	0.8	-	3.1	0.3
182 [a]	9.7	1.5	0.8	-	2.9	0.3

- not detected
a data are from TLC analyses, all others are from HPLC analyses
b Radioactivity distributed throughout regions of the chromatogram other than those specified and which did not contain any discrete radioactive components
* sediment extract samples at time zero, 1 and 4 hours were not analysed as the radioactivity present represented < 5% AR

Table B.8.2.2.3-20: Distribution of the radioactivity in the sediment phase of Swiss Lake aquatic sediment treated with ^{14}C-Captan (% applied radioactivity)*

Time	THPAM	THPI	THPAI	THCY	Polar	Others [b]
[days]	[% AR]					
0	-	4.6	-	-	-	0.1
0	-	6.2	-	-	-	0.2
2	-	4.9	-	0.7	-	0.4
2	-	5.4	-	0.7	-	0.5
7	1.3	4.9	-	0.8	-	0.5
7	1.4	5.6	-	0.7	-	0.6
15	2.8	4.6	0.3	1.0	-	0.9
15	2.5	5.7	0.3	0.7	-	0.5
30	2.5	4.8	0.4	0.8	-	0.7
30	2.3	4.6	0.3	1.4	-	0.4
100	3.4	1.5	0.6	0.9	0.6	0.6
100	4.0	1.6	0.7	1.1	0.4	0.6
182 [a]	3.5	1.0	0.5	-	2.1	0.3
182 [a]	4.1	1.2	0.9	-	2.0	0.5

- not detected
a Data are from TLC analyses, all others are from HPLC analyses

b Radioactivity distributed throughout regions of the chromatogram other than those specified and which did not contain any discrete radioactive components
* Soil extract samples at 1 and 4 hours and day 1 were not analysed as the radioactivity present represented < 5% AR

D. HALF-LIFE TIMES

The DT_{50} and DT_{90} values, according to NAFTA guidance, of the decline of Captan and its degradates (THPI and THCY) in the water and sediment phases of each aquatic sediment and in the total systems, are shown in the tables below.

Table B.8.2.2.3-21: DT_{50} and DT_{90} values of Captan

Water phase / Total system					
	Parameter		**Parameter**	**Prob>t**	**CI (95 %)**
Calwich Abbey Lake	DT_{50}	0.02 d (SFO)	k= 44.86	7.83E-004	
	DT_{90}	0.05 d (SFO)			
Swiss Lake	DT_{50}	0.03 d (IORE)*	k=11.36	0.02773	Contains 0
	DT_{90}	0.10 d (IORE)*			

SFO Single First Order
IORE Indeterminate Order of Rate Equation
*statistically not significant (Prob> t : >0.05 and/or CI contains 0)

Table B.8.2.2.3-22: DT_{50} and DT_{90} values of THPI and THCY

System		**THPI**				
		DT_{50}	**DT_{90}**	**Parameter**	**Prob>t**	**CI (95 %)**
Calwich Abbey Lake	Water	23.6 (DFOP)*	62.8 (DFOP)*	k1 = 0.9935	0.126	CI contains 0
	Sediment	122 (SFO)	404 (SFO)	k = 0.005701	0.002412	
	Total system	30.9 (DFOP)*	83.6 (DFOP)*	k1 = 0.9596	0.07708	CI contains 0
Swiss Lake	Water	46.6 (DFOP)*	126 (DFOP)*	k1 = 0.1445	0.07837	CI contains 0
	Sediment	70.7 (SFO)	235 (SFO)	k = 0.009809	1.49E-005	
	Total system	39.8 (IORE)*	132 (IORE)*	k = 0.003755	0.1505	CI contains 0
		THCY				
		DT_{50}	**DT_{90}**	**Parameter**	**Prob>t**	**CI (95 %)**
Calwich Abbey Lake	Water	32.4 (IORE)*	108 (IORE)*	k = 1.01E-004	0.2462	CI contains 0
	Sediment	-	-			
	Total system	78.6 (IORE)*	261 (IORE)*	k = 1.82E-005	0.2745	CI contains 0
Swiss Lake	Water	116 (IORE)*	386 (IORE)*	k = 7.07E-007	0.3515	CI contains 0
	Sediment	-	-			
	Total system	305 (IORE)*	1011 (IORE)*	k = 9.04E-008	0.371	CI contains 0

*statistically not significant (Prob> t : >0.05 and/or CI contains 0)

E. REDOXPOTENTIAL

The redox potential in water of Calwich Abbey Lake reached negative values during the acclimation period down to -99 mV but from day 0 onwards the redox potential was above 0 mV. The redox potential in water of Swiss lake showed mainly negative values (in the range of -16 to -69) during acclimation period and up to day 15, but from day 30 onward the values were above -1 mV. The oxygen conten (% saturation) was zero during the study with the exception of two occasions. According to the EPA GD the redox potential should be below -100 mV. The redox potential in the sediment was always below -200 mV (-210 mv to -315 mV for Calwich Abbey Lake, -256 to -296 mV for Swiss Lake) indicating anaerobic conditions in the sediment.

III. CONCLUSIONS

The dissipation of ^{14}C-Captan in two anaerobic aquatic sediment systems (Calwich Abbey Lake and Swiss Lake) was investigated at 20°C in the dark. ^{14}C-Captan rapidly dissipated from the water phase and total system. A DT_{50} value of 0.02 days (Calwich Abbey Lake) and 0.03 days (Swiss Lake) was calculated.

Captan was shown to degrade to THPI (up to 62.1%), THPAM (up to 61.8%), THCY (up to 43.6%), THPAI (up to 12.5%), polar material and two unidentified transient degradates, bound residue and carbon dioxide. The degradation of Captan proceeded via hydrolysis to THPI, then to THCY or THPAM and then to THPAI and then

to more highly degraded entities which were incorporated into bound residues and finally converted to carbon dioxide via mineralisation.

Comments RMS

No LOD and no LOQ were given.

The provided kinetic evaluation followed NAFTA guidance using the additional kinetic model IORE which is not one of the standard models recommended by FOCUS. Therefore, the RMS recalculated the kinetic evaluation following a stepwise approach (for the whole system) according to FOCUS using KINGUI 2:

Calwich Abbey Lake, whole system:
For captan only 3 sampling time points were available, no captan was detected after 1 day. Immediately after application captan degraded mainly to THPI (15.5 % AR), after 1 h and after 4 hours THCY (36.1/38.3 % AR) and unknown 1 (27/34.1 % AR) were detected at higher amounts than THPI (12/13.7 % AR). One day after application no unknown 1 was detectable. THPI reached its maximum of 44.5 % AR on day 1 and degraded to 1.5 % AR after 182 d, THCY reached its maximum of 38.3 % AR after 4 h and degraded to 5.3 % AR after 182 d. The metabolite THPAM was detected from day 1 onwards (24.8 % AR) and reached its maximum of 60.1 % AR after 100 d.
The amount of THPI increased from 4 h to 1 d after application although almost no captan was left. THPI might be generated from unknown 1 or /and THCY (via re-cyclisation).

Calwich Abbey Lake							
Substance	DT_{50}	DT_{90}	Kinetic model	Parameter	Visual fit	$\chi 2$	Prob > t, CI
Captan only, whole system							
Captan only	0.016	0.052	SFO	M0=97.447	acceptable	3.526	< 2e-16
				k=44.750			< 2e-16
Captan and metabolites, stepwise approach, whole system							
captan	0.016	0.052	SFO	Mo=97.42	acceptable	3.5	< 2e-16
				k=44.58688			< 2e-16
				ff to THPI=0.2927			
THPI			SFO	k=0.02228	Not acceptable	37.9	0.0158
				ff to THCY=1			
THCY			SFO	k=0.01826	Not acceptable	93.4	0.35
Degradation of metabolites from max onwards							
Whole system							
THPI	16.39	54.44	SFO	M0=38.870339	moderate	12.45	1.27e-08
				k=0.042296			0.000725
THCY			SFO		Not acceptable		ns
			FOMC				ns
			DFOP				ns
Water							
THPI	12.86	42.71	SFO	M0=35.74266	moderate	12.44	5.47e-07
				k=0.05391			0.0024
			FOMC				ns
			DFOP				ns
THCY			SFO		Not acceptable		
			FOMC				ns
			DFOP		Not acceptable		
Sediment							
THPI	121.6	403.9	SFO	M0=4.112594	acceptable	3.57	7.65e-07

				k=0.005700			0.00225

ns…not significant

For captan a DT_{50} value of 0.016 d and a DT_{90} value of 0.052 days were calculated for the dissipation in the whole system. For the metabolite THPI the following DT_{50} and DT_{90} values (SFO) were calculated: for the whole system 16.4 days and 54.4 days, for water 12.9 days and 42.7 days and for sediment 121.6 days and 403.9 days. For the metabolite THCY no acceptable and reliable DT_{50} values could be calculated.

Swiss Lake, whole system

For captan only 3 sampling time points were available, no captan was detected after 1 day. Immediately after application captan degraded to THPI (16.2 % AR), captan and THPI were further degraded to THCY and unknown 1. The metabolite Unknown 1 was only detected 1 h and 4 h after application with 12 and 22.9 % AR. THPI reached its maximum of 58.2 % AR two days after application and degraded to 1.1 % at the end of the study. THCY reached its maximum of 40.8 % AR four hour after application and degraded to 6.3 % AR after 182 d.

The metabolite THPAM was detected from day 1 onwards (24.8 % AR) and reached its maximum of 42.3 % AR after 100 d.

The amount of THPI increases from 4 h to 2 d after application although almost no captan is left. THPI could be generated from unknown 1 and from THCY (via re-cyclisation).

Swiss Lake							
Substance	DT_{50}	DT_{90}	Kinetic model	Parameter	Visual fit	$\chi 2$	Prob > t, CI
Captan only, whole system							
Captan	0.033	0.11	SFO	M0=83.601	Acceptable	1.4	2.16e-05
				k=20.959			0.00145
Captan and metabolites, stepwise approach, whole system							
Captan	0.034	0.11	SFO	Mo=83.25	acceptable	2.9	< 2e-16
				k=20.3383			< 2e-16
				ff to THPI=0.496			
THPI			SFO	k = 0.013056	Not acceptable	29.5	0.00183
				ff to THCY=1			
THCY				k = 0.024152	Not acceptable	90.9	0.21189 (CI contains 0)
Degradation of metabolites from max onwards							
Whole system							
THPI	29.02	96.42	SFO	M0=54.38	Acceptable	7.7	2.84e-10
				k=0.02388			4.55e-05
			FOMC				ns
			DFOP				ns
THCY			SFO		Not acceptable		
			FOMC				ns
			DFOP				ns
Water							
THPI	24.63	81.81	SFO	M0=49.65	Acceptable	8.2	3.99e-08
				k=0.028146			0.000450
			FOMC				ns
			DFOP				ns
THCY			SFO		Not acceptable		
			FOMC				ns
			DFOP				ns
Sediment							
THPI	70.67	234.75	SFO	M0=5.59	Acceptable	6.9	5.98e-12

				k=0.009809			1.96e-05
			FOMC				ns
			DFOP				ns

ns…not significant

For captan a DT50 value of 0.034 d and a DT90 value of 0.11 days were calculated for the dissipation in the whole system. For the metabolite THPI the following DT50 and DT90 values (SFO) were calculated: for the whole system 29.02 days and 96.42 days, for water 24.63 days and 81.81 days and for sediment 70.67 days and 234.75 days. For the metabolite THCY no acceptable and reliable DT50 values could be calculated.

The notifier provided an amendment to the anaerobic aquatic metabolism study which is summarised below.

Study 16 (2017)

Reference:	**Captan: Anaerobic aquatic metabolism – Report Amendment 1**
Notifier:	Arysta LifeScience S.A.S., ADAMA Makhteshim Ltd.
Author(s), year:	Anonymous, 2017
Report/Doc. number:	LEB0133/ R-35450
Guideline(s):	US EPA OCSPP 835.4100, Anaerobic aquatic metabolism, October 2008
GLP:	Yes
Deviations:	None
Validity:	Valid
Status:	Submitted for renewal

The following additional information was provided:

- HPLC-method:

For HPLC, the limit of detection (LOD) and limit of quantification (LOQ) is equivalent to radioactivity in gross amounts of less than twice the background level. The limit of detection was 0.1% of the applied radioactivity.

- Clarification of anaerobic system conditions:

During the acclimatisation period, oxygen levels in the water fell to zero and generally remained at this level (except on two occasions) for each aquatic sediment system. The zero levels of oxygen in the water phase indicated a reducing (anaerobic) environment, even though the redox values measured were greater than -100 mV.

- HPLC-Chromatogramms

Comments RMS

None.

B.8.3. REFERENCES RELIED ON

Fate and behavior in soil

Study number Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
Study 1 KCA 7.1.1.1	Anonymous	1992	AEROBIC METABOLISM OF [TRICHLOROMETHYL -14C] CAPTAN IN SOIL ICI Americas Inc. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S.		no		ADM/ ARY

Study number Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
			Report-no. PMS-320, R-9280/TMN-0323 GLP: yes Published: no				
Study 2 KCA 7.1.1.1	Anonymous	1988 a	AEROBIC SOIL METABOLISM OF [TRICHLOROMETHYL -14C] CAPTAN Chevron Chemical Company, Richmond, California ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. MEF 0060/8809887, R-4994/TMN-0324 GLP: yes Published: no		no		ADM/ ARY
Study 3 KCA 7.1.1.1/ 01	Anonymous	2016 a	[14C] CAPTAN AEROBIC DEGRADATION AND METABOLISM IN ONE SOIL AT 20°C IN THE DARK ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., S14-05275, R-35448 Eurofins Agroscience Services GmbH GLP: yes Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ ARY
Study 1 KCA 7.1.2.1	Anonymous	1992	AEROBIC METABOLISM OF [TRICHLOROMETHYL -14C] CAPTAN IN SOIL ICI Americas Inc. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. PMS-320, R-9280/TMN-0323 GLP: yes Published: no		no		ADM/ ARY
Study 2 KCA 7.1.2.1.1	Anonymous	1988 a	AEROBIC SOIL METABOLISM OF [TRICHLOROMETHYL -14C] CAPTAN Chevron Chemical Company, Richmond, California ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. MEF 0060/8809887, R-4994/TMN-0324 GLP: yes Published: no		no		ADM/ ARY
Study 3	Anonymous	2016 a	[14C] CAPTAN AEROBIC DEGRADATION AND METABOLISM IN ONE	no	yes	New data for active ingredient,	ADM/ ARY

Study number Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 7.1.2.1.1/02			SOIL AT 20°C IN THE DARK ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., S14-05275, R-35448 Eurofins Agroscience Services GmbH GLP: yes Published: no **Submitted in: KCA 7.1.1.1/01**			not previously submitted nor evaluated	
Study 4 KCA 7.1.2.1.1/01	Anonymous	2014	CAPTAN AEROBIC DEGRADATION IN ONE EUROPEAN SOIL ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., S14-00502 Eurofins Agroscience Services EcoChem GmbH GLP: yes Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ ARY
Study 5 KCA 7.1.2.1.1/03	Anonymous	2016	CALCULATION OF SOIL DEGRADATION VALUES FOR CAPTAN AND MAJOR METABOLITES ACCORDING TO THE RECOMMENDATIONS OF FOCUS DEGRADATION KINETICS WORKGROUP ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., 562961-CA-070102-01 GAB Consulting, Stade, Germany GLP/GEP: no Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ ARY
Study 6 KCA 7.1.2.1.1/04	Anonymous	2017	CALCULATION OF SOIL DEGRADATION VALUES FOR CAPTAN AND MAJOR METABOLITES THPI AND THPAM ACCORDING TO THE RECOMMENDATIONS OF FOCUS DEGRADATION KINETICS WORKGROUP USING CAKE 3.3 not available, 562961-CA-070102-02 not available GLP/GEP: no Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ ARY
Study 7 KCA 7.1.2.1.2	Anonymous	1993	TETRAHYDROPHTHALIMIDE : LABORATORY SOIL DEGRADATION STUDY (BBA) ICI Americas Inc.		no		ADM/ ARY

Study number Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
			ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. RJ1440B, R-7219/TMN-0346 GLP: yes Published: no				
Study 8 KCA 7.1.2.1.2	Anonymous	1993	CIS-TETRAHYDROPHTHALMIC ACID : LABORATORY SOIL DEGRADATION STUDY (BBA) ICI Americas Inc. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. RJ1441B, R-7220/TMN-0345 GLP: yes Published: no		no		ADM/ARY

Fate and behaviour in water and sediment

Study number Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
Study 1 KCA 7.2.1.1	Anonymous	1989 a	[TRICHLOROMETHYL-14C] CAPTAN - HYDROLYSIS AT 25°C ICI Americas Inc. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. WRC 89-44, R-5932/TMN-0361 GLP: yes Published: no		no		ADM/ARY
Study 2 KCA 7.2.1.1	Anonymous	1989 b	[RING-1-14C] CAPTAN - HYDROLYSIS AT 25°C ICI Americas Inc. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. RR 89-068B, R-8704/TMN-0360 GLP: yes Published: no		no		ADM/ARY
Study 3 KCA 7.2.1.1	Anonymous	2002 a	HYDROLYSIS DETERMINATION OF THPI AT DIFFERENT PH VALUES		no		ADM/ARY

Study number Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
			RCC Ltd. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. 833725, R 14370a/TMN-0369 GLP: yes Published: no				
Study 4 KCA 7.2.1.1	Anonymous	2002 b	HYDROLYSIS DETERMINATION OF THPAM AT DIFFERENT PH VALUES RCC Ltd. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. 833725, R-14370b/TMN-0370 GLP: yes Published: no		no		ADM/ ARY
Study 5 KCA 7.2.1.2	Anonymous	1986	PHOTOLYSIS OF CAPTAN: IN STERILE AQUEOUS SOLUTION Chevron Chemical Company, Richmond, California ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. MEF-0001, 870326, R-4393/TMN-0364 GLP: yes Published: no		no		ADM/ ARY
Study 6 KCA 7.2.1.2	Anonymous	2002 a	AQUEOUS PHOTOLYSIS OF THPI UNDER LABORATORY CONDITIONS AND DETERMINATION OF QUANTUM YIELD RCC Ltd. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. 833736, R-14256a/TMN-0369 GLP: yes Published: no		no		ADM/ ARY
Study 7 KCA 7.2.1.2	Anonymous	2002 b	AQUEOUS PHOTOLYSIS OF THPAM UNDER LABORATORY CONDITIONS AND DETERMINATION OF QUANTUM YIELD RCC Ltd. ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. 833747, R-14256b/TMN-0370		no		ADM/ ARY

Study number Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
			GLP: yes Published: no				
Study 8 KCA 7.2.2.1/01	Anonymous	2015	CAPTAN, [CARBOXYMIDE-14C] READY BIODEGRADABILITY MODIFIED STURM TEST (INCLUDING AMENDMENT 1) ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., NAU16289, R-34731 DR.U.NOACK-LABORATORIEN, Sarstedt, Germany GLP: yes Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ ARY
Study 9 KCA 7.2.2.2/01	Anonymous	2016b	AEROBIC MINERALISATION OF [14C] CAPTAN IN SURFACE WATER ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., S14-05599 Eurofins Agroscience Services EcoChem GmbH GLP: yes Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ ARY
Study 10 KCA 7.2.2.2/02	Anonymous	2016	AMENDMENT 1: AEROBIC MINERALISATION OF [14C] CAPTAN IN SURFACE WATER ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., S14-05599, R-35636 Eurofins Agroscience Services EcoChem GmbH GLP: yes Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ ARY
Study 11 KCA 7.2.2.2/03	Anonymous	2017	STATEMENT FOR REPORT AMENDMENT 1(NON-GLP): AEROBIC MINERALISATION OF [14C] CAPTAN IN SURFACE WATER ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., S14-05599, R-35636 Eurofins Agroscience Services EcoChem GmbH GLP: no Published: no	no		New data for active ingredient, not previously submitted nor evaluated	ADM/ ARY
Study 12	Anonymous	2017	AMENDMENT 2: AEROBIC	no	yes	New data for active	ADM/ ARY

Study number Data point	Author(s)	Year	Title Owner Report No. Source (where different from owner) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCA 7.2.2.2/04			MINERALISATION OF [14C] CAPTAN IN SURFACE WATER ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., S14-05599, R-35636 Eurofins Agroscience Services EcoChem GmbH GLP: yes Published: no			ingredient, not previously submitted nor evaluated	
Study 13 KCA 7.2.2.2/05	Anonymous	2016	METABOLISM OF CAPTAN IN THE ENVIRONMENT ADAMA Makhteshim Ltd., 1405319.UKO-4905, R-37590 Exponent International Ltd. GLP/GEP: no Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ARY
Study 14 KCA 7.2.2.3	Anonymous	1993	CAPTAN: DEGRADATION IN SEDIMENT - WATER SYSTEMS UNDER LABORATORY CONDITIONS ICI Agrochemicals, Jealott's Hill Research Station, UK ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S. Report-no. RJ1439B, R-6851/TMN-0365 GLP: yes Published: no		no		ADM/ARY
Study 15 KCA 7.2.2.3/01	Anonymous	2016	CAPTAN: ANAEROBIC AQUATIC METABOLISM ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., LEB0133, R-35450 ENVIGO CRS Limited, UK GLP: yes Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ARY
Study 16 KCA 7.2.2.3/02	Anonymous	2017	REPORT AMENDMENT 1 - CAPTAN: ANAEROBIC AQUATIC METABOLISM ADAMA Makhteshim Ltd / Arysta LifeScience S.A.S., LEB0133, R-35450 ENVIGO CRS Limited, UK GLP: yes Published: no	no	yes	New data for active ingredient, not previously submitted nor evaluated	ADM/ARY