



Draft Assessment Report

Evaluation of Active Substances

Plant Protection Products

Prepared according to **Regulation (EC) 1107/2009**
as it applies in Great Britain (GB PPP)

Cinmethylin (BAS 684 H)

Volume 3 – B.8 (AS)

Environmental Fate & Behaviour

Great Britain

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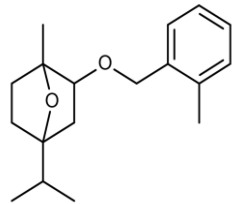
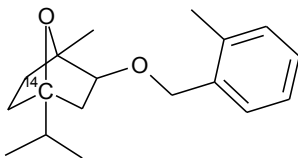
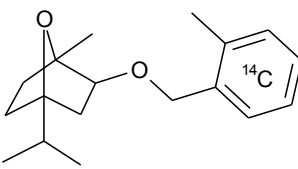
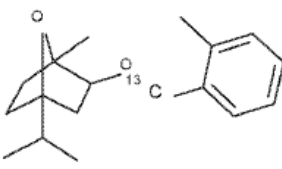
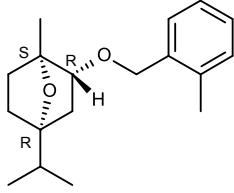
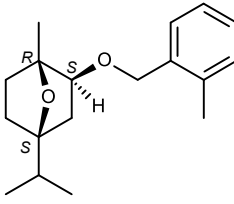
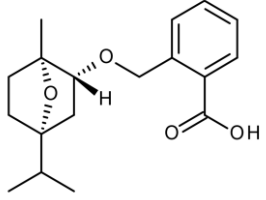
B.8. ENVIRONMENTAL FATE AND BEHAVIOUR

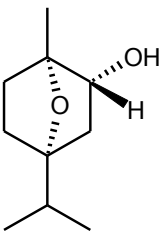
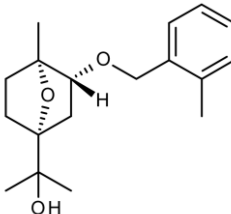
Cinmethylin (also known as BAS 684 H) is a broad-spectrum soil residual herbicide for the control of winter annual grass weed species and some broadleaf weeds in small grain cereals and oil seed rape. Spray application is at a proposed rate of up to 500 g a.s./ha. Cinmethylin targets a pre- to post-emergence application window of winter wheat (BBCH 00-29) and winter oil seed rape (BBCH 00-18), with targeted winter annual grass- and broadleaf weeds not yet emerged or within an early growth stage (BBCH 00-12).

All studies supplied by the Applicant were conducted in accordance with requirements contained in Regulation 1107. Studies were performed to investigate the environmentally relevant properties of cinmethylin using two different ¹⁴C-labeled compounds representing each ring system of cinmethylin: cyclohexane and phenyl. With these studies, a full environmentally relevant metabolic profile for cinmethylin was elucidated and this information was used to propose environmentally relevant exposure concentrations.

Cinmethylin comprises a racemic mixture of two enantiomers: (-)-cinmethylin (also known as Reg. No. 5925581); and (+)-cinmethylin (Reg No. 5925632). In all studies, this was applied as 50:50 ratio, consistent with the proposed ratio. The enantiomeric ratio was monitored throughout the studies via chiral HPLC analysis. An overview of the active substance, radiolabelled positions and metabolites discussed in this section is given below in Table CA 8.1-01.

Table CA 8.1-01. Summary of active substance and metabolites.

Substance name (plus synonyms)	Reg No.	Compartments assessed	Structure
Parent			
Cinmethylin / BAS 684 H	900202	Soil Surface water Groundwater Air	
[cyclohexane-4- ¹⁴ C]- cinmethylin	900202	Soil Surface water Groundwater Air	
[phenyl-U- ¹⁴ C]- cinmethylin (also referred to as benzyl-U- ¹⁴ C])	900202	Soil Surface water Groundwater Air	
[benzyl- ¹³ C]- cinmethylin	900202	Soil Surface water Groundwater	
Cinmethylin (-)-enantiomer	5925581	Soil Surface water Groundwater	
Cinmethylin (+)-enantiomer	5925632	Soil Surface water Groundwater	
Metabolites			
M684H001	6055521	Surface water	

M684H003	4539586	Surface water	
M684H004	6055480	Surface water	

For the soil and water environmental compartments, the assessment of the rate of degradation included the derivation of several endpoints through kinetic evaluation in accordance with the FOCUS Kinetics Guidance (2006; 2014). Regulatory endpoints, also known as trigger endpoints, were derived as regulatory endpoints used as triggers for higher-tier experiments. The endpoints are also used for predicting the environmental concentration of the active substance in soil (PEC_{soil}). The three triggers for the environmental fate and behaviour of an active substance are as follows:

- Field dissipation studies are required when the DT_{50} exceeds 60 days (20°C) or 90 days (10°C) in a laboratory study;
- Soil residue studies are required when the laboratory DT_{50} exceeds 1/3 of the period between application and harvest;
- Soil accumulation studies are required when the field DT_{90} exceeds one year.

Additionally, degradation rates are derived for use as input for pesticide fate models, also known as modelling endpoints. These are used to determine predicted environmental concentrations (PECs) in surface water, sediment and groundwater.

Degradation rates are also derived for the consideration of persistence criteria, known as persistence endpoints. These are used to conclude whether an active substance is a persistent organic pollutant (POP), or whether it fulfils persistence, bioaccumulation and toxicity (PBT) and very persistent, very bioaccumulative (vPvB) criteria.

B.8.1. FATE AND BEHAVIOUR IN SOIL

The Applicant submitted several laboratory and field studies to investigate the fate and behaviour of cinmethylin in the environment, with the route and rate of degradation studied for both the parent and its two enantiomers. The route and rate of degradation studies will be summarised in turn below, followed by a summary of the kinetics and selection of endpoints.

Route of degradation

For investigating the route of degradation, three laboratory studies were submitted, with kinetic evaluations for deriving trigger endpoints. A separate kinetic evaluation for the aerobic degradation study was submitted for modelling endpoints; this is covered in the summary for the rate of degradation. Table CA 8.1-01 summarises the relevant studies. Kinetic evaluations were performed for each study to derive best-fit laboratory degradation endpoints as triggers for additional work (trigger endpoints) for both cinmethylin and its

enantiomers; these are discussed in the summary for the rate of degradation. There were no major metabolites observed in the soil in these three studies, with no breakdown products observed above 5% of the applied radioactivity (AR) in each study.

Table CA 8.1-01 Laboratory studies investigating the route of cinmethylin degradation in soil.

Laboratory soil study	Study type	Endpoints calculated?
Stewart, L., Abernethy, A., 2016a KCA 7.1.1.1/1	Aerobic degradation	Trigger
Staudenmaier, H., Pape, L., 2017a KCA 7.1.1.2/1	Anaerobic degradation	Trigger
Hassink, J., 2017c KCA 7.1.1.3/1	Soil photolysis	Trigger

The aerobic degradation of cinmethylin was investigated under laboratory conditions in four soils: two from Europe and two from North America [see KCA 7.1.1.1/1]. Two radiolabelled positions were used: [cyclohexane-4-¹⁴C]- and [benzyl-U-¹⁴C]-cinmethylin; these sufficiently followed the metabolism of the parent. By the study end (120 DAT), cinmethylin accounted for between 0.6 – 47.3% total applied radioactivity (TAR) across the four soils. Non-extractable residues (NER)¹ peaked at 12 – 36.5% AR at 90 or 120 DAT, with some soils observing slight falls in NER levels by the study end at 120 DAT. CO₂ peaked at 23.3 – 47.7% total applied radioactivity (TAR) at 90 or 120 DAT; again, levels reduced slightly in some soils by 120 DAT. Aerobic degradation was therefore a major route of degradation for cinmethylin.

The anaerobic metabolism of cinmethylin was also studied in four soils, two European and two North American, under laboratory conditions using three labelled positions: [cyclohexane-4-¹⁴C]-cinmethylin, and [phenyl-U-¹⁴C]- and [benzyl-¹³C]-cinmethylin combined to form one treatment [see KCA 7.1.1.2/1]. All four soils undertook an aerobic incubation phase for between 10-30 days (corresponding to approximately one half-life in the respective soil) prior to flooding to induce anaerobic conditions for the remaining 103 – 105 days, giving a total duration of 118 – 120 days, depending on the soil. By the study end, cinmethylin accounted for 35.1 – 65.1% AR, with most of the degradation having occurred during the aerobic phase. NER were a major sink, accounting for 15 – 41.2% AR by 118/120 DAT, and CO₂ accounted for 8.1 – 17.0% AR. The HSE evaluator concluded that anaerobic metabolism is not a major route of degradation for cinmethylin.

The Applicant also investigated the soil photolysis of cinmethylin on one soil over 15 days under artificial, continuous lighting [see KCA 7.1.1.3/1]. Three labelled positions were used: [cyclohexane-4-¹⁴C]-, [phenyl-U-¹⁴C]- and [benzyl-¹³C]-cinmethylin, with the latter two combined to form one treatment. After 15 days of irradiation, cinmethylin accounted for 56.3 – 63.1% AR, NER accounted for 5.1 – 9.4% AR and volatiles accounted for 2.6 – 4.5% AR. In dark control samples, cinmethylin accounted for 61.7 – 71.8% AR, NER accounted for 7.3 – 11.1% AR and volatiles accounted for 6.9 – 7.2% AR after 15 days. Although the Applicant concluded there was no significant photolytic degradation taking place, the HSE evaluator concluded that photolysis is a minor route of degradation for cinmethylin.

¹ The HSE evaluator notes that the Applicant has referred to “non-extractable residues” (NER) throughout the assessment presented here. A more accurate term for these residues would be “unextracted residues”, as the proportion of unextracted residues varies based upon the extraction used. For consistency, the HSE evaluator has retained the use of “NER” throughout this assessment report but has made this note for clarity.

Overall, the radiolabelling was adequate for following the metabolism of cinmethylin in these studies.

Rate of degradation

For each laboratory study summarised above, the rate of degradation was calculated through the derivation of endpoints for cinmethylin. Table CA 8.1-02 summarises the trigger endpoints derived for cinmethylin and its two enantiomers from the aerobic degradation study. Table 8.1-03 summarises the modelling endpoints derived for cinmethylin and its two enantiomers. The maximum non-normalised DegT₅₀ was observed in the Lufa 2.2 soil at 93.6 days.

Anaerobic degradation occurred slowly for cinmethylin, with a maximum DT₅₀ of 1710 days (Table CA 8.1-04). Photolysis study DT₅₀s were 24.1 days for photolysis samples and 25.9 days for dark control samples, demonstrating a small influence of photolysis on the degradation of cinmethylin (Table CA 8.1-05). The HSE evaluator did not derive a photolysis-only degradation rate because of the use of biphasic kinetics for the photolysis degradation rate.

Field dissipation studies are necessary for the investigation of the rate of degradation for an active substance when the DegT₅₀ for the active substance, or DisT₅₀ for a metabolite exceeds 60 days in at least one soil in the aerobic degradation study. As the longest DT₅₀ for cinmethylin was 93.6 days, a field dissipation study was triggered.

Table CA 8.1-02

Summary of trigger/persistence endpoints for cinmethylin and its two enantiomers derived from the aerobic degradation study (conducted at 20°C and pF 2).

Cinmethylin (BAS 684 H)	Dark aerobic conditions (non-normalised trigger and persistence endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	93.6	541.4	0.9	DFOP
Lufa 5M	8.0	7.4	20	pF2	19.1	63.5	6.2	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	43.5	144.4	3.0	SFO
MSL-PF	6.7	6.3	20	pF2	18.5	178.1	3.1	DFOP
Maximum (non-normalised)					93.6	541.4		
(-)-enantiomer (Reg No. 5925581)	Dark aerobic conditions (non-normalised trigger and persistence endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	67.4	450.8	1.3	DFOP
Lufa 5M	8.0	7.4	20	pF2	15.4	51.1	4.5	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	34.7	115.4	4.1	SFO
MSL-PF	6.7	6.3	20	pF2	10.8	122.0	1.1	DFOP
Maximum (non-normalised)					67.4	450.8		
(+)-enantiomer (Reg No. 5925632)	Dark aerobic conditions (non-normalised trigger and persistence endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	113.5	450.2	2.2	DFOP
Lufa 5M	8.0	7.4	20	pF2	21.5	71.5	6.2	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	56.4	187.3	7.3	SFO
MSL-PF	6.7	6.3	20	pF2	36.5	206.5	0.5	DFOP
Maximum (non-normalised)					113.5	450.2		

Table CA 8.1-03

Summary of laboratory aerobic degradation modelling endpoints for cinmethylin and its two enantiomers Reg Nos. 5925581 and 5925632.

Cinmethylin (BAS 684 H)	Dark aerobic conditions (modelling endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	192.8 ^a	541.4	0.9	DFOP
Lufa 5M	8.0	7.4	20	pF2	19.1	63.5	6.18	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	43.5	144.4	3.02	SFO
MSL-PF	6.7	6.3	20	pF2	74.6 ^a	178.1	3.11	DFOP
Geometric mean					58.8			
(-)-enantiomer (Reg No. 5925581)	Dark aerobic conditions (modelling endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	165.0 ^a	450.8	1.3	DFOP
Lufa 5M	8.0	7.4	20	pF2	15.4	51.1	4.5	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	34.7	115.4	4.1	SFO
MSL-PF	6.7	6.3	20	pF2	54.6 ^a	122.0	1.1	DFOP
Geometric mean					46.8			
(+)-enantiomer (Reg No. 5925632)	Dark aerobic conditions (modelling endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	145.0 ^a	450.2	2.2	DFOP
Lufa 5M	8.0	7.4	20	pF2	21.5	71.5	6.2	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	56.4	187.3	7.3	SFO
MSL-PF	6.7	6.3	20	pF2	73.4 ^a	206.5	0.5	DFOP
Geometric mean					59.9			

^a Pseudo-SFO DT₅₀ derived from the DFOP slow phase (k₂) DT₅₀.

Table CA 8.1-04

Summary of trigger/persistence endpoints for cinmethylin in anaerobic conditions.

Cinmethylin (BAS 684 H)	Dark anaerobic conditions (non-normalised trigger and persistence endpoints)						
Soil type	pH (CaCl₂)	Temp °C	% MWHC	DT₅₀ (d)	DT₉₀ (d)	St. (χ^2)	Method of calculation
Lufa 2.2	5.4	20	Flooded Soil	1710	5660	1.1	SFO
Lufa 5M	7.2	20	Flooded Soil	651	2160	0.6	SFO
North Dakota	6.3	20	Flooded Soil	241	800	1.5	SFO
Wyoming	8.1	20	Flooded Soil	1680	5570	4.6	SFO
Maximum (non-normalised)				1710	5660		

Table CA 8.1-05

Summary of trigger/persistence endpoints for the photolytic degradation of cinmethylin.

Cinmethylin (BAS 684 H)	Photolysis study (non-normalised trigger and persistence endpoints)						
Experiment (LUFA 5M soil)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Method of calculation
Light	6.9 – 7.2	22	60	24.1	92.2	2.0	DFOP
Dark control			60	25.9	86.0	2.8	SFO
Photolysis only degradation rate				Not derived due to use of biphasic kinetics			

Enantiomeric ratio changes

Cinmethylin comprises a racemic mixture of two enantiomers; as a result, the Applicant investigated the enantiomeric ratio throughout the course of the laboratory degradation studies. In the aerobic degradation study (KCA 7.1.1.1/1), a more rapid degradation of the (-)-enantiomer was observed in some soils, leading to shifts in the enantiomeric ratio. For example, in the LAD-SCL-PF soil (cinmethylin DT₅₀ = 43.5 d), the ratio shifted to 23:77 after 120 days, with 9.4% of cinmethylin remaining. Conversely, in the soil displaying the longest DT₅₀ (Lufa 2.2; 192.8 d), the ratio measured 46:54 after 120 days, with 40% of cinmethylin remaining. Overall, there is a 13.1 day difference in the geomean modelling DT₅₀s for the aerobic degradation of enantiomers, with the (-)-enantiomer degrading faster.

A similar trend was observed in the aerobic phase of the anaerobic degradation study (KCA 7.1.1.2/1), with variable enantiomeric ratios observed by 10 DAT. The Lufa 2.2 soil displayed a slight shift to a ratio of 46:54 with 60.5% cinmethylin remaining after 10 days, whereas the North Dakota soil exhibited a ratio of 29:71 with 48% cinmethylin remaining after 10 days. However, all four soils showed little change in the enantiomeric ratio once anaerobic conditions had been established.

In the soil photolysis study (KCA 7.1.1.3/1), the enantiomeric ratio also did not display a notable change, shifting to 46:54 after 15 days with 56% of applied cinmethylin remaining.

The HSE evaluator concludes that changes in enantiomeric ratio are driven by the faster degradation of the (-)-enantiomer in aerobic soils. Anaerobic degradation and photolysis do

not appear to influence the enantiomeric ratio, consistent with the route of degradation being primarily aerobic degradation.

Field dissipation studies

The Applicant submitted two field studies to investigate the behaviour of cinmethylin under field conditions: one in Europe and one in the United States. The Applicant also supplied several studies to support the field studies. These are all summarised in Table CA 8.1-06 along with the associated kinetic evaluations.

Table CA 8.1-06 Cinmethylin applied field dissipation studies.

Field dissipation study	Field sites	Kinetic report(s)	Endpoints calculated? ^a
Gut, T., 2017a (CA 7.1.2.2.1/01) Gut, T., 2017b (CA 7.1.2.2.1/02)	Höltinghausen, Germany	He, W. and Pape, L., 2018a (KCA 7.1.2.2.1/03): trigger	Modelling and trigger
	Dugliolo di Budrio, Italy		
	Røllum, Denmark		
	Banbury, UK	He, W. and Pape, L., 2018b (KCA 7.1.2.2.1/04): modelling	
	Saint-Amand, Belgium		
	Almayate, Spain		
Mitchell J. <i>et al.</i> , 2018a (CA 7.1.2.2.1/05)	New York, US	Kinetic evaluations are reported within Mitchell, J. <i>et al.</i> , 2018a (KCA 7.1.2.2.1/05)	Modelling and trigger ^c
	North Carolina, US		
	North Dakota, US ^b		
	Texas, US		
	Washington, US		
	California, US		
Stewart, L., 2016a (KCA 7.1.2.2.1/06)	A study to compare the extraction methods to extract [¹⁴ C]-cinmethylin from soil.		
Bodsch J., 2017a (KCA 7.1.2.2.1/07)	A study to determine the storage stability of the cinmethylin racemate in soil.		
Perez, S. and Jones, A., 2018a (KCA 7.1.2.2.1/08)	A study to determine the freezer storage stability of cinmethylin (both enantiomers) in soil.		
Jeffries, M. and Warren, R., 2018a (KCA 7.1.2.2.1/09)	A study to determine European ecoregion similarity to terrestrial field dissipation sites in North America.		

^a Modelling or trigger endpoints. Trigger endpoints are defined as endpoints calculated to determine whether further work was triggered.

^b One soil, North Dakota, was excluded from derivation of modelling and trigger endpoints as the conditions were not ecologically relevant to Europe. The soil has been included in the study evaluations, but has not been included in final endpoints tables.

^c The Applicant supplied modelling endpoints following an information request from the HSE evaluator.

The degradation of cinmethylin was investigated under field conditions in six representative growing regions of Europe [see KCA 7.1.2.2.1/1 and KCA 7.1.2.2.1/2]. At these sites, the test item was incorporated immediately after application to exclude surface processes and to enable a straightforward generation of modelling endpoints to be used for calculation of predicted environmental concentrations as recommended by EFSA [EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT₅₀ values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662].

Kinetic evaluation was performed for cinmethylin and its enantiomers (-)-cinmethylin and (+)-cinmethylin according to the FOCUS kinetics guidance [FOCUS (2014)] and EFSA guidance [EFSA (2014)] in order to derive best-fit field degradation endpoints as triggers for additional work (trigger endpoints) [see KCA 7.1.2.2.1/3]. Additionally, normalised

degradation endpoints that could be used as input for modelling (modelling endpoints) were derived [see KCA 7.1.2.2.1/4].

As the laboratory DT₅₀ of cinmethylin exceeded 60 days in one case, an additional terrestrial field dissipation study was run in the US according to NAFTA guidelines at six different sites without incorporating the substance after application [see KCA 7.1.2.2.1/5]. Plot locations corresponded closely to the growing regions for the intended GAP though the test sites were not cropped. The application was also done according to intended GAP for the intended crops, although the studies themselves were not grown with actual crops (i.e. bare field plots).

The Applicant performed kinetic evaluations for cinmethylin and its enantiomers to derive trigger endpoints for the US field studies; these were undertaken according to FOCUS kinetics guidance. Following an information request, the Applicant also supplied modelling endpoints that were normalised according to the recommendations for legacy studies in the EFSA DegT₅₀ guidance [EFSA (2014)].

Several studies were performed in support of the field dissipation studies: extractability study, storage stability studies, and an ecoregion crosswalk study [see KCA 7.1.2.2.1/6, KCA 7.1.2.2.1/7, KCA 7.1.2.2.1/8 and KCA 7.1.2.2.1/9 respectively].

The extractability study was performed to demonstrate equivalent extractability between the methods used in the metabolism studies and the residue analytical methods used for the field samples [see KCA 7.1.2.2.1/6]. Storage stability of cinmethylin under frozen conditions was investigated in soil samples from the field studies conducted in Europe and the US [see KCA 7.1.2.2.1/7 and KCA 7.1.2.2.1/8]. The study relating to European soils demonstrated that cinmethylin was stable for at least 715 days when stored at -18°C or below, with reductions in recovery of < 10% observed. The study relating to US field soils demonstrated that storage at -25°C for 12 months (14 months for New York soils) did not lead to significant reductions in recoveries. The US study also demonstrated that cinmethylin was stable in final extracts in a refrigerator for at least 182 days. Both storage stability studies covered the sample storage periods for their respective field studies.

An ecoregion crosswalk exercise was performed with the OECD Europe – North America Soil Geographic Information for Pesticide Studies application (ENASGIPS v3.0) to determine if there are European ecoregions similar to the North American ecoregions containing the cinmethylin terrestrial field dissipation trial sites [see KCA 7.1.2.2.1/9]. The objective was to demonstrate that the data generated from the terrestrial dissipation study conducted in North America is representative of dissipation in similar European ecoregions. The study concluded that five out of six soils were representative of European ecoregions, with North Dakota being excluded on the basis that the conditions are not relevant to Europe. The HSE evaluator notes that the actual climatic conditions experienced during the field study were also assessed, with the HSE evaluator concluding that the conditions during the field studies were appropriate at the five accepted field sites, but not in North Dakota. Therefore, the HSE evaluator did not include North Dakota degradation rates when calculating modelling endpoint geomeans or when considering trigger endpoints.

Soil accumulation studies are required if the DisT₉₀ value of at least one field soil exceeds one year. For cinmethylin, the DT₉₀ value in European field soils was ≤ 207.6 days and ≤ 179.2 days in US field soils. Therefore, a field accumulation study is not necessary for cinmethylin.

Tables CA 8.1-07 – 09 present the final modelling endpoints for cinmethylin and its two enantiomers from field dissipation studies. Tables CA 8.1-10 – 12 present the final trigger endpoints. Discussion of pH dependence (referenced in the following tables) follows the field dissipation section.

Table CA 8.1-07

Summary of modelling endpoints for cinmethylin (time step normalisation performed).

Parent	Aerobic conditions								
Field dissipation study	Soil type (indicate if bare or cropped soil was used)	Location (country or USA state)	pH CaCl ₂ ^a	pH H ₂ O ^b	Depth (cm) ^c	St. (χ ²)	DT ₅₀ (d) Norm. ^d	DT ₉₀ (d) Norm.	Method of calculation
Gut, T., 2017a (KCA 7.1.2.2.1/01) Gut, T., 2017b (KCA 7.1.2.2.1/02)	Loamy fine sand, bare soil	Höltinghausen, Germany	4.80	-	0-15	9.7	29.9 ^e	99.4	FOMC
	Very fine sandy loam, bare soil	Dugliolo di Budrio, Italy	7.66	-	0-20	5.6	47.0 ^e	156.0	FOMC
	Sand, bare soil	Røllum, Denmark	4.62	-	0-30	9.4	15.3	50.7	SFO
	Loam, bare soil	Banbury, UK	6.70	-	0-25	8.1	5.4	18.0	SFO
	Silt, bare soil	Saint-Amand, Belgium	6.12	-	0-30	5.0	8.0 ^e	26.6	FOMC
	Coarse sandy loam, bare soil	Almayate, Spain	7.70	-	0-25	10.3	13.9	46.2	SFO
Mitchell et al., 2018a (KCA 7.1.2.2.1/5) ^f	Silt loam, bare soil	New York, US	5.14	5.7	0-45	9.7	19.2	63.8	SFO
	Sandy loam, bare soil	North Carolina, US	5.55	6.1	0-15	10.5	6.7	22.4	SFO
	Clay loam, bare soil	Texas, US	6.77	7.3	0-30	18.4	9.9	33.1	SFO
	Sand, bare soil	Washington, US	7.59	8.1	0-15	16.0	3.7	12.2	SFO
	Sandy loam, bare soil	California, US	7.69	8.2	0-30	9.9	5.2	17.3	SFO
Geometric mean (if not pH dependent)							11.1		
pH dependence							No		

^a pH values are mean values for the soil across the depths at which residues were detected. US field study pH values were converted to be expressed as a CaCl₂ pH value using the method reported in EFSA (2017).

^b Measured in a saturated soil paste made from distilled water. pH values are mean values for the soil across the depths at which residues were detected.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to 0.5 × LOD.

^d Normalised using a Q₁₀ of 2.58 and Walker equation coefficient of 0.7, values are DegT50matrix.

^e Calculated as DT₅₀ = DT₉₀ / 3.32 (less than 10% of initial concentration at last sampling).

^f One soil, North Dakota, was excluded from consideration of modelling endpoints as it was deemed not ecologically or climatically relevant to Europe following an ENASGIPS crosswalk exercise and consideration of the actual climatic conditions measured during the conduct of the field study.

Table CA 8.1-08

Summary of modelling endpoints for cinmethylin enantiomer
Reg. No. 5925581 (time step normalisation performed).

Parent	Aerobic conditions								
Field dissipation study	Soil type (indicate if bare or cropped soil was used)	Location (country or USA state)	pH CaCl ₂ ^a	pH H ₂ O ^b	Depth (cm) ^c	St. (χ ²)	DT ₅₀ (d) Norm. ^d	DT ₉₀ (d) Norm.	Method of calculation
Gut, T., 2017a (KCA 7.1.2.2.1/01) Gut, T., 2017b (KCA 7.1.2.2.1/02)	Loamy fine sand, bare soil	Höltinghausen, Germany	4.80	-	0-15	9.9	25.4 ^e	84.4	FOMC
	Very fine sandy loam, bare soil	Dugliolo di Budrio, Italy	7.66	-	0-20	5.9	40.6 ^e	134.8	FOMC
	Sand, bare soil	Røllum, Denmark	4.62	-	0-30	9.8	14.2	47.3	SFO
	Loam, bare soil	Banbury, UK	6.70	-	0-25	9.2	4.4	14.6	SFO
	Silt, bare soil	Saint-Amand, Belgium	6.12	-	0-30	5.4	6.4 ^e	21.3	FOMC
	Coarse sandy loam, bare soil	Almayate, Spain	7.70	-	0-25	10.5	10.7	35.5	SFO
Mitchell et al., 2018a (KCA 7.1.2.2.1/5) ^f	Silt loam, bare soil	New York, US	5.14	5.7	0-45	7.9	17.3	57.5	SFO
	Sandy loam, bare soil	North Carolina, US	5.55	6.1	0-15	10.0	6.5	21.6	SFO
	Clay loam, bare soil	Texas, US	6.77	7.3	0-30	18.5	8.7	28.9	SFO
	Sand, bare soil	Washington, US	7.59	8.1	0-15	15.6	3.5	11.7	SFO
	Sandy loam, bare soil	California, US	7.69	8.2	0-30	9.7	5.0	16.6	SFO
Geometric mean (if not pH dependent)							9.7		
pH dependence							No		

^a pH values are mean values for the soil across the depths at which residues were detected. US field study pH values were converted to be expressed as a CaCl₂ pH value using the method reported in EFSA (2017).

^b Measured in a saturated soil paste made from distilled water. pH values are mean values for the soil across the depths at which residues were detected.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

^d Normalised using a Q₁₀ of 2.58 and Walker equation coefficient of 0.7, values are DegT50matrix.

^e Calculated as $\text{DT}_{50} = \text{DT}_{90} / 3.32$ (less than 10% of initial concentration at last sampling).

^f One soil, North Dakota, was excluded from consideration of modelling endpoints as it was deemed not ecologically or climatically relevant to Europe following an ENASGIPS crosswalk exercise and consideration of the actual climatic conditions measured during the conduct of the field study.

Table CA 8.1-09

Summary of modelling endpoints for cinmethylin enantiomer
Reg. No. 5925632 (time step normalisation performed).

Parent	Aerobic conditions								
Field dissipation study	Soil type (indicate if bare or cropped soil was used)	Location (country or USA state)	pH CaCl ₂ ^a	pH H ₂ O ^b	Depth (cm) ^c	St. (χ ²)	DT ₅₀ (d) Norm. ^d	DT ₉₀ (d) Norm.	Method of calculation
Gut, T., 2017a (KCA 7.1.2.2.1/01) Gut, T., 2017b (KCA 7.1.2.2.1/02)	Loamy fine sand, bare soil	Höltinghausen, Germany	4.80	-	0-15	9.4	33.9 ^e	112.7	FOMC
	Very fine sandy loam, bare soil	Dugliolo di Budrio, Italy	7.66	-	0-20	5.5	52.5 ^e	174.2	FOMC
	Sand, bare soil	Røllum, Denmark	4.62	-	0-30	9.0	16.2	53.9	SFO
	Loam, bare soil	Banbury, UK	6.70	-	0-25	7.4	6.4	21.3	SFO
	Silt, bare soil	Saint-Amand, Belgium	6.12	-	0-30	5.0	9.4 ^e	31.4	FOMC
	Coarse sandy loam, bare soil	Almayate, Spain	7.70	-	0-25	9.2	17.2	57.2	SFO
Mitchell et al., 2018a (KCA 7.1.2.2.1/5) ^f	Silt loam, bare soil	New York, US	5.14	5.7	0-45	11.4	20.1	66.6	SFO
	Sandy loam, bare soil	North Carolina, US	5.55	6.1	0-15	11.0	7.0	23.2	SFO
	Clay loam, bare soil	Texas, US	6.77	7.3	0-30	18.3	11.5	37.6	SFO
	Sand, bare soil	Washington, US	7.59	8.1	0-15	16.3	3.8	12.7	SFO
	Sandy loam, bare soil	California, US	7.69	8.2	0-30	10.5	5.4	18.0	SFO
Geometric mean (if not pH dependent)							12.3		
pH dependence							No		

^a pH values are mean values for the soil across the depths at which residues were detected. US field study pH values were converted to be expressed as a CaCl₂ pH value using the method reported in EFSA (2017).

^b Measured in a saturated soil paste made from distilled water. pH values are mean values for the soil across the depths at which residues were detected.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

^d Normalised using a Q₁₀ of 2.58 and Walker equation coefficient of 0.7, values are DegT50matrix.

^e Calculated as $\text{DT}_{50} = \text{DT}_{90} / 3.32$ (less than 10% of initial concentration at last sampling).

^f One soil, North Dakota, was excluded from consideration of modelling endpoints as it was deemed not ecologically or climatically relevant to Europe following an ENASGIPS crosswalk exercise and consideration of the actual climatic conditions measured during the conduct of the field study.

Table CA 8.1-10

Summary of trigger/persistence endpoints for cinmethylin.

Parent	Aerobic conditions								
Field dissipation study	Soil type (indicate if bare or cropped soil was used)	Location (country or USA state)	pH-CaCl ₂ ^a	pH-H ₂ O ^b	Depth (cm) ^c	DT ₅₀ (d) actual	DT ₉₀ (d) actual	St. (χ ²)	Method of calculation
Gut, T., 2017a (KCA 7.1.2.2.1/01) Gut, T., 2017b (KCA 7.1.2.2.1/02)	Loamy fine sand, bare soil	Höltinghausen, Germany	4.80	-	0-15	38.7	191.4	10.6	FOMC
	Very fine sandy loam, bare soil	Dugliolo di Budrio, Italy	7.66	-	0-20	27.3	178.5	3.7	FOMC
	Sand, bare soil	Røllum, Denmark	4.62	-	0-30	38.9	207.6	11.2	FOMC
	Loam, bare soil	Banbury, UK	6.70	-	0-25	15.2	55.6	8.0	DFOP
	Silt, bare soil	Saint-Amand, Belgium	6.12	-	0-30	14.8	74.9	4.7	DFOP
	Coarse sandy loam, bare soil	Almayate, Spain	7.70	-	0-25	22.6	87.4	8.8	DFOP
Mitchell J. <i>et al.</i> , 2018a (KCA 7.1.2.2.1/05) ^d	Silt loam, bare soil	New York, US	5.14	5.7	0-45	14.9	170.9	9.4	DFOP
	Sandy loam, bare soil	North Carolina, US	5.55	6.1	0-15	4.2	18.2	3.3	FOMC
	Clay loam, bare soil	Texas, US	6.77	7.3	0-30	53.9	179.2	15.7	SFO
	Sand, bare soil	Washington Site, US	7.59	8.1	0-15	2.5	20.5	8.4	FOMC
	Sandy loam, bare soil	California Site, US	7.69	8.2	0-30	12.9	42.7	18.1	SFO
Maximum							207.6		

^a pH values are mean values for the soil across the depths at which residues were detected. US field study pH values were converted to be expressed as a CaCl₂ pH value using the method reported in EFSA (2017).

^b Measured in a saturated soil paste made from distilled water. pH values are mean values for the soil across the depths at which residues were detected.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

^d One soil, North Dakota, was excluded from consideration of trigger endpoints as it was deemed not ecologically or climatically relevant to Europe following an ENASGIPS crosswalk exercise and consideration of the actual climatic conditions measured during the conduct of the field study.

Table CA 8.1-11

Summary of trigger/persistence endpoints for cinmethylin enantiomer Reg. No. 5925581.

Parent	Aerobic conditions								
Field dissipation study	Soil type (indicate if bare or cropped soil was used)	Location (country or USA state)	pH-CaCl ₂ ^a	pH-H ₂ O ^b	Depth (cm) ^c	DT ₅₀ (d) actual	DT ₉₀ (d) actual	St. (χ ²)	Method of calculation
Gut, T., 2017a (KCA 7.1.2.2.1/01) Gut, T., 2017b (KCA 7.1.2.2.1/02)	Loamy fine sand, bare soil	Höltinghausen, Germany	4.80	-	0-15	32.9	169.0	11.0	FOMC
	Very fine sandy loam, bare soil	Dugliolo di Budrio, Italy	7.66	-	0-20	23.9	156.8	4.5	FOMC
	Sand, bare soil	Røllum, Denmark	4.62	-	0-30	35.6	192.0	11.4	FOMC
	Loam, bare soil	Banbury, UK	6.70	-	0-25	11.5	52.2	6.5	FOMC
	Silt, bare soil	Saint-Amand, Belgium	6.12	-	0-30	12.2	55.6	4.8	DFOP
	Coarse sandy loam, bare soil	Almayate, Spain	7.70	-	0-25	18.8	69.6	9.4	DFOP
Mitchell J. <i>et al.</i> , 2018a (KCA 7.1.2.2.1/05) ^d	Silt loam, bare soil	New York Site, US	5.14	5.7	0-45	12.2	147.1	8.0	DFOP
	Sandy loam, bare soil	North Carolina Site, US	5.55	6.1	0-15	4.2	18.2	3.3	FOMC
	Clay loam, bare soil	Texas Site, US	6.77	7.3	0-30	47.7	158.5	15.8	SFO
	Sand, bare soil	Washington Site, US	7.59	8.1	0-15	2.5	18.4	7.1	FOMC
	Sandy loam, bare soil	California Site, US	7.69	8.2	0-30	12.5	41.4	19.2	SFO
Maximum							192.0		

^a pH values are mean values for the soil across the depths at which residues were detected. US field study pH values were converted to be expressed as a CaCl₂ pH value using the method reported in EFSA (2017).

^b Measured in a saturated soil paste made from distilled water. pH values are mean values for the soil across the depths at which residues were detected.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

^d One soil, North Dakota, was excluded from consideration of trigger endpoints as it was deemed not ecologically or climatically relevant to Europe following an ENASGIPS crosswalk exercise and consideration of the actual climatic conditions measured during the conduct of the field study.

Table CA 8.1-12

Summary of trigger/persistence endpoints for cinmethylin enantiomer Reg. No. 5925632.

Parent	Aerobic conditions								
Field dissipation study	Soil type (indicate if bare or cropped soil was used)	Location (country or USA state)	pH-CaCl ₂ ^a	pH-H ₂ O ^b	Depth (cm) ^c	DT ₅₀ (d) actual	DT ₉₀ (d) actual	St. (χ ²)	Method of calculation
Gut, T., 2017a (KCA 7.1.2.2.1/01) Gut, T., 2017b (KCA 7.1.2.2.1/02)	Loamy fine sand, bare soil	Höltinghausen, Germany	4.80	-	0-15	44.7	211.3	10.2	FOMC
	Very fine sandy loam, bare soil	Dugliolo di Budrio, Italy	7.66	-	0-20	30.8	197.8	3.2	FOMC
	Sand, bare soil	Røllum, Denmark	4.62	-	0-30	42.4	220.7	11.1	FOMC
	Loam, bare soil	Banbury, UK	6.70	-	0-25	18.6	61.8	8.2	SFO
	Silt, bare soil	Saint-Amand, Belgium	6.12	-	0-30	17.9	91.7	4.4	DFOP
	Coarse sandy loam, bare soil	Almayate, Spain	7.70	-	0-25	26.8	104.6	8.7	DFOP
Mitchell J. <i>et al.</i> , 2018a (KCA 7.1.2.2.1/05) ^d	Silt loam, bare soil	New York Site, US	5.14	5.7	0-45	17.8	193.4	11.2	DFOP
	Sandy loam, bare soil	North Carolina Site, US	5.55	6.1	0-15	4.4	18.9	3.0	FOMC
	Clay loam, bare soil	Texas Site, US	6.77	7.3	0-30	60.2	200.1	15.6	SFO
	Sand, bare soil	Washington Site, US	7.59	8.1	0-15	2.6	22.9	9.6	FOMC
	Sandy loam, bare soil	California Site, US	7.69	8.2	0-30	13.2	44.0	17.2	SFO
Maximum							220.7		

^a pH values are mean values for the soil across the depths at which residues were detected. US field study pH values were converted to be expressed as a CaCl₂ pH value using the method reported in EFSA (2017).

^b Measured in a saturated soil paste made from distilled water. pH values are mean values for the soil across the depths at which residues were detected.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

^d One soil, North Dakota, was excluded from consideration of trigger endpoints as it was deemed not ecologically or climatically relevant to Europe following an ENASGIPS crosswalk exercise and consideration of the actual climatic conditions measured during the conduct of the field study.

pH Dependence

In physical/chemical property studies, the partition co-efficient ($\log P_{ow}$) for cinmethylin was 4.5 at pH 5.8 and 20°C (see KCA 2.7/001). Additionally, cinmethylin demonstrated no dissociation between pH 3.2 – 10.9 (see KCA 2.8/001). Therefore, no influence of pH on

degradation rates is anticipated. The HSE evaluator sought to confirm this hypothesis by investigating whether a relationship existed between cinmethylin degradation rates and soil pH in the laboratory aerobic degradation and field dissipation studies. The Input-Decision 3.3 tool (Federal Environment Agency, Germany) was utilised to conduct the Kendall Test on laboratory-derived DT₅₀s and field-derived DT₅₀s as two separate populations.

In the aerobic degradation study, four soils were investigated with a pH (CaCl₂) range of 5.6 – 8.0. Figure 8.1-1 illustrates the relationship between laboratory DT₅₀s for cinmethylin and its two enantiomers. In the field dissipation studies, 11 soils were investigated with a pH (CaCl₂) range of 4.6 – 7.7. Figure 8.1-2 illustrates the pH dependence for the field DT₅₀s. Kendall's Test statistics were calculated for cinmethylin, (-)-enantiomer and (+)-enantiomer both for laboratory and field populations; the results are reported in Table 8.1-14 and showed that there was no pH dependence between the degradation of cinmethylin or its enantiomers and the soil pH.

The HSE evaluator notes that the US field dissipation study soil pH values were measured in water. To harmonise the measurement methods used in the two field dissipation studies, it was necessary to convert these pH values to be expressed in terms of CaCl₂ pH. This was undertaken by rearranging a pH conversion equation used to convert a pH-CaCl₂ measurement to pH-H₂O; the new equation is shown below; the equation was derived from EFSA PEC_{soil} guidance (2017):

$$pH(CaCl_2) = \frac{pH(H_2O) - 0.648}{0.982}$$

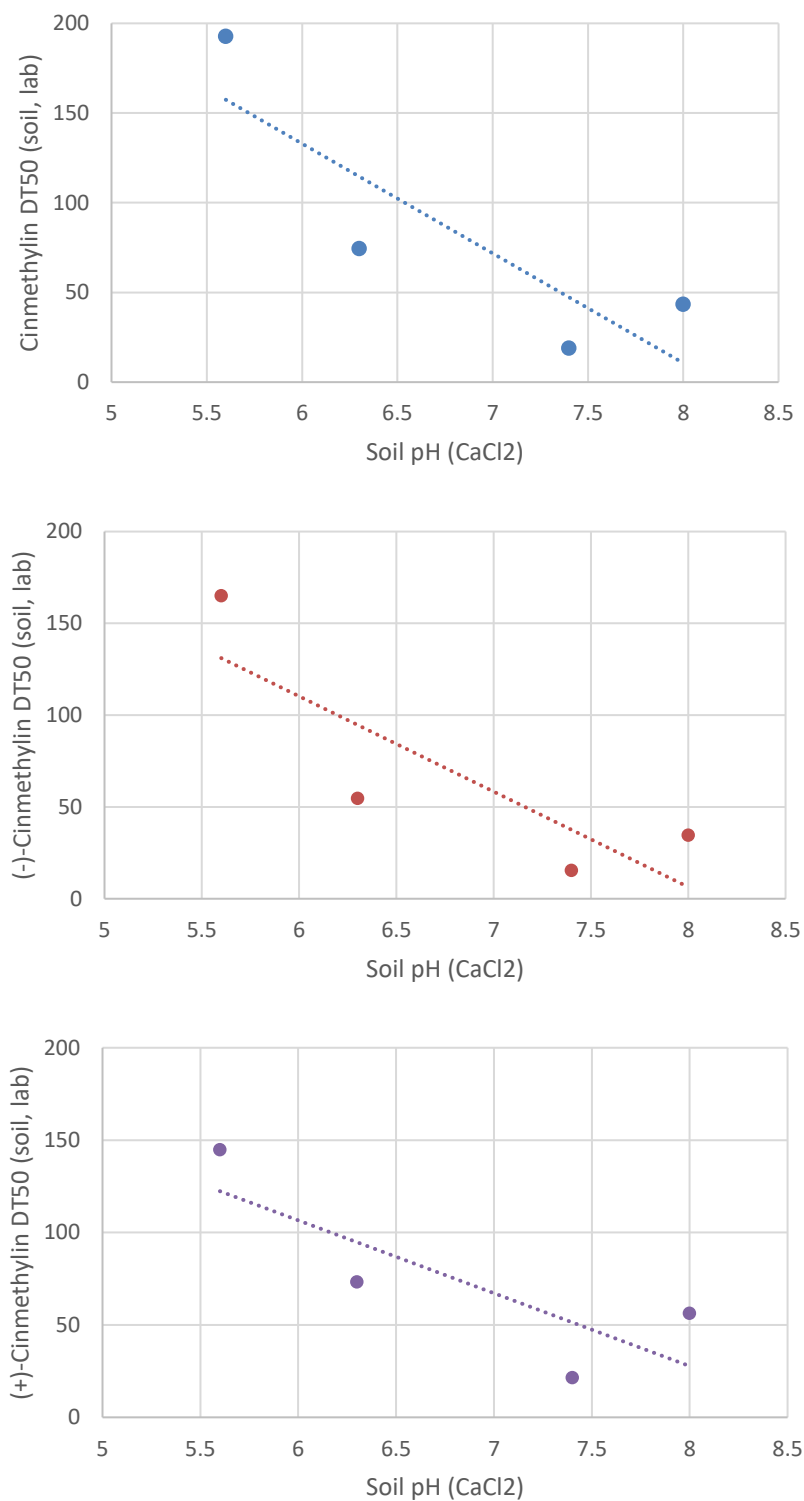


Figure 8.1-1

Relationship between laboratory soil DT₅₀ and soil pH. Top: cinmethylin. Middle: (-)-cinmethylin. Bottom: (+)-cinmethylin.

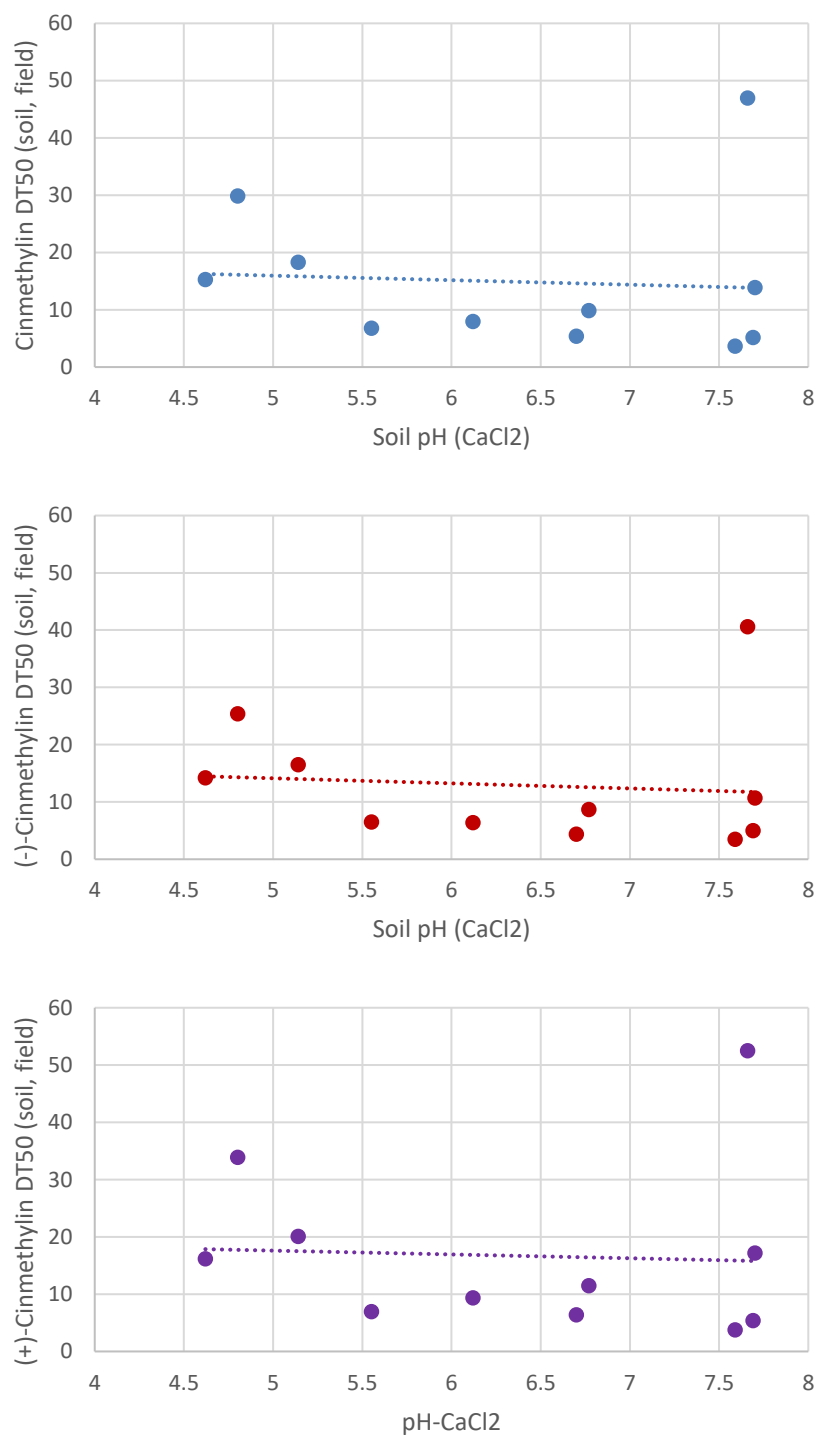


Figure 8.1-2

Relationship between field soil DT₅₀ and soil pH. Top: cinmethylin. Middle: (-)-cinmethylin. Bottom: (+)-cinmethylin.

Table 8.1-14

Kendall's test results investigating pH dependence of the degradation of cinmethylin and its enantiomers in soil in the laboratory and the field ($\alpha = 0.05$).

Substance	n	Tau	P	pH dependence?
Laboratory soils				
Cinmethylin	4	-0.667	0.308	No
(-)-enantiomer				
(+)-enantiomer				
Field soils				
Cinmethylin	11	-0.236	0.350	No
(-)-enantiomer		-0.236	0.350	No
(+)-enantiomer		-0.200	0.436	No

Sorption behaviour of cinmethylin

The Applicant submitted one laboratory study to investigate the sorption behaviour of cinmethylin, plus one study conducting QSAR estimation of adsorption coefficients. Table CA 8.1-15 provides details, with each study summarised below.

Table CA 8.1-15

Laboratory studies investigating the sorption behaviour of cinmethylin.

Laboratory soil study	Study type
Harder, U., Hegler, F., 2017a KCA 7.1.3.1.1/1	Adsorption study
Platz, K., 2017a KCA 7.1.3.1.2/1	QSAR estimation of sorption behaviour

The sorption behaviour of cinmethylin was investigated in eight soils (five European, two North American, one Japanese), using the batch equilibrium test [see KCA 7.1.3.1.1/1]. The study was conducted in accordance with the OECD 106 guidelines. The HSE evaluator notes that the Applicant could not study the desorption behaviour of cinmethylin due to the substance's tendency to volatilise. Five of the eight soils could be used to evaluate sorption behaviour; these are reported in Table CA 8.1-16. The HSE evaluator notes that no alkaline pH was tested; however, there was no observed pH dependence between K_{FOC} and pH, so this was not of concern. The sorption of cinmethylin to soil did not show pH dependence, though there was a strong dependence on organic carbon content. Additionally, K_F correlated with organic carbon.

Table CA 8.1-16

Overview of adsorption isotherms for cinmethylin on five soils.

Soil	Soil type (USDA)	C _{org} (%)	pH (CaCl ₂)	K _F (mL/g)	K _{FOC} (mL/g)	1/n	R ²
Li 10	Loamy sand	0.89	6.1	4.54	510.13	1.00	0.998
Lufa 2.3	Sandy loam	0.66	5.3	1.88	284.29	0.96	0.999
New Jersey	Loam	1.30	6.5	3.46	266.45	0.94	0.991
La Gironda	Silty clay loam	1.92	7.1	5.19	270.15	0.98	0.984
Gunma	Loam	4.34	4.4	13.49	310.77	0.96	0.993
Geomean					317.80		
Arithmetic mean						0.97	

The Applicant also conducted a QSAR exercise to determine the adsorption coefficient (K_{oc}) for three aqueous metabolites, M684H001, M684H003 and M6884H004 using the EPISUITE KocWIN tool. The results are summarised in Table CA 8.1-17.

Table CA 8.1-17 Estimated K_{oc} values for three cinmethylin metabolites arising in aqueous studies.

Metabolite	Log K_{ow} ¹	K_{oc} (mL/g) MCI Method	K_{oc} (mL/g) Log K_{ow} method
M684H001	3.54	430.2	85.63
M684H003	1.59	18.61	20.07
M684H004	3.05	422.4	104.6

¹ Log K_{ow} estimated by KowWIN.

Column leaching studies are triggered when the adsorption studies prove to be unreliable due to weak adsorption. As the K_{oc} of cinmethylin and its enantiomers was consistently above 25 mL/g, leaching studies were not necessary. Additionally, lysimeter and field leaching studies were not required for cinmethylin.

Selection of modelling endpoints

Following the evaluation of the laboratory and field studies, the HSE evaluator considered the differences in degradation rates observed in the laboratory and field studies. To do this, the HSE evaluator collated the laboratory aerobic degradation study DegT_{50s} (n = 4) and compared these with the field study DegT_{50s} (n = 11) using the EFSA DegT₅₀ Endpoint Selector tool [EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT₅₀ values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662]. Table 8.1-18 summarises the endpoints collated for comparison. From the results of the tool, it is concluded that the field studies show significantly shorter DegT_{50s} than the laboratory studies for cinmethylin (Student's t Test; t = 3.7; α = 0.25) and the two enantiomers (t = 3.3 (-); 3.4 (+); α = 0.25). Therefore, based on the EFSA DegT₅₀ guidance, it is recommended that the geomean of the field DegT_{50 matrix} be used instead of the laboratory derived DegT₅₀ for cinmethylin and its enantiomers. Table CA 8.1-19 summarises the final endpoints.

Table 8.1-18 Modelling endpoints derived from laboratory and field studies used to select the final modelling endpoints.

Laboratory modelling DT _{50s} (d)			Field modelling DT _{50s} (d)		
Cinmethylin	(-)- enantiomer	(+)- enantiomer	Cinmethylin	(-)- enantiomer	(+)- enantiomer
192.8 ^a	165.0 ^a	145.0 ^a	29.9 ^b	25.4 ^b	33.9 ^b
19.1	15.4	21.5	47.0 ^b	40.6 ^b	52.5 ^b
43.5	34.7	56.4	15.3	14.2	16.2
74.6 ^a	54.6 ^a	73.4 ^a	5.4	4.4	6.4
			8.0 ^b	6.4 ^b	9.4 ^b
			13.9	10.7	17.2
			19.2	17.3	21.1
			6.7	6.5	7.0
			9.9	8.7	11.5
			3.7	3.5	3.8
			5.2	5.0	5.4

^a Pseudo-SFO DT₅₀ derived from the DFOP slow phase (k₂) DT₅₀.

^b FOMC derived endpoints. Calculated as DT₅₀ = DT₉₀ / 3.32 (less than 10% of initial concentration at last sampling).

Table CA 8.1-19

Summary of final endpoints to be used for modelling the degradation of cinmethylin and its two enantiomers Reg Nos. 5925581 and 5925632 in soil.

	Geomean Field DegT _{50matrix} (d)
Cinmethylin	11.1
(-)-enantiomer	9.7
(+)-enantiomer	12.3

Persistence

Cinmethylin was found to be neither persistent (P) nor very persistent (vP) in the soil, in line with the DG SANCO definitions. See Section B.8.1.5 for further discussion of persistence.

B.8.1.1. Laboratory 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 (Data Requirement 7.1.1.1)

Report:	KCA 7.1.1.1/1; Stewart, L. and Abernethy, A. (2016)
Title	Cinmethylin - Aerobic degradation of [¹⁴ C]-Cinmethylin (Reg. No. 900202) in soil
Document No.:	2015/1186904
Guidelines:	<ul style="list-style-type: none"> • OECD Guidelines for the testing of chemicals 307: Aerobic Degradation in Soil (Apr 2002) • US EPA OPPTS Guidelines 835.4100: Anaerobic Soil Metabolism (Oct 2008) • GLP of Japanese Ministry of Agriculture, Forestry and Fisheries: No. 12-Nousan-8147, Agriculture Production Bureau (Nov 2000) • FOCUS Kinetics guidance (2006; 2014).
GLP:	Yes
Deviations	<ul style="list-style-type: none"> • One radiolabelled compound, [benzyl-U-¹⁴C]-cinmethylin, had a chemical purity below 95%. However, the radiochemical purity was 99.8%. The HSE evaluator does not consider this to have impacted upon the study's viability as radiochemical purity was high. • Two soils pre-incubated beyond 28 days though the HSE evaluator does not deem this to have impacted on the study's viability. • Low mass balance was observed in many samples, particularly in the Lufa 5M soil study.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

An aerobic soil route and rate study was conducted according to OECD guidelines (OECD 307: Aerobic Degradation in Soil) using cinmethylin radiolabelled in two positions:

[cyclohexane-4-¹⁴C]-cinmethylin (99.3% chemical purity; 99.4% radiochemical purity), and [benzyl-U-¹⁴C]-cinmethylin (90.5% chemical purity; 99.8% radiochemical purity). The HSE evaluator notes that the chemical purity of the benzyl-labelled compound is below the required 95% purity, which may result in less test substance being applied in the studies than expected. The HSE evaluator notes that the radiochemical purity is high at 99.8%, meaning the applied test substance can be efficiently tracked.

The study investigated the degradation rate in four fresh field soils under aerobic conditions (Lufa 2.2, Lufa 5M, LAD-SCL-PF, MSL-PF); additionally, the nature and rates of formation of potential degradation products were evaluated in two of the rate soils. Lufa 2.2 and MSL-PF soils were treated with both radiolabels to investigate both route and rate of degradation, while Lufa 5M and LAD-SCL-PF were treated with the benzyl-labelled compound only to investigate rate of degradation only.

Three of the four soils were incubated in darkness at $20 \pm 2^\circ\text{C}$ for up to 122 DAT, with one soil incubated further to 152 DAT to investigate low mass balance. The study was conducted to GLP and according to OECD 307 guidelines. Deviations from guidelines did occur and these were noted by the Applicant; these are discussed in later sections. However, the HSE evaluator concludes that these deviations were not significant enough to affect the outcomes of the study.

TEST PROCEDURES

1. Soil characteristics

Table 8.1.1.1/1-01 details the soil characteristics for the four soils used in this study. Based on experiment schedules provided by the Applicant, the HSE evaluator confirms that soils were sufficiently fresh (*i.e.* less than three months old) at the study start. Soil samples were pre-incubated, with times ranging 8 – 33 days depending on soil type. Experiments were carried out at $\text{pF} = 2$.

Soil microbial biomass was determined via fumigation extraction at three points: at the study start, at 60 days, and at the study end. All four soils demonstrated a decline in microbial biomass by the study end. The Applicant highlighted a lower than expected microbial biomass at day 60 in the LAD-SCL-PF soil; however, by the study end biomass had recovered and the Applicant concluded the soil was viable. There was also a notable reduction in biomass at day 60 in the Lufa 2.2 soil, though this was not highlighted by the Applicant and the biomass also recovered by the study end. The HSE evaluator noted these fluctuations in microbial biomass and concludes that the soils were still viable as microbial biomass as a proportion of organic carbon remained above 1% throughout the study.

Table 8.1.1.1/1-01: Characterisation of the four test soils used within the aerobic degradation study.

Soil designation	Lufa 2.2	Lufa 5M	LAD-SCL-PF	MSL-PF
Geographic location	Germany	Germany	Wyoming, US	North Dakota, US
Sampling date	06 Aug 2014	02 Dec 2014	02 Dec 2014	02 Dec 2014
Pesticide history	No pesticide use in last 5 years	No pesticide use in last 5 years	Pesticide free	Pesticide free
Sampling depth (cm)	25	~20	0 – 15	0 – 15
Storage conditions ^a	~4°C	~4°C	~4°C	~4°C
Soil textural class (DIN) ^b	Weak loamy sand	Sandy loam	Sandy clay loam	Loamy sand
USDA textural class	Loamy sand	Sandy loam	Clay loam	Sandy loam
Particle size distribution (%; DIN 4220)				
Sand 0.063 – 2 mm	80.0	54.0	32.0	62.0
Silt 0.002 – 0.063 mm	11.0	31.0	28.0	20.0
Clay < 0.002 mm	9.0	15.0	40.0	16.0
Particle size distribution (%; USDA Textural Class)				
Sand 0.05 – 2 mm	82.0	60.0	34.0	64.0
Silt 0.002 – 0.05 mm	10.0	26.0	26.0	20.0
Clay < 0.002 mm	8.0	14.0	40.0	16.0
Soil characteristics				
Organic carbon (%)	1.5	1.1	0.88	2.1
pH (H ₂ O)	6.3	8.0	8.2	6.7
pH (CaCl ₂)	5.6	7.4	8.0	6.3
Cation exchange capacity (meq/100 g)	7.2	8.5	27.0	17.2
Max. water holding capacity – 0.1 bar (pF 2.0; g/100 g dry weight)	20.4	23.0	33.5	29.0
Microbial biomass (mg C/100 g dry soil)				
Study start	35.3	25.7	43.4	35.7
Intermediate (Day 60)	27.2	25.9	15.1	34.9
Study end	34.8	23.7	34.4	35.1
Microbial biomass as % organic carbon ^c				
Study start	2.35	2.34	4.93	1.70
Intermediate (Day 60)	1.81	2.35	1.72	1.66
Study end	2.32	2.15	3.91	1.67

^a – Applicant states soil storage conditions applied upon arrival at study facility^b – DIN is the German soil classification scheme^c – Calculated as follows: (biomass (mg C/kg dry soil) ÷ % organic carbon) ÷ 100^d – Study end for studying microbial biomass was 120 or 122 DAT, depending on the soil, and was not extended to 152 DAT for Lufa 5M

2. Soil treatment

Each soil sample consisted 100 g soil (dry weight equivalent, 2 mm sieved) and samples were treated with [cyclohexane-4-¹⁴C]-cinmethylin or [benzyl-U-¹⁴C]-cinmethylin to achieve a nominal concentration of 2.0 µg a.i./g soil (field application rate equivalent 750 g a.i./ha, based on distribution in the top 2.5 cm soil layer and a soil density of 1.5 g/cm³). Table 8.1.1.1/1-02 outlines sample numbers, test solution concentrations and application volumes. Each soil sample was treated drop-wise and test flasks were tumbled by hand to incorporate the test solution. Actual application rates (corresponding to 100% AR at 0 DAT) are presented in Table 8.1.1.1/1-02. Volatiles were collected through a series of four traps: a

safety trap (a flask containing no liquid), ethylene glycol trap, 2M NaOH trap, and 1M H₂SO₄ trap.

Table 8.1.1.1/1-02: Cinmethylin test solution concentrations and application rates for each test item and soil

Soil	Test item	No. treated flasks	Application solution concentration (mg a.i./mL)	Application solution volume (μL)	Actual application rate (μg a.i./dose)	Field application rate equivalent (g a.i./ha)
Lufa 2.2	[cyclohexane-4- ¹⁴ C]-cinmethylin	33	2.0	100	197.1	739.1
	[benzyl-U- ¹⁴ C]-cinmethylin	33	2.0	100	207.3	777.4
Lufa 2.2 Sterile controls	[cyclohexane-4- ¹⁴ C]-cinmethylin	8	2.2	90	189.1	709.1
	[benzyl-U- ¹⁴ C]-cinmethylin	8	2.5	80	175.5	658.1
Lufa 5M	[benzyl-U- ¹⁴ C]-cinmethylin	22	2.2	90	223.5	838.1
LAD-SCL-PF	[benzyl-U- ¹⁴ C]-cinmethylin	22	2.2	90	224.6	842.3
MSL-PF	[cyclohexane-4- ¹⁴ C]-cinmethylin	33	2.0	100	209.3	784.9
	[benzyl-U- ¹⁴ C]-cinmethylin	33	2.0	100	216.2	810.8

3. Experimental Set Up

After application of the test item, the test flasks were connected to the incubation apparatus (one incubation apparatus per soil and per label) constructed using glass and PVC connectors. Each flask was connected to a series of four traps to collect any volatiles, the first acting as a safety, the second containing ethylene glycol, the third containing 2 M NaOH and the fourth containing 1 M H₂SO₄. The treated soils were incubated at 20 ± 2°C in the dark (with the exception of LUFA 2.2 soil for which from 49 DAT to 56 DAT the temperature decreased to 17°C). To maintain aerobic conditions, moist air was applied through the test system at a rate of one bubble per trap at any one time using a vacuum pump. pF2 was maintained throughout the study by replacing lost weight with milli-Q-water.

The soil flasks previously sterilised were attached to the incubation apparatus with filters between the flask and the incubation apparatus to maintain the sterility of the samples.

4. Sampling

At each sampling interval, triplicate soil samples were removed from the incubation apparatus for each route soil. Two samples were taken for immediate analysis, with the third sample stored as a spare at -20°C in case of further analysis. For the two route soils (Lufa 2.2 and MSL-PF), samples were taken at 0, 3, 7, 14, 24, 41, 59, 90 and 120 DAT.

For soils used for the rate study only (Lufa 5M and LAD-SCL-PF), duplicate samples were taken at 0, 3, 7, 14, 25, 40, 60, 90 and 122 DAT. Additionally, samples of Lufa 5M soil were taken at 152 DAT to investigate low mass balance.

5. Soil extraction methods

For all soils, the soil samples (100 g oven dry equivalent) were extracted in 200 mL acetonitrile on an end over end shaker for 30 minutes, and then centrifuged for 15 minutes at 3000 rpm. Following this, methods differed for each soil. For Lufa 2.2 soils, the supernatant was then removed and the soil pellet re-suspended in 200 mL acetonitrile:MilliQ water (80:20 v/v) and the extraction process repeated. The supernatants were combined, made up to a final volume of 450 mL with acetonitrile and identified as “Extract 1”. The remaining soil pellet was again re-suspended in 200 mL acetonitrile:MilliQ water (80:20 v/v) and extracted as outlined. The supernatant was removed and the soil pellet re-suspended in 200 mL acetonitrile:MilliQ water (50:50 v/v) and extracted as outlined. These supernatants were combined, made up to a final volume of 450 mL with acetonitrile and identified as “Extract 2”. Duplicate aliquots were taken for LSC analysis from both Extracts 1 and 2. Concentrated extracts were analysed by LSC and HPLC or liquid fraction collection if activity was low.

For Lufa 5M, LAD-SCL-PF and MSL-PF soils, four extractions were conducted. “Extract 1” was formed from the supernatant arising from the first extraction. The soil pellet was then re-suspended in 200 mL acetonitrile:MilliQ water (90:10 v/v) and the extraction repeated. The supernatant was made up to 450 mL with acetonitrile to form “Extract 2”. These steps were repeated again in 200 mL acetonitrile:MilliQ water (70:30 v/v) to form “Extract 3”. The steps were repeated once more in 200 mL acetonitrile:2% formic acid (aq) (50:50 v/v) to form “Extract 4”. Duplicate aliquots were taken from each extract for LSC analysis. For HPLC analysis, 25 mL subsamples of Extracts 1-4 were combined. 15-40 mL subsamples were transferred and concentrated to 5 mL, vortex mixed and sonicated. Concentrated extracts were analysed by HPLC using on-line detection or liquid fraction collection if activity was low.

Selected samples from all four soils were further extracted using less polar solvents, where non-extractable residues (NERs) were > 10% AR. The selected soil pellets were suspended in 200 mL tetrahydrofuran and the soil was extracted on an end over end shaker for 60 minutes. Samples were centrifuged for 15 minutes at 3000 rpm, and the supernatant volume was made up to 210 mL with tetrahydrofuran to form “Extract 3” for Lufa 2.2 samples, and “Extract 5” for the other three soils. Duplicate aliquots were taken for LSC analysis. The previous steps were then repeated once more with the soil pellet, re-suspending in 200 mL hexane. The supernatant was made up to 210 mL with hexane to form “Extract 4” for Lufa 2.2 and “Extract 6” for all other soil samples. Duplicate aliquots were taken for LSC analysis.

Samples were analysed as soon as possible; however, where storage was necessary, samples were refrigerated at 4°C or frozen at -20°C. The HSE evaluator notes that storage durations varied for each soil and sample batch; the storage period was typically about a month, with the longest storage period slightly over two months.

6. Analytical methods

NERs were determined by combusting 0.1 g of the post extraction soil pellets. The evolved $^{14}\text{CO}_2$ was trapped and measured by LSC. NERs were further characterised by organic matter fractionation analysis of selected samples (60 DAT for Lufa 2.2 soils, 40 DAT for Lufa 5M, LAD-SCL-PF and MSL-PF soils). Post-extraction soil pellets were extracted with 100 mL NaOH for 16 hours using an end over end shaker and were then centrifuged (3000 rpm; 15 minutes). The NaOH extraction was performed twice more and all three supernatants were combined for each sample. The supernatants were acidified to pH 1 and the humic and fulvic acid fractions were separated by centrifugation (3000 rpm for 10 minutes). Radioactivity in the fulvic acid fraction was determined by LSC; humic acid fraction radioactivity was determined by LSC following dissolution of the precipitate in 0.5M NaOH. Humin fraction radioactivity was determined by combustion analysis.

Cinmethylin identification was confirmed in selected soil extracts by qualitative mass spectrometry. Selected cyclohexane and benzyl labelled samples were analysed by LC-MS with radio-detection to identify spectra related to significant components. Retention times were compared against acquired radio-HPLC profiles for the selected samples. Qualitative mass spectrometry was also performed to identify unknown metabolites in a sterile sample (LC-MS with concurrent radio-detection). Retention times were compared against acquired radio-HPLC profiles for the selected sample. Chiral HPLC was conducted to quantify enantiomer levels.

The LSC LOQ was set as $\leq 0.4\%$ AR. The HPLC LOQ was set at $\leq 0.05\%$ AR or 0.001 mg/kg for the liquid fraction, and $\leq 0.8\%$ AR or 0.02 mg/kg for the online radio-HPLC quantification.

RESULTS AND DISCUSSION

1. Mass balance

Mass balances in non-sterile soils were 80.9 – 100% (Lufa 2.2), 81.0 – 100% (Lufa 5M), 87.5 – 100.1% (LAD-SCL-PF), and 80.6 – 100.1% (MSL-PF). The Applicant did not highlight the fact that recoveries fell below the guideline minimum mass balance of 90% for radiolabelled compounds for all soils. The HSE evaluator observed that, across both radiolabels, 33 of 110 soil samples had mass balances below 90%, with eight below 85%. Of particular concern were the low mass balances in the Lufa 5M soil treated with [benzyl- $U-^{14}C$]-cinmethylin, where four samples (out of 20) demonstrated mass balances below 85%. The Applicant investigated this by extending sampling to 152 DAT, and the results showed low extractability and low mass balance, both consistent with 122 DAT samples. Tables 8.1.1.1/1-03 – 8.1.1.1/1-08 present the radioactive residue characterisation in soil extracts. The HSE evaluator notes that the Applicant supplied a breakdown of the individual minor unknowns; this confirmed that no individual unknown was measured at levels above the regulatory trigger of 5%. As a result, the minor unknowns are presented as a sum of minor unknowns in the tables below.

Table 8.1.1.1/1-03: Characterisation/identification of radioactive residues in Lufa 2.2 soil extracts, expressed in % applied radioactivity, using the [cyclohexane-4-¹⁴C]-cinmethylin label.

Fraction (% AR)		Incubation time (days)								
		0	3	7	14	24	41	59	90	120
Cinmethylin	I	100.0	95.9	82.4	71.9	63.4	63.3	59.4	50.0	43.7
	II	99.5	89.9	83.0	72.1	70.7	56.5	62.3	49.3	50.9
	Mean	99.8	92.9	82.7	72.0	67.1	59.9	60.9	49.7	47.3
Sum minor unknowns ^a	I	ND	ND	1.8	4.2	5.3	2.3	2.0	5.4	6.3
	II	ND	ND	2.8	1.7	2.3	5.9	1.5	3.6	2.1
	Mean	NA	NA	2.3	3.0	3.8	4.1	1.8	4.5	4.2
Total extractables ^b	I	100.0	95.9	84.2	76.2	68.6	65.7	61.4	55.4	50.0
	II	99.5	89.9	85.8	73.8	72.9	62.5	63.8	53.0	53.0
	Mean	99.8	92.9	85.0	75.0	70.8	64.1	62.6	54.2	51.5
NER	I	0.2	4.1	4.8	7.2	9.3	9.9	10.4	11.5	9.7
	II	0.2	3.4	5.1	7.8	9.0	10.0	9.6	12.4	10.2
	Mean	0.2	3.8	5.0	7.5	9.2	10.0	10.0	12.0	10.0
¹⁴ CO ₂	I	NS	3.7	5.8	15.0	16.4	20.7	22.4	21.9	26.5
	II	NS	2.9	7.7	14.8	14.7	21.3	18.0	31.0	12.3
	Mean	NA	3.3	6.8	14.9	15.6	21.0	20.2	26.5	19.4
Organic volatiles	I	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.7	<LOQ
	II	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.6	<LOQ
	Mean	NA	NA	NA	NA	NA	NA	NA	0.7	NA
Total recovery	I	100.2	103.7	94.8	98.4	94.3	96.3	94.2	88.7	86.2
	II	99.7	96.2	98.6	96.4	96.6	93.8	91.4	97.0	75.5
	Mean	100.0	100.0	96.8	97.4	95.5	95.1	92.8	93.0	80.9

ND = not detected.

NA = not applicable due to no replicates having residues >LOQ.

NS = not sampled (0 DAT only).

<LOQ = residues were detected but these were below the LOQ of 0.05% AR.

^a – Sum of minor unknown components, none of which individually accounts for >3.4% AR.

^b – Total extractables = sum of cinmethylin and sum of minor unknowns. These values are then used to calculate total recovery.

Table 8.1.1.1/1-04: Characterisation/identification of radioactive residues in Lufa 2.2 soil extracts, expressed in % applied radioactivity, using the [benzyl-U-¹⁴C]-cinmethylin label.

Fraction (% AR)		Incubation time (days)								
		0	3	7	14	24	41	59	90	120
Cinmethylin	I	101.6	89.8	82.2	74.2	66.9	60.9	58.5	51.6	40.0
	II	98.0	92.1	86.5	76.7	65.2	58.5	53.6	50.5	45.3
	Mean	99.8	91.0	84.4	75.5	66.1	59.7	56.1	51.1	42.7
Sum minor unknowns ^a	I	ND	ND	ND	1.4	2.9	3.7	2.2	2.6	10.8
	II	ND	ND	ND	2.5	2.8	4.4	4.4	3.3	4.1
	Mean	NA	NA	NA	2.0	2.9	4.1	3.3	3.0	7.5
Total extractables ^b	I	101.6	89.8	82.2	75.6	69.8	64.6	60.7	54.3	50.9
	II	98.0	92.1	86.5	79.1	68.0	62.9	58.1	53.8	49.4
	Mean	99.8	91.0	84.4	77.4	68.9	63.8	59.4	54.1	50.2
NER	I	0.2	3.6	6.6	9.5	12.6	13.2	14.0	15.2	17.2
	II	0.2	2.4	5.0	7.8	11.6	12.1	14.1	16.2	14.5
	Mean	0.2	3.0	5.8	8.7	12.1	12.7	14.1	15.7	15.9
¹⁴ CO ₂	I	NS	<LOQ	<LOQ	3.2	7.7	19.0	6.6	23.9	23.3
	II	NS	<LOQ	3.7	3.1	14.0	17.7	21.5	22.6	22.4
	Mean	NA	NA	1.9	3.2	10.9	18.4	14.1	23.3	22.9
Organic volatiles	I	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
	II	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.2
	Mean	NA	NA	NA	NA	NA	NA	NA	NA	0.1
Total recovery	I	101.8	93.4	88.8	88.3	90.1	96.8	81.3	93.4	91.4
	II	98.2	94.5	95.2	90.0	93.6	92.7	93.7	92.6	86.3
	Mean	100.0	94.0	92.0	89.2	91.9	94.9	87.6	93.0	88.9

ND = not detected.

NA = not applicable due to no replicates having residues >LOQ.

NS = not sampled (0 DAT only).

<LOQ = residues were detected but these were below the LOQ of 0.05% AR.

^a – Sum of minor unknown components, none of which individually accounts for >3.3% AR.

^b – Total extractables = sum of cinmethylin and sum of minor unknowns. These values are then used to calculate total recovery.

Table 8.1.1.1/1-05: Characterisation/identification of radioactive residues in Lufa 5M soil extracts, expressed in % applied radioactivity, using the [benzyl-U-¹⁴C]-cinmethylin label.

Fraction (% AR)		Incubation time (days)									
		0	3	7	14	25	40	60	90	122	152
Cinmethylin	I	98.8	84.0	73.7	60.8	38.4	18.5	6.4	0.5	0.5	-
	II	99.8	80.9	73.5	63.6	50.0	22.9	6.7	1.2	0.7	-
	Mean	99.3	82.5	73.6	62.2	44.2	20.7	6.6	0.9	0.6	-
Sum minor unknowns ^a	I	ND	ND	3.3	3.6	8.8	9.9	7.5	4.4	3.7	-
	II	ND	2.9	3.8	4.8	5.4	5.7	8.4	5.6	3.8	-
	Mean	NA	1.5	3.6	4.2	7.1	7.8	8.0	5.0	3.8	-
Total extractables ^b	I	99.5	84.0	77.0	64.4	47.2	28.4	14.1	4.8	4.2	5.4
	II	99.8	83.7	77.3	68.4	55.4	28.7	15.0	6.8	4.5	3.9
	Mean	99.7	83.9	77.2	66.4	51.3	28.6	14.6	5.8	4.4	4.7
NER	I	0.4	7.5	8.4	14.1	23.7	28.7	31.9	35.7	33.4	33.5
	II	0.2	6.5	9.3	13.4	21.8	31.6	38.2	35.9	35.9	36.9
	Mean	0.3	7.0	8.9	13.8	22.8	30.2	35.1	35.8	34.7	35.2
¹⁴CO₂	I	NS	0.6	4.4	11.2	20.0	40.3	39.5	39.1	46.2	45.9
	II	NS	0.6	4.9	11.4	0.6	27.9	40.9	46.8	49.1	36.0
	Mean	NA	0.6	4.7	11.3	10.3	34.2	40.2	43.0	47.7	41.0
Organic volatiles	I	NS	0.1	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.2
	II	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.2
	Mean	NA	0.1	NA	NA	NA	NA	NA	NA	NA	0.3
Total recovery	I	99.9	92.2	89.8	89.7	90.9	97.4	85.5	79.6	83.8	85.0
	II	100.0	90.8	91.5	93.2	77.8	88.2	94.1	89.5	89.5	76.9
	Mean	100.0	91.5	90.7	91.5	84.4	92.9	89.8	84.6	86.8	81.0

ND = not detected.

NA = not applicable due to no replicates having residues >LOQ.

NS = not sampled (0 DAT only).

<LOQ = residues were detected but these were below the LOQ of 0.05% AR.

NA = not available due to measurements being below LOQ.

^a – Sum of minor unknown components, none of which individually accounts for >4.1% AR.

^b – Total extractables = sum of cinmethylin and sum of minor unknowns. These values are then used to calculate total recovery.

Table 8.1.1.1/1-06: Characterisation/identification of radioactive residues in LAD-SCL-PF soil extracts, expressed in % applied radioactivity, using the [benzyl-U-¹⁴C]-cinmethylin label.

Fraction (% AR)		Incubation time (days)								
		0	3	7	14	25	40	60	90	120
Cinmethylin	I	99.1	92.6	89.4	79.7	68.8	51.1	45.3	22.6	9.4
	II	100.4	91.3	84.4	73.6	67.2	55.5	36.8	20.9	10.2
	Mean	99.8	92.0	86.9	76.7	68.0	53.3	41.1	21.8	9.8
Sum minor unknowns ^a	I	ND	ND	1.9	2.4	5.5	8.2	5.4	9.8	6.5
	II	ND	2.1	5.0	5.4	5.9	6.3	10.6	6.7	7.3
	Mean	NA	1.1	3.5	3.9	5.7	7.3	8.0	8.3	6.9
Total extractables ^b	I	99.1	92.6	91.3	82.1	74.3	59.4	50.7	32.6	15.8
	II	100.4	93.4	89.4	79.1	73.2	61.8	47.5	27.6	17.5
	Mean	99.8	93.0	90.4	80.6	73.8	60.6	49.1	30.1	16.7
NER	I	0.3	3.1	3.9	7.3	11.7	20.9	26.0	27.4	36.8
	II	0.3	2.7	4.5	8.1	13.1	18.7	22.7	33.7	36.2
	Mean	0.3	2.9	4.2	7.7	12.4	19.8	24.4	30.6	36.5
¹⁴ CO ₂	I	NS	3.0	3.9	2.6	8.7	13.4	19.7	28.2	32.9
	II	NS	2.3	3.8	7.1	3.3	12.8	21.5	31.0	35.7
	Mean	NA	2.7	3.9	4.9	6.0	13.1	20.6	29.6	34.3
Organic volatiles	I	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
	II	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
	Mean	NA	NA	NA	NA	NA	NA	NA	NA	NA
Total recovery	I	99.4	98.7	99.1	92.0	94.7	93.7	96.4	88.2	85.5
	II	100.7	98.4	97.7	94.3	89.6	93.3	91.7	92.3	89.4
	Mean	100.1	98.6	98.4	93.2	92.2	93.5	94.1	90.3	87.5

ND = not detected.

NA = not applicable due to no replicates having residues >LOQ.

NS = not sampled (0 DAT only).

<LOQ = residues were detected but these were below the LOQ of 0.05% AR.

^a – Sum of minor unknown components, none of which individually accounts for >3.7% AR.

^b – Total extractables = sum of cinmethylin and sum of minor unknowns. These values are then used to calculate total recovery.

Table 8.1.1.1/1-07: Characterisation/identification of radioactive residues in MSL-PF soil extracts, expressed in % applied radioactivity, using the [cyclohexane-4-¹⁴C]-cinmethylin label.

Fraction (% AR)		Incubation time (days)								
		0	3	7	14	24	41	59	90	120
Cinmethylin	I	99.2	80.0	73.6	57.7	47.6	33.8	28.2	24.4	15.1
	II	100.4	76.6	70.2	56.5	40.7	30.5	30.4	20.6	17.3
	Mean	99.8	78.3	71.9	57.1	44.2	32.2	29.3	22.5	16.2
Sum minor unknowns ^a	I	ND	2.1	1.0	4.1	4.0	6.1	6.4	5.1	8.8
	II	ND	3.5	2.0	2.9	5.8	7.9	4.8	7.0	8.3
	Mean	NA	2.8	1.5	3.5	4.9	7.0	5.6	6.1	8.6
Total extractables ^b	I	99.2	82.1	74.6	61.8	51.5	39.7	34.6	29.4	23.9
	II	100.4	80.0	72.2	59.4	46.4	38.3	35.2	27.7	25.6
	Mean	99.8	81.1	73.4	60.6	49.0	39.0	34.9	28.6	24.8
NER	I	0.1	7.4	11.2	14.9	16.9	20.0	18.3	19.9	20.5
	II	0.1	8.5	10.5	14.7	17.8	19.9	20.5	20.5	22.9
	Mean	0.1	8.0	10.9	14.8	17.4	20.0	19.4	20.2	21.7
¹⁴ CO ₂	I	NS	3.2	8.1	15.4	22.8	31.7	29.3	42.4	26.8
	II	NS	4.2	7.5	16.5	25.7	35.1	33.8	39.6	41.2
	Mean	NA	3.7	7.8	16.0	24.3	33.4	31.6	41.0	34.0
Organic volatiles	I	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.1
	II	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.2
	Mean	NA	NA	NA	NA	NA	NA	NA	NA	0.2
Total recovery	I	99.3	92.7	93.9	92.1	91.2	91.4	82.2	91.7	71.3
	II	100.5	92.7	90.2	90.6	89.9	93.3	89.5	87.8	89.9
	Mean	99.9	92.7	92.1	91.4	90.6	92.4	85.9	89.8	80.6

ND = not detected.

NA = not applicable due to no replicates having residues >LOQ.

NS = not sampled (0 DAT only).

<LOQ = residues were detected but these were below the LOQ of 0.05% AR.

^a – Sum of minor unknown components, none of which individually accounts for >3.0% AR.

^b – Total extractables = sum of cinmethylin and sum of minor unknowns. These values are then used to calculate total recovery.

Table 8.1.1.1/1-08: Characterisation/identification of radioactive residues in MSL-PF soil extracts, expressed in % applied radioactivity, using the [benzyl-U-¹⁴C]-cinmethylin label.

Fraction (% AR)		Incubation time (days)								
		0	3	7	14	24	41	59	90	120
Cinmethylin	I	100.7	83.6	72.3	53.3	43.1	35.2	32.7	20.8	16.7
	II	99.2	78.4	70.9	54.2	44.2	36.8	33.1	25.7	15.7
	Mean	100.0	81.0	71.6	53.8	43.7	36.0	32.9	23.3	16.2
Sum minor unknowns ^a	I	ND	1.6	2.0	2.1	6.2	7.9	3.8	9.1	9.1
	II	ND	4.8	4.7	3.2	2.8	7.9	7.2	5.2	9.4
	Mean	NA	3.2	3.4	2.7	4.5	7.9	5.5	7.2	9.3
Total extractables ^b	I	100.7	85.2	74.3	55.4	49.4	43.0	36.5	30.0	25.9
	II	99.2	83.1	75.6	57.4	47.0	44.7	40.2	30.9	25.1
	Mean	100.0	84.2	75.0	56.4	48.2	43.9	38.5	30.5	25.5
NER	I	0.1	7.1	14.1	24.1	25.3	27.3	24.1	27.1	34.6
	II	0.1	7.3	13.5	29.1	27.8	27.1	24.8	27.2	28.7
	Mean	0.1	7.2	13.8	26.6	26.6	27.2	24.5	27.2	31.7
¹⁴ CO ₂	I	NS	1.7	4.3	13.0	18.8	16.9	25.3	31.6	30.0
	II	NS	1.5	4.5	12.3	16.0	22.2	23.3	32.6	34.1
	Mean	NA	1.6	4.4	12.7	17.4	19.6	24.4	32.1	32.1
Organic volatiles	I	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.2
	II	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.1
	Mean	NA	NA	NA	NA	NA	NA	NA	NA	0.2
Total recovery	I	100.8	94.0	92.7	92.5	93.5	87.2	85.9	88.7	90.7
	II	99.3	91.9	93.6	98.8	90.8	94.0	88.4	90.7	88.0
	Mean	100.1	93.0	93.2	95.7	92.2	90.6	87.2	89.7	89.4

ND = not detected.

NA = not applicable due to no replicates having residues >LOQ.

NS = not sampled (0 DAT only).

<LOQ = residues were detected but these were below the LOQ of 0.05% AR.

^a – Sum of minor unknown components, none of which individually accounts for >3.1% AR.

^b – Total extractables = sum of cinmethylin and sum of minor unknowns. These values are then used to calculate total recovery.

The Applicant characterised the non-extractable residues for all soils for one time point; these are summarised in Table 8.1.1.1/1-09 below. A small amount of radioactivity was associated with the humic acid fraction (max. 6.6% AR) and fulvic acid fraction (max. 5.7% AR). The majority of the radioactivity was associated with the humin fraction (max. 16.7% AR).

Table 8.1.1.1/1-09: Characterisation of non-extractable residues in all soils treated with [cyclohexane-4-¹⁴C]-cinmethylin and [benzyl-U-¹⁴C]-cinmethylin (% AR), as supplied by the Applicant.

Soil Type	Label	DAT ^(a)	Rep.	Pre-OMF residues	OMF ^(b)			OMF Recovery
					Humic acid	Fulvic acid	Humin	
Lufa 2.2	Cyclo	60	I	10.4	1.0	2.9	2.3	6.2
			II	9.6	0.9	2.8	2.4	6.1
			Mean	10.0	1.0	2.9	2.4	6.2
	Benzyl		I	14.0	1.6	3.6	2.6	7.8
			II	14.1	1.8	4.1	2.6	8.5
			Mean	14.1	1.7	3.9	2.6	8.2
Lufa 5M	Benzyl	40	I	28.7	5.3	5.7	15.2	26.2
			II	31.6	6.6	5.6	14.3	26.5
			Mean	30.2	6.0	5.7	14.8	26.4
LAD-SCL-PF	Benzyl		I	20.9	0.5	4.0	15.2	19.7
			II	18.7	0.5	4.4	16.7	21.6
			Mean	19.8	0.5	4.2	16.0	20.7
MSL-PF	Cyclo	40	I	20.0	1.6	3.3	8.5	13.4
			II	19.9	1.2	3.4	10.9	15.5
			Mean	20.0	1.4	3.4	9.7	14.5
	Benzyl		I	27.3	1.5	4.2	15.1	20.8
			II	27.1	2.0	3.9	14.2	20.1
			Mean	27.2	1.8	4.1	14.7	20.5

(a) = Days After Treatment

(b) = Organic Matter Fractionation

2. Metabolites

In all soils, cinmethylin was the principal component at the study start. No major metabolites were identified, with the largest minor component amounting to 3.4% in Lufa 2.2, 4.1% in Lufa 5M, 3.7% in LAD-SCL-PF, and 3.1% in MSL-PF. The Applicant supplied additional information showing minor unknown levels at each sampling time derived from radio-HPLC analysis, which confirms the maximum levels reported here. The HSE evaluator can confirm that no minor unknowns exceeded the regulatory triggers of 5%. In Lufa 2.2, mean total minor unknowns ranged 2.3% AR (7 DAT) to 4.5% AR (90 DAT) for [cyclohexane-4-¹⁴C]-cinmethylin, and 2.0% AR (14 DAT) to 7.5% AR (120 DAT) for [benzyl-U-¹⁴C]-cinmethylin. In Lufa 5M soil, mean total minor unknowns ranged 1.5% AR (3 DAT) to 8.0% AR (60 DAT; [benzyl-U-¹⁴C]-cinmethylin). In LAD-SCL-PF soil, mean total minor unknowns ranged 1.1% AR (3 DAT) to 8.3% AR (90 DAT; [benzyl-U-¹⁴C]-cinmethylin). For MSL-PF soils, mean total minor unknowns ranged 1.5% AR (7 DAT) to 8.6% AR (120 DAT) for [cyclohexane-4-¹⁴C]-cinmethylin, and 2.7% AR (14 DAT) to 9.3% AR (120 DAT) for [benzyl-U-¹⁴C]-cinmethylin.

The HSE evaluator notes that there could be a major metabolite of cinmethylin that is not being identified because of the low mass balances. The highest individual minor unknown was detected at 4.1% of AR in the Lufa 5M soil, where individual mass balances ranged 76.9-97.4% after 0 DAT. As a worst-case scenario, if the 4.1% AR minor unknown was upscaled

from a 76.9% mass balance to 100%, this would show formation of a major metabolite amounting to 5.3% AR. The HSE evaluator is therefore concerned by the potential for metabolite formation, though it is noted that no major metabolites were identified in the other three soils, where mass balance was acceptable. The HSE evaluator also notes that there were moderate rates of adsorption to the test vessel walls in the soil sorption study (KCA 7.1.3.1/1; Harder, U., Hegler, F., 2017a), and that high rates of volatilisation were observed from soil and plant surfaces (KCA 7.3.1/2; Hassink, J., 2017b). Therefore, the losses observed in the present study could be attributed to one or both of these processes.

3. Chiral analysis of enantiomers

As cinmethylin comprises two enantiomers (mixture ratio 50:50), the Applicant studied the ratio over time. These data are reported in Tables 8.1.1.1/1-10 – 8.1.1.1/1-15. Enantiomeric ratios remained relatively stable for both radiolabels in Lufa 2.2 soil between 0 and 120 DAT. However, in Lufa 5M and LAD-SCL-PF soils, the ratio changed from ~50:50 at 0 DAT to ~30:70 by 60 DAT. The HSE evaluator notes that these two soils also displayed faster degradation rates. For MSL-PF soils, the ratio shifted from approx. 50:50 at 0 DAT to ~40:60 at 59 DAT and ~30:70 at 120 DAT. The Applicant concluded that the two enantiomers do not degrade at the same rate; based on the chiral analysis presented below, the HSE evaluator agrees with this conclusion.

Table 8.1.1.1/1-10: Determination of enantiomeric ratios in Lufa 2.2 non-sterile soil treated with [cyclohexane-4-¹⁴C]-cinmethylin.

DAT	Replicate	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR) ^b	(+)-enantiomer (% AR) ^c	Enantiomer ratio (- : +)
0	II	99.5	51.0	48.5	51:49
	Mean	99.5	51.0	48.5	51:49
24	I	63.4	29.5	33.9	47:53
	II	70.7	32.0	38.7	45:55
	Mean	67.1	30.8	36.3	46:54
59	I	59.4	26.4	33.0	44:56
	II	62.3	29.5	32.8	47:53
	Mean	60.9	28.0	32.9	46:54
90	I	50.0	22.0	28.1	44:56
	II	49.3	22.3	27.0	45:55
	Mean	49.7	22.2	27.6	45:55
120	I	43.7	21.2	22.5	49:51
	Mean	43.7	21.2	22.5	49:51

^a – Retention time ~ 25 min (different HPLC method to the two below)

^b – Retention time ~ 33 min (Reg No. 5925581)

^c – Retention time ~ 35 min (Reg No. 5925632)

Table 8.1.1.1/1-11: Determination of enantiomeric ratios in Lufa 2.2 non-sterile soil treated with [benzyl-U-¹⁴C]-cinmethylin.

DAT	Replicate	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR) ^b	(+)-enantiomer (% AR) ^c	Enantiomer ratio (- : +)
0	II	98.0	50.8	47.2	52:48
	Mean	98.0	50.8	47.2	52:48
24	I	66.9	28.8	38.1	43:57
	II	65.2	30.9	34.3	47:53
	Mean	66.1	30.0	36.2	45:55
59	I	58.5	27.1	31.4	46:54
	II	53.6	23.8	29.8	44:56
	Mean	56.1	25.5	30.6	45:55
90	I	51.6	24.5	27.1	47:53
	II	50.5	24.5	26.0	49:51
	Mean	51.1	24.5	26.6	48:52
120	I	40.0	18.4	21.6	46:54
	Mean	40.0	18.4	21.6	46:54

^a – Retention time ~ 25 min (different HPLC method to the two below)^b – Retention time ~ 33 min (Reg No. 5925581)^c – Retention time ~ 35 min (Reg No. 5925632)**Table 8.1.1.1/1-12: Determination of enantiomeric ratios in Lufa 5M non-sterile soil treated with [benzyl-U-¹⁴C]-cinmethylin.**

DAT	Replicate	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR) ^b	(+)-enantiomer (% AR) ^c	Enantiomer ratio (- : +)
0	I	98.8	51.6	47.2	52:48
	Mean	98.8	51.6	47.2	52:48
14	I	60.8	27.9	32.9	46:54
	II	63.6	30.8	32.8	48:52
	Mean	62.2	29.4	32.9	47:53
40	I	18.5	6.8	11.7	37:63
	II	22.9	8.3	14.6	36:64
	Mean	20.7	7.6	13.2	37:63
60	I	6.4	2.1	4.3	33:67
	Mean	6.4	2.1	4.3	33:67

^a – Retention time ~ 25 min (different HPLC method to the two below)^b – Retention time ~ 33 min (Reg No. 5925581)^c – Retention time ~ 35 min (Reg No. 5925632)

Table 8.1.1.1/1-13: Determination of enantiomeric ratios in LAD-SCL-PF non-sterile soil treated with [benzyl-U-¹⁴C]-cinmethylin.

DAT	Replicate	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR) ^b	(+)-enantiomer (% AR) ^c	Enantiomer ratio (- : +)
0	I	99.1	48.2	50.9	49:51
	Mean	99.1	48.2	50.9	49:51
14	I	79.7	39.5	40.2	50:50
	II	73.6	36.5	37.1	50:50
	Mean	76.7	38.0	38.7	50:50
60	I	45.3	19.3	26.0	43:57
	II	36.8	10.9	25.9	30:70
	Mean	41.1	15.1	26.0	37:63
120	I	9.4	2.1	7.3	22:78
	Mean	9.4	2.1	7.3	22:78

^a – Retention time ~ 25 min (different HPLC method to the two below)^b – Retention time ~ 33 min (Reg No. 5925581)^c – Retention time ~ 35 min (Reg No. 5925632)**Table 8.1.1.1/1-14: Determination of enantiomeric ratios in MSL-PF non-sterile soil treated with [cyclohexane-4-¹⁴C]-cinmethylin.**

DAT	Replicate	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR) ^b	(+)-enantiomer (% AR) ^c	Enantiomer ratio (- : +)
0	I	99.2	51.7	47.5	52:48
	Mean	99.2	51.7	47.5	52:48
14	I	57.7	23.3	34.4	40:60
	II	56.5	23.1	33.4	41:59
	Mean	57.1	23.2	33.9	41:59
59	I	28.2	10.0	18.2	35:65
	II	30.4	12.0	18.4	39:61
	Mean	29.3	11.0	18.3	38:62
90	I	24.4	9.2	15.2	38:62
	II	20.6	6.8	13.8	33:67
	Mean	22.5	8.0	14.5	36:64
120	I	15.1	4.6	10.5	30:70
	Mean	15.1	4.6	10.5	30:70

^a – Retention time ~ 25 min (different HPLC method to the two below)^b – Retention time ~ 33 min (Reg No. 5925581)^c – Retention time ~ 35 min (Reg No. 5925632)

Table 8.1.1.1/1-15: Determination of enantiomeric ratios in MSL-PF non-sterile soil treated with [benzyl-U-¹⁴C]-cinmethylin.

DAT	Replicate	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR) ^b	(+)-enantiomer (% AR) ^c	Enantiomer ratio (- : +)
0	I	100.7	48.3	52.4	48:52
	Mean	100.7	48.3	52.4	48:52
14	I	53.3	21.4	31.9	40:60
	II	54.2	21.7	32.5	40:60
	Mean	53.8	21.6	32.2	40:60
59	I	32.7	10.1	22.6	31:69
	II	33.1	12.1	21.0	37:63
	Mean	32.9	11.1	21.8	34:66
90	I	20.8	7.3	13.5	35:65
	II	25.7	7.6	18.1	30:70
	Mean	23.3	7.5	15.8	32:68
120	I	16.7	5.0	11.7	30:70
	Mean	16.7	5.0	11.7	30:70

^a – Retention time ~ 25 min (different HPLC method to the two below)

^b – Retention time ~ 33 min (Reg No. 5925581)

^c – Retention time ~ 35 min (Reg No. 5925632)

GUIDELINE DEVIATIONS

The Applicant highlighted the following deviations from the standard guidelines:

- Two soils, Lufa 2.2 and MSL-PF were pre-incubated for longer than the 28 days recommended; however, this had no impact on study results as microbial biomass results indicated the soils were both viable and microbially active;
- For a seven-day period (49 – 56 DAT), the incubation temperature for the Lufa 2.2 soil samples dropped to 17°C, a deviation from the guideline incubation temperature of 20 ± 2°C;
- Mass balances in the Lufa 5M soil were low in several samples. The Applicant related this to inefficient trapping of ¹⁴CO₂. More traps were added at 125 DAT to investigate the low mass balance up to 152 DAT, but results continued to indicate low extractability and low mass balance, consistent with 122 DAT. The HSE evaluator notes that volatilisation from soil surfaces was high in a volatilisation study (KCA 7.3.1/2; Hassink, J., 2017b), and that this may have driven the low mass balances in this soil.

Additionally, the HSE evaluator identified the following deviations from the standard guidelines:

- The chemical purity of [benzyl-U-¹⁴C]-cinmethylin was 90.5%, below the guideline minimum purity of 95%. However, the radiochemical purity was 99.8%;
- Overall recoveries of AR were between 80.6 – 100.1%, with 33/110 samples below the guideline recovery limit and 8/33 below 85% recovery. The low mass balances were most prominent in the Lufa 5M soil, though they were observed in all soils. The Applicant noted that, where low mass balances were observed in individual replicates, these replicates also displayed lower CO₂ levels. The HSE evaluator agrees with this point and concludes that the low mass balance did not have a major impact.

It is evident from the microbial biomass values presented that the guideline deviations relating to pre-incubation times and incubation temperatures did not affect the viability of the soil. Therefore, the HSE evaluator does not consider these deviations to have significantly impacted upon the study results.

CONCLUSIONS

No major metabolites were characterised in this study. The study showed that the two enantiomers tended to degrade at different rates, with the (+)-enantiomer degrading at a slower rate than the (-)-enantiomer. As a result, the kinetic assessment was extended to the enantiomers. The study was well performed and conducted in compliance with GLP. The HSE evaluator considers the study acceptable for assessing the route and rate of degradation of [^{14}C]-Cinmethylin.

B.8.1.1.1.2. Anaerobic degradation (Data Requirement 7.1.1.2)

Report:	KCA 7.1.1.2/01; Staudenmaier, H. and Pape, L. (2017)
Title	Anaerobic soil metabolism of Cinmethylin (BAS 684 H) Report no. 2016/1053970
Guidelines	<ul style="list-style-type: none"> • OECD Guidelines for the testing of chemicals 307: Aerobic and anaerobic transformation in soil (Apr 2002) • US EPA fate, transport and transformation guidelines 835.4200: Anaerobic Soil Metabolism (Oct 2008) • FOCUS Degradation Kinetics (2006; 2014)
GLP?	Yes
Deviations	<ul style="list-style-type: none"> • One radiolabelled compound, [phenyl-$\text{U-}^{14}\text{C}$]-cinmethylin, had a chemical purity below 95%. However, the radiochemical purity was 99.8%. The HSE evaluator does not consider this to have impacted upon the study's viability as radiochemical purity was high. • One soil, Lufa 2.2, deviated from the OECD guidelines for pH and clay content; however, the HSE evaluator does not consider this to have impacted upon the study's viability.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

An anaerobic soil metabolism study was conducted according to OECD guidelines (OECD 307: Aerobic and anaerobic transformation in soil) using cinmethylin radiolabelled in two positions: [cyclohexane-4- ^{14}C]-cinmethylin (99.3% chemical purity; 99.4% radiochemical purity); and [phenyl- $\text{U-}^{14}\text{C}$]-cinmethylin (90.5% chemical purity; 99.8% radiochemical purity)². In addition, ^{13}C -labelled cinmethylin was used for structure elucidation ([benzyl- ^{13}C]-cinmethylin; 99.6% purity). The HSE evaluator notes that the chemical purity of the phenyl-labelled compound is below the required 95% threshold which may result in less test substance being applied in the studies than expected; however, the radiochemical purity is high at 99.8%, meaning the applied test substance can be efficiently tracked.

The study investigated metabolism in four agricultural soils under anaerobic conditions. All four soils undertook an aerobic incubation phase prior to flooding and were then incubated in darkness for 118 days (North Dakota and Wyoming soils), or 120 days (Lufa 2.2 and Lufa 5M soils). The Applicants performed a kinetic evaluation of cinmethylin based on the FOCUS kinetics guidance (2006; 2014). The study was conducted to GLP and according to

² [phenyl- $\text{U-}^{14}\text{C}$]-cinmethylin and [benzyl- $\text{U-}^{14}\text{C}$]-cinmethylin are both referenced within study reports. The UK evaluator assessed the certificates of analysis and confirms these two compounds are the same and of the same batch.

OECD 307 guidelines. There were two minor deviations from guidelines identified by the HSE evaluator; these are discussed in later sections. However, the HSE evaluator concludes that these deviations were not significant enough to affect the outcomes of the study.

TEST PROCEDURE

1. Soil characteristics

Table 8.1.1.2/01-01 details the soil characteristics for the four soils used in this study. Based on the experiment schedules provided by the applicant, the HSE evaluator confirms that soils were sufficiently fresh (*i.e.* less than three months old) at the study start. The HSE evaluator notes that the soil pH for Lufa 2.2 is below the required minimum of pH 5.5, the clay content is also below 10%; however, this deviation was not deemed significant enough to affect the study, especially as other soil properties were within guidelines. At study initiation, Lufa 2.2 pH was measured at an acceptable level (pH 5.6).

Table 8.1.1.2/01-01: Characterisation of the four test soils used within the anaerobic degradation study.

Soil designation	Lufa 2.2	Lufa 5M	North Dakota	Wyoming
Geographic location	Rheinland-Pfalz, Germany	Rheinland-Pfalz, Germany	North Dakota, US	Wyoming, US
Sampling date	24 Mar 2015	24 Mar 2015	24 Jul 2015	23 Jul 2015
Pesticide history	No pesticides or fertilisers in the past 5 years	No pesticides or fertilisers in the past 5 years	No pesticides or fertilisers in the past 5 years	No pesticides or fertilisers in the past 5 years
Sampling depth	0-20 cm	0-20 cm	0-15 cm	0-15 cm
Storage conditions ^a	~4°C	~4°C	~4°C	~4°C
Overall storage time (d)	28	84	60	61
Soil textural class (DIN 4220) ^b	Silty sand	Loamy sand	Sandy loam	Loamy clay
Soil texture (%; ISO 11277)				
Sand 0.063 – 2 mm	84.2	53.4	62	22
Silt 0.002 – 0.063 mm	11.0	34.2	17	29
Clay < 0.002 mm	4.8	12.4	21	49
Soil characteristics				
Organic carbon (%)	1.59	1.15	1.8	0.69
pH [CaCl ₂]	5.4	7.2	6.3	8.1
pH [H ₂ O]	6.0	7.7	6.7	8.3
Cation exchange capacity (cmol ⁺ /100 g)	6.3	10.3	15.5	31.0
Max. water holding capacity – 0.1 bar (pF 2.0; g/100 g dry soil)	33.6	29.7	47.5	51.1
Microbial biomass (mg C/100 g dry soil)	37.0	36.6	40.77	20.57
Microbial biomass as % organic carbon ^c	2.33	3.18	2.27	2.98

^a Applicant states soil storage conditions applied upon arrival at study facility

^b DIN is the German soil classification scheme

^c Calculated as follows: (biomass (mg C/kg dry soil) ÷ % organic carbon) ÷ 100

The aerobic incubation phase differed for each soil and corresponded to one half-life: 14 days for Lufa 2.2, 15 days for Lufa 5M, 10 days for North Dakota and 30 days for Wyoming. Soils were incubated at 20 ± 2°C in darkness, with soil moisture at 40% MWHC (Lufa 5M and North Dakota), and 50% MWHC (Lufa 2.2 and Wyoming); these achieved a pF of 2.0 – 2.5. To induce anaerobic conditions, each vessel was flooded with 50 mL degassed deionised

water to cover test vessels with a 1 cm water layer. A gentle stream of nitrogen gas flowed through each vessel to maintain anaerobic conditions. Incubation took place in the dark at $20 \pm 2^\circ\text{C}$.

For each soil, two samples were taken for immediate analysis, and a third was stored as a spare at -20°C in case of further analysis. All four soils were sampled ten times, with sampling times varying for each soil. For Lufa 2.2, samples were taken at 0, 3, 7, 14, 21, 30, 42, 59, 90, 120 DAT; for Lufa 5M samples were taken at 0, 3, 7, 15, 22, 30, 45, 59, 90, 120 DAT; for North Dakota samples were taken at 0, 3, 7, 10, 14, 29, 45, 59, 90, 118 DAT; for Wyoming samples were taken at 0, 3, 7, 14, 30, 38, 45, 59, 90, 118 DAT.

Additionally, benzyl/phenyl-labelled cinmethylin was applied to the North Dakota and Wyoming soils at an exaggerated rate of 6.65 mg a.s./kg dry soil (4 test vessels per soil) for structure elucidation of potential metabolites. Samples were taken at 10 DAT and 59 DAT for North Dakota samples, and 30 DAT for Wyoming samples.

2. Soil treatment

Each soil sample consisted 100 g soil (dry weight equivalent, 2 mm sieved). The target application rate for each test item was 1.33 mg/kg which corresponds to a field rate of 500 g a.s./Ha, assuming equal distribution in the top 2.5 cm soil layer and a soil density of 1.5 g/cm^3 . Soil was batch treated: for each test item, 4300 g soil was treated through 15-16 drops of application solution, each 3.46-3.77 mL in volume. After each addition, the soil was stirred with a hand mixer to ensure homogeneous distribution. Soil was then split into 100 g aliquots for the study. Table 8.1.1.2/01-02 outlines application rates for each soil and test item, as quantified by LSC. Actual application rates were 101-105% of the target 1.33 mg/kg. Volatiles were collected through four traps, with the fifth trap only used where necessary: ethylene glycol for organic volatiles; 0.5 M H_2SO_4 for alkaline volatiles; 0.5 M NaOH for CO_2 and acidic volatiles; 0.5 M NaOH; and 2 M NaOH. Due to high amounts of radioactivity being found in the second NaOH trap in the Lufa 2.2 soil, a third NaOH trap was installed for the rest of the study, and from the study start in the other three soils. When no further substantial amounts of radioactivity were detected in the second NaOH trap, the third NaOH trap was removed.

Table 8.1.1.2/01-02: Summary of actual ^{14}C -cinmethylin application rates for each soil.

Soil	Test item	Actual application rate (mg/kg)
Lufa 2.2	[Cyclohexane-4- ^{14}C]-cinmethylin	1.388
	[Phenyl- ^{14}C]-cinmethylin	1.376
Lufa 5M	[Phenyl- ^{14}C]-cinmethylin	1.401
North Dakota	[Phenyl- ^{14}C]-cinmethylin	1.374
	[Benzyl- ^{13}C]-cinmethylin	6.65 combined ¹
	[Phenyl- ^{14}C]-cinmethylin mix	
Wyoming	[Cyclohexane-4- ^{14}C]-cinmethylin	1.345
	[Benzyl- ^{13}C]-cinmethylin	6.65 combined ¹
	[Phenyl- ^{14}C]-cinmethylin mix	

¹ an exaggerated application rate was used for structure elucidation analysis. These application rates were not analytically verified.

3. Soil extraction methods

For aerobic phase samples, all soils were removed from their respective incubation vessel, filled into a centrifuge tube and consecutively extracted with five to seven extraction steps: $3 \times 100 \text{ mL}$ acetonitrile/water (50/50, v/v) and $2 \text{ to } 4 \times 100 \text{ mL}$ acetonitrile on a laboratory shaker at 150 rpm for 30 minutes. After each extraction step, the sample was centrifuged (10,000 rpm for 15 minutes). Supernatants were decanted into 100 mL volumetric flasks and

the volume was made up to the calibration mark with the respective solvent. Three aliquots of each extract were analysed via LSC. Exhaustive extraction was verified by the LSC results showing < 2% of AR in the last extract.

For anaerobic phase samples, the soil/water slurry was transferred to a centrifuge tube and 50 mL acetonitrile was added to achieve a final acetonitrile/water ratio of 50/50 (v/v). The samples were then extracted using the same procedure outlined for aerobic incubation phase samples.

For all samples, aliquots of the acetonitrile/water and acetonitrile extracts were combined and concentrated to 4 mL by evaporation with a stream of nitrogen. The concentrated solution was made up to 5 mL with acetonitrile/water (10/90, v/v). Three aliquots of the resulting sample were analysed by LSC, with recovery during concentration of extracts also checked via LSC. All recoveries were $\geq 94.6\%$. One sample was subjected to HPLC.

4. Determination of NERs

Extracted soils were dried at room temperature, ground in a mortar and five aliquots were combusted. The released $^{14}\text{CO}_2$ was trapped and analysed by LSC. If NER exceeded 5% AR, NER were further characterised in one replicate sample. Remaining residual dry soil was homogenised in an analytical mill. 50 g soil aliquots were shaken under nitrogen for 6-8 hours with 70 mL 0.5 M NaOH on a laboratory shaker. After centrifugation (10,000 rpm for 15 minutes), the supernatant was decanted, and the volume determined. The NaOH extraction was repeated, once overnight, and then for 6-8 hours. The remaining soil was washed with 40 mL distilled water, shaken for 30 minutes and centrifuged. Aliquots of the three NaOH extracts and washing solution were separately analysed by LSC, and then combined. To determine the humin fraction, the remaining soil was air-dried, weighed and homogenised with an analytical mill. Five aliquots were combusted and the resulting $^{14}\text{CO}_2$ was analysed by LSC. To separate the fulvic and humic acids, the combined NaOH extract was adjusted to pH 1-2 by adding 8.5 mL of concentrated HCl. After precipitation, the suspension was centrifuged (8000 rpm for 15 minutes) and the supernatant was decanted. The volume was adjusted to 250 mL with distilled water and three aliquots were analysed by LSC to determine fulvic acid residues. The precipitate was re-dissolved in 40 mL 0.5 M NaOH, the volume of the solution was adjusted to 50 mL with distilled water and three aliquots were analysed by LSC to determine the humic acid fraction.

The fulvic acid fraction was further extracted with 3×60 mL ethylacetate. For each extract and the remaining water phase, volume was determined, and three aliquots were analysed by LSC. The extracts were combined, concentrated to near dryness using a rotary evaporator, and then re-dissolved in 2 mL acetonitrile/water (50/50, v/v). Three aliquots were analysed by LSC, and one aliquot analysed via HPLC.

5. Analytical methods

Radioactivity was measured by LSC for all samples, and via combustion for solid samples. For LSC, values below < 0.1% AR were not reported. For combustion, five aliquots (0.4 – 1 g each) were taken. The limit of accurate determination was set to $2 \times$ background. The Applicant calculated the LOD and LOQ for the LSC analysis of labelled compounds, with $\text{LOD} = 2 \times \text{background}$ and $\text{LOQ} = 3 \times \text{background}$ and expressed as test item concentration per kg soil. For [cyclohexane-4- ^{14}C]-cinmethylin, the LOD was 0.065 $\mu\text{g/kg}$ and LOQ 0.097 $\mu\text{g/kg}$. For [phenyl-U- ^{14}C]-cinmethylin, the LOD was 0.068 $\mu\text{g/kg}$ and the LOQ 0.101 $\mu\text{g/kg}$.

The Applicant assessed cinmethylin stability in different pH regimes during the fractionation of NER. 15 μL of application solution containing [cyclohexane-4- ^{14}C]-cinmethylin was treated with 0.5 M NaOH, and 15 μL of application solution containing [phenyl-U- ^{14}C]-cinmethylin was treated with HCl at a pH of 1.5. Three aliquots of each solution were

analysed immediately by LSC, and one aliquot of each was subjected to HPLC analysis. Solutions were stored at room temperature for up to 30 hours to mimic the maximum workup time during NER fractionation. At intervals of 6, 24 and 30 hours, an aliquot of each solution was subjected to HPLC analysis. Cinmethylin recovery of $\geq 97.8\%$ was determined, and the Applicant concluded cinmethylin was stable during fractionation of NER.

Additionally, chiral HPLC was performed on one aliquot of concentrated, combined extract for one replicate sample per sample date. For these samples, the HPLC eluates of the two enantiomer peaks were collected separately and subjected to LSC measurement. For the two separated enantiomers, 93-99% recovery was achieved. The Applicant states that this confirms the two main chiral analysis peaks represented only the two enantiomers, and that no additional radioactivity was measured from potential metabolites.

RESULTS AND DISCUSSION

The anaerobic incubation phase for all soils demonstrated that soils remained anaerobic, with O₂ saturation levels of 0.2 – 2.0% for all soils by the study end, down from 65.5 – 88.3% at 0 days after flooding. Redox potential values indicate that anaerobic conditions were maintained throughout the study for all soils.

1. Mass balance and metabolites

Mass balances were 94.3 – 100.3% AR (Lufa 2.2), 90.8 – 100.0% (Lufa 5M), 93.2 – 100.1% (North Dakota), and 92.7 – 103.5% (Wyoming). Tables 8.1.1.2/01-03 – 8.1.1.2/01-07 present the radioactive residue characterisation in soil extracts. Two metabolites were characterised in extracts, M684H001 and M684H004, though neither were deemed to be major metabolites. The HSE evaluator notes that both metabolites started to form during aerobic incubation, which suggests these are not novel metabolites to the anaerobic degradation pathway. Respective maximum AR levels were 1.7% and 1.2% respectively in Lufa 2.2 ([phenyl-U-¹⁴C]-labelled); 1.0% and 1.8% in Lufa 5M ([phenyl-U-¹⁴C]-labelled); 3.0% for M684H004 in North Dakota ([phenyl-U-¹⁴C]-labelled); and 4.9% and 1.4% respectively in Wyoming samples ([phenyl-U-¹⁴C]-labelled). The HSE evaluator agrees that neither metabolite should be classed as a major metabolite.

Table 8.1.1.2/01-03: Distribution of radioactive residues in Lufa 2.2 soil extracts, expressed in % applied radioactivity, using the [cyclohexane-4-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	BAS684H (64.4 min)	Unknown (21.5 min)	M684H001 (52.3 min)	M684H004 (53.0 min)	Sum others ^a	Total extractables	NER	Volatiles			Mass balance
									CO ₂	Others	Total	
0	-	98.4	0.9	-	-	-	99.3	0.4	NA	NA	NA	99.7
0	-	99.1	0.8	-	-	-	99.9	0.4				100.3
0 (mean)	-	98.8	0.8	-	-	-	99.6	0.4				100.0
3	-	85.3	-	0.9	0.5	0.8	87.4	8.8	3.0	-	3.0	99.2
3	-	85.8	-	0.5	0.2	0.8	87.3	6.1				96.3
3 (mean)	-	85.5	-	0.7	0.3	0.8	87.3	7.4	3.0	-	3.0	97.7
7	-	73.3	-	1.1	0.8	1.5	76.6	13.0	7.2	-	7.2	96.8
7	-	72.1	-	0.8	0.8	1.9	75.6	12.7				95.5
7 (mean)	-	72.7	-	0.9	0.8	1.7	76.1	12.8	7.2	-	7.2	96.2
14	0	60.1	-	0.9	1.1	1.7	63.7	18.5	12.7	-	12.7	94.9
14	0	59.7	-	1.2	0.9	2.0	63.8	19.9				96.5
14 (mean)	0	59.9	-	1.0	1.0	1.9	63.8	19.2	12.7	-	12.7	95.7
21	7	60.5	-	1.4	0.8	2.7	65.4	16.1	13.3	-	13.3	94.7
21	7	60.2	-	1.3	1.2	2.3	65.1	17.1				95.4
21 (mean)	7	60.4	-	1.4	1.0	2.5	65.2	16.6	13.3	-	13.3	95.1
30	16	61.6	-	1.1	0.8	1.8	65.3	17.6	13.9	-	13.9	96.7
30	16	62.3	-	1.2	0.8	1.4	65.7	16.7				96.2
30 (mean)	16	61.9	-	1.2	0.8	1.6	65.5	17.1	13.9	-	13.9	96.5
42	28	61.4	0.6	1.3	0.9	1.3	65.5	16.7	14.5	-	14.5	96.6
42	28	61.5	0.7	1.3	0.8	1.9	66.2	16.1				96.8
42 (mean)	28	61.5	0.7	1.3	0.8	1.6	65.9	16.4	14.5	-	14.5	96.7
59	45	59.3	1.1	1.3	0.9	1.5	64.2	17.8	15.1	-	15.1	97.1
59	45	59.9	1.0	1.5	0.8	1.9	65.1	17.2				97.4
59 (mean)	45	59.6	1.0	1.4	0.8	1.7	64.6	17.5	15.1	-	15.1	97.3
90	76	59.0	1.7	1.3	0.8	1.7	64.4	17.1	15.6	-	15.6	97.2
90	76	58.3	1.6	1.6	0.8	1.2	63.5	16.4				95.6
90 (mean)	76	58.6	1.6	1.5	0.8	1.5	64.0	16.7	15.6	-	15.6	96.4
120	106	58.4	2.0	1.6	0.7	1.3	64.0	14.3	16.0	-	16.0	94.3
120	106	58.2	2.2	1.7	0.9	0.4	63.4	15.7				95.1
120 (mean)	106	58.3	2.1	1.6	0.8	0.9	63.7	15.0	16.0	-	16.0	94.7

NA = not analysed ^a ≤ 2% AR each (mean of two replicates)

Table 8.1.1.2/01-04: Distribution of radioactive residues in Lufa 2.2 soil extracts, expressed in % applied radioactivity, using the [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	BAS684H (64.4 min)	M684H001 (52.3 min)	M684H004 (53.0 min)	Sum others ^a	Total extractables	NER	Volatiles			Mass balance
								CO ₂	Others	Total	
0	-	98.7	-	-	0.8	99.5	0.3	NA	NA	NA	99.8
0	-	99.1	-	-	0.7	99.8	0.4				100.2
0 (mean)	-	98.9	-	-	0.7	99.7	0.3				100.0
3	-	86.5	0.5	0.6	0.7	88.2	7.8	2.1	-	2.1	98.1
3	-	87.0	0.6	-	0.7	88.2	8.0				98.3
3 (mean)	-	86.7	0.5	0.3	0.7	88.2	7.9	2.1	-	2.1	98.2
7	-	73.3	1.0	0.5	1.6	76.4	15.3	5.5	-	5.5	97.1
7	-	73.5	1.2	0.7	1.2	76.6	15.2				97.3
7 (mean)	-	73.4	1.1	0.6	1.4	76.5	15.2	5.5	-	5.5	97.2
14	0	60.1	0.8	1.2	2.0	64.1	23.3	9.5	-	9.5	96.9
14	0	60.5	1.2	0.8	1.8	64.3	21.5				95.4
14 (mean)	0	60.3	1.0	1.0	1.9	64.2	22.4	9.5	-	9.5	96.1
21	7	63.7	1.6	0.7	1.3	67.2	20.2	9.9	-	9.9	97.4
21	7	62.9	1.7	0.6	1.7	66.8	20.0				96.7
21 (mean)	7	63.3	1.6	0.7	1.5	67.0	20.1	9.9	-	9.9	97.1
30	16	63.3	1.3	0.7	1.5	66.8	19.3	10.4	-	10.4	96.4
30	16	63.7	1.3	0.7	0.8	66.6	19.1				96.1
30 (mean)	16	63.5	1.3	0.7	1.2	66.7	19.2	10.4	-	10.4	96.3
42	28	60.9	1.3	0.9	1.6	64.7	20.3	10.8	-	10.8	95.8
42	28	60.2	1.5	0.8	2.2	64.7	19.3				94.8
42 (mean)	28	60.5	1.4	0.9	1.9	64.7	19.8	10.8	-	10.8	95.3
59	45	58.8	1.4	0.9	1.2	62.4	22.0	11.2	-	11.2	95.5
59	45	62.8	1.6	0.7	1.2	66.2	19.5				96.9
59 (mean)	45	60.8	1.5	0.8	1.2	64.3	20.8	11.2	-	11.2	96.2
90	76	61.0	1.3	0.7	1.0	64.1	18.8	11.4	-	11.4	94.3
90	76	59.7	1.5	1.1	1.3	63.5	19.8				94.8
90 (mean)	76	60.3	1.4	0.9	1.1	63.8	19.3	11.4	-	11.4	94.5
120	106	60.0	1.4	0.7	1.6	63.7	20.3	11.8	-	11.8	95.7
120	106	59.4	1.7	0.9	1.4	63.4	19.5				94.7
120 (mean)	106	59.7	1.5	0.8	1.5	63.5	19.9	11.8	-	11.8	95.2

NA = not analysed ^a ≤ 2% AR each (mean of two replicates)

Table 8.1.1.2/01-05: Distribution of radioactive residues in Lufa 5M soil extracts, expressed in % applied radioactivity, using the [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	BAS684H (64.4 min)	M684H001 (52.3 min)	M684H004 (53.0 min)	Sum others ^a	Total extractables	NER	Volatiles			Mass balance
								CO ₂	Others	Total	
0	-	98.8	-	-	0.9	99.7	0.3	NA	NA	NA	100.0
0	-	99.1	-	-	0.5	99.7	0.3				100.0
0 (mean)	-	98.9	-	-	0.7	99.7	0.3	NA	NA	NA	100.0
3	-	85.8	1.0	0.5	-	87.3	8.7	1.8	-	1.8	97.8
3	-	86.9	0.9	-	-	87.7	8.9				98.5
3 (mean)	-	86.3	0.9	0.2	-	87.5	8.8	1.8	-	1.8	98.1
7	-	74.2	0.8	1.0	0.5	76.6	16.0	5.2	-	5.2	97.8
7	-	74.4	0.7	0.7	0.8	76.7	15.0				96.9
7 (mean)	-	74.3	0.8	0.9	0.7	76.7	15.5	5.2	-	5.2	97.4
15	0	57.7	0.6	1.2	1.2	60.7	23.8	11.7	-	11.7	96.2
15	0	58.3	0.6	1.4	0.9	61.3	24.2				97.2
15 (mean)	0	58.0	0.6	1.3	1.1	61.0	24.0	11.7	-	11.7	96.7
22	7	57.1	0.5	1.7	0.8	60.0	24.6	12.2	-	12.2	96.8
22	7	56.7	0.5	1.3	0.7	59.1	24.8				96.2
22 (mean)	7	56.9	0.5	1.5	0.7	59.6	24.7	12.2	-	12.2	96.5
30	15	56.2	0.6	1.4	-	58.2	24.0	12.7	-	12.7	94.9
30	15	56.6	0.3	1.3	0.5	58.7	23.2				94.7
30 (mean)	15	56.4	0.4	1.4	0.3	58.4	23.6	12.7	-	12.7	94.8
45	30	55.6	0.5	1.4	-	57.5	23.2	13.5	-	13.5	94.2
45	30	55.6	0.4	1.5	-	57.5	23.4				94.4
45 (mean)	30	55.6	0.5	1.4	-	57.5	23.3	13.5	-	13.5	94.3
59	44	55.9	0.4	1.8	-	58.2	24.9	14.2	-	14.2	97.3
59	44	55.7	0.3	1.1	-	57.1	23.7				95.0
59 (mean)	44	55.8	0.3	1.5	-	57.6	24.3	14.2	-	14.2	96.1
90	75	53.1	0.4	1.6	-	55.1	23.2	15.4	-	15.4	93.8
90	75	52.4	-	1.5	-	53.9	21.5				90.8
90 (mean)	75	52.7	0.2	1.5	-	54.5	22.4	15.4	-	15.4	92.3
120	105	51.4	0.5	1.5	-	53.4	23.1	16.2	-	16.2	92.8
120	105	51.9	0.4	1.6	-	53.9	24.5				94.6
120 (mean)	105	51.6	0.4	1.6	-	53.6	23.8	16.2	-	16.2	93.7

NA = not analysed

^a ≤ 2% AR each (mean of two replicates)

Table 8.1.1.2/01-06: Distribution of radioactive residues in North Dakota soil extracts, expressed in % applied radioactivity, using the [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	BAS684H (64.4 min)	M684H004 (53.0 min)	Sum others ^a	Total extractables	NER	Volatiles			Mass balance
							CO ₂	Others	Total	
0	-	98.1	-	1.3	99.4	0.7	NA	NA	NA	100.1
0	-	98.5	-	0.7	99.2	0.7				99.9
0 (mean)	-	98.3	-	1.0	99.3	0.7	NA	NA	NA	100.0
3	-	73.5	-	2.6	76.2	16.6	3.5	-	3.5	96.4
3	-	73.7	-	2.8	76.5	16.6				96.6
3 (mean)	-	73.6	-	2.7	76.3	16.6	3.5	-	3.5	96.5
7	-	56.5	1.1	2.8	60.3	25.9	9.0	-	9.0	95.3
7	-	55.2	1.4	3.4	60.0	26.3				95.3
7 (mean)	-	55.8	1.2	3.1	60.1	26.1	9.0	-	9.0	95.3
10	0	47.6	2.6	2.9	53.1	29.5	12.8	-	12.8	95.4
10	0	47.9	2.3	3.1	53.3	28.1				94.3
10 (mean)	0	47.7	2.4	3.0	53.2	28.8	12.8	-	12.8	94.8
14	4	45.5	2.3	2.7	50.5	29.6	13.4	-	13.4	93.6
14	4	47.0	2.6	1.9	51.5	28.3				93.3
14 (mean)	4	46.3	2.4	2.3	51.0	29.0	13.4	-	13.4	93.4
29	19	45.8	2.6	2.5	50.9	29.0	14.7	-	14.7	94.6
29	19	44.8	2.4	2.9	50.2	28.4				93.2
29 (mean)	19	45.3	2.5	2.7	50.5	28.7	14.7	-	14.7	93.9
45	35	43.6	3.0	1.9	48.5	29.6	15.4	0.1	15.5	93.6
45	35	44.4	2.4	2.0	48.8	29.2				93.6
45 (mean)	35	44.0	2.7	2.0	48.6	29.4	15.4	0.1	15.5	93.6
59	49	41.9	2.2	2.1	46.2	32.1	15.9	0.1	16.0	94.4
59	49	43.0	2.4	-	45.3	32.9				94.2
59 (mean)	49	42.4	2.3	1.0	45.8	32.5	15.9	0.1	16.0	94.3
90	80	36.9	2.2	-	39.1	39.4	16.6	0.1	16.7	95.2
90	80	36.4	2.1	-	38.5	40.0				95.2
90 (mean)	80	36.7	2.2	-	38.8	39.7	16.6	0.1	16.7	95.2
118	108	35.4	1.7	-	37.0	41.0	17.0	0.1	17.1	95.2
118	108	34.8	2.1	-	36.9	41.4				95.4
118 (mean)	108	35.1	1.9	-	37.0	41.2	17.0	0.1	17.1	95.3

NA = not analysed ^a ≤ 2% AR each (mean of two replicates)

Table 8.1.1.2/01-07: Distribution of radioactive residues in Wyoming soil extracts, expressed in % applied radioactivity, using the [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	BAS684H (64.4 min)	M684H001 (52.3 min)	M684H004 (53.0 min)	Sum others ^a	Total extractables	NER	Volatiles			Mass balance
								CO ₂	Others	Total	
0	-	101.5	-	-	1.1	102.6	0.3	NA	NA	NA	102.9
0	-	95.7	-	-	1.0	96.7	0.4				97.1
0 (mean)	-	98.6	-	-	1.0	99.7	0.3				100.0
3	-	99.2	-	-	-	99.2	2.2	0.3	-	0.3	101.7
3	-	99.2	-	-	-	99.2	2.2				101.7
3 (mean)	-	99.2	-	-	-	99.2	2.2				101.7
7	-	90.2	1.1	-	-	91.3	5.9	0.9	-	0.9	98.0
7	-	93.7	0.9	-	-	94.6	4.9				100.4
7 (mean)	-	91.9	1.0	-	-	92.9	5.4				99.2
14	-	86.0	3.0	-	-	89.0	10.6	2.0	-	2.0	101.6
14	-	85.9	3.1	-	-	89.0	8.8				99.8
14 (mean)	-	86.0	3.0	-	-	89.0	9.7				100.7
30	0	64.5	4.8	0.8	0.7	70.8	18.4	5.0	-	5.0	94.2
30	0	67.1	4.9	1.2	0.8	74.0	19.1				98.1
30 (mean)	0	65.8	4.8	1.0	0.8	72.4	18.7				96.1
38	8	74.9	4.0	1.0	-	79.9	17.3	5.3	-	5.3	102.5
38	8	72.0	4.6	0.8	-	77.3	15.8				98.4
38 (mean)	8	73.4	4.3	0.9	-	78.6	16.6				100.4
45	15	72.2	4.6	0.7	-	77.5	16.8	5.5	-	5.5	99.8
45	15	72.6	4.5	0.9	-	78.1	16.8				100.3
45 (mean)	15	72.4	4.5	0.8	-	77.8	16.8				100.1
59	29	79.1	3.5	1.0	-	83.6	14.0	5.9	-	5.9	103.5
59	29	73.4	3.5	0.9	-	77.9	15.5				99.4
59 (mean)	29	76.3	3.5	1.0	-	80.7	14.8				101.4
90	60	74.7	3.8	1.1	-	79.7	15.9	7.4	-	7.4	103.0
90	60	73.7	4.3	1.0	-	79.0	16.3				102.7
90 (mean)	60	74.2	4.0	1.1	-	79.3	16.1				102.8
118	88	63.8	3.6	0.9	-	68.3	16.2	8.1	-	8.1	92.7
118	88	66.3	3.9	1.4	-	71.6	16.4				96.1
118 (mean)	88	65.1	3.8	1.1	-	69.9	16.3				94.4

NA = not analysed

^a ≤ 2% AR each (mean of two replicates)

2. Enantiomer ratio

As cinmethylin consists two enantiomers (mixture ratio 50:50), the Applicants studied the ratio over time in each soil. These data are reported in Tables 8.1.1.2/01-08 – 8.1.1.2/01-12. In Lufa 2.2 and Lufa 5M, the enantiomeric ratio of both labels changed from approximately 50:50 to 40:60 (- : +) by the end of the aerobic incubation phase (14/15 DAT), and remained relatively stable through the anaerobic period. In the North Dakota samples, the ratio changed to approximately 30:70 by the end of the aerobic phase (10 DAT), and remained relatively stable through the anaerobic phase. In the Wyoming soil, the ratio did not markedly change throughout the whole incubation period. The Applicant suggests the change in enantiomeric ratio is caused by different degradation rates for the two enantiomers and is not caused by conversion. They also note that the (-)-enantiomer degrades faster than the (+)-enantiomer in three soils (Lufa 2.2, Lufa 5M, North Dakota), as indicated by the reductions in AR shown in the tables below, though this difference was not observed in the Wyoming soil samples.

Table 8.1.1.2/01-08: Determination of enantiomeric ratios in Lufa 2.2 soil treated with [cyclohexane-4-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR)	(+)-enantiomer (% AR)	Enantiomer ratio (- : +)
0	-	98.4	50.3	48.1	51:49
3	-	85.3	40.8	44.5	48:52
7	-	73.3	33.3	40.0	45:55
14	0	60.1	24.3	35.9	40:60
21	7	60.5	24.7	35.8	41:59
30	16	61.6	25.8	35.8	42:58
42	28	61.4	25.7	35.8	42:58
59	45	59.3	24.9	34.5	42:58
90	76	59.0	24.7	34.2	42:58
120	106	58.4	25.2	33.2	43:57

^a Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

Table 8.1.1.2/01-09: Determination of enantiomeric ratios in Lufa 2.2 soil treated with [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR)	(+)-enantiomer (% AR)	Enantiomer ratio (- : +)
0	-	98.7	51.2	47.5	52:48
3	-	86.5	41.8	44.7	48:52
7	-	73.3	33.4	39.9	46:54
14	0	60.1	25.7	34.4	43:57
21	7	63.7	27.7	36.0	43:57
30	16	63.3	26.9	36.4	42:58
42	28	60.9	25.9	35.0	43:57
59	45	58.8	24.8	34.0	42:58
90	76	61.0	25.6	35.4	42:58
120	106	60.0	26.5	33.5	44:56

^a Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

Table 8.1.1.2/01-10: Determination of enantiomeric ratios in Lufa 5M soil treated with [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR)	(+)-enantiomer (% AR)	Enantiomer ratio (- : +)
0	-	98.8	50.6	48.1	51:49
3	-	85.8	41.4	44.4	48:52
7	-	74.2	34.3	40.0	46:54
15	0	57.7	23.5	34.2	41:59
22	7	57.1	23.7	33.4	42:58
30	15	56.2	22.9	33.3	41:59
45	30	55.6	22.2	33.4	40:60
59	44	55.9	23.2	32.8	41:59
90	75	53.1	22	31.1	41:59
120	105	51.4	21.1	30.3	41:59

^a Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

Table 8.1.1.2/01-11: Determination of enantiomeric ratios in North Dakota soil treated with [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR)	(+)-enantiomer (% AR)	Enantiomer ratio (- : +)
0	-	98.1	50.6	47.5	52:48
3	-	73.5	30.9	42.6	42:58
7	-	56.5	19.0	37.4	34:66
10	0	47.6	13.9	33.7	29:71
14	4	45.5	12.6	32.9	28:72
29	19	45.8	13.2	32.6	29:71
45	35	43.6	12.7	30.9	29:71
59	49	41.9	12.3	29.6	29:71
90	80	36.9	10.7	26.2	29:71
118	108	35.1	9.5	25.9	27:73

^a Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

Table 8.1.1.2/01-12: Determination of enantiomeric ratios in Wyoming soil treated with [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	Cinmethylin (% AR) ^a	(-)-enantiomer (% AR)	(+)-enantiomer (% AR)	Enantiomer ratio (- : +)
0	-	101.5	52.3	49.2	52:48
3	-	99.2	50.6	48.6	51:49
7	-	90.2	45.8	44.4	51:49
14	-	86.0	44.0	42.0	51:49
30	0	64.5	30.2	34.4	47:53
38	8	74.9	35.6	39.3	48:52
45	15	72.2	35.1	37.2	49:51
59	29	79.1	38.5	40.6	49:51
90	60	74.7	35.1	39.7	47:53
118	88	63.8	29.8	34.0	47:53

^a Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

3. Non-extractable residues (NERs)

The Applicant characterised the NERs, apportioning them to humin, humic acid and fulvic acid fractions. These are summarised in Tables 8.1.1.2/01-13 – 8.1.1.2/01-17. In Lufa 2.2 soils treated with [cyclohexane-4-¹⁴C]-cinmethylin, on average 33% of NERs were attributed to the fulvic acid fraction, 42% to the humic acid fraction, and 25% to the humin fraction. For the phenyl-labelled Lufa 2.2 treatment, 28% were attributed to fulvic acids, 48% to humic acid, and 24% to humin. In Lufa 5M, 26% of NERs were attributed to fulvic acids, 36% to humic acid, and 38% to humin. In North Dakota samples, 29% were attributed to fulvic acids, 29% to humic acid, and 42% to humin fraction. In Wyoming samples, 31% were attributed to fulvic acids, 9% to humic acid, and 59% to humin.

Table 8.1.1.2/01-13: Characterisation of NERs in Lufa 2.2 soil treated with [cyclohexane-4-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	NER (% AR)	NER in fraction (% NER)		
			Fulvic acid	Humic acid	Humin
3	-	8.8	40%	42%	18%
7	-	13.0	33%	44%	23%
14	0	19.9	32%	45%	22%
21	7	17.1	31%	44%	25%
30	16	17.6	30%	44%	25%
42	28	16.7	31%	43%	26%
59	45	17.8	31%	41%	28%
90	76	17.1	34%	38%	28%
120	106	15.7	34%	38%	29%

Table 8.1.1.2/01-14: Characterisation of NERs in Lufa 2.2 soil treated with [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	NER (% AR)	NER in fraction (% NER)		
			Fulvic acid	Humic acid	Humin
3	-	8.0	30%	50%	20%
7	-	15.3	28%	50%	22%
14	0	23.3	27%	50%	23%
21	7	20.2	27%	51%	22%
30	16	19.3	27%	50%	24%
42	28	20.3	25%	49%	25%
59	45	22.0	27%	46%	27%
90	76	19.8	28%	42%	29%
120	106	20.3	29%	44%	27%

Table 8.1.1.2/01-15: Characterisation of NERs in Lufa 5M soil treated with [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	NER (% AR)	NER in fraction (% NER)		
			Fulvic acid	Humic acid	Humin
3	-	8.9	27%	42%	31%
7	-	16.0	28%	38%	35%
15	0	24.2	27%	36%	37%
22	7	24.8	27%	36%	38%
30	15	24.0	25%	36%	39%
45	30	23.4	25%	36%	39%
59	44	24.9	25%	36%	38%
90	75	23.2	25%	34%	41%
120	105	24.5	25%	33%	42%

Table 8.1.1.2/01-16: Characterisation of NERs in North Dakota soil treated with [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	NER (% AR)	NER in fraction (% NER)		
			Fulvic acid	Humic acid	Humin
3	-	16.6	28%	34%	38%
7	-	26.3	29%	32%	39%
10	0	29.5	30%	31%	39%
14	4	29.6	28%	31%	41%
29	19	29.0	26%	31%	43%
45	35	29.6	26%	31%	43%
59	49	32.9	32%	27%	41%
90	80	40.0	29%	24%	47%
118	108	41.4	33%	23%	44%

Table 8.1.1.2/01-17: Characterisation of NERs in Wyoming soil treated with [phenyl-U-¹⁴C]-cinmethylin label.

Days after treatment	Days after flooding	NER (% AR)	NER in fraction (% NER)		
			Fulvic acid	Humic acid	Humin
7	-	5.9	37%	10%	54%
14	-	10.6	33%	9%	58%
30	0	19.1	31%	9%	59%
38	8	17.3	29%	9%	61%
45	15	16.8	28%	9%	62%
59	29	15.5	28%	9%	63%
90	60	16.3	29%	8%	63%
118	88	16.4	34%	11%	55%

GUIDELINE DEVIATIONS

The HSE evaluator identified two minor deviations from the standard guidelines:

- The chemical purity of [phenyl-U-¹⁴C]-cinmethylin was 90.5%, below the minimum purity of 95%. However, the radiochemical purity was 99.8%;
- One soil, Lufa 2.2, deviated from the OECD guidelines for both pH and clay content at the point of soil classification. However, pH was at an acceptable level at study initiation and throughout the study.

The HSE evaluator does not consider that either of these deviations impacted upon the study or on the data quality.

CONCLUSIONS

Degradation of cinmethylin was fast under aerobic conditions, though under anaerobic conditions the degradation rate slowed considerably or remained stable. Kinetic evaluations of the anaerobic degradation rates are reported in section KCA 7.1.2.1.3/1; Staudenmaier, H. and Pape, L. (2017).

No major metabolites were observed; two minor metabolites (M684H001 and M684H004) were formed mainly during aerobic incubation, though amounts never exceeded 4.8% and 2.7% AR respectively. The major sink for cinmethylin was formation of non-extractable residues, with maximum values ranging 15.0 – 41.2% AR, with NERs predominantly found in the humin fraction.

Chiral analysis indicated that the ratio of the two enantiomers changed during the aerobic incubation phase for three soils (Lufa 2.2, Lufa 5M, North Dakota), and then remained stable during the anaerobic phase. For one soil, Wyoming, the ratio remained stable throughout. The Applicant concluded that the change in ratio was due to different degradation rates for the two enantiomers; the HSE evaluator agrees with this conclusion and notes that the result is consistent with the conclusion of the aerobic degradation study (KCA 7.1.1.1/1; Stewart, L. and Abernethy, A. 2016).

B.8.1.1.1.3. Soil photolysis (Data Requirement 7.1.1.3)

Report:	KCA 7.1.1.3/01; Hassink, J. (2017c)
Title	Soil photolysis of BAS 684 H Report no. 2016/1333357
Guidelines	<ul style="list-style-type: none"> • OECD Draft Guideline “Phototransformation of chemicals on soil surfaces” (Jan 2002) • US EPA Fate, Transport and Transformation Guidelines 835.2410: photodegradation on soil (Oct 2008) • US EPA Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate: Photodegradation Studies on Soil (Oct 1982) • FOCUS Kinetics guidance (2006; 2014).
GLP?	Yes
Deviations	<ul style="list-style-type: none"> • Air temperature throughout the study was held at $22 \pm 1^{\circ}\text{C}$; however, the HSE evaluator does not deem the higher temperature to have significantly affected test outcomes. • Low mass balances were achieved with over half of the phenyl/benzyl-labelled soil samples in both light and dark sample groups, with 3/22 samples below 85% recovery. The HSE evaluator concludes that the degree of low recovery did not significantly impact upon the test outcomes. • The Applicant included analysis of the condensed water from within test systems to improve mass balances. The HSE evaluator concludes this was an acceptable deviation considering the poor mass balances observed.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

A soil photolysis study was conducted according to OECD draft guidelines and US EPA guidelines using cinmethylin labelled in three positions: [cyclohexane-4- ^{14}C]-cinmethylin (99.3% chemical purity; 99.4% radiochemical purity); [phenyl- ^{14}C]-cinmethylin (97.0% chemical purity; 98.9% radiochemical purity); and [benzyl- ^{13}C]-cinmethylin (99.6% chemical purity). Phenyl- and benzyl-labelled compounds were combined to form the phenyl/benzyl-labelled treatments. The HSE evaluator notes that the two radiolabelled compounds appear to be the same radiolabelling position, with differing names and isotopes.

The study investigated photolysis on one soil, Lufa 5M, under artificial light in a laboratory for 15 days of continuous irradiation. The study was conducted to GLP. The Applicant also provided kinetic evaluation of cinmethylin conducted to FOCUS Kinetics guidance (2006; 2014). There were deviations from guidelines identified by the Applicant and the HSE evaluator; these are discussed in later sections. However, the HSE evaluator concludes that these deviations were not significant enough to affect study outcomes.

TEST PROCEDURE

1. Soil characteristics and test set up

Table 8.1.1.3/01-01 details the soil characteristics for the two soil batches used in this study. Two batches of the same soil were used for the photolysis study, with the first batch (June 2015) used for the phenyl/benzyl-labelled samples, and the second batch (August) used for the cyclohexane-labelled study.

Table 8.1.1.3/01-01: Characterisation of the test soil used in the photolysis study.

Soil designation	Lufa 5M	
Geographic location	Rheinland-Pfalz, Germany	
Sampling date	5 Jun 2015	19 Aug 2015
Pesticide history	No pesticide or fertiliser use in the past 5 years	
Sampling depth	0-20 cm	
Soil texture (%; ISO 11277)		
Soil textural class (DIN 4220) ^a	Loamy sand	
Sand 0.063 – 2 mm	53.4	57.8
Silt 0.002 – 0.063 mm	34.3	30.2
Clay < 0.002 mm	12.4	12.0
USDA Particle size distribution (%)	Sandy loam	
Sand 0.050 – 2 mm	59.3	63.6
Silt 0.002 – 0.050 mm	28.3	24.4
Clay < 0.002 mm	12.4	12.0
Soil characteristics		
Organic carbon (%)	1.05	1.21
pH [CaCl ₂]	6.9	7.2
pH [H ₂ O]	7.4	7.9
Cation exchange capacity (cmol ⁺ /100 g)	12.5	12.7
Max. water holding capacity – 0.1 bar (pF 2.0; g/100 g dry soil)	29.4	26.4
Microbial biomass (mg C/100 g dry soil)	29.9	27.8
Microbial biomass as % organic carbon ^b	2.85	2.30

^a DIN is the German soil classification scheme

^b Calculated as follows: (biomass (mg C/kg dry soil) ÷ % organic carbon) ÷ 100

Twenty-two samples were created for each radiolabel, with ten dishes for the photolysis test and ten dishes for the dark control. Samples were taken in duplicate on 0, 2, 5, 7, 12 and 15 DAT from both the photolysis and dark samples, except on 0 DAT where no dark control samples were taken. Both photolysis and dark samples were incubated at a steady temperature of $22 \pm 1^\circ\text{C}$. The HSE evaluator notes that this target temperature and error placed the incubation temperature at the top end of the draft OECD guidelines; however, inspection of the measured temperatures showed that mean temperatures across the studies ranged $21.70 - 22.01^\circ\text{C}$, therefore, the HSE evaluator did not deem this deviation to have impacted on the study.

The photolysis experiment was performed with SUNTEST apparatus, with a xenon lamp providing a light intensity of 3 mW/cm^2 continuously for 15 days at 315-400 nm. A filter was

used to cut off wavelengths < 290 nm. The Applicant stated that this set up simulated a clear summer day in Limburgerhof, Germany, which is at 49°N. The HSE evaluator notes that 3 mW/cm² (30 W/m²) is lower than the values given in the draft OECD guidance for irradiance for natural summer sunlight. The HSE evaluator has calculated that the duration of the study, 15 days, is equivalent to 18.4 days of summer sunlight at 50°N. Dark control samples were placed in an incubator to eliminate light.

2. Soil treatment

Each sample consisted 30 g dry weight equivalent soil in an aluminium dish. Soils were adjusted in bulk to 60% MWHC prior to weighing into sample dishes; this corresponded to pH 2.0 – 2.5. Cinmethylin application was based on the recommended field application rate of 500 g/Ha. Based on a 1 cm soil layer and a bulk density of 1.5 g/cm³, the application rate was deemed to correspond to 3.34 mg test item/kg dry soil. Test substances were applied dropwise by pipette, with each replicate treated individually. Based on LSC measurements provided by the Applicant, the HSE evaluator calculated that the cyclohexane-labelled application corresponded to 3.34 mg/kg dry soil, and the phenyl/benzyl-labelled application corresponded to 3.35 mg/kg of dry soil. Throughout the study, moisture loss through evaporation was quantified daily, and samples adjusted appropriately to maintain water content. Volatiles were collected through five traps: 0.5 M NaOH, 0.5 M NaOH, H₂O, ethylene glycol, and 0.5 M H₂SO₄. The Applicant noted that, due to low recovery in preliminary studies, any condensed water found within the bowl of the test set up was collected at each sampling time, and the bowl was rinsed with acetonitrile. The HSE evaluator notes that this additional step is included in the mass balance tables presented in the results.

3. Soil extraction methods

To determine extractable radioactivity, each soil sample was extracted three times with 40 mL acetonitrile, and twice with 40 mL ACN/water (70/30, v/v). For each extraction step, the suspension was shaken for 30 minutes at 220 rpm then centrifuged for 10 minutes at 13000 rpm. The extract was decanted and made up to 50 mL with the appropriate solvent (acetonitrile or ACN/water). Each extract was analysed by LSC, and extracts were then combined. After the fifth extraction, soil residues were dried and stored at room temperature. To determine NERs, dried soils were homogenised with an analytical mill, and three aliquots weighing up to 1 g were combusted in a sample oxidiser. Collected ¹⁴CO₂ was measured by LSC.

4. NER characterisation

Further analyses were conducted to characterise NERs due to residues exceeding 5% AR. Samples of the photolysis study from 7 DAT onwards and dark control samples from 5 DAT onwards (phenyl/benzyl-labelled) were selected. In the cyclohexane-labelled treatment, photolysis samples from 12 and 15 DAT and dark control samples from 5 DAT onwards were selected. Only the second replicate from each time point was extracted.

Samples were extracted three times with 50 mL 0.5 M NaOH on a rotary shaker (200 rpm for a minimum of 6 hours) and then centrifuged for 10 minutes at 13000 rpm. The headspace of each vessel was purged with nitrogen before shaking. The supernatant was decanted, filtered, and made up to 50 mL with water. Soil residues were washed twice with 25 mL water, centrifuged and then the water was decanted and filtered into volumetric flasks. Extracts were

analysed by LSC and then pooled. Further analysis was performed on phenyl/benzyl-labelled samples as the combined extracts showed > 5% AR. Combined extracts were acidified to pH 1.5 and stored for three days in a refrigerator. To separate fulvic and humic acids, the samples were then centrifuged for 10 minutes at 13000 rpm and the supernatant fulvic acids were analysed by LSC. Precipitates were redissolved with 10 mL 0.5 M NaOH, stored overnight, and measured by LSC the next day. Finally, the insoluble soil residue from the NaOH extraction was air-dried, homogenised and weighed, then three aliquots were combusted and analysed by LSC to determine radioactivity in the humin fraction.

5. Analytical methods

All samples were measured for radioactivity by LSC. The combined acetonitrile extracts of each sample and the condensed water of each sampling day were analysed by HPLC to determine the metabolite pattern. Aliquots of all combined acetonitrile extracts were diluted with water (1/1, v/v) and characterised by chiral HPLC analysis to determine the enantiomeric composition.

For the phenyl/benzyl-labelled samples, the LSC LOD was 0.012% AR, and the LOQ was 0.018% AR. For HPLC analysis, the LOD was 0.207%, and the LOQ was 0.277%. For the cyclohexane-labelled samples, the LSC LOD was 0.013% AR and the LOQ was 0.019%. For HPLC analysis, the LOD was 0.166% and the LOQ was 0.225%.

RESULTS AND DISCUSSION

1. Mass balance and metabolites

Tables 8.1.1.3/01-02 – 05 summarise the mass balance for photolysis tests and dark controls for both radiolabelled compounds applied to Lufa 5M soils. By 15 DAT, total extractables had dropped from 99.7% to 63.5% in photolysis, and to 67.1% in dark control samples in the phenyl/benzyl-labelled samples. In cyclohexane-labelled samples, extractables dropped from 99.9% to 69.2% and 77.8% in photolysis and dark control samples respectively. By 15 DAT, 4% fewer extractables were recovered from phenyl/benzyl photolysis samples than dark controls; in cyclohexane-labelled samples, 7.9% fewer extractables were recovered from photolysis samples than in dark control. As previously mentioned, an additional sink for radioactivity was included by the Applicant in condensed water. The HSE evaluator notes that, without the inclusion of this measure, mass balances would be unacceptably low in the photolysis samples for both labels. Overall, the HSE evaluator notes that mass balances ranged 80.5 – 100.7% for phenyl/benzyl-labelled samples, and 87.0 – 100.2% for cyclohexane-labelled samples. In phenyl/benzyl-labelled samples, 3/22 replicates fell below 85%, though no cyclohexane-labelled samples fell below this threshold. A similar issue with low mass balances was observed in the aerobic soil study (KCA 7.1.2.1.1/01; Stewart, L. and Abernethy, A. (2016)), but not in the anaerobic soil study (KCA 7.1.2.1.3/01; Staudenmaier, H. and Pape, L. (2017)). Based on these observations, the HSE evaluator suggests CO₂ and/or volatiles may be being lost within the test system.

Table 8.1.1.3/01-02: Distribution of radioactive residues in Lufa 5M soil extracts following 15 days continuous UVA irradiation, expressed in % applied radioactivity (% AR), using the [phenyl-U-¹⁴C]/[benzyl-¹³C]-cinmethylin label. Cinmethylin and “sum others” values are derived from HPLC analysis; all other values are derived from LSC analysis.

DAT	Replicate	Cinmethylin	Sum others ^a	Total extractables ^b	NER	Volatiles ^c	Condensed water ^c	Mass balance
0	I	98.0	0.7	100.5	0.2	NA	NA	100.7
	II	97.3	ND	99.0	0.3			99.3
	Mean	97.6	0.4	99.7	0.3			100.0
2	I	75.5	2.1	79.5	1.9	0.3	1.1	82.8
	II	82.0	1.9	85.9	2.1			89.4
	Mean	78.8	2.0	82.7	2.0			86.1
5	I	79.1	4.2	85.3	4.5	1.2	2.7	93.7
	II	70.3	4.7	76.7	4.7			85.3
	Mean	74.7	4.4	81.0	4.6			89.5
7	I	70.7	4.4	77.1	6.7	1.9	3.8	89.5
	II	76.4	3.9	82.1	5.4			93.2
	Mean	73.6	4.1	79.6	6.1			91.3
12	I	70.9	5.5	78.4	7.4	3.5	6.2	95.5
	II	63.5	4.6	70.0	9.2			89.0
	Mean	67.2	5.1	74.2	8.3			92.2
15	I	50.6	5.6	58.0	9.4	4.5	8.6	80.5
	II	61.9	5.1	68.9	7.7			89.7
	Mean	56.3	5.4	63.5	8.6			85.1

NA = not analysed ND = none detected

^a Individual replicate peaks do not exceed 3.1% AR

^b Total extractables may not accurately reflect the sum of cinmethylin + sum others; this is due to total extractables being derived from LSC analysis while the individual values are derived from HPLC analysis.

^c Volatiles and condensed water measures are derived from a single measurement for both replicates because of the experimental design.

Table 8.1.1.3/01-03: Distribution of radioactive residues in Lufa 5M soil extracts from the dark control test, expressed in % applied radioactivity (% AR), using the [phenyl-U-¹⁴C]/[benzyl-¹³C]-cinmethylin label. Cinmethylin and “sum others” values are derived from HPLC analysis; all other values are derived from LSC analysis.

DAT	Replicate	Cinmethylin	Sum others ^a	Total extractables ^b	NER	Volatiles ^c	Condensed water ^c	Mass balance
2	I	81.3	0.9	84.3	3.3	0.9	0.01	88.5
	II	89.8	1.2	93.1	3.4			97.4
	Mean	85.5	1.1	88.7	3.4			93.6
5	I	76.0	1.1	79.2	8.2	1.5	0.05	89.0
	II	79.7	1.3	83.6	8.5			93.6
	Mean	77.9	1.2	81.4	8.4			91.3
7	I	73.6	1.9	77.2	9.4	3.1	0.09	89.8
	II	74.2	1.7	77.8	9.3			90.3
	Mean	73.9	1.8	77.5	9.4			90.1
12	I	65.4	2.8	71.0	10.6	6.5	0.41	88.5
	II	65.0	4.7	72.6	10.8			90.3
	Mean	65.2	3.8	71.8	10.7			90.1
15	I	64.1	3.1	69.7	10.9	7.2	0.70	88.5
	II	59.2	3.2	64.5	11.5			83.9
	Mean	61.7	3.2	67.1	11.1			86.2

NA = not analysed

^a Individual replicate peaks do not exceed 2.6% AR

^b Total extractables may not accurately reflect the sum of cinmethylin + sum others; this is due to total extractables being derived from LSC analysis while the individual values are derived from HPLC analysis.

^c Volatiles and condensed water measures are derived from a single measurement for both replicates because of the experimental design.

Table 8.1.1.3/01-04: Distribution of radioactive residues in Lufa 5M soil extracts following 15 days continuous UVA irradiation, expressed in % applied radioactivity (% AR), using the [cyclohexane-4-¹³C]-cinmethylin label. Cinmethylin and “sum others” values are derived from HPLC analysis; all other values are derived from LSC analysis.

DAT	Replicate	Cinmethylin	Sum others ^a	Total extractables ^b	NER	Volatiles ^c	Condensed water ^c	Mass balance
0	I	98.8	0.4	100.1	0.1	NA	NA	100.2
	II	97.5	1.1	99.7	0.1			99.8
	Mean	98.1	0.7	99.9	0.1			100.0
2	I	91.3	0.5	93.8	1.4	0.0	1.8	97.1
	II	87.9	ND	90.2	1.5			93.5
	Mean	89.6	0.3	92.0	1.4			95.3
5	I	80.5	1.3	84.0	2.9	0.8	4.6	92.3
	II	79.0	1.2	82.1	3.2			90.7
	Mean	79.7	1.2	83.1	3.0			91.5
7	I	76.1	1.7	80.1	4.0	1.2	6.3	91.6
	II	79.0	2.0	83.1	4.2			94.8
	Mean	77.5	1.8	81.6	4.1			93.2
12	I	73.1	1.7	77.5	4.9	2.1	10.7	95.2
	II	69.7	2.6	75.6	6.0			94.4
	Mean	71.4	2.1	76.6	5.5			94.8
15	I	60.5	3.6	66.5	5.0	2.6	13.0	87.0
	II	65.6	3.6	72.0	5.2			92.7
	Mean	63.1	3.6	69.2	5.1			89.9

NA = not analysed

^a Individual peaks do not exceed 2.6% AR

^b Total extractables may not accurately reflect the sum of cinmethylin + sum others; this is due to total extractables being derived from LSC analysis while the individual values are derived from HPLC analysis.

^c Volatiles and condensed water measures are derived from a single measurement for both replicates because of the experimental design.

Table 8.1.1.3/01-05: Distribution of radioactive residues in Lufa 5M soil extracts from the dark control test, expressed in % applied radioactivity (% AR), using the [cyclohexane-4-¹⁴C]-cinmethylin label. Cinmethylin and “sum others” values are derived from HPLC analysis; all other values are derived from LSC analysis.

DAT	Replicate	Cinmethylin	Sum others ^a	Total extractables ^b	NER	Volatiles ^c	Condensed water ^c	Mass balance
2	I	92.0	ND	94.3	2.4	1.0	0.07	97.8
	II	92.4	0.3	95.0	2.3			98.5
	Mean	92.2	0.2	94.7	2.4			98.1
5	I	82.1	0.7	85.2	4.4	2.7	0.17	92.5
	II	84.3	1.6	88.2	4.7			95.8
	Mean	83.2	1.2	86.7	4.6			94.2
7	I	75.1	1.6	79.7	5.7	3.8	0.24	89.4
	II	82.3	1.4	86.4	6.0			96.4
	Mean	78.7	1.5	83.1	5.8			92.9
12	I	74.2	2.7	80.1	7.5	6.1	0.66	94.3
	II	75.4	2.5	81.0	8.3			96.1
	Mean	74.8	2.6	80.6	7.9			95.2
15	I	72.4	2.5	78.2	7.0	6.9	1.01	93.1
	II	71.2	3.2	77.5	7.7			93.1
	Mean	71.8	2.9	77.8	7.3			93.1

NA = not analysed ND = none detected

^a Individual peaks < 5% AR

^b Total extractables may not accurately reflect the sum of cinmethylin + sum others; this is due to total extractables being derived from LSC analysis while the individual values are derived from HPLC analysis.

^c Volatiles and condensed water measures are derived from a single measurement for both replicates because of the experimental design.

The Applicant identified a number of minor metabolites in both light and dark samples, though none of these were classified as major metabolites as % AR did not exceed 5% at any point. For the [phenyl-U-¹⁴C]/[benzyl-¹³C]-cinmethylin label, peak metabolite formation was 3.13% at 5 DAT in light samples, and 2.59% at 15 DAT in dark samples. For the [cyclohexane-4-¹⁴C]-cinmethylin label, peak metabolite formation was 1.41% at 15 DAT in light and 1.92% at 12 DAT in dark samples. As previously noted, low mass balances were observed. To investigate whether any of these metabolite levels could be of concern assuming a 100% mass balance, the HSE evaluator upscaled these metabolite levels and found that metabolite levels were no higher than 3.67% AR. Therefore, the HSE evaluator agrees that none of the metabolites trigger classification as major metabolites.

2. Enantiomer ratio

As cinmethylin consists two enantiomers (mixture ratio 50:50), the Applicants studied the ratio over time via chiral HPLC analysis. These data are reported in Tables 8.1.1.3/01-06 – 07. There was only a slight shift in enantiomeric ratio in the phenyl/benzyl-labelled compound, with the ratio becoming 46:54 by 15 DAT in photolysis samples. Dark control

sample ratios were 49:51 at 15 DAT. There was little change in ratio in cyclohexane-labelled samples, with the ratio at 49:51 at 15 DAT in photolysis samples and also dark controls.

Table 8.1.1.3/01-06: Determination of enantiomeric ratios in photolysis and dark control samples treated with the [phenyl-U-¹⁴C]/[benzyl-¹³C]-cinmethylin label.

DAT	Replicate	Cinmethylin (% AR) ^a	(-)-enantiomer (% cinmethylin)	(+)-enantiomer (% cinmethylin)
0	I	98.0	50.5	49.5
	II	97.3	51.5	48.5
	Mean	97.6	51.0	49.0
2	I	75.5	51.0	49.0
	II	82.0	50.5	49.5
	Mean	78.8	50.7	49.3
5	I	79.1	49.8	50.2
	II	70.3	50.5	49.5
	Mean	74.7	50.2	49.8
7	I	70.7	50.3	49.7
	II	76.4	49.1	50.9
	Mean	73.6	49.7	50.3
12	I	70.9	47.4	52.6
	II	63.5	47.3	52.7
	Mean	67.2	47.3	52.7
15	I	50.6	46.0	54.0
	II	61.9	46.6	53.4
	Mean	56.3	46.3	53.7
Dark 15	I	64.1	48.3	51.7
	II	59.2	50.0	50.0
	Mean	61.7	49.1	50.9

^a Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

Table 8.1.1.3/01-07: Determination of enantiomeric ratios in photolysis and dark control samples treated with the [cyclohexane-4-¹⁴C]-cinmethylin label.

DAT	Replicate	Cinmethylin (% AR) ^a	(-)-enantiomer (% cinmethylin)	(+)-enantiomer (% cinmethylin)
0	I	98.8	49.4	50.6
	II	97.5	49.4	50.6
	Mean	98.1	49.4	50.6
15	I	60.5	48.1	51.9
	II	65.6	49.0	51.0
	Mean	63.1	48.5	51.5
Dark 15	I	72.4	48.6	51.4
	II	71.2	48.6	51.4
	Mean	71.8	48.6	51.4

^a Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

3. Non-extractable residues (NERs)

The Applicant characterised the NERs for the sampling dates displaying NERs of > 5% AR by sampling the second replicate for each date of interest. NERs were apportioned, where possible, to fulvic acids, humic acids, and humin. These results are summarised in Tables 8.1.1.3/01-08 – 09. In phenyl/benzyl-labelled samples, most NERs were found in the fulvic acids (37% of initial NER), with 14% found in humic acids and 24% in the humin fraction. The HSE evaluator notes that, with the majority of NERs being associated with the fulvic acids, there is a greater possibility of the NERs being re-released with weathering and turnover of soil. In cyclohexane-labelled samples, the Applicant could only identify the humin fraction (mean 26% of initial NER).

Table 8.1.1.3/01-08: Characterisation of NERs in photolysis and dark control samples treated with the [phenyl-U-¹⁴C]/[benzyl-¹³C]-cinmethylin label.

Sample type	DAT	Initial NER (% AR)	NER in fraction (% Initial NER)		
			Fulvic acid	Humic acid	Humin
Photolysis	7	5.4	38.9	13.0	24.1
	12	9.2	35.9	13.0	21.7
	15	7.7	40.3	15.6	26.0
Dark	5	8.5	35.3	14.1	24.7
	7	9.3	37.6	16.1	24.7
	12	10.8	36.1	14.8	23.1
	15	11.5	32.2	13.0	20.9

Table 7.1.1.3/01-09: Characterisation of NERs in photolysis and dark control samples treated with the [cyclohexane-4-¹⁴C]-cinmethylin label.

Sample type	DAT	Initial NER (% AR)	NER in humin fraction (% Initial NER)
Photolysis	12	6.0	28.3
	15	5.2	28.8
Dark	5	4.7	23.4
	7	6.0	26.7
	12	8.3	22.9
	15	7.7	27.3

KINETIC EVALUATION

The Applicant provided a kinetic evaluation of the photolytic degradation of Cinmethylin in soil using KinGUI version 2 to derive DegT₅₀ and DegT₉₀ values for photolytic and dark control samples. The Applicant conducted the evaluation to FOCUS kinetic guidance (2006; 2014). The HSE evaluator notes that the Applicant did not supply kinetic evaluation for the degradation of the two enantiomers (Reg. Nos. 5925581 and 5925632); however, these were deemed to not be necessary as photolysis is not a significant route of degradation. As two labels were applied to the same soil, the replicates were all considered together, giving four replicates per sampling point. Individual replicates were considered with no averaging. Data were derived from the HPLC analysis of extractables, and only considered the parent compound, except for 0 DAT where the full material balance derived by LSC was given as the initial concentration.

The HSE evaluator assessed the supplied kinetic evaluation in CAKE version 3.2. The degradation data reported here were used to derive endpoints for both photolysis and dark control samples.

The kinetic evaluation was conducted to determine degradation parameters according to the FOCUS degradation kinetics guidance (2006; 2014). Figures 7.1.1.3/01-02 - 7.1.1.3/01-03 display the model fit and residuals for the parent compound in the photolysis and dark samples. Table 8.1.1.3/01-10 summarises the kinetic models and derived endpoints for each sample as supplied by the Applicant. For the photolysis samples, the SFO fit was acceptable with large residuals (Figure 8.1.1.3/01-02). The FOMC model offered a comparatively better fit which led to the exploration of DFOP. The Applicant concluded the DFOP fit best described the data with the lowest χ^2 error, a good visual fit and estimated parameters are significantly above zero.

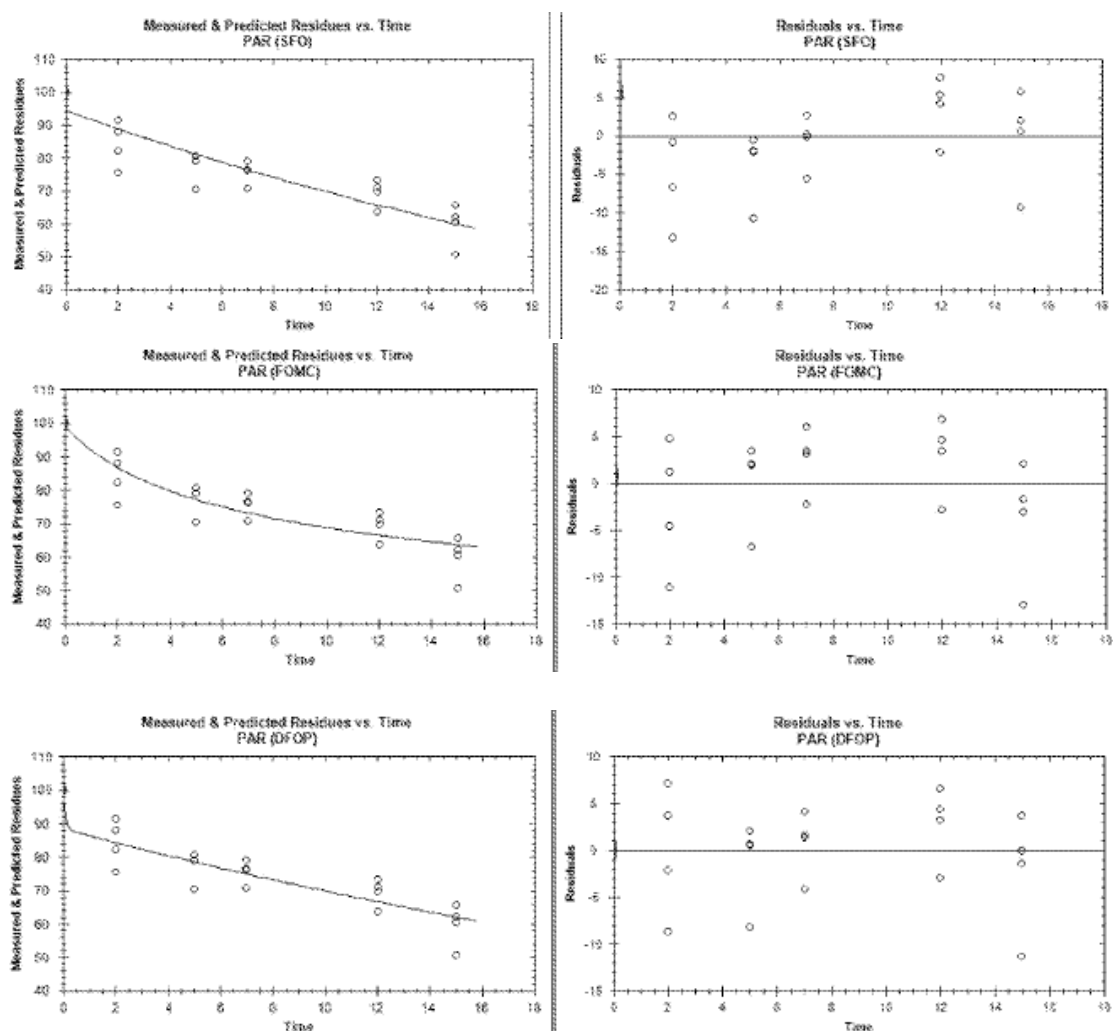


Figure 8.1.1.3/01-02: Model fits and residuals for the photolysis experiment. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final model: DFOP.

For the dark control samples, the SFO fit was deemed acceptable by the Applicant (Figure 8.1.1.3/01-03), though χ^2 error was lower in the FOMC model. The DFOP model offered lower χ^2 error, but the model parameters were not significantly different to zero. Therefore, the Applicant concluded the SFO model was most suitable for deriving degradation rates.

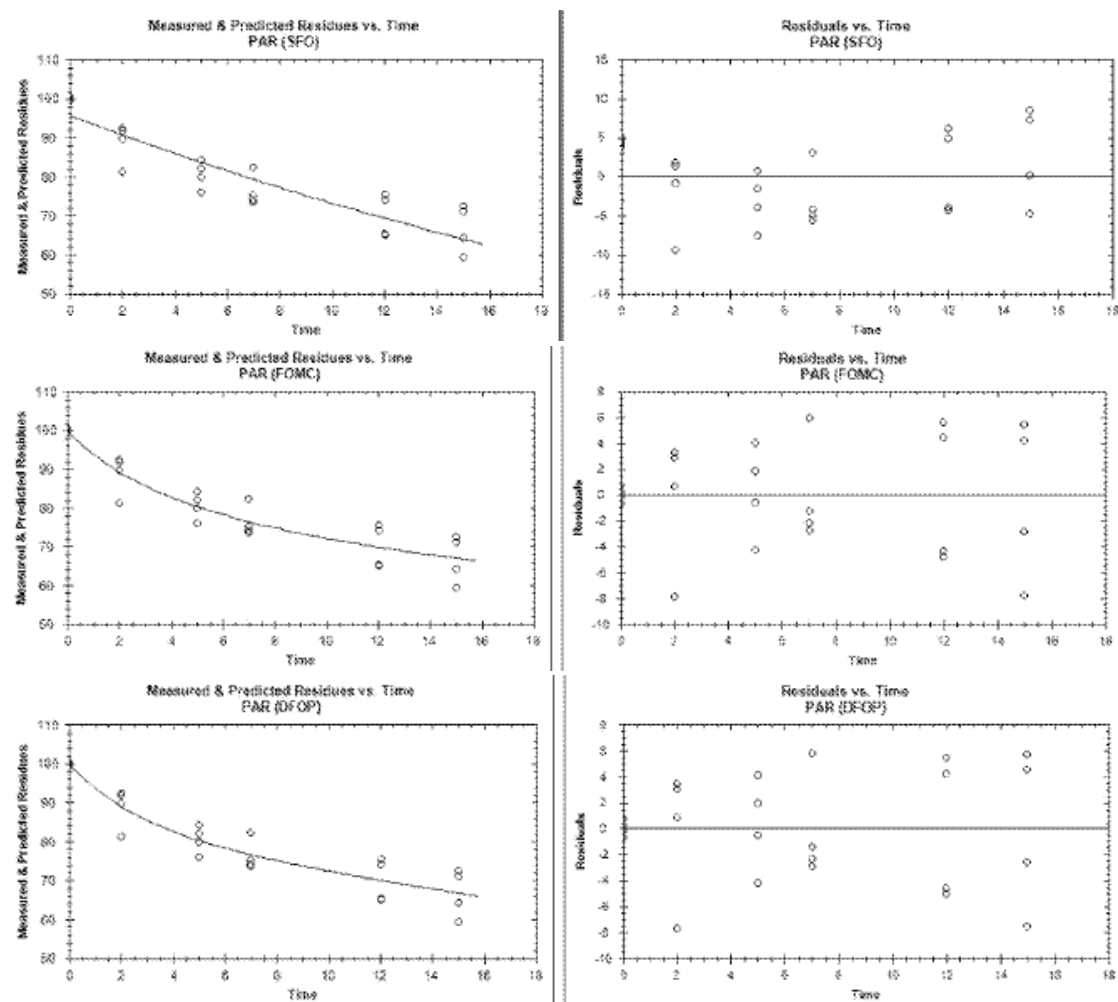


Figure 8.1.1.3/01-03: Model fits and residuals for the dark control samples. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final model: SFO.

Table 8.1.1.3/01-10: Summary of degradation rates, the kinetic models used, estimated parameters and associated χ^2 test error rate for photolysis and dark control samples. Final kinetic model choices are highlighted in bold.

Experiment	Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Photolysis	SFO	Acceptable	100.0	M_0 : 94.2890 k (d): 0.0303	90.165 – 98.413	< 0.0001	3.8	22.9	76.0
	FOMC	Acceptable	100.0	M_0 : 99.3297 α : 0.2254 β : 2.4001	94.291 – 104.368 0.0778 – 0.373 -0.959 – 5.759		2.8	49.5	> 1000
	DFOP	Good	100.0	M_0: 100.0 k1 (d): 1.138 k2 (d): 0.0236 g: 0.1172	95.190 – 104.811 1.138 – 11.377 0.0172 – 0.030 0.0529 – 0.182	< 0.0001 < 0.0001	2.05	24.1	92.2
Dark Control	SFO	Acceptable	100.0	M_0: 95.587 k (d): 0.0268	92.018 – 99.159	0.0026	2.82	25.9	86.0
	FOMC	Good	100.0	M_0 : 99.9303 α : 0.2271 β : 2.9831	95.847 – 104.013 0.0844 – 0.361 -0.7822 – 6.748		0.23	64.1	> 1000
	DFOP	Good	100.0	M_0 : 99.9726 k1 (d): 0.3740 k2 (d): 0.0154 g: 0.1601	95.730 – 104.215 -0.351 – 1.099 -0.003 – 0.034 -0.052 – 0.373	0.1619 0.0617	0.21	33.7	138.2

The HSE evaluator has evaluated and accepted the decisions made by the Applicant and the resulting modelling endpoints.

GUIDELINE DEVIATIONS

The Applicant highlighted one deviation from the standard guidelines: to improve mass balance, they collected the condensed water from within the test set up at each time point and quantified the radioactivity. The HSE evaluator requested further information relating to cinmethylin and its potential metabolites within the condensed water. In response, the Applicant supplied additional chromatograms to demonstrate that HPLC peak patterns were consistent for condensed water samples covering the time periods of 7 – 12 DAT and 12 – 15 DAT. The HSE evaluator assessed the supplied chromatograms, comparing the peak patterns for 7 – 12 DAT and 12 – 15 DAT samples for both radiolabels and agreed with the Applicant's assertions that the only major peak was cinmethylin and that the peak pattern remained consistent over time. Therefore, the HSE evaluator concluded that this was an acceptable deviation as the additional work helped to improve mass balances.

In addition, the HSE evaluator identified the following deviations from the standard guidelines:

- Air temperature throughout the study was held at $22 \pm 1^\circ\text{C}$;
- Low mass balances were identified in some of the samples.

The HSE evaluator does not feel that either of these deviations impacted upon the study or on the data quality.

CONCLUSIONS

The Applicant concluded there was no significant influence of light on the degradation behaviour, or metabolite formation in soil in this experiment, though the HSE evaluator notes that there were differences of up to 11% in extractable residues between photolysis and dark samples after 15 days. The HSE evaluator has not explored this further by calculating a photolysis only DT_{50} as the application of biphasic kinetics makes this a complex step; however, the HSE evaluator notes that the difference between photolysis and dark samples was very small. Chiral analysis showed that there was no influence of light on the enantiomeric ratio, with the ratio remaining relatively stable throughout. Cinmethylin DT_{50} s were calculated to be 24.1 days (photolysis) and 25.9 days (dark control) in the artificial light test system.

B.8.1.1.2. Rate of degradation in soil**B.8.1.1.2.1. Aerobic degradation (Data Requirement 7.1.2.1.1 and 7.1.2.1.2)**

Report:	KCA 7.1.2.1.1/1; Stewart, L. and Abernethy, A. (2016)
Title	Cinmethylin - Aerobic degradation of [¹⁴ C]-Cinmethylin (Reg.No. 900202) in soil
Document No.:	2015/1186904
Guidelines:	<ul style="list-style-type: none"> • OECD Guidelines for the testing of chemicals 307: Aerobic Degradation in Soil (Apr 2002) • US EPA OPPTS Guidelines 835.4100: Anaerobic Soil Metabolism (Oct 2008) • GLP of Japanese Ministry of Agriculture, Forestry and Fisheries: No. 12-Nousan-8147, Agriculture Production Bureau (Nov 2000) • FOCUS Kinetics guidance (2006; 2014).
GLP:	Yes
Deviations	None for modelling
Previous evaluations:	None – report submitted as part of a new active substance registration.

Evaluator note: The study evaluation is presented in section 'Aerobic degradation (Data Requirement 7.1.1.1)' under KCA 8.1.1.1/1; Stewart, L. and Abernethy, A. (2016). Only the kinetic evaluation for trigger endpoints is provided here.

KINETIC EVALUATION (TRIGGER ENDPOINTS)**1. Introduction**

A kinetic evaluation was undertaken by the Applicant to investigate the degradation behaviour of cinmethylin and its two enantiomers in four fresh soils under aerobic conditions. The kinetic evaluation was conducted to derive degradation parameters for trigger endpoints according to the FOCUS degradation kinetics guidance (2006; 2014). A separate study (KCA 7.1.2.1/1; He, W. 2018a) was submitted to derive modelling endpoints. The Applicant derived trigger endpoints for cinmethylin using KinGUI version 2 using IRLS optimisation. Model fits were initially derived from the single first order (SFO) and first order multi-compartment (FOMC) models, as per FOCUS guidance. Through detailed statistical analysis including visual assessment of the goodness of fit, Chi² scaled-error criterion and t-test significance, the Applicant compared the two model fits; if SFO was preferable, no further analysis was required; if not, other biphasic models were explored. The Applicant then chose the best-fit model. Due to the parent not dropping below 10% AR by the study end, the Applicant determined double first order in parallel (DFOP) to be the most appropriate biphasic model to test and did not test the hockey stick (HS) model.

The Applicant assessed data derived from the radio-HPLC analysis of extractables, and considered the parent compound, except for 0 DAT where total extractable residues (TER) derived by LSC were given as the initial concentration. The two enantiomers were also assessed using chiral HPLC analysis data. The HSE evaluator notes that the Applicant used

TER data at 0 DAT when full material balance is recommended in FOCUS guidance; however, the HSE evaluator concludes that this minor deviation did not affect endpoints due to the small differences in TER and mass balance values at 0 DAT. As the experiments were conducted at reference conditions (soil moisture of pF 2 and at 20°C), no normalisation procedure was applied by the Applicant. The Applicant did not identify or exclude any outliers or apply any other data processing methods. The HSE evaluator agrees with these decisions.

Degradation endpoints were derived for each soil as triggers for additional work. Where two radiolabels were studied (Lufa 2.2 and MSL-PF soils), all samples were treated as individual replicates. Therefore, these soils had four replicates for each sampling time point instead of the usual two. The HSE evaluator accepts this decision. Tables 8.1.2.1.1/1-01 – 04 display the data used for kinetic evaluation.

Table 8.1.2.1.1/1-01: Data values used to quantify the aerobic degradation of cinmethylin and its two enantiomers in the Lufa 2.2 soil.

Parent		Enantiomers		
Time (Days)	Cinmethylin (% AR)	Time (Days)	(-)-cinmethylin (% AR)	(+)-cinmethylin (% AR)
0	100.2	0	51	48.5
0	99.7	0	50.8	47.2
0	101.8	24	29.5	33.9
0	98.2	24	32	38.7
3	95.9	24	28.8	38.1
3	89.9	24	30.9	34.3
3	89.8	59	26.4	33
3	92.1	59	29.5	32.8
7	82.4	59	27.1	31.4
7	83	59	23.8	29.8
7	82.2	90	22	28.1
7	86.5	90	22.3	27
14	71.9	90	24.5	27.1
14	72.1	90	24.5	26
14	74.2	120	21.2	22.5
14	76.7	120	18.4	21.6
24	63.4			
24	70.7			
24	66.9			
24	65.2			
41	63.3			
41	56.5			
41	60.9			
41	58.5			
59	59.4			
59	62.3			
59	58.5			
59	53.6			
90	50			
90	49.3			
90	51.6			
90	50.5			
120	43.7			
120	50.9			
120	40			
120	45.3			

Table 8.1.2.1.1/1-02: Data values used to quantify the aerobic degradation of cinmethylin and its two enantiomers in the Lufa 5M soil.

Parent		Enantiomers		
Time (Days)	Cinmethylin (% AR)	Time (Days)	(-)-cinmethylin (% AR)	(+)-cinmethylin (% AR)
0	99.9	0	51.6	47.2
0	100	14	27.9	32.9
3	84	14	30.8	32.8
3	80.9	40	6.8	11.7
7	73.7	40	8.3	14.6
7	73.5	60	2.1	4.3
14	60.8			
14	63.6			
25	38.4			
25	50			
40	18.5			
40	22.9			
60	6.4			
60	6.7			
90	0.5			
90	1.2			
122	0.5			
122	0.7			

Table 8.1.2.1.1/1-03: Data values used to quantify the aerobic degradation of cinmethylin and its two enantiomers in the LAD-SCL-PF soil.

Parent		Enantiomers		
Time (Days)	Cinmethylin (% AR)	Time (Days)	(-)-cinmethylin (% AR)	(+)-cinmethylin (% AR)
0	99.4	0	51.6	47.2
0	100.7	14	27.9	32.9
3	92.6	14	30.8	32.8
3	91.3	40	6.8	11.7
7	89.4	40	8.3	14.6
7	84.4	60	2.1	4.3
14	79.7			
14	73.6			
25	68.8			
25	67.2			
40	51.1			
40	55.5			
60	45.3			
60	36.8			
90	22.6			
90	20.9			
120	9.4			
120	10.2			

Table 8.1.2.1.1/1-04: Data values used to quantify the aerobic degradation of cinmethylin and its two enantiomers in the MSL-PF soil.

Parent		Enantiomers		
Time (Days)	Cinmethylin (% AR)	Time (Days)	(-)-cinmethylin (% AR)	(+)-cinmethylin (% AR)
0	99.3	0	51.7	47.5
0	100.5	0	48.3	52.4
0	100.8	14	23.3	34.4
0	99.3	14	23.1	33.4
3	80	14	21.4	31.9
3	76.6	14	21.7	32.5
3	83.6	59	10	18.2
3	78.4	59	12	18.4
7	73.6	59	10.1	22.6
7	70.2	59	12.1	21
7	72.3	90	9.2	15.2
7	70.9	90	6.8	13.8
14	57.7	90	7.3	13.5
14	56.5	90	7.6	18.1
14	53.3	120	4.6	10.5
14	54.2	120	5	11.7
24	47.6			
24	40.7			
24	43.1			
24	44.2			
41	33.8			
41	30.5			
41	35.2			
41	36.8			
59	28.2			
59	30.4			
59	32.7			
59	33.1			
90	24.4			
90	20.6			
90	20.8			
90	25.7			
120	15.1			
120	17.3			
120	16.7			
120	15.7			

The HSE evaluator assessed the supplied kinetic evaluation by deriving trigger endpoints for the parent and two enantiomers in CAKE version 3.2, with this evaluation also following FOCUS guidance on deriving trigger endpoints. The HSE evaluator agreed with the procedures used by the Applicant to conduct the kinetic evaluation.

2. Kinetic fits

The HSE evaluator has evaluated and accepted the decisions made by the Applicant and the resulting trigger endpoints. Therefore, the results presented are derived from the Applicant's assessment. Kinetic evaluations for the parent and two enantiomers are presented below for the four soils. Visual assessment of goodness of fit, estimated parameters and degradation endpoints are each discussed in turn.

Lufa 2.2

Figure 8.1.2.1.1/01-01 displays the model fit and residuals for cinmethylin in Lufa 2.2. For the parent, the SFO visual fit was poor, with residuals showing tendencies to both underestimate and overestimate residues; however, FOMC offered a better fit. DFOP offered a good model fit and the residuals were smaller and randomly scattered. Figures 8.1.2.1.1/01-02 – 03 display the model fit and residuals for the two enantiomers in Lufa 2.2. Consistent with the parent compound, SFO was a poor fit to both enantiomers, with FOMC offering a better fit. As with the parent, DFOP was the most appropriate fit for both enantiomers.

The kinetic models and derived endpoints for each soil, as supplied by the Applicant, are summarised in Tables 8.1.2.1.1/01-05 – 07. The HSE evaluator has evaluated and accepted the process followed and the decisions made by the Applicant, and the resulting endpoints.

Table 8.1.2.1.1/01-05: Summary of kinetic model evaluation of aerobic degradation of cinmethylin in the Lufa 2.2 soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	M ₀ : 88.91 k: 0.006997	85.29 – 92.52	<0.0001	7.3	99.1	329.1
FOMC	Good	M ₀ : 100.1406 α : 0.26118 β : 6.81393	97.513 – 102.769 0.220 – 0.303 3.858 – 9.770		1.6	90.0	>1000
DFOP	Good	M ₀ : 99.78 k1 (d): 0.0979 k2 (d): 0.0036 g: 0.3000	0.0696 – 0.126 0.0027 – 0.004 0.2522 – 0.348	<0.0001 <0.0001	0.9	93.6	541.4

Table 8.1.2.1.1/01-06: Summary of kinetic model evaluation of aerobic degradation of (-)-cinmethylin (Reg No. 5925581) in the Lufa 2.2 soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	M ₀ : 43.3089 k: 0.007731	38.401 – 48.220	<0.0001	11.9	89.7	297.8
FOMC	Good	M ₀ : 50.8708 α : 0.2341 β : 3.2160	48.236 – 53.506 0.150 – 0.318 -0.434 – 6.866		3.1	58.9	>1000
DFOP	Good	M ₀ : 50.90 k1 (d): 1.092 k2 (d): 0.0042 g: 0.3366	48.58 – 53.222 1.092 – 1.092 0.003 – 0.005 0.282 – 0.392	<0.0001 <0.0001	1.3	67.4	450.8

Table 8.1.2.1.1/01-07: Summary of kinetic model evaluation of aerobic degradation of (+)-cinmethylin (Reg No. 5925632) in the Lufa 2.2 soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor ^a	M ₀ : 44.709 k: 0.0059	42.319 – 47.098	<0.0001	4.5	117.2	389.3
FOMC	Good	M ₀ : 47.385 α : 0.4545 β : 35.1105	44.622 – 50.147 0.1559 – 0.753 -6.0747 – 76.296		3.5	126.3	>1000
DFOP	Good	M ₀ : 47.85 k ₁ (d): 1.466 k ₂ (d): 0.0048 g: 0.1399	45.5 – 50.201 1.466 – 1.466 0.0039 – 0.006 0.0738 – 0.206	<0.0001 <0.0001	2.2	113.5	450.2

^a The Applicant described the visual fit as poor; however, the HSE evaluator deemed the visual fit to be acceptable. This difference in opinion did not alter the decision made on the best model fit.

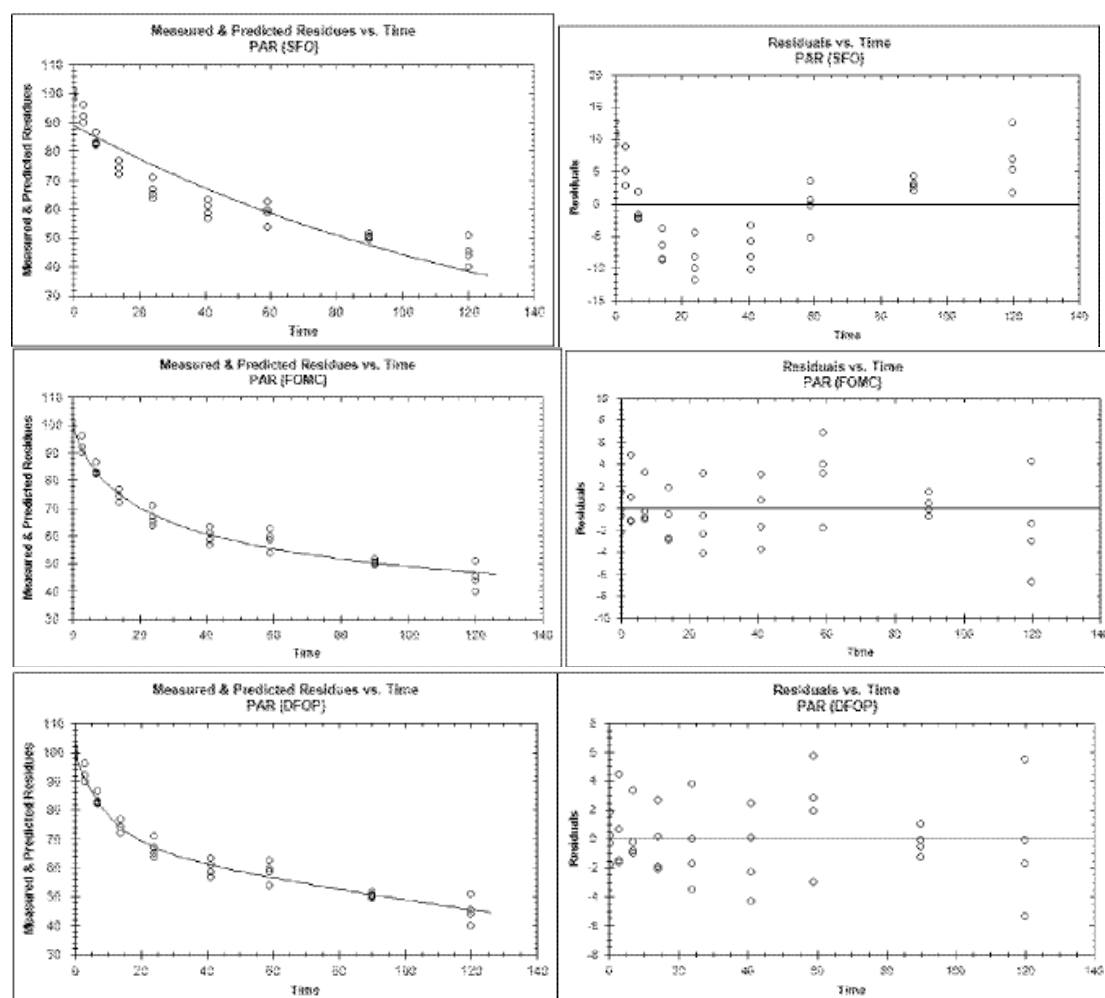


Figure 8.1.2.1.1/01-01: Model fits and residuals for cinmethylin in Lufa 2.2 soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final model fit: DFOP.

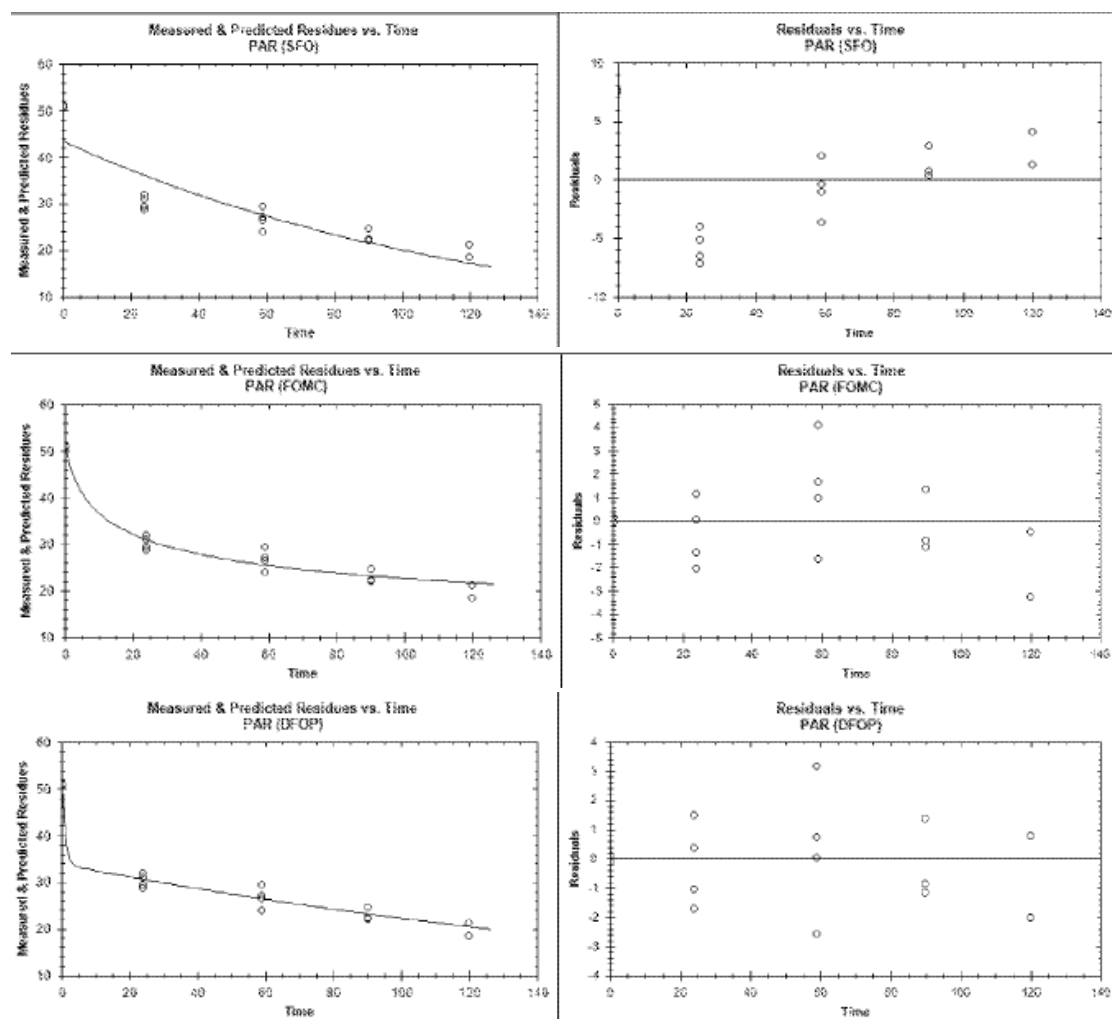


Figure 8.1.2.1.1/01-02: Model fits and residuals for (-)-cinmethylin (Reg No. 5925581) in Lufa 2.2 soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final model fit: DFOP.

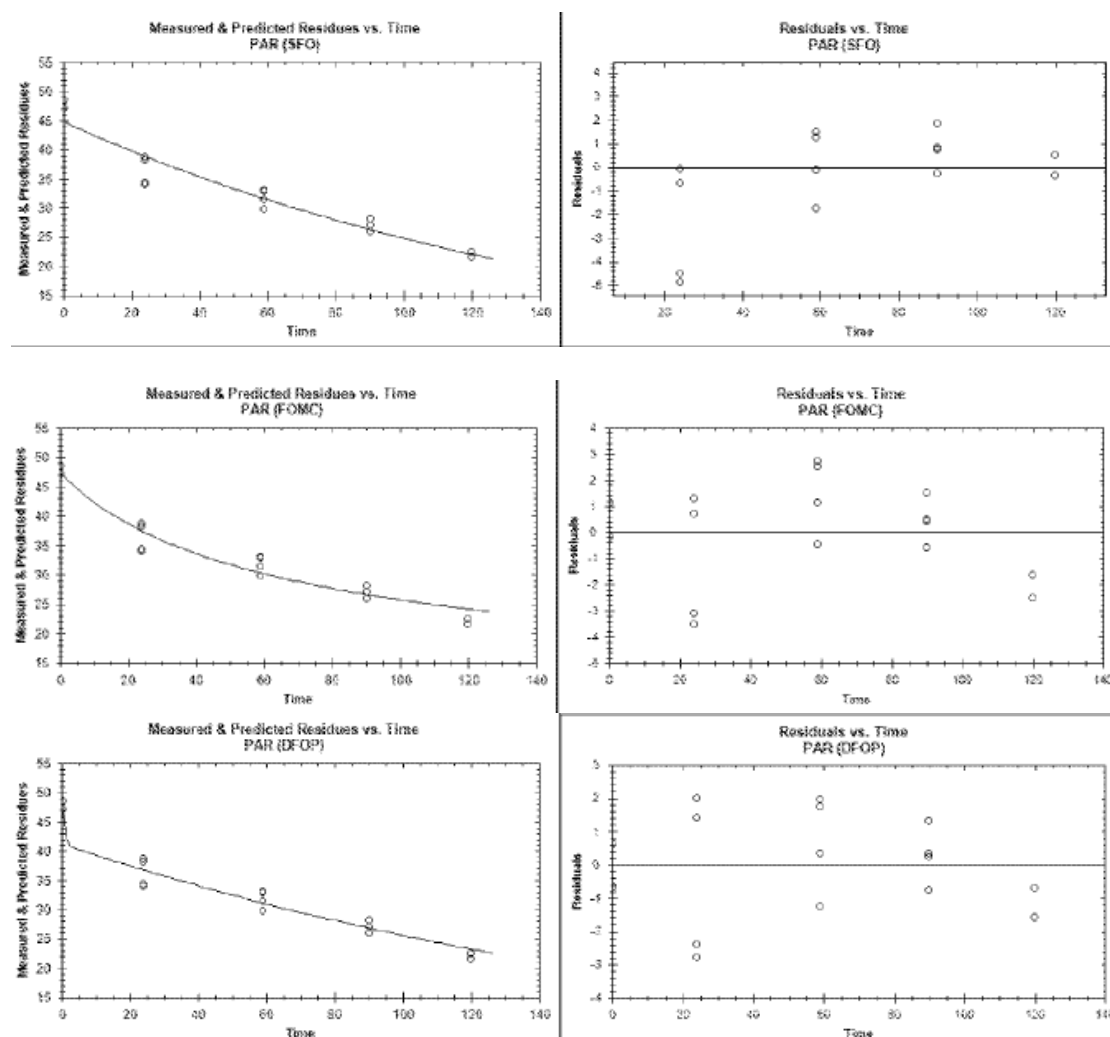


Figure 8.1.2.1.1/01-03: Model fits and residuals for (+)-cinmethylin (Reg No. 5925632) in Lufa 2.2 soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final model fit: DFOP.

Lufa 5M

For Lufa 5M, the SFO and FOMC model fits were very similar and displayed a good fit against the measured parent data (Figure 8.1.2.1.1/01-04). χ^2 error was lower for the SFO fit, therefore, this was the most appropriate model. SFO was also the most appropriate fit for both enantiomers (Figures 8.1.2.1.1/01-05 – 06).

The kinetic models and derived endpoints for each soil, as supplied by the Applicant, are summarised in Tables 8.1.2.1.1/01-08 – 10. The HSE evaluator has evaluated and accepted the processes followed and the decisions made by the Applicant, and the resulting endpoints.

Table 8.1.2.1.1/01-08: Summary of kinetic model evaluation of aerobic degradation of cinmethylin in the Lufa 5M soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	M ₀ : 97.042 k: 0.0362	92.884 – 101.20	<0.0001	6.2	19.1	63.5
FOMC	Good	M ₀ : 97.04 α : 18920.0 β : 521900	92.75 – 101.3 16810.0 – 21028.9 521800 – 521987		6.5	19.1	63.5

Table 8.1.2.1.1/01-09: Summary of kinetic model evaluation of aerobic degradation of (-)-cinmethylin (Reg No. 5925581) in the Lufa 5M soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	M ₀ : 52.595 k: 0.0451	49.063 – 56.126	<0.0001	4.5	15.4	51.1
FOMC	Good	M ₀ : 52.59 α : 21161.9 β : 469419.0	48.52 – 56.67 17996.7 – 24327.2 469276 – 469561		1.3	15.4	51.1

Table 8.1.2.1.1/01-10: Summary of kinetic model evaluation of aerobic degradation of (+)-cinmethylin (Reg No. 5925632) in the Lufa 5M soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	M ₀ : 48.840 k: 0.03221	44.845 – 52.835	0.00014	6.2	21.5	71.5
FOMC	Good	M ₀ : 48.84 α : 15120 β : 469400	44.23 – 53.45 12270 – 17974.8 469300 - 469474		7.7	21.5	71.5

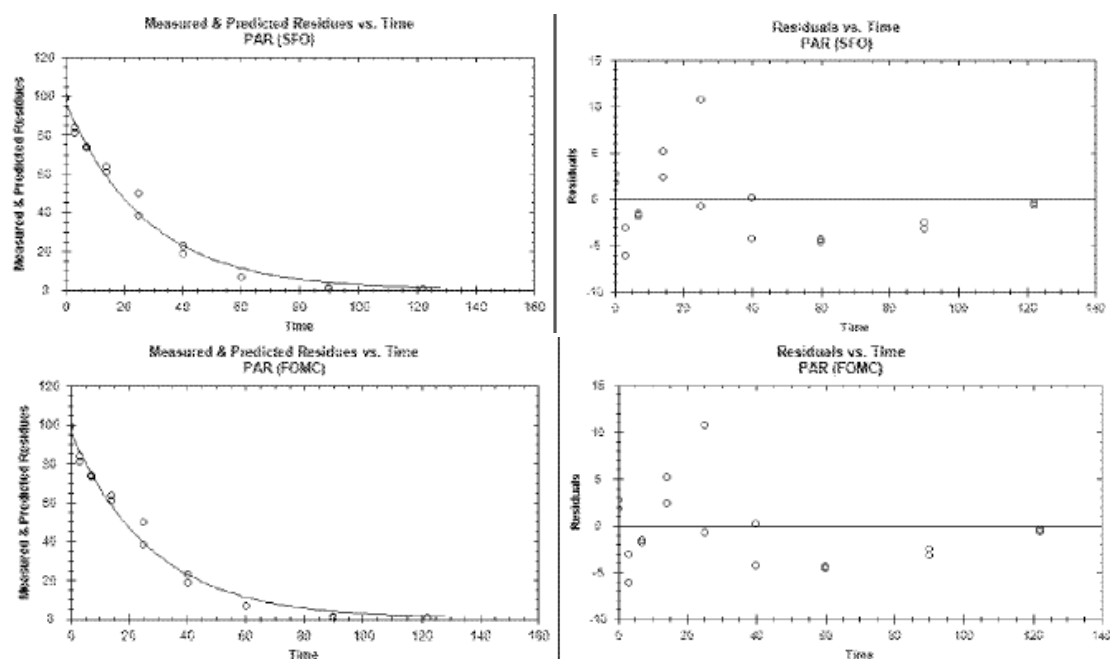


Figure 8.1.2.1.1/01-04: Model fits and residuals for cinmethylin in Lufa 5M soil. Top row: SFO. Bottom row: FOMC. Final model: SFO.

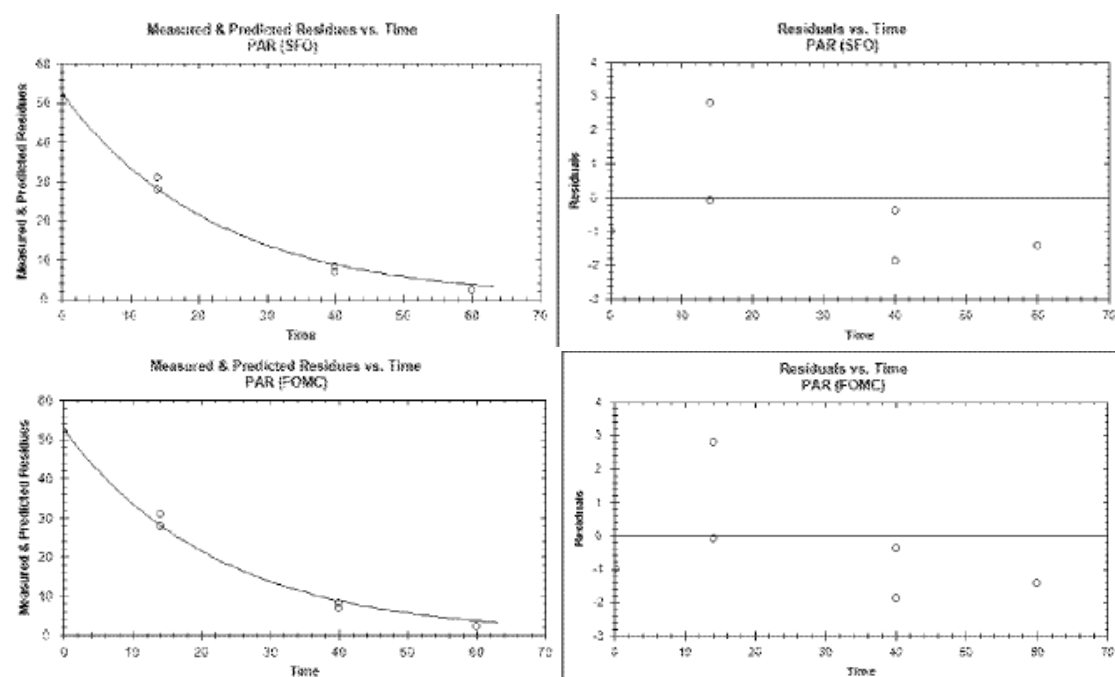


Figure 8.1.2.1.1/01-05: Model fits and residuals for (-)-cinmethylin (Reg No. 5925581) in Lufa 5M soil. Top row: SFO. Bottom row: FOMC. Final model: SFO.

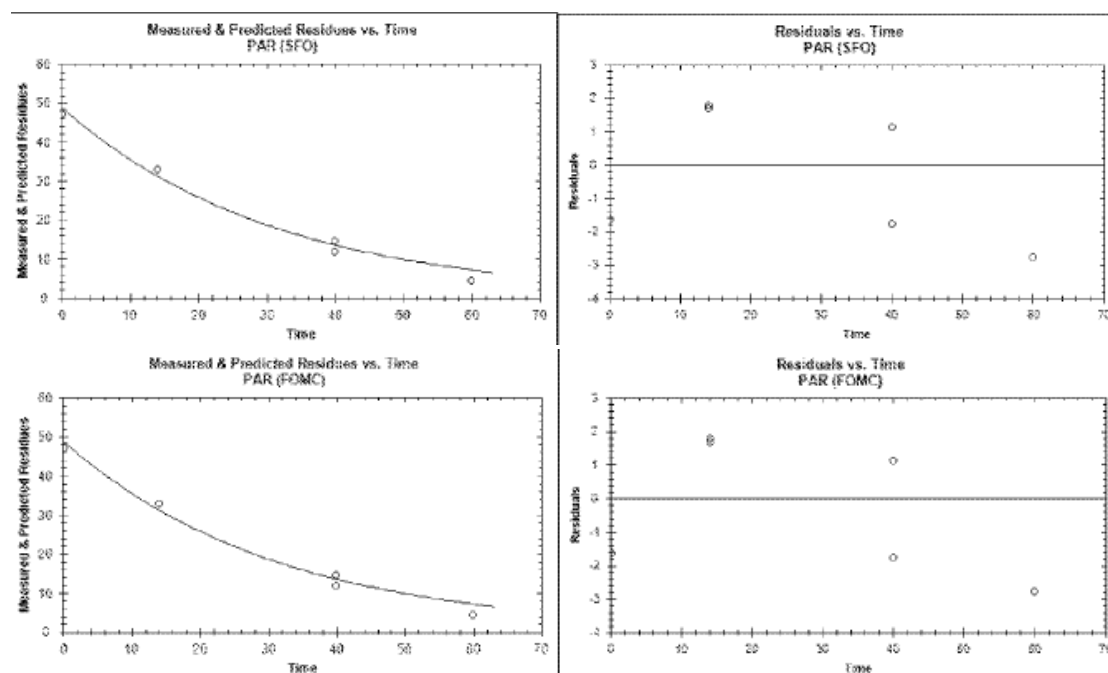


Figure 8.1.2.1.1/01-06: Model fits and residuals for (+)-cinmethylin (Reg No. 5925632) in Lufa 5M soil. Top row: SFO. Bottom row: FOMC. Final model: SFO.

LAD-SCL-PF

For LAD-SCL-PF, the SFO and FOMC model fits were very similar and both displayed a good fit against the measured parent data (Figure 8.1.2.1.1/01-07). χ^2 error was lower for the SFO fit, therefore, this was the most appropriate model. SFO was also the most appropriate fit for both enantiomers due to lower χ^2 error (Figures 8.1.2.1.1/01-08 – 09).

The kinetic models and derived endpoints for each soil, as supplied by the Applicant, are summarised in Tables 8.1.2.1.1/01-11 – 13. The HSE evaluator has evaluated and accepted the processes followed and the decisions made by the Applicant, and the resulting endpoints; however, it is noted that the kinetic fits for the enantiomers only include four time points.

Table 8.1.2.1.1/01-11: Summary of kinetic model evaluation of aerobic degradation of cinmethylin in the LAD-SCL-PF soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	M ₀ : 98.2074 k: 0.0159	95.485 – 100.930	<0.0001	3.02	43.5	144.4
FOMC	Good	M ₀ : 98.21 α : 10290 β : 645500	95.40 – 101.0 9475.0 – 11111 645500 - 645557		3.2	43.5	144.4

Table 8.1.2.1.1/01-12: Summary of kinetic model evaluation of aerobic degradation of (-)-cinmethylin (Reg No. 5925581) in the LAD-SCL-PF soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	M ₀ : 49.2630 k: 0.0199	43.868 – 54.658	0.0009	4.1	34.7	115.4
FOMC	Good	M ₀ : 49.260 α : 24330 β : 1219000	43.030 – 55.490 16870 – 31800 1219000 - 1220000		5.1	34.7	115.4

Table 8.1.2.1.1/01-13: Summary of kinetic model evaluation of aerobic degradation of (+)-cinmethylin (Reg No. 5925632) in the LAD-SCL-PF soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	M ₀ : 48.6943 k: 0.01229	43.737 – 53.655	0.001	7.31	56.4	187.3
FOMC	Good	M ₀ : 48.70 α : 5717.0 β : 465100	42.97 – 54.42 3905.0 – 7528.59 465100 – 465103		9.13	56.4	187.4

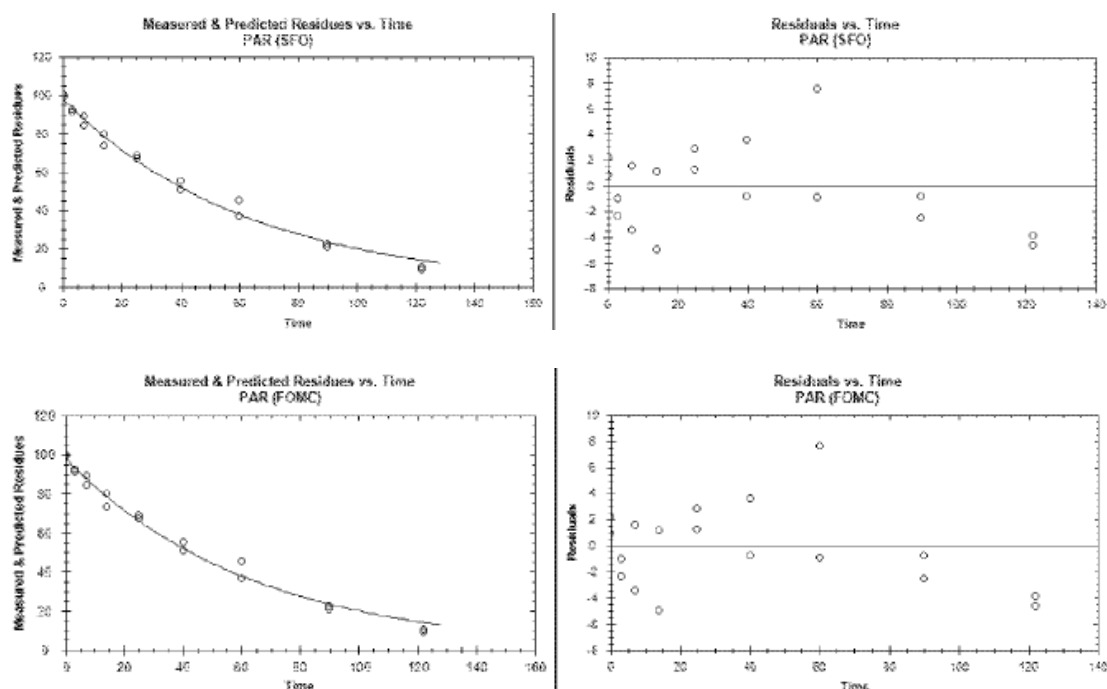


Figure 8.1.2.1.1/01-07: Model fits and residuals for cinmethylin in LAD-SCL-PF soil. Top row: SFO. Bottom row: FOMC. Final model: SFO.

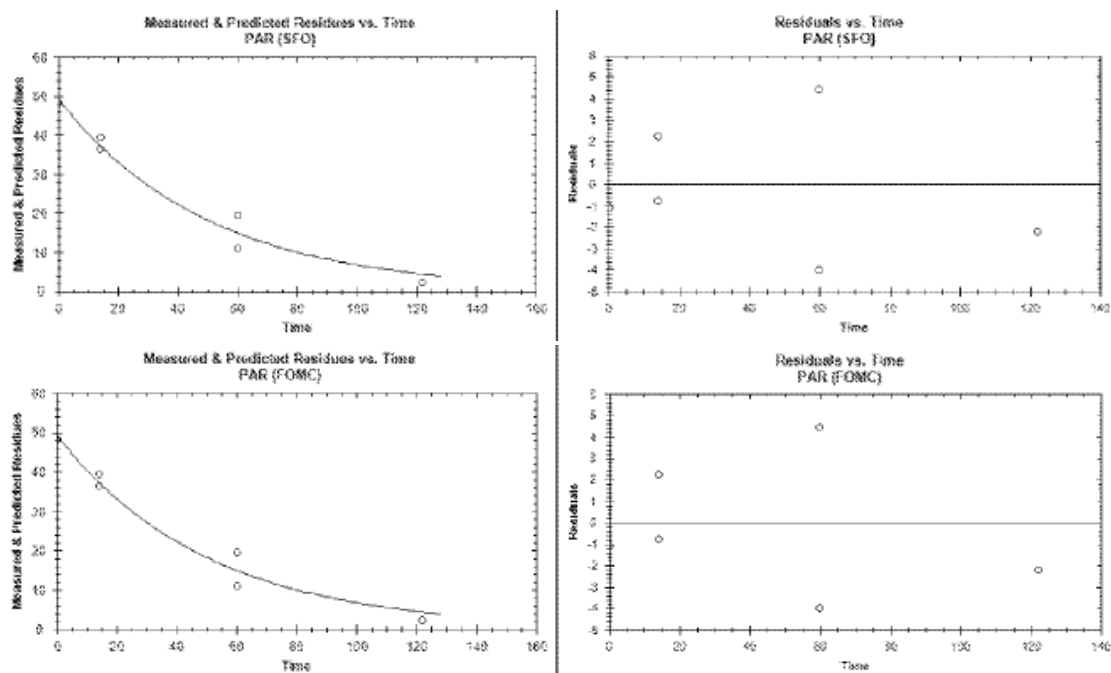


Figure 8.1.2.1.1/01-08: Model fits and residuals for (-)-cinmethylin (Reg No. 5925581) in LAD-SCL-PF soil. Top row: SFO. Bottom row: FOMC. Final model: SFO.

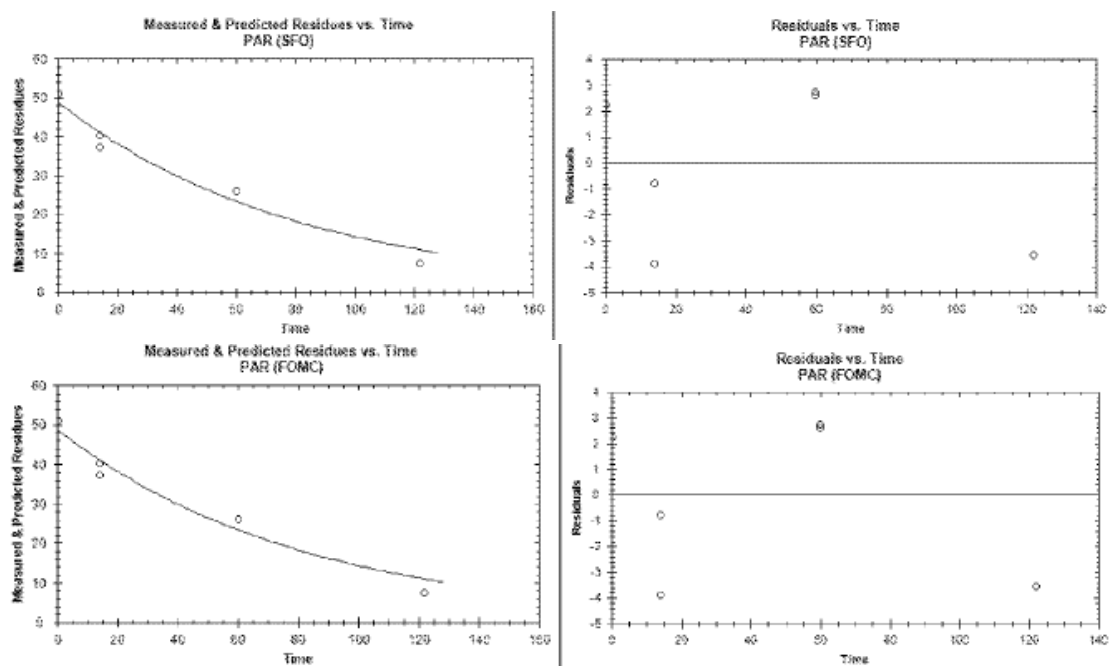


Figure 8.1.2.1.1/01-09: Model fits and residuals for (+)-cinmethylin (Reg No. 5925632) in LAD-SCL-PF soil. Top row: SFO. Bottom row: FOMC.

MSL-PF

For cinmethylin in MSL-PF soil, the SFO visual fit was poor with large residuals indicating both under and overestimation of residues; however, FOMC offered a better fit (Figure 8.1.2.1.1/01-10). Consistent with Lufa 2.2, DFOP offered a good model fit with smaller, randomly scattered residuals.

Figures 8.1.2.1.1/01-11 – 12 display the model fit and residuals for the two enantiomers in MSL-PF. Consistent with the parent compound, SFO was a poor fit to both enantiomers, with FOMC offering a better fit. As with the parent, DFOP was the most appropriate fit for both enantiomers.

The kinetic models and derived endpoints for each soil, as supplied by the Applicant, are summarised in Tables 8.1.2.1.1/01-14 – 16. The HSE evaluator has evaluated and accepted the processes followed and the decisions made by the Applicant, and the resulting endpoints.

Table 8.1.2.1.1/01-14 Summary of kinetic model evaluation of aerobic degradation of cinmethylin in the MSL-PF soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	M ₀ : 85.9578 k: 0.0202	80.883 – 91.033	<0.0001	12.52	34.24	113.7
FOMC	Good	M ₀ : 98.6926 α : 0.6267 β : 9.3326	96.118 – 101.27 0.543 – 0.710 6.679 – 11.990		3.20	18.9	358.5
DFOP	Good	M₀: 98.34 k1 (d): 0.1134 k2 (d): 0.0093 g: 0.4762	95.85 – 100.82 0.0866 – 0.140 0.00746 – 0.011 0.4139 – 0.539	<0.0001 <0.0001	3.11	18.5	178.1

Table 8.1.2.1.1/01-15: Summary of kinetic model evaluation of aerobic degradation of (-)-cinmethylin (Reg No. 5925581) in the MSL-PF soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	M ₀ : 42.294 k: 0.0264	35.982 – 48.606	<0.0001	21.6	26.2	87.1
FOMC	Good	M ₀ : 49.9655 α : 0.690 β : 6.4798	48.052 – 51.879 0.562 – 0.818 3.782 – 9.178		4.01	11.2	175.8
DFOP	Good	M₀: 50.0 k1 (d): 0.1634 k2 (d): 0.0127 g: 0.5296	48.384 – 51.616 0.040 – 0.287 0.0083 – 0.017 0.375 – 0.684	0.0117 <0.0001	1.07	10.84	122.0

Table 8.1.2.1.1/01-16: Summary of kinetic model evaluation of aerobic degradation of (+)-cinmethylin (Reg No. 5925632) in the MSL-PF soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	M ₀ : 44.2285 k: 0.0129	40.610 – 47.847	<0.0001	10.0	53.5	177.9
FOMC	Good	M ₀ : 49.7324 α : 0.6336 β : 16.2525	46.846 – 52.619 0.426 – 0.842 5.281 – 27.224		3.6	32.3	599.3
DFOP	Good	M ₀ : 49.9501 k1 (d): 0.1330 k2 (d): 0.0094 g: 0.2976	47.318 – 52. 0.0992 – 0.496	0.089 0.0001	0.506	36.5	206.5

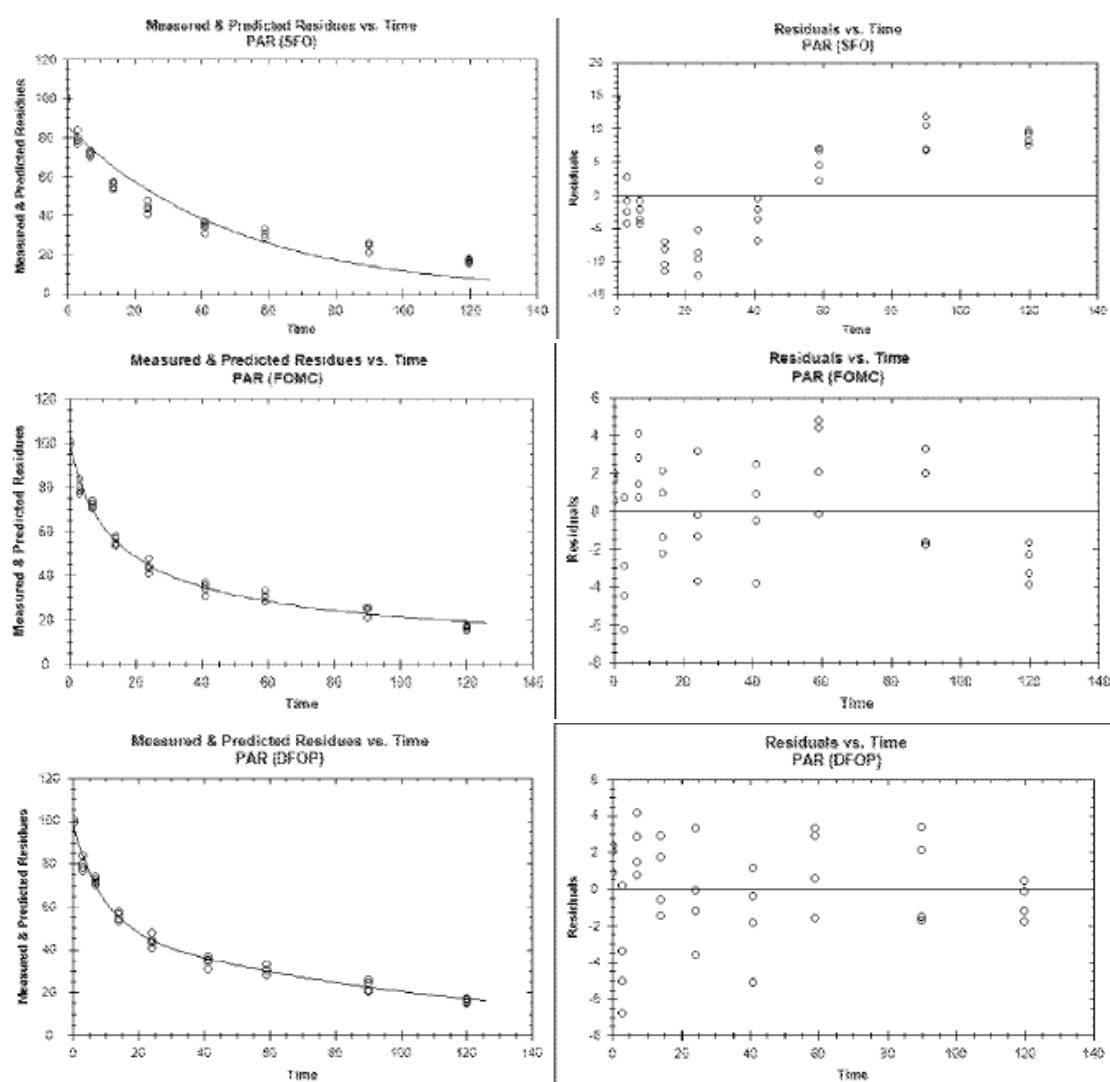


Figure 8.1.2.1.1/01-10: Model fits and residuals for cinmethylin in MSL-PF soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final model: DFOP.

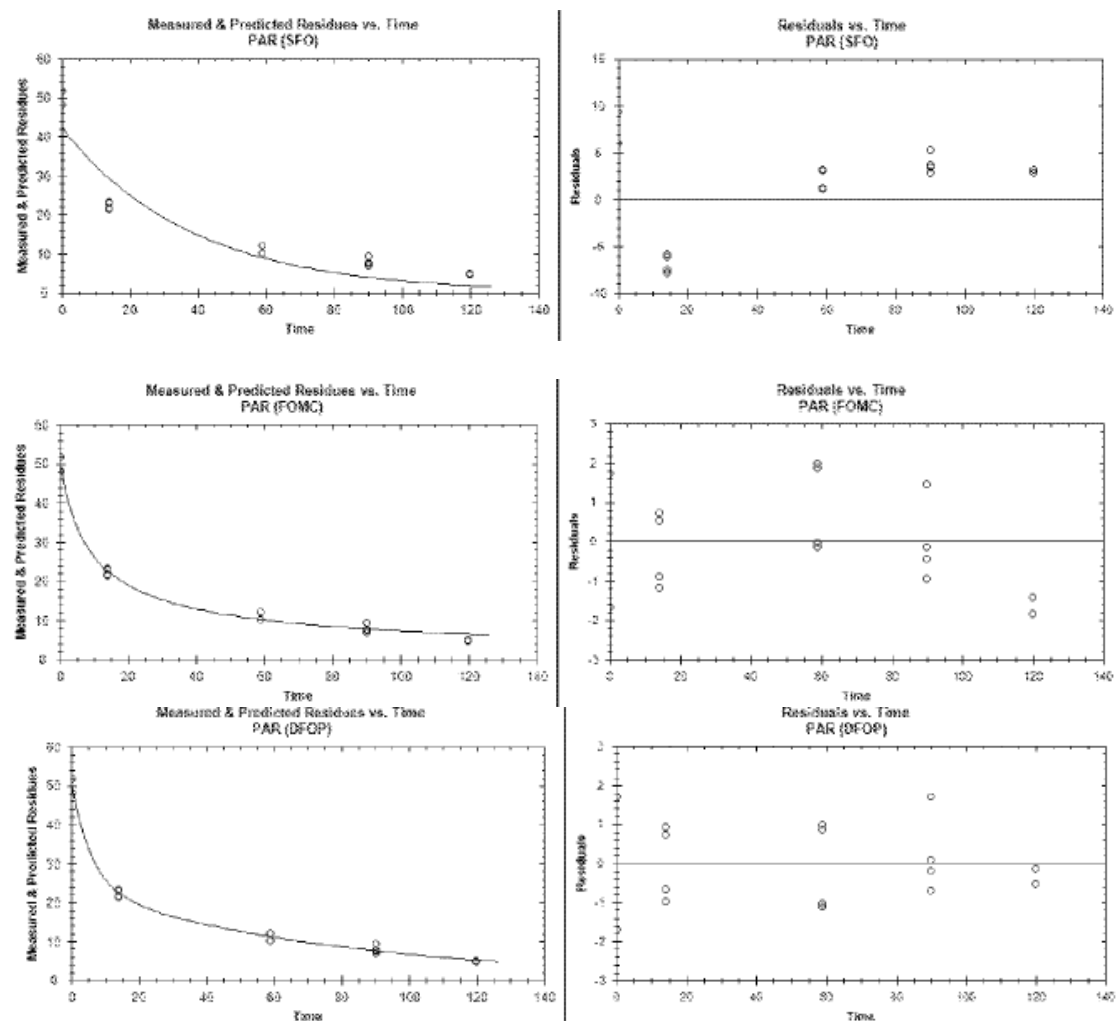
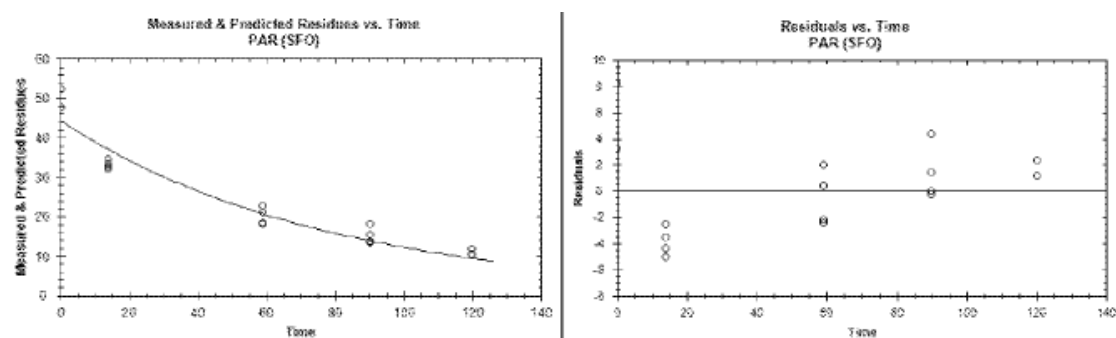


Figure 8.1.2.1.1/01-11: Model fits and residuals for (-)-cinmethylin (Reg No. 5925581) in MSL-PF soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final model: DFOP.



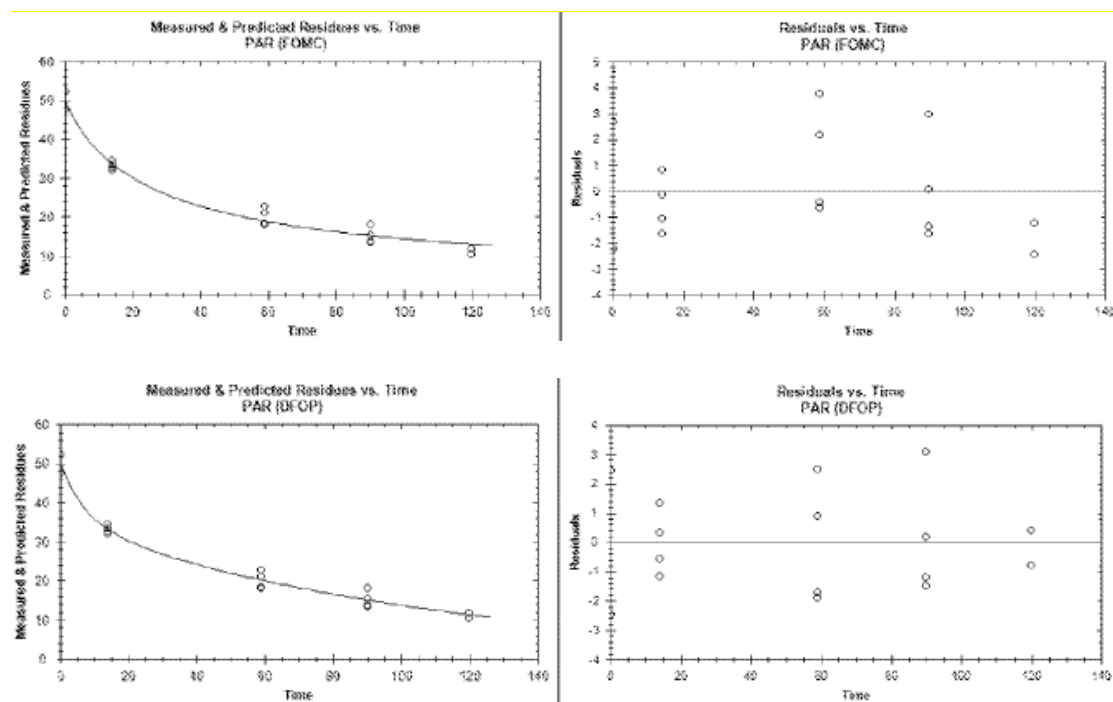


Figure 8.1.2.1.1/01-12: Model fits and residuals for (+)-cinmethylin (Reg No. 5925632) in MSL-PF soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final model: DFOP.

CONCLUSION

The DegT₅₀ and DegT₉₀ endpoints of cinmethylin and its two enantiomers are summarised in Table 8.1.2.1.1/01-17. The Applicant stated that the endpoints were derived for use as triggers for additional work, and that the visual assessment and statistical testing show plausible fits and that the resulting endpoints are reliable. The HSE evaluator accepts this summary and the following endpoints, which show that the (+)-enantiomer (Reg No. 5925632) degrades at a slower rate than the (-)-enantiomer (Reg No. 5925581) in all four soils.

As the parent and enantiomers show DegT₅₀s beyond 60 days in Lufa 2.2, the HSE evaluator notes that the trigger endpoints indicated the need for field dissipation studies.

Table 8.1.2.1.1/01-17: Calculated trigger and persistence endpoints for cinmethylin and its two enantiomers in four aerobic soils in laboratory conditions.

Cinmethylin (BAS 684 H)	Dark aerobic conditions (non-normalised trigger and persistence endpoints)							
Soil type	pH (H₂O)	pH (CaCl₂)	Temp °C	% MWHC	DT₅₀ (d)	DT₉₀ (d)	St. (χ^2)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	192.5	541.4	0.9	DFOP
Lufa 5M	8.0	7.4	20	pF2	19.1	63.5	6.2	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	43.5	144.4	3.0	SFO
MSL-PF	6.7	6.3	20	pF2	18.5	178.1	3.1	DFOP
Maximum (non-normalised)					93.6	541.4		
(-)-enantiomer (Reg No. 5925581)	Dark aerobic conditions (non-normalised trigger and persistence endpoints)							
Soil type	pH (H₂O)	pH (CaCl₂)	Temp °C	% MWHC	DT₅₀ (d)	DT₉₀ (d)	St. (χ^2)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	67.4	450.8	1.3	DFOP
Lufa 5M	8.0	7.4	20	pF2	15.4	51.1	4.5	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	34.7	115.4	4.1	SFO
MSL-PF	6.7	6.3	20	pF2	10.8	122.0	1.1	DFOP
Maximum (non-normalised)					67.4	450.8		
(+)-enantiomer (Reg No. 5925632)	Dark aerobic conditions (non-normalised trigger and persistence endpoints)							
Soil type	pH (H₂O)	pH (CaCl₂)	Temp °C	% MWHC	DT₅₀ (d)	DT₉₀ (d)	St. (χ^2)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	113.5	450.2	2.2	DFOP
Lufa 5M	8.0	7.4	20	pF2	21.5	71.5	6.2	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	56.4	187.3	7.3	SFO
MSL-PF	6.7	6.3	20	pF2	36.5	206.5	0.5	DFOP
Maximum (non-normalised)					113.5	450.2		

Report:	KCA 7.1.2.1.1/02 He, 2018
Title	Kinetic evaluation of laboratory aerobic soil degradation studies with BAS 684 H: determination of modelling endpoints according to FOCUS. Document ID: 2017/1217117
Guidelines	FOCUS Degradation kinetics (2006) FOCUS Degradation kinetics (2014)
GLP?	No – kinetic modelling conducted in compliance with the Codex of Good Modelling Practices.
Deviations	The Applicant did not include non-extractable residues (NER) at 0 DAT; however, the HSE evaluator notes that NER levels were < 0.5% on day 0 and concludes that this had no effect on overall outcomes.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

A kinetics study was undertaken by the Applicant to investigate the degradation behaviour of cinmethylin and its two enantiomers (Reg. Nos. 5925581 and 5925632) in four fresh soils under aerobic conditions. Data were derived from the laboratory aerobic degradation study conducted by Stewart and Abernethy (2016; KCA 7.1.1.1/1). The kinetic evaluation was conducted to derive degradation parameters for modelling endpoints according to the FOCUS degradation kinetics guidance (2006; 2014).

TEST PROCEDURE

The Applicant derived modelling endpoints for cinmethylin using KinGUI version 2 using IRLS optimisation. Model fits were preferably derived from the single first order (SFO) model, as per FOCUS guidance; however, if the SFO model was not appropriate based on detailed statistical analysis including visual assessment of the goodness of fit, Chi² scaled-error criterion and t-test significance, bi-phasic models were chosen according to the FOCUS guidance and conservative pseudo-SFO degradation rates were derived. Where this was necessary, cinmethylin levels were still at > 10% AR; therefore, the Applicant selected the DFOP kinetic model. The HSE evaluator accepts this decision. As the original experiments were conducted at reference conditions (soil moisture of pF 2 and at 20°C), no normalisation procedure was applied by the Applicant. The HSE evaluator agrees with this decision.

The HSE evaluator assessed the supplied kinetic evaluation by deriving modelling endpoints in CAKE version 3.2. The degradation data reported by Stewart and Abernethy (2016; KCA 7.1.1.1/1) were used to derive endpoints for each soil, with this evaluation also following FOCUS guidance on deriving modelling endpoints. Data for the parent only were used for analysis, apart from 0 DAT where the mass balance was used. This is consistent with the FOCUS kinetics guidance. The HSE evaluator notes that the Applicant did not include non-extractable residues (NER) in the 0 DAT values in their evaluation; however, NER levels were < 1% in all replicates on day 0 and the HSE evaluator confirms there were no significant

differences in the kinetic fits derived when NERs were included in the day 0 values. Therefore, the HSE evaluator accepted the Applicant's kinetic evaluations, and these are presented in the following sections..

Degradation endpoints were generated for each soil. Where two radiolabels were studied (Lufa 2.2 and MSL-PF soils), all samples were treated as individual replicates. Therefore, these soils had four replicates for each sampling time point instead of the usual two. Tables 8.1.2.1.1/2-01 – 04 display the data used by the Applicant to derive modelling endpoints

Table 8.1.2.1.1/2-01: Data values used to derive modelling endpoints for cinmethylin and its two enantiomers in the Lufa 2.2 soil.

Parent		Enantiomers		
Time (Days)	Cinmethylin (% AR)	Time (Days)	(-)-cinmethylin (% AR)	(+)-cinmethylin (% AR)
0	100.0	0	51	48.5
0	99.5	0	50.8	47.2
0	101.6	24	29.5	33.9
0	98.0	24	32	38.7
3	95.9	24	28.8	38.1
3	89.9	24	30.9	34.3
3	89.8	59	26.4	33
3	92.1	59	29.5	32.8
7	82.4	59	27.1	31.4
7	83.0	59	23.8	29.8
7	82.2	90	22	28.1
7	86.5	90	22.3	27
14	71.9	90	24.5	27.1
14	72.1	90	24.5	26
14	74.2	120	21.2	22.5
14	76.7	120	18.4	21.6
24	63.4			
24	70.7			
24	66.9			
24	65.2			
41	63.3			
41	56.5			
41	60.9			
41	58.5			
59	59.4			
59	62.3			
59	58.5			
59	53.6			
90	50.0			
90	49.3			
90	51.6			
90	50.5			
120	43.7			
120	50.9			
120	40.0			
120	45.3			

Note: Day 0 parent values reflect total recovery.

Table 8.1.2.1.1/2-02: Data values used to derive modelling endpoints for cinmethylin and its two enantiomers in the Lufa 5M soil.

Parent		Enantiomers		
Time (Days)	Cinmethylin (% AR)	Time (Days)	(-)-cinmethylin (% AR)	(+)-cinmethylin (% AR)
0	98.8	0	51.6	47.2
0	99.8	14	27.9	32.9
3	84.0	14	30.8	32.8
3	80.9	40	6.8	11.7
7	73.7	40	8.3	14.6
7	73.5	60	2.1	4.3
14	60.8			
14	63.6			
25	38.4			
25	50.0			
40	18.5			
40	22.9			
60	6.4			
60	6.7			
90	0.5			
90	1.2			
122	0.5			
122	0.7			

Note: Day 0 parent values reflect total recovery

Table 8.1.2.1.1/2-03: Data values used to derive modelling endpoints for cinmethylin and its two enantiomers in the LAD-SCL-PF soil.

Parent		Enantiomers		
Time (Days)	Cinmethylin (% AR)	Time (Days)	(-)-cinmethylin (% AR)	(+)-cinmethylin (% AR)
0	99.1	0	51.6	47.2
0	100.4	14	27.9	32.9
3	92.6	14	30.8	32.8
3	91.3	40	6.8	11.7
7	89.4	40	8.3	14.6
7	84.4	60	2.1	4.3
14	79.7			
14	73.6			
25	68.8			
25	67.2			
40	51.1			
40	55.5			
60	45.3			
60	36.8			
90	22.6			
90	20.9			
120	9.4			
120	10.2			

Table 8.1.2.1.1/2-04: Data values used to derive modelling endpoints for cinmethylin and its two enantiomers in the MSL-PF soil.

Parent		Enantiomers		
Time (Days)	Cinmethylin (% AR)	Time (Days)	(-)-cinmethylin (% AR)	(+)-cinmethylin (% AR)
0	99.2	0	51.7	47.5
0	100.4	0	48.3	52.4
0	100.7	14	23.3	34.4
0	99.3	14	23.1	33.4
3	80	14	21.4	31.9
3	76.6	14	21.7	32.5
3	83.6	59	10	18.2
3	78.4	59	12	18.4
7	73.6	59	10.1	22.6
7	70.2	59	12.1	21
7	72.3	90	9.2	15.2
7	70.9	90	6.8	13.8
14	57.7	90	7.3	13.5
14	56.5	90	7.6	18.1
14	53.3	120	4.6	10.5
14	54.2	120	5	11.7
24	47.6			
24	40.7			
24	43.1			
24	44.2			
41	33.8			
41	30.5			
41	35.2			
41	36.8			
59	28.2			
59	30.4			
59	32.7			
59	33.1			
90	24.4			
90	20.6			
90	20.8			
90	25.7			
120	15.1			
120	17.3			
120	16.7			
120	15.7			

RESULTS AND DISCUSSION

Visual assessment of goodness of fit is an important step in the kinetic evaluation process. This assessment is covered in the sections below for cinmethylin, (-)-enantiomer (Reg. No. 5925581) and (+)-enantiomer (Reg. No. 5925632).

Cinmethylin

Figures 8.1.2.1.1/2-01 – 04 display the model fit and residuals for each soil.

For Lufa 2.2, the SFO visual fit was poor, with residuals showing tendencies to both underestimate and overestimate residues (Figure 8.1.2.1.1/2-01). Due to the parent not dropping below 10% AR by the study end, DFOP was the most appropriate biphasic model to test, and it offered a good model fit and the residuals were randomly scattered.

Table 8.1.2.1.1/2-05: Summary of kinetic model evaluation of aerobic degradation of cinmethylin in the Lufa 2.2 soil. Final model is highlighted in bold.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	M ₀ : 88.91 k: 0.006997	85.29 – 92.52	<0.0001	7.3	99.1	329.1
DFOP	Good	M₀: 99.78 k₁ (d): 0.0979 k₂ (d): 0.0036 g: 0.3000	0.0696 – 0.126 0.0027 – 0.004 0.2522 – 0.348	<0.0001 <0.0001 <0.0001	0.9	k₁: 6.9 192.5^a	541.4

^a k₁ DT₅₀ = fast phase DT₅₀. Slow phase DT₅₀ = ln(2)/k₂

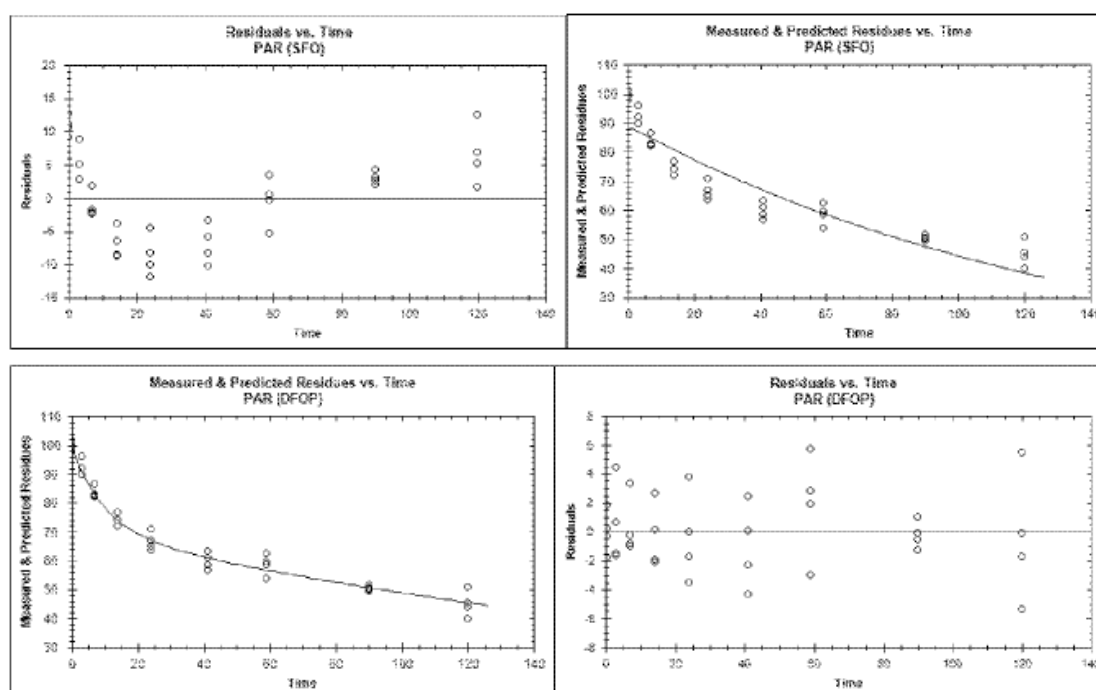


Figure 8.1.2.1.1/2-01: Model fits and residuals for Lufa 2.2 soil. Top row: SFO. Bottom row: DFOP.

For Lufa 5M, the SFO model displayed a good fit against the measured data, and the residuals were scattered (Figure 8.1.2.1.1/2-02). Table 8.1.2.1.1/2-06 summarises the kinetic model and derived endpoint for LUFA 5M soil as supplied by the Applicant.

Table 8.1.2.1.1/2-06: Summary of kinetic model evaluation of aerobic degradation of cinmethylin in the Lufa 5M soil.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	M ₀ : 97.04 k: 0.0362	92.88 – 101.2	<0.0001	6.18	19.1	63.53

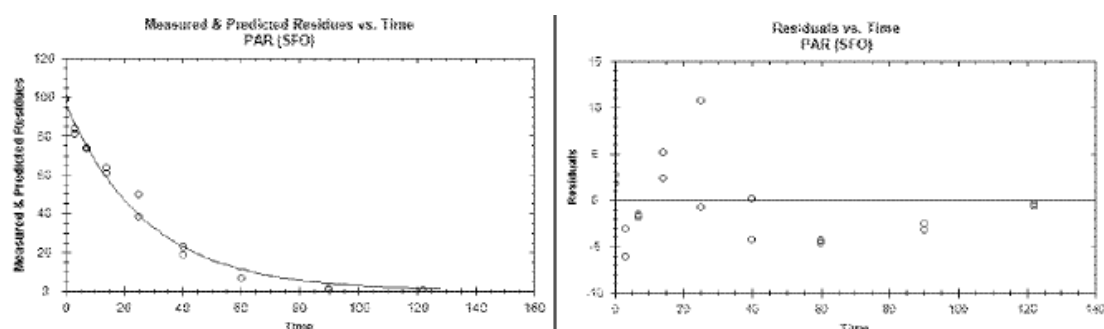


Figure 8.1.2.1.1/2-02: SFO model fit and residuals for Lufa 5M soil.

SFO was also a good fit for the LAD-SCL-PF soil data with randomly scattered residuals (Figure 8.1.2.1.1/2-03). Table 8.1.2.1.1/2-07 summarises the kinetic model and derived endpoint for LAD-SCL-PF soil as supplied by the Applicant.

Table 8.1.2.1.1/2-07: Summary of kinetic model evaluation of aerobic degradation of cinmethylin in the LAD-SCL-PF soil.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	99.75	M ₀ : 98.2074 k: 0.0159	95.485 – 100.930	<0.0001	3.02	43.47	144.4

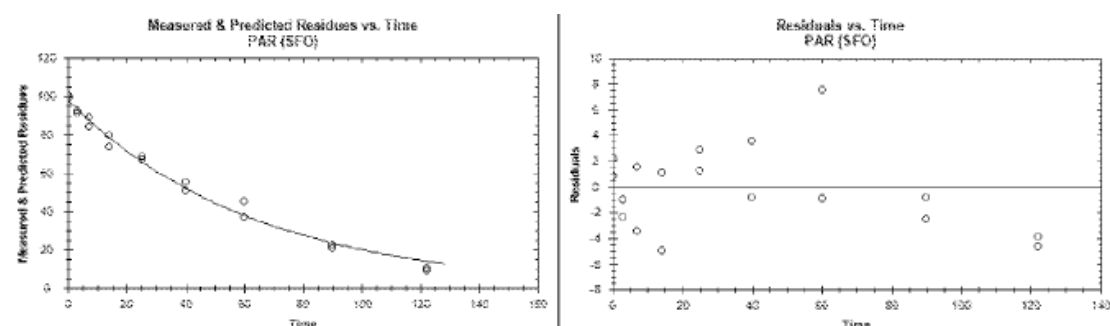


Figure 8.1.2.1.1/2-03: SFO model fit and residuals for LAD-SCL-PF soil.

For the MSL-PF soil, the SFO model showed a poor fit and residuals indicated a tendency to both overestimate and underestimate residues (Figure 8.1.2.1.1/2-04). Due to the parent not dropping below 10% AR by the study end, DFOP was the most appropriate biphasic model to test, and it offered a very good model fit and the residuals were both small and randomly scattered. Table 8.1.2.1.1/2-04 summarises the kinetic model and derived endpoint for MSL-PF soil as supplied by the Applicant.

Table 8.1.2.1.1/2-08: Summary of kinetic model evaluation of aerobic degradation of cinmethylin in the MSL-PF soil. Final model is highlighted in bold.

Kinetic model	Visual fit	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	M ₀ : 85.9578 k: 0.0202	80.883 – 91.033	<0.0001	12.52	34.2	113.7
DFOP	Good	M₀: 98.34 k₁ (d): 0.1134 k₂ (d): 0.0093 g: 0.4762	95.85 – 100.82 0.0866 – 0.140 0.00746 – 0.011 0.4139 – 0.539	<0.0001 <0.0001 <0.0001 <0.0001	3.11	fast: 6.1 slow: 74.5^a	178.1

^a Fast phase DT₅₀ = ln2/k₁. Slow phase DT₅₀ (used as pseudo-SFO DT₅₀) = ln(2)/k₂

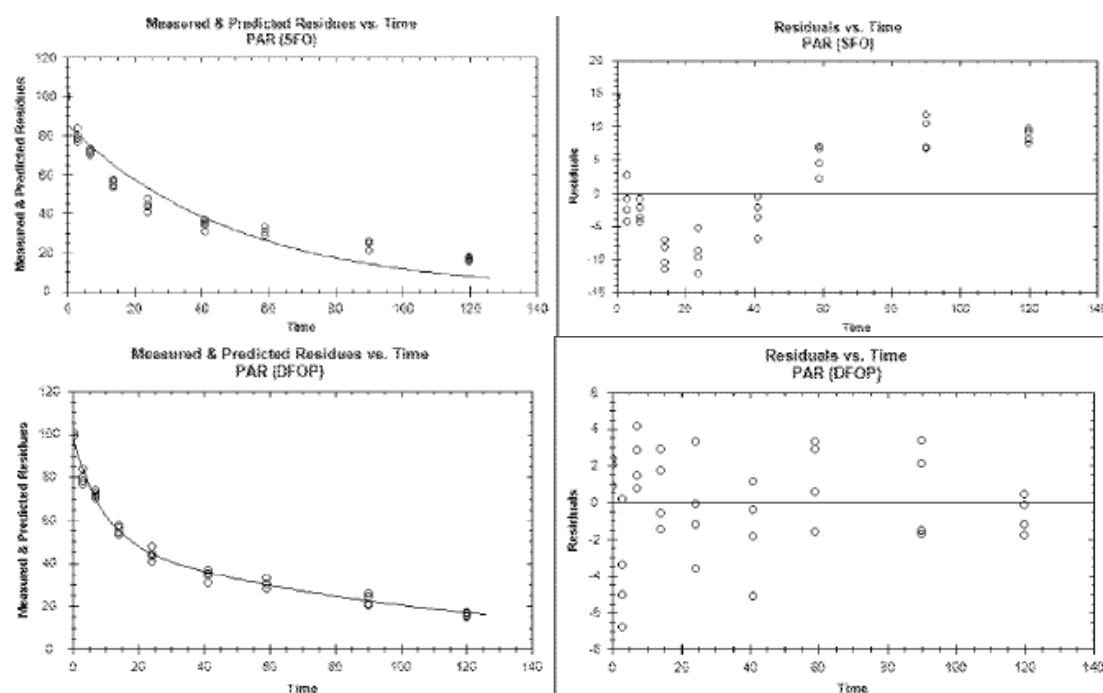


Figure 8.1.2.1.1/02-04: Model fits for MSL-PF soil. Top row: SFO. Bottom row: DFOP.

(-)-Cinmethylin

Figures 8.1.2.1.1/2-05 – 08 display the model fit and residuals for each soil. Tables 8.1.2.1.1/2-09 – 13 summarise kinetic model evaluations.

For (-)-cinmethylin degradation in Lufa 2.2, the SFO visual fit was poor, with residuals showing tendencies to both underestimate and overestimate residues (Figure 8.1.2.1.1/2-05). Due to the parent not dropping below 10% AR by the study end, DFOP was the most appropriate biphasic model to test, and it offered a good model fit and the residuals were randomly scattered.

Table 8.1.2.1.1/2-09: Summary of kinetic model evaluation of aerobic degradation of (-)-cinmethylin in the Lufa 2.2 soil. Final model highlighted in bold.

Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	43.31	k: 0.0077	0.005 – 0.010	<0.0001	11.9	89.7	297.8
DFOP	Good	50.90	k1 (d): 1.092 k2 (d): 0.004 g: 0.337	1.092 – 1.092 0.003 – 0.005 0.282 – 0.392	<0.0001 <0.0001 <0.0001	1.3	k1 67.4 (173.3)^a	450.8

^a k1 DT₅₀ = fast phase DT₅₀. Pseudo-SFO DT₅₀ = ln(2)/k₂

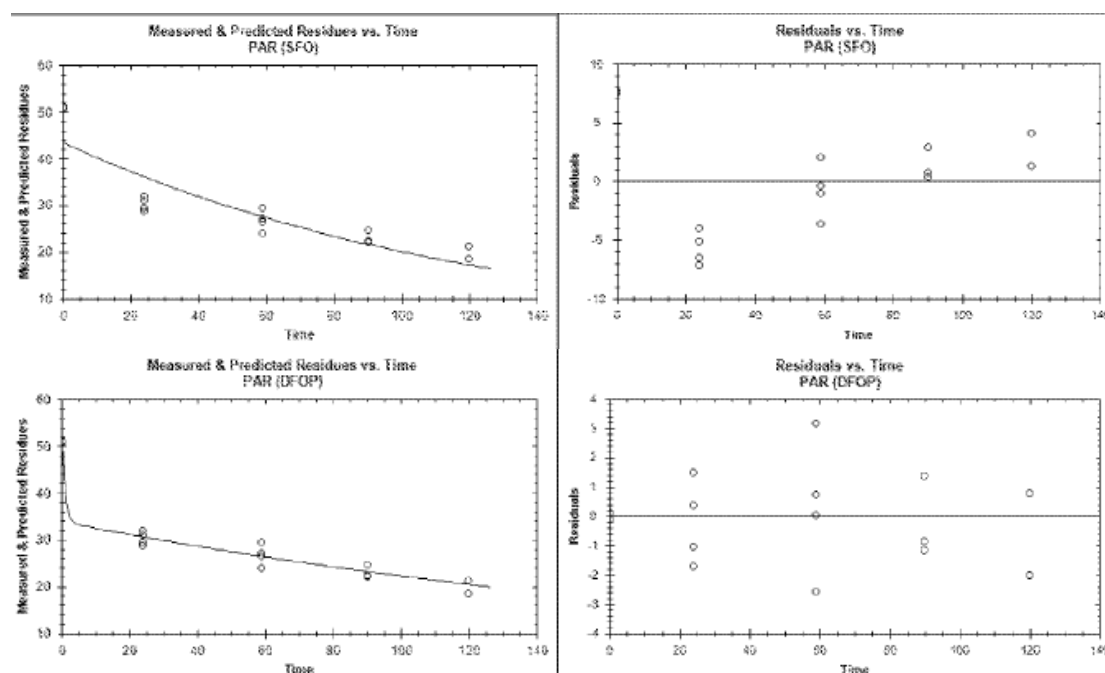


Figure 8.1.2.1.1/2-05: Model fits and residuals for (-)-cinmethylin in Lufa 2.2 soil. Top row: SFO. Bottom row: DFOP.

For Lufa 5M, the SFO model displayed a good fit against the measured data for (-)-cinmethylin, and the residuals were scattered (Figure 8.1.2.1.1/2-06). Table 8.1.2.1.1/2-10 summarises the kinetic model and derived endpoint for LUFA 5M soil as supplied by the Applicant. The HSE evaluator notes that there are only four time points for this soil when FOCUS guidance (2006; 2014) recommends a minimum of five time points. The HSE evaluator concludes that this is not a major deviation and does not invalidate the kinetic evaluation.

Table 8.1.2.1.1/2-10: Summary of kinetic model evaluation of aerobic degradation of (-)-cinmethylin in the Lufa 5M soil.

Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	52.60	k: 0.045	0.037 – 0.053	<0.0001	4.5	15.4	51.1

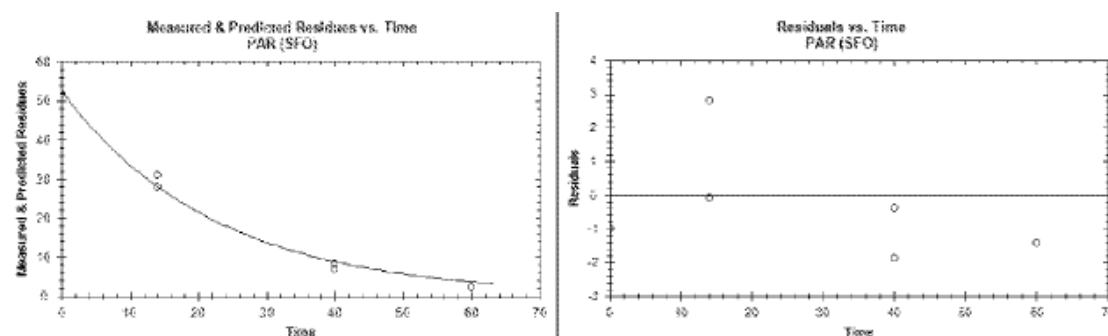


Figure 8.1.2.1.1/2-06: SFO model fit and residuals for (-)-cinmethylin degradation in Lufa 5M soil.

SFO was a good fit against the measured data for (-)-cinmethylin in LAD-SCL-PF soil with randomly scattered residuals (Figure 8.1.2.1.1/2-07). Table 8.1.2.1.1/2-11 summarises the kinetic model and derived endpoint for LAD-SCL-PF soil as supplied by the Applicant. The HSE evaluator notes that there are only four time points for this soil; again, this is not a major deviation and does not invalidate the kinetic evaluation.

Table 8.1.2.1.1/2-11: Summary of kinetic model evaluation of aerobic degradation of (-)-cinmethylin in the LAD-SCL-PF soil.

Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	49.26	k: 0.020	0.012 – 0.028	0.0009	4.1	34.7	115.4

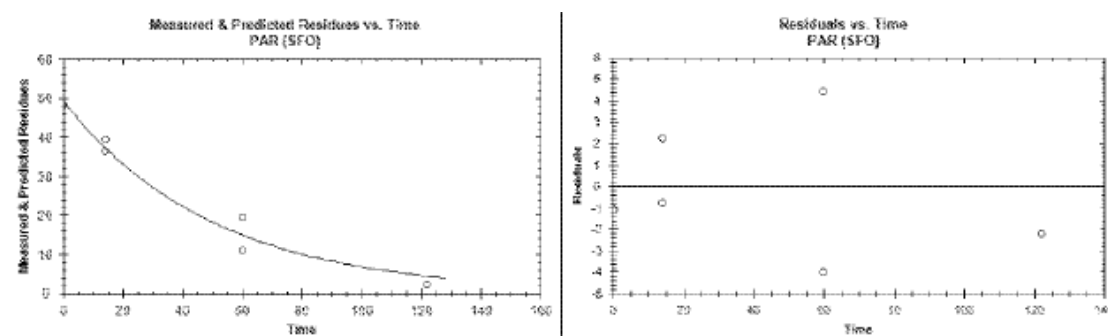


Figure 8.1.2.1.1/2-07: SFO model fit and residuals for (-)-cinmethylin degradation in LAD-SCL-PF soil.

For the MSL-PF soil, the SFO model showed a poor fit and residuals indicated a tendency to both overestimate and underestimate residues (Figure 8.1.2.1.1/2-08). DFOP offered a very good model fit and the residuals were both small and randomly scattered. Table 8.1.2.1.1/2-12 summarises the kinetic model and derived endpoint for MSL-PF soil as supplied by the Applicant.

Table 8.1.2.1.1/2-12: Summary of kinetic model evaluation of aerobic degradation of (-)-cinmethylin in the MSL-PF soil. Final model highlighted in bold.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	42.29	k: 0.026	0.017 – 0.036	<0.0001	12.5	34.2	113.7
DFOP	Good	50.0	k1 (d): 0.163 k2 (d): 0.013 g: 0.530	0.040 – 0.287 0.008 – 0.017 0.375 – 0.684	0.0117 <0.0001 <0.0001	1.1	k1 10.4 (53.3)^a	122.0

^a k1 DT₅₀ = fast phase DT₅₀. Pseudo-SFO DT₅₀ = ln(2)/k₂

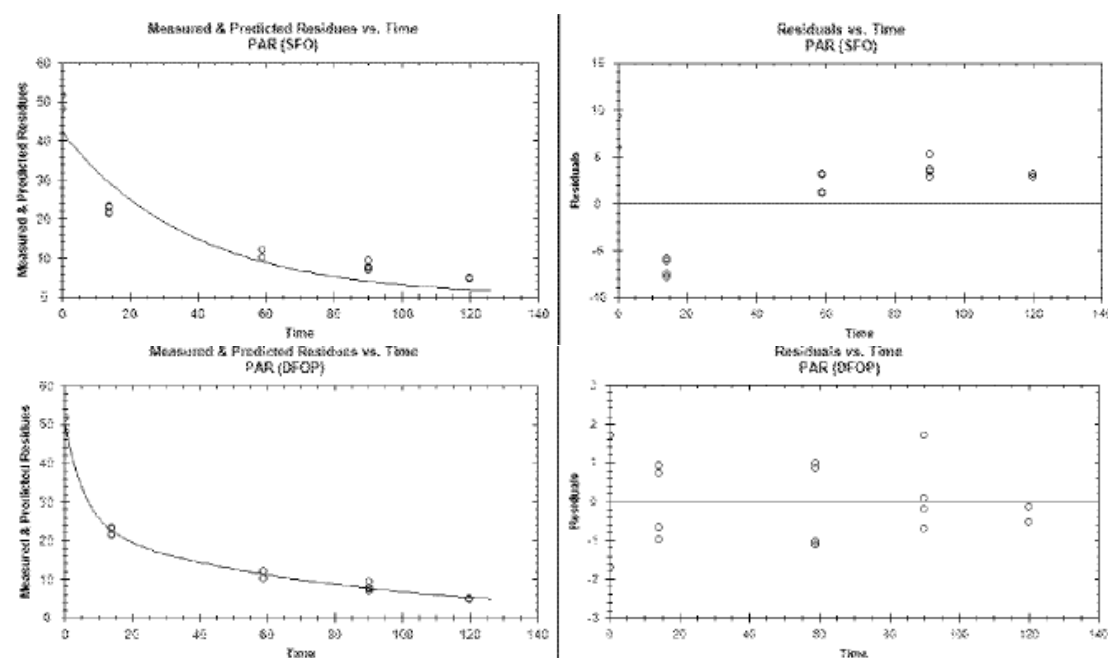


Figure 8.1.2.1.1/2-08: Model fits for (-)-cinmethylin degradation in MSL-PF soil. Top row: SFO. Bottom row: DFOP.

The HSE evaluator has evaluated the procedure followed by the Applicant and notes that DFOP was chosen to derive modelling endpoints where SFO proved to be an unsuitable model. The HSE evaluator accepts this decision and procedure, and therefore accepts the resulting modelling endpoints.

(+)-Cinmethylin

Figures 8.1.2.1.1/2-09 – 12 display the model fit and residuals for each soil. Tables 8.1.2.1.1/2-13 – 16 summarise kinetic model evaluations. Final model fits were consistent with those chosen for (-)-cinmethylin.

For (+)-cinmethylin degradation in Lufa 2.2, the SFO visual fit was poor, with residuals showing tendencies to both underestimate and overestimate residues (Figure 8.1.2.1.1/2-05). Due to the parent not dropping below 10% AR by the study end, DFOP was the most appropriate biphasic model to test, and it offered a good model fit and the residuals were randomly scattered.

Table 8.1.2.1.1/2-13: Summary of kinetic model evaluation of aerobic degradation of (+)-cinnmethylin in the Lufa 2.2 soil. Final model highlighted in bold.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	44.71	k: 0.006	0.005 – 0.007	<0.0001	4.5	117.2	389.3
DFOP	Good	47.85	k1 (d): 1.466 k2 (d): 0.005 g: 0.140	1.466 – 1.466 0.0039 – 0.006 0.0738 – 0.206	<0.0001 <0.0001 0.0007	2.2	113.5 (138.6)^a	450.2

^a k1 DT₅₀ = fast phase DT₅₀. Pseudo-SFO DT₅₀ = ln(2)/k₂

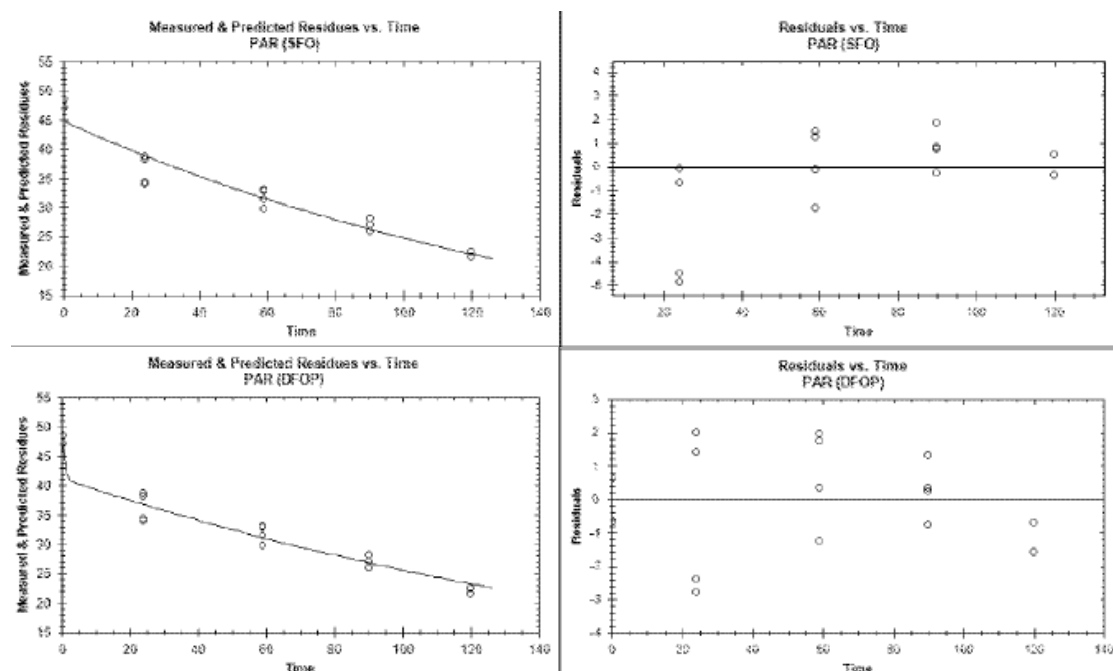


Figure 8.1.2.1.1/2-09: Model fits and residuals for (+)-cinnmethylin in Lufa 2.2 soil. Top row: SFO. Bottom row: DFOP.

For Lufa 5M, the SFO model displayed a good fit against the measured data for (+)-cinnmethylin, and the residuals were scattered (Figure 8.1.2.1.1/2-06). Table 8.1.2.1.1/2-14 summarises the kinetic model and derived endpoint for LUFA 5M soil as supplied by the Applicant. The HSE evaluator notes that there are only four time points for this soil; again, this is not a major deviation and does not invalidate the kinetic evaluation.

Table 8.1.2.1.1/2-14: Summary of kinetic model evaluation of aerobic degradation of (+)-cinnmethylin in the Lufa 5M soil.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	48.84	k: 0.032	0.024 – 0.040	0.0001	6.2	21.5	71.5

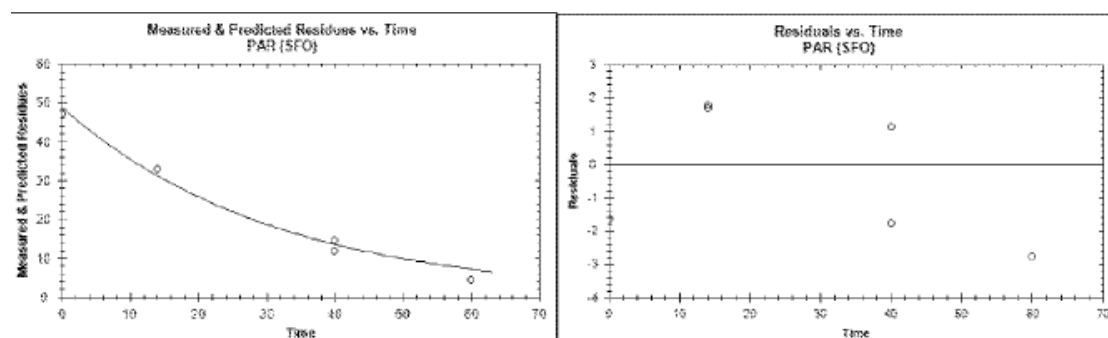


Figure 8.1.2.1.1/2-10: SFO model fit and residuals for (+)-cinmethylin degradation in Lufa 5M soil.

SFO was a good fit against the measured data for Reg. No. 5925581 in LAD-SCL-PF soil with randomly scattered residuals (Figure 8.1.2.1.1/2-07). Table 8.1.2.1.1/2-15 summarises the kinetic model and derived endpoint for LAD-SCL-PF soil as supplied by the Applicant. The HSE evaluator notes that there are only four time points for this soil; again, this is not a major deviation and does not invalidate the kinetic evaluation.

Table 8.1.2.1.1/2-15: Summary of kinetic model evaluation of aerobic degradation of Reg. No. 5925632 in the LAD-SCL-PF soil.

Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	48.69	k: 0.012	0.007 – 0.017	0.001	7.3	56.4	187.3

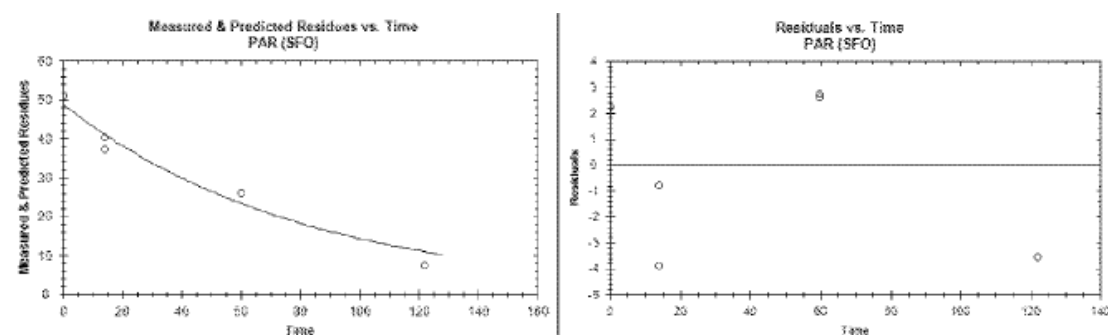


Figure 8.1.2.1.1/2-11: SFO model fit and residuals for Reg. No. 5925632 degradation in LAD-SCL-PF soil.

For the MSL-PF soil, the SFO model showed a poor fit and residuals indicated a tendency to both overestimate and underestimate residues (Figure 8.1.2.1.1/2-08). DFOP offered a very good model fit and the residuals were both small and randomly scattered. Table 8.1.2.1.1/2-16 summarises the kinetic model and derived endpoint for MSL-PF soil as supplied by the Applicant. The HSE evaluator notes that the DFOP k1 parameter is not significantly different to zero; additionally, the 95% confidence intervals contain 0. However, the visual fit is markedly better than the SFO visual fit. Based on this, the improved residuals and lower error, the HSE evaluator agrees that the DFOP model fit is the most appropriate.

Table 8.1.2.1.1/2-16: Summary of kinetic model evaluation of aerobic degradation of (+)-cinmethylin in the MSL-PF soil. Final model highlighted in bold.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	44.23	k: 0.013	0.010 – 0.015	<0.0001	12.5	34.2	113.7
DFOP	Good	49.95	k1 (d): 0.133 k2 (d): 0.009 g: 0.298	-0.069 – 0.335 0.005 – 0.013 0.077 – 0.518	0.089 0.0001	0.51	36.5 (77.0)^a	206.5

^a Pseudo-SFO DT₅₀ = ln(2)/k_{slow}

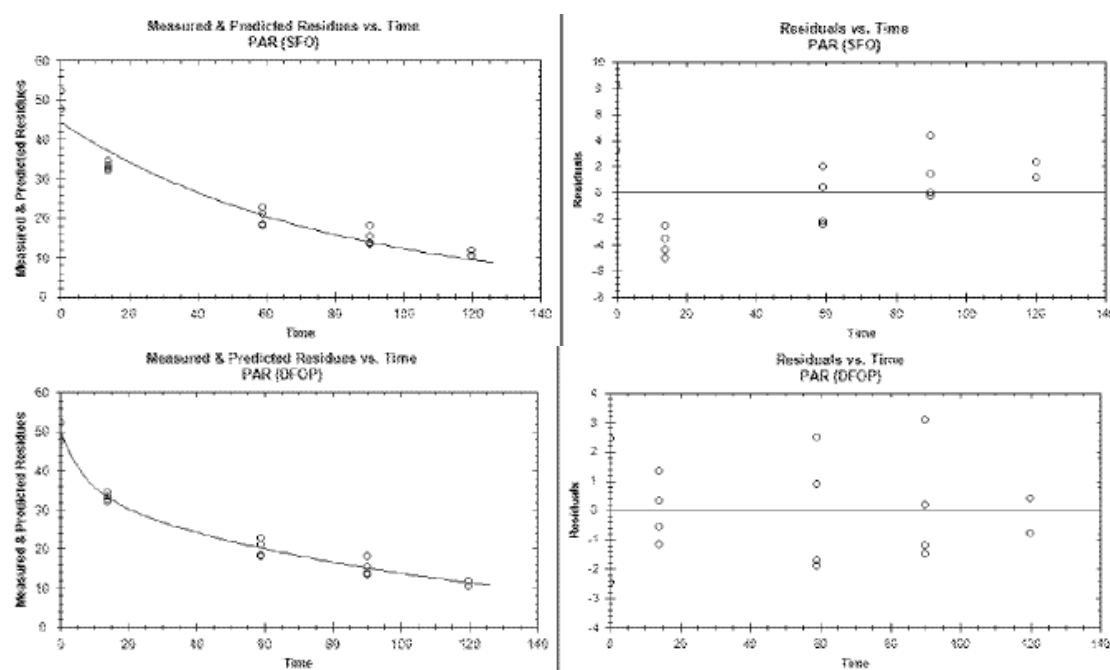


Figure 8.1.2.1.1/2-12: Model fits for (+)-cinmethylin degradation in MSL-PF soil. Top row: SFO. Bottom row: DFOP.

The HSE evaluator has evaluated and agrees with the procedure followed by the Applicant; therefore, the HSE evaluator accepts the modelling endpoints presented by the Applicant.

GUIDELINE DEVIATIONS

There were no guideline deviations reported by the Applicant; however, the HSE evaluator noted that the Applicant did not use mass balances at 0 DAT as recommended in FOCUS kinetics guidance. Following kinetic evaluation, the HSE evaluator concluded that, due to the low levels of NERs, this deviation had no significant effect on the modelling decisions or on subsequent endpoints, and so has accepted the endpoints and parameters provided by the Applicant.

CONCLUSIONS

The Applicant presented degradation rates as modelling endpoints for the four soils investigated in the laboratory aerobic degradation study. The same models were chosen for trigger endpoints in Stewart and Abernethy (2016). No normalisation procedure was necessary as the experiment was conducted at soil moisture of pF 2 and at a temperature of 20°C. Tables 8.1.2.1.1/2-17 – 19 summarise the modelling endpoints for cinmethylin and its

enantiomers; these endpoints were presented by the Applicant and evaluated and accepted by the HSE evaluator.

Table 8.1.2.1.1/2-17: Calculated modelling endpoints for cinmethylin in four aerobic soils in laboratory conditions. Values in parentheses are pseudo-SFO endpoints used for calculation of the geometric mean.

Parent	Dark aerobic conditions (normalised modelling endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	192.5 ^a	541.4	0.9	DFOP
Lufa 5M	8.0	7.4	20	pF2	19.1	63.5	6.18	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	43.5	144.4	3.02	SFO
MSL-PF	6.7	6.3	20	pF2	74.5 ^b	178.1	3.11	DFOP
Geometric mean (if not pH dependent)					58.8			
pH dependence					No			

^{a)} $k_1 = 0.0979$, $k_2 = 0.0036$, $g = 0.3000$. Slow phase DT₅₀ calculated using $\ln(2)/k_2$

^{b)} $k_1 = 0.1134$, $k_2 = 0.0093$, $g = 0.4762$. Slow phase DT₅₀ calculated using $\ln(2)/k_2$

Table 8.1.2.1.1/2-18: Calculated modelling endpoints for (-)-cinmethylin in four aerobic soils in laboratory conditions. Values in parentheses are pseudo-SFO endpoints used for calculation of the geometric mean.

Parent	Dark aerobic conditions (normalised modelling endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	173.3 ^a	450.8	1.3	DFOP
Lufa 5M	8.0	7.4	20	pF2	15.4	51.1	4.5	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	34.7	115.4	4.1	SFO
MSL-PF	6.7	6.3	20	pF2	53.3 ^b	122.0	1.1	DFOP
Geometric mean (if not pH dependent)					47.1			
pH dependence					No			

^{a)} $k_1 = 1.092$, $k_2 = 0.004$, $g = 0.3370$. Slow phase DT₅₀ calculated using $\ln(2)/k_2$

^{b)} $k_1 = 0.163$, $k_2 = 0.013$, $g = 0.5296$. Slow phase DT₅₀ calculated using $\ln(2)/k_2$

Table 8.1.2.1.1/2-19: Calculated modelling endpoints for (+)-cinmethylin in four aerobic soils in laboratory conditions. Values in parentheses are pseudo-SFO endpoints used for calculation of the geometric mean.

Parent	Dark aerobic conditions (normalised modelling endpoints)							
Soil type	pH (H ₂ O)	pH (CaCl ₂)	Temp °C	% MWHC	DT ₅₀ (d)	DT ₉₀	St. (χ ²)	Method of calculation
Lufa 2.2	6.3	5.6	20	pF2	138.6 ^a	450.2	2.2	DFOP
Lufa 5M	8.0	7.4	20	pF2	21.5	71.5	6.2	SFO
LAD-SCL-PF	8.2	8.0	20	pF2	56.4	187.3	7.3	SFO
MSL-PF	6.7	6.3	20	pF2	77.0 ^b	206.5	0.5	DFOP
Geometric mean (if not pH dependent)					60.0			
pH dependence					No			

^a) $k_1 = 1.466$, $k_2 = 0.005$, $g = 0.1399$. Slow phase DT₅₀ calculated using $\ln(2)/k_2$

^b) $k_1 = 0.133$, $k_2 = 0.009$, $g = 0.2976$. Slow phase DT₅₀ calculated using $\ln(2)/k_2$

B.8.1.1.2.2. Anaerobic degradation (Data Requirement 7.1.2.1.3 and 7.1.2.1.4)

Report:	KCA 7.1.2.1.3/01; Staudenmaier, H. and Pape, L. (2017)
Title	Anaerobic soil metabolism of Cinmethylin (BAS 684 H) Report no. 2016/1053970
Guidelines	OECD Guidelines for the testing of chemicals 307: Aerobic and anaerobic transformation in soil (Apr 2002) US EPA fate, transport and transformation guidelines 835.4200: Anaerobic Soil Metabolism (Oct 2008) FOCUS Degradation Kinetics (2006; 2014)
GLP?	Yes
Deviations	None for modelling.

Previous evaluations:	None – report submitted as part of a new active substance registration. The study evaluation is presented in section ‘Anaerobic degradation (Data Requirement 7.1.1.2)’ under KCA 7.1.1.2/01; Staudenmaier, H. and Pape, L. (2017). Only the kinetic evaluation for trigger endpoints is provided here.
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KINETIC EVALUATION

1. Introduction

The Applicant performed a kinetic analysis and calculation of DegT₅₀ and DegT₉₀ values for cinmethylin in the four soils using KinGUI version 2 using IRLS optimisation. The Applicant assessed data from both the aerobic and anaerobic phases together, giving one set of endpoints per soil. For the Lufa 2.2 soil, where two radiolabels were used, the data for the two labels were considered together, thus giving four replicates per sampling time compared to the usual two replicates. The Applicant applied the biphasic hockey stick (HS) model to all four soils. All replicates were considered individually, with no averaging.

The HSE evaluator rejected the Applicant’s kinetic evaluation due to their assessment of both aerobic and anaerobic phases together. The HSE evaluator conducted new evaluations on the

parent compound from the point each soil was flooded, meaning only the anaerobic phase was assessed.

The HSE evaluator conducted the kinetic evaluation in CAKE version 3.2. The degradation data reported here were used to derive endpoints for each soil, with this evaluation also following FOCUS guidance on deriving trigger endpoints to identify the best model fit for the anaerobic phase. The single first order (SFO) and first order multiple compartment (FOMC) model fits were both evaluated to determine the most appropriate fit, as per FOCUS guidance; in this case the SFO model was most appropriate for all four soils so other biphasic models were not explored further. As the experiment was conducted at reference conditions (soil moisture of pF 2 and temperature of 20°C), no normalisation procedure was applied by the Applicant. The HSE evaluator agreed with this decision and did not normalise data for the new evaluation.

One set of endpoints were generated for each soil. For Lufa 2.2, where two radiolabels were studied, all samples were treated as individual replicates, giving four replicates per sampling time instead of the usual two. Table 8.1.2.1.3/1-01 displays the data used for the kinetic evaluation.

Table 8.1.2.1.1/1-01: Data values used to quantify the aerobic degradation of cinmethylin and its two enantiomers in the Lufa 2.2 soil.

Lufa 2.2		Lufa 5M		North Dakota		Wyoming	
Time (Days)	Cinmethylin (% AR)	Time (Days)	Cinmethylin (% AR)	Time (Days)	Cinmethylin (% AR)	Time (Days)	Cinmethylin (% AR)
0	60.1	0	57.7	0	47.6	0	64.5
0	59.7	0	58.3	0	47.9	0	67.1
0	60.1	7	57.1	4	45.5	8	74.9
0	60.5	7	56.7	4	47	8	72
7	60.5	15	56.2	19	45.8	15	72.2
7	60.2	15	56.6	19	44.8	15	72.6
7	63.7	30	55.6	35	43.6	29	79.1
7	62.9	30	55.6	35	44.4	29	73.4
16	61.6	44	55.9	49	41.9	60	74.7
16	62.3	44	55.7	49	43	60	73.7
16	63.3	75	53.1	80	36.9	88	63.8
16	63.7	75	52.4	80	36.4	88	66.3
28	61.4	105	51.4	108	35.4		
28	61.5	105	51.9	108	34.8		
28	60.9						
28	60.2						
45	59.3						
45	59.9						
45	58.8						
45	62.8						
76	59						
76	58.3						
76	61						
76	59.7						
106	58.4						
106	58.2						
106	60						
106	59.4						

2. Kinetic fits

The Applicant provided kinetic evaluations for anaerobic degradation of cinmethylin in four soils to determine trigger endpoints in the studied soil using parent compound data from both the aerobic and anaerobic phases. Based on this, the HSE evaluator rejected the kinetic evaluation and endpoints derived by the Applicant, and re-calculated endpoints based upon cinmethylin in the anaerobic phase only.

Tables 8.1.2.1.3/1-02 – 05 summarise the kinetic models and derived endpoints for each soil derived by the HSE evaluator. For all soils, there was little difference in visual fit or residuals between SFO and FOMC, and in all cases, χ^2 error was lower with SFO fits. Visual fits were generally good or acceptable, with scattered residuals. Figures 8.1.2.1.3/1-01 – 04 display both SFO and FOMC model fits and residuals for the anaerobic degradation of cinmethylin in each soil. In one soil, Wyoming, the visual fits were relatively poor and the SFO k parameter failed the t test, though FOMC did not offer a better model fit. The HSE evaluator concluded that SFO was the most appropriate model for all four soils, though ultimately, anaerobic degradation is not a significant route of degradation for cinmethylin.

Table 8.1.2.1.3/1-02: Summary of kinetic model evaluation of anaerobic degradation of cinmethylin in the Lufa 2.2 soil.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	61.6	M ₀ : 61.6 k: 0.000407	0.0011	1.1	1710	5660
FOMC	Good	61.78	M ₀ : 61.78 α : 0.651 β : 1310	N/A	1.19	3290	>10,000

Table 8.1.2.1.3/1-03: Summary of kinetic model evaluation of anaerobic degradation of cinmethylin in the Lufa 5M soil.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	57.63	M ₀ : 57.63 k: 0.001065	<0.0001	0.608	651	2160
FOMC	Good	57.64	M ₀ : 57.64 α : 2.722 β : 2510	N/A	0.657	690	2710

Table 8.1.2.1.3/1-04: Summary of kinetic model evaluation of anaerobic degradation of cinmethylin in the North Dakota soil.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Good	47.72	M ₀ : 47.72 k: 0.002879	<0.0001	1.45	241	800
FOMC	Good	47.77	M ₀ : 47.77 α : 3.39 β : 1130	N/A	1.57	256	1100

Table 8.1.2.1.3/1-05: Summary of kinetic model evaluation of anaerobic degradation of cinmethylin in the Wyoming soil.

Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
SFO	Poor	72.17	M ₀ : 72.17 k: 0.000414	0.2647	4.62	1680	5570
FOMC	Poor	71.19	M ₀ : 71.19 α : 3.04×10^{-11} β : 0.02016	N/A	5.22	>10,000	>10,000

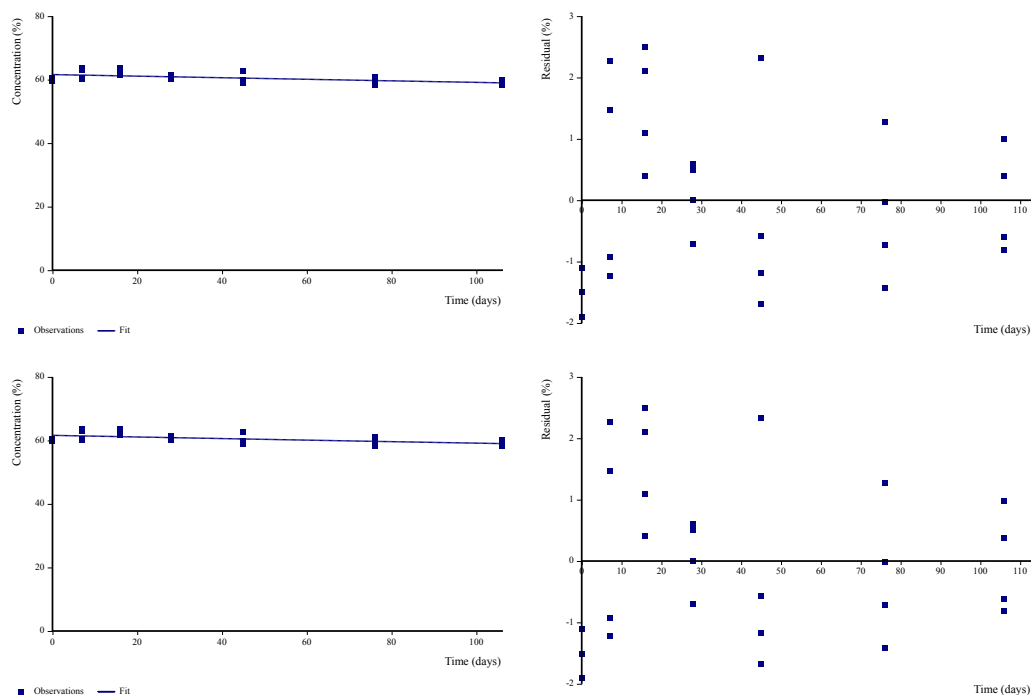


Figure 8.1.2.1.3/1-01: Model fits and residuals for the anaerobic degradation of cinmethylin in the Lufa 2.2 soil. Top row: SFO. Bottom row: FOMC. Final model fit: SFO.

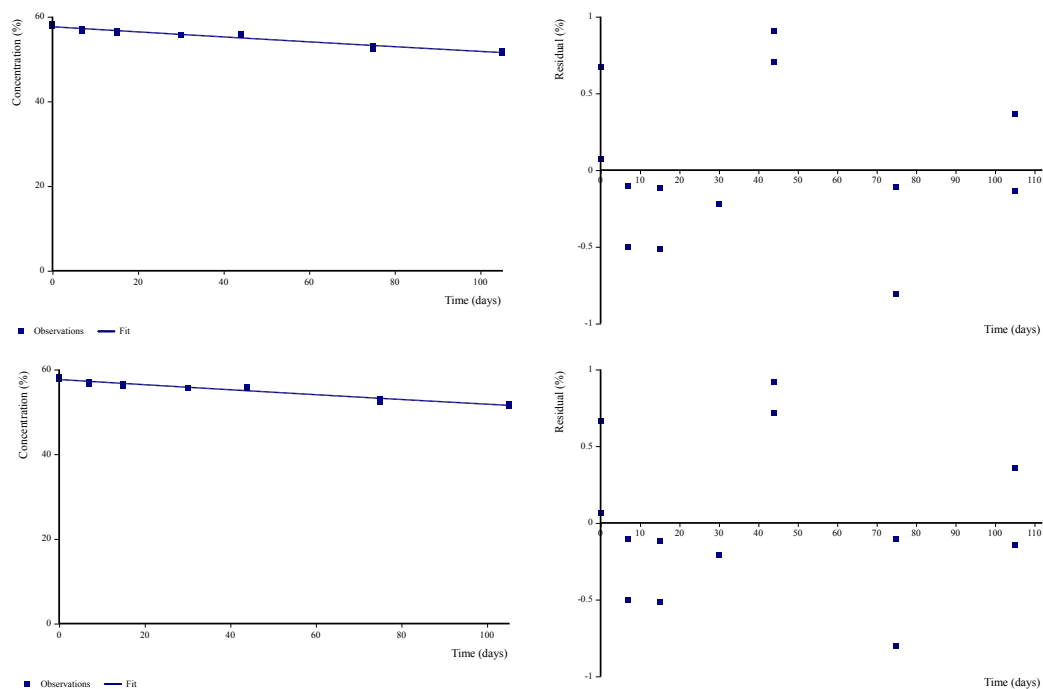


Figure 8.1.2.1.3/1-02: Model fits and residuals for the anaerobic degradation of cinmethylin in the Lufa 5M soil. Top row: SFO. Bottom row: FOMC. Final model fit: SFO.

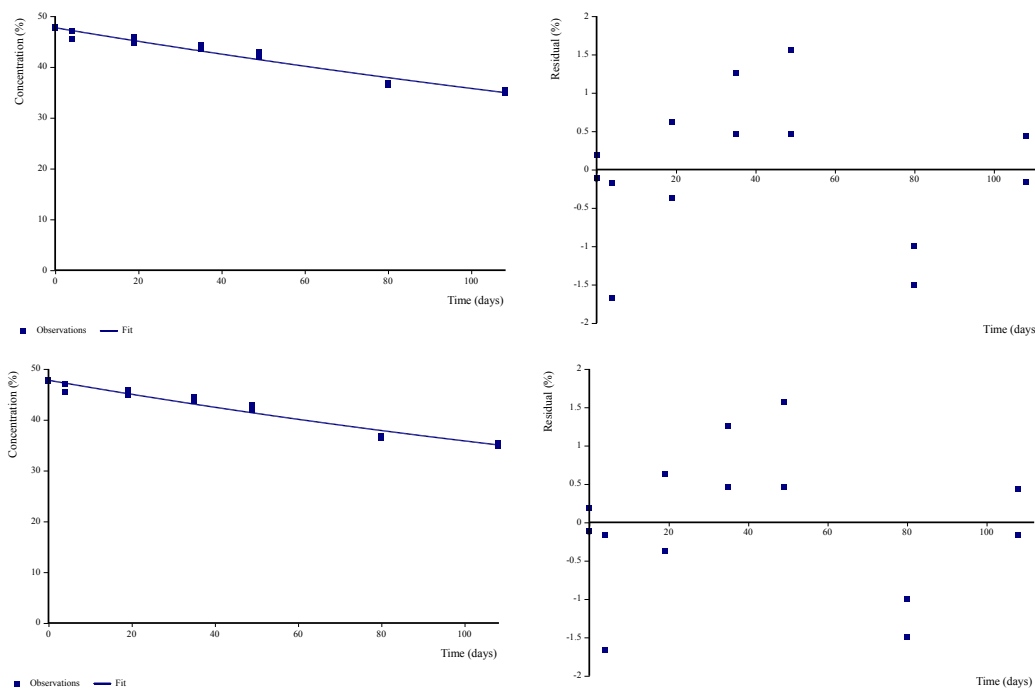


Figure 8.1.2.1.3/1-03: Model fits and residuals for the anaerobic degradation of cinmethylin in the North Dakota soil. Top row: SFO. Bottom row: FOMC. Final model fit: SFO.

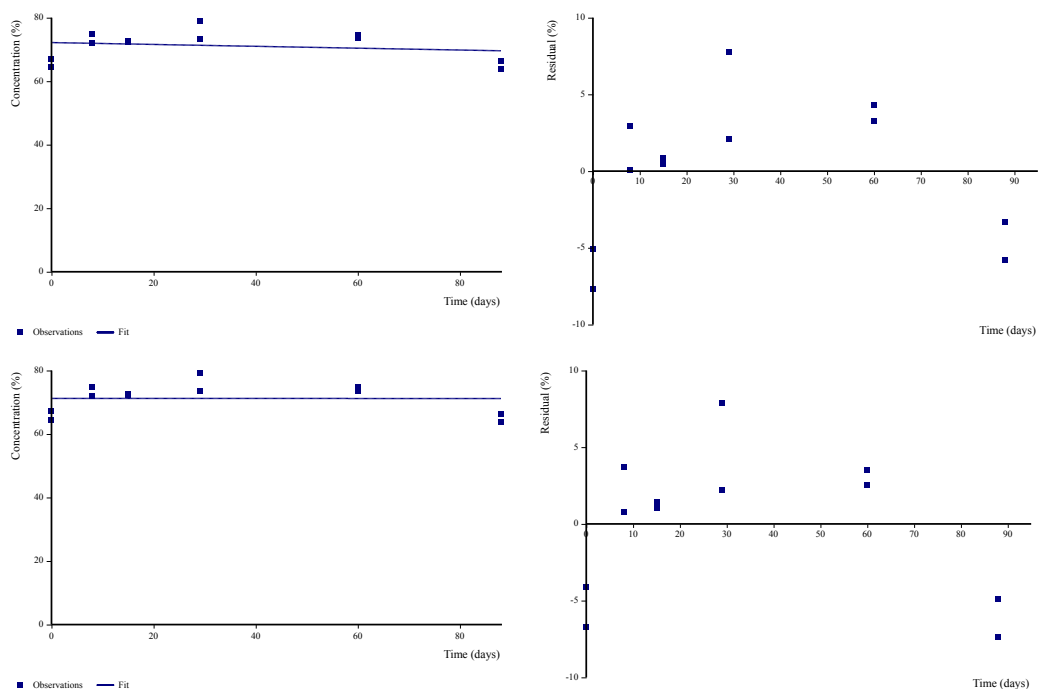


Figure 8.1.2.1.3/1-04: Model fits and residuals for the anaerobic degradation of cinmethylin in the Wyoming soil. Top row: SFO. Bottom row: FOMC. Final model fit: SFO.

CONCLUSIONS

Degradation of cinmethylin under anaerobic conditions was slow or remained stable. Kinetic evaluation of the anaerobic degradation rates submitted by the Applicant were rejected and the data re-evaluated by the HSE evaluator; no normalisation procedure was necessary as the experiment was conducted at a temperature of 20°C. Trigger endpoints were derived and are presented in Table 8.1.2.1.3/1-06.

Table 8.1.2.1.3/1-06: Calculated trigger endpoints for cinmethylin in four anaerobic soils in laboratory conditions

Cinmethylin	Dark anaerobic conditions (non-normalised trigger and persistence endpoints)							
Soil type	pH (H₂O)	pH (CaCl₂)	Temp °C	% MWHC	DT₅₀ (d)	DT₉₀ (d)	St. (χ²)	Method of calculation
Lufa 2.2	6.0	5.4	20	-	1710	5660	1.1	SFO
Lufa 5M	7.7	7.2	20	-	651	2160	0.608	SFO
LAD-SCL-PF	6.7	6.3	20	-	241	800	1.45	SFO
MSL-PF	8.3	8.1	20	-	1680	5570	4.62	SFO
Maximum (non-normalised)					1710	5660		

No major metabolites were observed; two minor metabolites (M684H001 and M684H004) were formed mainly during aerobic incubation, though amounts peaked at 4.8% and 2.7% AR respectively. The major sink for cinmethylin was formation of non-extractable residues, with maximum values ranging 15.0 – 41.2% AR, with NERs predominantly found in the humin fraction.

Chiral analysis indicated that the ratio of the two enantiomers changed during the aerobic incubation phase for three soils (Lufa 2.2, Lufa 5M, North Dakota), and then remained stable during the anaerobic phase. For one soil, Wyoming, the ratio remained stable throughout. The Applicant concluded that the change in ratio was due to different degradation rates for the two enantiomers; the HSE evaluator agrees with this conclusion and notes that the result is consistent with the conclusion of the aerobic degradation study (Stewart and Abernethy, 2016a).

B.8.1.2. Field Studies

B.8.1.2.1. Soil dissipation studies (Data Requirement 7.1.2.2.1)

Report:	CA 7.1.2.2.1/1 Gut, T. 2017a
Title	Field soil dissipation study of BAS 684 H in the formulation BAS 684 02 H on bare soil at 6 different sites in Northern and Southern Europe, 2015-2017
Document No.:	2017/1190305
Guidelines:	<ul style="list-style-type: none"> • SANCO/3029/99 rev. 4 (11 July 2000) • NAFTA Guidance Document for Conducting Terrestrial Field Dissipation Studies Regulatory Directive DIR2006-01 (March 2006), • EPA (environmental Protection Agency) US: Fate, Transport and Transformation Test Guidelines, OPPTS 835.6100, Terrestrial Field Dissipation, October 2008. • European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662.
GLP:	Yes
Deviations	None

Report:	CA 7.1.2.2.1/2 Gut, T. 2017b
Title	Amendment 1: Field soil dissipation study of BAS 684 H in the formulation BAS 684 02 H on bare soil at 6 different sites in Northern and Southern Europe, 2015-2017
Document No.:	2017/1217703
Guidelines:	<ul style="list-style-type: none"> • SANCO/3029/99 rev. 4 (11 July 2000) • NAFTA Guidance Document for Conducting Terrestrial Field Dissipation Studies Regulatory Directive DIR2006-01 (March 2006), • EPA (environmental Protection Agency) US: Fate, Transport and Transformation Test Guidelines, OPPTS 835.6100, Terrestrial Field Dissipation, October 2008. • European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662.
GLP:	Yes
Deviations	None

SUMMARY

The dissipation of cinmethylin in the formulation BAS 684 02 H (EC formulation) under field conditions was investigated at six sites in Europe representative of Northern and Southern EU conditions. One trial each was performed in Germany, Italy, Denmark, United Kingdom, Belgium and Spain. All sites represent typical regions of agricultural practice representative for growing crops including cereals which are among the most important crops for the use of cinmethylin. The trial sites consisted of an untreated and a treated plot, the latter being subdivided into 3 subplots that were assigned for replicates.

The product BAS 684 02 H, formulated as an emulsifiable concentrate (EC), was broadcast applied to bare soil in a single application at a nominal rate of 500 g a.s. ha⁻¹ using a target water volume of 100 – 400 L ha⁻¹. Applications were conducted in April and May 2015 for the two spring trials (Germany and Italy) and in September 2015 for the autumn trials (Denmark, UK, Belgium and Spain) using a calibrated boom sprayer. The actual application rates for each trial, determined by quantifying the amount of spray discharged, ranged from 483.8 to 512.8 g a.s. ha⁻¹, with an average of 488.3

(Denmark) to 509.6 (Belgium) g a.s. ha⁻¹, calculated based on the actual content of a.s. in the test item. Dose verification conducted via application monitors (petri dishes) yielded recovery values for the individual sites ranging from 97.7 to 118% of the target rate for enantiomer Reg. No. 5925581 and between 102 and 129% of the target rate for enantiomer Reg. No. 5925632.

Immediately after application of the test item, the plots were harrowed to incorporate the test item into the soil to approx. 4-10 cm depth to protect the applied product from surface processes like photolysis or volatilization, and to exclude any potential impact on the degradation of the test item caused by any of these processes.

No tillage or fertilization was performed during the study and no crops were grown throughout any of the trials. The plots were kept free of vegetation via the application of glyphosate and in one case (Germany) with pelargonic acid to keep the plot free of moss growth.

Actual weather data was collected at each test site. No additional irrigation was performed to supplement natural rainfall.

Soil specimens were taken at intervals up to 538 days after application (spring trials in Germany and Italy) or up to 420 days after application (autumn trials in Denmark, UK, Belgium and Spain) and down to a maximum soil depth of 50 cm. Soil cores were cut into 10 cm sections. Soil segments of the same depth and subplot from a defined sampling event were pooled and homogenised and a representative sub-specimen of each depth was taken for residue analysis. All soil specimens were stored at about -18°C within a maximum of 6 hours and 12 minutes after sampling and remained frozen until analysis. The HSE evaluator notes that the longest time period from sampling to analysis (date of extraction) of the field soil specimens was 545 days. The results from the storage stability study shows that cinmethylin is stable over a period of at least 715 days when stored in the dark at -18°C

In order to demonstrate stability of the residues in soil during storage and shipment, shipment verification specimens were prepared at selected sampling occasions by fortifying untreated soil from the field sites with known amounts of cinmethylin. These specimens were stored and shipped under the same conditions as the actual residue specimens. Analysis of the shipping verification specimens on cinmethylin yielded average recovery values, corrected for procedural recovery, of 96.9-106% for enantiomer Reg. No. 5925581 and of 101-113% for enantiomer Reg. No. 5925632 across all sites confirming residue stability during all storage and shipment procedures.

Soil specimens were analysed for cinmethylin (BAS 684 02 H). The two enantiomers Reg. No. 5925581 and Reg. No. 5925632 contained in the test item were analysed and are reported separately and as sum in the results tables. The analytical method involved extraction of the soil with acetonitrile in a first step and acetonitrile / water (60/40, v/v) in a second step. The combined liquid phases, diluted to measuring concentration if necessary, were analysed by LC-MS/MS with a limit of quantification (LOQ) of 0.005 mg/kg for each analyte. Field soil specimens from the treated plot were analysed down to a depth until at least one consecutive soil segments were free of quantifiable residues (< LOD). Analysis was performed until a maximum of 538 days after application (DAA). Application monitors (Petri dish specimens) and shipping verification specimens were analysed for cinmethylin using the same analytical method.

Residue values of cinmethylin in mg/kg dry soil were converted to residue rates in g ha⁻¹ and were summed up for all depths between 0 and 50 cm analysed. Residue values were not corrected for procedural recoveries except for results obtained from petri dish and shipment verification analysis.

Cinmethylin degraded moderately fast under field conditions in soil at all six European field sites. For enantiomer Reg. No. 5925581, the total residues in the soil profiles decreased from an average of 192.3 g ha⁻¹ at day 0 to residues below 5 g ha⁻¹ within 18 months. For enantiomer Reg. No. 5925632, the total residues in the soil profiles decreased from an average of 205.5 g ha⁻¹ at day 0 to residues

below 5.7 g ha⁻¹ within 18 months. For the a.s. cinmethylin (sum of both enantiomers), the total residues in the soil profiles decreased from an average of 398.5 g ha⁻¹ at day 0 to residues below the 10.4 g ha⁻¹ within 18 months. DT₅₀ values for modelling and trigger endpoints are calculated within He, W. and Pape, L. (2018a, CA 7.1.2.2.1/03) and He, W. and Pape, L. (2018b, CA 7.1.2.2.1/04) respectively.

Residues of cinmethylin in the soil profiles were exclusively detected at concentrations above the LOQ in the upper 20 cm of the soils. No residues above the LOQ were detected below 20 cm in any specimen at any time. Altogether, it can be concluded that cinmethylin does not show any significant tendency to move into deeper soil layers indicating low potential for cinmethylin residues to leach to groundwater.

I. MATERIAL AND METHODS

A. MATERIALS

1. Test Material

Test item (formulation):	BAS 684 02 H
Active ingredient:	cinmethylin
	The active ingredient consists of the two enantiomers Reg. No. 5925581 and Reg. No. 5925632 as racemate in a ratio of 50:50
Chemical name (IUPAC):	(1S,2R,4R)-1-methyl-2-[(2-methylbenzyl)oxy]-4-(propan-2-yl)-7-oxabicyclo[2.2.1]heptane
Molar mass:	274.4 g mol ⁻¹
Batch No.:	FD-150116-0001 (containing 744.3 g cinmethylin L ⁻¹)
Type of formulation:	EC
Density of formulation:	1.019 g/cm ³

2. Test sites

The dissipation of cinmethylin under field conditions was investigated at six sites in Europe representative of Northern and Southern EU conditions. One trial each was performed in Germany, Italy, Denmark, United Kingdom, Belgium and Spain. The homogeneity of the upper soil layer was verified prior to the start of the trials. The site characteristics including soil taxonomy, the basic soil parameters of the corresponding soil horizons as well as soil bulk density in 10-20 cm depth are presented in Table 8.1.2.2.1-1 to Table 8.1.2.2.1-3. All sites represent typical regions of agricultural practice representative for growing cereals which is among the most important crops for the use of cinmethylin. No product containing the test item a.s. had been used on the test plots in the last three years. The trial sites consisted of an untreated and a treated plot, the latter being subdivided into 3 subplots that were assigned for replicates.

Table 8.1.2.2.1-1: Characteristics of the trial sites used to investigate the field dissipation of cinmethylin

Trial	15/03314437-01			15/03314437-02	
Location	Höltinghausen, Germany			Dugliolo di Budrio, Italy	
Soil properties	0 - 15 cm	15 - 35 cm	35 - 50 cm	0 - 20 cm	20 – 41 cm ^d
Soil class (DIN 4220)	Poor silty sand (Su2)	Poor silty sand (Su2)	Poor silty sand (Su2)	High loamy sand (Sl4)	High loamy sand (Sl4)
sand [%]	81.0	80.3	85.1	47.1	48.5
silt [%]	16.3	16.3	12.6	39.6	37.9
clay [%]	2.8	3.3	2.3	13.3	13.5
Soil class (USDA)	Loamy fine sand	Loamy fine sand	Fine sand	Very fine sandy loam	Very fine sandy loam
sand [%]	83.9	83.9	88.1	52.8	54.3
silt [%]	12.8	13.0	9.2	33.7	32.3
clay [%]	3.3	3.2	7.7	13.5	13.4
Total organic C [%]	0.67	0.68	0.17	0.65	0.64
Organic matter [%] ^a	1.16	1.17	0.29	1.12	1.10
pH [CaCl ₂]	4.80	4.83	5.60	7.66	7.73
pH [H ₂ O]	5.30	5.32	6.36	8.48	8.56
CEC [mval Ba 100 g ⁻¹ dry weight]	6.4	6.5	3.0	8.5	8.5
MWHC [g 100 g ⁻¹ dry weight]	32.6	33.0	28.0	42.1	35.7
WHC at pF 2.0 [g 100 g ⁻¹ dry weight] ^b	12.9	12.9	11.9	26.2	28.2
WHC at pF 2.5 [g 100 g ⁻¹ dry weight] ^b	7.3	7.1	5.4	17.6	20.1
Dry bulk density [g cm ⁻³] ^c	1.31	-	-	1.48	-
Soil taxonomy	Gleyic Cambisol			Calcaric Cambisol	

^a organic matter = organic carbon x 1.724^b water retention characteristics, soil moisture at 0.1 (pF2) or 0.33 bar (pF2.5)^c specimens taken at 10-15 cm depth (mean of 3 replicates)^d liners filled to different depths between 31.5 and 41 cm

CEC = cation exchange capacity

MWHC = maximum water holding capacity

Table 8.1.2.2.1-2: Characteristics of the trial sites used to investigate the field dissipation of cinmethylin

Trial	15/03314437-03		15/03314437-04	
Location	Røllum, Denmark		Banbury, UK	
Soil properties	0 - 30 cm	30 - 50 cm	0 - 25 cm	25 - 50 cm
Soil class (DIN 4220)	Pure sand (Ss)	Pure Sand (Ss)	Poor clay loam	Poor clay loam
sand [%]	88.5	94.4	(Lt2)	(Lt2)
silt [%]	7.7	3.5	28.6	26.2
clay [%]	3.8	2.1	45.3	45.4
			26.2	28.4
Soil class (USDA)	Sand	Sand	Loam	Clay loam
sand [%]	89.6	95.0	31.4	29.2
silt [%]	6.2	2.7	42.3	42.2
clay [%]	4.2	2.3	26.3	28.6
Total organic C [%]	1.13	0.60	2.26	0.80
Organic matter [%] ^a	1.95	1.03	3.90	1.38
pH [CaCl ₂]	4.62	4.82	6.70	6.99
pH [H ₂ O]	5.36	5.51	7.44	7.86
CEC [mval Ba 100 g ⁻¹ dry weight]	9.2	6.8	27.1	19.7
MWHC [g 100 g ⁻¹ dry weight]	31.0	27.6	59.7	47.8
WHC at pF 2.0 [g 100 g ⁻¹ dry weight] ^b	12.9	10.3	40.7	39.6
WHC at pF 2.5 [g 100 g ⁻¹ dry weight] ^b	7.4	4.8	30.3	31.6
Dry bulk density [g cm ⁻³] ^c	1.46	-	1.08	-
Soil taxonomy	glacial meltwater washouts – sand and gravel		well drained brashy fine and coarse loamy ferruginous soils over ironstone	

^a organic matter = organic carbon x 1.724^b water retention characteristics, soil moisture at 0.1 (pF2) or 0.33 bar (pF2.5)^c specimens taken at 10-15 cm depth (mean of 3 replicates)

CEC = cation exchange capacity

MWHC = maximum water holding capacity

Table 8.1.2.2.1-3: Characteristics of the trial sites used to investigate the field dissipation of cinmethylin

Trial	15/03314437-05		15/03314437-06	
Location	Saint-Amand, Belgium		Almayate, Spain	
Soil properties	0 - 30 cm	30 - 50 cm	0 - 25 cm	25 - 50 cm
Soil class (DIN 4220)	Pure silt (Uu)	Poor clay silt (Ut2)	Medium loamy sand (Sl3)	Medium loamy sand (Sl3)
sand [%]	6.2		70.5	66.3
silt [%]	87.8	5.7	18.4	22.2
clay [%]	6.0	83.3 11.0	11.1	11.5
Soil class (USDA)	Silt	Silt	Coarse sandy loam	Coarse sandy loam
sand [%]	9.4	8.4	71.4	67.3
silt [%]	83.9	80.4	17.6	20.7
clay [%]	6.7	11.2	11.0	12.0
Total organic C [%]	1.45	0.04	1.43	0.42
Organic matter [%] ^a	2.50	0.07	2.47	0.72
pH [CaCl ₂]	6.12	6.31	7.70	7.79
pH [H ₂ O]	6.83	7.12	8.47	8.72
CEC [mval Ba 100 g ⁻¹ dry weight]	13.9	11.9	8.6	7.4
MWHC [g 100 g ⁻¹ dry weight]	63.9	53.6	45.6	40.1
WHC at pF 2.0 [g 100 g ⁻¹ dry weight] ^b	32.1	35.1	17.0	17.5
WHC at pF 2.5 [g 100 g ⁻¹ dry weight] ^b	25.2	25.3	14.1	15.0
Dry bulk density [g cm ⁻³] ^c	1.45	-	1.21	-
Soil taxonomy	wet (moist limestone soils)		holocene quaternary alluvial sediments	

^a organic matter = organic carbon x 1.724^b water retention characteristics, soil moisture at 0.1 (pF2) or 0.33 bar (pF2.5)^c specimens taken at 10-15 cm depth (mean of 3 replicates)

CEC = cation exchange capacity

MWHC = maximum water holding capacity

B. STUDY DESIGN

1. Experimental conditions

The trial area at each site was divided into two plots, one untreated control plot (size: 22.5 – 54 m²) and one treated plot (size: 337.5 – 564 m²). The untreated control plot was subdivided into three subplots of equal size. The treated plot also consisted of three equal sized subplots A, B and C that were assigned for replicates. Each of the three treated subplots was subdivided into 15 subplots of equal size and two buffer strips at each end. The width of the treated subplots was 3 m, except for trial 15/03314437-05, where the width of the subplots was 4 m, and adapted to the size of the spraying boom used. The buffer strips at beginning and end of each treated subplot were treated with the test item but were not sampled.

The distance between the treated subplots was at least 3 m, the distance between treated and untreated plot at least 10 m. The sites were flat without any significant slope.

The product, formulated as an emulsifiable concentrate (EC), was broadcast applied to bare soil in a single application at a nominal rate of 500 g a.s. ha⁻¹ using a target water volume between 300 and 400 L ha⁻¹. Applications were conducted in April and May 2015 (trials 15/03314437-01 and 15/03314437-02) and in September 2015 (trials 15/03314437-03 to 15/03314437-06) using a calibrated boom sprayer. Treated plots were three-fold replicated with subplot size ranging from 112.5 to 188 m². For each treated replicate, a separate spray mixture was prepared, and the test item was applied to each subplot individually. Each spray mixture was visually checked for homogeneity and small aliquots of the spray mixture were taken before and after application of each individual subplot for later analysis.

The actual application rates determined by quantifying the amount of spray discharged ranged from 490.5 to 509.6 g a.s. ha⁻¹ averaged over the three replicates of each treated plot. In addition, the dose was verified by means of sampling Petri dishes filled with top soil of the respective sites (approximately 50 g per dish, sieved to 2 mm). The petri dishes were placed on the treated plot (ten in each subplot) before application and analysed thereafter. Details of the application are presented in Table 8.1.2.2.1-4.

Immediately after application of the test item and before subsequent soil sampling, the treated replicates were harrowed to incorporate the test item in the soil to minimize the impact of surface processes (e.g. photolysis, volatilization) on the DegT₅₀. The incorporation was conducted mechanically by or using power harrows or rotary harrows pulled by tractors. The incorporation depth was between 4 -10 cm.

No tillage or fertilization was performed during the study from first to last sampling and no crops were grown throughout any of the trials. The plots were kept free of vegetation via the application of glyphosate.

Table 8.1.2.2.1-4: Application parameters of field trial sites treated with BAS 684 02 H (EC)

Trial Country	Application Method	No. of applications	Subplot (m ²)	Application rate per treatment				Application date
				nominal [g a.s. ha ⁻¹]	actual ^a [g a.s. ha ⁻¹]	dose verification ^b		
						[g a.s ha ⁻¹]	% of nominal	
15/033144 37-01 Germany	broadcast spray to bare soil	1	A (120)	500	512.8	219 + 237	85.5 + 92.5	21-April-2015
			B (120)	500	509.8	271 + 306	106 + 120	
			C (120)	500	500.2	253 + 300	101 + 120	
			Average	500	507.6	248 + 281	97.7 + 111	
15/033144 37-02 Italy	broadcast spray to bare soil	1	A (118.5)	500	497.9	259 + 296	104 + 119	07-May-2015
			B (118.5)	500	492.0	258 + 290	105 + 118	
			C (118.5)	500	493.5	261 + 296	106 + 120	
			Average	500	494.5	259 + 294	105 + 119	
15/033144 37-03 Denmark	broadcast spray to bare soil	1	A (156)	500	489.7	251 + 281	101 + 113	29-Sep-2015
			B (156)	500	491.2	239 + 266	97.3 + 108	
			C (156)	500	483.8	265 + 290	107 + 118	
			Average	500	488.3	252 + 279	102 + 113	
15/033144 37-04 UK	broadcast spray to bare soil	1	A (118.5)	500	492.7	283 + 308	113 + 124	23-Sep-2015
			B (118.5)	500	497.9	310 + 337	126 + 137	
			C (118.5)	500	500.2	285 + 307	115 + 124	
			Average	500	496.9	293 + 318	118 + 129	
15/033144 37-05 Belgium	broadcast spray to bare soil	1	A (188)	500	512.8	257 + 278	103 + 112	29-Sep-2015
			B (188)	500	511.3	276 + 297	112 + 121	
			C (188)	500	504.6	268 + 287	109 + 116	
			Average	500	509.6	267 + 287	108 + 116	
15/033144 37-06 Spain	broadcast spray to bare soil	1	A (112.5)	500	483.8	241 + 238	96.6 + 95.6	16-Sep-2015
			B (112.5)	500	489.7	244 + 254	99.1 + 103	
			C (112.5)	500	497.9	241 + 264	97.8 + 107	
			Average	500	490.5	242 + 252	97.9 + 102	

^a determined by calculation of spray liquid applied, taking actual content of a.s. in test item into account.

^b determined by means of petri dishes filled with soil; values for both enantiomers Reg. No. 5925581 and Reg. No. 5925632 given separately.

Actual weather data are based on records of appropriate weather stations located on-site. Monthly summary results on temperature and precipitation are presented in Table 8.1.2.2.1-5. No additional irrigation was necessary. The Applicant states that only in case of precipitation of less than 10 mm within 4 weeks would irrigation be needed. However, precipitation within four-week intervals always exceeded 10 mm. No additional irrigation to supplement rainfall was done during the study from application until last sampling at any trial.

Historical (long-term) weather data on precipitation and average air temperature from at least 10 years were taken from official or other available weather stations located nearby (<1 - 17 km distance to trial site). The historical and actual data, each averaged over the complete duration of the individual trials, are presented in Table 8.1.2.2.1-6. The actual air temperature recorded at the field sites during the study period was similar to the historic values, with a difference of 1.1 °C or less between historic temperature and average temperature during the study period. The precipitation amounts during the study period differed from the historic averages. The trials 15/03314437-01 (Germany), 15/03314437-03 (Denmark, 15/03314437-04 (UK) and 15/03314437-06 (Spain) were dryer than usual, whereas the sites of trials 15/03314437-02 (Italy) and 15/03314437-05 (Belgium) were wetter than usual.

Table 8.1.2.2.1-5: Summary of climatic conditions at field sites used to investigate the dissipation of cinmethylin

Trial	15/03314437-01		15/03314437-02	
Location	Höltinghausen		Dugliolo di Budrio	
	Germany		Italy	
Climatic conditions	T_{mean} Air [°C]	Prec. [mm]	T_{mean} Air [°C]	Prec. [mm]
Month		Σ		Σ
Apr 2015	9.1	13.2	-	-
May 2015	11.7	39.0	18.5	53.4
Jun 2015	14.9	32.8	22.4	50.4
Jul 2015	18.1	128.4	26.9	0.2
Aug 2015	18.7	118.0	24.7	44.6
Sep 2015	13.2	62.2	19.8	57.0
Oct 2015	9.1	58.4	13.7	186.6
Nov 2015	8.6	161.2	8.6	50.4
Dec 2015	8.7	47.8	4.4	2.6
Jan 2016	1.6	59.2	3.3	37.4
Feb 2016	3.4	121.2	7.2	179.4
Mar 2016	4.6	61.0	9.4	76.0
Apr 2016	7.9	67.6	14.2	40.2
May 2016	14.3	24.4	17.1	121.4
Jun 2016	17.2	34.8	21.5	119.6
Jul 2016	16.8	29.0	25.3	17.8
Aug 2016	17.4	11.1	23.4	48.3
Sep 2016	17.5	11.1	20.8	79.6
Oct 2016	9.7	8.2	13.4	126.6
Total	Mean: 11.7	Sum: 1088.6	Mean: 16.4	Sum: 1291.5

Trial	15/03314437-03		15/03314437-04		15/03314437-05		15/03314437-06	
Location	Røllum		Banbury		Saint-Amand		Almayate	
	Denmark		UK		Belgium		Spain	
Climatic conditions	T_{mean} Air [°C]	Prec. [mm]	T_{mean} Air [°C]	Prec. [mm]	T_{mean} Air [°C]	Prec. [mm]	T_{mean} Air [°C]	Prec. [mm]
Month		Σ		Σ		Σ		Σ
Sep 2015	9.4	0.0	11.7	0.0	11.4	0.0	21.6	9.2
Oct 2015	9.8	58.4	10.6	53.8	9.8	38.2	20.0	86.6
Nov 2015	7.8	153.2	9.3	47.0	9.4	95.6	16.7	48.8
Dec 2015	7.3	113.4	9.2	77.1	9.0	73.8	14.4	0.2
Jan 2016	0.9	54.2	9.2	66.9	4.5	87.4	13.9	32.2
Feb 2016	2.9	8.6	3.3	24.9	4.5	98.6	14.0	19.8
Mar 2016	4.0	9.2	5.0	22.4	5.0	31.0	14.5	15.8
Apr 2016	6.4	10.6	6.8	62.4	8.3	65.0	16.6	44.8
May 2016	12.7	46.0	12.0	39.4	13.9	43.4	18.5	45.8
Jun 2016	16.2	132.4	14.4	63.4	16.2	178.4	22.2	0.0
Jul 2016	15.0	51.0	16.6	22.8	18.7	36.0	24.9	0.6
Aug 2016	15.9	60.8	16.9	47.6	18.5	52.4	25.4	0.2
Sep 2016	16.0	55.2	15.4	45.6	17.5	14.8	23.2	0.8
Oct 2016	9.3	74.0	10.1	24.6	9.5	35.6	20.1	60.0
Nov 2016	2.8	36.4	5.0	26.2	6.7	63.0	18.0	2.4
Total	Mean: 9.1	Sum: 863.4	Mean: 10.4	Sum: 624.1	Mean: 10.9	Sum: 913.2	Mean: 18.8	Sum: 367.2

Weather data refer to time period from start of trial (day of application) until end of trial (last sampling events)
Prec. – precipitation

Table 8.1.2.2.1-6: Summary of historical and actual weather data at field trial sites averaged over entire trial duration

Trial Country	T _{mean} Air [°C] (average over trial period)		Precipitation [mm] (sum over trial period)		Sum of actual precipitation [mm]	% of historic precipitation
	Historic ^a	Actual	Historic ^a	Actual		
15/03314437-01 Germany	11.3	11.7	1202.4	1088.6	1088.6	91
15/03314437-02 Italy	15.74	16.4	950.83	1291.5	1291.5	136
15/03314437-03 Denmark	9.3	9.1	1065.0	863.4	863.4	81
15/03314437-04 UK	10.3	10.4	757.2	624.1	624.1	82
15/03314437-05 Belgium	9.8	10.9	812.0	913.2	913.2	112
15/03314437-06 Spain	18.1	18.8	697.2	367.2	367.2	53

^a at least over ten years

The HSE evaluator notes that the trial location in Spain (15/03314437-06) only had 53 % precipitation of historic levels and questions whether the site should have been irrigated. However, the site is drier than previous years and so the degradation of BAS 684 02 H would be slower than in wetter conditions. Because this would result in a longer DT₅₀ and a more conservative endpoint, the HSE evaluator considers the site selection acceptable.

No product containing the test item a.s. has been used on the test plots in the last three years. The applicant presented the crop and pesticide history of the trial sites for three years and the HSE evaluator can confirm that cinmethylin was not used on the test sites during this time. The pesticides that were used did not have the same mode of action or common metabolites to cinmethylin.

2. Sampling

Replicate soil specimens (10 per treated subplot and 10 or 15 per control plot) were taken at intervals up to 538 days and down to a maximum soil depth of 50 cm. At day 0, immediately after application, and at all following sampling events, the treated plots were sampled down to a depth of 50 cm. The detailed sampling intervals are presented in Table 8.1.2.2.1-7.

Table 8.1.2.2.1-7: Summary of sampling intervals at each field trial site

Trial	Country	Sampling intervals [days after application]
15/03314437-01	Germany	-1, 0, 6, 14, 29, 62, 90, 121, 176, 238, 303, 413, 538
15/03314437-02	Italy	-1, 0, 7, 13, 28, 60, 90, 119, 181, 245, 312, 413, 536
15/03314437-03	Denmark	-8, 0, 7, 14, 29, 58, 85, 122, 176, 245, 293, 414
15/03314437-04	UK	-1, 0, 6, 16, 28, 63, 86, 119, 177, 247, 301, 413
15/03314437-05	Belgium	-5, -1, 0, 6, 14, 30, 58, 85, 119, 176, 239, 300, 420
15/03314437-06	Spain	-6, 0, 6, 14, 28, 62, 89, 118, 181, 239, 301, 420

Untreated specimens were collected from the control plot on two occasions (trials 15/03314437-01 and 15/03314437-02), at one day before application down to a depth of 50 cm, and after about one year to a depth of 10 cm. At trials 15/03314437-03 to 15/03314437-06, the control plot was sampled only

once, between 8 and 1 days before application down to a depth of 50 cm. The specimens were taken from the assigned subplot of the treated plot each time and pooled to one specimen per sampling event. The 15 cores collected at the first sampling interval were taken using a common soil probe equipped with a plastic liner of 4.6 cm diameter in all trials except trial 15/03314437-04, where the diameter was 4.4 cm. The 10 cores taken after about one year were collected with a metal tube of minimum 11.0 cm diameter.

Treated soil specimens were taken randomly from ten points of each of the three treated subplots A – C and pooled according to subplot and depth. After sampling, the remaining holes were filled with untreated soil from outside the plots.

In addition to the main sampling, a second complete sampling (double sampling) was carried out for all residue and control soil specimens. The double specimens were generally stored and shipped under the same conditions as the main specimens, but care was taken that the double specimens were not transported in the same freezer trucks and at the same time than the main specimens.

All soil specimens intended for residue analysis were placed into freezer storage at about -18°C within less than 6 hours of being taken, with a few exceptions, where this limit was exceeded to a maximum of 6 hours and 12 minutes. They remained frozen at about -18°C or below until shipment to the test facility. Shipment to the test facility took place in a freezer truck.

Upon arrival at the test facility, all soil specimens were immediately placed in a freezer storage area maintained at temperatures around or below -18 C and kept at this temperature until processing or shipment to the analytical laboratory.

Processing was conducted in frozen state. The frozen soil segments were weighed and segmented into 10 cm segments (except 0-10 cm specimens, which were weighed and directly homogenised). Segmentation was conducted with a circular buzz saw, and care has been taken to avoid contamination. Segments of the same sampling event, subplot and soil depth were combined in a polyethylene bag, double bagged and the pooled specimen was labeled. The remains of the plastic liners were disposed of. Then, the pooled specimens of each 10 cm segment were weighted again after segmentation. The segmentation was done in a time period short enough so that defrosting of the specimens could be avoided, and if necessary, dry ice was added on top of the soil liners. Additional material below 50 cm soil segments was discarded.

Subsequently, the specimens were stored at temperatures around or below -18 C again until further processing for homogenisation of the specimens. The specimens were homogenised by grinding in a STEPHAN mill together with dry ice to keep the specimens frozen. Afterwards, the specimens were mixed further if necessary by use of either a kitchen blender or concrete mixer, depending on the amount of the specimen. If larger stones (>2 cm in diameter) were visible, they were removed from the bulk specimen before the homogenisation process. If that was the case, the weight of the removed specimens was recorded. After grinding and mixing, representative aliquots of the homogenised soil segments were packed as separate sub-specimens into appropriately labelled plastic containers (two containers of 500 mL and remaining specimen material in an additional bag per specimen). The specimens were further stored at temperatures around or below -18 C until shipment to the analytical laboratory.

3. Shipment verification

At nominal sampling events 0 DAA, 30 DAA and 90 DAA, shipping verification specimens were prepared at all field test sites to demonstrate stability of the residues in soil during storage and through any shipping process. 20 g specimens of top soil from the untreated control plot were weighed into four glass bottles. Three of them were dosed with 0.5 or 1 mL of a solution containing cinmethylin

with a concentration of 12 µg/mL (both enantiomers in a ratio of 50:50). The fourth bottle with soil remained untreated as control specimen.

The analytical results demonstrated no losses from the shipping verification specimens. The average amount of cinmethylin from the spiked field specimens was between 88.3 and 119 % across all trials. It was concluded that cinmethylin was stable in all soils under the storage and shipping conditions used. Storage stability of cinmethylin in frozen soil is investigated in a separate study [see CA 7.1.2.2.1/7 2017] with soils originating from the individual trial sites of the present terrestrial field dissipation study.

4. Description of analytical procedure

Field soil specimens were analysed for cinmethylin. The analytical method involved extraction of the soil with acetonitrile in a first step and acetonitrile / water (60/40, v/v) in a second step. The combined liquid phases, diluted to measuring concentration if necessary, were analysed by LC-MS/MS with a limit of quantification (LOQ) of 0.005 mg/kg for each individual enantiomer. The limit of detection (LOD) was set at 0.0015 mg/kg (30% of LOQ).

Analysis of field soil specimens originating from the treated plots was conducted down to a depth until at least one consecutive soil segment was free of quantifiable residues (< LOD). Analysis was performed up to a maximum of 540 days after application (DAA). For all trials, double specimens of the 0-10 soil layer were analysed as well. If deviations higher than 30% occurred between the residues of main and double specimen the results were verified by an additional duplicate analysis of each of the specimens. In order to determine the variation between main and double specimens, the larger of the two residue values was set as 100%. Mean values of the 0-10 cm layer were calculated by:

- 1) Averaging multiple determinations of main and double specimen separately,
- 2) Mean of all single values of main and double specimen.

If questionable results occurred in any of the field soil specimens it was re-analysed in duplicate. If the results were still inconclusive the double specimen was analysed additionally.

II. RESULTS AND DISCUSSION

Spray solution

Spray mixtures were sampled before and after application of each subplot and analysed for cinmethylin. Each specimen was analysed in triplicate. The specimens were analysed for the two enantiomers Reg. No. 5925581 and Reg. No. 5925632 and the results were reported for both enantiomers separately, see Table 8.1.2.2.1-8.

Table 8.1.2.2.1-8: Summary of the recoveries of the spray application mixtures analysed for Reg. No. 5925581 and Reg. No. 5925632.

	Recoveries of the spray application (%)	
	Reg. No. 5925581	Reg. No. 5925632
15/03314437-01 (Germany)	61.8 – 85.0	67.8 – 89.4
15/03314437-02 (Italy)	64.8 – 77.4	72.4 – 81.5
15/03314437-03 (Denmark)	84.5 – 90.0	95.2 – 101
15/03314437-04 (United Kingdom)	67.9 – 85.9	75.6 – 90.7
15/03314437-05 (Belgium)	41.5 – 49.2	51.3 – 60.1
15/03314437-06 (Spain)	48.6 – 65.5	55.5 – 70.1

The low recoveries of the spray mixture stand in contradiction to the recoveries of the application verification (petri dish) specimens, where the recoveries of all trials proved the correct rate of application and the 0 DAA residue results which are in agreement with the anticipated expected ones.

The study report stated that the low recoveries of the spray mixture may be due to the long storage period from sampling until analysis (611 days) combined with freezing storage conditions.

Application verification

Procedural recovery experiments were conducted. Mean recoveries of each analysed set of specimens for cinmethylin ranged from 97.4 – 105 % for Reg. No. 5925581 and 97.2 – 105 % for Reg. No. 5925632 across all trials.

Residue levels of cinmethylin achieved on extraction and analysis of the application monitors (Petri dishes filled with soil) were corrected for the mean procedural recovery of the respective analytical set and converted into residue rates (in g/ha) taking into account the area of the Petri dishes (91.6 cm²). The obtained rates for the individual trials ranged from 219-310 g/ha representing 85.5 – 126 % of the target application rate for enantiomer Reg. No. 5925581 and from 237 – 337 g/ha representing 92.5 – 137 % of the target application rate for enantiomer Reg. No. 5925632.

Residues in field soil specimens

Untreated soil specimens (control specimens) of the respective soil depths from each trial were analysed for residues of Reg. No. 5925581 and Reg. No. 5925632. No residues above the LOD of any analyte were detected in any of the control specimens proving that there were no interferences of the untreated soil material with the analytical procedures used. A peak in the chromatogram for a sample <LOD was questioned by the HSE evaluator. However, the applicant highlighted that the peak was also observed for the control sample at this retention time. The retention time of the peak also does not exactly match the reference substance. The HSE evaluator agrees that the peak is regarded as background and not test substance related.

Procedural recovery experiments performed with untreated field soil specimens spiked with a mix of the two analytes at concentration levels of 0.005 to 0.5 mg/kg yielded overall mean recovery rates for the individual analytes between 95.5 and 96.9%, confirming the validity of the analytical method used in this study. A summary of the individual procedural recovery results is provided in the actual study report. These data prove that the analytical method applied was able to accurately determine residues of cinmethylin in soil specimens down to a concentration of 0.005 mg/kg for each analyte.

Field soil specimens from the treated plots were analysed down to a depth until at least one soil segment was free of quantifiable residues (< LOD of 0.0015 mg/kg, maximum depth of 50 cm).

For all trials, double specimens of the 0-10 soil layer were analysed as well. If deviations higher than 30% occurred between the residues of main and double specimen the results were verified by an additional duplicate analysis of each of the specimens. Mean values for the 0-10 cm layer were calculated by:

- 1) Averaging multiple determinations of main and double specimen separately
- 2) Mean of all single values of main and double specimen

Mean value calculations were done down to the LOD level. Generally, if questionable results occurred in any of the field soil specimens it was re-analysed in duplicate. If the results were still inconclusive the double specimen was analysed additionally.

The analytical average results are summarised in Table 8.1.2.2.1-9 to Table 8.1.2.2.1-20. All residue values presented in these tables are related to the dry weight of the soil and are not corrected for procedural recoveries. Residue levels of the analyte in mg/kg dry soil were converted to residue rates in g ha⁻¹ taking into account the actual dry soil density of the field specimens and were summed up for all depths between 0 and 50 cm if analysed. In Table 8.1.2.2.1-21 to Table 8.1.2.2.1-26 the sum in g ha⁻¹ of the enantiomers Reg. No. 5925581 and Reg. No. 5925632 is presented.

Table 8.1.2.2.1-9: Summary of cinmethylin enantiomer Reg. No. 5925581 residues in treated soil specimens of trial 15/03314437-01 (Höltinghausen, Germany) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-01											
Sampling No.	8	9	10	11	13	14	16	17	18	20	21	22
DAA	0	6	14	29	62	90	121	176	238	303	413	538
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b											
0 – 10	170.7 ^a	124.5 ^a	137.4 ^a	92.2 ^a	64.0 ^a	40.5 ^a	13.6 ^a	6.6 ^a	12.6 ^a	6.5 ^a	3.9 ^a	2.2 ^a
10 – 20	3.9	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	174.6	124.5	137.4	92.2	64.0	40.5	13.6	6.6	12.6	6.5	3.9	2.2
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b											
0 – 10	192.6 ^a	154.8 ^a	130.7 ^a	114.8 ^a	68.3 ^a	51.2 ^a	25.5 ^a	11.3 ^a	15.0 ^a	9.6 ^a	5.5 ^a	2.2 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	192.6	154.8	130.7	114.8	68.3	51.2	25.5	11.3	15.0	9.6	5.5	2.2
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b											
0 – 10	262.9 ^a	161.1 ^a	168.6 ^a	133.1 ^a	59.2 ^a	43.0 ^a	27.3 ^a	19.0 ^a	12.8 ^a	10.3 ^a	8.6 ^a	0 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	262.9	161.1	168.6	133.1	59.2	43.0	27.3	19.0	12.8	10.3	8.6	0

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-10: Summary of cinmethylin enantiomer Reg. No. 5925632 residues in treated soil specimens of trial 15/03314437-01 (Höltinghausen, Germany) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-01											
Sampling No.	8	9	10	11	13	14	9	16	17	18	20	21
DAA	0	6	14	29	62	90	121	176	238	303	413	538
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	182.5 ^a	139.8 ^a	160.1 ^a	114.8 ^a	89.7 ^a	60.6 ^a	25.1 ^a	11.9 ^a	20.1 ^a	11.8 ^a	6.3 ^a	2.7 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	182.5	139.8	160.1	114.8	89.7	60.6	25.1	11.9	20.1	11.8	6.3	2.7
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	207.1 ^a	177.5 ^a	149.8 ^a	136.5 ^a	87.1 ^a	67.7 ^a	34.0 ^a	18.2 ^a	23.6 ^a	15.3 ^a	8.3 ^a	3.2 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	207.1	177.5	149.8	136.5	87.1	67.7	34.0	18.2	23.6	15.3	8.3	3.2
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	277.0 ^a	170.1 ^a	188.5 ^a	167.4 ^a	76.6 ^a	58.2 ^a	40.5 ^a	30.6 ^a	19.7 ^a	14.4 ^a	12.6 ^a	0 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	277.0	170.1	188.5	167.4	76.6	58.2	40.5	30.6	19.7	14.4	12.6	0

- specimen taken, but not analysed

^a mean value of main and double specimens (multiple determinations)

^b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-11: Summary of cinmethylin enantiomer Reg. No. 5925581 residues in treated soil specimens of trial 15/03314437-02 (Dugliolo di Budrio, Italy) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-02											
Sampling No.	8	9	10	11	13	14	16	17	18	20	21	22
DAA	0	7	13	28	60	90	119	181	245	312	413	536
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b											
0 – 10	182.4 ^a	178.7 ^a	137.0 ^a	91.5 ^a	50.9 ^a	38.3 ^a	27.3 ^a	8.9 ^a	8.4 ^a	8.9 ^a	5.3 ^a	3.5 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	182.4	178.7	137.0	91.5	50.9	38.3	27.3	8.9	8.4	8.9	5.3	3.5
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b											
0 – 10	190.3 ^a	134.5 ^a	139.7 ^a	74.4 ^a	50.9 ^a	37.7 ^a	21.7 ^a	14.5 ^a	9.9 ^a	11.4 ^a	7.7 ^a	2.9 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	190.3	134.5	139.7	74.4	50.9	37.7	21.7	14.5	9.9	11.4	7.7	2.9
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b											
0 – 10	210.1 ^a	138.5 ^a	128.8 ^a	82.9 ^a	47.0 ^a	36.1 ^a	23.4 ^a	15.4 ^a	8.3 ^a	12.2 ^a	9.4 ^a	4.7 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	210.1	138.5	128.8	82.9	47.0	36.1	23.4	15.4	8.3	12.2	9.4	4.7

- specimen taken, but not analysed

^a mean value of main and double specimens (multiple determinations)

^b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-12: Summary of cinmethylin enantiomer Reg. No. 5925632 residues in treated soil specimens of trial 15/03314437-02 (Dugliolo di Budrio, Italy) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-02											
Sampling No.	8	9	10	11	13	14	16	17	18	20	21	22
DAA	0	7	13	28	60	90	119	181	245	312	413	536
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	201.0 ^a	211.0 ^a	161.8 ^a	120.9 ^a	68.8 ^a	53.1 ^a	41.0 ^a	13.4 ^a	13.6 ^a	13.9 ^a	5.9 ^a	4.5 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	201.0	211.0	161.8	120.9	68.8	53.1	41.0	13.4	13.6	13.9	5.9	4.5
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	205.2 ^a	163.9 ^a	157.8 ^a	94.5 ^a	66.0 ^a	52.1 ^a	29.7 ^a	23.4 ^a	14.1 ^a	15.5 ^a	9.0 ^a	3.6 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	205.2	163.9	157.8	94.5	66.0	52.1	29.7	23.4	14.1	15.5	9.0	3.6
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	232.0 ^a	159.2 ^a	151.5 ^a	109.2 ^a	65.3 ^a	50.2 ^a	32.9 ^a	21.8 ^a	14.8 ^a	19.2 ^a	12.6 ^a	5.7 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	232.0	159.2	151.5	109.2	65.3	50.2	32.9	21.8	14.8	19.2	12.6	5.7

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-13: Summary of cinmethylin enantiomer Reg. No. 5925581 residues in treated soil specimens of trial 15/03314437-03 (Røllum, Denmark) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-03										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	7	14	29	58	85	122	176	245	293	414
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	172.4 ^a	182.6 ^a	136.5 ^a	97.0 ^a	67.2 ^a	44.5 ^a	36.1 ^a	27.8 ^a	4.6 ^a	2.6 ^a	-
10 – 20	0	0	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	172.4	182.6	136.5	97.0	67.2	44.5	36.1	27.8	4.6	2.6	-
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	194.6 ^a	206.6 ^a	138.2 ^a	121.3 ^a	60.9 ^a	40.4 ^a	45.9 ^a	43.4 ^a	6.3 ^a	0 ^a	-
10 – 20	2.5	0	0	0	0	0	2.1	8.4	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	197.1	206.6	138.2	121.3	60.9	40.4	48.0	51.8	6.3	0	-
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	184.5 ^a	173.9 ^a	112.3 ^a	111.8 ^a	55.1 ^a	51.7 ^a	39.7 ^a	20.3 ^a	6.2 ^a	0	-
10 – 20	0	0	0	0	0	0	2.0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	184.5	173.9	112.3	111.8	55.1	51.7	41.7	20.3	6.2	1.1	-

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-14: Summary of cinmethylin enantiomer Reg. No. 5925632 residues in treated soil specimens of trial 15/03314437-03 (Røllum, Denmark) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-03										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	7	14	29	58	85	122	176	245	293	414
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925632 1 [g ha ⁻¹] – converted ^b										
0 – 10	186.5 ^a	203.7 ^a	158.6 ^a	118.0 ^a	79.6 ^a	57.4 ^a	46.3 ^a	32.7 ^a	5.8 ^a	0 ^a	-
10 – 20	0	1.9	0	0	2.6	3.2	2.8	0	0	0	-
20 – 30	0	0	0	0	2.8	0	0	0	0	0	-
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	186.5	205.6	158.6	118.0	85.0	60.6	49.1	32.7	5.8	0	-
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	211.7 ^a	222.1 ^a	150.7 ^a	138.8 ^a	74.6 ^a	49.1 ^a	57.4 ^a	51.1 ^a	7.9 ^a	0 ^a	-
10 – 20	3.1	0	0	0	0	0	2.9	11.4	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	214.8	222.1	150.7	138.8	74.6	49.1	60.3	62.5	7.9	0	-
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	199.5 ^a	190.5 ^a	124.7 ^a	128.2 ^a	69.4 ^a	64.2 ^a	53.0 ^a	25.1 ^a	8.4 ^a	0 ^a	-
10 – 20	0	0	0	0	0	2.5	3.3	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	199.5	190.5	124.7	128.2	69.4	66.7	56.3	25.1	8.4	0	-

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-15: Summary of cinmethylin enantiomer Reg. No. 5925581 residues in treated soil specimens of trial 15/03314437-04 (Banbury, UK) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-04										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	16	28	63	86	119	177	247	301	413
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	163.3 ^a	102.7 ^a	64.2 ^a	41.9 ^a	7.5 ^a	7.3 ^a	3.0 ^a	2.6 ^a	2.7 ^a	0 ^a	-
10 – 20	0	2.5	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	163.3	105.2	64.2	41.9	7.5	7.3	3.0	2.6	2.7	0	
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	175.0 ^a	102.1 ^a	68.9 ^a	58.2 ^a	8.2 ^a	5.5 ^a	4.7 ^a	3.5 ^a	2.1 ^a	0 ^a	-
10 – 20	0	3.2	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	175.0	105.3	68.9	58.2	8.2	5.5	4.7	3.5	2.1	0	
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	191.6 ^a	151.1 ^a	61.0 ^a	42.2 ^a	6.1 ^a	4.9 ^a	3.2 ^a	3.4 ^a	1.9 ^a	0 ^a	-
10 – 20	0	2.6	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	191.6	153.7	61.0	42.2	6.1	4.9	3.2	3.4	1.9	0	

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-16: Summary of cinmethylin enantiomer Reg. No. 5925632 residues in treated soil specimens of trial 15/03314437-04 (Banbury, UK) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-04										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	16	28	63	86	119	177	247	301	413
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	174.2 ^a	131.0 ^a	94.3 ^a	67.5 ^a	11.5 ^a	11.6 ^a	5.2 ^a	4.0 ^a	2.9 ^a	0 ^a	-
10 – 20	0	2.7	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	174.2	133.7	94.3	67.5	11.5	11.6	5.2	4.0	2.9	0	-
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	185.6 ^a	127.8 ^a	98.0 ^a	89.8 ^a	14.4 ^a	8.7 ^a	7.8 ^a	5.2 ^a	2.6 ^a	0 ^a	-
10 – 20	0	3.6	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	185.6	131.4	98.0	89.8	14.4	8.7	7.8	5.2	2.6	0	-
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	205.3 ^a	185.2 ^a	86.5 ^a	70.3 ^a	8.2 ^a	7.4 ^a	4.9 ^a	4.7 ^a	2.7 ^a	1.8 ^a	-
10 – 20	1.7	2.6	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	207.0	187.8	86.5	70.3	8.2	7.4	4.9	4.7	2.7	1.8	-

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-17: Summary of cinmethylin enantiomer Reg. No. 5925581 residues in treated soil specimens of trial 15/03314437-05 (Saint-Amand, Belgium) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-05										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	14	30	58	85	119	176	239	300	420
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	171.0 ^a	128.9 ^a	83.6 ^a	50.1 ^a	15.5 ^a	15.8 ^a	10.5 ^a	9.0 ^a	4.9 ^a	4.2 ^a	1.7 ^a
10 – 20	43.7	15.8	8.2	5.7	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	214.7	144.7	91.8	55.8	15.5	15.8	10.5	9.0	4.9	4.2	1.7
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	160.1 ^a	123.6 ^a	83.9 ^a	41.4 ^a	15.0 ^a	16.0 ^a	10.3 ^a	8.3 ^a	5.0 ^a	4.3 ^a	2.3 ^a
10 – 20	34.8	31.4	9.0	7.4	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	194.9	155.0	92.9	48.8	15.0	16.0	10.3	8.3	5.0	4.3	2.3
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	175.8 ^a	108.0 ^a	68.9 ^a	40.4 ^a	13.8 ^a	8.9	6.6 ^a	7.6 ^a	4.0 ^a	3.0 ^a	0 ^a
10 – 20	29.7	6.3	18.6	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	205.5	114.3	87.5	40.4	13.8	8.9	6.6	7.6	4.0	3.0	0

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-18: Summary of cinmethylin enantiomer Reg. No. 5925632 residues in treated soil specimens of trial 15/03314437-05 (Saint-Amand, Belgium) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-05										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	14	30	58	85	119	176	239	300	420
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	183.7 ^a	148.5 ^a	107.2 ^a	72.2 ^a	24.9 ^a	23.7 ^a	14.4 ^a	12.8 ^a	6.3 ^a	3.7 ^a	2.1 ^a
10 – 20	46.9	18.7	10.5	8.3	2.4	0	0	0	2.4	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	230.6	167.2	117.7	80.5	27.3	23.7	14.4	12.8	8.7	3.7	2.1
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	170.4 ^a	145.3 ^a	115.3 ^a	69.8 ^a	30.8 ^a	29.1 ^a	17.9 ^a	14.9 ^a	7.9 ^a	7.7 ^a	2.3 ^a
10 – 20	35.8	36.4	14.0	8.3	6.7	0	0	0	2.2	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	206.2	181.7	129.3	78.1	37.5	29.1	17.9	14.9	10.1	7.7	2.3
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	186. ^a 0	127.1 ^a	95.1 ^a	68.7 ^a	25.2 ^a	13.4 ^a	10.2 ^a	10.5 ^a	6.1 ^a	3.8 ^a	1.9 ^a
10 – 20	30.4	6.7	26.8	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	5.6	0	0	0	0	0	0
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	216.4	133.8	121.9	68.7	30.8	13.4	10.2	10.5	6.1	3.8	1.9

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-19: Summary of cinmethylin enantiomer Reg. No. 5925581 residues in treated soil specimens of trial 15/03314437-06 (Almayate, Spain) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-06										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	14	28	62	89	118	181	239	301	420
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	116.9 ^a	72.7 ^a	43.0 ^a	40.6 ^a	12.1 ^a	9.3 ^a	4.0 ^a	3.9 ^a	0 ^a	0 ^a	0 ^a
10 – 20	87.7	35.0	18.1	18.8	4.6	4.6	0	0	0	2.0	0
20 – 30	7.0	6.0	8.1	0	0	0	0	0	0	0	0
30 – 40	0	0	0	0	0	-	-	-	-	-	-
40 – 50	0	0	0	0	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	211.6	113.7	69.2	59.4	16.7	13.9	4.0	3.9	0	2.0	0
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	102.6 ^a	101.4 ^a	95.9 ^a	41.1 ^a	11.7 ^a	9.5 ^a	10.2 ^a	2.3 ^a	2.6 ^a	0 ^a	0 ^a
10 – 20	52.9	49.6	53.8	12.6	2.1	2.8	4.4	0	0	1.8	0
20 – 30	0	0	5.2	0	0	0	0	0	0	0	0
30 – 40	-	-	0	0	0	-	-	-	-	-	-
40 – 50	-	-	0	0	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	155.5	151.0	154.9	53.7	13.8	12.3	14.6	2.3	2.6	1.8	0
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 [g ha ⁻¹] – converted ^b										
0 – 10	115.0 ^a	89.7 ^a	67.5 ^a	59.6 ^a	6.8 ^a	8.8 ^a	6.6 ^a	5.5 ^a	0 ^a	2.3 ^a	0 ^a
10 – 20	67.2	34.0	45.5	27.5	2.9	2.0	3.3	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	182.2	123.7	113.0	87.1	9.7	10.8	9.9	5.5	0	2.3	0

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-20: Summary of cinmethylin enantiomer Reg. No. 5925632 residues in treated soil specimens of trial 15/03314437-06 (Almayate, Spain) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-06										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	14	28	62	89	118	181	239	301	420
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	121.1 ^a	87.2 ^a	52.0 ^a	57.0 ^a	27.2 ^a	19.4 ^a	7.7 ^a	7.2 ^a	2.1 ^a	2.9 ^a	0 ^a
10 – 20	92.6	43.7	24.7	34.1	11.7	11.5	4.5	3.4	0	2.9	0
20 – 30	7.9	7.7	13.1	0	0	0	0	0	0	0	0
30 – 40	0	0	0	0	0	-	-	-	-	-	-
40 – 50	0	0	0	0	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	221.6	138.6	89.8	91.1	38.9	30.9	12.2	10.6	2.1	5.8	0
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	110.4 ^a	116.1 ^a	110.5 ^a	58.2 ^a	25.0 ^a	21.7 ^a	21.5 ^a	4.6 ^a	5.9 ^a	4.0 ^a	0 ^a
10 – 20	59.0	59.1	76.8	19.6	5.3	7.4	11.3	0	0	0	0
20 – 30	0	0	7.3	0	0	0	0	0	0	0	0
30 – 40	-	-	0	0	0	-	-	-	-	-	-
40 – 50	-	-	0	0	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	169.4	175.2	194.6	77.8	30.3	29.1	32.8	4.6	5.9	4.0	0
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	120.1 ^a	102.9 ^a	83.9 ^a	79.8 ^a	13.0 ^a	15.4 ^a	12.1 ^a	11.3 ^a	2.9 ^a	5.1 ^a	5.1 ^a
10 – 20	74.4	40.6	58.9	41.6	5.8	4.1	7.2	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	194.5	143.5	142.8	121.4	18.8	19.5	19.3	11.3	2.9	5.1	5.1

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-21: Summary of total cinmethylin (sum of both enantiomers Reg. No. 5925581 and Reg. No. 5925632) residues in treated soil specimens of trial 15/03314437-01 (Höltinghausen, Germany) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-01											
Sampling No.	8	9	10	11	13	14	16	17	18	20	21	22
DAA	0	6	14	29	62	90	121	176	238	303	413	538
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	353.2 ^a	264.3 ^a	297.5 ^a	207.0 ^a	153.7 ^a	101.1 ^a	38.7 ^a	18.5 ^a	32.7 ^a	18.3 ^a	10.2 ^a	4.9 ^a
10 – 20	3.9	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	357.1	264.3	297.5	207.0	153.7	101.1	38.7	18.5	32.7	18.3	10.2	4.9
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	399.7 ^a	332.3 ^a	280.5 ^a	251.3 ^a	155.4 ^a	118.9 ^a	59.5 ^a	29.5 ^a	38.6 ^a	24.9 ^a	13.8 ^a	5.4 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	399.7	332.3	280.5	251.3	155.4	118.9	59.5	29.5	38.6	24.9	13.8	5.4
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	539.9 ^a	331.2 ^a	357.1 ^a	300.5 ^a	135.8 ^a	101.2 ^a	67.8 ^a	49.6 ^a	32.5 ^a	24.7 ^a	21.2 ^a	0 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	539.9	331.2	357.1	300.5	135.8	101.2	67.8	49.6	32.5	24.7	21.2	0

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-22: Summary of total cinmethylin (sum of both enantiomers Reg. No. 5925581 and Reg. No. 5925632) residues in treated soil specimens of trial 15/03314437-02 (Dugliolo di Budrio, Italy) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-02											
Sampling No.	8	9	10	11	13	14	16	17	18	20	21	22
DAA	0	7	13	28	60	90	119	181	245	312	413	536
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	383.4 ^a	389.7 ^a	298.8 ^a	212.4 ^a	119.7 ^a	91.4 ^a	68.3 ^a	22.3 ^a	22.0 ^a	22.8 ^a	11.2 ^a	8.0 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	383.4	389.7	298.8	212.4	119.7	91.4	68.3	22.3	22.0	22.8	11.2	8.0
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	395.5 ^a	298.4 ^a	297.5 ^a	168.9 ^a	116.9 ^a	89.8 ^a	51.4 ^a	37.9 ^a	24.0 ^a	26.9 ^a	16.7 ^a	6.5 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	395.5	298.4	297.5	168.9	116.9	89.8	51.4	37.9	24.0	26.9	16.7	6.5
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b											
0 – 10	442.1 ^a	297.7 ^a	280.3 ^a	192.1 ^a	112.3 ^a	86.3 ^a	56.3 ^a	37.2 ^a	23.1 ^a	31.4 ^a	22.0 ^a	10.4 ^a
10 – 20	0	0	0	0	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	442.1	297.7	280.3	192.1	112.3	86.3	56.3	37.2	23.1	31.4	22.0	10.4

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-23: Summary of total cinmethylin (sum of both enantiomers Reg. No. 5925581 and Reg. No. 5925632) residues in treated soil specimens of trial 15/03314437-03 (Røllum, Denmark) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-03										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	7	14	29	58	85	122	176	245	293	414
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	358.9 ^a	386.3 ^a	295.1 ^a	215.0 ^a	146.8 ^a	101.9 ^a	82.4 ^a	60.5 ^a	10.4 ^a	2.6 ^a	-
10 – 20	0	1.9	0	0	2.6	3.2	2.8	0	0	0	-
20 – 30	0	0	0	0	2.8	0	0	0	0	0	-
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	358.9	388.2	295.1	215.0	152.2	105.1	85.2	60.5	10.4	2.6	-
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	406.3 ^a	428.7 ^a	288.9 ^a	260.1 ^a	135.5 ^a	89.5 ^a	103.3 ^a	94.5 ^a	14.2 ^a	0 ^a	-
10 – 20	5.6	0	0	0	0	0	5.0	19.8	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	411.9	428.7	288.9	260.1	135.5	89.5	108.3	114.3	14.2	0	-
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	384.0 ^a	364.4 ^a	237.0 ^a	240.0 ^a	124.5 ^a	115.9 ^a	92.7 ^a	45.4 ^a	14.6 ^a	0 ^a	-
10 – 20	0	0	0	0	0	2.5	5.3	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	384.0	364.4	237.0	240.0	124.5	118.4	98.0	45.4	14.6	0	-

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-24: Summary of total cinmethylin (sum of both enantiomers Reg. No. 5925581 and Reg. No. 5925632) residues in treated soil specimens of trial 15/03314437-04 (Banbury, UK) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-04										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	16	28	63	86	119	177	247	301	413
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	337.5 ^a	233.7 ^a	158.5 ^a	109.4 ^a	19.0 ^a	18.9 ^a	8.2 ^a	6.6 ^a	5.6 ^a	0 ^a	-
10 – 20	0	5.2	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	337.5	238.9	158.5	109.4	19.0	18.9	8.2	6.6	5.6	0	
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	360.6 ^a	229.9 ^a	166.9 ^a	148.0 ^a	22.6 ^a	14.2 ^a	12.5 ^a	8.7 ^a	4.7 ^a	0 ^a	-
10 – 20	0	6.8	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	360.6	236.7	166.9	148.0	22.6	14.2	12.5	8.7	4.7	0	
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	396.9 ^a	336.3 ^a	147.5 ^a	112.5 ^a	14.3 ^a	12.3 ^a	8.1 ^a	8.1 ^a	4.6 ^a	1.8 ^a	-
10 – 20	1.7	5.2	0	0	0	0	0	0	0	0	-
20 – 30	0	0	0	0	0	0	0	0	0	0	-
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	398.6	341.5	147.5	112.5	14.3	12.3	8.1	8.1	4.6	1.8	

- specimen taken, but not analysed;

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-25: Summary of total cinmethylin (sum of both enantiomers Reg. No. 5925581 and Reg. No. 5925632) residues in treated soil specimens of trial 15/03314437-05 (Saint-Amand, Belgium) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-05										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	14	30	58	85	119	176	239	300	420
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	354.7 ^a	277.4 ^a	190.8 ^a	122.3 ^a	40.4 ^a	39.5 ^a	24.9 ^a	21.8 ^a	11.2 ^a	7.9 ^a	3.8 ^a
10 – 20	90.6	34.5	18.7	14.0	2.4	0	0	0	2.4	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	445.3	311.9	209.5	136.3	42.8	39.5	24.9	21.8	13.6	7.9	3.8
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	330.5 ^a	268.9 ^a	199.2 ^a	111.2 ^a	45.8 ^a	45.1 ^a	28.2 ^a	23.2 ^a	12.9 ^a	12.0 ^a	4.6 ^a
10 – 20	70.6	67.8	23.0	15.7	6.7	0	0	0	2.2	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	401.1	336.7	222.2	126.9	52.5	45.1	28.2	23.2	15.1	12.0	4.6
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	361.8 ^a	235.1 ^a	164.0 ^a	109.1 ^a	39.0 ^a	22.3 ^a	16.8 ^a	18.1 ^a	10.1 ^a	6.8 ^a	1.9 ^a
10 – 20	60.1	13.0	45.4	0	0	0	0	0	0	0	0
20 – 30	0	0	0	0	5.6	0	0	0	0	0	0
30 – 40	-	-	-	-	0	0	0	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	421.9	248.1	209.4	109.1	44.6	22.3	16.8	18.1	10.1	6.8	1.9

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Table 8.1.2.2.1-26: Summary of total cinmethylin (sum of both enantiomers Reg. No. 5925581 and Reg. No. 5925632) residues in treated soil specimens of trial 15/03314437-06 (Almayate, Spain) converted to g ha⁻¹ (Replicate A, B, C)

	15/03314437-06										
Sampling No.	8	9	10	11	13	14	16	17	18	20	21
DAA	0	6	14	28	62	89	118	181	239	301	420
depth [cm]	Replicate A: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	238.0 ^a	159.9 ^a	95.0 ^a	97.6 ^a	39.3 ^a	28.7 ^a	11.7 ^a	11.1 ^a	2.1 ^a	2.9 ^a	0 ^a
10 – 20	180.3	78.7	42.8	52.9	16.3	16.1	4.5	3.4	0	4.9	0
20 – 30	14.9	13.7	21.2	0	0	0	0	0	0	0	0
30 – 40	0	0	0	0	0	-	-	-	-	-	-
40 – 50	0	0	0	0	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	433.2	252.3	159.0	150.5	55.6	44.8	16.2	14.5	2.1	7.8	0
	Replicate B: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	213.0 ^a	217.5 ^a	206.4 ^a	99.3 ^a	36.7 ^a	31.2 ^a	31.7 ^a	6.9 ^a	8.5 ^a	4.0 ^a	0 ^a
10 – 20	111.9	108.7	130.6	32.2	7.4	10.2	15.7	0	0	1.8	0
20 – 30	0	0	12.5	0	0	0	0	0	0	0	0
30 – 40	-	-	0	0	0	-	-	-	-	-	-
40 – 50	-	-	0	0	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	324.9	326.2	349.5	131.5	44.1	41.4	47.4	6.9	8.5	5.8	0
	Replicate C: Residues of cinmethylin enantiomer Reg. No. 5925581 + Reg. No. 5925632 [g ha ⁻¹] – converted ^b										
0 – 10	235.1 ^a	192.6 ^a	151.4 ^a	139.4 ^a	19.8 ^a	24.2 ^a	18.7 ^a	16.8 ^a	2.9 ^a	7.4 ^a	5.1 ^a
10 – 20	141.6	74.6	104.4	69.1	8.7	6.1	10.5	0	0	0	0
20 – 30	0	0	0	0	0	0	0	0	0	0	0
30 – 40	-	-	-	-	-	-	-	-	-	-	-
40 – 50	-	-	-	-	-	-	-	-	-	-	-
total residues in soil profile [g ha ⁻¹]	376.7	267.2	255.8	208.5	28.5	30.3	29.2	16.8	2.9	7.4	5.1

- specimen taken, but not analysed

a mean value of main and double specimens (multiple determinations)

b calculations are based on the total amount of residue and the respective surface area of the individual soil layers; for residue values < 0.0015 mg/kg (< LOD), no conversions were made and values are reported as zero

DAA = days after application

Residues of cinmethylin in the soil profiles were exclusively detected at concentrations above the LOQ in the upper 20 cm of the soils for the trials 15/03314437-01 to 15/03314437-05 and in the upper 30 cm for trial 15/03314437-06 (Spain). No residues above the LOD were detected below 30 cm in any specimen at any time. Altogether, it can be concluded that cinmethylin does not show any significant tendency to move into deeper soil layers indicating low potential for cinmethylin residues to leach to groundwater.

III. CONCLUSION

Cinmethylin degraded moderately fast under field conditions in soil at all six European field sites. For enantiomer Reg. No. 5925581, the total residues in the soil profiles decreased from an average of 192.3 g ha⁻¹ at day 0 to residues below 5 g ha⁻¹ within 18 months. For enantiomer Reg. No. 5925632, the total residues in the soil profiles decreased from an average of 205.5 g ha⁻¹ at day 0 to residues below 5.7 g ha⁻¹ within 18 months. For the a.s. cinmethylin (sum of both enantiomers), the total residues in the soil profiles decreased from an average of 398.5 g ha⁻¹ at day 0 to residues below the 10.4 g ha⁻¹ within 18 months. DT₅₀ values are calculated within He, W. and Pape, L. (2018a, CA 7.1.2.2.1/03) and He, W. and Pape, L. (2018b, CA 7.1.2.2.1/04).

Residues of cinmethylin in the soil profiles were exclusively detected at concentrations above the LOQ in the upper 20 cm of the soils. No residues above the LOQ were detected below 20 cm in any specimen at any time. Altogether, it can be concluded that cinmethylin does not show any significant tendency to move into deeper soil layers indicating low potential for cinmethylin residues to leach to groundwater.

Report:	CA 7.1.2.2.1/03 He, W. and Pape, L. 2018a
Title	Kinetic evaluation of a field dissipation study with BAS 684 H conducted in 2015 to 2017: Determination of trigger endpoints for the racemate and its enantiomers (Reg. No. 5925581 and Reg. No. 5925632) according to FOCUS
Document No.:	2017/1199007
Guidelines:	<ul style="list-style-type: none"> • FOCUS Kinetics (2006) “Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration” Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0, 434 pp • FOCUS Kinetics (2014) “Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration” Version 1.1, 440 pp • European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662
GLP:	None
Deviations	None; acceptable for use as trigger endpoints.

SUMMARY

The degradation behaviour of the herbicide cinmethylin in soil has been investigated in a field dissipation study including six field trials located in Germany, Italy, Denmark, UK, Belgium and Spain. The purpose of this evaluation was to analyse the degradation kinetics of cinmethylin and its two enantiomers Reg. No. 5925581 and Reg. No. 5925632 observed in the soils according to the current guidance of the FOCUS workgroup on degradation kinetics in order to derive best-fit field degradation parameters as triggers for additional work (trigger endpoints). The HSE evaluator has also included conservative back calculated (pseudo) SFO DT₅₀ values for simple Tier 1 PEC_{soil} calculations.

The study design was compliant with EFSA’s recommendations for obtaining DegT50 values in soil from field studies for modelling purposes, as dissipation caused by surface processes like photolysis or volatilization was minimized by incorporating of the test item residues to a depth of 4 – 10 cm directly after the applications of all treated subplots were completed. Hence, the reported trigger endpoints represent a conservative estimate of the dissipation behaviour of cinmethylin and its enantiomers in soil.

The kinetic evaluation showed that the degradation behaviour of cinmethylin and its two enantiomers was best described with biphasic kinetic models (FOMC and DFOP). For all models considered appropriate, the visual assessment and goodness-of-fit statistics indicate plausible fit. Therefore, the resulting endpoints can be considered reliable.

The trigger endpoints (DegT50 and DegT90) for cinmethylin and its two enantiomers are summarised in the tables below.

Table 8.1.2.2.1-27: Summary of trigger endpoints of cinmethylin

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error [%]	DegT50 [d]	DegT90 [d]
15/03314437-01 (Germany)	Loamy fine sand	4.80	FOMC	10.6	38.7 ^c / 57.6 ^d	191.4
15/03314437-02 (Italy)	Very fine sandy loam	7.66	FOMC	3.7	27.3 ^c / 53.7 ^d	178.5
15/03314437-03 (Denmark)	Sand	4.62	FOMC	11.2	38.9 ^c / 62.5 ^d	207.6
15/03314437-04 (UK)	Loam	6.70	DFOP	8.0	15.2 ^c / 16.7 ^d	55.6
15/03314437-05 (Belgium)	Silt	6.12	DFOP	4.7	14.8 ^c / 22.6 ^d	74.9
15/03314437-06 (Spain)	Coarse sandy loam	7.70	DFOP	8.8	22.6 ^c / 26.3 ^d	87.4

^a Soil characteristics of the uppermost horizon^b Measured in CaCl₂^c Overall DT₅₀ for use as trigger endpoints^d Calculated DT₅₀ = DT₉₀/3.32 for use in PEC_{SOIL} calculations**Table 8.1.2.2.1-28: Summary of trigger endpoints of Reg. No. 5925581**

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error [%]	DegT50 [d]	DegT90 [d]
15/03314437-01 (Germany)	Loamy fine sand	4.80	FOMC	11.0	32.9 ^c / 50.9 ^d	169.0
15/03314437-02 (Italy)	Very fine sandy loam	7.66	FOMC	4.5	23.9 ^c / 47.2 ^d	156.8
15/03314437-03 (Denmark)	Sand	4.62	FOMC	11.4	35.6 ^c / 57.8 ^d	192.0
15/03314437-04 (UK)	Loam	6.70	FOMC	6.5	11.5 ^c / 15.7 ^d	52.2
15/03314437-05 (Belgium)	Silt	6.12	DFOP	4.8	12.2 ^c / 16.7 ^d	55.6
15/03314437-06 (Spain)	Coarse sandy loam	7.70	DFOP	9.4	18.8 ^c / 21.0 ^d	69.6

^a Soil characteristics of the uppermost horizon^b Measured in CaCl₂^c Overall DT₅₀ for use as trigger endpoints^d Calculated DT₅₀ = DT₉₀/3.32 for use in PEC_{SOIL} calculations

Table 8.1.2.2.1-29: Summary of trigger endpoints of Reg. No. 5925632

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error [%]	DegT50 [d]	DegT90 [d]
15/03314437-01 (Germany)	Loamy fine sand	4.80	FOMC	10.2	44.7 ^c / 63.6 ^d	211.3
15/03314437-02 (Italy)	Very fine sandy loam	7.66	FOMC	3.2	30.8 ^c / 59.6 ^d	197.8
15/03314437-03 (Denmark)	Sand	4.62	FOMC	11.1	42.4 ^c / 66.4 ^d	220.7
15/03314437-04 (UK)	Loam	6.70	SFO	8.2	18.6	61.8
15/03314437-05 (Belgium)	Silt	6.12	DFOP	4.4	17.9 ^c / 27.6 ^d	91.7
15/03314437-06 (Spain)	Coarse sandy loam	7.70	DFOP	8.7	26.8 ^c / 31.5 ^d	104.6

^a Soil characteristics of the uppermost horizon

^b Measured in CaCl₂

^c Overall DT₅₀ for use as trigger endpoints

^d Calculated DT₅₀ = DT₉₀/3.32 for use in PEC_{soil} calculations

I. MATERIAL AND METHODS

The degradation behaviour of the herbicide cinmethylin in soil has been investigated in a field dissipation study including six field trials located in Germany, Italy, Denmark, UK, Belgium and Spain [see KCA 7.1.2.2.1/1 and KCA 7.1.2.2.1/2].

The purpose of this evaluation was to analyse the degradation kinetics of cinmethylin and its two enantiomers Reg. No. 5925581 and Reg. No. 5925632 observed in the two soils according to the current guidance of the FOCUS workgroup on degradation kinetics [FOCUS (2014)] in order to derive best-fit field degradation parameters as triggers for additional work (trigger endpoints). The HSE evaluator has also included conservative back calculated (pseudo) SFO DT₅₀ values for simple Tier 1 PEC_{soil} calculations.

The study design was compliant with EFSA's recommendations for obtaining DegT50 values in soil from field studies for modelling purposes, as dissipation caused by surface processes like photolysis or volatilization was minimized by incorporating of the test item residues to a depth of 4 – 10 cm directly after the applications of all treated subplots were completed. Hence, the reported trigger endpoints represent a conservative estimate of the dissipation behaviour of cinmethylin and its enantiomers in soil.

Samples were analysed for residues of the two enantiomers contained in the test item. The limit of quantification (LOQ) was 0.005 mg/kg for each analyte. The limit of detection (LOD) was set at 0.0015 mg/kg (30% of LOQ).

Kinetic modelling

Kinetic evaluation was performed for the parent substance cinmethylin and the two enantiomers Reg. No. 5925581 and Reg. No. 5925632.

Kinetic models included in the assessment

The kinetic models SFO, FOMC and DFOP recommended by FOCUS (2014) were applied. Trigger endpoints were derived from the kinetic models that provided the best fit to the measured data. The goodness-of-fit of kinetic models SFO and FOMC were compared first. If FOMC resulted in a better fit or no clear decision could be made further biphasic models i.e. DFOP was tested.

A kinetic model is considered appropriate if the residuals are randomly distributed around zero, the χ^2 error indicates a sufficient quality of the fit (i.e. value is <15%). However, this value should not be taken as a cut-off criterion. In field studies, the data points are often scattered around the curve, which results in a large error value. In some cases fits with higher error value (i.e. χ^2 error value >15%) are still acceptable if they represent the degradation behaviour well. According to FOCUS, the t-test for the degradation parameters should be passed at 5% error level. In cases where the t-test failed a decision was made whether this has an influence on the estimated endpoint.

The overall DT50 has been accepted by the HSE evaluator

Data handling

For the evaluation of each field trial, the residue data of the two enantiomers Reg. No. 5925581 and Reg. No. 5925632 in g ha⁻¹ were taken from the study report. The evaluation started at the day of application (0 DAT). Data from the three subplots were considered separately as replicates. For each of the two enantiomers, measured residues below LOQ or LOD were handled according to FOCUS (2014), where all samples < LOD were set to ½ LOD and all samples after the first non-detect were omitted unless positive detections above LOQ were made later in the experiment. For the corrections the LOQ or LOD values in mg/kg were converted into g ha⁻¹ based on the respective dry sample weights and the total surface areas of liners, using the same method as described in the study report [see KCA 7.1.2.2.1/1 and KCA 7.1.2.2.1/2]. Corrections along the sampling depth were made for each sampling date and each subplot. In addition, corrections along the sampling dates were made, if no residue values above LOD were detected in any sampling depth. Then, the residue data of each enantiomer were cumulated over the entire sampling depth. The resulting data sets were directly used for kinetic evaluation for the two enantiomers. For the kinetic evaluation for the test item cinmethylin, the data of the two enantiomers were summed up.

Due to the corrections described above the resulting datasets used for kinetic analysis (in g ha⁻¹) are different from the measured residues data (in g ha⁻¹) given in the study report.

Software for kinetic evaluation

The software package used by the Applicant was KinGUI (version 2.2014.224.1704) was used for parameter fitting. The error tolerance and the maximum number of iterations of the optimization tool (IRLS) were set to 10⁻⁶ and 100, respectively. The HSE evaluator has validated the Applicants modelling using CAKE v.3.2.

Experimental data

The data sets submitted to kinetic analysis are provided in Table 8.1.2.2.1-30 to Table 8.1.2.2.1-32.

Table 8.1.2.2.1-30: Experimental data, Subplot A, B and C used for kinetic evaluation of cinmethylin (sum of both enantiomers Reg. No. 5925581 and Reg. No. 5925632 and all depths summed)

15/03314437-01 (Germany)				15/03314437-02 (Italy)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	359.6	402.1	542.2	0	385.9	398.2	444.2
6	266.6	334.4	333.8	7	391.9	300.8	299.8
14	299.8	282.8	359.5	13	301.5	300.0	282.7
29	209.3	253.3	302.5	28	214.8	171.2	194.4
62	156.0	158.0	138.2	60	121.9	119.5	114.8
90	103.2	121.1	103.3	90	93.6	91.8	88.5
121	41.0	61.9	69.9	119	70.3	53.5	57.9
176	20.6	31.3	51.7	181	24.7	40.4	39.5
238	34.3	40.6	34.6	245	24.3	26.7	25.6
303	20.6	27.1	26.8	312	25.3	29.2	33.6
413	12.0	15.7	23.3	413	13.5	19.0	24.2
538	7.0	7.5	5.1	536	9.9	9.0	12.7
15/03314437-03 (Denmark)				15/03314437-04 (UK)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	360.8	414.1	386.2	0	339.2	362.4	400.3
7	390.1	430.8	365.9	6	240.5	238.3	343.1
14	297.0	290.9	238.8	16	160.3	168.7	149.2
29	217.1	262.1	241.9	28	111.2	149.7	114.2
58	154.4	139.3	126.8	63	20.2	24.2	16.0
85	107.3	91.3	118.2	86	20.5	15.9	13.8
122	87.4	110.5	100.3	119	9.5	13.8	9.4
176	62.9	116.6	47.7	177	8.3	10.4	10.1
245	12.5	16.4	16.8	247	7.7	6.8	6.7
293	7.7 ^c	4.2 ^a	6.6 ^a	301	3.0 ^a	2.8 ^a	3.4 ^a
414	- ^b	- ^b	- ^b	413	- ^b	- ^b	- ^b
15/03314437-05 (Belgium)				15/03314437-06 (Spain)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	447.6	403.4	424.2	0	435.6	327.3	379.0
6	313.8	338.7	250.1	6	255.1	328.7	269.7
14	211.6	224.3	211.4	14	161.7	351.9	258.1
30	138.3	128.8	111.6	28	152.8	133.7	210.9
58	44.8	54.6	45.2	62	58.2	46.8	31.0
85	41.4	47.1	24.3	89	47.2	43.8	32.9
119	26.9	30.3	18.9	118	13.0	49.8	31.7
176	23.9	25.4	20.3	181	16.7	9.2	18.8
239	15.8	17.2	12.4	239	4.4	10.8	7.1
300	10.2	14.3	9.1	301	10.0	7.8	9.2
420	7.5	6.8	6.5	420	3.9	5.0	9.7

^a The residues below the LOD were set to ½ LOD (in accordance to FOCUS guidance) along the sampling depth and sampling dates. LOQ or LOD values in mg/kg were converted into g ha⁻¹ based on the respective dry sample weights and surface areas of liners.

^b Specimen taken but not analysed

^c Residue value between LOD and LOQ

Table 8.1.2.2.1-31: Experimental data, Subplot A, B and C used for kinetic evaluation of Reg. No. 5925581

15/03314437-01 (Germany)				15/03314437-02 (Italy)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	175.8	193.8	264.0	0	183.7	191.6	211.2
6	125.7	155.8	162.4	7	179.8	135.7	139.5
14	138.5	131.8	169.8	13	138.3	140.9	130.0
29	93.4	115.8	134.1	28	92.7	75.6	84.0
62	65.1	69.6	60.4	60	52.0	52.2	48.3
90	41.6	52.3	44.0	90	39.4	38.8	37.3
121	14.7	26.7	28.4	119	28.3	22.7	24.2
176	7.6	12.2	20.0	181	10.1	15.8	16.5
238	13.4	16.0	13.9	245	9.6	11.3	9.6
303	7.7	10.7	11.3	312	10.1	12.5	13.3
413	4.8	6.4	9.7	413	6.5	8.8	10.5
538	3.2	3.2	0.9	536	4.4	4.1	5.9
15/03314437-03 (Denmark)				15/03314437-04 (UK)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	173.3	198.3	185.6	0	164.2	175.9	192.5
7	183.4	207.6	174.7	6	106.0	106.1	154.5
14	137.4	139.2	113.2	16	65.1	69.8	61.8
29	98.1	122.3	112.8	28	42.8	59.1	43.0
58	68.3	62.0	56.2	63	8.1	9.0	6.9
85	45.5	41.3	52.8	86	8.1	6.4	5.6
122	37.2	49.1	42.9	119	3.6	5.3	3.9
176	29.0	53.0	21.4	177	3.4	4.4	4.4
245	5.7	7.4	7.3	247	3.7	3.2	3.0
293	3.9 ^a	0.9 ^a	3.3 ^a	301	0.7 ^a	0.7 ^a	0.7 ^a
414	- ^b	- ^b	- ^b	413	- ^b	- ^b	- ^b
15/03314437-05 (Belgium)				15/03314437-06 (Spain)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	215.8	196.1	206.7	0	212.8	156.7	183.3
6	145.7	156.0	115.3	6	115.1	152.2	124.9
14	92.9	93.9	88.5	14	70.6	156.1	114.2
30	56.9	49.8	41.6	28	60.6	54.8	88.3
58	16.5	16.0	14.8	62	18.0	15.2	11.0
85	16.7	17.0	9.9	89	15.2	13.5	12.1
119	11.5	11.3	7.6	118	4.2	15.8	11.1
176	10.0	9.4	8.7	181	4.9	3.5	6.5
239	6.0	6.1	5.2	239	1.0	3.8	3.0
300	5.4	5.4	4.2	301	3.1	3.0	3.2
420	4.4	3.4	3.4	420	1.0	0.9	3.8

^a The residues below the LOD were set to ½ LOD (in accordance to FOCUS guidance) along the sampling depth and sampling dates. LOQ or LOD values in mg/kg were converted into g ha⁻¹ based on the respective dry sample weights and surface areas of liners.

^b Specimen taken but not analysed

Table 8.1.2.2.1-32: Experimental data, Subplot A, B and C used for kinetic evaluation of Reg. No. 5925632

15/03314437-01 (Germany)				15/03314437-02 (Italy)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	183.8	208.3	278.2	0	202.2	206.5	233.1
6	140.9	178.6	171.4	7	212.1	165.1	160.2
14	161.3	151.0	189.7	13	163.1	159.0	152.7
29	116.0	137.5	168.4	28	122.1	95.6	110.4
62	90.9	88.4	77.8	60	69.9	67.3	66.5
90	61.6	68.7	59.2	90	54.2	53.1	51.3
121	26.3	35.2	41.6	119	42.0	30.8	33.7
176	13.0	19.1	31.6	181	14.6	24.6	23.0
238	20.8	24.6	20.8	245	14.7	15.5	16.0
303	12.9	16.4	15.5	312	15.1	16.7	20.3
413	7.3	9.2	13.7	413	7.0	10.1	13.7
538	3.8	4.3	4.2	536	5.5	4.8	6.8
15/03314437-03 (Denmark)				15/03314437-04 (UK)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	187.5	215.9	200.6	0	175.1	186.5	207.8
7	206.8	223.1	191.3	6	134.5	132.2	188.6
14	159.6	151.7	125.6	16	95.2	98.9	87.4
29	119.1	139.8	129.2	28	68.4	90.7	71.1
58	86.1	77.3	70.6	63	12.1	15.2	9.1
85	61.8	50.0	65.3	86	12.4	9.5	8.2
122	50.2	61.4	57.4	119	5.8	8.5	5.5
176	33.9	63.7	26.2	177	4.9	6.0	5.7
245	6.8	9.0	9.5	247	3.9	3.7	3.8
293	3.8 ^a	3.4 ^a	3.3 ^a	301	2.3 ^a	2.1 ^a	2.7 ^c
414	- ^b	- ^b	- ^b	413	- ^b	- ^b	- ^b
15/03314437-05 (Belgium)				15/03314437-06 (Spain)			
DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a			DAT [d]	Data according to FOCUS [g ha ⁻¹] ^a		
	Subplot A	Subplot B	Subplot C		Subplot A	Subplot B	Subplot C
0	231.8	207.3	217.6	0	222.8	170.6	195.6
6	168.2	182.7	134.9	6	140.0	176.5	144.8
14	118.7	130.4	122.9	14	91.1	195.8	143.9
30	81.5	79.0	70.0	28	92.3	79.0	122.6
58	28.3	38.6	30.4	62	40.2	31.6	20.1
85	24.7	30.1	14.4	89	32.1	30.3	20.8
119	15.4	18.9	11.3	118	8.7	34.0	20.6
176	13.8	16.0	11.6	181	11.8	5.8	12.3
239	9.8	11.1	7.2	239	3.4	7.0	4.1
300	4.9	8.9	4.9	301	6.9	4.8	6.0
420	3.1	3.4	3.1	420	3.0	4.0	5.9

^a The residues below the LOD were set to ½ LOD (in accordance to FOCUS guidance) along the sampling depth and sampling dates. LOQ or LOD values in mg/kg were converted into g ha⁻¹ based on the respective dry sample weights and surface areas of liners.

^b Specimen taken but not analysed

^c Residue value between LOD and LOQ

II. RESULTS AND DISCUSSION

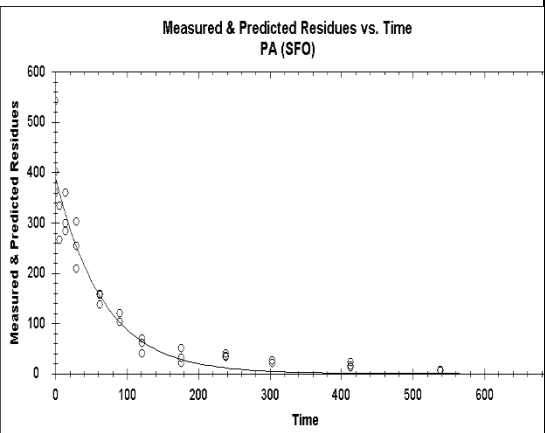
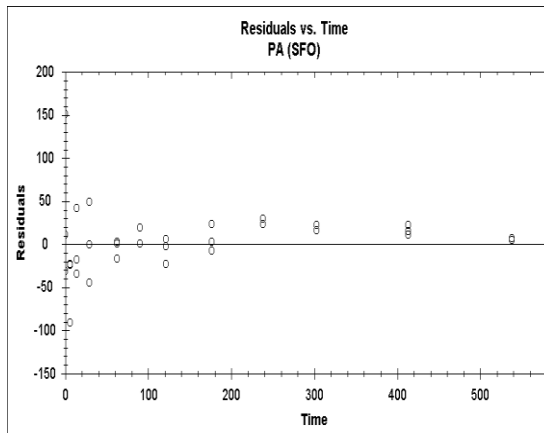
The degradation behaviour of cinmethylin and its two enantiomers Reg. No. 5925581 and Reg. No. 5925632 in the six field trials was analysed in order to derive trigger endpoints. As degradation caused by surface processes like photolysis or volatilization was minimized by incorporating of the test item residues to a depth of 4 – 10 cm directly after the treatments, the

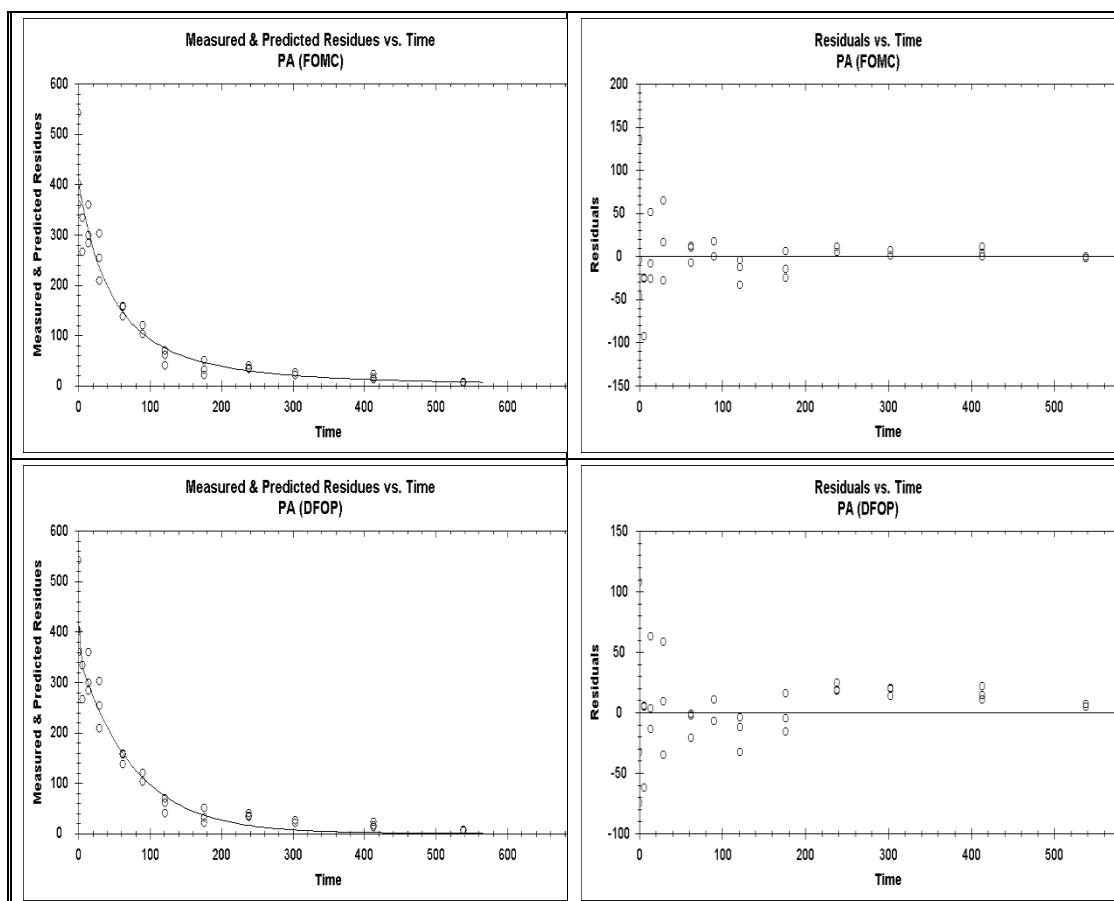
reported endpoints represent a conservative estimate of the dissipation behaviour of cinmethylin and its enantiomers in soil.

Kinetic evaluation for cinmethylin

The kinetic evaluation showed that the degradation behaviour of cinmethylin was best described with biphasic kinetic models (FOMC and DFOP). The kinetic models tested and the respective visual and statistical assessments are summarised in Table 8.1.2.2.1-33 to Table 8.1.2.2.1-38.

Table 8.1.2.2.1-33: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for cinmethylin in field trial 15/03314437-01 (Germany)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	11.9	k: <0.001	acceptable	46.4	154.2
	FOMC	10.6	α : 2.25 β : 107.3	good	38.7 ^a / 57.6 ^b	191.4
The SFO visual fit is acceptable, the χ^2 error value is below 15%, and k is significantly different from zero. The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	7.9	k1 = 2.528 (>0.05) k2 = 0.013 (<0.01) g = 0.1815	acceptable	37.9 ^a / 48.7 ^b	161.6
The DFOP model does not further improve the visual fit compared to the FOMC fit and the k1 value is not statistically different from zero. Conclusion: FOMC is appropriate for derivation of trigger endpoints.						
<div style="display: flex; justify-content: space-around;">   </div>						

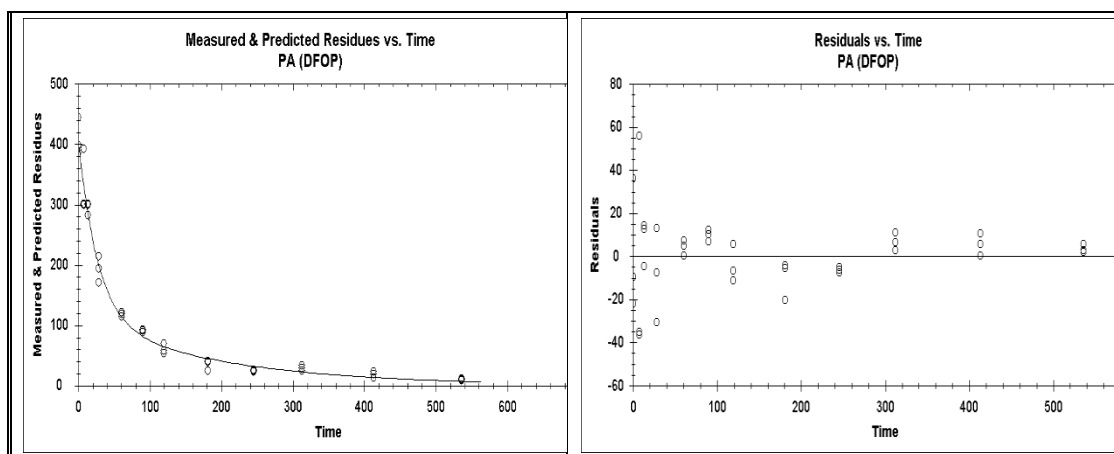


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-34: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for cinmethylin in field trial 15/03314437-02 (Italy)

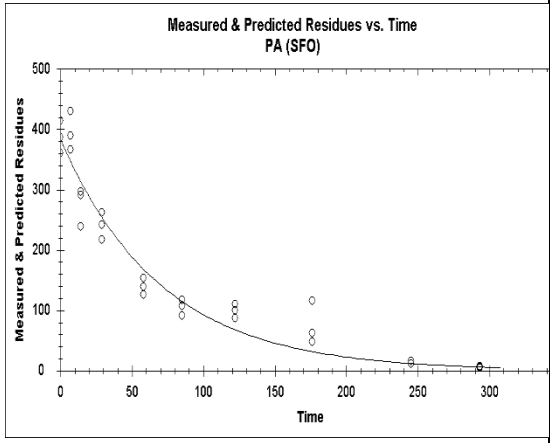
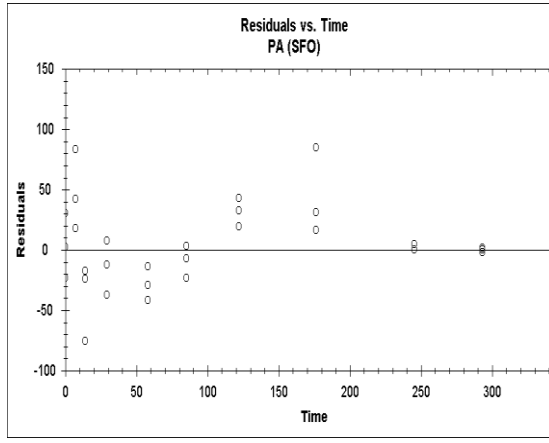
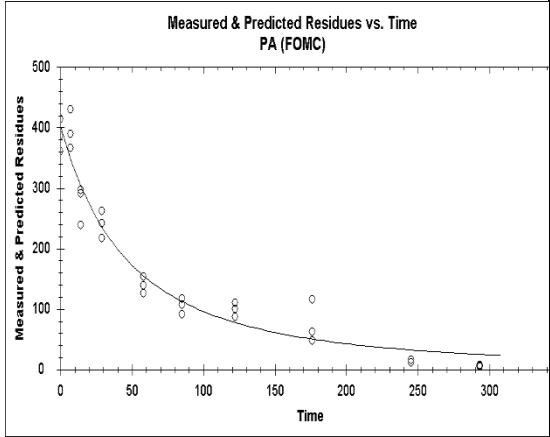
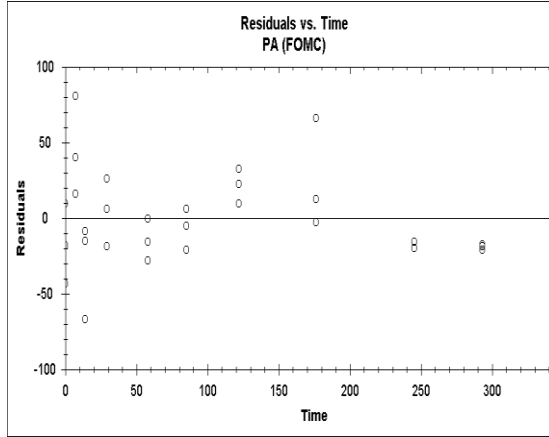
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	12.1	k: <0.001	poor	37.1	123.4
	FOMC	3.7	α : 1.397 β : 42.51	good	27.3 ^a / 53.7 ^b	178.5
The SFO visual fit is poor as residuals are large and deviate systematically from zero. The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	4.3	k1 = 0.037 (<0.001) k2 = 0.005 (<0.001) g = 0.7218	good	27.5 ^a / 59.8 ^b	198.4
The DFOP model does not further improve the visual fit compared to the FOMC fit and provides a higher χ^2 error value. Conclusion: FOMC is appropriate for derivation of trigger endpoints.						
Measured & Predicted Residues vs. Time PA (SFO)		Residuals vs. Time PA (SFO)				
Measured & Predicted Residues vs. Time PA (FOMC)		Residuals vs. Time PA (FOMC)				

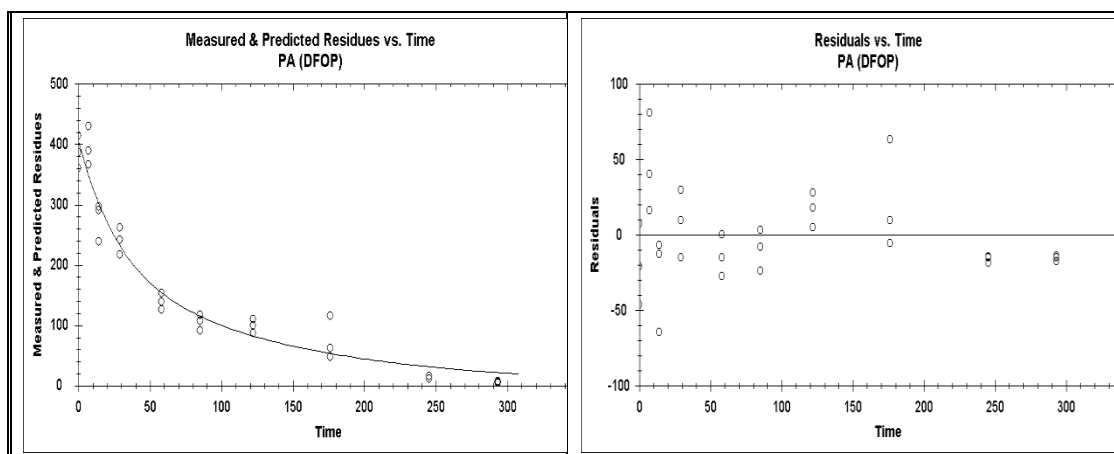


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-35: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for cinmethylin in field trial 15/03314437-03 (Denmark)

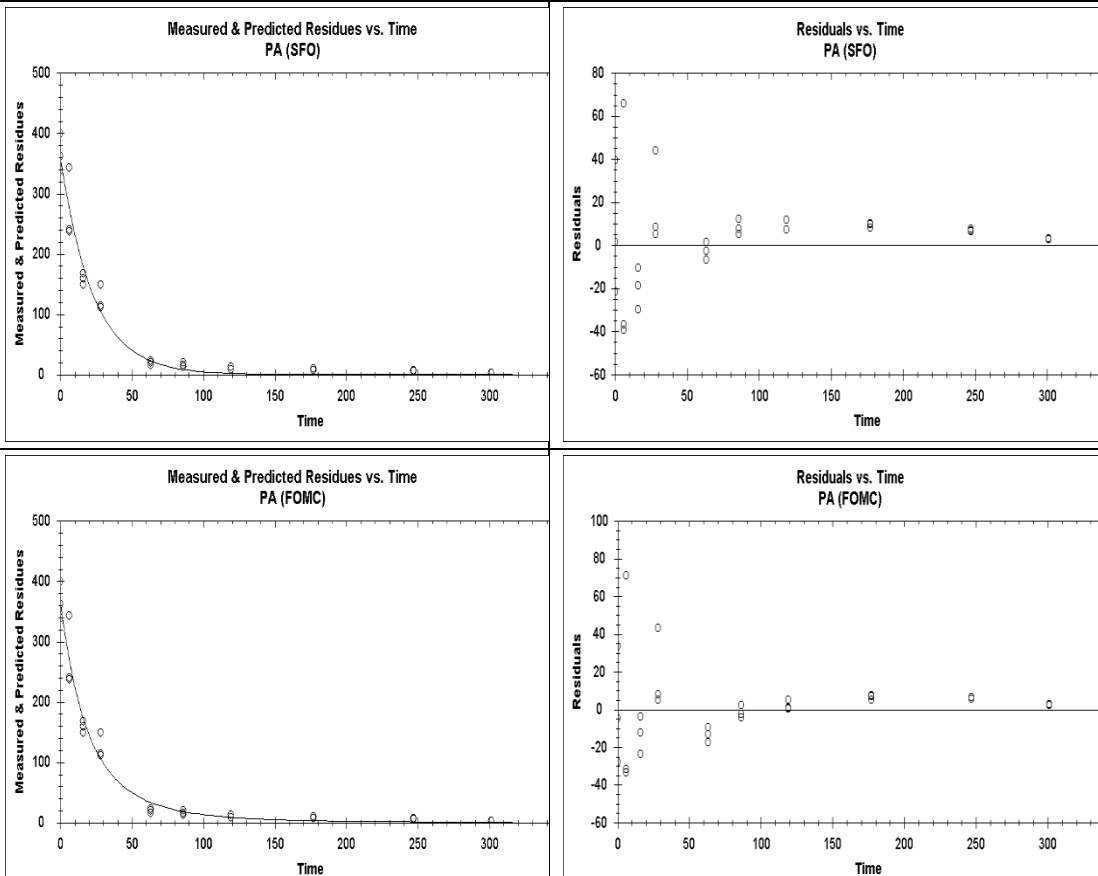
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	13.0	k: <0.001	acceptable	48.7	161.9
	FOMC	11.2	α : 1.919 β : 89.45	acceptable	38.9 ^a / 62.5 ^b	207.6
The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	11.4	k1 = 0.038 (<0.05) k2 = 0.008 (<0.05) g = 0.4952	acceptable	37.4 ^a / 63.3 ^b	210.2
The DFOP model does not further improve the visual fit compared to the FOMC fit and provides a higher χ^2 error value.						
Conclusion: FOMC is appropriate for derivation of trigger endpoints.						
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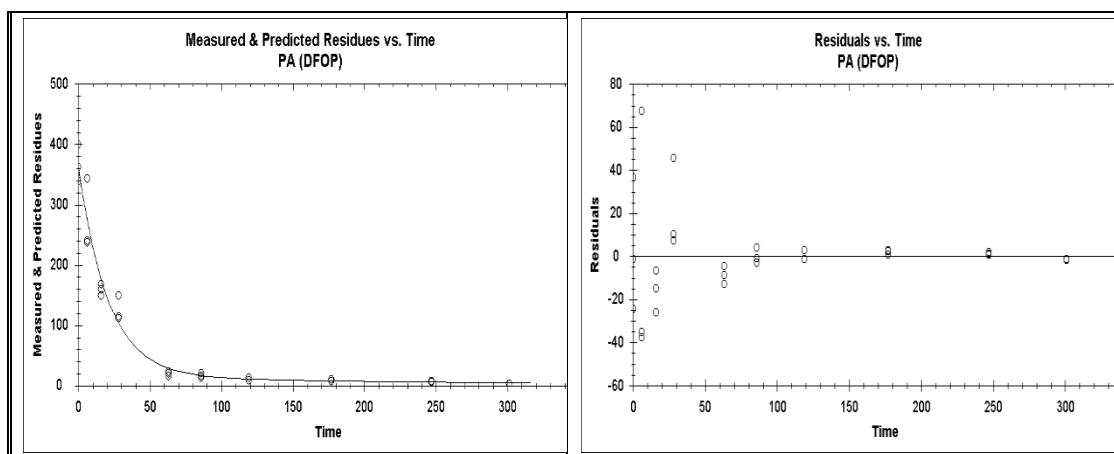


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-36: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for cinmethylin in field trial 15/03314437-04 (UK)

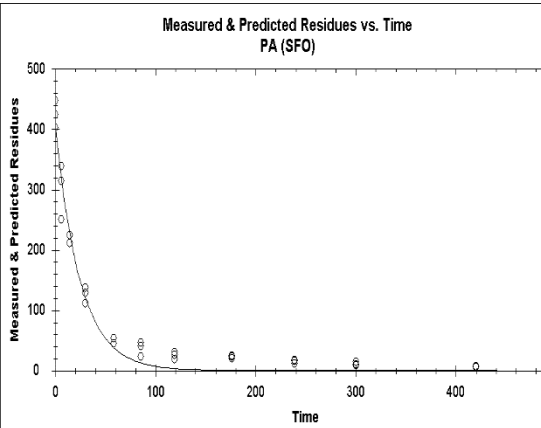
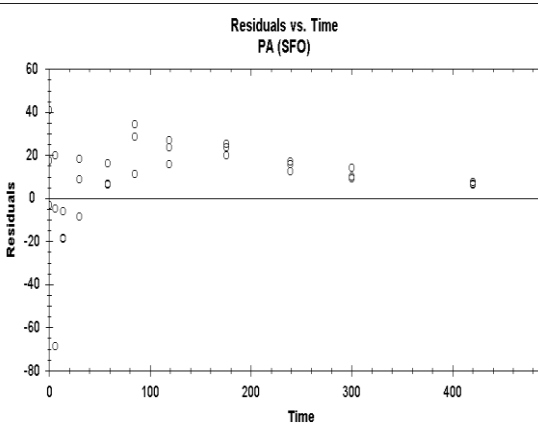
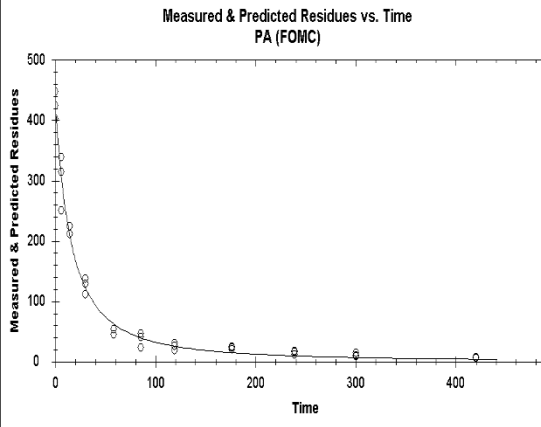
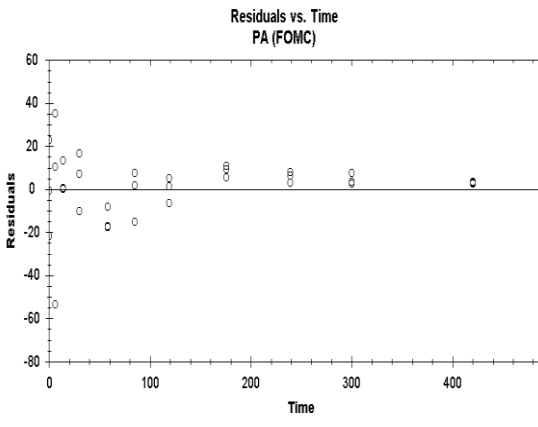
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	8.5	k: <0.001	good	15.8	52.6
	FOMC	7.6	α : 4.018 β : 77.43	good	14.6 ^a / 18.0 ^b	59.9
The SFO visual fit is good, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	8.0	k1 = 0.048 (<0.001) k2 = 0.004 (not sig.) g = 0.9562	good	15.2 ^a / 16.7 ^b	55.6
The DFOP model further improves the visual fit, residuals are randomly scattered around zero. The parameter k2 is not significantly different from zero, which is acceptable as the degradation is mainly driven by the fast degradation phase, indicated by the g value of 0.9562.						
Conclusion: DFOP is appropriate for derivation of trigger endpoints.						
						

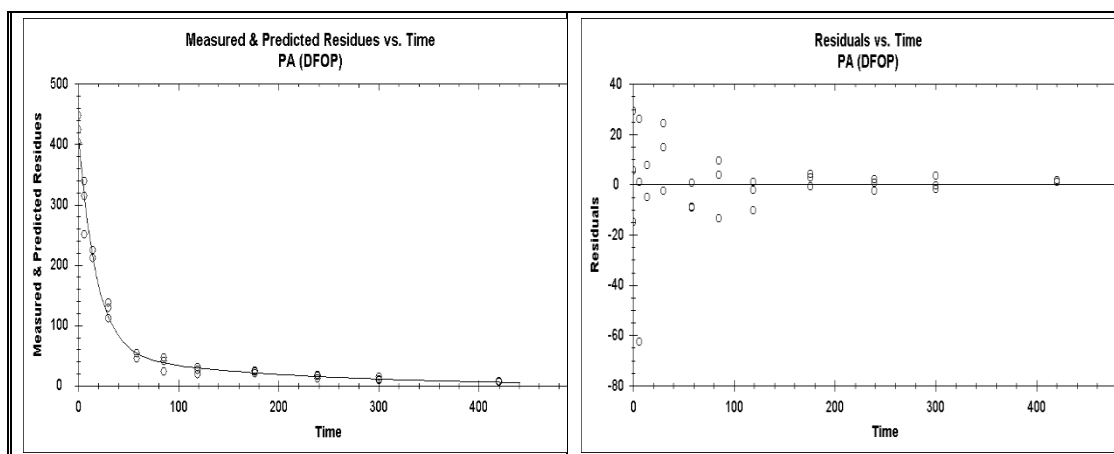


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-37: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for cinmethylin in field trial 15/03314437-05 (Belgium)

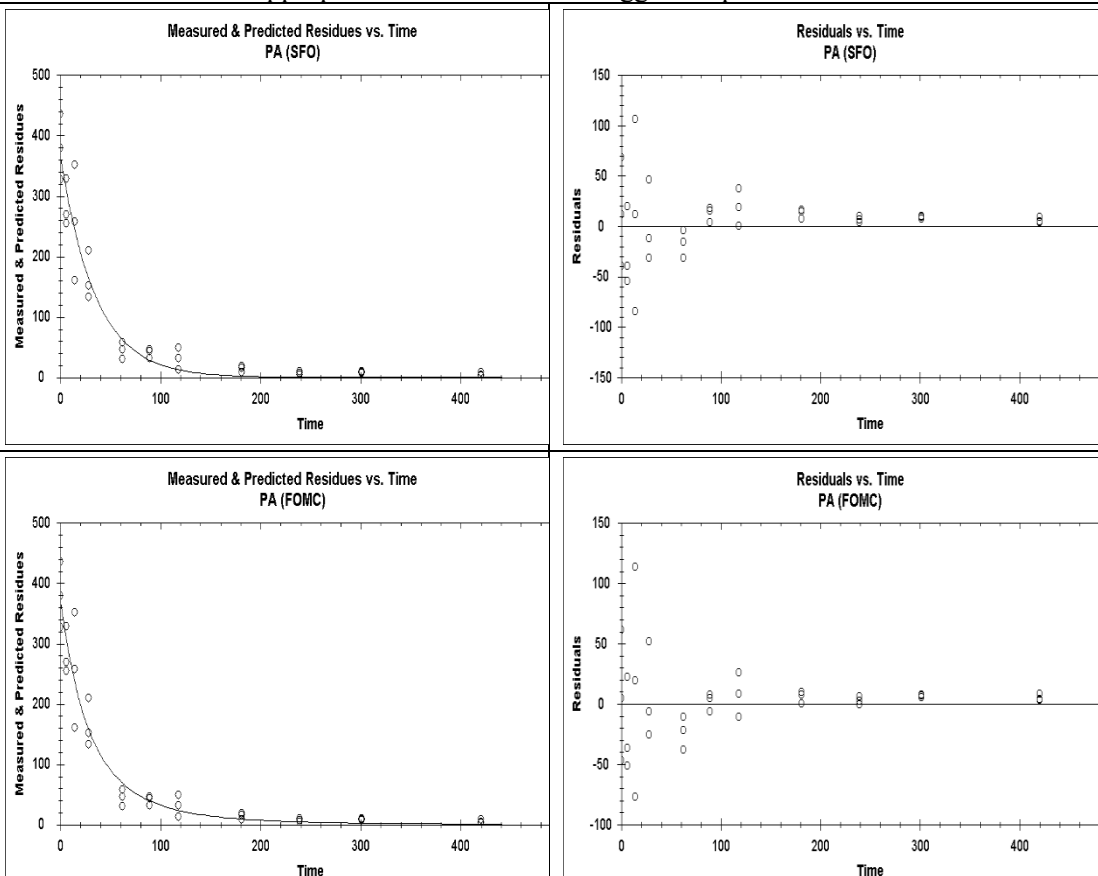
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	11.9	k: <0.001	poor	17.1	56.7
	FOMC	4.5	α : 1.66 β : 26.71	acceptable	13.8 ^a / 24.1 ^b	80.2
The SFO visual fit is poor as residuals are large and deviate systematically from zero. The FOMC model improves the visual fit and provides lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	4.7	k1 = 0.056 (<0.001) k2 = 0.005 (<0.05) g = 0.8693	good	14.8 ^a / 22.6 ^b	74.9
The DFOP model further improves the visual fit, residuals are randomly scattered around zero. The parameters k1 and k2 are significantly different from zero. Conclusion: DFOP is appropriate for derivation of trigger endpoints.						
<div>   </div> <div>   </div>						

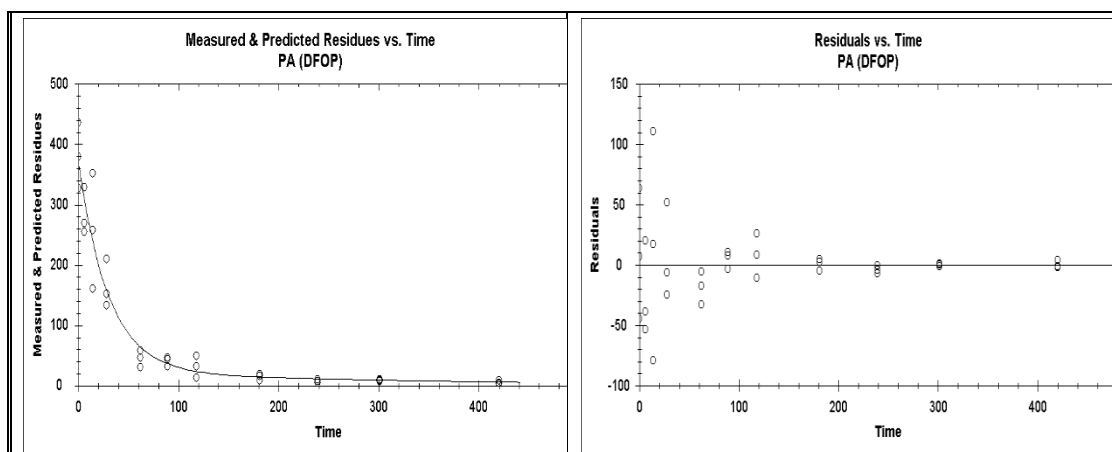


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-38: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for cinmethylin in field trial 15/03314437-06 (Spain)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	9.8	k: <0.001	acceptable	24.2	80.4
	FOMC	9.2	α : 3.931 β : 114.9	good	22.2 ^a / 27.6 ^b	91.5
The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	8.8	k1 = 0.033 (<0.001) k2 = 0.003 (not sig.) g = 0.9325	good	22.6 ^a / 26.3 ^b	87.4
The DFOP model further improves the visual fit and provides the lowest χ^2 error, residuals are randomly scattered around zero. The parameter k2 is not significantly different from zero, which is acceptable as the degradation is mainly driven by the fast degradation phase indicated by the g value of 0.9325.						
Conclusion: DFOP is appropriate for derivation of trigger endpoints.						
						



^a Overall DT₅₀

^b Calculated DT₅₀ = DT₉₀/3.32

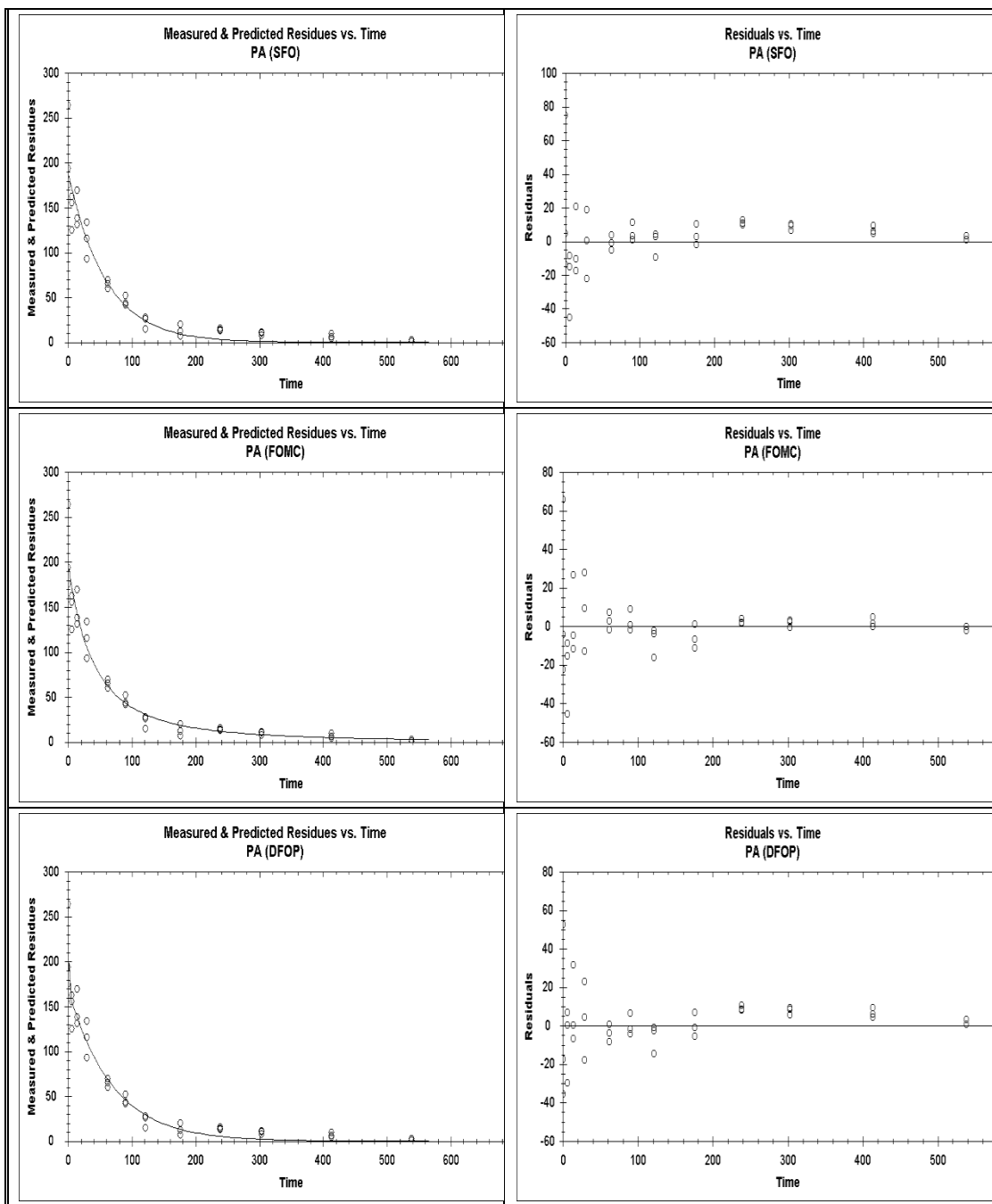
Kinetic evaluation for enantiomers

The kinetic evaluation showed that the degradation behaviour of the enantiomers Reg. No. 5925581 and Reg. No. 5925632 was best described with biphasic kinetic models (FOMC and DFOP) except one evaluation (Reg. No. 5925632 for field trial 15/03314437-04 (UK)). The kinetic models tested and the respective visual and statistical assessments are summarised in Table 8.1.2.2.1-39 to Table 8.1.2.2.1-50.

Reg. No. 5925581

Table 8.1.2.2.1-39: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925581 in field trial 15/03314437-01 (Germany)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	12.7	k: <0.001	acceptable	40.7	135.1
	FOMC	11.0	α : 2.065 β : 82.49	good	32.9 ^a / 50.9 ^b	169.0
The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero. The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	7.4	k1 = 2.471 (not sig.) k2 = 0.01451 (<0.001) g = 0.1976	acceptable	32.6 ^a / 43.4 ^b	143.5
The DFOP model does not further improve the visual fit compared to the FOMC fit and k1 is not significantly different from zero. Conclusion: FOMC is appropriate for derivation of trigger endpoints.						

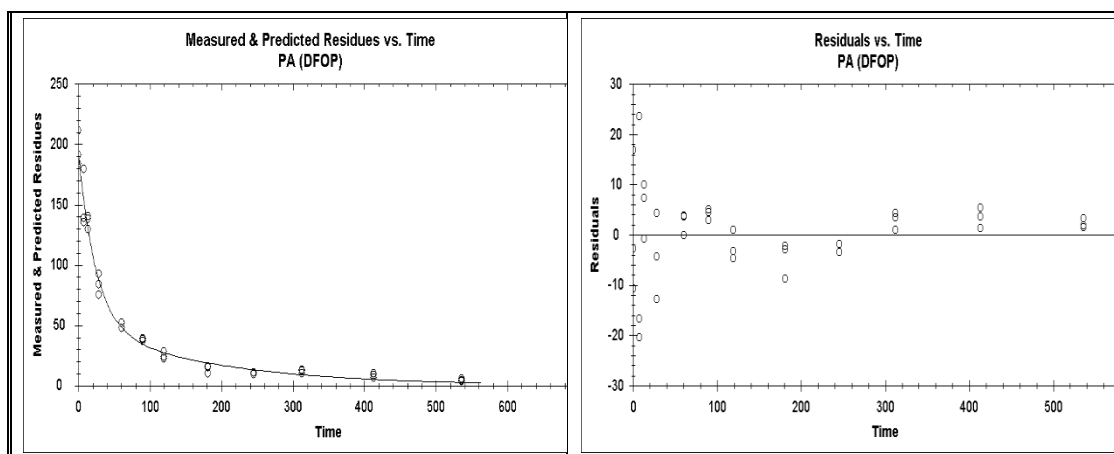


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-40: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925581 in field trial 15/03314437-02 (Italy)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	13.0	k: <0.001	poor	32.5	108.1
	FOMC	4.5	α : 1.393 β : 37.12	good	23.9 ^a / 47.2 ^b	156.8
The SFO visual fit is poor as residuals are large and deviate systematically from zero. The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	5.2	k1 = 0.04165 (<0.001) k2 = 0.00555 (<0.001) g = 0.7373	good	24.1 ^a / 52.7 ^b	174.9
The DFOP model does not further improve the visual fit compared to the FOMC fit and provides a higher χ^2 error value. Conclusion: FOMC is appropriate for derivation of trigger endpoints.						
Measured & Predicted Residues vs. Time PA (SFO)		Residuals vs. Time PA (SFO)				
Measured & Predicted Residues vs. Time PA (FOMC)		Residuals vs. Time PA (FOMC)				

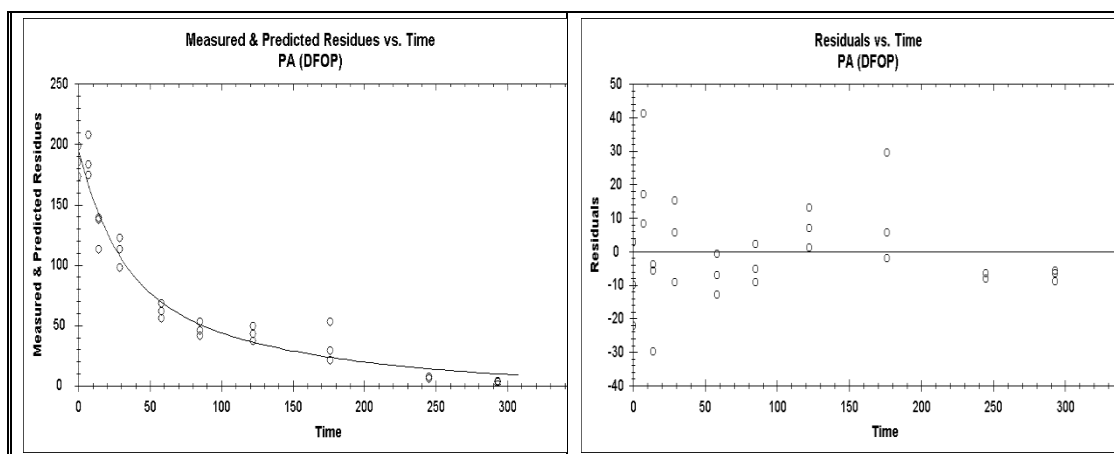


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-41: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925581 in field trial 15/03314437-03 (Denmark)

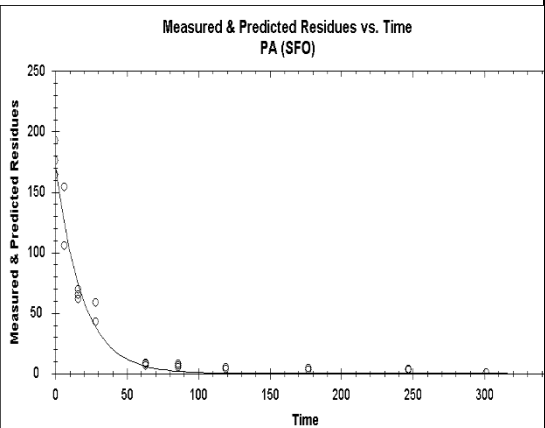
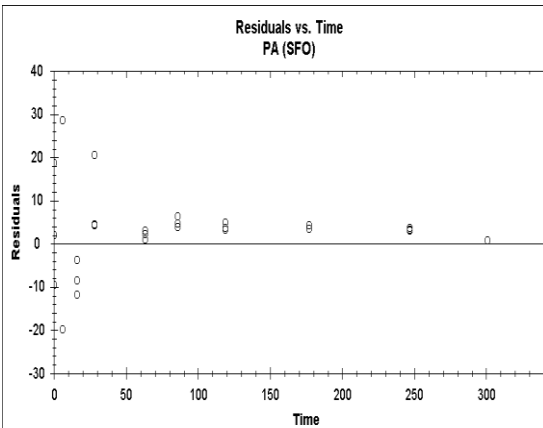
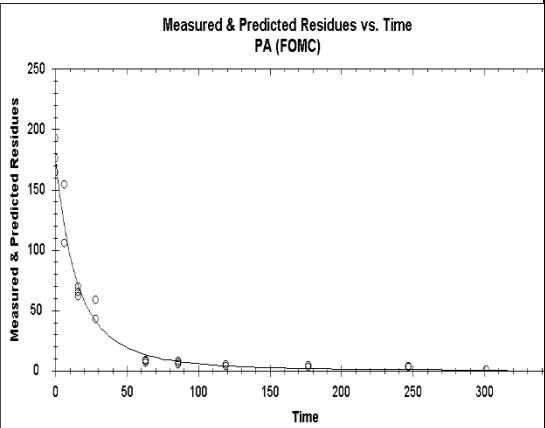
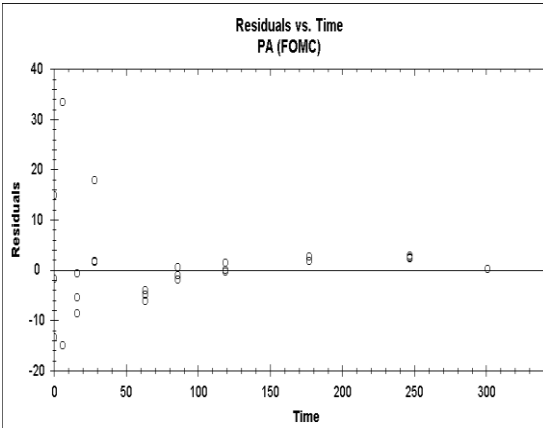
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	13.4	k: <0.001	acceptable	44.6	148.1
	FOMC	11.4	α : 1.882 β : 80.02	acceptable	35.6 ^a / 57.8 ^b	192.0
The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	11.6	k1 = 0.03664 (<0.05) k2 = 0.00744 (<0.05) g = 0.5599	acceptable	34.3 ^a / 60.1 ^b	199.5
The DFOP model does not further improve the visual fit compared to the FOMC fit and provides a higher χ^2 error value						
Conclusion: FOMC is appropriate for derivation of trigger endpoints.						

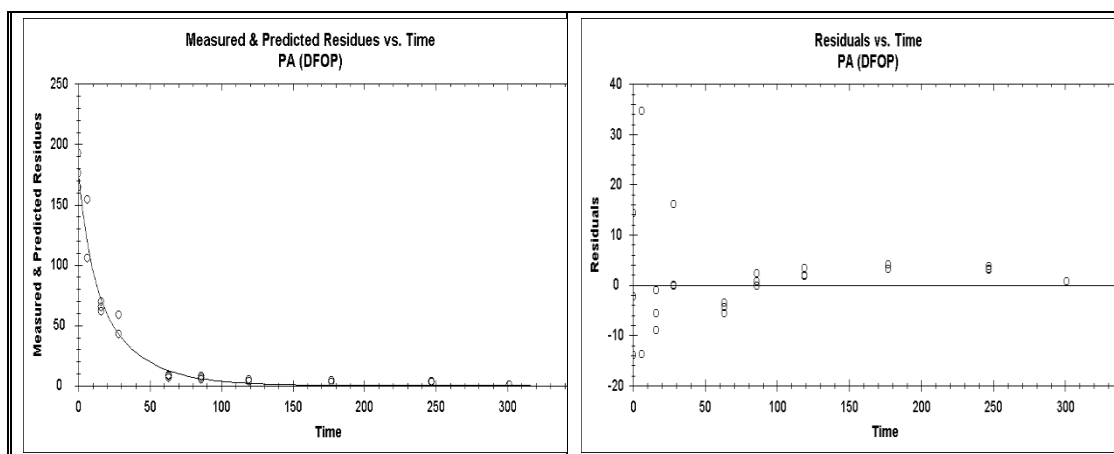


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-42: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925581 in field trial 15/03314437-04 (UK)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	9.3	k: <0.001	good	12.9	42.8
	FOMC	6.5	α : 2.796 β : 40.84	good	11.5 ^a 15.7 ^b	/ 52.2
The SFO visual fit is good, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	6.9	k1 = 0.1286 (not sig.) k2 = 0.03403 (<0.01) g = 0.404	good	11.3 ^a / 15.8 ^b	52.6
The DFOP model does not further improve the visual fit and the parameter k1 is not significantly different from zero.						
Conclusion: FOMC is appropriate for derivation of trigger endpoints.						
Measured & Predicted Residues vs. Time PA (SFO)		Residuals vs. Time PA (SFO)				
						
Measured & Predicted Residues vs. Time PA (FOMC)		Residuals vs. Time PA (FOMC)				
						

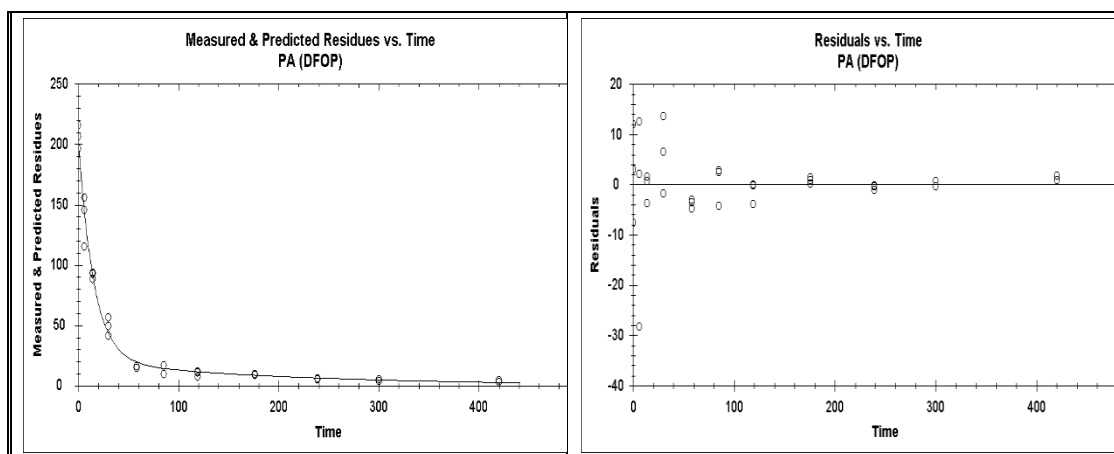


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-43: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925581 in field trial 15/03314437-05 (Belgium)

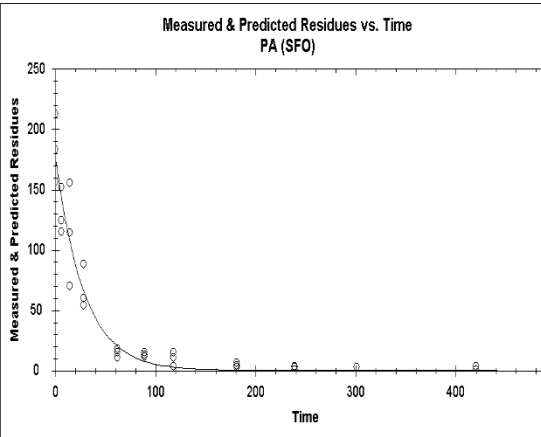
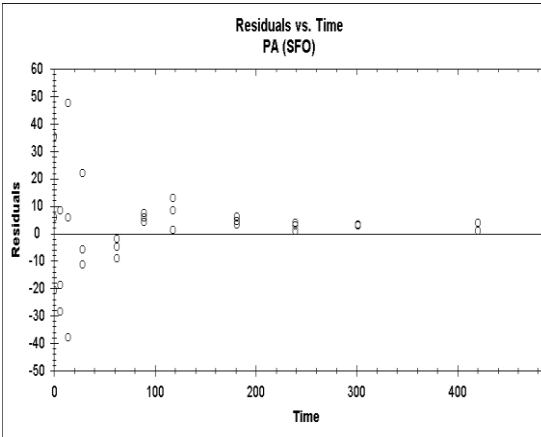
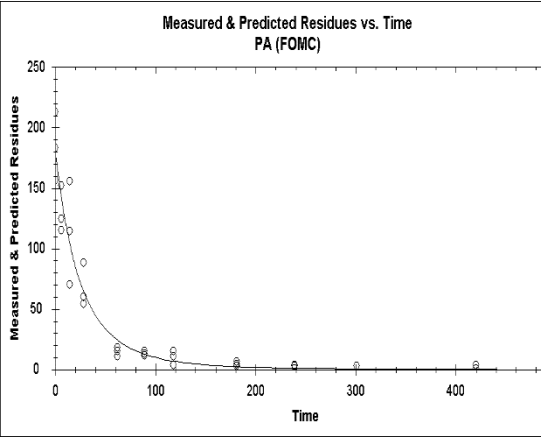
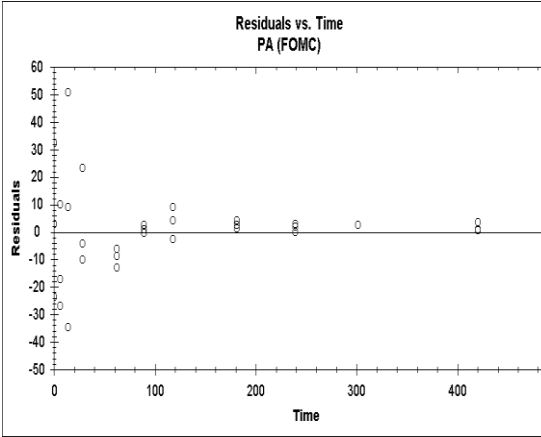
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	12.0	k: <0.001	poor	13.6	45.0
	FOMC	5.2	α : 1.741 β : 23.15	good	11.3 ^a / 19.2 ^b	63.8
The SFO visual fit is poor as residuals are large and deviate systematically from zero. The FOMC model improves the visual fit and provides lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	4.8	k1 = 0.06566 (<0.001) k2 = 0.00497 (<0.05) g = 0.8989	good	12.2 ^a / 16.7 ^b	55.6
The DFOP model further improves the visual fit and provides the lowest χ^2 error value, residuals are randomly scattered around zero. The parameters k1 and k2 are significantly different from zero.						
Conclusion: DFOP is appropriate for derivation of trigger endpoints.						
Measured & Predicted Residues vs. Time PA (SFO)		Residuals vs. Time PA (SFO)				
Measured & Predicted Residues vs. Time PA (FOMC)		Residuals vs. Time PA (FOMC)				

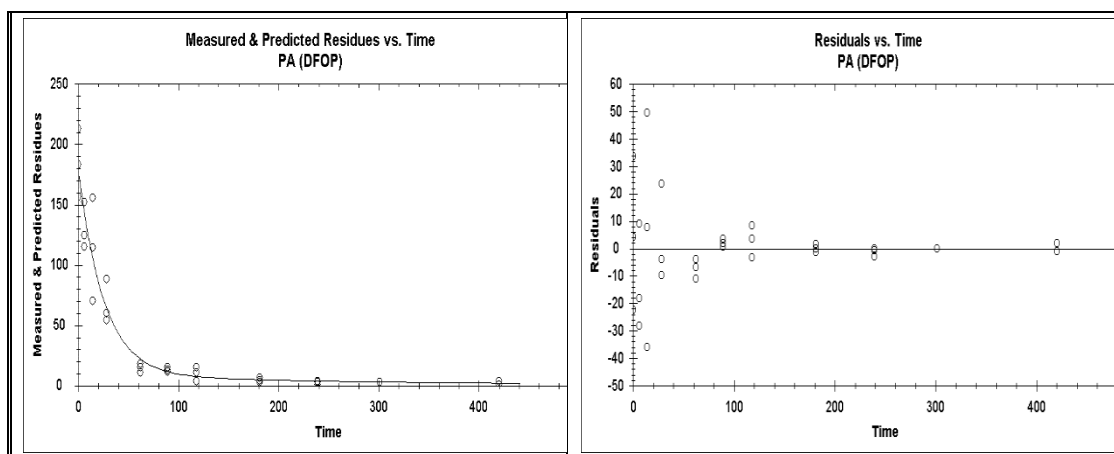


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-44: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925581 in field trial 15/03314437-06 (Spain)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	9.8	k: <0.001	good	19.7	65.5
	FOMC	9.5	α : 4.512 β : 110.2	good	18.3 ^a / 22.1 ^b	73.4
The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	9.4	k1 = 0.03941 (<0.001) k2 = 0.00357 (not sig.) g = 0.9504	good	18.8 ^a / 21.0 ^b	69.6
The DFOP model further improves the visual fit and provides the lowest χ^2 error, residuals are randomly scattered around zero. The parameter k2 is not significantly different from zero, which is acceptable as the degradation is mainly driven by the fast degradation phase, indicated by the g value of 0.9504.						
Conclusion: DFOP is appropriate for derivation of trigger endpoints.						
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<div>   </div>						



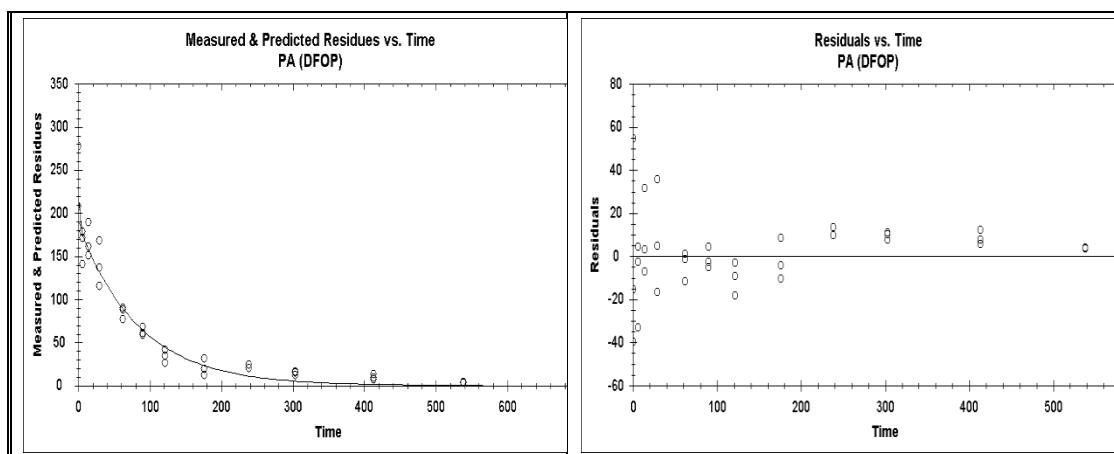
^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Reg. No. 5925632

Table 8.1.2.2.1-45: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925632 in field trial 15/03314437-01 (Germany)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	11.3	k: <0.001	acceptable	52.0	172.8
	FOMC	10.2	α : 2.51 β : 140.6	good	44.7 ^a / 63.6 ^b	211.3
The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	8.4	k1 = 2.732 (not sig.) k2 = 0.01185 (<0.001) g = 0.1641	acceptable	43.4 ^a / 53.9 ^b	179.2
The DFOP model does not further improve the visual fit compared to the FOMC fit and the k1 parameter is not significantly different to zero.						
Conclusion: FOMC is appropriate for derivation of trigger endpoints.						

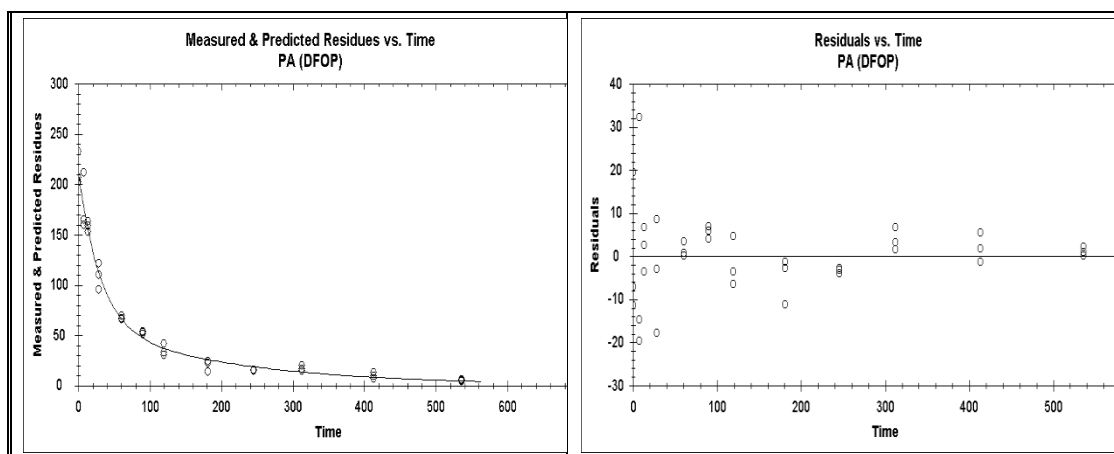


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-46: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925632 in field trial 15/03314437-02 (Italy)

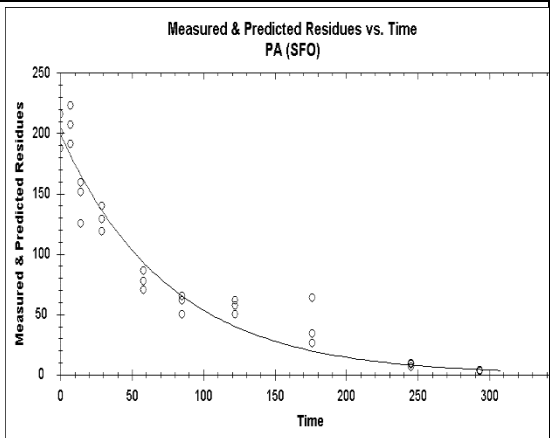
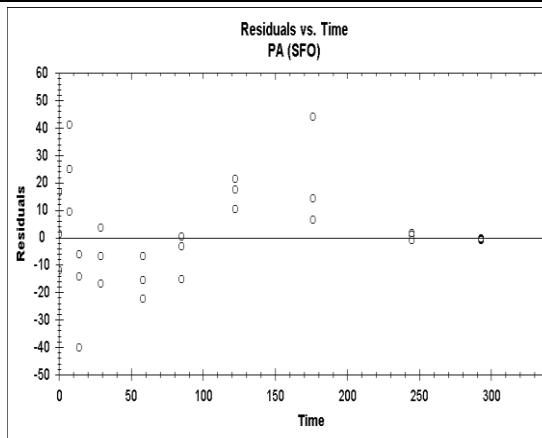
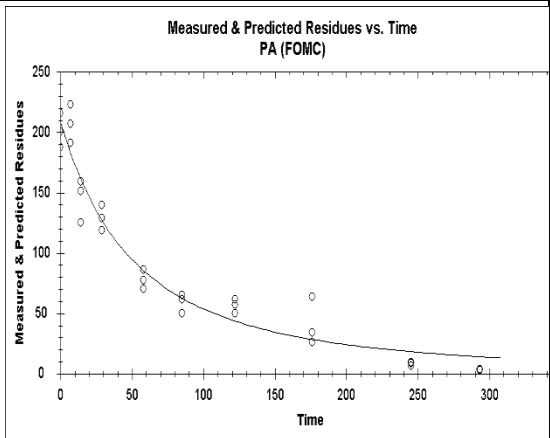
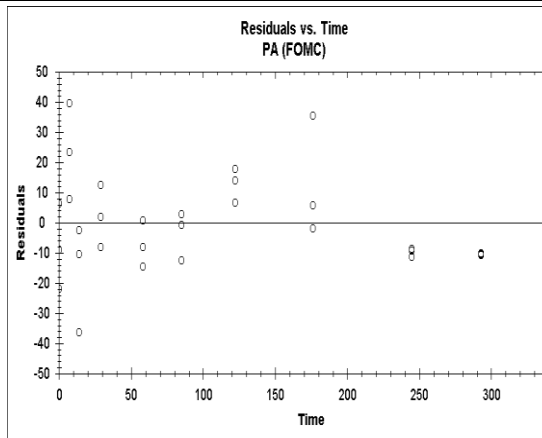
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	11.3	k: <0.001	poor	41.4	137.6
	FOMC	3.2	α : 1.428 β : 49.29	good	30.8 ^a / 59.6 ^b	197.8
The SFO visual fit is poor as residuals are large and deviate systematically from zero. The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	3.7	k1 = 0.03331 (<0.001) k2 = 0.00485 (<0.01) g = 0.7132	good	31.1 ^a / 65.7 ^b	218.1
The DFOP model does not further improve the visual fit compared to the FOMC fit and provides a higher χ^2 error value. Conclusion: FOMC is appropriate for derivation of trigger endpoints.						
Measured & Predicted Residues vs. Time PA (SFO)		Residuals vs. Time PA (SFO)				
Measured & Predicted Residues vs. Time PA (FOMC)		Residuals vs. Time PA (FOMC)				

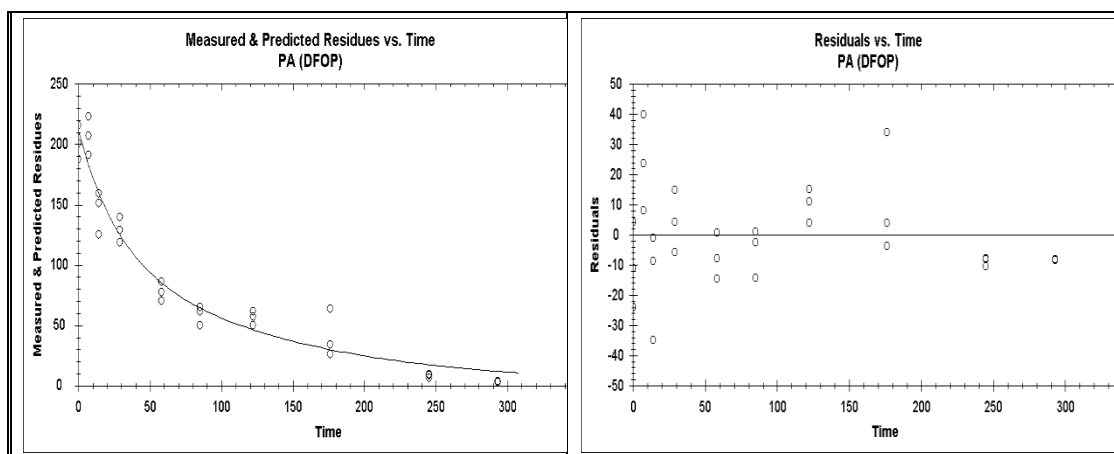


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-47: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925632 in field trial 15/03314437-03 (Denmark)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	12.5	k: <0.001	acceptable	52.6	174.7
	FOMC	11.1	α : 2.009 β : 102.9	acceptable	42.4 ^a / 66.4 ^b	220.7
The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	11.2	k1 = 0.03859 (<not sig.) k2 = 0.00790 (<0.01) g = 0.4365	acceptable	40.6 ^a / 66.0 ^b	219.0
The DFOP model does not further improve the visual fit compared to the FOMC and the k1 parameter is not significantly different to zero.						
Conclusion: FOMC is appropriate for derivation of trigger endpoints.						
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<div>   </div>						



^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

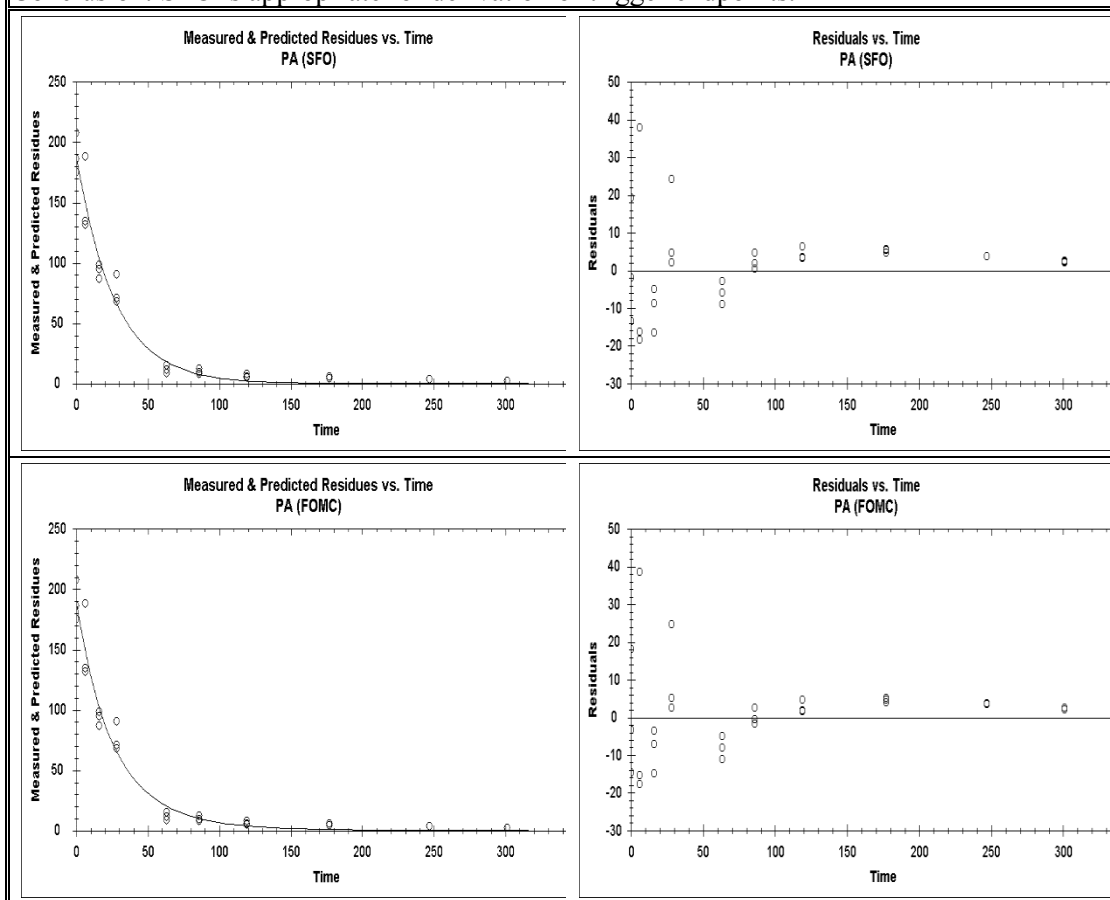
Table 8.1.2.2.1-48: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925632 in field trial 15/03314437-04 (UK)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	8.2	k: <0.001	good	18.6	61.8
	FOMC	8.4	α : 10.39 β : 261.2	good	18.0 ^a / 19.5 ^b	64.8

The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero.

The FOMC model does not improve the visual fit and provides a higher χ^2 error value.

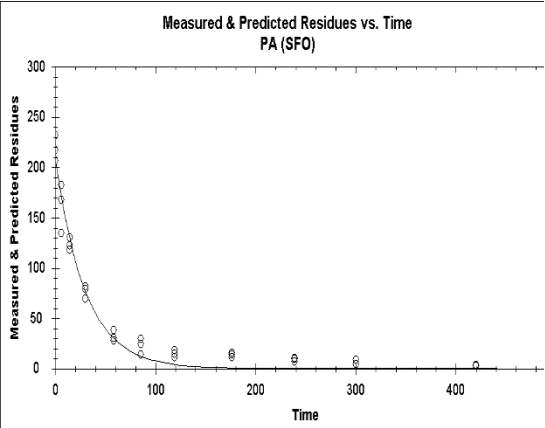
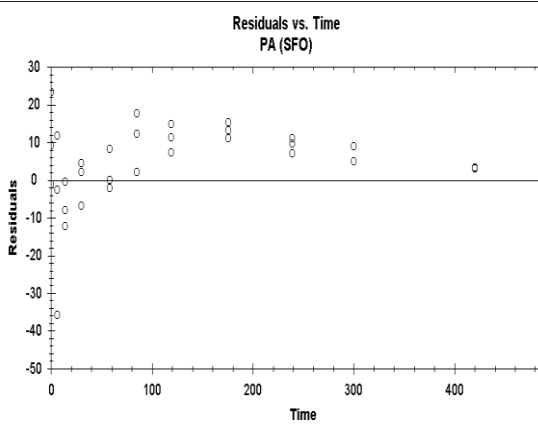
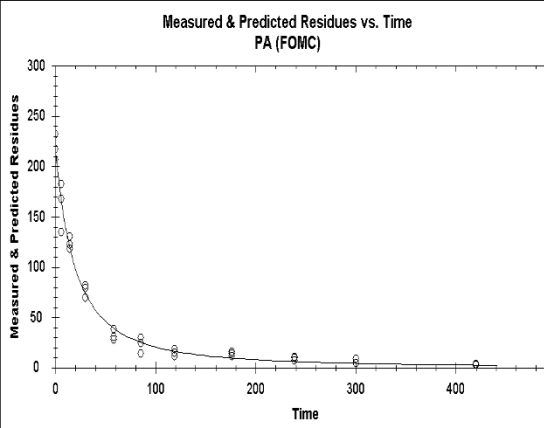
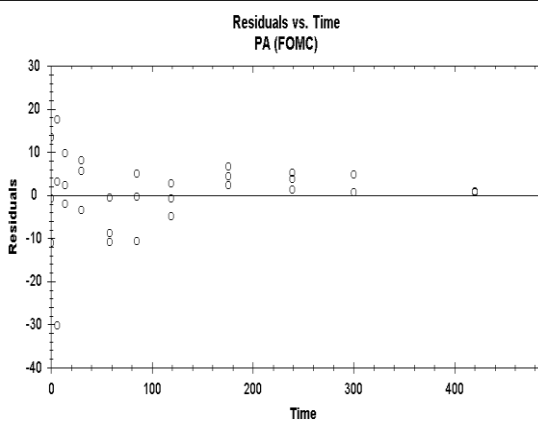
Conclusion: SFO is appropriate for derivation of trigger endpoints.

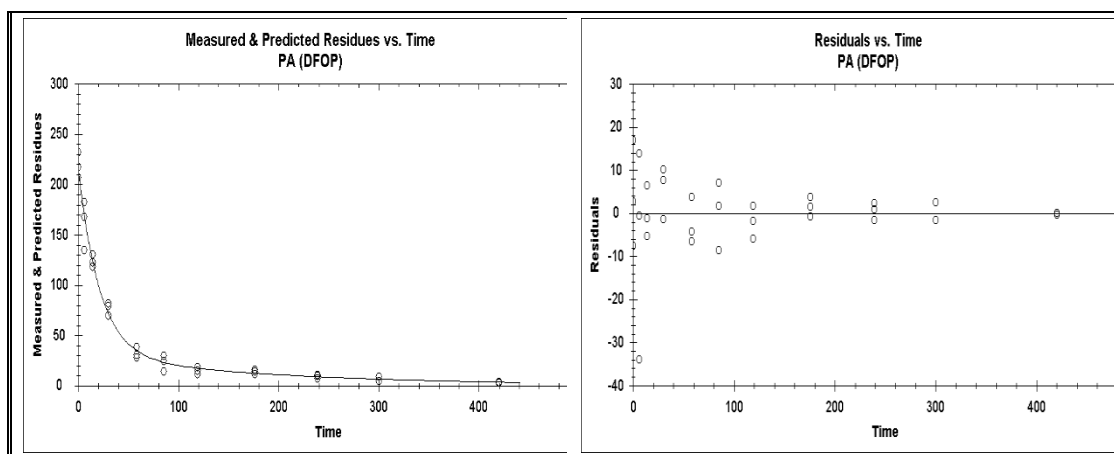


^a Overall DT₅₀

^b Calculated DT₅₀ = DT₉₀/3.32

Table 8.1.2.2.1-49: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925632 in field trial 15/03314437-05 (Belgium)

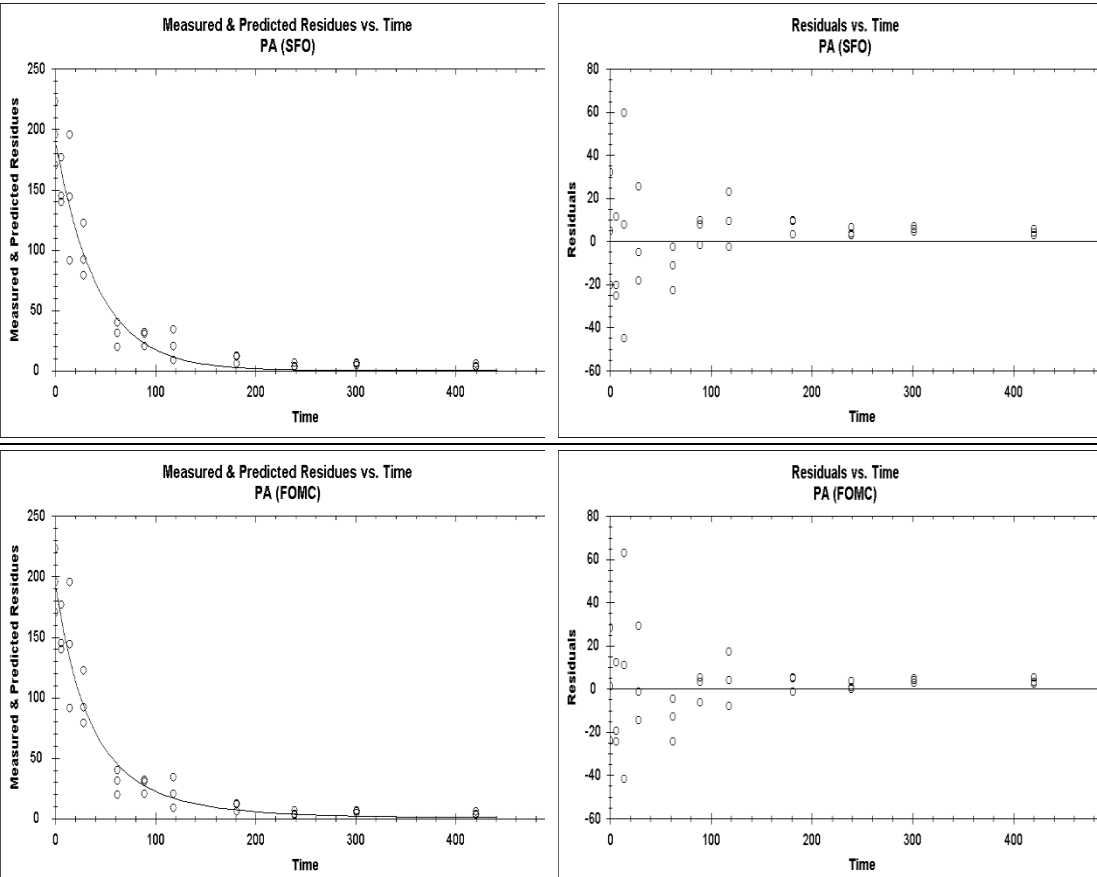
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	11.0	k: <0.001	poor	20.9	69.3
	FOMC	4.5	α : 1.744 β : 34.59	good	16.9 ^a / 28.6 ^b	94.9
The SFO visual fit is poor as residuals are large and deviate systematically from zero. The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	4.4	k1 = 0.04693 (<0.001) k2 = 0.00522 (<0.05) g = 0.8574	good	17.9 ^a / 27.6 ^b	91.7
The DFOP model further improves the visual fit and provides the lowest χ^2 error value, residuals are randomly scattered around zero. The parameters k1 and k2 are significantly different from zero.						
Conclusion: DFOP is appropriate for derivation of trigger endpoints.						
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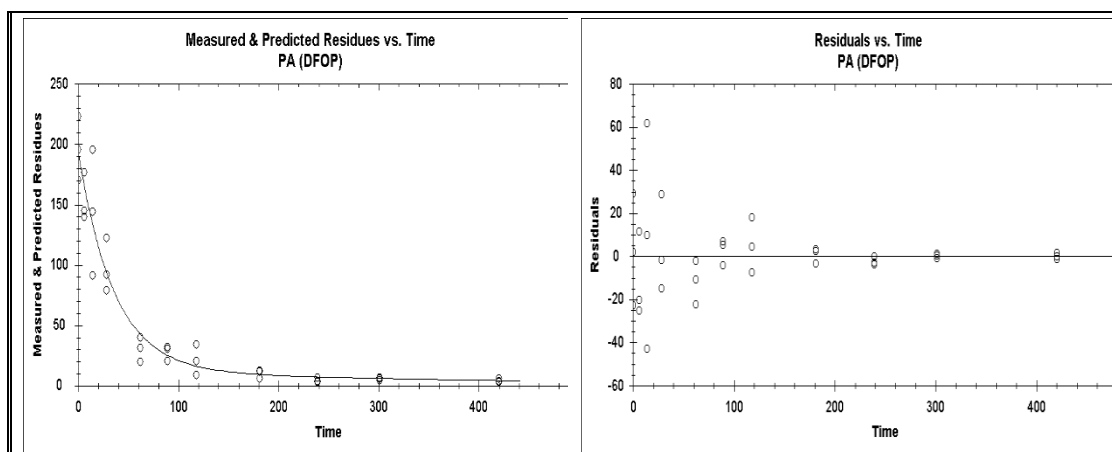


^a Overall DT_{50}

^b Calculated $DT_{50} = DT_{90}/3.32$

Table 8.1.2.2.1-50: Statistical and visual assessment of kinetic models for derivation of trigger endpoints for Reg. No. 5925632 in field trial 15/03314437-06 (Spain)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO & FOMC	SFO	9.6	k: <0.001	acceptable	28.8	95.7
	FOMC	9.1	α : 4.055 β : 141.8	good	26.4 ^a / 32.6 ^b	108.4
The SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero.						
The FOMC model improves the visual fit and provides a lower χ^2 error value → test further biphasic model (DFOP).						
Run DFOP	DFOP	8.7	k1 = 0.02833 (<0.001) k2 = 0.00278 (not sig.) g = 0.9305	good	26.8 ^a / 31.5 ^b	104.6
The DFOP model further improves the visual fit and provides the lowest χ^2 error, residuals are randomly scattered around zero. The parameters k2 is not significantly different from zero, which is acceptable as the degradation is mainly driven by the fast degradation phase, indicated by the g value of 0.9305.						
Conclusion: DFOP is appropriate for derivation of trigger endpoints.						
 <p>The figure contains four subplots arranged in a 2x2 grid. The top-left plot is titled 'Measured & Predicted Residues vs. Time PA (SFO)' and shows a decreasing curve with open circles representing data points. The top-right plot is titled 'Residuals vs. Time PA (SFO)' and shows residuals scattered around zero. The bottom-left plot is titled 'Measured & Predicted Residues vs. Time PA (FOMC)' and shows a similar decreasing curve with open circles. The bottom-right plot is titled 'Residuals vs. Time PA (FOMC)' and shows residuals scattered around zero. All plots have 'Time' on the x-axis (0 to 400) and 'Measured & Predicted Residues' or 'Residuals' on the y-axis.</p>						



^a Overall DT₅₀

^b Calculated DT₅₀ = DT₉₀/3.32

III. CONCLUSION

The degradation behaviour of the herbicide cinmethylin and its two enantiomers Reg. No. 5925581 and Reg. No. 5925632 in soil has been investigated in a field dissipation study including six field trials located in Germany, Italy, Denmark, UK, Belgium and Spain. Kinetic evaluations were performed to analyse the degradation kinetics of cinmethylin and its two enantiomers observed in the six soils according to the current guidance of the FOCUS workgroup on degradation kinetics in order to derive the trigger endpoints.

For all models considered appropriate, the visual assessment and goodness-of-fit statistics indicate plausible fit. Therefore, the resulting endpoints can be considered reliable.

Report:	CA 7.1.2.2.1/04 He, W. and Pape, L. 2018b
Title	Kinetic evaluation of a field dissipation study with BAS 684 H conducted in 2015 to 2017: Determination of modelling endpoints for the racemate and its enantiomers (Reg.No. 5925581 and Reg.No. 5925632) according to FOCUS
Document No.:	2017/1199008
Guidelines:	<ul style="list-style-type: none"> • FOCUS Kinetics (2006) “Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration” Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0, 434 pp • FOCUS Kinetics (2014) “Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration” Version 1.1, 440 pp • European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662
GLP:	None
Deviations	None; acceptable for use as modelling endpoints.

SUMMARY

The degradation behaviour of the herbicide cinmethylin in soil has been investigated in a field dissipation study including six field trials located in Germany, Italy, Denmark, UK, Belgium and Spain. The purpose of this evaluation was to analyse the degradation kinetics of cinmethylin and its two enantiomers Reg. No. 5925581 and Reg. No. 5925632 according to the current guidance of the FOCUS workgroup on degradation kinetics in order to derive normalized modelling endpoints.

Prior to kinetic analysis, the sampling intervals of the field studies were normalized to reference conditions (20°C, pF2) regarding soil moisture and temperature according to the time-step normalization technique. Kinetic evaluation was performed on the time-step normalized dataset.

The respective degradation parameters were derived based on a visual and statistical assessment under the consideration of the recommendations of the FOCUS kinetics working group. The appropriate kinetic models and resulting normalized modelling endpoints for cinmethylin and its two enantiomers are summarised in the tables below.

The study design was compliant with EFSA's recommendations for obtaining DegT50 values in soil from field studies for modelling purposes, as dissipation caused by surface processes like photolysis or volatilization was minimized by incorporating the test item residues to a depth of 4 – 10 cm directly after the applications. Hence, the reported modelling endpoints are suitable for use in environmental fate models.

For all models considered appropriate, the visual assessment and goodness-of-fit statistics indicate plausible fit. The t-test was passed for the respective model parameters. Therefore, the resulting endpoints can be considered reliable.

The modelling endpoints for cinmethylin and its two enantiomers are summarised in the tables below.

Table 8.1.2.2.1-51: Summary of modelling endpoints of cinmethylin

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error [%]	Normalized DegT50 [d]
15/03314437-01 (Germany)	Loamy fine sand	4.80	FOMC	9.7	29.9 ^c
15/03314437-02 (Italy)	Very fine sandy loam	7.66	FOMC	5.6	47.0 ^c
15/03314437-03 (Denmark)	Sand	4.62	SFO	9.4	15.3
15/03314437-04 (UK)	Loam	6.70	SFO	8.1	5.4
15/03314437-05 (Belgium)	Silt	6.12	FOMC	5.0	8.0 ^c
15/03314437-06 (Spain)	Coarse sandy loam	7.70	SFO	10.3	13.9

^a Soil characteristics of the uppermost horizon^b Measured in CaCl₂^c Calculated as DT50 = DT90 / 3.32 (less than 10% of initial concentration at last sampling)**Table 8.1.2.2.1-52: Summary of modelling endpoints of Reg. No. 5925581**

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error [%]	Normalized DegT50 [d]
15/03314437-01 (Germany)	Loamy fine sand	4.80	FOMC	9.9	25.4 ^c
15/03314437-02 (Italy)	Very fine sandy loam	7.66	FOMC	5.9	40.6 ^c
15/03314437-03 (Denmark)	Sand	4.62	SFO	9.8	14.2
15/03314437-04 (UK)	Loam	6.70	SFO	9.2	4.4
15/03314437-05 (Belgium)	Silt	6.12	FOMC	5.4	6.4 ^c
15/03314437-06 (Spain)	Coarse sandy loam	7.70	SFO	10.5	10.7

^a Soil characteristics of the uppermost horizon^b Measured in CaCl₂^c Calculated as DT50 = DT90 / 3.32 (less than 10% of initial concentration at last sampling)

Table 8.1.2.2.1-53: Summary of modelling endpoints of Reg. No. 5925632

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error [%]	Normalized DegT50 [d]
15/03314437-01 (Germany)	Loamy fine sand	4.80	FOMC	9.4	33.9 ^c
15/03314437-02 (Italy)	Very fine sandy loam	7.66	FOMC	5.5	52.5 ^c
15/03314437-03 (Denmark)	Sand	4.62	SFO	9.0	16.2
15/03314437-04 (UK)	Loam	6.70	SFO	7.4	6.4
15/03314437-05 (Belgium)	Silt	6.12	FOMC	5.0	9.4 ^c
15/03314437-06 (Spain)	Coarse sandy loam	7.70	SFO	9.2	17.2

^a Soil characteristics of the uppermost horizon^b Measured in CaCl₂^c Calculated as DT50 = DT90 / 3.32 (less than 10% of initial concentration at last sampling)

I. MATERIAL AND METHODS

Description of the field dissipation study

The degradation behaviour of the herbicide cinmethylin and its two enantiomers Reg. No. 5925581 and Reg. No. 5925632 in soil has been investigated in a field dissipation study including six field trials located in Germany, Italy, Denmark, UK, Belgium and Spain [see KCA 7.1.2.2.1/1 and KCA 7.1.2.2.1/2]. The sites represent typical regions of agricultural practice representative for growing cereals which are among the most important crops for the use of cinmethylin.

The study design was compliant with EFSA's recommendations for obtaining DegT50 values in soil from field studies for modelling purposes [EFSA (2014)], as dissipation caused by surface processes like photolysis or volatilization was minimized by incorporating the test item to a depth of 4 – 10 cm directly after the applications. Hence, the reported modelling endpoints are suitable for use in environmental fate models.

Cinmethylin was applied in the formulation BAS 684 02 H as an emulsifiable concentrate (EC) to bare soil on three replicate plots per trial (Subplots A, B and C) in a single application at an intended application rate of 500 g a.s. ha⁻¹ using a calibrated boom sprayer. Immediately after application of the test item, but before subsequent soil sampling all plots were harrowed to a soil depth of approximately 4 to 10 cm in order to incorporate residues in soil and thus minimize the impact of surface processes (e.g. photolysis, volatilization) on the degradation of cinmethylin as recommended by EFSA [EFSA (2014)].

No tillage or fertilization was performed during the course of the study and no crops were grown throughout the trial. The plots were kept free of vegetation via the application of glyphosate and in one case (Germany) with pelargonic acid in order to keep the plot free of moss growth. Additional irrigation to supplement rainfall was not performed during the course of the study.

For all trials, each sampling was conducted per replicate plot and down to a maximum soil depth of 50 cm, generating one set of main and one set of double samples.

Details on the applied amounts of test item, the application dates and the sampling dates are given in [see KCA 7.1.2.2.1/1 and KCA 7.1.2.2.1/2].

Samples were analysed for residues of the two enantiomers contained in the test item. The limit of quantification (LOQ) was 0.005 mg/kg for each analyte. The limit of detection (LOD) was set at 0.0015 mg/kg (30% of LOQ).

Residues of cinmethylin in the soil profiles were exclusively detected at concentrations above the LOQ in the upper 20 cm of the soils. No residues above the LOQ were detected below 20 cm in any specimen at any time.

Data handling

As surface processes had been minimized by incorporating of the test item residues to a depth of 4 – 10 cm directly after the treatments, all data points were considered in this evaluation regardless of the 10 mm rain criterion described in EFSA [EFSA (2014)].

For the evaluation of each field trial, the residue data of the two enantiomers Reg. No. 5925581 and Reg. No. 5925632 in g ha⁻¹ were taken from the study report. The evaluation started at the day of application (0 DAT). Data from the three subplots were considered separately as replicates. For each of the two enantiomers, measured residues below LOQ or LOD were corrected according to FOCUS [FOCUS (2014)]. For the corrections the LOQ or LOD values in mg/kg were converted into g ha⁻¹ based on the respective dry sample weights and the total surface areas of liners, using the same method as described in the study report [KCA 7.1.2.2.1/1]. Corrections along the sampling depth were made for each sampling date and each subplot. In addition, corrections along the sampling dates were made, if no residue values above LOD were detected in any sampling depth. Then, the residue data of each enantiomer were cumulated over the entire sampling depth. The resulting datasets were directly used for kinetic evaluation for the two enantiomers. For the kinetic evaluation for the test item cinmethylin, the data of the two enantiomers were summed up.

Due to the corrections described above the resulting datasets used for kinetic analysis (in g ha⁻¹) are different from the measured residues data (in g ha⁻¹) given in the study report.

Time-step normalization approach

The normalization procedure was carried out based on the recommendations of FOCUS [FOCUS (2014)] for all the six field trials by reducing or increasing day lengths depending on soil temperature and moisture by means of correction factors (f_{temp} and f_{moist}). Daily soil moisture and soil temperature values were calculated by FOCUS-PEARL 4.4.4. Based on these model results, daily correction factors for the normalized day length were calculated, and the cumulative time between sampling points was determined and used as input for a standard kinetic evaluation according to FOCUS (2014). The HSE evaluator validated the applicants daily soil moisture and soil temperature using FOCUS-PEARL 4.4.4 and can confirm the values used by the applicant are correct.

The daily soil temperature and moisture used for the temperature and moisture correction of the different field trial data were calculated for each day of the study period from the respective day of application until the last sampling day.

Temperature correction factors (f_{temp}) were determined to account for differences between actual daily soil temperatures as calculated by FOCUS-PEARL and a reference soil temperature of 20°C using a Q10 value of 2.58.

Moisture correction factors (f_{moist}) were determined to account for differences between actual daily soil moisture as calculated by FOCUS-PEARL and the reference soil moisture at field capacity (pF 2).

For DAT 0, no normalization was considered and application was assumed to occur at time point zero. Normalized sampling days (D_{norm}) after application were calculated by cumulatively summing up normalized day lengths.

Kinetic models included in the assessment

For each trial, the appropriate kinetic model was identified based on the visual and statistical assessment considering the procedures and kinetic models proposed by the FOCUS kinetics guidance (2014) to derive modelling endpoints. The modelling endpoints were derived preferably from the SFO model. If the SFO model was not appropriate, pragmatic procedures were used to derive conservative pseudo-SFO degradation rates from the appropriate bi-phasic model. For the current evaluation, the SFO kinetic model and as 10% initially measured concentration were reached within the experimental period the FOMC kinetic model were applied, as recommended by FOCUS. There are no relevant soil metabolites in the field or laboratory degradation studies so the HSE evaluator accepts the Applicants approach to use FOMC kinetic model if the SFO model is not appropriate.

A kinetic model is considered appropriate if the residuals are randomly distributed around zero, the χ^2 error indicates a sufficient quality of the fit (i.e. value is <15%). However, this value should not be taken as a cut-off criterion. In field studies, the data points are often scattered around the curve, which results in a large error value. In some cases fits with higher error value (i.e. χ^2 error value >15%) are still acceptable if they represent the degradation behaviour well. The t test for the degradation parameters should be passed at 5% error level.

Software for kinetic evaluation

The Applicant used the software package KinGUI version 2.2014.224.1704 for parameter fitting. The error tolerance and the number of iterations of the optimization tool (IRLS) were set to the default values of 1×10^{-6} and 100, respectively. The HSE evaluator has validated the Applicants kinetic evaluation using CAKE v3.2.

Experimental data

The data sets submitted to kinetic analysis are provided in Table 8.1.2.2.1-54 to Table 8.1.2.2.1-56.

Table 8.1.2.2.1-54: Experimental data, Subplot A, B and C used for kinetic evaluation of cinmethylin

15/03314437-01 (Germany)					15/03314437-02 (Italy)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		
		Subplot A	Subplot B	Subplot C			Subplot A	Subplot B	Subplot C
0	0.0	359.6	402.1	542.2	0	0.0	385.9	398.2	444.2
6	2.1	266.6	334.4	333.8	7	3.5	391.9	300.8	299.8
14	4.4	299.8	282.8	359.5	13	6.8	301.5	300.0	282.7
29	9.9	209.3	253.3	302.5	28	17.2	214.8	171.2	194.4
62	21.2	156.0	158.0	138.2	60	47.8	121.9	119.5	114.8
90	41.4	103.2	121.1	103.3	90	79.2	93.6	91.8	88.5
121	66.6	41.0	61.9	69.9	119	111.0	70.3	53.5	57.9
176	99.2	20.6	31.3	51.7	181	151.8	24.7	40.4	39.5
238	120.4	34.3	40.6	34.6	245	170.4	24.3	26.7	25.6
303	134.9	20.6	27.1	26.8	312	189.0	25.3	29.2	33.6
413	176.8	12.0	15.7	23.3	413	256.9	13.5	19.0	24.2
538	269.8	7.0	7.5	5.1	536	389.6	9.9	9.0	12.7
15/03314437-03 (Denmark)					15/03314437-04 (UK)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		
		Subplot A	Subplot B	Subplot C			Subplot A	Subplot B	Subplot C
0	0.0	360.8	414.1	386.2	0	0.0	339.2	362.4	400.3
7	2.0	390.1	430.8	365.9	6	1.9	240.5	238.3	343.1
14	4.8	297.0	290.9	238.8	16	5.6	160.3	168.7	149.2
29	10.3	217.1	262.1	241.9	28	9.4	111.2	149.7	114.2
58	20.1	154.4	139.3	126.8	63	22.2	20.2	24.2	16.0
85	28.2	107.3	91.3	118.2	86	31.0	20.5	15.9	13.8
122	33.9	87.4	110.5	100.3	119	41.9	9.5	13.8	9.4
176	44.5	62.9	116.6	47.7	177	56.5	8.3	10.4	10.1
245	67.5	12.5	16.4	16.8	247	79.2	7.7	6.8	6.7
293	97.3	7.7	4.2	6.6	301	110.1	3.0	2.8	3.4
414	161.5	- ^c	- ^c	- ^c	413	170.7	- ^c	- ^c	- ^c
15/03314437-05 (Belgium)					15/03314437-06 (Spain)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		

		Subplot A	Subplot B	Subplot C			Subplot A	Subplot B	Subplot C
0	0.0	447.6	403.4	424.2	0	0.0	435.6	327.3	379.0
6	1.8	313.8	338.7	250.1	6	3.0	255.1	328.7	269.7
14	4.8	211.6	224.3	211.4	14	6.9	161.7	351.9	258.1
30	9.6	138.3	128.8	111.6	28	14.5	152.8	133.7	210.9
58	19.6	44.8	54.6	45.2	62	40.7	58.2	46.8	31.0
85	28.9	41.4	47.1	24.3	89	56.0	47.2	43.8	32.9
119	37.1	26.9	30.3	18.9	118	69.9	13.0	49.8	31.7
176	50.7	23.9	25.4	20.3	181	99.8	16.7	9.2	18.8
239	76.5	15.8	17.2	12.4	239	134.5	4.4	10.8	7.1
300	124.7	10.2	14.3	9.1	301	188.2	10.0	7.8	9.2
420	201.2	7.5	6.8	6.5	420	278.6	3.9	5.0	9.7

^a Normalized day lengths (20°C, pF2)

^b The residues below the LOD were set to ½ LOD (in accordance to FOCUS guidance) along the sampling depth and sampling dates. LOQ or LOD values in mg/kg were converted into g ha⁻¹ based on the respective dry sample weights and surface areas of liners.

^c Specimen taken but not analysed

Table 8.1.2.2.1-55: Experimental data, Subplot A, B and C used for kinetic evaluation of Reg. No. 5925581

15/03314437-01 (Germany)					15/03314437-02 (Italy)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		
		Subplot A	Subplot B	Subplot C			Subplot A	Subplot B	Subplot C
0	0.0	175.8	193.8	264.0	0	0.0	183.7	191.6	211.2
6	2.1	125.7	155.8	162.4	7	3.5	179.8	135.7	139.5
14	4.4	138.5	131.8	169.8	13	6.8	138.3	140.9	130.0
29	9.9	93.4	115.8	134.1	28	17.2	92.7	75.6	84.0
62	21.2	65.1	69.6	60.4	60	47.8	52.0	52.2	48.3
90	41.4	41.6	52.3	44.0	90	79.2	39.4	38.8	37.3
121	66.6	14.7	26.7	28.4	119	111.0	28.3	22.7	24.2
176	99.2	7.6	12.2	20.0	181	151.8	10.1	15.8	16.5
238	120.4	13.4	16.0	13.9	245	170.4	9.6	11.3	9.6
303	134.9	7.7	10.7	11.3	312	189.0	10.1	12.5	13.3
413	176.8	4.8	6.4	9.7	413	256.9	6.5	8.8	10.5
538	269.8	3.2	3.2	0.9	536	389.6	4.4	4.1	5.9
15/03314437-03 (Denmark)					15/03314437-04 (UK)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		
		Subplot A	Subplot B	Subplot C			Subplot A	Subplot B	Subplot C
0	0.0	173.3	198.3	185.6	0	0.0	164.2	175.9	192.5
7	2.0	183.4	207.6	174.7	6	1.9	106.0	106.1	154.5
14	4.8	137.4	139.2	113.2	16	5.6	65.1	69.8	61.8
29	10.3	98.1	122.3	112.8	28	9.4	42.8	59.1	43.0
58	20.1	68.3	62.0	56.2	63	22.2	8.1	9.0	6.9
85	28.2	45.5	41.3	52.8	86	31.0	8.1	6.4	5.6
122	33.9	37.2	49.1	42.9	119	41.9	3.6	5.3	3.9
176	44.5	29.0	53.0	21.4	177	56.5	3.4	4.4	4.4
245	67.5	5.7	7.4	7.3	247	79.2	3.7	3.2	3.0
293	97.3	3.9 ^d	0.9 ^d	3.3 ^d	301	110.1	0.7 ^d	0.7 ^d	0.7 ^d
414	161.5	- ^c	- ^c	- ^c	413	170.7	- ^c	- ^c	- ^c
15/03314437-05 (Belgium)					15/03314437-06 (Spain)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		
		Subplot A	Subplot B	Subplot C			Subplot A	Subplot B	Subplot C
0	0.0	215.8	196.1	206.7	0	0.0	212.8	156.7	183.3
6	1.8	145.7	156.0	115.3	6	3.0	115.1	152.2	124.9
14	4.8	92.9	93.9	88.5	14	6.9	70.6	156.1	114.2
30	9.6	56.9	49.8	41.6	28	14.5	60.6	54.8	88.3
58	19.6	16.5	16.0	14.8	62	40.7	18.0	15.2	11.0
85	28.9	16.7	17.0	9.9	89	56.0	15.2	13.5	12.1
119	37.1	11.5	11.3	7.6	118	69.9	4.2	15.8	11.1
176	50.7	10.0	9.4	8.7	181	99.8	4.9	3.5	6.5
239	76.5	6.0	6.1	5.2	239	134.5	1.0	3.8	3.0

300	124.7	5.4	5.4	4.2	301	188.2	3.1	3.0	3.2
420	201.2	4.4	3.4	3.4	420	278.6	1.0	0.9	3.8

^a Normalized day lengths (20°C, pF2)

^b The residues below the LOD were set to ½ LOD (in accordance to FOCUS guidance) along the sampling depth and sampling dates. LOQ or LOD values in mg/kg were converted into g ha⁻¹ based on the respective dry sample weights and surface areas of liners.

^c Specimen taken but not analysed

Table 8.1.2.2.1-56: Experimental data, Subplot A, B and C used for kinetic evaluation of Reg. No. 5925632

15/03314437-01 (Germany)					15/03314437-02 (Italy)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		
		Subplot t A	Subplot t B	Subplot C			Subplot A	Subplot B	Subplot t C
0	0.0	183.8	208.3	278.2	0	0.0	202.2	206.5	233.1
6	2.1	140.9	178.6	171.4	7	3.5	212.1	165.1	160.2
14	4.4	161.3	151.0	189.7	13	6.8	163.1	159.0	152.7
29	9.9	116.0	137.5	168.4	28	17.2	122.1	95.6	110.4
62	21.2	90.9	88.4	77.8	60	47.8	69.9	67.3	66.5
90	41.4	61.6	68.7	59.2	90	79.2	54.2	53.1	51.3
121	66.6	26.3	35.2	41.6	119	111.0	42.0	30.8	33.7
176	99.2	13.0	19.1	31.6	181	151.8	14.6	24.6	23.0
238	120.4	20.8	24.6	20.8	245	170.4	14.7	15.5	16.0
303	134.9	12.9	16.4	15.5	312	189.0	15.1	16.7	20.3
413	176.8	7.3	9.2	13.7	413	256.9	7.0	10.1	13.7
538	269.8	3.8	4.3	4.2	536	389.6	5.5	4.8	6.8
15/03314437-03 (Denmark)					15/03314437-04 (UK)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		
		Subplot t A	Subplot t B	Subplot C			Subplot A	Subplot A	Subplot t B
0	0.0	187.5	215.9	200.6	0	0.0	175.1	186.5	207.8
7	2.0	206.8	223.1	191.3	6	1.9	134.5	132.2	188.6
14	4.8	159.6	151.7	125.6	16	5.6	95.2	98.9	87.4
29	10.3	119.1	139.8	129.2	28	9.4	68.4	90.7	71.1
58	20.1	86.1	77.3	70.6	63	22.2	12.1	15.2	9.1
85	28.2	61.8	50.0	65.3	86	31.0	12.4	9.5	8.2
122	33.9	50.2	61.4	57.4	119	41.9	5.8	8.5	5.5
176	44.5	33.9	63.7	26.2	177	56.5	4.9	6.0	5.7
245	67.5	6.8	9.0	9.5	247	79.2	3.9	3.7	3.8
293	97.3	3.8	3.4	3.3	301	110.1	2.3	2.1	2.7
414	161.5	- ^c	- ^c	- ^c	413	170.7	- ^c	- ^c	- ^c
15/03314437-05 (Belgium)					15/03314437-06 (Spain)				
DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b			DAT [d]	Dnorm [d] ^a	Data according to FOCUS [g ha-1] ^b		
		Subplot t A	Subplot t B	Subplot C			Subplot A	Subplot A	Subplot B
0	0.0	231.8	207.3	217.6	0	0.0	222.8	170.6	195.6
6	1.8	168.2	182.7	134.9	6	3.0	140.0	176.5	144.8
14	4.8	118.7	130.4	122.9	14	6.9	91.1	195.8	143.9
30	9.6	81.5	79.0	70.0	28	14.5	92.3	79.0	122.6
58	19.6	28.3	38.6	30.4	62	40.7	40.2	31.6	20.1
85	28.9	24.7	30.1	14.4	89	56.0	32.1	30.3	20.8
119	37.1	15.4	18.9	11.3	118	69.9	8.7	34.0	20.6
176	50.7	13.8	16.0	11.6	181	99.8	11.8	5.8	12.3
239	76.5	9.8	11.1	7.2	239	134.5	3.4	7.0	4.1

300	124.7	4.9	8.9	4.9	301	188.2	6.9	4.8	6.0
420	201.2	3.1	3.4	3.1	420	278.6	3.0	4.0	5.9

^a Normalized day lengths (20°C, pF2)

^b The residues below the LOD or LOD were set to ½ LOD (in accordance to FOCUS guidance) along the sampling depth and sampling dates. LOQ or LOD values in mg/kg were converted into g ha⁻¹ based on the respective dry sample weights and surface areas of liners.

^c Specimen taken but not analysed

II. RESULTS AND DISCUSSION

Kinetic evaluation for cinmethylin

For all trials, the simulated soil moisture overestimated the measured soil moisture and therefore represents a conservative estimate with regard to derivation of normalized DegT50. Therefore, the results of the FOCUS-PEARL simulations were considered adequate to be used for subsequent time-step normalization.

Normalized day lengths were determined using the correction factors for soil temperature and moisture calculated from the differences between the simulated daily actual soil temperature and moisture and the standard soil temperature of 20°C and soil moisture of pF 2.

The degradation behaviour of cinmethylin in the six field trials was analysed in order to derive kinetic endpoints for environmental fate modelling using the normalized data sets.

The kinetic evaluation of cinmethylin showed that for trial 15/03314437-01 (Germany), 15/03314437-02 (Italy) and 15/03314437-05 (Belgium) the FOMC kinetic model is appropriate to derive modelling endpoints, whereas for trial 15/03314437-03 (Denmark), 15/03314437-04 (UK) and 15/03314437-06 (Spain) the SFO kinetic model is appropriate to derive modelling endpoints. The kinetic models tested and the respective statistical and visual assessments are summarised in Table 8.1.2.2.1-57 to Table 8.1.2.2.1-62.

For modelling endpoints, an SFO model fit should be accepted if the fit is statistically and visually acceptable. If an SFO model fit is not acceptable then bi-phasic models must be explored. An HS or DFOP model would be accepted if statistically and visually acceptable and 10 % of the initial measured concentration is not reached within the experimental period. An FOMC model should be accepted if statistically and visually acceptable and 10 % of the initial measured concentration is reached. An FOMC model can also only be accepted if there are no soil metabolites.

Table 8.1.2.2.1-57: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for cinmethylin in field trial 15/03314437-01 (Germany)

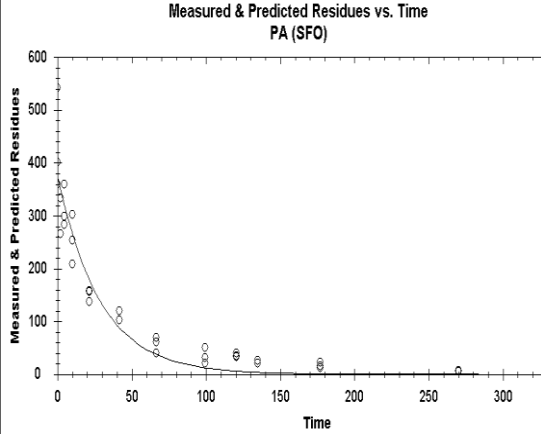
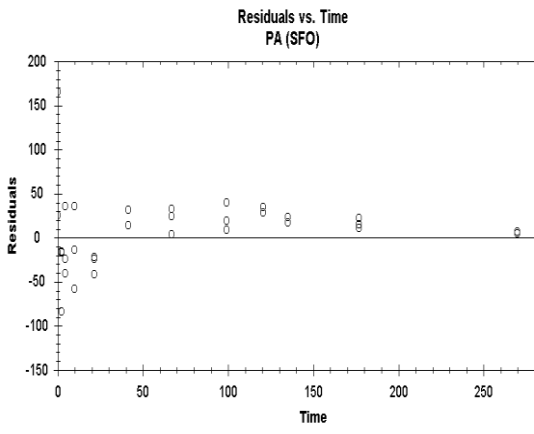
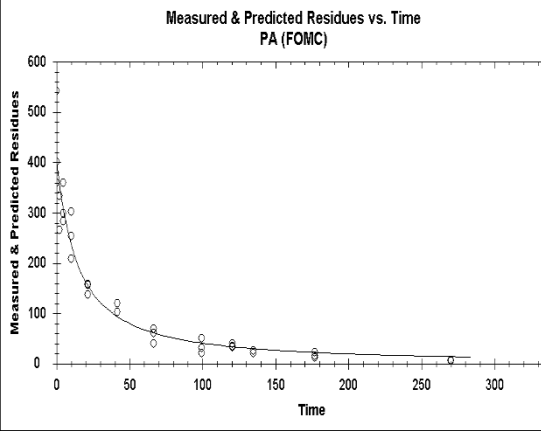
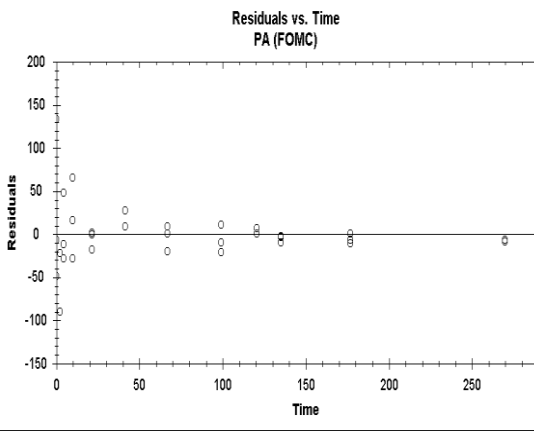
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	15.2	k: <0.001	poor	19.9	66.2
SFO visual fit is poor as residuals are large and deviate systematically from zero, the χ^2 error value is above 15% → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	9.7	$\alpha = 1.211$ B = 17.44	good	29.9 (DT90/3.32)	99.4
The FOMC visual fit is good, the χ^2 error value is below 15%, residuals are randomly scattered around zero.						
Conclusion: The HSE evaluator considers FOMC is appropriate for derivation of modelling endpoints because there are no soil metabolites.						
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Table 8.1.2.2.1-58: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for cinmethylin in field trial 15/03314437-02 (Italy)

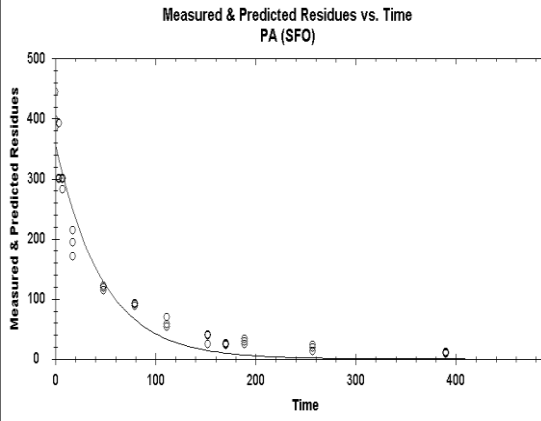
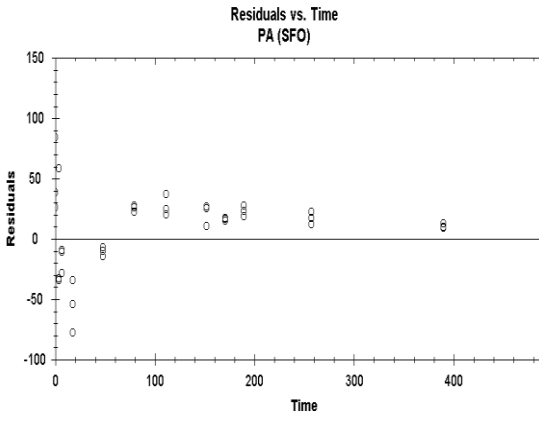
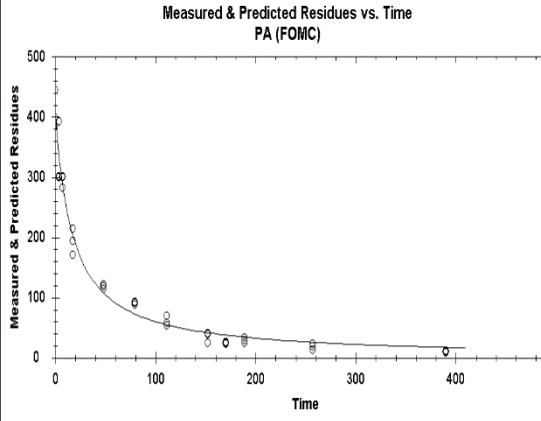
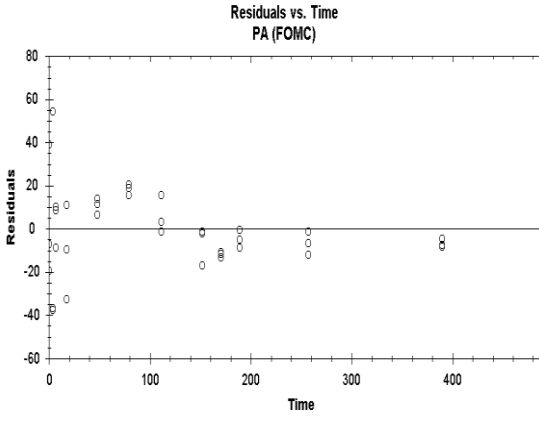
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	16.4	k: <0.001	poor	32.3	107.4
SFO visual fit is poor as residuals are large and deviate systematically from zero, the χ^2 error value is above 15% → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	5.6	$\alpha = 1.004$ $\beta = 17.51$	good	47.0 (DT90/3.32)	156.0
The FOMC visual fit is good and the χ^2 error value is below 15%. Conclusion: The HSE evaluator considers FOMC is appropriate for derivation of modelling endpoints because there are no soil metabolites.						
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Table 8.1.2.2.1-59: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for cinmethylin in field trial 15/03314437-03 (Denmark)

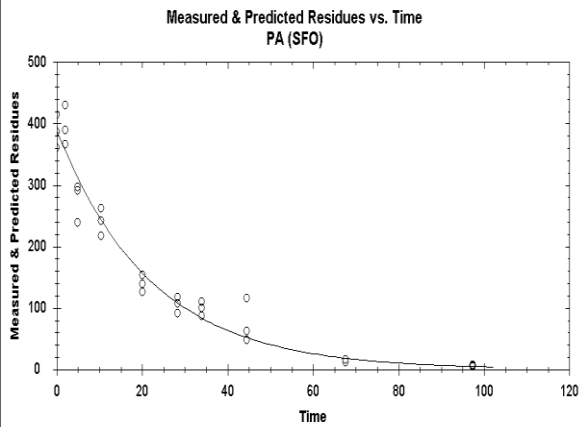
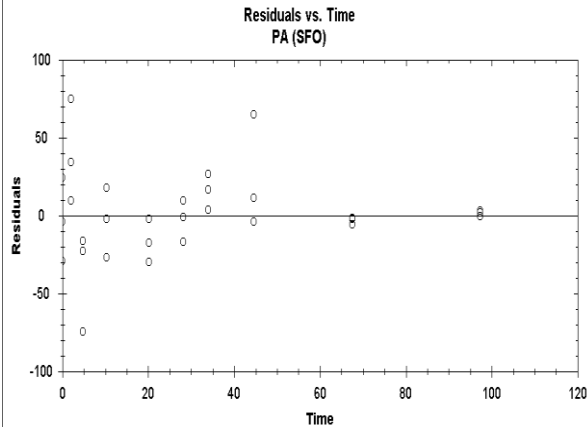
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	9.4	k: <0.001	acceptable	15.3	50.7
SFO visual fit is acceptable, the χ^2 error value is below 15%. k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;">   </div>						

Table 8.1.2.2.1-60: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for cinmethylin in field trial 15/03314437-04 (UK)

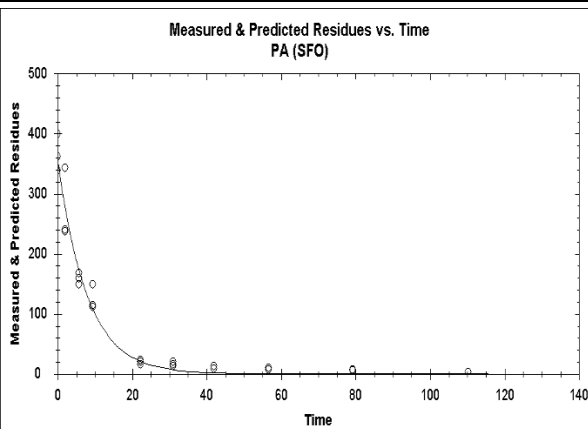
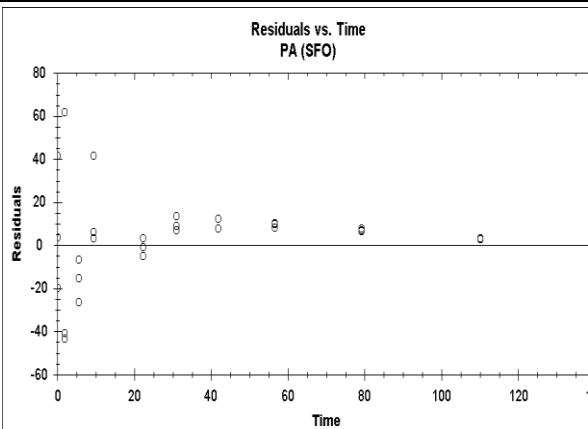
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	8.1	k: <0.001	acceptable	5.4	18.0
SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;">   </div>						

Table 8.1.2.2.1-61: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for cinmethylin in field trial 15/03314437-05 (Belgium)

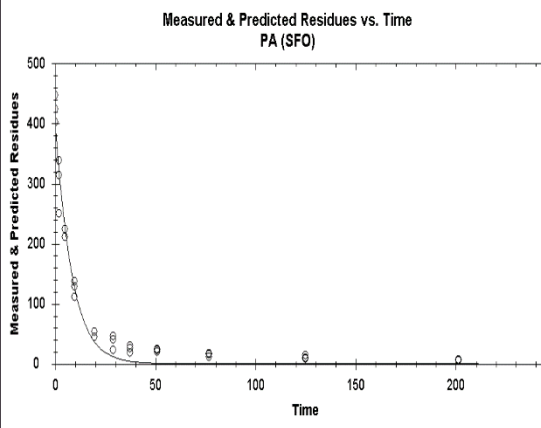
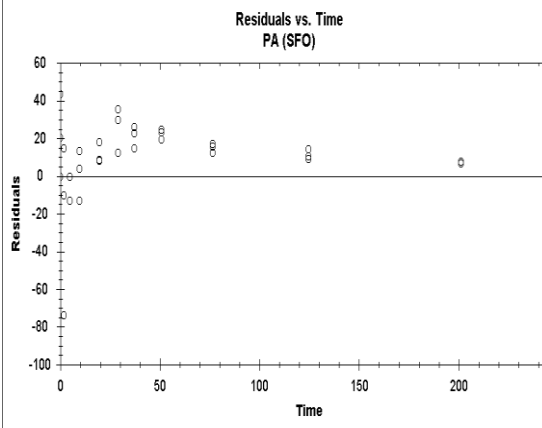
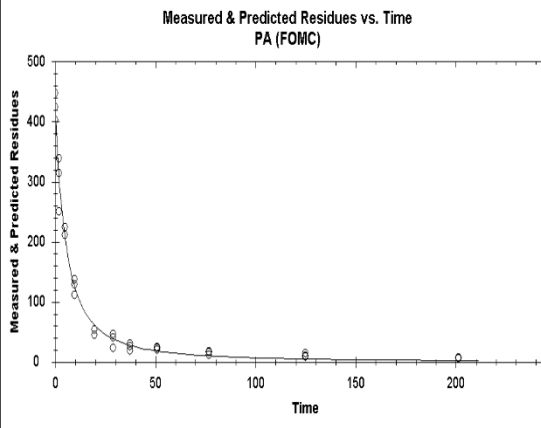
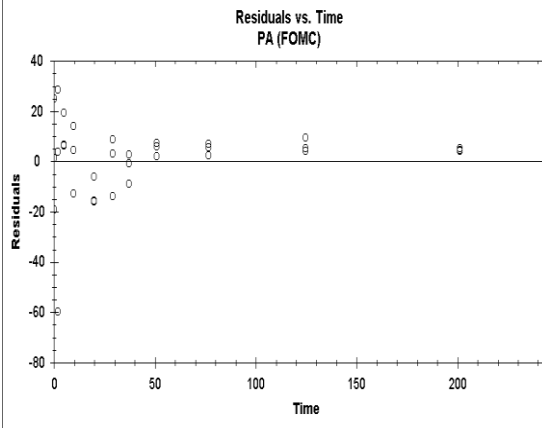
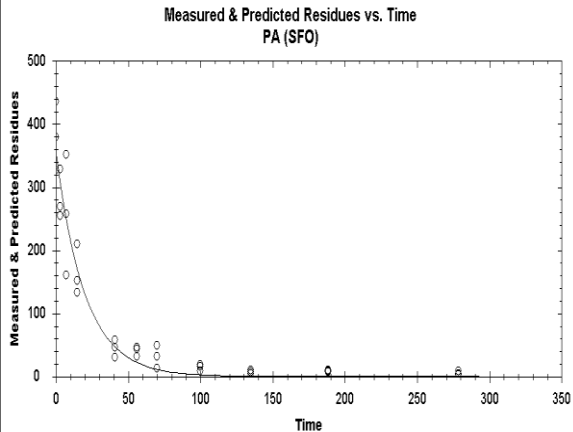
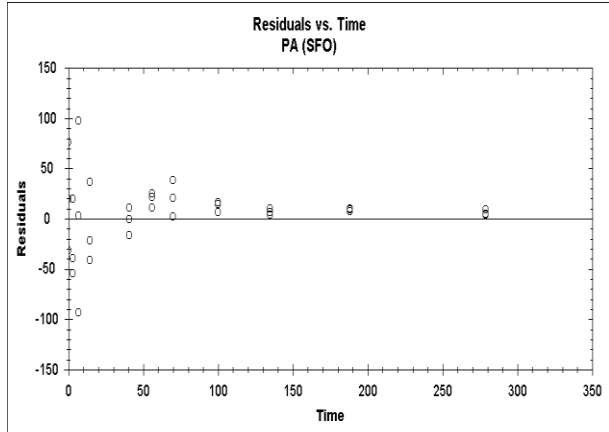
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	12.3	k: <0.001	poor	5.7	18.8
SFO visual fit is poor as residuals are large and deviate systematically from zero → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	5.0	$\alpha = 1.634$ $\beta = 8.614$	good	8.02 (DT90/3.32)	26.6
The FOMC visual fit is good, the χ^2 error value is low. Conclusion: The HSE evaluator considers FOMC is appropriate for derivation of modelling endpoints because there are no soil metabolites.						
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Table 8.1.2.2.1-62: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for cinmethylin in field trial 15/03314437-06 (Spain)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	10.3	k: <0.001	acceptable	13.9	46.2
SFO visual fit is acceptable, the χ^2 error value is below 15%, k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;">  </div> <div style="text-align: center;">  </div> </div>						

Kinetic evaluation for enantiomers

The degradation behaviour of Reg. No. 5925581 and Reg. No. 5925632 in the six field trials was analysed in order to derive kinetic endpoints for environmental fate modelling using the normalized data sets. For both enantiomers, the kinetic evaluation showed that for trial 15/03314437-01 (Germany), 15/03314437-02 (Italy) and 15/03314437-05 (Belgium) the FOMC kinetic model is appropriate to derive modelling endpoints, whereas for trial 15/03314437-03 (Denmark), 15/03314437-04 (UK) and 15/03314437-06 (Spain) the SFO kinetic model is appropriate to derive modelling endpoints. The kinetic models tested and the respective statistical and visual assessment are summarised in Table 8.1.2.2.1-63 to Table 8.1.2.2.1-74.

Reg. No. 5925581

Table 8.1.2.2.1-63: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for Reg. No. 5925581 in field trial 15/03314437-01 (Germany)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	16.1	k: <0.001	poor	16.3	54.1
SFO visual fit is poor as residuals are large and deviate systematically from zero, the χ^2 error value is above 15% → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	9.9	$\alpha = 1.158$ $\beta = 13.39$	good	25.4 (DT90/3.32)	84.4
The FOMC visual fit is good, the χ^2 error value is below 15%, residuals are randomly scattered around zero.						
Conclusion: FOMC is appropriate for derivation of modelling endpoints.						
<p>Measured & Predicted Residues vs. Time PA (SFO)</p>		<p>Residuals vs. Time PA (SFO)</p>				
<p>Measured & Predicted Residues vs. Time PA (FOMC)</p>		<p>Residuals vs. Time PA (FOMC)</p>				

Table 8.1.2.2.1-64: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for Reg. No. 5925581 in field trial 15/03314437-02 (Italy)

Table 8.1.2.2.1-64: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for Reg. No. 5925581 in field trial 15/03314437-02 (Italy)

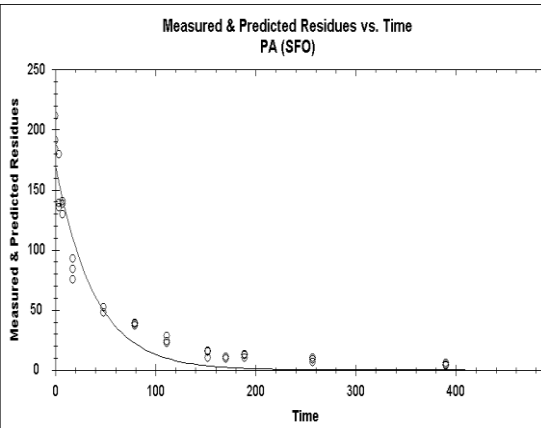
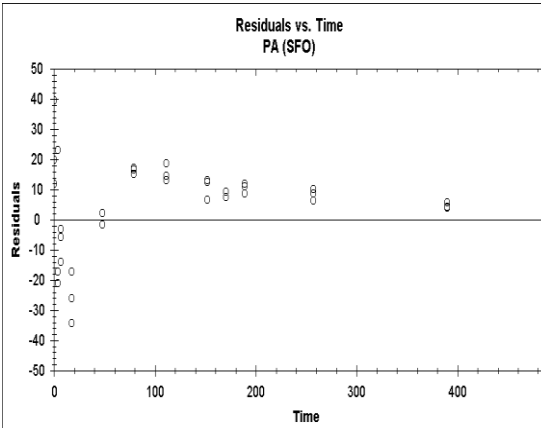
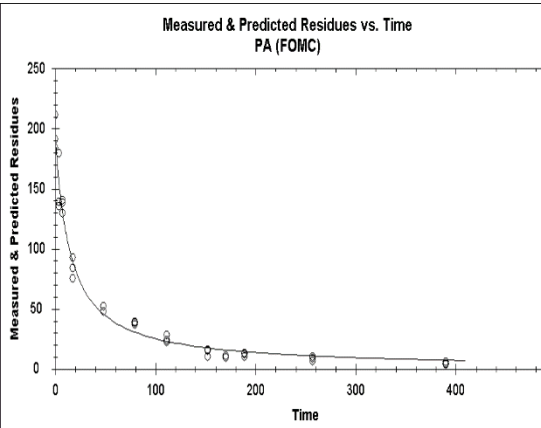
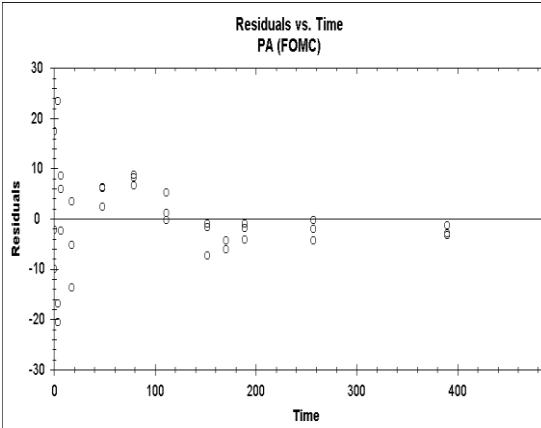
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	18.0	k: <0.001	poor	26.8	89.0
SFO visual fit is poor as residuals are large and deviate systematically from zero, the χ^2 error value is above 15% → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	5.9	$\alpha = 0.9835$ $\beta = 14.36$	good	40.6 (DT90/3.32)	134.8
The FOMC visual fit is good and the χ^2 error value is below 15%. Conclusion: FOMC is appropriate for derivation of modelling endpoints.						
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Table 8.1.2.2.1-65: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for Reg. No. 5925581 in field trial 15/03314437-03 (Denmark)

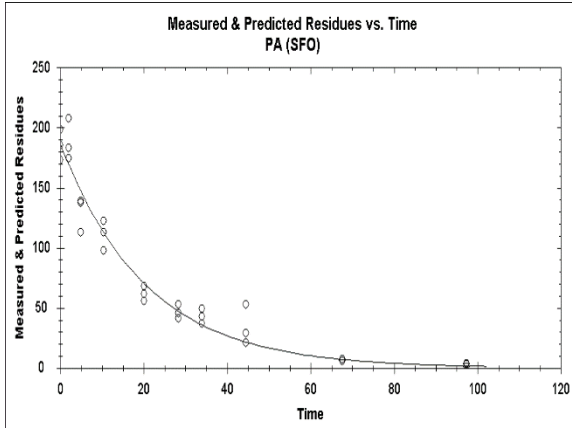
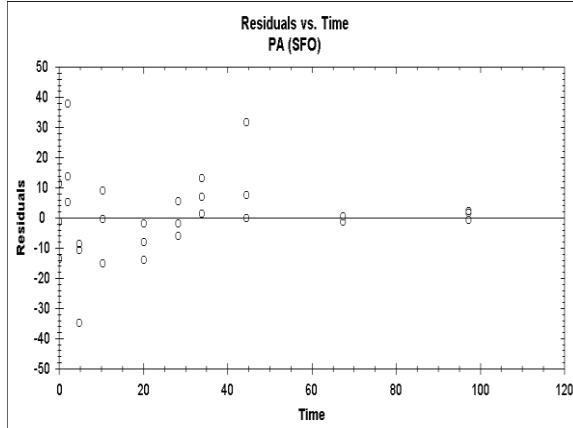
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	9.8	k: <0.001	acceptable	14.2	47.3
SFO visual fit is acceptable, the χ^2 error value is below 15% and k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;">   </div>						

Table 8.1.2.2.1-66: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for Reg. No. 5925581 in field trial 15/03314437-04 (UK)

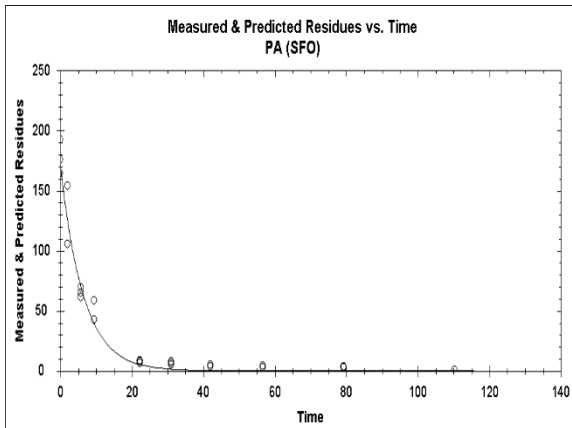
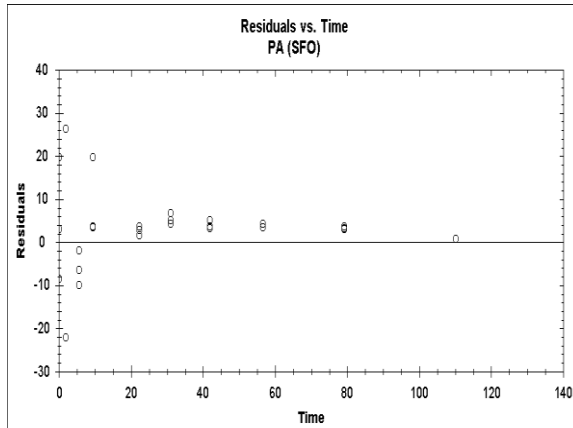
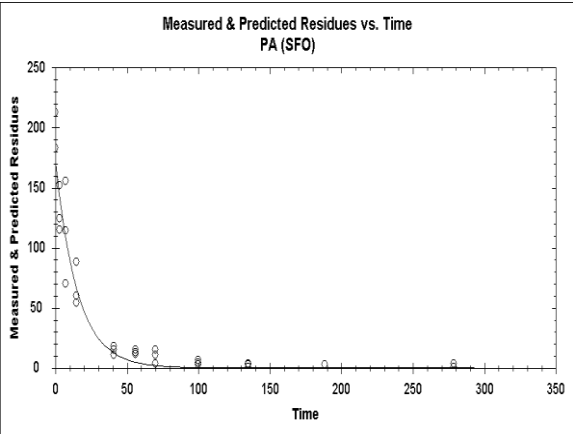
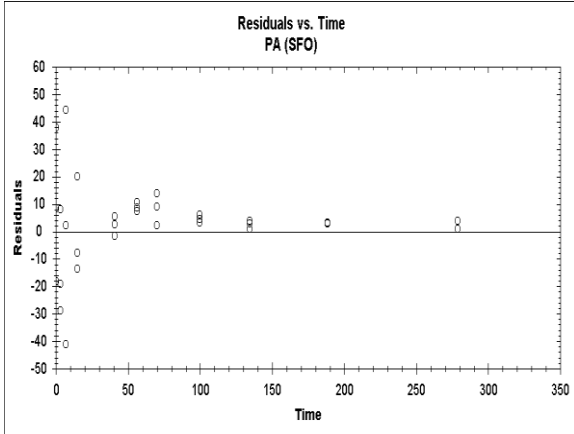
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	9.2	k: <0.001	acceptable	4.4	14.6
SFO visual fit is acceptable, the χ^2 error value is below 15% and k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;">   </div>						

Table 8.1.2.2.1-67: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for Reg. No. 5925581 in field trial 15/03314437-05 (Belgium)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	12.4	k: <0.001	poor	4.5	14.9
SFO visual fit is poor as residuals are large and deviate systematically from zero → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	5.4	$\alpha = 1.671$ $\beta = 7.166$	good	6.4 (DT90/3.32)	21.3
The FOMC visual fit is good and the χ^2 error value is low. Conclusion: FOMC is appropriate for derivation of modelling endpoints.						
Measured & Predicted Residues vs. Time PA (SFO)		Residuals vs. Time PA (SFO)				
Measured & Predicted Residues vs. Time PA (FOMC)		Residuals vs. Time PA (FOMC)				

Table 8.1.2.2.1-68: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for Reg. No. 5925581 in field trial 15/03314437-06 (Spain)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	10.5	k: <0.001	acceptable	10.7	35.5
SFO visual fit is acceptable, the χ^2 error value is below 15% and k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;">  </div> <div style="text-align: center;">  </div> </div>						

Reg. No. 5925632

Table 8.1.2.2.1-69: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for Reg. No. 5925632 in field trial 15/03314437-01 (Germany)

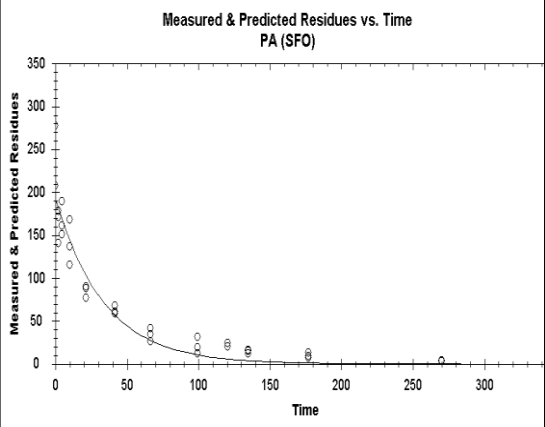
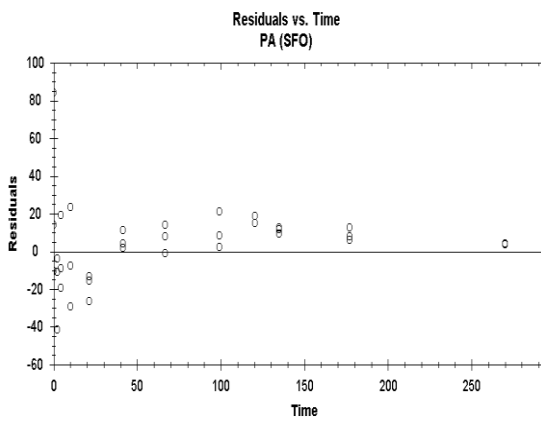
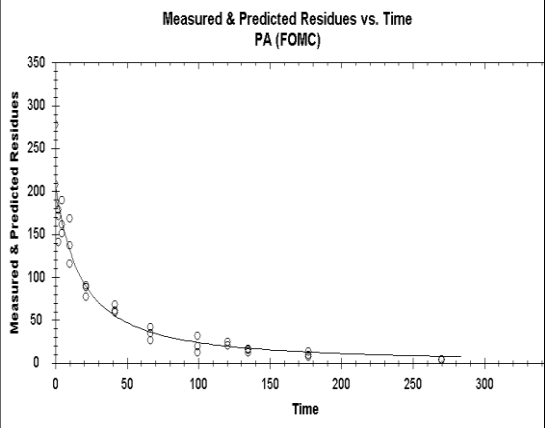
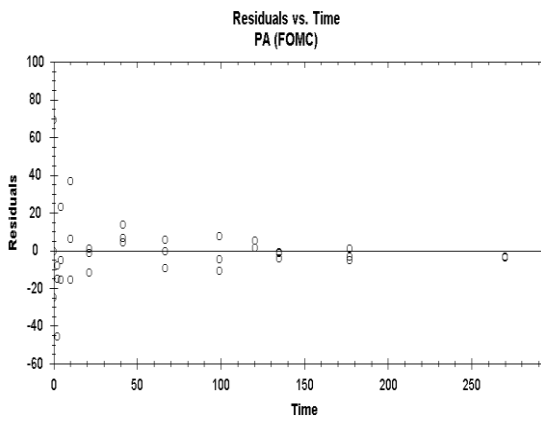
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	14.1	k: <0.001	poor	23.6	78.3
SFO visual fit is poor as residuals are large and deviate systematically from zero → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	9.4	$\alpha = 1.305$ $\beta = 23.3$	good	33.9 (DT90/3.32)	112.7
The FOMC visual fit is good and provides a lower χ^2 error value. Residuals are randomly scattered around zero.						
Conclusion: FOMC is appropriate for derivation of modelling endpoints.						
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Table 8.1.2.2.1-70: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for Reg. No. 5925632 in field trial 15/03314437-02 (Italy)

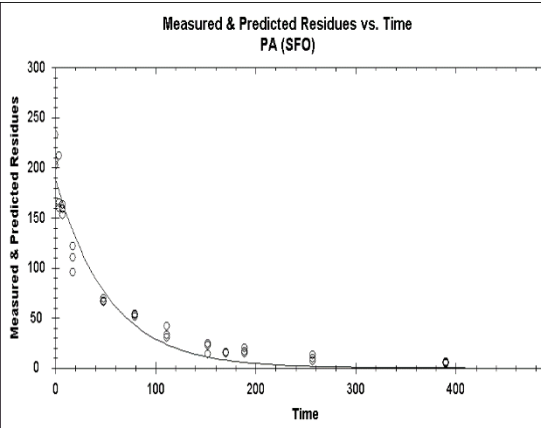
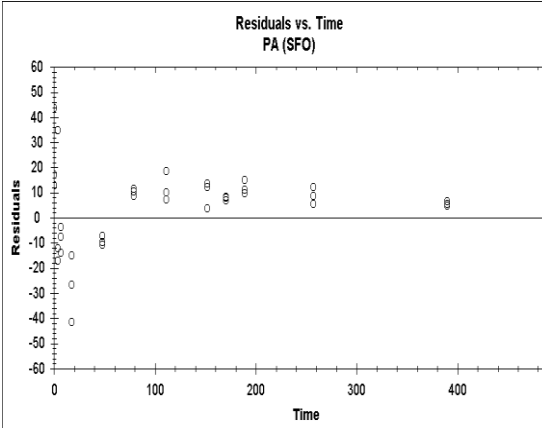
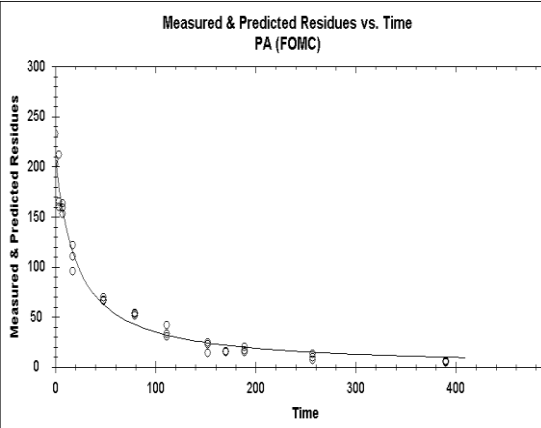
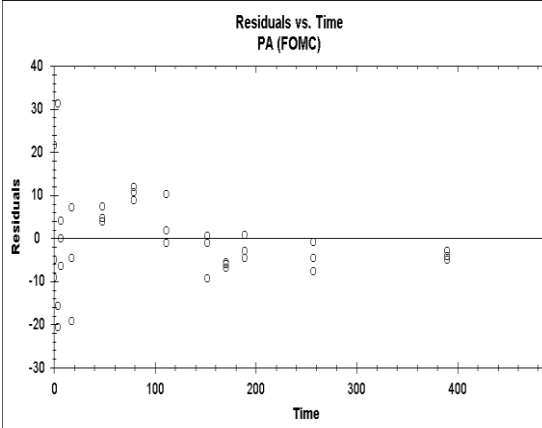
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	14.8	k: <0.001	poor	36.9	122.5
SFO visual fit is poor as residuals are large and deviate systematically from zero → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	5.5	$\alpha = 1.049$ $\beta = 21.81$	good	52.5 (DT90/3.32)	174.2
The FOMC visual fit is good and the χ^2 error value is below 15%. Conclusion: FOMC is appropriate for derivation of modelling endpoints.						
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Table 8.1.2.2.1-71: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for Reg. No. 5925632 in field trial 15/03314437-03 (Denmark)

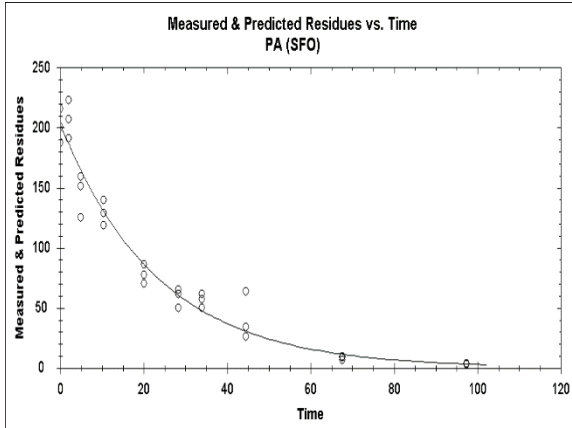
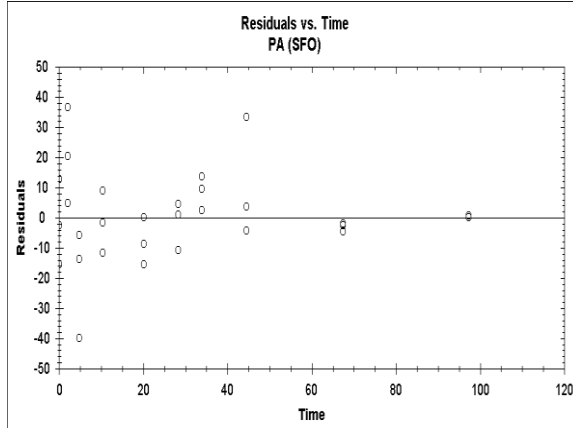
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	9.0	k: <0.001	acceptable	16.2	53.9
SFO visual fit is acceptable, the χ^2 error value is below 15% and k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;">   </div>						

Table 8.1.2.2.1-72: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for Reg. No. 5925632 in field trial 15/03314437-04 (UK)

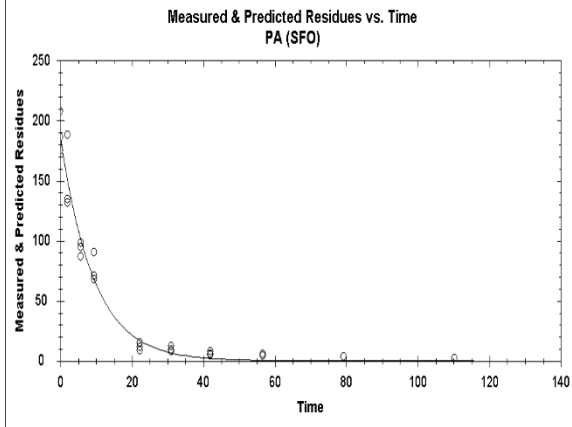
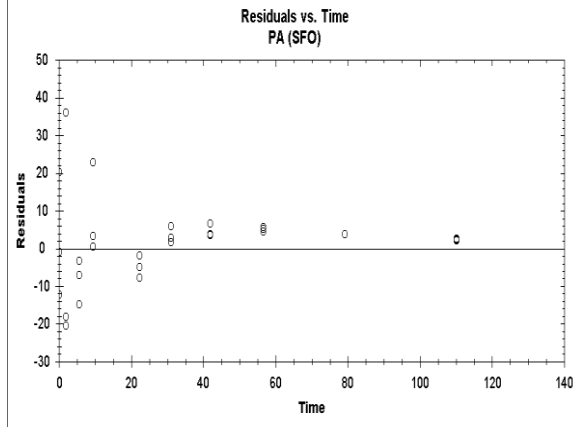
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	7.4	k: <0.001	acceptable	6.4	21.3
SFO visual fit is acceptable, the χ^2 error value is below 15% and k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;">   </div>						

Table 8.1.2.2.1-73: Statistical and visual assessment of kinetic models for derivation of modelling endpoints for Reg. No. 5925632 in field trial 15/03314437-05 (Belgium)

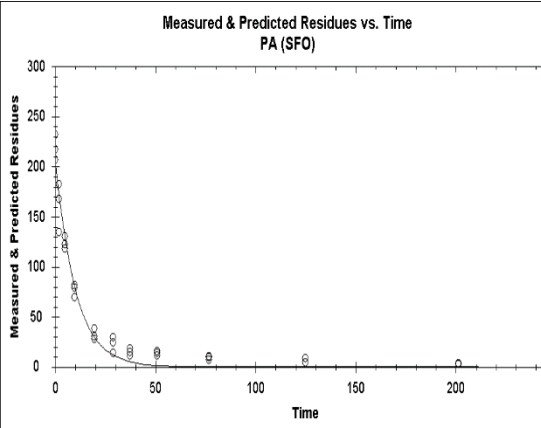
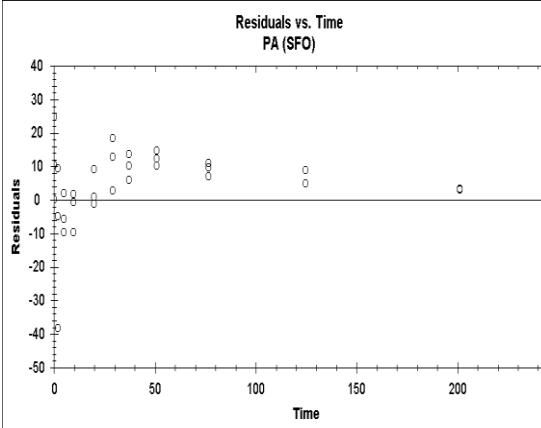
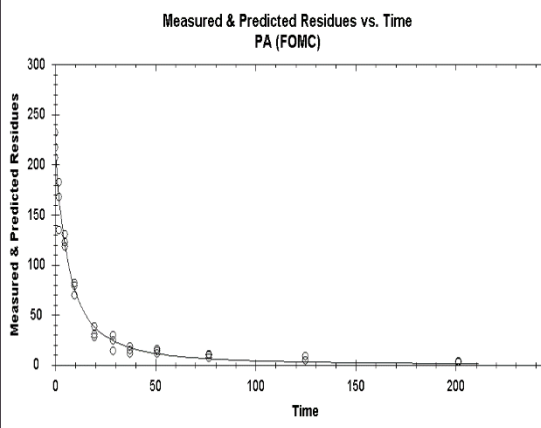
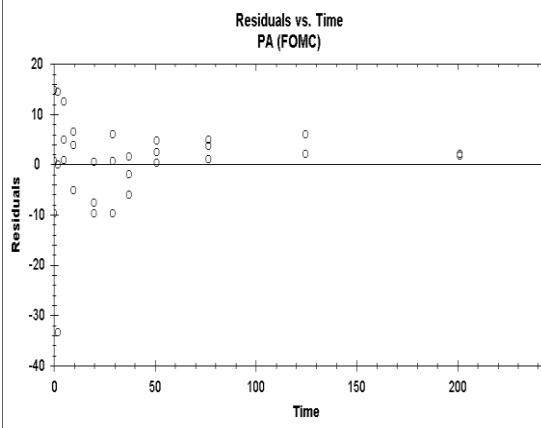
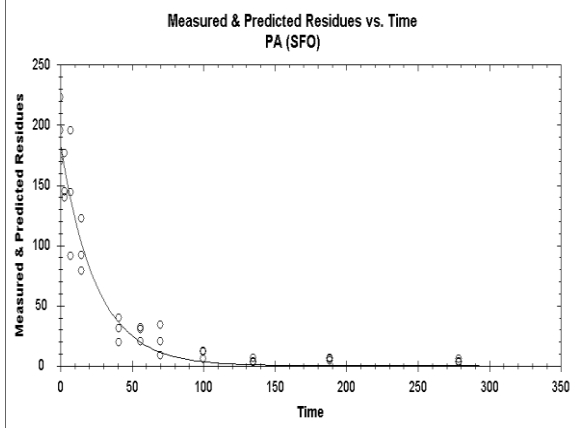
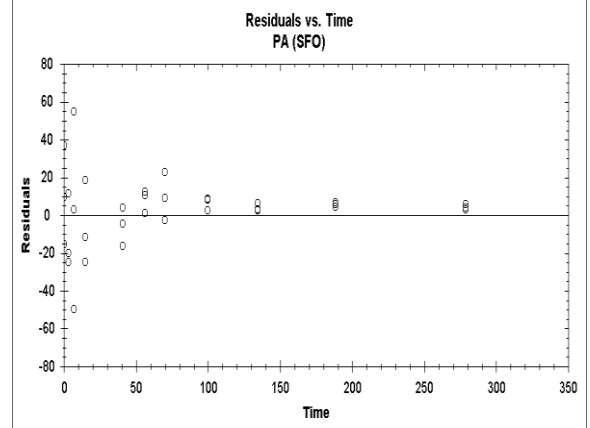
Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	11.2	k: <0.001	poor	7.0	23.1
SFO visual fit is poor as residuals are large and deviate systematically from zero → test FOMC (less than 10% of initial concentration at last sampling).						
Run FOMC	FOMC	5.0	$\alpha = 1.755$ $\beta = 11.55$	good	9.44 (DT50/3.32)	31.4
The FOMP visual fit is good and the χ^2 error value is low. Conclusion: FOMC is appropriate for derivation of modelling endpoints.						
<div>   </div> <div>   </div>						

Table 8.1.2.2.1-74: Statistical and visual assessment of the SFO kinetic model for derivation of modelling endpoints for Reg. No. 5925632 in field trial 15/03314437-06 (Spain)

Step in FOCUS flowchart	Kinetic model	χ^2 error [%]	Prob > t (t-test)	Visual assessment	DegT50 [d]	DegT90 [d]
Run SFO	SFO	9.2	k: <0.001	acceptable	17.2	57.2
SFO visual fit is acceptable, the χ^2 error value is below 15% and k is significantly different from zero. Conclusion: SFO is appropriate for derivation of modelling endpoints.						
<div style="display: flex; justify-content: space-around;">   </div>						

A summary of all parameters is presented in Table 8.1.2.2.1-51 to Table 8.1.2.2.1-53.

III. CONCLUSION

Kinetic evaluations were performed to analyse the degradation kinetics of cinmethylin and its two enantiomers observed in the six soils according to the current guidance of the FOCUS workgroup on degradation kinetics in order to derive the modelling endpoints.

For all models considered appropriate, the visual assessment and goodness-of-fit statistics indicate plausible fit. The t-test was passed for the respective model parameters. Therefore, the resulting endpoints can be considered reliable.

Report:	KCA 7.1.2.2.1/5; Mitchell, J., Perez, R., Warren, R., Saha, M. (2018)
Title	Terrestrial field dissipation of the herbicide BAS 684 H following broadcast applications of BAS 684 02 H (EC)
Report No.	2017/7017329
Guidelines	OPPTS 835.6100, Terrestrial Field Dissipation, US EPA Residue Chemistry Test Guideline FOCUS Kinetics guidance (2006; 2014). European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662
GLP?	Yes, except for some electronic data loss (see below)
Deviations	<ul style="list-style-type: none"> For the North Dakota site, due to frozen field conditions, the 90 DALA soil samples were collected at 180 DALA; For the Texas site, 60 DALA samples from the 3-6 inch depth were not analysed due to inadvertent oversight. The Applicant assumed the worst-case scenario and applied concentrations from 30 DALA.

Report:	KCA 7.1.2.2.1/5; Mitchell, J., Perez, R., Warren, R., Saha, M. (2018)
Title	Amended final report: Terrestrial field dissipation of the herbicide BAS 684 H following broadcast applications of BAS 684 02 H (EC)
Report No.	2019/7002321
Guidelines	OPPTS 835.6100, Terrestrial Field Dissipation, US EPA Residue Chemistry Test Guideline FOCUS Kinetics guidance (2006; 2014). European Food Safety Authority, 2014. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662
GLP?	Yes, except for some electronic data loss (see below)
Deviations	<ul style="list-style-type: none"> For the North Dakota site, due to frozen field conditions, the 90 DALA soil samples were collected at 180 DALA; For the Texas site, 60 DALA samples from the 3-6 inch depth were not analysed due to inadvertent oversight. The Applicant assumed the worst-case scenario and applied concentrations from 30 DALA.

Previous evaluations:	None – report submitted as part of a new active substance registration.
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INTRODUCTION

A terrestrial field dissipation study was conducted at six field sites across the United States to determine the persistence and mobility of cinmethylin, formulated as an emulsifiable concentrate (EC) when applied under field conditions to a bare soil plot. The bare soil experiment was used to determine the dissipation kinetics in soil and to evaluate the leaching

potential. The study was conducted according to US EPA guidelines (OPPTS 835.6100, Terrestrial Field Dissipation) and to GLP. The Applicant also conducted a kinetic evaluation according to FOCUS Kinetics guidance (2006; 2014) with the aim of deriving trigger endpoints for cinmethylin and its two enantiomers in all six soils. The field portion of the study was undertaken from October 2015 to July 2017. Following submission of the field study, the Applicant supplied a kinetic evaluation for deriving modelling endpoints from the dissipation study in order to determine DegT_{50 matrix} values following the EFSA guidance for obtaining DegT₅₀ values (EFSA, 2014).

The test substance for this study was BAS 684 02 H (EC, nominal concentration 750 g a.i./L; batch number FD-150416-0012) and this was applied in a single application to bare soil of 500 g a.i./ha. The Applicant stated that application timing was appropriate for herbicide applications targeting weeds in the representative crops for that region, and that depending on site, both spring/summer and fall applications were evaluated. The HSE evaluator agreed that timings were appropriate.

The HSE evaluator notes that, for the US field dissipation study evaluated here, one reference item was cinmethylin formulated with an enantiomeric ratio of 78.5:21.5 (-):(+) , batch number L83-264. The Applicant has applied for approval to use cinmethylin in the UK formulated with a ratio of 50:50, and all preceding European laboratory soil studies investigated degradation of cinmethylin using batches containing the ratio of 50:50. The HSE evaluator sought clarification from the Applicant, who confirmed that this batch of reference item was used for Speedisk sample quantitation, and that all field sample quantitation was based on calibrations derived from individual reference items for each enantiomer. Although this is not a guideline deviation, the HSE evaluator concludes this required noting as the (+) enantiomer degrades at a slower rate in the aerobic degradation study (Stewart and Abernethy, 2016a; KCA 7.1.1.1/1). The HSE evaluator accepts the Applicant's clarification and concludes that this did not affect the overall study conduct or interpretation.

TEST SITES

Six field sites across the United States were chosen for this study, and were in the states of New York, North Carolina, North Dakota, Texas, Washington and California. Table 8.1.2.2.1/5-01 provides a summary description of each field site. The Applicant stated that the test sites were geographically appropriate for the use of cinmethylin in the U.S.. The Applicant has provided an ecoregion similarity study to demonstrate the relevance of the U.S. field sites to Europe (Jeffries and Warren, 2018a; KCA 7.1.2.2.1/09). This has been evaluated separately; however, the HSE evaluator agreed with the conclusion that five field sites were relevant to Europe. The test sites were bare soil plots suitable for field crops, leafy and fruiting vegetable crops, or vineyard/orchard crops in the test region.

Table 8.1.2.2.1/5-01: Summary of geographic location and site description for the six field study sites

Details		New York (NY)	North Carolina (NC)	North Dakota (ND)	Texas (TX)	Washington (WA)	California (CA)
Location	Site	Wayne County	Wayne County	Cass County	Armstrong County	Grant County	Tulare County
	State	New York	North Carolina	North Dakota	Texas	Washington	California
	Country	United States					
	Latitude	43.196800	35.262328	47.12038	35.11592	47.134461	36.004450
	Longitude	-76.920850	-77.890983	-96.98456	-101.35772	-119.555044	-119.077166
	Ecoregion ¹	8.1 Mixed Wood Plains	8.3 Southeastern USA Plains	9.2 Temperate Prairies	9.4 South Central Semi-Arid Prairies	10.1 Cold Deserts	11.1 Mediterranean California
	MLRA ²	Ontario-Erie Plain and Finger Lakes	Southern Coastal Plain	Red River Valley of the North	North Central Prairies	Columbia Basin	Sacramento and San Joaquin Valleys
Soil series		Niagara silt loam	Wickham sandy loam	Bearden/Lindaas	Pullman	Quincy	Nord
Slope Gradient (%)		0	0.5	< 1	~2	0 – 1	~1
Depth to ground water (m)		1.2	2.0	0.5 – 1.1	2.03	22.9	~77

¹ http://www.epa.gov/wed/pages/ecoregions/na_eco.htm² MLRA – Major Land Resource Area (USDA Handbook 296, 2006).

Soil characteristics

The Applicant stated that all test site soils were representative of where the product could be used. Tables KCA 7.1.2.2.1/5-02-07 outline the soil characteristics for each field site, split into eight depth profiles for each soil site. In summary, the Applicant described the soils as follows:

- New York soil was a Niagara silt loam, a very deep, somewhat poorly drained soil formed in silty glacio-lacustrine deposits (Table 8.1.2.2.1/5-02);
- North Carolina soil was a Wickham sandy loam, very deep, well drained and formed in fluvial and marine sediments (Table 8.1.2.2.1/5-03);
- North Dakota soil was a Bearden-Lindaas silty clay loam, a very deep, somewhat poorly drained soil formed in calcareous silt loam and silty clay loam lacustrine sediments (Table 8.1.2.2.1/5-04);
- Texas soil was a Pullman silty clay loam, very deep, well drained and formed in clayey eolian deposits (Table 8.1.2.2.1/5-05);
- Washington soil was a Quincy loamy fine sand, a very deep, excessively drained soil formed in sands on dunes and terraces (Table 8.1.2.2.1/5-06);
- California soil was a Nord fine sandy loam, very deep, well drained and formed in mixed alluvium dominantly from granitic and sedimentary rocks (Table 8.1.2.2.1/5-07).

The HSE evaluator has checked and confirmed the taxonomic classifications and soil mapping units provided by the Applicant.

Table 8.1.2.2.1/5-02: Characterisation of the soil from the New York field site.

Property	Depth (inches)							
	0-3	3-6	6-12	12-18	18-24	24-30	30-36	36-42
USDA Textural classification	Silt loam	Silt loam	Silt loam	Loam	Silty clay loam	Silty clay loam	Silt loam	Silt loam
% Sand	28	32	30	32	18	16	22	20
% Silt	60	56	58	46	52	56	52	54
% Clay	12	12	12	22	30	28	26	26
pH ¹	5.7	5.4	5.3	5.2	5.7	5.6	5.7	5.6
% Organic matter	4.1	3.9	3.9	0.32	0.28	0.28	0.11	0.15
% Organic carbon	2.4	2.3	2.2	0.19	0.16	0.16	0.06	0.09
Salinity ¹ (mmhos/cm)	0.30	0.53	0.56	0.18	0.15	0.16	0.13	0.15
CEC (meq/100 g)	8.8	8.8	8.3	8.1	12.0	10.0	10.0	9.4
AEC (cmol (-)/kg) @ pH 5.0 – 6.0	0.13	0.13	0.21	0.33	0.3	0.22	0.25	0.19
Bulk density (g/cm ³) – disturbed	1.00	1.02	0.98	1.20	1.15	1.16	1.11	1.15
Gravimetric moisture (%)	0.33 Bar	27.7	26.6	28.6	21.0	25.0	24.5	24.0
	15 bar	9.8	9.8	9.5	9.5	12.6	12.0	11.5
Taxonomic classification ²	Niagara – fine-silty, mixed, active, mesic Aeric Endoaqualfs							
Soil mapping unit ³	Niagara silt loam (mapping unit symbol Ng)							

¹ pH and salinity were measured in a saturated paste comprising soil and distilled water

² Taxonomic classification from https://soilseries.sc.egov.usda.gov/OSD_Docs/N/NIAGARA.html (HSE evaluator note: link checked 10/1/2019)

³ Soil mapping unit derived from <https://websoilsurvey.sc.egov.usda.gov/App/HomePage.htm> (HSE evaluator note: link checked 10/1/2019)

Table 8.1.2.2.1/5-03: Characterisation of the soil from the North Carolina field site.

Property	Depth (inches)							
	0-3	3-6	6-12	12-18	18-24	24-30	30-36	36-42
USDA Textural classification	Sandy loam	Loamy sand	Sandy loam	Sandy clay loam	Clay	Clay	Sandy clay loam	Sandy clay loam
% Sand	75	77	67	55	37	33	45	51
% Silt	18	16	22	22	22	26	22	20
% Clay	7	7	11	23	41	41	33	29
pH ¹	6.1	5.5	5.4	4.8	4.6	4.7	4.7	4.7
% Organic matter	1.3	1.2	1.04	0.39	0.39	0.35	0.17	0.17
% Organic carbon	0.73	0.68	0.61	0.23	0.23	0.20	0.10	0.10
Salinity ¹ (mmhos/cm)	0.70	0.49	0.33	0.22	0.23	0.27	0.80	0.29
CEC (meq/100 g)	4.9	4.9	5.2	6.5	10.3	10.4	9.6	8.6
AEC (cmol (-)/kg) @ pH 5.0 – 6.0	-0.03	-0.02	0.05	0.34	0.59	1.13	0.98	0.71
Bulk density (g/cm ³) – disturbed	1.28	1.23	1.28	1.24	1.13	1.08	1.12	1.13
Gravimetric moisture (%)	0.33 Bar	18.9	20.5	20.2	22.2	32.7	33.4	31.6
	15 bar	3.6	3.9	4.3	8.1	15.9	16.2	14.8
Taxonomic classification ²	Wickham – Fine-loamy, mixed, semiactive, thermic Typic Hapludults							
Soil mapping unit ³	Wickham sandy loam (mapping unit symbol WkB2)							

¹ pH and salinity were measured in a saturated paste comprising soil and distilled water

² Taxonomic classification from https://soilseries.sc.egov.usda.gov/OSD_Docs/W/WICKHAM.html (HSE evaluator note: link checked 10/1/2019)

³ Soil mapping unit derived from <https://websoilsurvey.sc.egov.usda.gov/App/HomePage.htm> (HSE evaluator note: link checked 10/1/2019)

Table 8.1.2.2.1/5-04: Characterisation of the soil from the North Dakota field site.

Property		Depth (inches)							
		0-3	3-6	6-12	12-18	18-24	24-30	30-36	36-42
USDA classification		Clay	Clay	Clay	Clay	Clay	Clay	Clay	Clay
Textural									
% Sand		21	23	21	19	21	19	17	17
% Silt		35	33	35	33	35	33	29	35
% Clay		44	44	44	48	44	48	54	48
pH ¹		7.4	7.5	7.6	7.7	7.6	7.7	7.8	7.8
% Organic matter		4.6	3.8	2.5	1.4	1.05	1.05	0.92	1.1
% Organic carbon		2.7	2.2	1.5	0.82	0.61	0.61	0.54	0.64
Salinity ¹ (mmhos/cm)		0.64	0.39	0.31	0.30	0.36	0.49	0.97	0.30
CEC (meq/100 g)		25.8	27.2	23.8	24.6	24.7	26.3	26.9	23.8
AEC (cmol (-)/kg) @ pH 5.0 – 6.0		-0.42	-0.28	-0.16	-0.03	-0.05	-0.32	-0.13	-0.12
Bulk density (g/cm ³) – disturbed		1.04	1.08	1.11	1.09	1.08	1.11	1.08	1.10
Gravimetric moisture (%)	0.33 Bar	38.1	36.1	33.1	32.3	35.7	37.8	40.8	36.5
	15 bar	22.1	20.8	20.7	22.6	23.4	24.1	25.3	23.6
Taxonomic classification ²		Bearden – Fine-silty, mixed, superactive, frigid Aeric Calciaquolls Lindaas – Fine, smectitic, frigid Typic Argiaquolls							
Soil mapping unit ³		Bearden-Lindaas silty clay loams (mapping unit symbol I492A)							

¹ pH and salinity were measured in a saturated paste comprising soil and distilled water² Taxonomic classifications from https://soilseries.sc.egov.usda.gov/OSD_Docs/B/BEARDEN.html and https://soilseries.sc.egov.usda.gov/OSD_Docs/L/LINDAAS.html (HSE evaluator checked links 10/1/2019)³ Soil mapping unit derived from <https://websoilsurvey.sc.egov.usda.gov/App/HomePage.htm> (HSE evaluator note: link checked 10/1/2019)**Table 8.1.2.2.1/5-05: Characterisation of the soil from the Texas field site.**

Property		Depth (inches)							
		0-3	3-6	6-12	12-18	18-24	24-30	30-36	36-42
USDA Textural classification		Clay loam	Clay loam	Clay loam	Clay	Clay	Clay	Clay	Clay
% Sand		24	26	28	20	24	26	20	22
% Silt		37	35	33	33	29	31	31	33
% Clay		39	39	39	47	47	43	49	45
pH ¹		7.3	7.0	7.4	7.6	7.7	7.7	7.9	7.8
% Organic matter		2.8	2.4	1.7	1.1	0.93	0.89	0.73	0.52
% Organic carbon		1.6	1.4	1.0	0.66	0.54	0.52	0.42	0.30
Salinity ¹ (mmhos/cm)		1.09	1.23	0.67	0.45	0.39	0.26	0.42	0.53
CEC (meq/100 g)		24.4	25.2	26.6	27.9	26.5	26.6	24.5	25.6
AEC (cmol (-)/kg) @ pH 5.0 – 6.0		-0.27	-0.29	-0.14	-0.14	-0.13	-0.09	-0.18	0.03
Bulk density (g/cm ³) – disturbed		1.10	1.15	1.14	1.19	1.11	1.14	1.14	1.14
Gravimetric moisture (%)	0.33 Bar	30.1	30.1	30.3	29.9	28.7	28.5	29.2	28.7
	15 bar	19.5	19.9	22.3	24.0	22.6	20.9	20.3	44.6
Taxonomic classification ²		Pullman – fine, mixed, superactive, thermic Torrtic Palustolls							
Soil mapping unit ³		Pullman silty clay loam (mapping unit symbol PuB)							

¹ pH and salinity were measured in a saturated paste comprising soil and distilled water ² Taxonomic classifications from https://soilseries.sc.egov.usda.gov/OSD_Docs/P/PULLMAN.html (HSE evaluator note: link checked 10/1/2019)³ Soil mapping unit derived from <https://websoilsurvey.sc.egov.usda.gov/App/HomePage.htm> (HSE evaluator note: link checked 10/1/2019)

Table 8.1.2.2.1/5-06: Characterisation of the soil from the Washington field site.

Property		Depth (inches)							
		0-3	3-6	6-12	12-18	18-24	24-30	30-36	36-42
USDA Textural classification		Sand	Sand	Sand	Sand	Sand	Loamy sand	Loamy sand	Loamy sand
% Sand		87	91	91	93	89	85	79	83
% Silt		13	9	9	7	11	15	21	17
% Clay		0	0	0	0	0	0	0	0
pH ¹		8.1	8.0	8.0	7.9	7.8	7.8	8.2	8.4
% Organic matter		1.2	1.1	0.47	0.34	0.43	0.20	0.20	0.25
% Organic carbon		0.69	0.66	0.27	0.20	0.25	0.12	0.12	0.14
Salinity ¹ (mmhos/cm)		0.56	0.68	0.45	0.44	0.40	0.33	0.41	0.46
CEC (meq/100 g)		8.7	8.7	9.0	8.9	9.1	8.4	10.1	10.7
AEC (cmol (-)/kg) @ pH 5.0 – 6.0		-0.11	-0.1	-0.04	-0.04	-0.09	-0.09	-0.06	0.01
Bulk density (g/cm ³) – disturbed		1.35	1.38	1.45	1.45	1.51	1.48	1.51	1.56
Gravimetric moisture (%)	0.33 Bar	8.6	8.2	6.7	6.4	6.4	6.9	8.4	7.6
	15 bar	4.6	4.3	4.5	4.3	4.1	3.8	3.9	3.8
Taxonomic classification ²	Quincy – Mixed, mesic Xeric Torripsamments								
Soil mapping unit ³	Quincy loamy fine sand (mapping unit symbol 98)								

¹ pH and salinity were measured in a saturated paste comprising soil and distilled water

² Taxonomic classifications from https://soilseries.sc.egov.usda.gov/OSD_Docs/Q/QUINCY.html (HSE evaluator note: link checked 10/1/2019)

³ Soil mapping unit derived from <https://websoilsurvey.sc.egov.usda.gov/App/HomePage.htm> (HSE evaluator note: link checked 10/1/2019)

Table 8.1.2.2.1/5-07: Characterisation of the soil from the California field site.

Property	Depth (inches)							
	0-3	3-6	6-12	12-18	18-24	24-30	30-36	36-42
USDA Textural classification	Sandy loam	Sandy loam	Sandy loam	Sandy loam	Sandy loam	Sandy loam	Sandy loam	Sandy loam
% Sand	56	60	60	64	64	64	54	52
% Silt	35	31	35	31	31	31	39	39
% Clay	9	9	5	5	5	5	7	9
pH ¹	8.2	8.2	8.6	8.6	8.7	8.8	8.8	8.7
% Organic matter	0.82	0.74	0.43	0.30	0.35	0.35	0.35	0.35
% Organic carbon	0.48	0.43	0.25	0.18	0.20	0.20	0.20	0.20
Salinity ¹ (mmhos/cm)	1.37	2.07	1.20	1.54	1.07	1.27	0.89	1.02
CEC (meq/100 g)	8.8	9.6	8.4	8.5	8.5	10.1	9.7	10.9
AEC (cmol (-)/kg) @ pH 5.0 – 6.0	-0.08	0.02	-0.11	-0.08	-0.11	-0.14	-0.19	-0.10
Bulk density (g/cm ³) – disturbed	1.13	1.11	1.13	1.12	1.12	1.08	1.06	1.03
Gravimetric moisture (%)	0.33 Bar	16.7	17.2	13.6	13.8	13.8	17.6	18.5
	15 bar	6.5	6.5	5.4	5.1	5.1	6.1	7.8
Taxonomic classification ²	Nord – coarse-loamy, missed, superactive, thermic Cumulic Haploxerolls							
Soil mapping unit ³	Nord fine sandy loam (mapping unit symbol 130)							

¹ pH and salinity were measured in a saturated paste comprising soil and distilled water

² Taxonomic classifications from https://soilseries.sc.egov.usda.gov/OSD_Docs/N/NORD.html (HSE evaluator note: link checked 10/1/2019)

³ Soil mapping unit derived from <https://websoilsurvey.sc.egov.usda.gov/App/HomePage.htm> (HSE evaluator note: link checked 10/1/2019)

Experimental conditions

Each test site consisted of two bare soil test plots: one treated and one control. At all sites the plots were separated by at least 23 m and, where possible, the control plot was located up-slope and upwind of the prevailing wind. The treated plot at each site was divided into three replicate subplots ranging from 209 m² (New York) to 418 m² (Washington), and averaged 300 m². Plots were kept in a bare soil condition throughout the study through the spray application of glyphosate and Paraquat. The pesticides that were used did not have the same mode of action or common metabolites to cinmethylin.

All field test sites had pesticide use in the three years prior to the field test commencement. Table 8.1.2.2.1/5-08 was provided by the Applicant as a summary of crop and chemical use at the six field sites between 2012 and 2015.

Table 8.1.2.2.1/5-08: Crop, cultivation and chemical use history for the six field test sites between 2012 and 2015, as provided by the Applicant.

Use	Year	New York	North Carolina	North Dakota	Texas	Washington	California ¹
Crops grown	2015	--	Fallow	Wheat	--	--	Bare ground
	2014	Bare ground	Fallow	Wheat, Fallow	Wheat	Fallow, Spring wheat	Bare ground
	2013	Bare ground	Peanut	Soybean, Fallow	Fallow	Spring wheat, Fallow	Bare ground
	2012	Bare ground	--	Soybean	Fallow	Fallow	Bare ground
Pesticides used	2015	--	Glyphosate	MCPA	--	--	None
	2014	Glyphosate	None	Thiencarbazone-methyl Pyrasulfotole Bromoxynil	2,4-D	Glyphosate MCPA	Gramoxone
	2013	Glyphosate Gramoxone	Bentazon Acifluorfen Metolachlor Clethodim Sethoxydim Esfenvalerate Chlorothalonil	Glyphosate	Glyphosate	Glyphosate	Fungicide Gramoxone
	2012	Gramoxone Glyphosate	--	Glyphosate	Glyphosate 2,4-D	2,4-D Diquat dibromide Glyphosate	None
Fertilizers used	2015	--	Not reported	Not reported	--	--	Not reported
	2014	Not reported	Not reported	Nitrogen, Phosphorus	Not reported	Not reported	Not reported
	2013	Not reported	Not reported	Nitrogen, Phosphorus	Not reported	Not reported	Not reported
	2012	Not reported	--	Not reported	Not reported	Not reported	Not reported
Cultivation methods, if provided (e.g., Tillage)	2015	--	Not reported	Not reported	--	--	Not reported
	2014	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
	2013	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
	2012	Not reported	--	--	Not reported	Not reported	Not reported

¹ Site usage and history based on treated plot.

Climatic conditions

The Applicant provided detailed information of the climatic measurement regimes for each field site. Daily precipitation, air temperature, relative humidity, solar radiation, wind speed, evapotranspiration (ET_o) and soil temperature were all collected for each site. In all six field sites, soil temperature was collected within the treated plot at the surface, 12, 24 and 36 inch depths. Recording of climatic conditions varied for each site; details are summarised for each field site in turn below:

New York – Weather station was positioned on site approx. 0.25 miles from the test plots. The Applicant collected additional soil temperature data at 2 and 6 inches.

North Carolina – Weather station was positioned on site approx. 650 ft from the test plots. The weather station collected daily precipitation, air temperature, relative humidity and solar radiation. Wind speed and ET_o were collected from the Goldsboro IAG weather station, situated approx. 12 miles from test site. The HSE evaluator notes that no significant topography was identified on satellite maps between the test site and second weather station.

North Dakota – Weather station was positioned on site within 1000 ft of the test plots. The weather station collected all measurements except ET_o, which the Applicant states was calculated based on other measures. The Applicant noted exceptions where meteorological data were collected from other weather stations: during Nov 2015 – Mar 2016 and Feb – Apr 2017, air temperature, wind speed and precipitation data were collected from the NAOO Fargo International Airport station,

approx. 18 miles from the test site; solar radiation and ETo data were collected from the Fargo NDAWN station approx. 17 miles from the test site. The HSE evaluator notes that no significant topography was identified on satellite maps between the test site and second weather station.

Texas – Weather station was positioned on site approx. 30 ft from the test plots and collected all information except for ETo.

Washington – Weather station was positioned on site approx. 1 mile from the test plots. The Applicant collected additional soil temperature data at 3 and 6 inches.

California – Weather station was positioned on site approx. 500 ft from the test plots. Daily measurements were taken for air temperature, relative humidity, solar radiation, wind speed and ETo. Rainfall data were collected using a manual rain gauge. The Applicant collected additional soil temperature data at 2 and 6 inches. The Applicant noted two exceptions: between Dec 2016 and Jan 2017 data were collected from Delano CIMIS Station 182, approx. 15 miles from the test site; in Feb 2017 data were collected from Porterville CIMIS Station 169 approx. 5 miles from the test site.

Table 8.1.2.2.1/5-09: Summary of climatic conditions at the six field sites used to investigate the dissipation of cinmethylin

Location	New York			North Carolina		
Climatic conditions	T _{mean} Air (°C)	Prec. (mm)	Irrigation (mm)	T _{mean} Air (°C)	Prec. (mm)	Irrigation (mm)
Month		Σ	Σ		Σ	Σ
Oct 2015	9.8	91.9	19.1	-	-	-
Nov 2015	7.4	37.3	0.0	-	-	-
Dec 2015	5.4	151.4	0.0	-	-	-
Jan 2016	-2.7	59.9	0.0	-	-	-
Feb 2016	-1.6	89.9	0.0	-	-	-
Mar 2016	3.9	68.8	0.0	-	-	-
Apr 2016	5.4	38.4	57.2	-	-	-
May 2016	14.3	85.6	19.1	-	-	-
Jun 2016	19.3	37.3	76.2	27.1	11.9	58.2
Jul 2016	23.1	29.7	57.2	29.1	94.2	43.9
Aug 2016	23.5	69.1	38.1	28.6	62.7	71.6
Sep 2016	18.5	42.2	76.2	25.7	182.1	0.0
Oct 2016	11.8	174.8	0.0	-	-	-
Nov 2016	6.5	64.3	0.0	-	-	-
Dec 2016	-0.7	73.4	0.0	-	-	-
Jan 2017	-0.8	105.7	0.0	-	-	-
Feb 2017	1.2	60.2	0.0	-	-	-
Mar 2017	-1.3	16.5	0.0	-	-	-
Total	Mean: 8.0	Sum: 1296.4	Sum: 342.9	Mean: 27.6	Sum: 351.0	Sum: 524.8

Weather data refer to time period from start of trial (day of application) until end of trial (last sampling events)
Prec. – precipitation

Table 8.1.2.2.1/5-09 continued

Location	North Dakota			Texas		
Climatic conditions	T _{mean} Air (°C)	Prec. (mm)	Irrigation (mm)	T _{mean} Air (°C)	Prec. (mm)	Irrigation (mm)
Month		Σ	Σ		Σ	Σ
Oct 2015	8.7	35.3	0.0	-	-	-
Nov 2015	2.5	33.8	0.0	6.3	44.7	12.7
Dec 2015	-4.8	16.3	0.0	5.1	13.7	0.0
Jan 2016	-10.3	17.5	0.0	4.2	3.0	0.0
Feb 2016	-4.6	7.6	0.0	8.2	14.2	0.0
Mar 2016	3.6	24.4	0.0	11.1	5.1	37.8
Apr 2016	5.3	40.6	0.0	14.4	65.5	0.0
May 2016	15.6	67.6	0.0	17.6	53.8	52.3
Jun 2016	20.2	45.5	0.0	25.1	51.3	66.8
Jul 2016	21.5	104.6	0.0	27.9	24.4	71.4
Aug 2016	20.3	94.2	0.0	25.0	137.9	0.0
Sep 2016	15.7	51.6	17.8	21.8	32.5	44.5
Oct 2016	8.3	50.8	0.0	18.8	4.3	55.9
Nov 2016	4.1	35.3	0.0	10.8	16.3	0.0
Dec 2016	-10.2	13.7	0.0	2.9	10.2	0.0
Jan 2017	-11.1	0.8	0.0	3.5	56.1	0.0
Feb 2017	-4.2	20.1	0.0	8.4	13.0	0.0
Mar 2017	-1.2	8.4	0.0	11.8	54.6	0.0
Apr 2017	8.6	0.3	0.0	14.4	19.3	6.9
May 2017	-	-	-	13.9	57.4	0.0
Total	Mean: 4.6	Sum: 668.0	Sum: 17.8	Mean: 13.2	Sum: 600.7	Sum: 341.4

Weather data refer to time period from start of trial (day of application) until end of trial (last sampling events)
 Prec. – precipitation

Table 8.1.2.2.1/5-09 continued

Location	Washington			California		
Climatic conditions	T _{mean} Air (°C)	Prec. (mm)	Irrigation (mm)	T _{mean} Air (°C)	Prec. (mm)	Irrigation (mm)
Month		Σ	Σ		Σ	Σ
Oct 2015	12.5	6.4	24.4	-	-	-
Nov 2015	2.6	6.6	0.0	-	-	-
Dec 2015	-1.1	58.7	0.0	-	-	-
Jan 2016	-0.7	68.6	0.0	-	-	-
Feb 2016	4.2	10.4	0.0	-	-	-
Mar 2016	7.4	35.1	0.0	-	-	-
Apr 2016	13.9	6.1	135.1	16.2	0.0	50.8
May 2016	16.9	17.3	213.9	19.8	3.0	88.9
Jun 2016	19.6	21.6	240.8	24.7	0.0	152.4
Jul 2016	21.4	6.1	100.1	26.1	0.0	247.7
Aug 2016	21.9	0.0	39.6	24.9	0.0	266.7
Sep 2016	16.2	0.8	10.9	21.8	0.0	190.5
Oct 2016	9.9	63.8	0.0	16.8	19.8	50.8
Nov 2016	6.5	19.1	0.0	11.8	8.4	63.5
Dec 2016	-4.9	10.4	0.0	7.3	57.9	50.8
Jan 2017	-6.2	27.9	0.0	8.3	106.4	0.0
Feb 2017	-2.6	54.6	0.0	7.1	60.2	6.4
Mar 2017	5.6	27.9	0.0	12.7	20.8	50.8
Apr 2017	-	-	-	14.8	25.9	12.7
May 2017	-	-	-	19.7	0.0	101.6
Jun 2017	-	-	-	24.7	0.0	114.3
Jul 2017	-	-	-	27.7	0.0	108.0
Total	Mean: 7.9	Sum: 441.2	Sum: 764.8	Mean: 17.8	Sum: 276.6	Sum: 1219.2

Weather data refer to time period from start of trial (day of application) until end of trial (last sampling events)
Prec. – precipitation

The Applicant indicated whether the monthly average air temperatures and total water input (precipitation + irrigation) during the study were within 30-year normal levels for air temperature and precipitation.

New York – Air temperature was within -2.8 to 6.5°C of historical averages. Total water input was 16% more than the 30-year annual average.

North Carolina – Air temperature was within 1.9 to 2.2°C of historical averages. Total water input was 27% more than the 30-year annual average.

North Dakota – Air temperature was within -1.1 to 6.9°C of historical averages. Total water input was 1% less than the 30-year annual average.

Texas – Air temperature was within -3.8 to 4.4°C of historical averages. Total water input was 6% less than the 30-year annual average.

Washington – Air temperature was within -4.1 to 3.3°C of historical averages. Total water input was 21% more than the 30-year annual average.

California – Air temperature was within -5.2 to -0.6°C of historical averages. Total water input was 55% more than the 30-year annual average.

METHODS

Field application

Table 8.1.2.2.1/5-10 outlines the field application dates and study durations for each study site. The Applicant stated that application dates allowed evaluation of both spring/summer and fall applications that were agronomically appropriate timings for the application of herbicides to target weeds in the representative crops. In File MCA 3/001 the Applicant states that, in Europe, cinmethylin will be used for the targeted control of winter annual grass and

broadleaf weeds in pre- and post-emergent winter wheat (BBCH 00-29) and winter oilseed rape (BBCH 00-18). The HSE evaluator agrees with the Applicant's statement that the field test application dates were agronomically appropriate.

Table 8.1.2.2.1/5-10: Field application dates and study durations for each field site location.

Field site	Field application date	Study duration (days)
New York	2 October 2015	540
North Carolina	20 June 2016	93
North Dakota	6 October 2015	549
Texas	13 November 2015	545
Washington	6 October 2015	540
California	19 April 2016	449

Test substance applications were verified in three ways at each field site: measurement of calibrated sprayer pass times over the plot; measurement of cinmethylin recovered from spray interception devices (C₁₈ Speedisks) placed on the plot surface; and measurement of cinmethylin recovered from pans of soil placed on the plot surface. Table 8.1.2.2.1/5-11 summarises the application parameters for each field site treated with the test substance in formulation as an emulsifiable concentrate (BAS 684 02 H). Application verification is discussed in more detail later.

Table 8.1.2.2.1/5-11: Application parameters of field sites treated with cinmethylin formulated as an emulsifiable concentrate (BAS 684 02 H)

Details	New York	North Carolina	North Dakota	Texas	Washington	California
Application rate(s) used [g a.s. ha ⁻¹]	Target: 500					
	513	511	513	504	499	499
Was the maximum proposed label rate per ha used in study?	Yes (103% of target)	Yes (102% of target)	Yes (103% of target)	Yes (101% of target)	Yes (99.8% of target)	Yes (99.9% of target)
Number of applications	One	One	One	One	One	One
Application rate at Day 0 (mg a.s. kg soil ⁻¹) ^a	0.673	0.524	0.647	0.601	0.485	0.580
Application method	Spraying	Spraying	Spraying	Spraying	Spraying	Spraying
Type of spray equipment	Tractor-Mounted Boom Sprayer	Tractor-Mounted Boom Sprayer	Tractor-Mounted Boom Sprayer	Spider Self-Propelled Sprayer	Tractor-Mounted Boom Sprayer	Tractor-Mounted Boom Sprayer
Total volume of spray solution applied/plot OR total amount broadcasted/plot ^b	10025 mL	21819 mL	23733 mL	13121 mL	22101 mL	13220 mL
Volume of carrier	18900 mL	36790 mL	40000 mL	19971.5 mL	63085 mL	37801 mL

^a Calculated for the 0-3 inch soil depth and based on the site-specific 0-3 inch segment disturbed bulk density from GLP Soil Characterization Reports for each site (Table 8.1.2.2.1/5-07) and the calculated application rate for each application event

^b Calculated based on reported spray boom discharge rate (mL sec⁻¹) × sprayer pass time (sec)

Soil sampling

The sampling intervals for each field site are presented in Table 8.1.2.2.1/5-12. The soil sampling procedure is summarised in Table 8.1.2.2.1/5-13. The Applicant provided a freezer

storage stability study for cinmethylin (KCA 7.1.2.2.1/8); this has been assessed separately by the HSE evaluator.

Table 8.1.2.2.1/5-12: Actual soil sampling dates and intervals after field application for each test site.

Planned Sampling Event [days]	New York	North Carolina	North Dakota	Texas	Washington	California
	[days after last application (DALA)]					
First Application Date:	2-Oct-15	20-Jun-16	6-Oct-15	13-Nov-15	6-Oct-15	19-Apr-16
Prior to Application 1 (-T1)	-1	-2	-4	-1	-4	-1
Application 1 (T1)	0	0	0	0	0	0
3 DALA	3	3	3	3	3	3
7 DALA	7	7	7	7	7	7
15 DALA	15	15	15	12	15	15
30 DALA	31	30	34	28	30	30
60 DALA	61	65	63	61	63	63
90 DALA	90	93	192 ^b	90	100	90
180 DALA	180	-- ^a		192	181	181
270 DALA	270	--	269	262	269	273
360 DALA	360	--	357	356	360	357
450 DALA	452	--	429	445	524	449 ^c
540 DALA	540	--	549	545	540	NS
Untreated Plots						
Prior to Application 1 (-T1)	-1	-2	-4	-1	-4	-1
3 DALA	3	3	3	3	3	3
30 DALA	31	30	34	28	30	30
180 DALA	180	--	--	192	181	181
360 DALA	360	--	357	356	360	357

NS = Not Sampled

DALA = Days After Last Application

^a The North Carolina field trial site was severely flooded due to Hurricane Matthew; therefore, no sampling events occurred following the 90 DALA sampling interval.

^b The 90 DALA sampling event was taken on 15 Apr 16 due to the ground being frozen at the actual 90 DALA sampling interval. Since the 90 DALA sampling interval occurred on 192 DALA, the 180 DALA sampling interval was not conducted.

^c Due to the dissipation of cinmethylin residues, no further sampling intervals were conducted.

Table 8.1.2.2.1/5-13: Soil sampling procedure and storage conditions for the field soil samples.

Details	Treated test plots (all sites)
Method of sampling (random or systematic)	Random
Method of soil collection (e.g., cores)	Cores
Sampling depth	42-inch (approx. 106.7 cm)
Number of cores collected	NY, NC, ND, TX, WA: 15 cores per site per sampling period (5 per subplot) CA: 15 6-42 inch cores and 24 0-6 inch cores per site per sampling period (5 and 8 per subplot) Duplicate 0-3 inch depth core samples were taken on the day of application.
Number of segments per core ^a	8
Length of soil segments ^{a, b}	3- or 6-inch
Core diameters	Soil samples were collected in two steps. First, a large diameter sampler (minimum of 3.5 inch) was used to collect a 0-6 inch depth core sample. A smaller diameter sampler (minimum of 1.4 inch) was then used to collect a 6-42 inch depth core sample.
Method of sample processing	The 0-6 inch depth core samples were divided into 0-3 and 3-6 inch sections in the field. The 6-42 inch depth core samples were divided into 6-12, 12-18, 18-24, 24-30, 30-36, and 36-42 inch sections either immediately in the field or soon after at a nearby facility.
Storage conditions	Frozen
Storage length	Treated plot, post-application samples were stored for a maximum of 140 days (NC) to 395 days (NY).

^a After sectioning the soil cores.^b 1 inch corresponds to 2.54 cm.**Field application verification**

The Applicant verified the field application through three methods. The pass time of the calibrated sprayer in the treated plot at each field site was used to calculate the delivery of cinmethylin. To confirm the amount of test compound applied to a given area, ten Speedisks were placed randomly on the soil surface in each subplot in locations where soil would not be sampled (e.g. -T1 subplots and along subplot borders). Disks were collected once the plot was relatively dry, transported on dry ice or ice packs and frozen until analysis. Each disk was fortified with a racemic solution of cinmethylin at 800 µg, left to dry, then eluted with two 20 mL aliquots of acetonitrile. The extract was made up to 500 mL with acetonitrile; a 0.5 mL aliquot was diluted to 10 mL with acetonitrile and analysed by LC-MS/MS. If necessary, further dilutions were made using acetonitrile/water (80/20, v/v) and analysed by LC-MS/MS.

Soil pans were also used for application verification. Three soil pans were placed randomly in each subplot prior to application of cinmethylin in locations that were not to be soil sampled. Soils were collected once the plot was relatively dry post-application and soils were collected, transported on dry ice or ice packs and frozen prior to extraction. Soil pan samples were subjected to the same handling, shipping and storage conditions as field trial samples.

Shipping verification

Shipping verification (SV) samples were prepared using soil from the control plot and were prepared to coincide with the sampling intervals at each field site. At each interval, four 20 g soil aliquots were weighed into 50 mL Falcon tubes. One sample was designated the control sample. The concentration in the remaining three SV samples based on 1 mL of a 10 µg/mL fortification solution added to a nominal 20 g soil sample was 500 µg/kg. All SV samples were subjected to the same handling, shipping, and storage conditions as field trial samples.

The SV samples were analysed for both cinmethylin enantiomers. The Applicant concluded that recoveries $\geq 70\%$ would demonstrate acceptable sample stability during shipping.

Sample shipment and storage

Soil, application verification, and shipping verification samples were shipped frozen from the six field trial sites to BASF Crop Protection (Research Triangle Park, NC) for processing and homogenisation of soil samples. The frozen composite soil samples were homogenised in a soil mill in the presence of liquid nitrogen to maintain frozen conditions. Processed soil samples were shipped on dry ice. A freezer soil storage stability study for cinmethylin was conducted for a 12- to 14-month period [see KCA 7.1.2.2.1/8 2018/7001858]. The HSE evaluator has assessed this separately and concluded that storing samples for up to 14 months at -25°C did not affect the recovery of cinmethylin from soils.

Soil extraction method

Samples were homogenised using a soil mill in the presence of liquid nitrogen to maintain frozen conditions. For each site, three composite samples, one from each replicate treated plot, were analysed at each sampling interval and depth. On the day of application (T1) three additional composite samples (0-3 inch (0 – 7.6 cm) depth only), one from each replicate treated plot, were also collected for analysis. Composite samples were generally analysed once, though several samples were analysed multiple times to confirm original results.

A 5 g soil sample was extracted twice by shaking: the first extraction was with 10 mL pure acetonitrile; the second extraction was with acetonitrile-water (60/40 v/v). These extracts were combined and the cinmethylin residues in the soil extracts were directly determined by LC-MS/MS. The analytical method allowed for separate quantification of both enantiomers present. Moisture content (%) of samples was determined by a moisture analyser. Residue results for soil samples between 0-6 inches and samples with residues $\geq \text{LOD}$ were corrected for moisture content.

Analytical methods

Soil core sample analysis was conducted using a BASF analytical method (L0308/01; see file KCA 4.1.2/1). The HSE evaluator notes that the analytical method has been evaluated separately and the method was deemed valid. The Applicant reported results of the soil analysis on a dry weight basis for residue determination and that field treated soil sample weights were corrected for moisture content. Control plots were used for procedural recovery experiments; these were fortified with cinmethylin prior to extraction and analysed with samples from the treated plots. The LOD and LOQ for residues of the parent and two enantiomers are $1.5 \mu\text{g kg}^{-1}$ and $5 \mu\text{g kg}^{-1}$, respectively.

As there were no metabolites of concern identified during the laboratory studies, the Applicant did not include any metabolites in the field soil residue methods.

Kinetic evaluation

A kinetic study was undertaken by the Applicant to assess the dissipation of cinmethylin from the time of application in six field site locations. The Applicant used single first-order (SFO), first-order multi compartment (FOMC), and double first-order in parallel (DFOP) kinetic models to derive endpoints using the trigger endpoint flowchart described in FOCUS Kinetics guidance (2006; 2014).

The Applicant used analyte mass data in g/ha terms to conduct the kinetic evaluation. These values were derived using analytical dry weight residue concentrations, sample fresh weights, soil moisture content, and soil core diameters. Mass values for core segments were summed over depth to give the total mass of each analyte in the entire 0-42 inch (0-107 cm) sampled soil profile at each sampling time. Total mass values were expressed on a g/ha basis, so they could be easily related to the target amount applied. The calculations used by the Applicant

are presented below; the HSE evaluator has checked these and considers this manipulation to be valid:

$$g/Ha = \frac{(ppb \times \text{dry sample weight (kg)} \times g/10^6 \mu g)}{(\text{sampling area (cm}^2\text{)} \times ha/10^8 \text{ cm}^2)}$$

Where:

$$\text{dry sample weight (kg)} = \frac{\text{fresh sample weight (kg)}}{\left[\frac{\text{moisture \%}}{100} + 1\right]}$$

The Applicant also provided an example of the sampling area calculation, based on the 0-3 and 3-6 inch cores with 11 cm diameter (5.5 cm radius):

$$\text{Area (cm)} = \pi 5.5^2 \times 5 \text{ cores per sample} = 475.17 \text{ cm}^2$$

The analytical LOQ was 5 µg/kg and the LOD was 1.5 µg/kg for both enantiomers. The Applicant stated that analytical values between the LOD and LOQ were used as reported (as per FOCUS kinetics guidance), and noted that quantification at these levels may be somewhat less certain than those above LOQ. Additionally, a depth segment (3 inches deep for 0-3 and 3-6 inches; 6 inches deep for segments thereafter) was deemed by the Applicant to be residue free if the average concentration of the three replicates at that depth was < LOD for all analytes. Values < LOD were set to zero except in specific cases listed below, where values < LOD were set to 0.5 × LOD (0.75 µg/kg) for g/ha calculation. The Applicant applied this where:

- A later concentration in the same depth and replicate was ≥ LOQ;
- The value at the previous sampling event in the same depth and replicate was ≥ LOD;
- The value in the overlying depth segment at the same event and in the same replicate was ≥ LOD;
- At the same event and replicate, the underlying depth segment at the same event and in the same replicate was ≥ LOD.

Table 8.1.2.2.1/5-14, below, is an example provided by the Applicant to show how the above data manipulations would be applied on example data. These were then converted to g/ha as outlined previously. The HSE evaluator notes that this data processing was in agreement with FOCUS guidance, except for the conversion to g/ha, which the Applicant undertook to better contextualise the data.

Table 8.1.2.2.1/5-14: Example table with theoretical values to show how data manipulations were applied, as supplied by the Applicant.

Days After Application	Analytical Values (µg/kg)			Adjusted Values (µg/kg)		
	0-3	3-6	6-12	0-3	3-6	6-12
0	300.0	<LOD	<LOD	300.0	0.25 ¹	0.00
3	75.0	<LOD	<LOD	75.0	0.25 ¹	0.00
7	10.0	<LOD	<LOD	10.0	0.25 ¹	0.00
15	1.0	1.5	<LOD	1.0	1.5	0.25 ²
30	0.75	0.75	<LOD	0.75	0.75	0.25 ²
60	0.50	<LOD	<LOD	0.50	0.25 ³	0.00
90	<LOD	<LOD	<LOD	0.25 ⁴	0.00	0.00

¹ These values were set to ½ LOD for two reasons: a) the value in the overlying depth segment at the same event was ≥ LOD; and b) a later concentration at the same depth was ≥ LOQ.

² These values were set to ½ LOD since the value in the overlying depth segment at the same event was ≥ LOD.

³ This value was set to ½ LOD for two reasons: a) the value in the overlying depth segment at the same event was ≥ LOD; and b) the value at the previous sampling event was ≥ LOD.

⁴ This value was set to ½ LOD since the value at the previous sampling event was ≥ LOD.

n.b. The HSE evaluator notes the LOD used in this example is not the actual LOD from the present study.

The Applicant noted the following data manipulations for handling specific issues within the datasets:

- For the Texas site, 60 DAA samples from the 3-6 inch (7.6-15.2 cm) depth were not analysed due to inadvertent oversight. The concentrations of the 3-6 inch (7.6-15.2 cm) samples from 30 DAA were assumed for the 60 DAA samples;
- In cases where a concentration value was assigned and there was no soil moisture value available, the soil moisture content at 15 bar for the applicable soil (taken from the soil characterisation data) was assumed for calculations to convert residues to g ha⁻¹.

The HSE evaluator agrees with the above data manipulations as the Applicant has applied decisions that assume a worst-case scenario.

The Applicant used the kinetic evaluation software package KinGUI version 2 to derive endpoints. Time-series plots and residual plots were also generated using KinGUI. Model fits were selected based on detailed statistical analysis including visual assessment of the goodness of fit, Chi² scaled-error criterion and t-test significance.

The HSE evaluator conducted an evaluation of the Applicant's kinetic assessment by conducting their own assessments of the dissipation of cinmethylin and its two enantiomers in each of the six soils studied in the present study. The HSE evaluator used Cake v.3.2 for the kinetic evaluation and followed the trigger endpoint pathway to achieve the best model fit, as described in the FOCUS Kinetics Guidance (2006; 2014).

RESULTS AND DISCUSSION

Field application verification

Application verification via pass time and sprayer calibration data indicated that the target field application rates were precise and accurate. Individual application rates ranged from 100 – 103% of target with an average (n = 6) of 102%. Table 8.1.2.2.1/5-15 reports the individual application rates for each field site.

Table 8.1.2.2.1/5-15: Individual application rates for application of BAS 684 02 H based on pass time and sprayer calibration data in six field sites

Site	Sprayer output (Gal per Acre)	Application rate		% of Target Rate
		lb a.i./A	g a.i./ha	
New York	51.28	0.4581	513	103
North Carolina	53.66	0.4561	511	102
North Dakota	49.66	0.4581	513	103
Texas	50.33	0.4492	504	101
Washington	49.87	0.4450	499	100
California	50.71	0.4455	499	100

Application verification via C₁₈ Speedisks placed on the soil surface within plots were also analysed. The calculated theoretical total µg expected in each C₁₈ Speedisk sample was approximately 795.22 µg. Table 8.1.2.2.1/5-16 reports application verification results arising from extraction of C₁₈ Speedisks. Average recoveries ranged 52 – 111% with an average of 74%. The Applicant highlighted the low recoveries at the North Carolina (57%) and California (52%) sites; however, the HSE evaluator concludes that overall, the Speedisk recoveries were poor and that this method was not a good method for verifying field applications.

Table 8.1.2.2.1/5-16: Cinmethylin recoveries arising from analysis of C₁₈ Speedisks from the six field sites (n = 3 per site)

Site	Theoretical cinmethylin mass (µg)	Mean cinmethylin found (µg)			Mean Recovery (%)	RSD (%)
		(+)	(-)	Total		
New York	795.22	444.05	436.69	880.740	111	4.5
North Carolina		229.56	225.97	455.533	57	7.9
North Dakota		297.10	265.04	562.147	71	3.0
Texas		322.35	270.78	593.140	75	2.9
Washington		325.66	295.21	620.873	78	5.7
California		207.0	202.89	409.893	52	1.7

Finally, soil pans (not described by the Applicant) were used at each field site as a third application verification method. Three soil pans were distributed in each replicate of the treated plot. The Applicant calculated theoretical concentrations expected in each soil pan sample and compared this to the actual residues; these data are presented in KCA 7.1.2.2.1/5-17 below. Overall recoveries were 93% ((+)-enantiomer) and 87.5% ((-)-enantiomer) and ranged 74-119% and 72-111% respectively. The HSE evaluator notes that recoveries from Texas soil pans demonstrated high variation with RSDs of 17.6 and 19.9% for (+) and (-) respectively, and this combined with relatively low recoveries; however, this was not a significant issue.

Table 8.1.2.2.1/5-17: Mean cinmethylin recoveries arising from analysis of soil pans from the six field sites (n = 3 per site)

Site	Mean Sample weight (g)	Theoretical cinmethylin mass (µg/kg)	Mean cinmethylin found (µg)		Mean Recovery (%)		RSD (%)	
			(+)	(-)	(+)	(-)	(+)	(-)
New York	1650.0	3561.28	4244.48	3969.39	119	111	3.1	3.6
North Carolina	2400.0	2448.38	2175.17	2142.88	89	88	5.4	2.4
North Dakota	2400.0	2358.87	2435.21	2191.94	103	93	6.4	4.6
Texas	1650.0	4398.82	3264.0	3203.41	74	73	17.6	19.9
Washington	3600.0	1632.26	1586.05	1435.09	97	88	7.4	6.0
California	2476.67	2286.25	1768.29	1634.88	77	72	9.4	3.8

The HSE evaluator concludes that, based on the pass time/sprayer calibration and soil pan recovery techniques, the spray applications were valid at all sites.

Shipping verification samples

Recoveries of cinmethylin following sampling, handling, shipping and storage of samples are summarised in Table 8.1.2.2.1/5-18. All replicates demonstrated recoveries > 90% and mean recoveries ranged 94-122% ((-)-enantiomer) and 93-120% ((+)-enantiomer).

Table 8.1.2.2.1/5-18: Cinmethylin recoveries arising from shipping verification sample analysis for the six field sites as provided by the Applicant. Mean recoveries are presented in parentheses.

Site (RCN) [Reference]	Sampling Interval (DALA)	Analyte	Spike Level (µg/kg)	% Recovery (Mean)	
				Procedural	Shipping Verification
New York (R150283) [Table 5]	180	BAS 684 H (-)	500	96, 94 (95)	109, 101, 102 (104)
	270				112, 111, 110 (111)
	180	BAS 684 H (+)		94, 92 (93)	101, 98, 98 (99)
	270				111, 116, 111 (113)
North Carolina (R150284) [Table 10]	30	BAS 684 H (-)	500	93, 91 (92)	102, 97, 102 (100)
	90				92, 94, 96 (94)
	30	BAS 684 H (+)		95, 92 (94)	100, 96, 101 (99)
	90				92, 90, 96 (93)
North Dakota (R150285) [Table 15]	180	BAS 684 H (-)	500	103, 103 (103)	120, 121, 123 (122)
	270				117, 118, 115 (117)
	180	BAS 684 H (+)		101, 100 (101)	122, 121, 116 (120)
	270				113, 112, 110 (112)
Texas (R150286) [Table 20]	180	BAS 684 H (-)	500	109, 104 (106)	108, 116, 112 (112)
	180	BAS 684 H (+)		99, 98 (99)	111, 116, 111 (113)
Washington (R150287) [Table 25]	180	BAS 684 H (-)	500	98, 96 (97)	105, 103, 104 (104)
	270				111, 112, 109 (111)
	180	BAS 684 H (+)		99, 96 (98)	103, 105, 102 (103)
	270				108, 108, 109 (108)
California (R150288) [Table 30]	30	BAS 684 H (-)	500	99, 102 (100)	99, 100, 94 (98)
	90				109, 136, 107 (118)
	30	BAS 684 H (+)		99, 98 (98)	100, 96, 93 (97)
	90				106, 134, 106 (115)

Method recoveries

Procedural recoveries were tested by studying four spike levels for each enantiomer: 5, 50, 500 and 1000 µg/kg (1x, 10x, 100x, 200x LOQ). New York and North Carolina soils were tested at all four spike levels, while the other four soils were tested at 5, 50 and 1000 µg/kg only. Results are presented for each field site in Tables KCA 7.1.2.2.1/5-19-24. Mean recoveries reported by the Applicant for both enantiomers ranged 94-98% for New York, 90-98% for North Carolina, 96-100% for North Dakota, 89-94% for Texas, 87-95% for Washington, and 85-100% for California. The HSE evaluator notes that, based upon the published ranges, no samples were found to be below the required 70-120% range, though a number were observed to be above 120% at the lowest spike level (5 µg/kg). The HSE evaluator does not deem this to have been problematic as only three New York spike samples were above 120%, and therefore concludes the applied methods is valid.

Cinmethylin dissipation in soils

The Applicant stated that, due to the use of non-radiolabelled material, mass balances were not determined. Therefore, it was not possible to quantify non-extractable residues or losses of volatile CO₂ from the mineralisation of cinmethylin.

Where a replicate was measured several times, the Applicant averaged these before calculating the overall mean. On the application day sampling event (T1), the Applicant collected a duplicate topsoil sample (0-3 inches; 0-7.6 cm) in addition to the primary 0-42 inch (0-106.7 cm) sample from each replicate and analysed them separately. Both the primary and the duplicate samples were comprised of five individual cores composited together. The primary and duplicate topsoil segment residue values were averaged to give one value per replicate. Non-detectable residues (< LOD or < 1.5 µg/kg) were set to zero (0) when calculating the mean.

At each sampling interval, the Applicant analysed segments down to the core depth at which no residues were detected. This was defined by the Applicant as when the average residue of the three replicates was < LOD for both enantiomers.

The Applicant reported that no cinmethylin residues were detected in the control soil samples.

Results are summarised on the following pages split by field site in Table 8.1.2.2.1/5-19 (New York), Table 8.1.2.2.1/5-20 (North Carolina), Table 8.1.2.2.1/5-21 (North Dakota), Table 8.1.2.2.1/5-22 (Texas), Table 8.1.2.2.1/5-23 (Washington), and Table 8.1.2.2.1/5-24 (California).

New York (Table 8.1.2.2.1/5-19). The Applicant described the dissipation of cinmethylin as happening at a moderate rate. The maximum mean concentrations were observed at 0 DALA, with 259.2 and 274.0 µg/kg observed for the (-) and (+) enantiomers respectively in the 0-3 inch (0-7.6 cm) segment. By 61 DALA the Applicant reported 79 and 74% reductions against the levels observed at 0 DALA (55.3 and 71 µg/kg) respectively.

North Carolina (Table 8.1.2.2.1/5-20). The Applicant described the dissipation of cinmethylin as being rapid. Mean maximum concentrations of cinmethylin (-)-enantiomer and (+)-enantiomer were observed at 0 DALA, with 125.7 and 130.2 µg/kg at 0-3 inch depth respectively. By 15 DALA, mean concentrations had reduced by 90% and 88% to 12.7 and 15.5 µg/kg respectively. By the time the study was terminated due to hurricane damage at 65 DALA, mean concentrations were < LOD throughout the soil profile, though the HSE evaluator observes that for both enantiomers, one replicate measured just above LOD (1.95 and 1.61 µg/kg respectively).

North Dakota (Table 8.1.2.2.1/5-21). The Applicant described the dissipation of cinmethylin as being moderate. Mean maximum concentrations of cinmethylin (-)-enantiomer and (+)-

enantiomer were observed at 0 DALA, with 304.8 and 318.4 µg/kg at 0-3 inch depth respectively. By 63 DALA, mean concentrations had reduced by 72% and 69% respectively to 85.6 and 99.2 µg/kg.

Texas (Table 8.1.2.2.1/5-22). The Applicant described the dissipation of cinmethylin as being moderate. Mean maximum concentrations of cinmethylin (-)-enantiomer and (+)-enantiomer were observed 7 DALA, with 195.7 and 210.3 µg/kg observed respectively at 0-3 inch depth. By 90 DALA the mean concentrations had reduced by 76% and 71% respectively to 46.4 and 60.9 µg/kg.

Washington (Table 8.1.2.2.1/5-23). The Applicant described the dissipation of cinmethylin as being rapid. Mean maximum concentrations of cinmethylin (-)-enantiomer and (+)-enantiomer were observed at 0 DALA, with 163.1 and 165.7 µg/kg observed respectively at 0-3 inch depth. By 30 DALA the mean concentrations had reduced by 95% and 93% respectively to 8.41 and 11.4 µg/kg.

California (Table 8.1.2.2.1/5-24). The Applicant described the dissipation of cinmethylin as being rapid. Mean maximum concentrations of cinmethylin (-)-enantiomer and (+)-enantiomer were observed 3 DALA, with 63.11 and 67.85 µg/kg observed respectively at 0-3 inch depth. By 30 DALA the mean concentrations had reduced by 95% and 93% respectively to 8.41 and 11.4 µg/kg.

Table 8.1.2.2.1/5-19: Mean dry weight residues of cinmethylin enantiomers ($\mu\text{g a.s./kg dry soil}$) in treated soil samples from the New York field site. The residues presented are means of three replicate values (i.e. mean result for replicate 1, 2 and 3 for each soil depth).

Analyte	Soil depth (Inches (cm))	Targeted days after last application (DALA; actual DALA shown in parentheses)										
		T1	3	7	15	30	60	90	180	270	360	450
		(0)	(3)	(7)	(15)	(31)	(61)	(90)	(180)	(270)	(360)	(452)
Cinmethylin (-)- enantiomer	0-3 (0-7.6)	259.208	176.528	136.435	127.940	106.214	55.342	23.662	25.219	7.769	3.677	< LOD
	3-6 (7.6- 15.2)	2.330	< LOD	6.751	2.420	< LOD ^a	1.615	20.151	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD ^a	NA	NA	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA	NA
	Total	261.537	177.278	144.110	132.781	106.964	57.707	44.563	25.969	8.519	4.427	0.750
Cinmethylin (+)- enantiomer	0-3 (0-7.6)	273.958	223.854	144.060	154.663	123.322	71.004	29.942	36.761	11.867	7.723	< LOD
	3-6 (7.6- 15.2)	2.555	< LOD	8.029	4.093	1.867	2.324	27.501	< LOD	< LOD ^a	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD ^a	NA	NA	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA	NA
	Maximum	276.512	224.604	152.839	159.506	125.939	74.078	58.193	37.511	12.617	8.473	0.750

< LOD = Below limit of detection (< 1.5 $\mu\text{g/kg}$); NA = Not analysed; NS = Not sampled.

n.b. < LOD in italics denotes where, for kinetic evaluation, the value was set to $0.5 \times \text{LOD}$ (0.75 $\mu\text{g/kg}$). This has been included in the total value for each sample date.

^a Denotes instance where the mean for all replicates was < LOD (< 1.5 $\mu\text{g/kg}$), but one or two replicates contained detectable residue.

Table 8.1.2.2.1/5-20: Mean dry weight residues of cinmethylin enantiomers ($\mu\text{g a.s./kg dry soil}$) in treated soil samples from the North Carolina field site. The residues presented are means of three replicate values (i.e. mean result for replicate 1, 2 and 3 for each soil depth). The 90 DALA samples are included for completeness; however, these values were not considered for kinetic evaluation and are highlighted in grey to reflect this.

Analyte	Soil depth (Inches (cm))	Targeted days after last application (DALA; actual DALA shown in parentheses)						
		T1 (0)	3 (3)	7 (7)	15 (15)	30 (30)	60 (65)	90 (93)
Cinmethylin (-)-enantiomer	0-3 (0-7.6)	125.737	73.116	43.309	12.650	6.137	< LOD ^a	< LOD
	3-6 (7.6- 15.2)	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	NA	< LOD	< LOD	NA	NA	NA
	12-18 (30.5-45.7)	NS	NA	< LOD	< LOD	NA	NA	NA
	Total	126.487	73.866	44.059	13.40	6.887	0.75	0.75
Cinmethylin (+)-enantiomer	0-3 (0-7.6)	130.209	78.803	46.929	15.520	7.339	< LOD ^a	< LOD
	3-6 (7.6- 15.2)	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	NA	< LOD	< LOD	NA	NA	NA
	12-18 (30.5-45.7)	NS	NA	< LOD	< LOD	NA	NA	NA
	Total	130.959	79.553	47.679	16.270	8.089	0.75	0.75

< LOD = Below limit of detection (< 1.5 $\mu\text{g/kg}$); NA = Not analysed; NS = Not sampled.

n.b. < LOD in italics denotes where, for kinetic evaluation, the value was set to $0.5 \times \text{LOD}$ (0.75 $\mu\text{g/kg}$). This has been included in the total value for each sample date.

^a Denotes instance where the mean for all replicates was < LOD (< 1.5 $\mu\text{g/kg}$), but one or two replicates contained detectable residue.

Table 8.1.2.2.1/5-21: Mean dry weight residues of cinmethylin enantiomers (µg a.s./kg dry soil) in treated soil samples from the North Dakota field site. The residues presented are means of three replicate values (i.e. mean result for replicate 1, 2 and 3 for each soil depth).

Analyte	Soil depth (Inches (cm))	Targeted days after last application (DALA; actual DALA shown in parentheses)								
		T1	3	7	15	30	60	90	270	360
		(0)	(3)	(7)	(15)	(34)	(63)	(192)	(269)	(357)
Cinmethylin (-)- enantiomer	0-3 (0-7.6)	304.754	254.126	277.965	106.322	101.103	85.594	31.061	9.571	< LOD ^a
	3-6 (7.6- 15.2)	< LOD	< LOD ^a	< LOD ^a	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA	NA
	Total	305.504	254.876	278.715	107.072	101.853	86.344	31.811	10.321	0.75
Cinmethylin (+)- enantiomer	0-3 (0-7.6)	318.448	265.80	290.093	109.812	114.569	99.159	38.838	13.654	3.004
	3-6 (7.6- 15.2)	< LOD	1.5445	< LOD ^a	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	< LOD ^a	< LOD	NA	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA	NA
	Total	319.198	268.094	290.843	110.562	115.319	99.909	39.588	14.404	3.754

< LOD = Below limit of detection (< 1.5 µg/kg); NA = Not analysed; NS = Not sampled.

n.b. < LOD in italics denotes where, for kinetic evaluation, the value was set to 0.5 × LOD (0.75 µg/kg). This has been included in the total value for each sample date.

^a Denotes instance where the mean for all replicates was < LOD (< 1.5 µg/kg), but one or two replicates contained detectable residue.

Table 8.1.2.2.1/5-22: Mean dry weight residues of cinmethylin enantiomers ($\mu\text{g a.s./kg dry soil}$) in treated soil samples from the Texas field site. The residues presented are means of three replicate values (i.e. mean result for replicate 1, 2 and 3 for each soil depth).

Analyte	Soil depth (Inches (cm))	Targeted days after last application (DALA; actual DALA shown in parentheses)										
		T1	3	7	15	30	60	90	180	270	360	450
		(0)	(3)	(7)	(12)	(28)	(61)	(90)	(192)	(262)	(356)	(445)
Cinmethylin (-)- enantiomer	0-3 (0-7.6)	146.903	145.805	195.676	125.043	84.295	67.222	46.429	2.151	< LOD	< LOD	< LOD
	3-6 (7.6- 15.2)	< LOD ^a	2.781	< LOD	< LOD	< LOD	NA ^b	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA	NA	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA	NA	NA
	Total	147.653	149.337	196.426	125.793	85.045	67.972	47.179	2.901	0.75	0.75	0.75
Cinmethylin (+)- enantiomer	0-3 (0-7.6)	155.256	153.457	210.286	136.851	97.244	83.048	60.910	8.683	2.702	< LOD	< LOD
	3-6 (7.6- 15.2)	< LOD ^a	3.7652	< LOD	< LOD	< LOD ^a	NA ^b	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA	NA	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA	NA	NA	NA
	Total	156.006	157.973	211.036	137.601	97.994	83.798	61.660	9.433	3.452	0.75	0.75

< LOD = Below limit of detection (< 1.5 $\mu\text{g/kg}$); NA = Not analysed; NS = Not sampled.

n.b. < LOD in italics denotes where, for kinetic evaluation, the value was set to $0.5 \times \text{LOD}$ (0.75 $\mu\text{g/kg}$). This has been included in the total value for each sample date.

^a Denotes instance where the mean for all replicates was < LOD (< 1.5 $\mu\text{g/kg}$), but one or two replicates contained detectable residue.

^b Sample was not analysed. Applicant assumed the worst-case scenario and applied the 30 DALA residue level here (0.75 $\mu\text{g/kg}$). This has been included in the total values.

Table 8.1.2.2.1/5-23: Mean dry weight residues of cinmethylin enantiomers ($\mu\text{g a.s./kg dry soil}$) in treated soil samples from the Washington field site. The residues presented are means of three replicate values (i.e. mean result for replicate 1, 2 and 3 for each soil depth).

Analyte	Soil depth (Inches (cm))	Targeted days after last application (DALA; actual DALA shown in parentheses)								
		T1	3	7	15	30	60	90	180	270
		(0)	(3)	(7)	(15)	(30)	(63)	(100)	(181)	(269)
Cinmethylin (-)- enantiomer	0-3 (0-7.6)	163.119	72.312	45.291	15.439	8.413	4.735	3.939	< LOD	< LOD
	3-6 (7.6- 15.2)	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA
	Total	163.869	73.062	46.041	16.189	9.163	5.485	4.689	0.75	0.75
Cinmethylin (+)- enantiomer	0-3 (0-7.6)	165.659	73.432	52.946	18.946	11.396	5.867	5.653	< LOD	< LOD
	3-6 (7.6- 15.2)	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD	NA
	Total	166.409	74.182	53.696	19.696	12.146	6.617	6.403	0.75	0.75

< LOD = Below limit of detection (< 1.5 $\mu\text{g/kg}$); NA = Not analysed; NS = Not sampled.

n.b. < LOD in italics denotes where, for kinetic evaluation, the value was set to $0.5 \times \text{LOD}$ (0.75 $\mu\text{g/kg}$). This has been included in the total value for each sample date.

Table 8.1.2.2.1/5-24: Mean dry weight residues of cinmethylin enantiomers ($\mu\text{g a.s./kg dry soil}$) in treated soil samples from the California field site. The residues presented are means of three replicate values (i.e. mean result for replicate 1, 2 and 3 for each soil depth).

Analyte	Soil depth (Inches (cm))	Targeted days after last application (DALA; actual DALA shown in parentheses)							
		T1	3	7	15	30	60	90	180
		(0)	(3)	(7)	(15)	(30)	(63)	(90)	(181)
Cinmethylin (-)- enantiomer	0-3 (0-7.6)	50.521	63.112	55.575	22.277	2.441	< LOD	< LOD	< LOD
	3-6 (7.6- 15.2)	< LOD	1.5589	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NS	< LOD	< LOD	< LOD	< LOD	NA	NA	NA
	12-18 (30.5-45.7)	NS	< LOD	< LOD	< LOD	< LOD	NA	NA	NA
	Total	51.271	65.421	56.325	23.027	3.191	0.75	0.75	0.75
Cinmethylin (+)- enantiomer	0-3 (0-7.6)	55.030	67.850	60.642	24.156	7.426	< LOD	< LOD	< LOD
	3-6 (7.6- 15.2)	< LOD	1.6971	< LOD	< LOD	< LOD	< LOD	< LOD	< LOD
	6-12 (15.2-30.5)	NA	< LOD	< LOD	< LOD	< LOD	NA	NA	NA
	12-18 (30.5-45.7)	NA	< LOD	< LOD	< LOD	< LOD	NA	NA	NA
	Total	55.780	70.297	61.392	24.906	8.176	0.75	0.75	0.75

< LOD = Below limit of detection (< 1.5 $\mu\text{g/kg}$); NA = Not analysed; NS = Not sampled.

n.b. < LOD in italics denotes where, for kinetic evaluation, the value was set to $0.5 \times \text{LOD}$ (0.75 $\mu\text{g/kg}$). This has been included in the total value for each sample date.

Leaching potential

The Applicant stated that limited mobility was observed in both cinmethylin enantiomers at all six field sites, with neither enantiomer being observed at a replicate average > LOD beyond 6 inches (15.2 cm). The HSE evaluator agrees that the data shows limited mobility in field soils.

KINETIC EVALUATION: TRIGGER ENDPOINTS**Evaluation Data**

The Applicant's kinetic evaluation was conducted to derive trigger endpoints and utilised results for soil core samples collected and analysed from the time of application through to the last analysed sampling event, which ranged from 63 days (California) to 360 days (New York) after the application. The Applicant converted the total mass values from µg/kg to g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. This allowed the data to be easily related to the target amount applied. Tables KCA 7.1.2.2.1/5-25-30 present the data used by the Applicant and HSE evaluator for the kinetic evaluation of the dissipation of cinmethylin and the two enantiomers. These data are reproduced as presented by the Applicant, and have been evaluated by the HSE evaluator and deemed valid.

Table 8.1.2.2.1/5-25: Data values used to quantify dissipation of cinmethylin (sum of (-) and (+) enantiomers), and the two enantiomers in soil at the New York field site. Values are expressed in g/ha.

Actual Days After Application	Replicate	(-)-enantiomer		(+) -enantiomer		Sum cinmethylin (g/ha) ^{a,b}
		Residue (g/ha) ^{a,b}	Residue depth (inches) ^c	Residue (g/ha) ^{a,b}	Residue depth (inches)	
0	A	295.9	0-6	312.5	0-6	608.4
0	A (duplicate)	281.8	0-3	306.3	0-3	588.1
0	B	127.4	0-6	138.3	0-6	265.7
0	B (duplicate)	206.3	0-3	216.2	0-3	422.5
0	C	232.7	0-6	236.9	0-6	469.6
0	C (duplicate)	200.4	0-3	210.6	0-3	411.0
3	A	157.4	0-6	191.2	0-6	348.6
3	B	106.7	0-6	143.3	0-6	250.0
3	C	184.0	0-6	232.4	0-6	416.4
7	A	128.4	0-12	147.5	0-12	275.9
7	B	134.3	0-6	140.0	0-12	274.3
7	C	96.51	0-6	95.24	0-6	191.8
15	A	94.63	0-6	113.9	0-6	208.5
15	B	146.4	0-12	190.7	0-12	337.1
15	C	108.2	0-6	122.5	0-12	230.7
31	A	59.78	0-6	74.50	0-12	134.3
31	B	109.2	0-12	123.1	0-12	232.3
31	C	99.88	0-6	118.0	0-6	217.9
61	A	69.09	0-6	84.50	0-6	153.6
61	B	60.93	0-12	80.33	0-12	141.3
61	C	27.34	0-6	37.45	0-6	64.79
90	A	28.51	0-12	46.12	0-12	74.63
90	B	44.52	0-12	53.81	0-12	98.33
90	C	40.43	0-12	48.46	0-12	88.89
180	A	36.32	0-6	52.12	0-6	88.44
180	B	31.85	0-18	45.84	0-18	77.69
180	C	31.83	0-6	45.55	0-6	77.38
270	A	8.474	0-6	13.20	0-6	21.67
270	B	4.264	0-6	7.484	0-6	11.75
270	C	7.780	0-6	10.74	0-6	18.52
360	A	2.2258	0-6	4.077	0-6	6.303
360	B	6.433	0-6	11.66	0-6	18.09
360	C	2.687	0-6	5.614	0-6	8.301

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected both spatially and temporally according to FOCUS (2014).

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

Table 8.1.2.2.1/5-26: Data values used to quantify dissipation of cinmethylin (sum of (-) and (+) enantiomers), and the two enantiomers in soil at the North Carolina field site. Values are expressed in g/ha.

Actual Days After Application	Replicate	(-)-enantiomer		(+) -enantiomer		cinmethylin (g/ha) ^{a,b}
		Residue (g/ha) ^{a,b}	Residue depth (inches) ^c	Residue (g/ha) ^{a,b}	Residue depth (inches)	
0	A	149.4	0-6	150.1	0-6	299.5
0	A (duplicate)	132.7	0-3	137.7	0-3	270.4
0	B	144.5	0-6	140.5	0-6	285.0
0	B (duplicate)	184.2	0-3	195.5	0-3	379.7
0	C	139.9	0-6	141.8	0-6	281.7
0	C (duplicate)	127.3	0-3	143.3	0-3	270.6
3	A	85.69	0-6	91.73	0-6	177.4
3	B	108.1	0-6	116.8	0-6	224.9
3	C	64.45	0-6	69.68	0-6	134.1
7	A	51.78	0-6	56.43	0-6	108.2
7	B	45.86	0-6	51.71	0-6	97.57
7	C	53.09	0-6	54.90	0-6	108.0
15	A	11.96	0-6	15.09	0-6	27.05
15	B	17.02	0-6	21.67	0-6	38.69
15	C	17.24	0-6	19.17	0-6	36.41
30	A	10.08	0-6	12.70	0-6	22.78
30	B	7.679	0-6	8.504	0-6	16.18
30	C	5.789	0-6	6.457	0-6	12.25
65	A	3.182	0-6	0.8413	0-3	4.023
65	B	<i>0.8950</i>	0-3	<i>0.8950</i>	0-3	1.790
65	C	<i>0.7931</i>	0-3	2.613	0-6	3.406
93	A	<i>1.000</i>	0-3	0.0000	-	1.000
93	B	0.0000	-	0.0000	-	0.0000
93	C	0.0000	-	<i>0.9362</i>	0-3	0.9362

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

Table 8.1.2.2.1/5-27: Data values used to quantify dissipation of cinmethylin (sum of (-) and (+) enantiomers), and the two enantiomers in soil at the North Dakota field site. Values are expressed in g/ha.

Actual Days After Application	Replicate	(-)-enantiomer		(+) -enantiomer		Sum cinmethylin (g/ha) ^{a,b}
		Residue (g/ha) ^{a,b}	Residue depth (inches) ^c	Residue (g/ha) ^{a,b}	Residue depth (inches)	
0	A	258.8	0-6	282.4	0-6	541.2
0	A (duplicate)	233.9	0-3	246.5	0-3	480.4
0	B	217.7	0-6	221.9	0-6	439.6
0	B (duplicate)	328.3	0-3	330.3	0-3	658.6
0	C	231.7	0-6	249.3	0-6	481.0
0	C (duplicate)	231.5	0-3	235.5	0-3	467.0
3	A	162.2	0-6	169.7	0-6	331.9
3	B	224.4	0-6	232.8	0-6	457.2
3	C	180.4	0-12	190.7	0-12	371.1
7	A	188.3	0-6	196.3	0-6	384.6
7	B	229.9	0-6	241.0	0-6	470.9
7	C	161.3	0-12	167.2	0-12	328.5
15	A	112.3	0-6	116.0	0-6	228.3
15	B	74.17	0-6	75.90	0-6	150.1
15	C	99.22	0-6	103.1	0-6	202.3
34	A	71.23	0-6	87.15	0-18	158.4
34	B	82.96	0-6	94.05	0-6	177.0
34	C	110.9	0-6	124.2	0-6	235.1
63	A	51.95	0-6	58.19	0-6	110.1
63	B	95.62	0-6	111.8	0-6	207.4
63	C	54.73	0-6	63.99	0-6	118.7
192	A	18.26	0-6	19.92	0-6	38.18
192	B	32.25	0-6	38.22	0-6	70.47
192	C	24.54	0-6	35.48	0-6	60.02
269	A	6.940	0-6	10.04	0-6	16.98
269	B	10.23	0-6	13.67	0-6	23.9
269	C	9.157	0-6	12.96	0-6	22.12
357	A	<i>0.6492</i>	0-3	2.798	0-6	3.447
357	B	3.659	0-6	4.744	0-6	8.403
357	C	<i>0.6701</i>	0-3	3.022	0-6	3.692

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

Table 8.1.2.2.1/5-28: Data values used to quantify dissipation of cinmethylin (sum of (-) and (+) enantiomers), and the two enantiomers in soil at the Texas field site. Values are expressed in g/ha.

Actual Days After Application	Replicate	(-)-enantiomer		(+) -enantiomer		Sum cinmethylin (g/ha) ^{a,b}
		Residue (g/ha) ^{a,b}	Residue depth (inches) ^c	Residue (g/ha) ^{a,b}	Residue depth (inches)	
0	A	112.0	0-6	116.5	0-6	228.5
0	A (duplicate)	107.6	0-3	110.4	0-3	218.0
0	B	130.6	0-6	139.3	0-6	269.9
0	B (duplicate)	224.5	0-3	239.6	0-3	464.1
0	C	98.86	0-6	107.7	0-6	206.6
0	C (duplicate)	68.78	0-3	70.52	0-3	139.3
3	A	95.55	0-12	104.0	0-12	199.6
3	B	103.8	0-6	110.8	0-6	214.6
3	C	133.0	0-6	137.5	0-12	270.5
7	A	144.6	0-6	157.6	0-12	302.2
7	B	164.7	0-6	178.1	0-6	342.8
7	C	120.5	0-6	132.8	0-12	253.3
12	A	95.08	0-6	107.4	0-6	202.5
12	B	87.18	0-6	91.62	0-6	178.8
12	C	89.03	0-6	97.14	0-6	186.2
28	A	46.33	0-6	56.14	0-12	102.5
28	B	80.81	0-6	94.02	0-6	174.8
28	C	63.47	0-6	73.48	0-6	137.0
61	A	47.64	0-6	65.69	0-12	113.3
61	B	51.92	0-6	63.00	0-6	114.9
61	C	71.37	0-6	85.72	0-6	157.1
90	A	45.28	0-6	58.31	0-6	103.6
90	B	51.83	0-6	68.13	0-6	120.0
90	C	34.12	0-6	45.04	0-6	79.16
192	A	7.301	0-6	19.48	0-6	26.78
192	B	<i>0.6814</i>	0-3	4.953	0-6	5.634
192	C	<i>0.7089</i>	0-3	3.553	0-6	4.262
262	A	<i>0.6315</i>	0-3	3.164	0-6	3.796
262	B	0.0000	-	<i>0.5607</i>	0-3	0.5607
262	C	0.0000	-	4.789	0-6	4.789

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

Table 8.1.2.2.1/5-29: Data values used to quantify dissipation of cinmethylin (sum of (-) and (+) enantiomers), and the two enantiomers in soil at the Washington field site. Values are expressed in g/ha.

Actual Days After Application	Replicate	(-)-enantiomer		(+) -enantiomer		Sum cinmethylin (g/ha) ^{a,b}
		Residue (g/ha) ^{a,b}	Residue depth (inches) ^c	Residue (g/ha) ^{a,b}	Residue depth (inches)	
0	A	166.0	0-6	169.6	0-6	335.6
0	A (duplicate)	185.8	0-3	190.0	0-3	375.8
0	B	195.2	0-6	203.6	0-6	398.8
0	B (duplicate)	189.3	0-3	191.9	0-3	381.2
0	C	157.5	0-6	157.0	0-6	314.5
0	C (duplicate)	183.5	0-3	182.4	0-3	365.9
3	A	105.7	0-6	108.4	0-6	214.1
3	B	62.23	0-6	62.87	0-6	125.1
3	C	63.33	0-6	63.46	0-6	126.8
7	A	60.01	0-6	68.62	0-6	128.6
7	B	59.53	0-6	67.38	0-6	126.9
7	C	34.93	0-6	44.33	0-6	79.26
15	A	20.97	0-6	25.83	0-6	46.80
15	B	20.31	0-6	25.14	0-6	45.45
15	C	8.621	0-6	9.494	0-6	18.12
30	A	9.863	0-6	12.50	0-6	22.36
30	B	7.196	0-6	8.890	0-6	16.09
30	C	10.05	0-6	14.27	0-6	24.32
63	A	10.81	0-6	13.52	0-6	24.33
63	B	<i>0.7983</i>	0-3	<i>0.7983</i>	0-3	1.5966
63	C	5.878	0-6	6.666	0-6	12.54
100	A	7.169	0-6	9.488	0-6	16.66
100	B	0.0000	-	0.0000	-	0.0000
100	C	7.397	0-6	10.60	0-6	18.00
181	A	<i>0.6715</i>	0-3	<i>0.6715</i>	0-3	1.343
181	B	0.0000	-	0.0000	-	0.0000
181	C	<i>0.7141</i>	0-3	<i>0.7141</i>	0-3	1.428

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

Table 8.1.2.2.1/5-30: Data values used to quantify dissipation of cinmethylin (sum of (-) and (+) enantiomers), and the two enantiomers in soil at the California field site. Values are expressed in g/ha.

Actual Days After Application	Replicate	(-)-enantiomer		(+) -enantiomer		cinmethylin (g/ha) ^{a,b}
		Residue (g/ha) ^{a,b}	Residue depth (inches) ^c	Residue (g/ha) ^{a,b}	Residue depth (inches)	
0	A	27.51	0-6	36.31	0-6	63.82
0	A (duplicate)	33.84	0-3	50.78	0-3	84.62
0	B	113.3	0-6	108.6	0-6	221.9
0	B (duplicate)	91.77	0-3	102.6	0-3	194.4
0	C	60.37	0-6	68.24	0-6	128.6
0	C (duplicate)	122.6	0-3	122.3	0-3	244.9
3	A	95.53	0-12	100.8	0-12	196.3
3	B	60.59	0-12	66.15	0-12	126.7
3	C	94.64	0-6	102.3	0-6	196.9
7	A	62.44	0-6	72.05	0-6	134.5
7	B	84.62	0-6	86.44	0-6	171.1
7	C	71.74	0-6	79.96	0-6	151.7
15	A	42.66	0-6	47.98	0-6	90.64
15	B	22.57	0-6	24.98	0-6	47.55
15	C	22.63	0-6	21.96	0-6	44.59
30	A	8.461	0-6	20.01	0-6	28.47
30	B	4.056	0-6	12.57	0-6	16.63
30	C	<i>1.186</i>	0-3	<i>1.186</i>	0-3	2.372
63	A	<i>1.555</i>	0-3	<i>1.555</i>	0-3	3.110
63	B	<i>1.576</i>	0-3	<i>1.576</i>	0-3	3.152
63	C	0.0000	-	0.0000	-	0.0000

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

The HSE evaluator assessed the supplied kinetic evaluation and accepted the methods and decisions made by the Applicant for all field sites except North Carolina. The results for New York, North Dakota, Texas, Washington and California that are presented below are derived from the kinetic evaluation supplied by the Applicant. The results for North Carolina are derived from the HSE evaluator's own kinetic evaluation.

Visual assessment of goodness of fit was an important step in the kinetic evaluation process. The model fit and residuals for each soil and each test substance are displayed below and are grouped by substance. These are followed by the model fit parameters for each soil and tables summarising the derived endpoints.

Dissipation of cinmethylin (sum)

Figures KCA 7.1.2.2.1/5-01-06 show the model fits and residuals for cinmethylin in each soil. Model evaluation and parameters are summarised per soil in Table 8.1.2.2.1/5-31.

New York

Based on visual assessment and consideration of Chi^2 error, FOMC offered a better fit and lower error than SFO for the New York site, therefore DFOP was explored and found to be the best model fit (Figure 8.1.2.2.1/5-01). The HSE evaluator agrees with this decision.

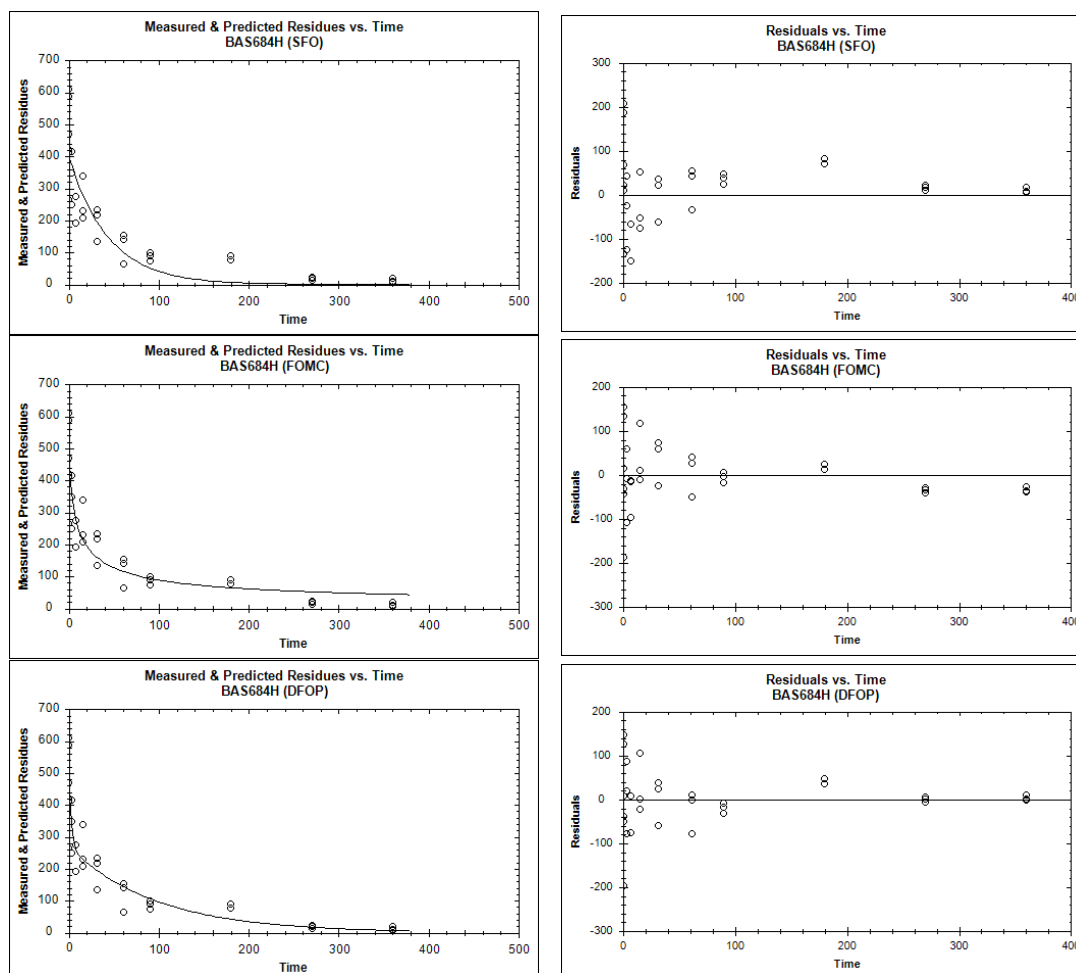


Figure 8.1.2.2.1/5-01: Model fits and residuals for cinmethylin in New York soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: DFOP. DisT_{50} = 14.9 days; DisT_{90} = 170.9 days. Chi^2 error = 9.4%.

North Carolina

For North Carolina, the Applicant assessed SFO and FOMC and concluded that SFO was most appropriate as it was the simplest model of the two. The HSE evaluator disagreed with this as the process had not explored all model fit options to determine the best fit. The HSE evaluator compared SFO and FOMC fits and concluded that FOMC offered a better visual fit and χ^2 error rate, so DFOP was explored and found to be the best model fit. The k_2 value initially failed the t test ($P = 0.32$) and was therefore not significantly > 0 ; the k_2 value was then fixed assuming a worst-case DT_{50} of 1000 days. This increased the χ^2 error value from 3.08% to 4.72%; therefore, FOMC was the most appropriate model for trigger endpoints (Figure 8.1.2.2.1/5-02).

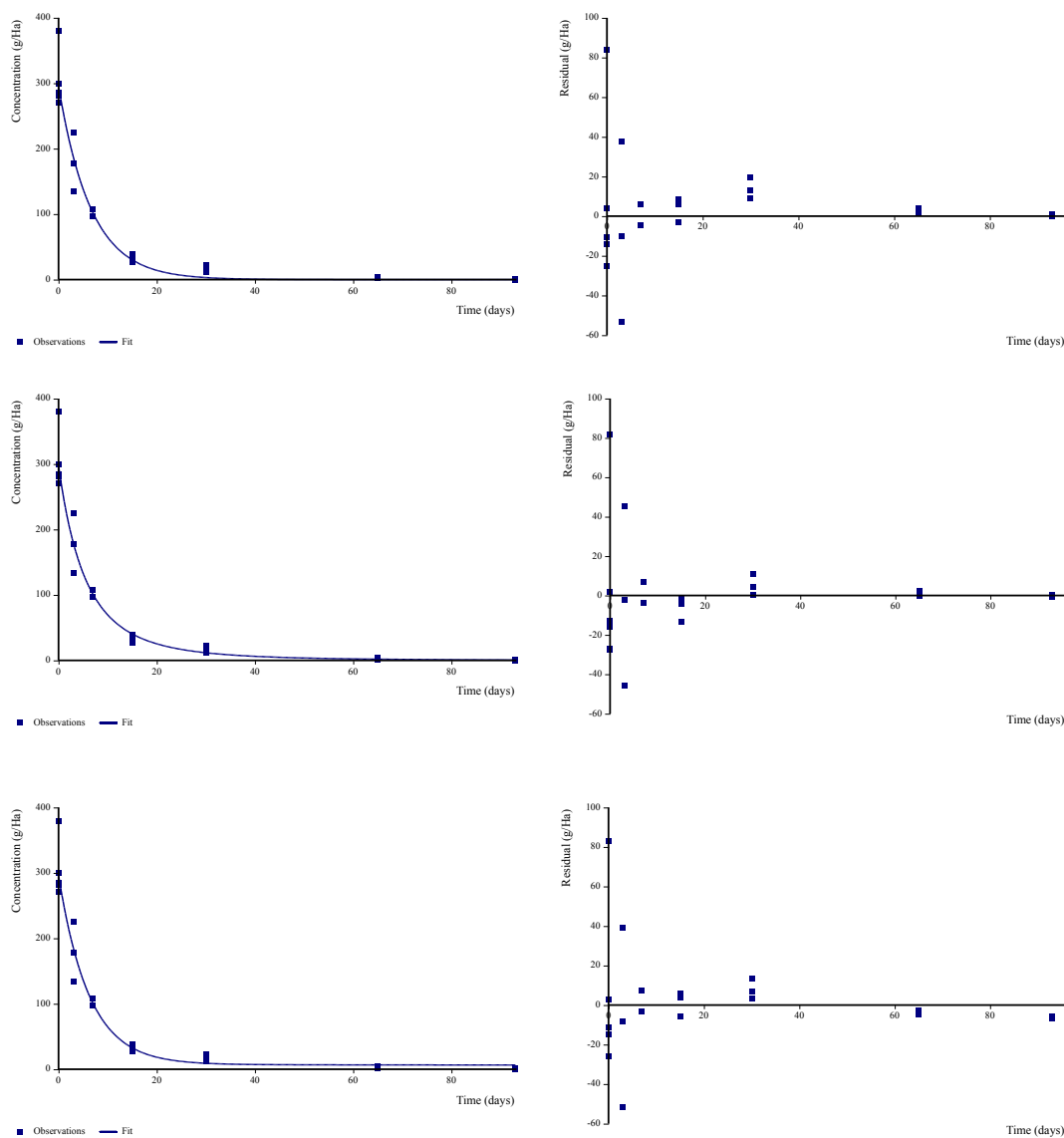


Figure 8.1.2.2.1/5-02: Model fits and residuals for cinmethylin in North Carolina soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: FOMC. $DisT_{50} = 4.2$ days; $DisT_{90} = 18.2$ days. χ^2 error = 3.3%.

North Dakota

For the North Dakota field site, the Applicant concluded that FOMC offered a better χ^2 error and visual fit than SFO. DFOP was explored and found to be the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-03). The HSE evaluator agrees with this decision.

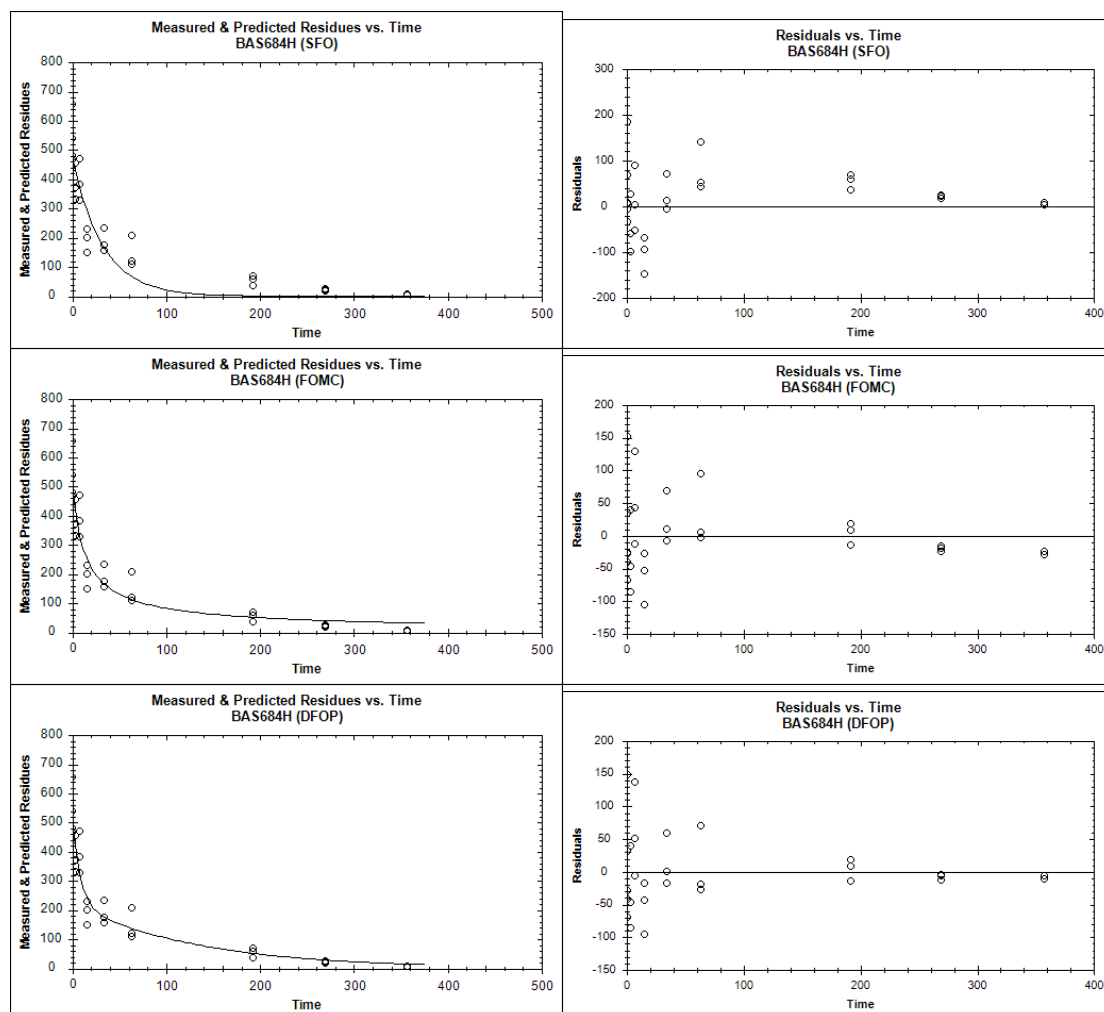


Figure 8.1.2.2.1/5-03: Model fits and residuals for cinmethylin in North Dakota soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: DFOP. DisT_{50} = 13.7 days; DisT_{90} = 193.6 days. χ^2 error = 12.5%.

Texas

For the Texas field site, the Applicant concluded that SFO offered a better χ^2 error and visual fit than FOMC. The Applicant concluded that SFO offered the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-04). The HSE evaluator agrees with this decision.

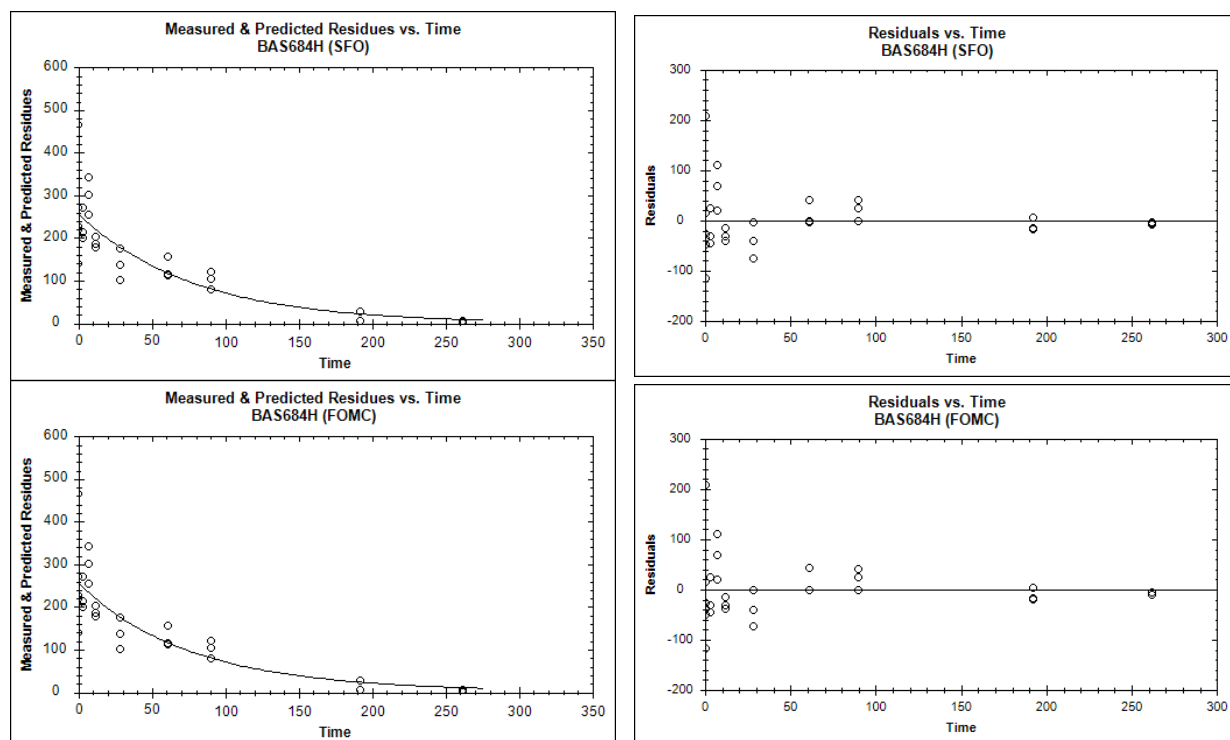


Figure 8.1.2.2.1/5-04: Model fits and residuals for cinmethylin in Texas soil. Top row: SFO. Bottom row: FOMC. Final fit: SFO. DisT_{50} = 53.9 days; DisT_{90} = 179.2 days. χ^2 error = 15.7%.

Washington

For the Washington field site, the Applicant compared SFO and FOMC fits and concluded that FOMC offered a better χ^2 error and visual fit. The Applicant then investigated DFOP and concluded that FOMC offered the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-05). The HSE evaluator agrees with this decision.

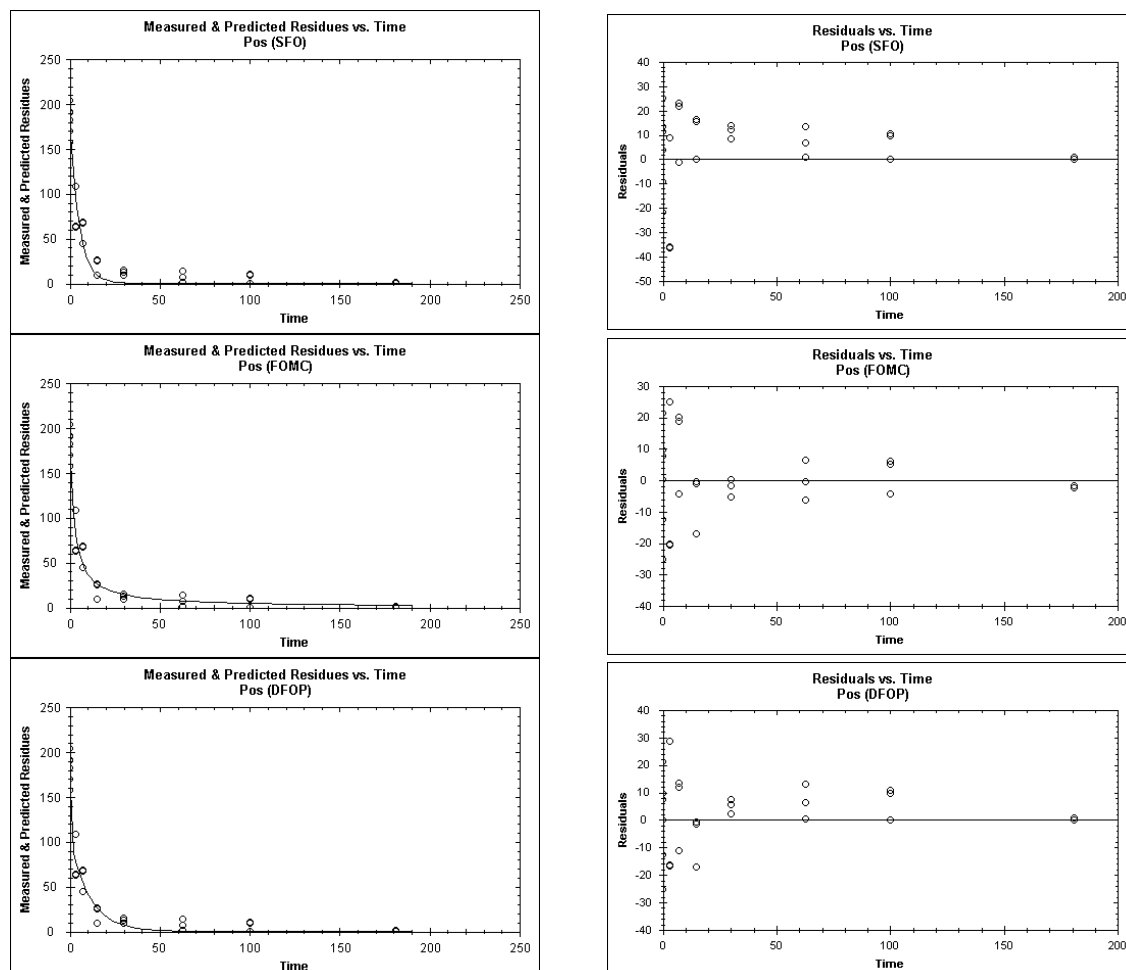


Figure 8.1.2.2.1/5-05: Model fits and residuals for cinmethylin in Washington soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: FOMC. DisT_{50} = 2.5 days; DisT_{90} = 20.5 days. χ^2 error = 8.4%.

California

For the California field site, the Applicant compared SFO and FOMC fits and concluded that FOMC offered no improvement to Chi^2 error and visual fit. The Applicant concluded SFO was the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-06). The HSE evaluator noted that 0 DALA residue values from the A subplot were inexplicably low compared to the other replicates and checked the kinetic evaluations without the A subplot 0 DALA values. Endpoints reduced slightly, but the HSE evaluator could not identify a reason to consider these values outliers. As such, the HSE evaluator agrees with the Applicant's kinetic evaluation and trigger endpoints as they offer conservative dissipation rates.

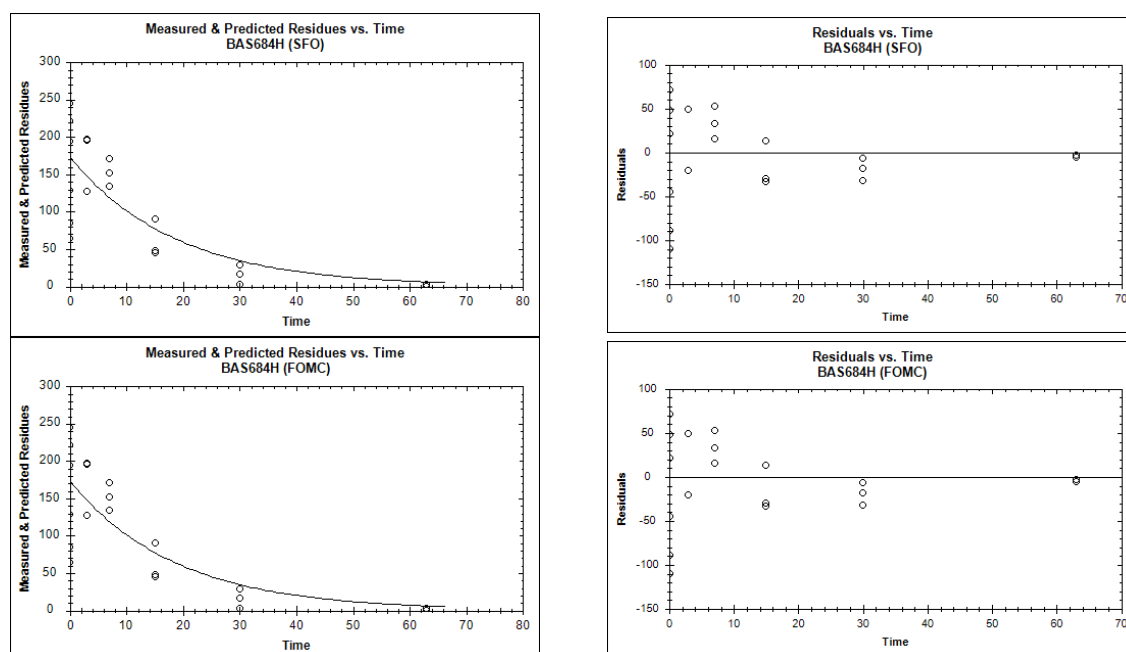


Figure 8.1.2.2.1/5-06: Model fits and residuals for cinmethylin in California soil. Top row: SFO. Bottom row: FOMC. Final fit: SFO. DisT_{50} = 12.9 days; DisT_{90} = 42.7 days. Chi^2 error = 18.1%.

Table 8.1.2.2.1/5-31: Summary of kinetic model evaluation of field dissipation of cinmethylin (sum of enantiomers) in six US soils.

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
New York	SFO	30.3	100.6	Fair	20.8	400.4	k = 0.0229	< 0.0001	0.01319	0.033
	FOMC	13.8	342.6	Fair	12.8	453.7	$\alpha = 0.5577$ $\beta = 5.606$	N/A	0.2233 -2.277	0.892 13.490
	DFOP	14.9	170.9	Good	9.43	461.7	k ₁ = 0.3419 k ₂ = 0.0103 g = 0.4203	0.0773 0.0026 0.0001	-0.1366 0.0033 0.2149	0.8200 0.0170 0.6260
Applicant's proposal: FOMC better fit than SFO, therefore explore DFOP. DFOP better fit overall – use DFOP for trigger endpoint. HSE evaluator agrees.										
North Carolina	SFO	4.6	15.1	Good	5.78	295.8	k = 0.1521	< 0.0001	0.1199	0.1840
	FOMC	4.2	18.2	Good	3.27	297.8	$\alpha = 3.345$ $\beta = 18.37$	N/A	-2.992 -23.17	9.682 59.92
	DFOP (fixed k ₂)	4.46	15.8	Good	4.72	297.4	k ₁ = 0.1872 k ₂ = 0.000693 g = 0.8725	< 0.0001 (fixed)	0.1189 (fixed) 0.9157	0.2030 (fixed) 1.0370
Applicant's proposal: FOMC offered improved Chi² error and visual fit, but error was < 6% for both models – use the simpler model, SFO, for trigger endpoints. HSE evaluator disagrees; the kinetic assessment shown above is the evaluator's own. The HSE evaluator accepts that FOMC offers improved error and visual fit, and as a result investigated the DFOP fit. Initially the DFOP fit was best overall; however, k₂ value failed the t test so this value was fixed assuming the worst-case scenario of a DT₅₀ of 1000 days. Following fixing of the k₂ value the visual fit for FOMC became the best overall. Conclusion: use FOMC for trigger endpoint.										

Table 8.1.2.2.1/5-31 continued

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
North Dakota	SFO	22.4	74.3	Poor	19.8	473.7	k = 0.031	< 0.0001	0.0201	0.0420
	FOMC	15.2	197.3	Fair	13.6	507.3	$\alpha = 0.7683$ $\beta = 10.37$	N/A	0.3036 -1.602	1.233 22.340
	DFOP	13.7	193.6	Good	12.5	509.6	k ₁ = 0.1207 k ₂ = 0.0076 g = 0.5643	0.0082 0.0104 < 0.0001	0.0240 0.0013 0.3444	0.217 0.014 0.784
Applicant's proposal: SFO better fit than FOMC, therefore explored DFOP. DFOP best overall fit with lower Chi² error and better predicted values – use DFOP for trigger endpoint. HSE evaluator agrees.										
Texas	SFO	53.9	179.2	Good	15.7	255.2	k = 0.0129	0.0001	0.00066	0.0190
	FOMC	52.9	184.4	Good	16.6	256.0	$\alpha = 16.72$ $\beta = 1249$	N/A	-342.0 -2.181E+4	375.4 2.90E+4
Applicant's proposal: SFO and FOMC provided similar visual fits, with similar Chi² errors. SFO had the slightly lower error – use SFO for trigger endpoint. The HSE evaluator notes that one 0 DALA replicate was markedly higher than the others at 464 g/ha and conducted a kinetic assessment with this value excluded. Chi² errors increased and the DT₅₀ was extended to 61 days; however, the HSE evaluator could not identify a reason for the result to be considered an outlier and so did not exclude the value. The HSE evaluator concluded that the Applicant's original model fits sufficiently represented the field dissipation and has accepted their decisions. Conclusion: HSE evaluator agrees.										

Table 8.1.2.2.1/5-31 continued

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
Washington	SFO	3.4	11.2	Poor	18.1	355.6	k = 0.2048	< 0.0001	0.1607	0.2490
	FOMC	2.5	20.5	Good	8.35	361.6	$\alpha = 1.084$ $\beta = 2.786$	N/A	0.4543 -0.0456	1.714 5.617
	DFOP	1.6	17.7	Fair	8.55	362.0	k ₁ = 2125 k ₂ = 0.1002 g = 0.4136	0.5 < 0.0001 < 0.0001	-996.5 0.053 0.2466	1010 0.147 0.581
Applicant's proposal: FOMC better visual fit than SFO and DFOP throughout the whole sampling period and offers best Chi ² error – use FOMC for trigger endpoint. HSE Evaluator agrees.										
California	SFO	12.9	42.7	Fair	18.1	173.3	k = 0.0539	0.0025	0.0185	0.0890
	FOMC	12.9	42.7	Fair	19.9	173.3	$\alpha = 11150$ $\beta = 2.068E+5$	N/A	-1950 -3.6E+4	2710 5.0E+4
Applicant's proposal: SFO and FOMC similarly predicted observed data throughout. SFO offered slightly smaller Chi ² error. FOMC did not improve statistical or visual results – use SFO for trigger endpoints. HSE evaluator noted that 0 DALA samples from subplot A were markedly lower than those observed in the other two subplots and conducted a kinetic assessment with these values excluded to investigate whether fit improved. Dissipation times were shortened slightly, but the HSE evaluator could not identify a reason for the results to be considered outliers and so did not exclude these data. Therefore, the HSE evaluator agrees with the Applicant's kinetic evaluation and endpoints as they offer a conservative dissipation rate.										

Dissipation of (-)-enantiomer

Figures 8.1.2.2.1/5-07-12 show the model fits and residuals for cinmethylin (-)-enantiomer in each soil. Model evaluation and parameters are summarised per soil in Table 8.1.2.2.1/5-32. All decisions were consistent with those reported for the overall cinmethylin assessment.

New York

For the New York site, FOMC offered a better visual fit and lower χ^2 error than SFO for the New York site, therefore DFOP was explored and found to be the best model fit (Figure 8.1.2.2.1/5-07). The HSE evaluator notes that the k_1 value fails the t-test ($P = 0.0911$); however, this is likely due to rapid dissipation of the enantiomer. The HSE evaluator therefore agrees with this decision.

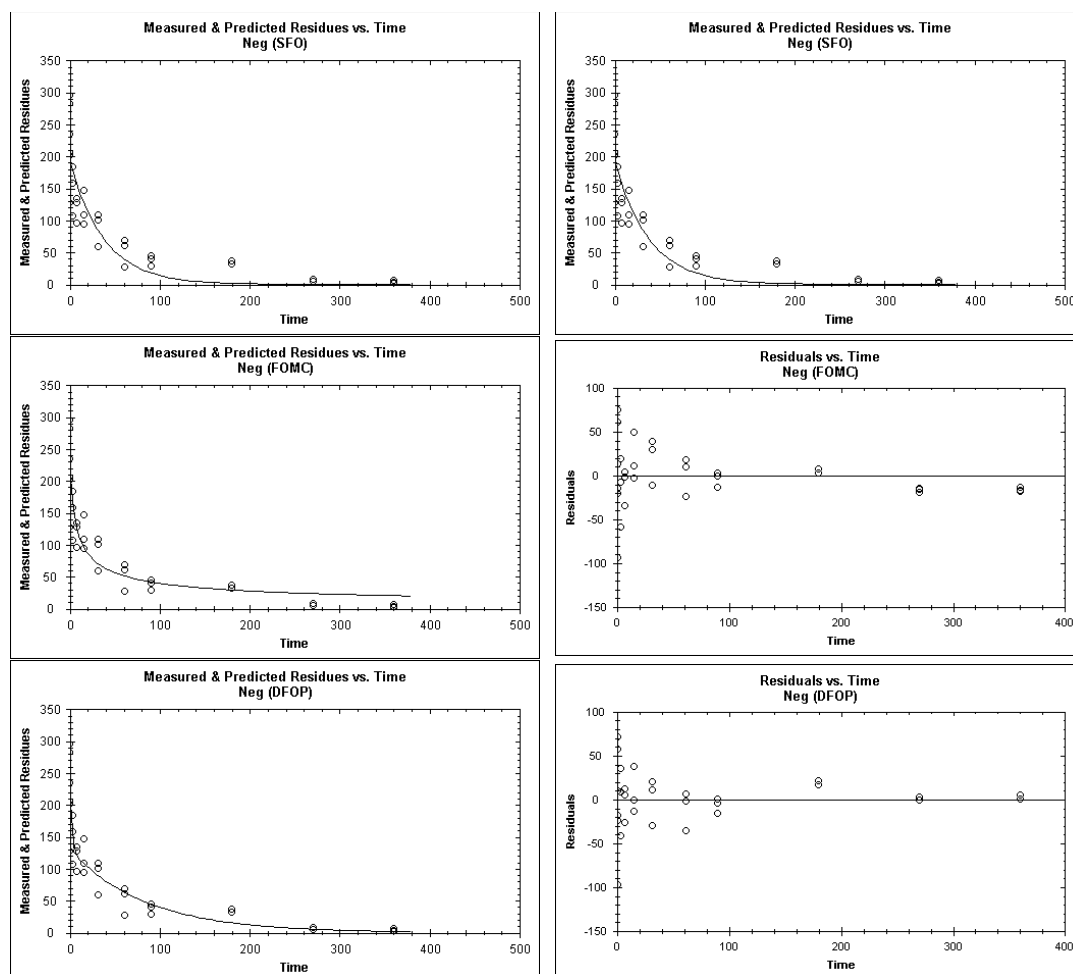


Figure 8.1.2.2.1/5-07: Model fits and residuals for cinmethylin (-)-enantiomer in New York soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: DFOP. $\text{DisT}_{50} = 12.2$ days; $\text{DisT}_{90} = 147.1$ days. χ^2 error = 8.0%.

North Carolina

For North Carolina, the Applicant assessed SFO and FOMC and concluded that visual fits were similar and Chi^2 errors were both below 6%. The Applicant concluded that SFO was most appropriate as it was the simplest model of the two. The HSE evaluator disagreed with this as the process had not explored all model fit options to determine the best fit. The HSE evaluator compared SFO and FOMC fits and concluded that FOMC offered a better visual fit and Chi^2 error rate, so DFOP was explored and found to be the best model fit. The k_2 value initially failed the t test ($P = 0.33$) and was therefore not significantly > 0 ; the k_2 value was then fixed assuming a worst-case DT_{50} of 1000 days. This increased the Chi^2 error value from 3.08% to 4.72%; therefore, FOMC was the most appropriate model for trigger endpoints (Figure 8.1.2.2.1/5-08).

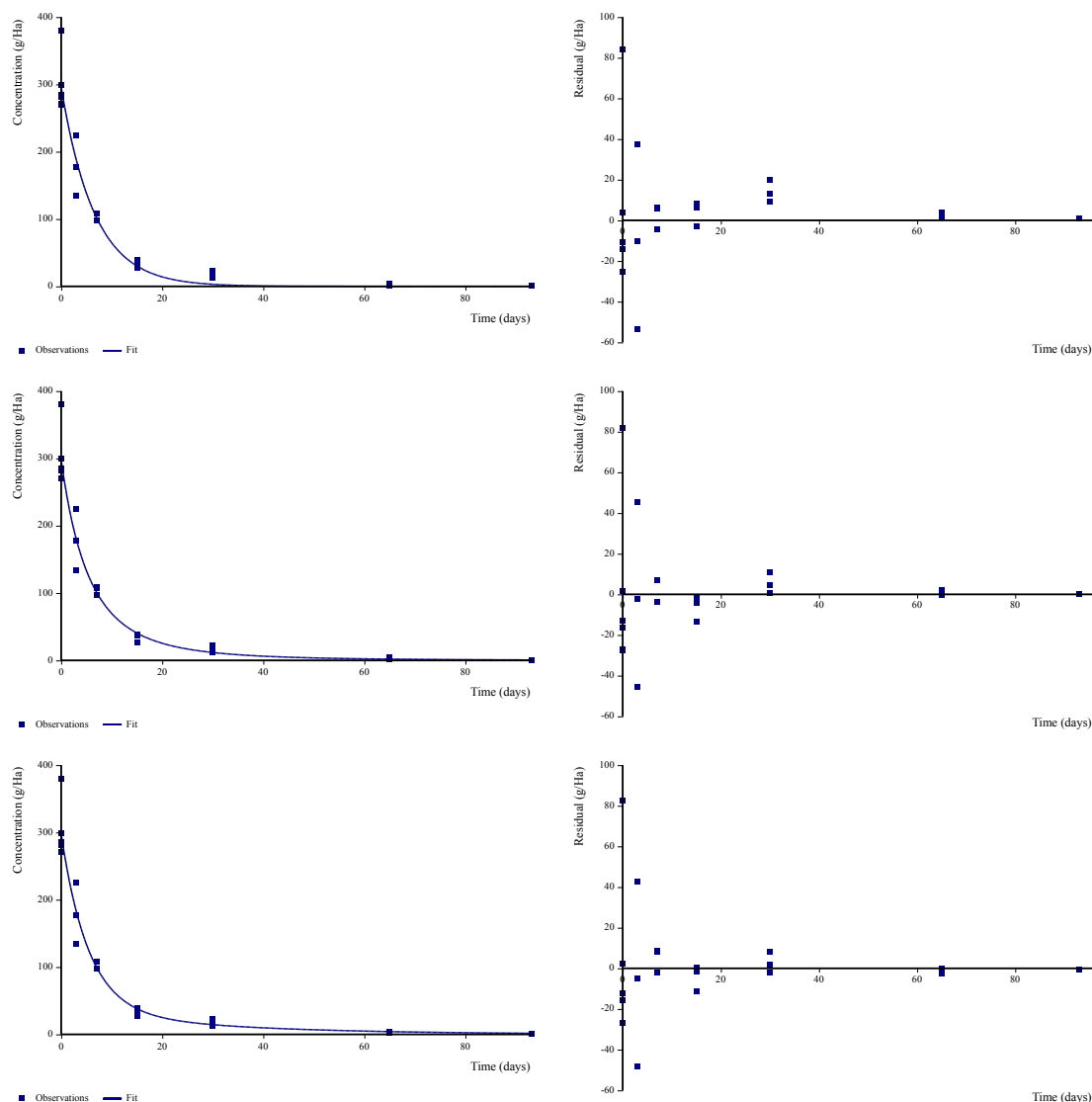


Figure 8.1.2.2.1/5-08: Model fits and residuals for cinmethylin (-)-enantiomer in North Carolina soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: FOMC. $\text{DisT}_{50} = 4.2$ days; $\text{DisT}_{90} = 18.2$ days. Chi^2 error = 3.3%.

North Dakota

For the North Dakota field site, the Applicant concluded that FOMC offered a better χ^2 error and visual fit than SFO. DFOP was explored and found to be the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-09). The HSE evaluator agrees with this decision.

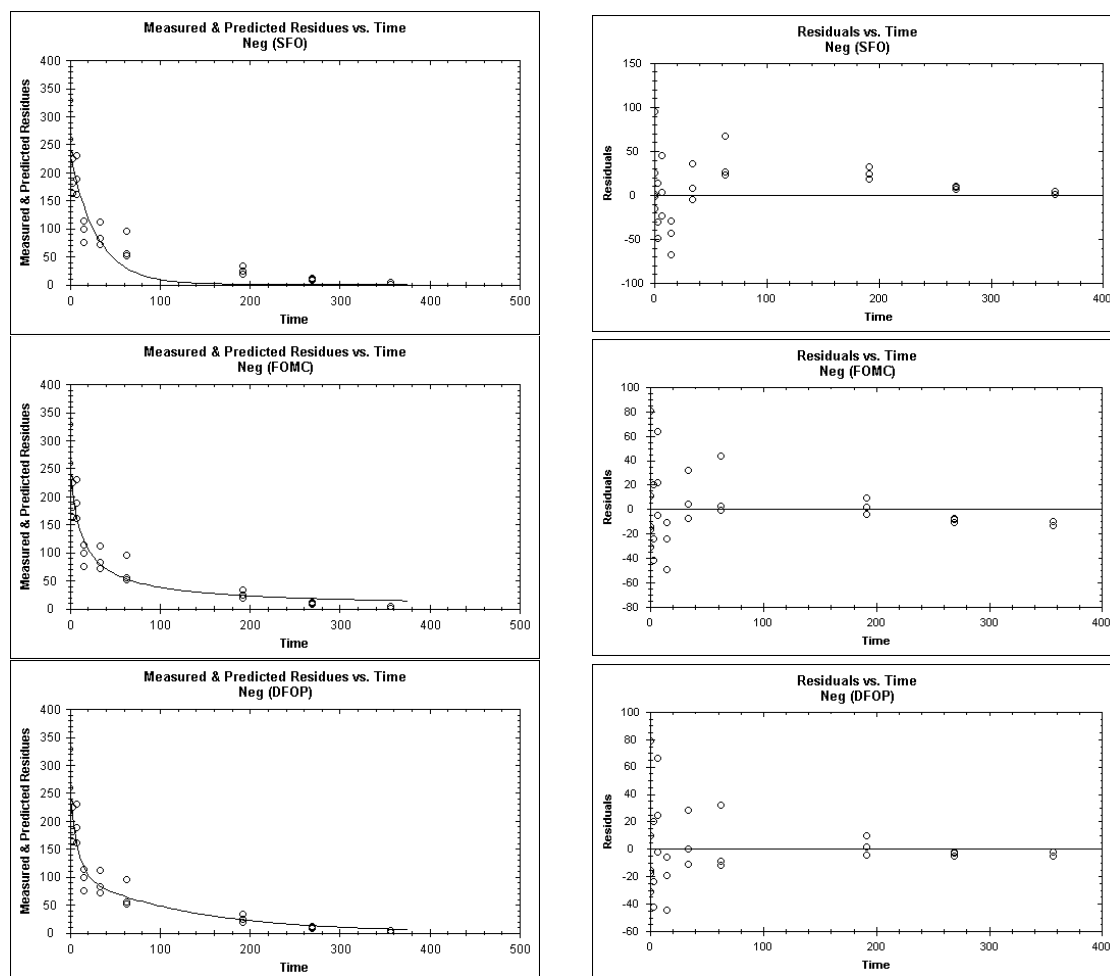


Figure 8.1.2.2.1/5-09: Model fits and residuals for cinmethylin (-)-enantiomer in North Dakota soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: DFOP. DisT_{50} = 13.5 days; DisT_{90} = 181.3 days. χ^2 error = 12.3%.

Texas

For the Texas field site, the Applicant concluded that SFO offered a better χ^2 error and visual fit than FOMC. The Applicant concluded that SFO offered the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-10). The HSE evaluator agrees with this decision.

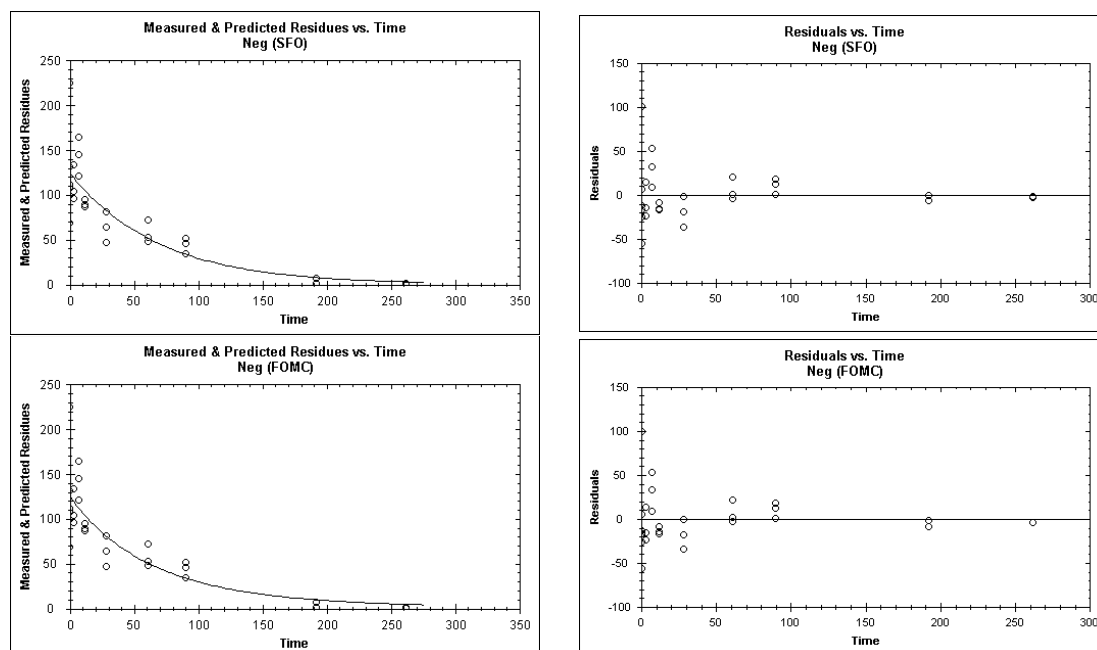


Figure 8.1.2.2.1/5-10: Model fits and residuals for cinmethylin (-)-enantiomer in Texas soil. Top row: SFO. Bottom row: FOMC. Final fit: SFO. DisT₅₀ = 47.7 days; DisT₉₀ = 158.5 days. χ^2 error = 15.8%.

Washington

For the Washington field site, the Applicant compared SFO and FOMC fits and concluded that FOMC offered a better χ^2 error and visual fit. The Applicant then investigated DFOP and concluded that FOMC continued to offer the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-11). The HSE evaluator agrees with this decision.

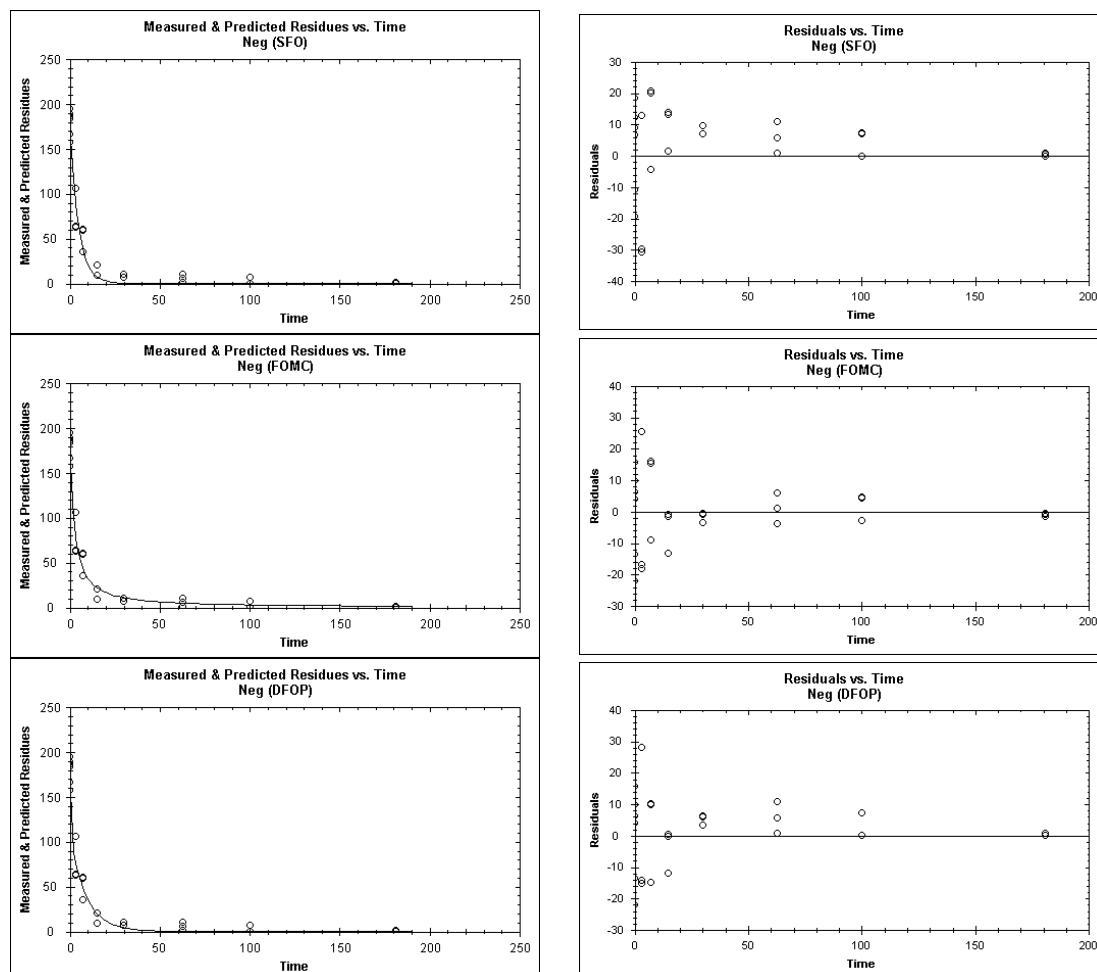


Figure 8.1.2.2.1/5-11: Model fits and residuals for cinmethylin (-)-enantiomer in Washington soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: FOMC. DisT₅₀ = 2.5 days; DisT₉₀ = 18.4 days. χ^2 error = 7.1%.

California

For the California field site, the Applicant compared SFO and FOMC fits and concluded that FOMC offered no improvement to Chi^2 error and visual fit. The Applicant concluded SFO was the best model fit for persistence endpoints (Figure 8.1.2.2.1/5-12). The HSE evaluator noted that 0 DALA residue values from the A subplot were markedly low compared to the other replicates and checked the kinetic evaluations without the A subplot 0 DALA values. Endpoints reduced slightly, but the HSE evaluator could not identify a reason to consider these values as outliers. As such, the HSE evaluator agrees with the Applicant's kinetic evaluation and trigger endpoints as they offer conservative dissipation rates.

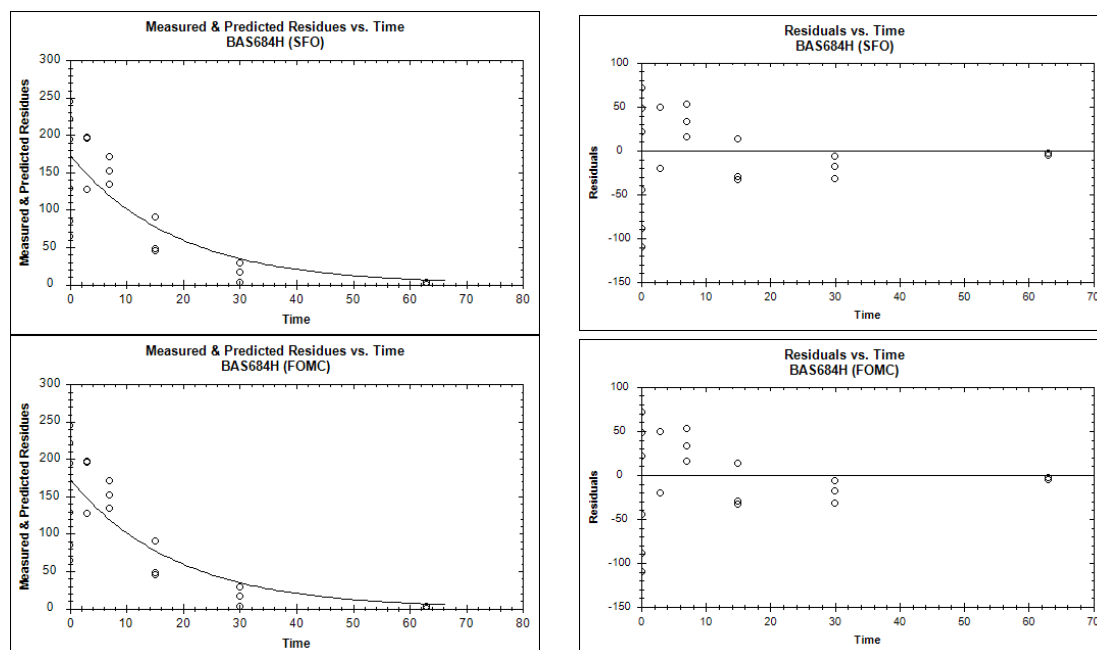


Figure 8.1.2.2.1/5-12: Model fits and residuals for cinmethylin (-)-enantiomer in California soil. Top row: SFO. Bottom row: FOMC. Final fit: SFO. DisT_{50} = 12.5 days; DisT_{90} = 41.4 days. Chi^2 error = 19.2%.

Table 8.1.2.2.1/5-32: Summary of kinetic model evaluation of field dissipation of cinmethylin (-)-enantiomer in six US soils.

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
New York	SFO	26.2	86.9	Fair	22.2	193.1	k = 0.0265	< 0.0001	0.015	0.038
	FOMC	11.1	302.8	Fair	13.1	220.9	α = 0.5357 β = 4.174	-	0.2185 -1.606	0.816 9.388
	DFOP	12.2	147.1	Good	7.98	224.4	k ₁ = 0.4644 k ₂ = 0.0119 g = 0.4233	0.0911 0.0018	-0.245 0.004	1.173 0.02
Applicant's proposal: FOMC better fit than SFO, therefore explore DFOP. DFOP better fit overall – use DFOP for trigger endpoint. HSE evaluator notes that the k₁ value fails the t-test, but still agrees that DFOP is most appropriate.										
North Carolina	SFO	4.56	15.1	Good	5.78	295.8	k = 0.1521	< 0.0001	0.119	0.185
	FOMC	4.23	18.2	Good	3.27	297.8	α = 3.338 β = 18.33	-	-3.165 -24.31	9.842 60.97
	DFOP (fixed k ₂)	4.4	15.9	Good	4.69	296.5	k ₁ = 0.02127 k ₂ = 0.00096 g = 0.9738	< 0.0001 (fixed)	0.118 (fixed)	0.206 (fixed)
Applicant's proposal: FOMC offered improved Chi² error and visual fit, but error was < 6% for both models – use the simpler model, SFO, for trigger endpoints. HSE evaluator disagrees; the kinetic assessment shown above is the Evaluator's own. The HSE evaluator accepts that FOMC offers improved error and visual fit, and as a result investigated the DFOP fit. Initially the DFOP fit was best overall; however, k₂ value failed the t test (P = 0.33) so this value was fixed assuming the worst-case scenario of a DT₅₀ of 1000 days. Following fixing of the k₂ value, the visual fit for FOMC became the best overall. Conclusion: use FOMC for trigger endpoint.										

Table 8.1.2.2.1/5-32 continued

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
North Dakota	SFO	21.0	69.8	Poor	19.1	233.4	k = 0.033	< 0.0001	0.0217	0.044
	FOMC	14.8	173.1	Fair	14.8	173.1	$\alpha = 0.8218$ $\beta = 11.18$	-	0.3009 -1.901	1.343 24.270
	DFOP	13.5	181.3	Good	12.3	249.3	k ₁ = 0.1148 k ₂ = 0.0079 g = 0.5806	0.008 0.016	0.0228 7.4E-4	0.207 0.015
Applicant's proposal: SFO better fit than FOMC, therefore explored DFOP. DFOP best overall fit with lower Chi² error and better predicted values – use DFOP for trigger endpoint. HSE evaluator agrees.										
Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
Texas	SFO	47.7	158.5	Good	15.8	124.1	k = 0.0145	0.0001	0.0071	0.022
	FOMC	45.6	168.6	Good	16.7	125.0	$\alpha = 7.806$ $\beta = 491.5$	-	-29.39 -2027	38.77 2590
Applicant's proposal: SFO and FOMC provided similar visual fits, with similar Chi² errors. SFO had the slightly lower error – use SFO for trigger endpoint. The HSE evaluator notes that one 0 DALA replicate was markedly higher than the others at 464 g/ha and conducted a kinetic assessment with this value excluded. Chi² errors increased and the DT₅₀ was extended to 61 days; however, the HSE evaluator could not identify a reason for the result to be considered an outlier and so did not exclude the value. The HSE evaluator concluded that the Applicant's original model fits sufficiently represented the field dissipation and has accepted their decisions. Conclusion: HSE evaluator agrees.										

Table 8.1.2.2.1/5-32 continued

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
Washington	SFO	3.2	10.7	Poor	16.4	176.9	k = 0.2146	< 0.0001	0.1694	0.260
	FOMC	2.5	18.4	Good	7.09	179.4	$\alpha = 1.193$ $\beta = 3.113$	-	0.4264 -0.2175	1.92 6.286
	DFOP	1.7	16.2	Fair	7.58	179.6	k ₁ = 1740 k ₂ = 0.1111 g = 0.3976	< 0.0001 < 0.0001	-744.3 0.0579	753.9 0.1640
Applicant's proposal: FOMC better visual fit than SFO and DFOP throughout the whole sampling period and offers best Chi² error – use FOMC for trigger endpoint. HSE Evaluator agrees.										
California	SFO	12.5	41.4	Fair	19.2	83.39	k = 0.0556	0.0045	0.01403	0.0970
	FOMC	12.5	41.4	Fair	21.1	83.39	$\alpha = 18110$ $\beta = 3.257E+5$	-	5619 3.250E+5	30611.3 3.264E+5
Applicant's proposal: SFO and FOMC similarly predicted observed data throughout. SFO offered slightly smaller Chi² error. FOMC did not improve statistical or visual results – use SFO for trigger endpoints. HSE evaluator noted that 0 DALA samples from subplot A were markedly lower than those observed in the other two subplots and conducted a kinetic assessment with these values excluded to investigate whether fit improved. Dissipation times were shortened slightly, but the HSE evaluator could not identify a reason for the results to be considered outliers and so did not exclude these data. Therefore, the HSE evaluator agrees with the Applicant's kinetic evaluation and endpoints as they offer a conservative dissipation rate.										

Dissipation of (+)-enantiomer

Figures KCA 7.1.2.2.1/5-13-18 show the model fits and residuals for cinmethylin (+)-enantiomer in each soil. Model evaluation and parameters are summarised per soil in Table 8.1.2.2.1/5-33. The HSE evaluator notes that all decisions were consistent with those reported for the overall cinmethylin and (-)-enantiomer assessments.

New York

For the New York site, FOMC offered a better visual fit and lower Chi² error than SFO for the New York site, therefore DFOP was explored and found to be the best model fit (Figure 8.1.2.2.1/5-13). The HSE evaluator notes that the k1 value fails the t test, likely due to rapid dissipation of the enantiomer in the initial stages of the field study. However, the HSE evaluator still agrees that DFOP is the most appropriate model for trigger endpoints.

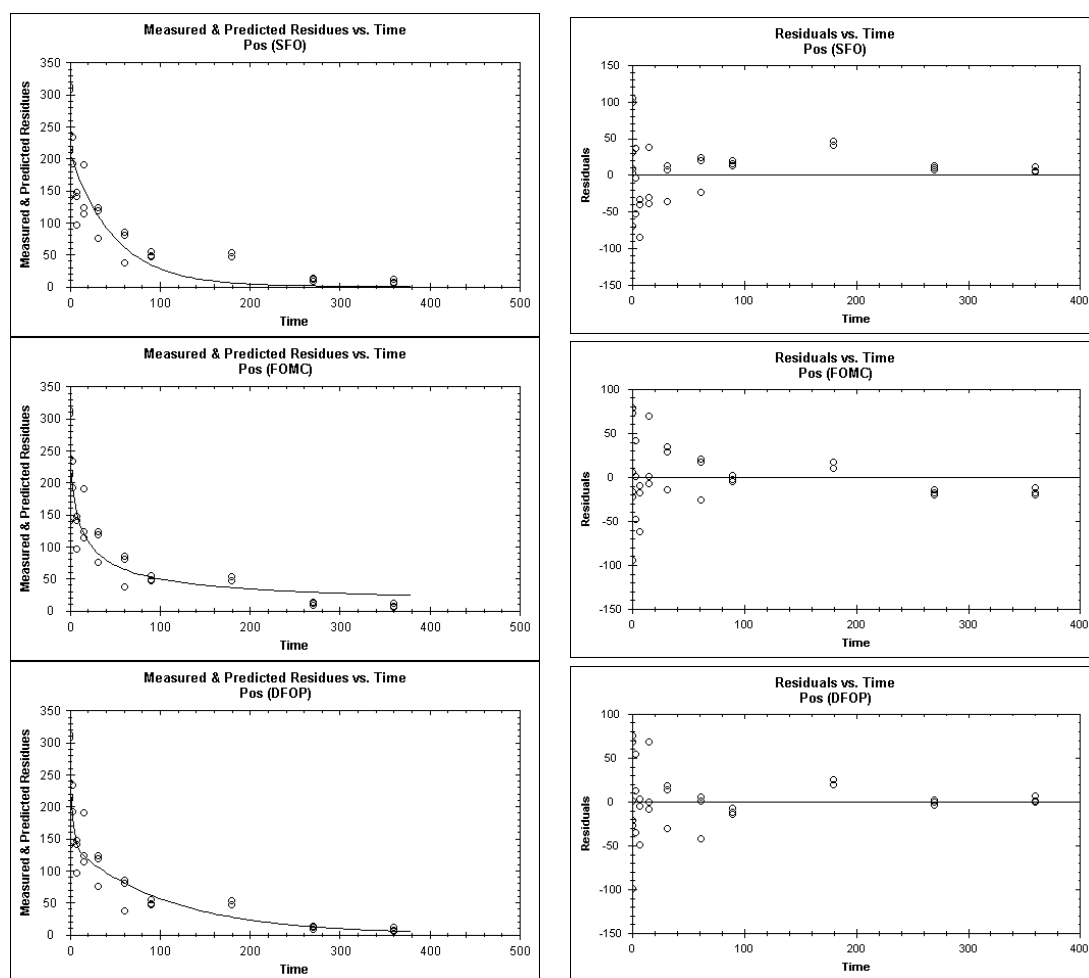


Figure 8.1.2.2.1/5-13: Model fits and residuals for cinmethylin (+)-enantiomer in New York soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: DFOP. DisT₅₀ = 17.8 days; DisT₉₀ = 193.4 days. Chi² error = 11.2%.

North Carolina

For North Carolina, the Applicant assessed SFO and FOMC and concluded that visual fits were similar and χ^2 errors were both below 5%. The Applicant concluded that SFO was most appropriate as it was the simplest model of the two. The HSE evaluator disagreed with this as the process had not explored all model fit options to determine the best fit. The HSE evaluator compared SFO and FOMC fits and concluded that FOMC offered a better visual fit and χ^2 error rate, so DFOP was explored and found to be the best model fit. The k_2 value initially failed the t test ($P = 0.34$) and was therefore not significantly > 0 ; the k_2 value was then fixed assuming a worst-case DT_{50} of 1000 days. This increased the χ^2 error value from 2.61% to 4.49%; therefore, FOMC was the most appropriate model for trigger endpoints (Figure 8.1.2.2.1/5-14).

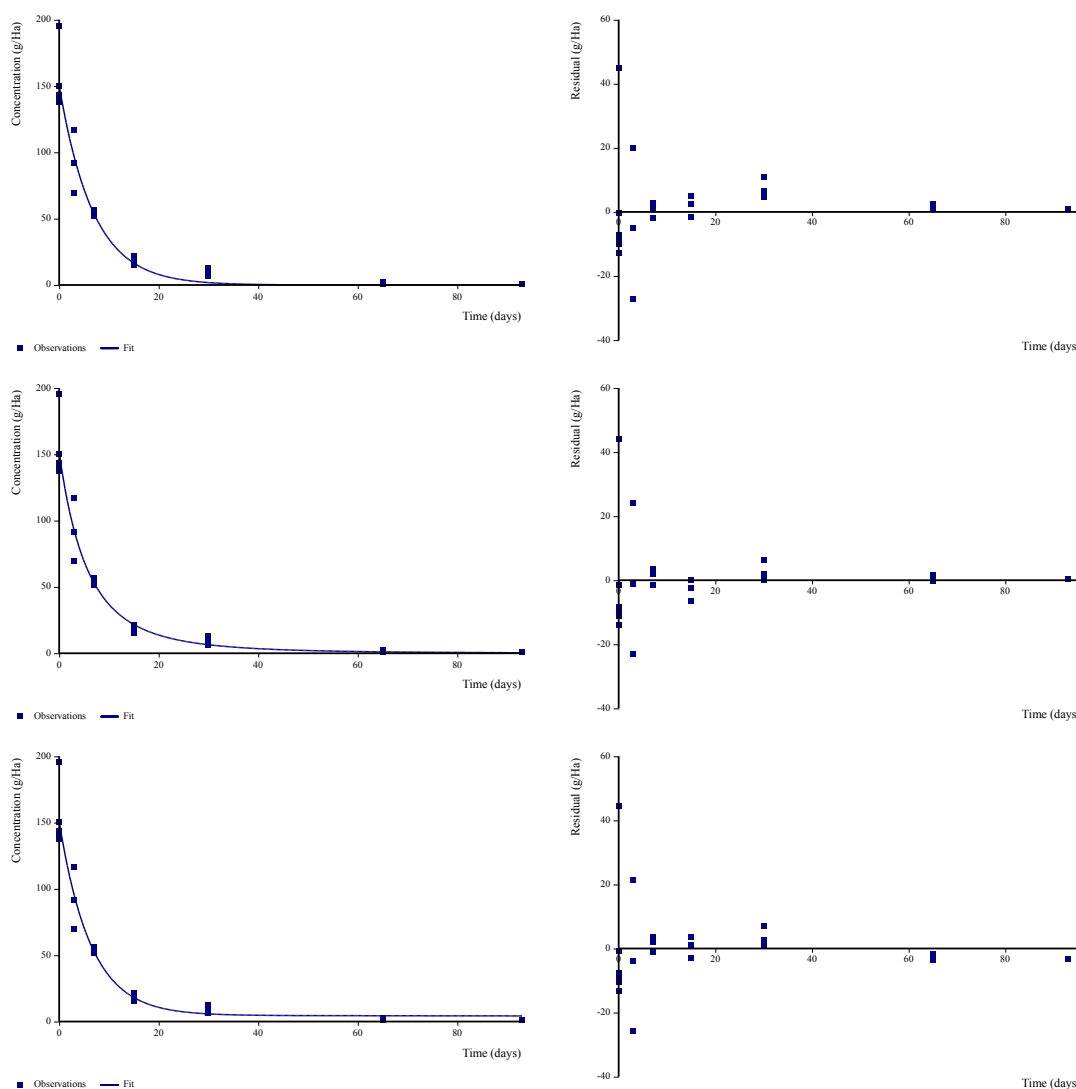


Figure 8.1.2.2.1/5-14: Model fits and residuals for cinmethylin (+)-enantiomer in North Carolina soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: FOMC. $DisT_{50} = 4.4$ days; $DisT_{90} = 18.9$ days. χ^2 error = 3.0%.

North Dakota

For the North Dakota field site, the Applicant concluded that FOMC offered a better χ^2 error and visual fit than SFO. DFOP was explored and found to be the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-15). The HSE evaluator agrees with this decision.

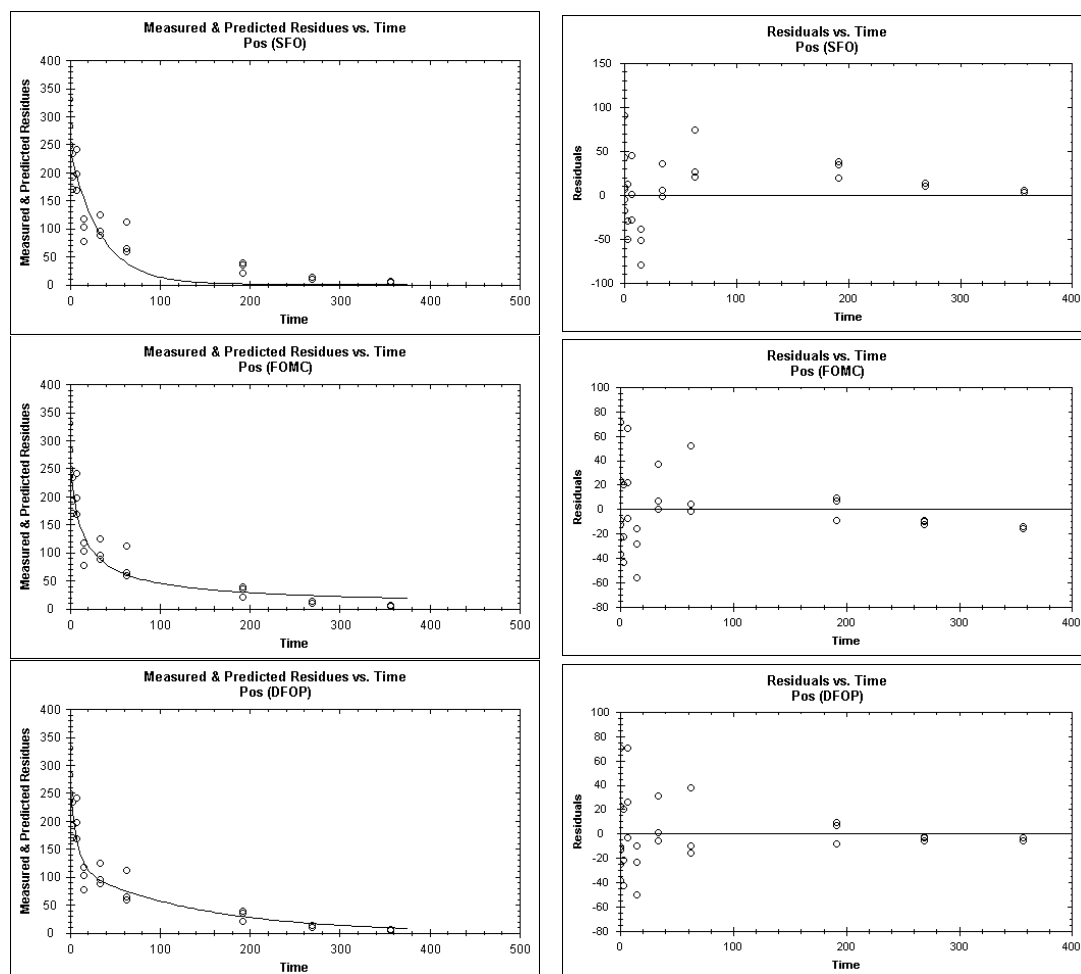


Figure 8.1.2.2.1/5-15: Model fits and residuals for cinmethylin (+)-enantiomer in North Dakota soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: DFOP. $\text{DisT}_{50} = 14.0$ days; $\text{DisT}_{90} = 205.4$ days. χ^2 error = 12.6%.

Texas

For the Texas field site, the Applicant concluded that FOMC did not improve on the goodness of SFO fit, or the χ^2 error rate. The Applicant concluded that SFO offered the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-16). The HSE evaluator agrees with this decision.

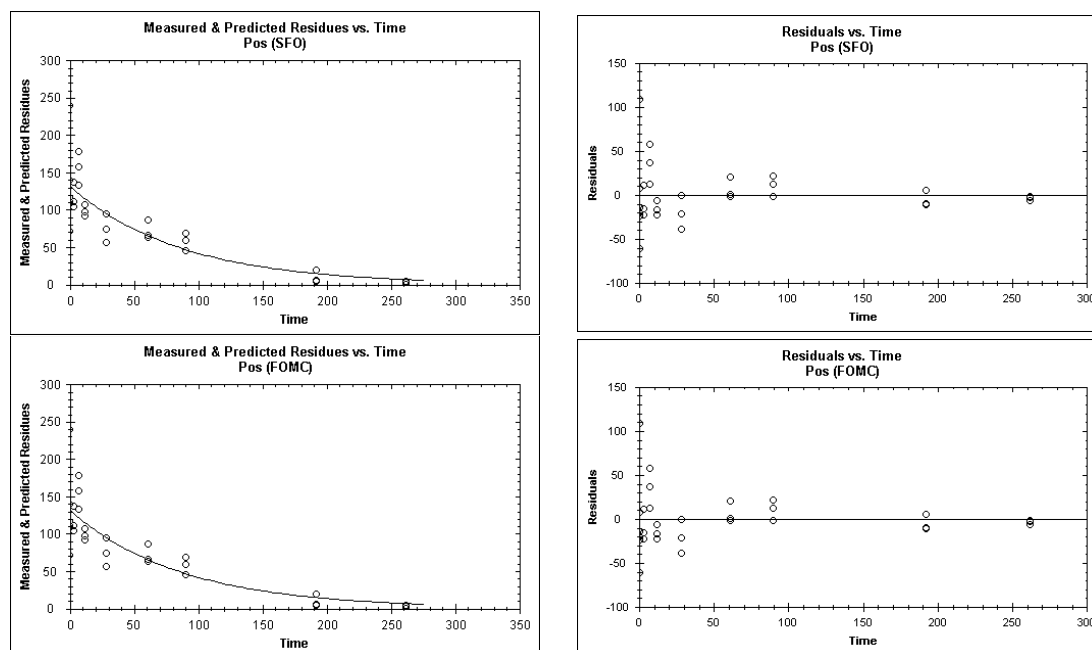


Figure 8.1.2.2.1/5-16 – Model fits and residuals for cinmethylin (+)-enantiomer in Texas soil. Top row: SFO. Bottom row: FOMC. Final fit: SFO. DisT_{50} = 60.2 days; DisT_{90} = 200.1 days. χ^2 error = 15.6%.

Washington

For the Washington field site, the Applicant compared SFO and FOMC fits and concluded that FOMC offered a better χ^2 error and visual fit. The Applicant then investigated DFOP and concluded that FOMC offered the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-17). The HSE evaluator agrees with this decision.

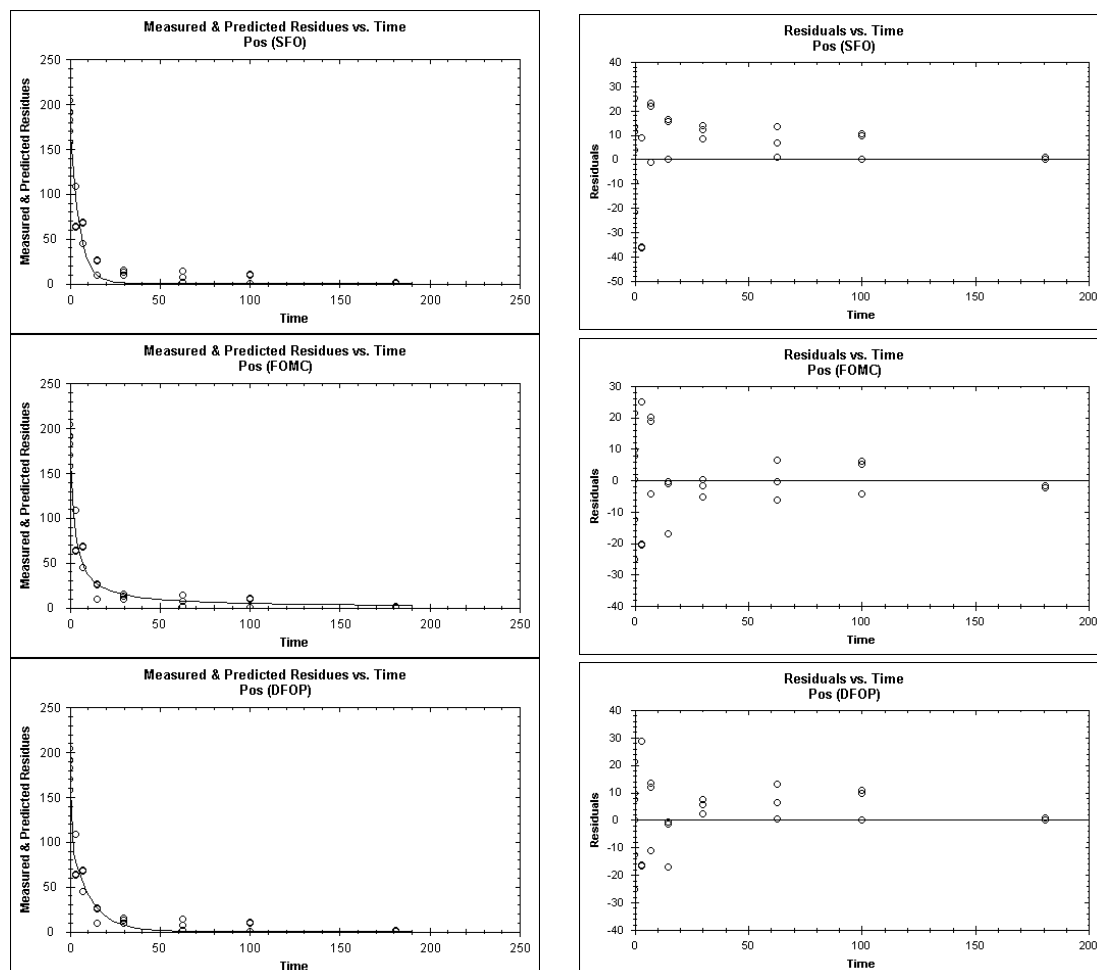


Figure 8.1.2.2.1/5-17: Model fits and residuals for cinmethylin (+)-enantiomer in Washington soil. Top row: SFO. Middle row: FOMC. Bottom row: DFOP. Final fit: FOMC. DisT_{50} = 2.5 days; DisT_{90} = 23.4 days. χ^2 error = 10%.

California

For the California field site, the Applicant compared SFO and FOMC fits and concluded that FOMC offered no improvement to χ^2 error and visual fit. The Applicant concluded SFO was the best model fit for trigger endpoints (Figure 8.1.2.2.1/5-18). The HSE evaluator noted that 0 DALA residue values from the A subplot were markedly low compared to the other replicates and checked the kinetic evaluations without the A subplot 0 DALA values. Endpoints reduced slightly, but the HSE evaluator could not identify a reason to consider these values as outliers. As such, the HSE evaluator agrees with the Applicant's kinetic evaluation and trigger endpoints as they offer conservative dissipation rates.

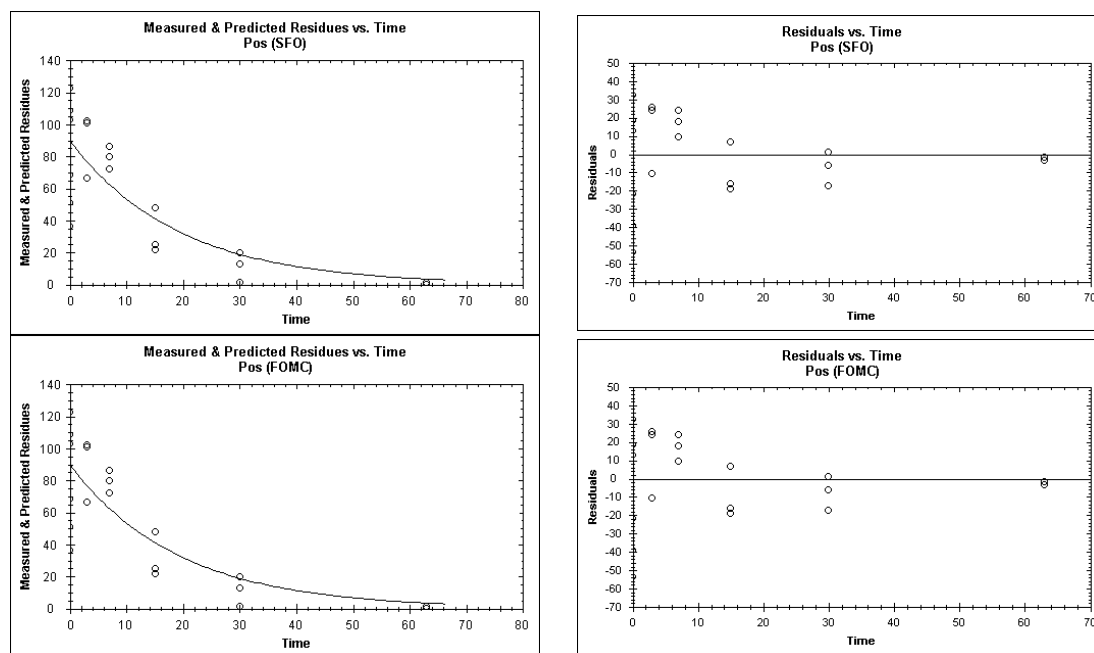


Figure 8.1.2.2.1/5-18: Model fits and residuals for cinmethylin (+)-enantiomer in California soil. Top row: SFO. Bottom row: FOMC. Final fit: SFO. DisT_{50} = 13.2 days; DisT_{90} = 44.0 days. χ^2 error = 17.2%.

Table 8.1.2.2.1/5-33 – Summary of kinetic model evaluation of field dissipation of cinmethylin (+)-enantiomer in six US soils.

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
New York	SFO	34.3	113.9	Fair	20.1	208.0	k = 0.0202	< 0.0001	0.0197	0.0280
	FOMC	16.7	378.8	Fair	13.2	233.6	α = 0.5790 β = 7.239	-	0.2206 -2.9902	0.938 17.469
	DFOP	17.8	193.4	Good	11.2	238.1	k ₁ = 0.2743 k ₂ = 0.0091 g = 0.4152	0.0794 0.0091	-0.09732 0.00295	0.6460 0.0150
Applicant's proposal: FOMC better fit than SFO, therefore explore DFOP. DFOP better fit overall – use DFOP for trigger endpoint. HSE evaluator notes that the k₁ value for DFOP fails the t-test; however, this does not change the conclusion. DFOP is a more conservative representation of sampling points between 30 and 100 days, and better representative of the later sampling points. Therefore, the HSE evaluator agrees.										
North Carolina	SFO	4.7	15.7	Fair	5.7	150.5	k = 0.1472	< 0.0001	0.1134	0.1810
	FOMC	4.4	18.9	Good	3.0	151.5	α = 3.305 β = 18.74	-	-3.448 -27.02	10.06 64.5
	DFOP (k ₂ fixed)	4.6	16.6	Good	4.5	151.3	k ₁ = 0.1824 k ₂ = 0.00096 g = 0.869	< 0.0001 Fixed	0.1113 Fixed	0.206 Fixed
Applicant's proposal: FOMC offered improved Chi² error and visual fit, but error was < 5% for both models – use the simpler model, SFO, for trigger endpoints. HSE evaluator disagrees; the kinetic assessment shown above is the Evaluator's own. The HSE evaluator accepts that FOMC offers improved error and visual fit, and as a result investigated the DFOP fit. Initially the DFOP fit was best overall; however, k₂ value failed the t test (P = 0.34) so this value was fixed assuming the worst-case scenario of a DT₅₀ of 1000 days. Following fixing of the k₂ value, the visual fit for FOMC became the best overall. Conclusion: use FOMC for trigger endpoints.										

Table 8.1.2.2.1/5-33 continued

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
North Dakota	SFO	23.8	79.1	Poor	20.4	240.2	k = 0.0291	< 0.0001	0.01904	0.0390
	FOMC	15.6	224.2	Fair	14.0	258.9	$\alpha = 0.7234$ $\beta = 9.699$	-	0.3186 -0.9819	1.1280 20.380
	DFOP	14.0	205.4	Good	12.6	260.3	k ₁ = 0.1266 k ₂ = 0.0073 g = 0.5492	0.0087 0.0071	0.0289 0.0019	0.2240 0.0130
Applicant's proposal: SFO better fit than FOMC, therefore explored DFOP. DFOP best overall fit with lower Chi² error and better predicted values – use DFOP for trigger endpoint. HSE evaluator agrees.										
Texas	SFO	60.2	200.1	Good	15.6	131.2	k = 0.0115	0.0001	0.0114	148.154
	FOMC	60.2	200.1	Good	16.5	131.2	$\alpha = 1232$ $\beta = 1.07E+5$	-	-1.847E+6 -1.604E+8	1.849E+6 1.607E+8
Applicant's proposal: SFO and FOMC provided similar visual fits, with similar Chi² errors. SFO had the slightly lower error – use SFO for trigger endpoint. The HSE evaluator notes that one 0 DALA replicate was markedly higher than the others at 239.6 g/ha and conducted a kinetic assessment with this value excluded. Chi² errors decreased and the DT₅₀ was extended to 68 days; however, the HSE evaluator could not identify a reason for the result to be considered an outlier and so did not exclude the value. The HSE evaluator concluded that the Applicant's original model fits sufficiently represented the field dissipation and has accepted their decisions. Conclusion: HSE evaluator agrees.										

Table 8.1.2.2.1/5-33 continued

Field Site	Kinetic Model	DT ₅₀ (d)	DT ₉₀ (d)	Visual assessment	Chi ² error %	M ₀ (g/ha)	Parameters	Prob >t	Lower 95 %	Upper 95 %
Washington	SFO	3.6	11.8	Poor	19.5	178.7	k = 0.1952	< 0.0001	0.1525	0.2380
	FOMC	2.6	22.9	Good	9.63	182.2	$\alpha = 1.001$ $\beta = 2.550$	-	0.4591 0.0399	1.5440 5.0610
	DFOP	1.5	19.2	Fair	9.57	182.4	k ₁ = 9.886 k ₂ = 0.091 g = 0.426	0.5 < 0.0001	-Infinity 0.0508	+Infinity 0.1310
Applicant's proposal: FOMC better visual fit than SFO and DFOP throughout the whole sampling period and offers best Chi² error – use FOMC for trigger endpoint. HSE Evaluator agrees.										
California	SFO	13.2	44.0	Fair	17.2	89.95	k = 0.0523	0.0014	0.0226	0.0820
	FOMC	13.2	44.0	Fair	19.0	89.95	$\alpha = 3941$ $\beta = 7.53E+4$	-	-2.434E+7 -4.651E+8	2.434E+7 4.652E+8
Applicant's proposal: SFO and FOMC similarly predicted observed data throughout. SFO offered slightly smaller Chi² error. FOMC did not improve statistical or visual results – use SFO for trigger endpoints. HSE evaluator noted that 0 DALA samples from subplot A were markedly lower than those observed in the other two subplots and conducted a kinetic assessment with these values excluded to investigate whether fit improved. Dissipation times were shortened slightly, but the HSE evaluator could not identify a reason for the results to be considered outliers and so did not exclude these data. Therefore, the HSE evaluator agrees with the Applicant's kinetic evaluation and endpoints as they offer a conservative dissipation rate.										

KINETIC EVALUATION: MODELLING ENDPOINTS

Background

The Applicant evaluated the dissipation behaviour of the herbicide cinmethylin in a field dissipation study involving six US soils located in New York, North Carolina, North Dakota, Texas, Washington and California. The Applicant supplied a kinetic evaluation for deriving trigger endpoints (see previous section). At the time of dossier evaluation, the Applicant had not supplied a kinetic evaluation for deriving modelling endpoints for the field dissipation study. This acted against the current guidance of the FOCUS workgroup on degradation kinetics (EFSA, 2014; also referred to as DegT50 guidance), which issued guidance on how to design field dissipation studies to allow for the derivation of degradation rates (DegT50) as opposed to dissipation rates (DisT50) through the elimination of surface processes such as photolysis. The guidance includes instructions on how to process and normalise data from “legacy studies” that were not conducted in accordance with the 2014 guidance to derive normalised modelling endpoints (DegT50s) from the field dissipation study.

Following a request from the HSE evaluator, the Applicant supplied a report that provided the degradation kinetics of cinmethylin in US soils in accordance with the current guidance to derive normalised modelling endpoints. The Applicant provided this to the HSE evaluator following Applicant commenting as a formal report, detailed below.

Report:	KCA 7.1.2.2.1/XX; Donaldson, F.P. (2020)
Title	Kinetic evaluation of a field dissipation study with BAS 684 H conducted in the USA from 2015 to 2017: Determination of modeling endpoints according to FOCUS. Report no. 2019/2052931
Guidelines	<ul style="list-style-type: none"> • FOCUS Degradation Kinetics (2006; 2014) • EFSA Guidance to obtain DegT50 values in soil (2014)
GLP?	Yes
Deviations	None.

Summary

The Applicant analysed the degradation kinetics of cinmethylin according to EFSA guidance to derive normalised modelling endpoints from five US soils: New York, North Carolina, Texas, Washington and California. The Applicant noted that kinetic evaluation was not included for North Dakota as, in an ecoregion similarity assessment, no matching European ecoregions were identified (KCA 7.1.2.2.1/9; Jeffries, M., Warren, R., 2018a). This study was assessed separately, with the HSE evaluator agreeing with the conclusion.

The Applicant did not submit kinetic evaluation for the two enantiomers, Reg. No. 5925581 ((-)-cinmethylin) and Reg. No. 5925632 ((+)-cinmethylin); as such, these assessments were conducted by the HSE evaluator.

The original study was not compliant with EFSA recommendations for obtaining DegT50 values in soil from field studies for modelling purposes; as a result, the Applicant followed the approach described for legacy studies in the EFSA guidance (2014), to be applied where surface processes have not been minimised. Degradation was considered using sampling points after cumulative rainfall and irrigation exceeded 10 mm. Prior to analysis, the sampling intervals were normalised to reference conditions (20°C, pF2) regarding soil moisture and temperature according to the time-step normalisation technique. Kinetic evaluation was then performed on the time-step normalised dataset. Respective degradation parameters were

derived based on a visual and statistical assessment following FOCUS kinetics guidance (2006; 2014).

The appropriate kinetic models and resulting normalised modelling endpoints for cinmethylin and its two enantiomers are summarised in the tables below. For all models, the visual assessment and goodness-of-fit statistics indicate plausible fit. The t-test was passed for the respective model parameters. Therefore, the resulting modelling endpoints can be considered reliable.

Table 8.1.2.2.1/5-34: Summary of modelling endpoints for cinmethylin.

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error (%)	Normalised DegT50 (d)
New York	Silt loam	5.7	SFO	9.6	18.3
North Carolina	Sandy loam	6.1	SFO	10.4	6.8
Texas	Clay loam	7.3	SFO	18.4	9.9
Washington	Sand	8.1	SFO	16.0	3.7
California	Sandy loam	8.2	SFO	9.9	5.2

^a Soil characteristic of the uppermost horizon

^b pH measured in a soil paste containing distilled water

Table 8.1.2.2.1/5-35: Summary of modelling endpoints for Reg. No. 5925581 ((-)-enantiomer).

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error (%)	Normalised DegT50 (d)
New York	Silt loam	5.7	SFO	7.8	16.5
North Carolina	Sandy loam	6.1	SFO	9.9	6.5
Texas	Clay loam	7.3	SFO	18.5	8.7
Washington	Sand	8.1	SFO	15.6	3.5
California	Sandy loam	8.2	SFO	9.7	5.0

^a Soil characteristic of the uppermost horizon

^b pH measured in a soil paste containing distilled water

Table 8.1.2.2.1/5-36: Summary of modelling endpoints for Reg. No. 5925632 ((+)-enantiomer).

Field trial	Soil type (USDA) ^a	pH ^b	Kinetic model	χ^2 error (%)	Normalised DegT50 (d)
New York	Silt loam	5.7	SFO	11.3	20.1
North Carolina	Sandy loam	6.1	SFO	10.9	7.0
Texas	Clay loam	7.3	SFO	18.3	11.5
Washington	Sand	8.1	SFO	16.3	3.8
California	Sandy loam	8.2	SFO	10.5	5.4

^a Soil characteristic of the uppermost horizon

^b pH measured in a soil paste containing distilled water

Methods

Data handling and time step normalisation

Residue data for cinmethylin and its two enantiomers were expressed in g/ha for kinetic evaluation, consistent with the data set used for deriving trigger endpoints. The normalisation procedure was carried out by the Applicant based on the recommendations of FOCUS (2014) for the five selected trial sites by increasing or decreasing day lengths depending on soil temperature and moisture by means of correction factors (f_{temp} and f_{moist}). The Applicant derived the van Genuchten parameter and reference soil moisture values at pF 2 through using soil properties derived from the soil analysis certificates. The Applicant also calculated soil bulk density using organic matter content for each soil.

Temperature correction factors (f_{temp}) were determined to account for differences between actual daily soil temperatures (as calculated by FOCUS-PEARL), and a reference soil temperature of 20°C using a Q10 value of 2.58. Moisture correction factors (f_{moist}) were determined by comparing the measured soil moisture with the reference soil moisture, both converted to be expressed as volumetric soil moisture. The f_{moist} value was used to account for differences between actual daily soil moisture (as calculated by FOCUS-PEARL), and the reference soil moisture at field capacity (pF 2).

In accordance with EFSA DegT50 guidance for normalising legacy studies, the Applicant identified the first sampling point at which 10 mm of rainfall and/or irrigation had occurred. Daily soil moisture and temperature values were calculated using FOCUS-PEARL 4.4.4, calculated from measured soil moisture values. Based on the model results, daily correction factors were calculated for the normalised day length. No normalisation was applied to the new 0 DAA. Normalised sampling days after application were calculated by cumulative addition of normalised day lengths.

The HSE evaluator validated the Applicant's daily soil moisture and temperature corrections and subsequent time step normalisation using FOCUS-PEARL 4.4.4 and concluded that the values applied by the Applicant were correct.

In addition to the time step normalisation, the Applicant was also required to only consider sampling points that fell after a cumulative 10 mm of precipitation and irrigation had occurred at the field site. The HSE evaluator assessed the Applicant's use of the "10 mm rule" and agreed with their decisions for all five soils. Table 8.1.2.2.1/5-37 displays the application of the "10 mm rule". The HSE evaluator notes that the Applicant included additional time-step normalisation for the complete North Carolina dataset without consideration of the "10 mm rule" due to the need to consider biphasic kinetic models for this field site. The HSE evaluator also agrees with this time-step normalisation.

Table 8.1.2.2.1/5-37: Time-step normalised sampling days supplied by the Applicant and verified by the HSE evaluator. The Applicant removed sampling times that took place before a cumulative 10 mm of precipitation had occurred.

New York		North Carolina	
DAT [d]	D _{norm} [d]	DAT [d]	D _{norm} [d]
7 ^a	0.0	3 ^b	0.0
15	4.1	7	4.2
31	9.5	15	17.4
61	19.3	30	40.6
90	26.6	65	103.9
180	37.4	93	153.5
270	90.6	-	-
360	205.4	-	-
Texas		Washington	
DAT [d]	D _{norm} [d]	DAT [d]	D _{norm} [d]
7 ^c	0.0	7 ^d	0.0
12	1.4	15	4.5
28	5.3	30	10.5
61	10.9	63	15.5
90	16.8	100	18.6
192	64.2	181	38.8
262	170.3	-	-
California		North Carolina ^f	
DAT [d]	D _{norm} [d]	DAT [d]	D _{norm} [d]
3 ^e	0.0	0	0.0
7	2.2	3	3.9
15	6.9	7	8.1
30	19.4	15	21.3
63	52.3	30	44.5
-	-	65	107.8
-	-	93	157.4

^a 10mm rain+irrigation was achieved at 3 DAT. Therefore, next sampling time (7 DAT) set to time zero for kinetic evaluation.

^b 10mm rain+irrigation was achieved at 0 DAT. Therefore, next sampling time (3 DAT) set to time zero for kinetic evaluation.

^c 10mm rain+irrigation was achieved at 3 DAT. Therefore, next sampling time (7 DAT) set to time zero for kinetic evaluation.

^d 10mm rain+irrigation was achieved at 6 DAT. Therefore, next sampling time (7 DAT) set to time zero for kinetic evaluation.

^e 10mm rain+irrigation was achieved at 1 DAT. Therefore, next sampling time (3 DAT) set to time zero for kinetic evaluation.

^f Complete dataset with normalized days was used to fit biphasic DFOP and HS models, as per EFSA guidance.

Kinetic evaluation

For each trial, the Applicant identified the appropriate kinetic model based on the visual and statistical assessment based on the FOCUS kinetics guidance for deriving modelling endpoints (2006; 2014). The Applicant tested the SFO, FOMC and DFOP models using Cake v3.3 with the error tolerance set to 1×10^{-5} and iterations of the optimisation tool (IRLS) set to 100. The HSE evaluator validated the Applicant's kinetic evaluations using Cake v3.2 with the same error tolerance and optimisation tool iteration settings.

The HSE evaluator agreed with the data used for the kinetic evaluation. The HSE evaluator assessed the data handling and kinetic evaluations supplied by the Applicant as Cake outputs. The HSE evaluator accepted the kinetic evaluation for all five soils. As a result, the Applicant's kinetic evaluations and decision-making process is presented in the following sections.

As cinmethylin decline does not show a lag phase or long-term sorption kinetics, it was appropriate to initially assess the SFO model fitted to the normalised data including sampling

points following 10 mm precipitation. If SFO did not sufficiently describe the decline of cinmethylin, then DFOP and HS were considered where necessary using the EFSA DegT50 guidance (2014).

A kinetic model is considered appropriate if the residuals are randomly distributed around zero and the χ^2 error indicates sufficient quality of the fit (i.e. value is < 15%). However, this value was not taken as a cut-off criterion as field studies often have large scatter to the data, leading to large error values. In some cases, fits with higher error values (i.e. χ^2 error value > 15%) are still acceptable if they represent the degradation behaviour well. The t test for the degradation parameters should be passed at 5% error level.

Experimental data

The field residue data used to derive modelling endpoints were time-step normalised and considered only sampling points that occurred after a cumulative 10 mm precipitation + irrigation had fallen at the field site, as per EFSA DegT50 guidance for using legacy studies. Tables 8.1.2.2.1/5-38-42 display the residue data used to derive modelling endpoints for cinmethylin and its two enantiomers. The HSE evaluator notes that the cinmethylin column consists the sum of the two enantiomer concentrations. The HSE evaluator notes that the residue values are the same as those used for trigger endpoints in the previous section, and that the data handling and processing has been explained previously. All zero values were also included in the kinetic evaluation, and not treated as missing values.

Table 8.1.2.2.1/5-38: Experimental data used for the kinetic evaluation of the degradation of cinmethylin and its two enantiomers in the New York soil.

Days after application (d)		Field residues (g/ha) ^{a, b}		
Original	Normalised	Cinmethylin	(-)-enantiomer	(+)-enantiomer
7	0.0	275.9	128.4	147.5
7	0.0	274.3	134.3	140.0
7	0.0	191.8	96.51	95.24
15	4.1	208.5	94.63	113.9
15	4.1	337.1	146.4	190.7
15	4.1	230.7	108.2	122.5
31	9.5	134.3	59.78	74.50
31	9.5	232.3	109.2	123.1
31	9.5	217.9	99.88	118.0
61	19.3	153.6	69.09	84.50
61	19.3	141.3	60.93	80.33
61	19.3	64.79	27.34	37.45
90	26.6	74.63	28.51	46.12
90	26.6	98.33	44.52	53.81
90	26.6	88.89	40.43	48.46
180	37.4	88.44	36.32	52.12
180	37.4	77.69	31.85	45.84
180	37.4	77.38	31.83	45.55
270	90.6	21.67	8.474	13.20
270	90.6	11.75	4.264	7.484
270	90.6	18.52	7.780	10.74
360	205.4	6.303	2.226	4.077
360	205.4	18.09	6.433	11.66
360	205.4	8.301	2.687	5.614

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected both spatially and temporally according to FOCUS (2014).

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Field Study Methods section for explanation.

Table 8.1.2.2.1/5-39: Experimental data used for the kinetic evaluation of the degradation of cinmethylin and its two enantiomers in the North Carolina soil.

Days after application (d)			Field residues (g/ha) ^{b, c}		
Original	Normalised (SFO) ^a	Normalised (biphasic) ^a	Cinmethylin	(-)-enantiomer	(+)-enantiomer
0	-	0	299.5	149.4	150.1
0	-	0	270.4	132.7	137.7
0	-	0	285.0	144.5	140.5
0	-	0	379.7	184.2	195.5
0	-	0	281.7	139.9	141.8
0	-	0	270.6	127.3	143.3
3	0.0	3.9	177.4	85.69	91.73
3	0.0	3.9	224.9	108.1	116.8
3	0.0	3.9	134.1	64.45	69.68
7	4.2	8.1	108.2	51.78	56.43
7	4.2	8.1	97.57	45.86	51.71
7	4.2	8.1	108.0	53.09	54.90
15	17.4	21.3	27.05	11.96	15.09
15	17.4	21.3	38.69	17.02	21.67
15	17.4	21.3	36.41	17.24	19.17
30	40.6	44.5	22.78	10.08	12.70
30	40.6	44.5	16.18	7.679	8.504
30	40.6	44.5	12.25	5.789	6.457
65	103.9	107.8	4.023	3.182	0.8413
65	103.9	107.8	1.790	<i>0.8950</i>	<i>0.8950</i>
65	103.9	107.8	3.406	<i>0.7931</i>	2.613
93	153.5	157.4	1.000	<i>1.000</i>	0.0000
93	153.5	157.4	0.0000	0.0000	0.0000
93	153.5	157.4	0.9362	0.0000	<i>0.9362</i>

^a Two time-step normalisations were undertaken as it was necessary to consider both SFO and biphasic (DFOP and HS) model fits for the North Carolina data. For the biphasic model fits, EFSA DegT50 guidance does not require the exclusion of sampling times where 10 mm cumulative precipitation had not occurred. Therefore, time-step normalisation for the biphasic normalisation started at 0 DAA.

^b Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected by the Applicant both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^c Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

Table 8.1.2.2.1/5-40: Experimental data used for the kinetic evaluation of the degradation of cinmethylin and its two enantiomers in the Texas soil.

Days after application (d)		Field residues (g/ha) ^{a, b}		
Original	Normalised	Cinmethylin	(-)-enantiomer	(+)-enantiomer
7.0	0.0	302.2	144.6	157.6
7.0	0.0	342.8	164.7	178.1
7.0	0.0	253.3	120.5	132.8
12.0	1.4	202.5	95.08	107.4
12.0	1.4	178.8	87.18	91.62
12.0	1.4	186.2	89.03	97.14
28.0	5.3	102.5	46.33	56.14
28.0	5.3	174.8	80.81	94.02
28.0	5.3	137.0	63.47	73.48
61.0	10.9	113.3	47.64	65.69
61.0	10.9	114.9	51.92	63.00
61.0	10.9	157.1	71.37	85.72
90.0	16.8	103.6	45.28	58.31
90.0	16.8	120.0	51.83	68.13
90.0	16.8	79.16	34.12	45.04
192.0	64.2	26.78	7.301	19.48
192.0	64.2	5.634	<i>0.6814</i>	4.953
192.0	64.2	4.262	<i>0.7089</i>	3.553
262.0	170.3	3.796	<i>0.6315</i>	3.164
262.0	170.3	0.5607	0.0000	<i>0.5607</i>
262.0	170.3	4.789	0.0000	4.789

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected by the Applicant both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

Table 8.1.2.2.1/5-41: Experimental data used for the kinetic evaluation of the degradation of cinmethylin and its two enantiomers in the Washington soil.

Days after application (d)		Field residues (g/ha) ^{a, b}		
Original	Normalised	Cinmethylin	(-)-enantiomer	(+)-enantiomer
7	0.0	128.6	60.01	68.62
7	0.0	126.9	59.53	67.38
7	0.0	79.26	34.93	44.33
15	4.5	46.80	20.97	25.83
15	4.5	45.45	20.31	25.14
15	4.5	18.12	8.621	9.494
30	10.5	22.36	9.863	12.50
30	10.5	16.09	7.196	8.890
30	10.5	24.32	10.05	14.27
63	15.5	24.33	10.81	13.52
63	15.5	1.5966	<i>0.7983</i>	<i>0.7983</i>
63	15.5	12.54	5.878	6.666
100	18.6	16.66	7.169	9.488
100	18.6	0.0000	0.0000	0.0000
100	18.6	18.00	7.397	10.60
181	38.8	1.343	<i>0.6715</i>	<i>0.6715</i>
181	38.8	0.0000	0.0000	0.0000
181	38.8	1.428	<i>0.7141</i>	<i>0.7141</i>

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected by the Applicant both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

Table 8.1.2.2.1/5-42: Experimental data used for the kinetic evaluation of the degradation of cinmethylin and its two enantiomers in the California soil.

Days after application (d)		Field residues (g/ha) ^{a, b}		
Original	Normalised	Cinmethylin	(-)-enantiomer	(+)-enantiomer
3.0	0.0	196.3	95.53	100.8
3.0	0.0	126.7	60.59	66.15
3.0	0.0	196.9	94.64	102.3
7.0	2.2	134.5	62.44	72.05
7.0	2.2	171.1	84.62	86.44
7.0	2.2	151.7	71.74	79.96
15.0	6.9	90.64	42.66	47.98
15.0	6.9	47.55	22.57	24.98
15.0	6.9	44.59	22.63	21.96
30.0	19.4	28.47	8.461	20.01
30.0	19.4	16.63	4.056	12.57
30.0	19.4	2.372	<i>1.186</i>	<i>1.186</i>
63.0	52.3	3.110	<i>1.555</i>	<i>1.555</i>
63.0	52.3	3.152	<i>1.576</i>	<i>1.576</i>
63.0	52.3	0.0000	0.0000	0.0000

^a Analytical values between the LOQ (5 µg/kg) and LOD (1.5 µg/kg) were used as reported, while values <LOD were corrected by the Applicant both spatially and temporally according to FOCUS (2014). Values set to $0.5 \times \text{LOD}$, corrected based on sample size and moisture level, are highlighted in italics.

^b Analyte soil concentrations in µg/kg were converted into g/ha based on the respective sample dry weights and surface area based on the soil sampling probe diameter. See the Methods section for explanation.

^c Residue depth refers to the depths at which residues were detected, plus the following depth where the Applicant added values corresponding to $0.5 \times \text{LOD}$.

Results and Discussion

Kinetic evaluations for cinmethylin and its two enantiomers are covered in turn below for each of the five US soils. For some fits, error values above 15% were obtained; these can be attributed to the scatter of the measured data due to large variation between replicates. As the observed data were generally well described by the fitted curves, the HSE evaluator concluded that the high error values are acceptable.

Cinmethylin kinetic evaluation

Table 8.1.2.2.1/5-43 summarises the statistical assessment of kinetic models for cinmethylin in the five US soils. Visual assessment is discussed for each soil in turn in the table below, with model fits and residuals displayed in Figures 8.1.2.2.1/5-18-22.

Table 8.1.2.2.1/5-43: Summary of kinetic model evaluation for deriving modelling endpoints for cinmethylin in five US soils using time-step normalised data.

Soil	Kinetic model	Visual fit	Initial value (Mo)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
New York	SFO	Acceptable	247.3	k: 0.0361	0.0255 – 0.047	< 0.0001	9.7	19.2	63.8
Applicant: SFO visual fit is acceptable, the error value is below 15%. Conclusion: SFO is appropriate for derivation of modelling endpoints. HSE evaluator agrees. Use SFO.									
North Carolina	SFO	Acceptable	174.3	k: 0.1029	0.0696 – 0.1360	< 0.001	10.5	6.7	22.4
	DFOP	Good	297.8	k ₁ : 0.1561 k ₂ : 0.0211 g: 0.8682	0.0668 – 0.2450 -0.0505 – 0.0930 0.480 – 1.2560	0.00134 0.2854 0.0001	1.2	5.3	24.0
	HS	Good	297.8	k ₁ : 0.1298 k ₂ : 0.0292 tb: 15.397	0.1009 – 0.1590 -0.0380 – 0.0960 4.0529 – 27.7410	< 0.0001 0.2024 0.0075	0.4	5.3	25.8
Applicant: SFO visual fit is acceptable, though data beyond 40.6 days onward are systematically underestimated → test DFOP with entire (normalised) dataset. DFOP visual fit is good, g is > 0.75, but k ₂ is not statistically significant → test HS with entire (normalised) dataset. The HS visual fit is good, but k ₂ is not statistically significant. As k ₂ parameters are unreliable for both biphasic models, select SFO model Conclusion: SFO is appropriate for derivation of modelling endpoints. HSE evaluator agrees. Use SFO.									
Texas	SFO	Good	251.5	k: 0.0697	0.0448 – 0.0950	< 0.0001	18.4	9.9	33.1
Applicant: SFO visual fit is acceptable, residuals are randomly scattered. Although the error value is above 15%, the visual fit is acceptable. Conclusion: SFO is appropriate for derivation of modelling endpoints. HSE evaluator agrees. Use SFO.									
Washington	SFO	Acceptable	108.8	k: 0.1883	0.1261 – 0.250	< 0.0001	16.0	3.7	12.2
Applicant: SFO visual fit is acceptable, residuals are randomly scattered. Although the error value is above 15%, the visual fit is acceptable. Conclusion: SFO is appropriate for derivation of modelling endpoints. HSE evaluator agrees. Use SFO.									
California	SFO	Good	181.6	k: 0.1335	0.0848 – 0.182	< 0.0001	9.9	5.2	17.3
Applicant: SFO visual fit is acceptable, the error value is below 15%. Conclusion: SFO is appropriate for derivation of modelling endpoints. HSE evaluator agrees. Use SFO.									

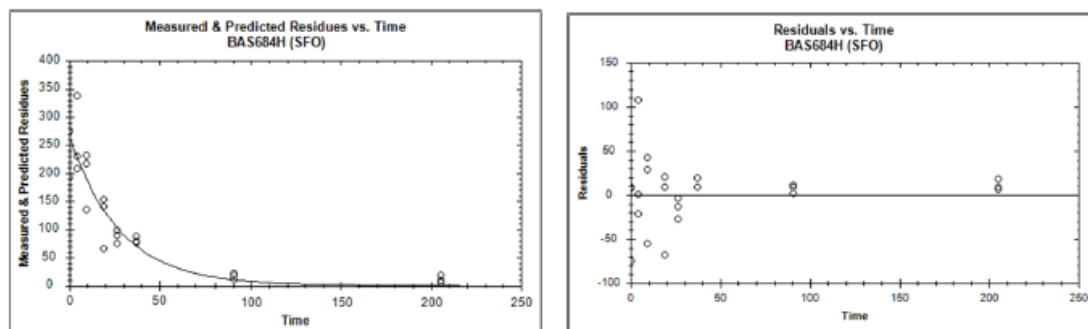


Figure 8.1.2.2.1/5-18: SFO model fit and residuals for cinmethylin in New York soil.

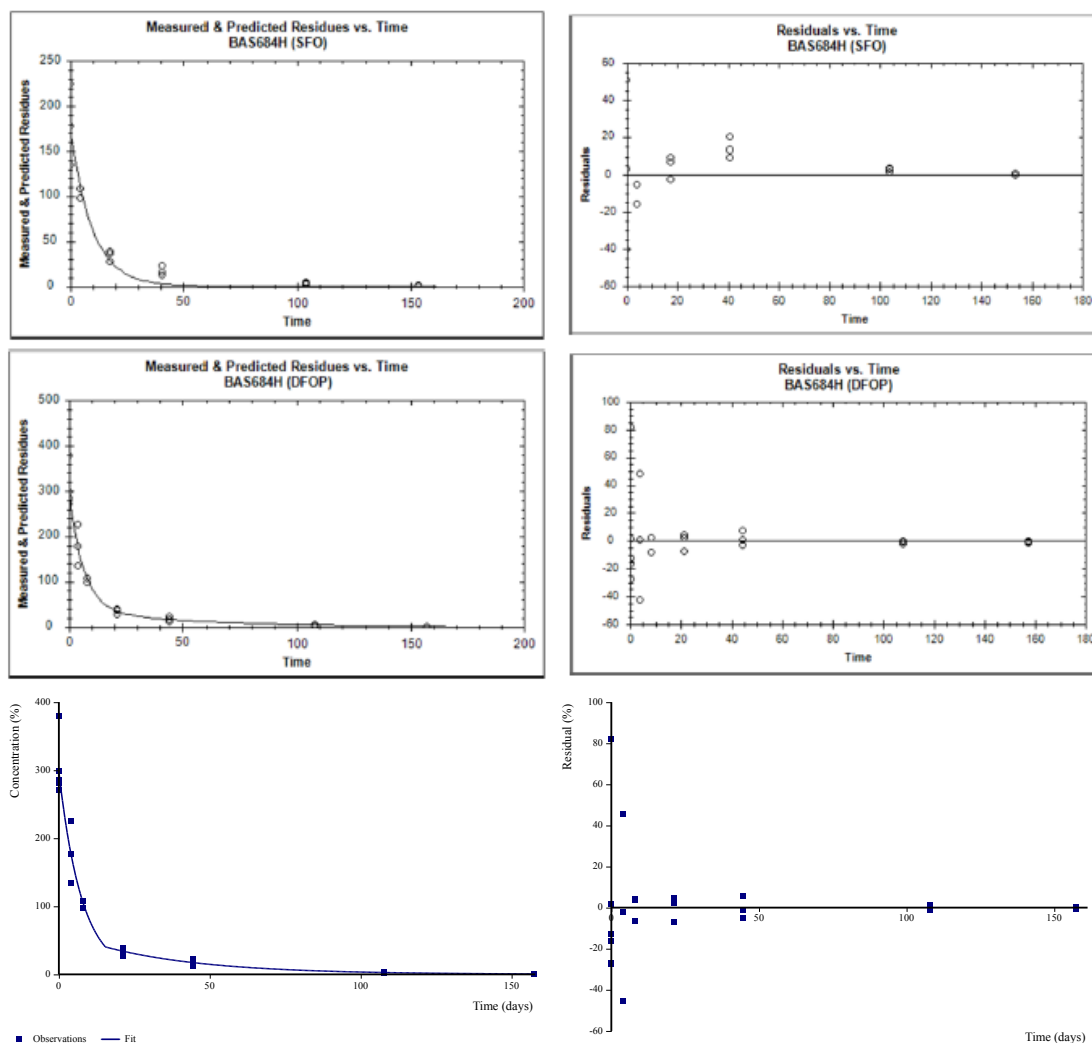


Figure 8.1.2.2.1/5-19: Model fits and residuals for cinmethylin in North Carolina soil. Top row: SFO. Middle row: DFOP. Bottom row: HS. Final model: SFO. Note that the HS model fit is the HSE evaluator's own as the Applicant did not present the correct visual fit in their report.

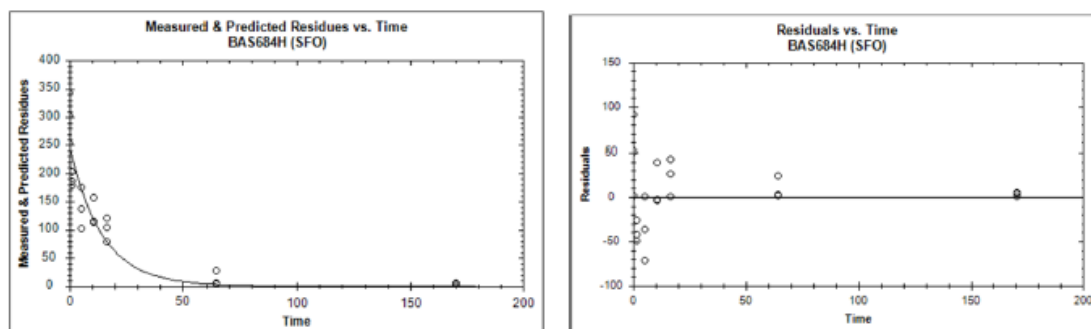


Figure 8.1.2.2.1/5-20: SFO model fit and residuals for cinmethylin in Texas soil.

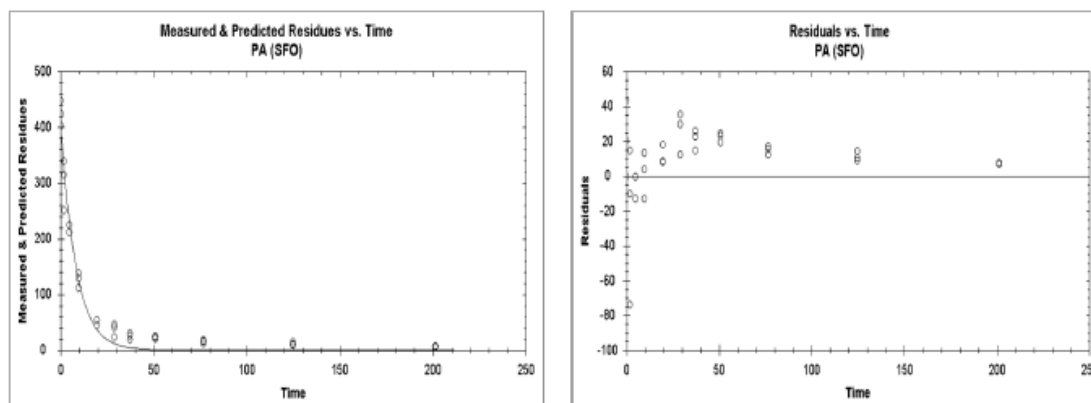


Figure 8.1.2.2.1/5-21: SFO model fit and residuals for cinmethylin in Washington soil.

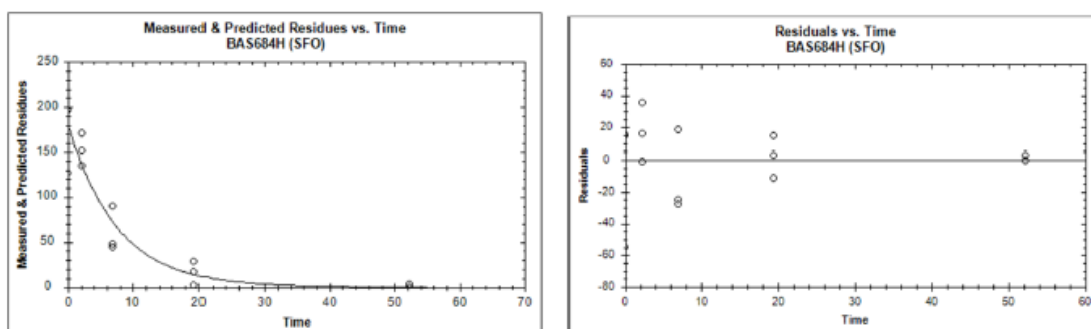


Figure 8.1.2.2.1/5-22: SFO model fit and residuals for cinmethylin in California soil.

(-)-Enantiomer kinetic evaluation

The Applicant did not supply kinetic evaluations for the individual enantiomers, therefore the following evaluations are the HSE evaluator's own, utilising the Applicant's timestep normalisation. Table 8.1.2.2.1/5-44 summarises the statistical assessment of kinetic models for the (-)-enantiomer in the five US soils. Visual assessment is discussed for each soil in turn in the table below, with model fits and residuals displayed in Figures 8.1.2.2.1/5-23-27.

Table 8.1.2.2.1/5-44: Summary of kinetic model evaluation for deriving modelling endpoints for the (-)-enantiomer in five US soils using time-step normalised data.

Soil	Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
New York	SFO	Good	126.3	k: 0.0401	0.0290 – 0.0510	< 0.0001	7.9	17.3	57.5
HSE evaluator: SFO offers a good visual fit, though underestimates measurements after 35.5 DAA. Residuals are large but randomly scattered, and the χ^2 error rate is below 15%. Conclusion: use SFO to derive modelling endpoints.									
North Carolina	SFO	Acceptable	84.22	k: 0.1065	0.0694 – 0.1440	< 0.0001	10.0	6.5	21.6
	DFOP ^a	Good	146.4	k ₁ : 0.1583 k ₂ : 0.0202 g: 0.8813	0.0680 – 0.2490 -0.0562 – 0.0970 0.5033 – 1.2590	< 0.0001 0.294	0.85	k ₁ : 4.4 k ₂ : 34.3	22.6
	HS ^a	Good	146.2	k ₁ : 0.1335 k ₂ : 0.0280 tb: 15.71	0.1025 – 0.1650 -0.0452 – 0.1010 3.6960 – 27.730	<0.0001 0.217	0.88	k ₁ : 5.2 k ₂ : 24.8	23.0
HSE Evaluator: SFO offers a good fit to the first three time points; however, it significantly underestimates the field data for three time points from 40.6 DAA onwards. The HSE evaluator followed the EFSA DegT50 guidance legacy study modelling flowchart ³ and explored DFOP with all data points (i.e. from the actual 0 DAA) with timestep normalisation applied. The visual fit improved, however the g value was > 0.75. Therefore, HS was explored. HS offered a good visual fit but again the k ₂ value was not significantly above 0. As the k ₂ values were unreliable in the biphasic fits, and there was little difference to the DT50 due to rapid degradation, the HSE evaluator opted for SFO. Conclusion: Use SFO for modelling endpoints.									
Texas	SFO	Acceptable	121.8	k: 0.0797	0.0511 – 0.1080	< 0.0001	18.5	8.7	28.9
SFO offers an acceptable visual fit with large but randomly scattered visuals. The χ^2 error rate is above 15%; however, the model describes the data well. Conclusion: use SFO to derive modelling endpoints.									
Washington	SFO	Good	50.35	k: 0.1964	0.1234 – 0.2690	< 0.0001	15.6	3.5	11.7
SFO offers a good visual fit with small, randomly scattered residuals. The and the χ^2 error rate is slightly above 15%, however the model describes the data well. Conclusion: use SFO to derive modelling endpoints.									
California	SFO	Good	87.87	k: 0.1390	0.0830 – 0.1950	< 0.0001	9.7	5.0	16.6
SFO offers a good visual fit to the measured data with randomly scattered residuals and a χ^2 error rate below 10%. Conclusion: use SFO to derive modelling endpoints.									

^a Biphasic models were fitted to the whole dataset, i.e. from 0 DAA. The whole dataset was time step normalised as per EFSA DegT50 guidance (2014).

³ The legacy study modelling flowchart can be found on page 8 of the EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil (EFSA, 2014).

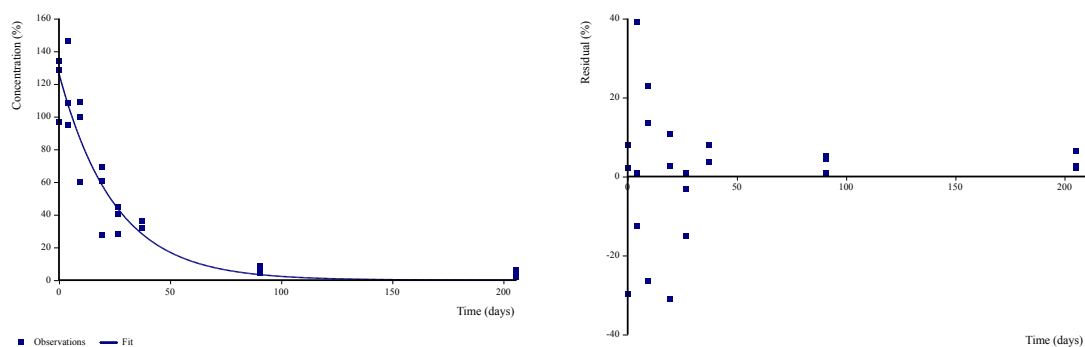


Figure 8.1.2.2.1/5-22: SFO model fit and residuals for (-)-enantiomer in New York soil.

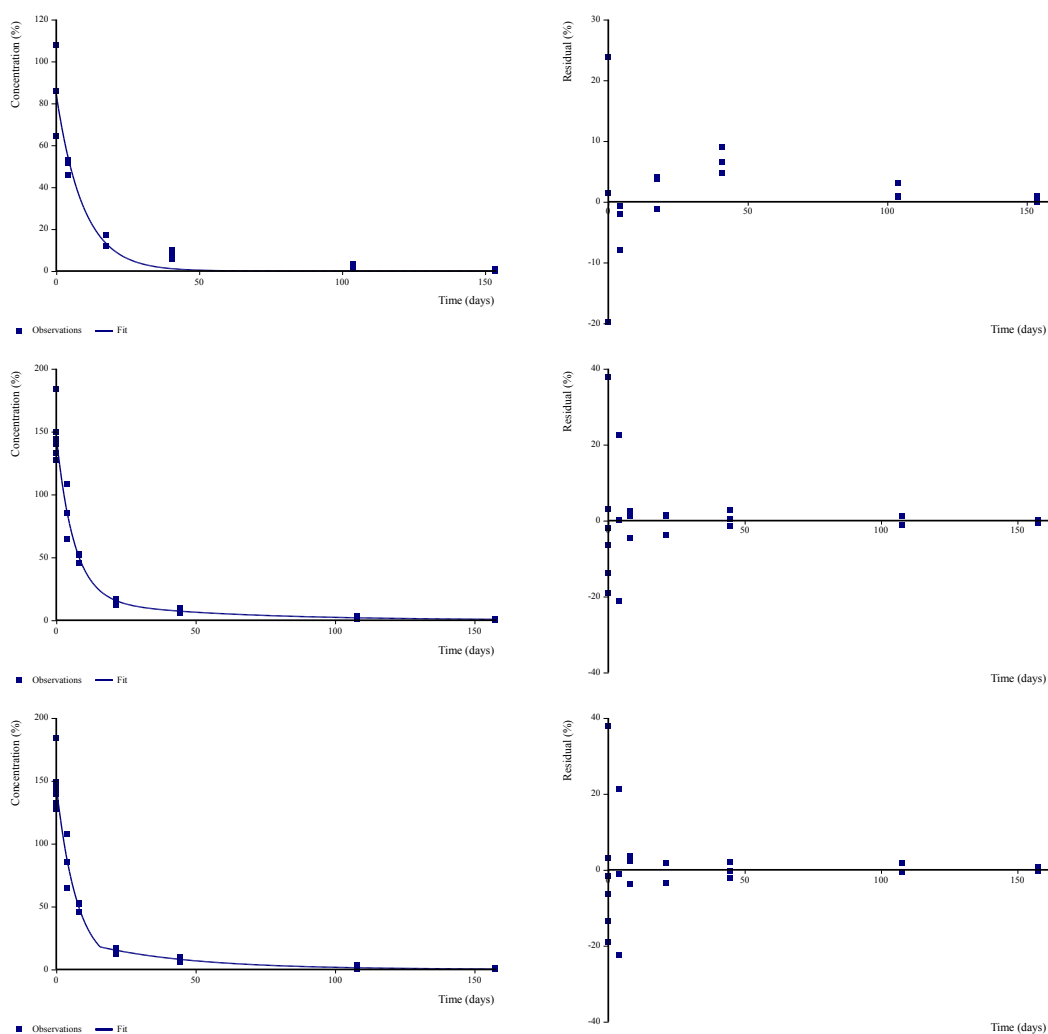


Figure 8.1.2.2.1/5-23: Model fits and residuals for (-)-enantiomer in North Carolina soil. Top row: SFO. Middle row: DFOP. Bottom row: HS. Final model: SFO.

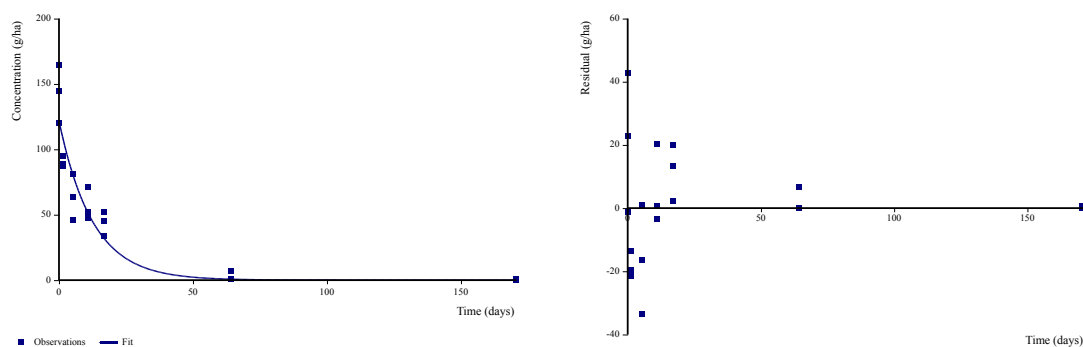


Figure 8.1.2.2.1/5-24: SFO model fit and residuals for (-)-enantiomer in Texas soil.

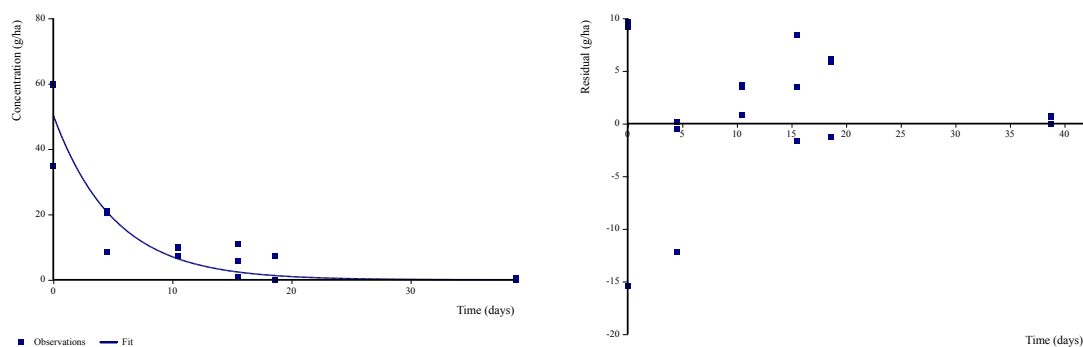


Figure 8.1.2.2.1/5-25: SFO model fit and residuals for (-)-enantiomer in Washington soil.

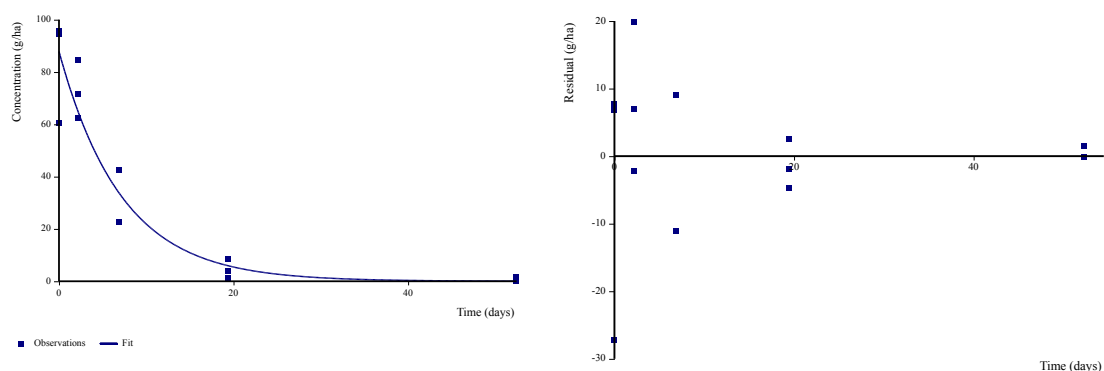


Figure 8.1.2.2.1/5-26: SFO model fit and residuals for (-)-enantiomer in California soil.

(+)-enantiomer kinetic evaluation

Table 8.1.2.2.1/5-45 summarises the HSE evaluator's statistical assessment of kinetic models for the (+)-enantiomer in the five US soils. Visual assessment is discussed for each soil in turn in the table below, with model fits and residuals displayed in Figures 8.1.2.2.1/5-27-31.

Table 8.1.2.2.1/5-45: Summary of kinetic model evaluation for deriving modelling endpoints for the (+)-enantiomer in five US soils using time-step normalised data.

Soil	Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
New York	SFO	Good	140.7	k: 0.0329	0.0215 – 0.0440	< 0.0001	11.4	21.1	70.0
HSE evaluator: SFO offers a good visual fit, though underestimates measurements after 35.5 DAA. Residuals are large but randomly scattered, and the χ^2 error rate is below 15%. Conclusion: use SFO to derive modelling endpoints.									
North Carolina	SFO	Acceptable	90.07	k: 0.0995	0.0644 – 0.1340	< 0.0001	11	7.0	23.2
	DFOP ^a	Good	151.7	k ₁ : 0.1540 k ₂ : 0.0218 g: 0.8554	0.0523 – 0.2560 -0.0557 – 0.0990 0.3982 – 1.313	0.003 0.282	1.7	k ₁ : 4.5 k ₂ : 31.8	25.5
	HS ^a	Good	151.5	k ₁ : 0.1263 k ₂ : 0.0301 tb: 15.12	0.0951 – 0.1570 -0.0410 – 0.1010 2.7160 – 27.530	<0.0001 0.194	0.17	k ₁ : 5.5 k ₂ : 23.0	28.2
HSE Evaluator: SFO offers a good fit to the first three time points; however, it significantly underestimates the field data for three time points from 40.6 DAA onwards. The HSE evaluator followed the EFSA DegT50 guidance legacy study modelling flowchart and explored DFOP with all data points (i.e. from the actual 0 DAA) with timestep normalisation applied. The visual fit improved, however the g value was > 0.75. Therefore, HS was explored. HS offered a good visual fit but again the k ₂ value was not significantly above 0. As the k ₂ values were unreliable in the biphasic fits, the HSE evaluator opted for SFO. Conclusion: Use SFO for modelling endpoints.									
Texas	SFO	Good	130.0	k: 0.06133	0.0363 – 0.0860	< 0.0001	18.3	11.5	37.6
SFO offers a good visual fit with residuals randomly scattered. The χ^2 error rate is above 15%; however, the model describes the data well. Conclusion: use SFO to derive modelling endpoints.									
Washington	SFO	Good	58.46	k: 0.1817	0.1184 – 0.2450	< 0.0001	16.3	3.8	12.7
SFO offers a good visual fit with small, randomly scattered residuals. The χ^2 error rate is above 15%; however, the model describes the data well. Conclusion: use SFO to derive modelling endpoints.									
California	SFO	Good	93.73	k: 0.1281	0.0753 – 0.1810	< 0.0001	10.5	5.4	18.0
SFO offers a good visual fit to the measured data with randomly scattered residuals and a χ^2 error rate below 15%. Conclusion: use SFO to derive modelling endpoints.									

^a Biphasic models were fitted to the whole dataset, i.e. from 0 DAA. The whole dataset was time step normalised as per EFSA DegT50 guidance (2014).

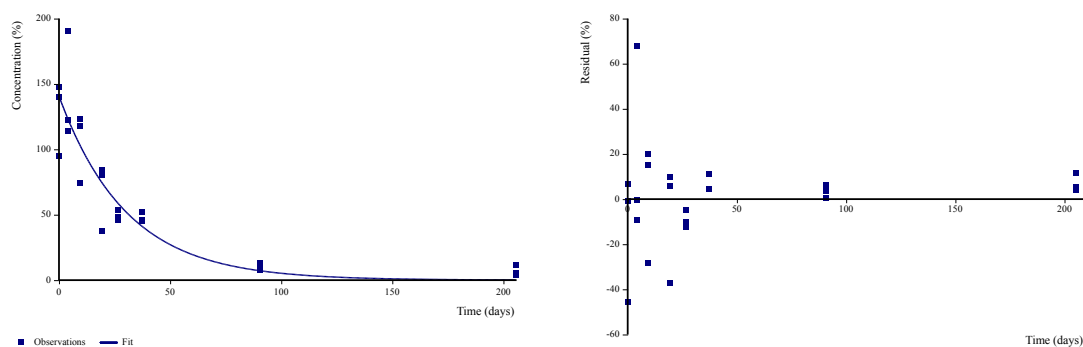


Figure 8.1.2.2.1/5-27: SFO model fit and residuals for (+)-enantiomer in New York soil.

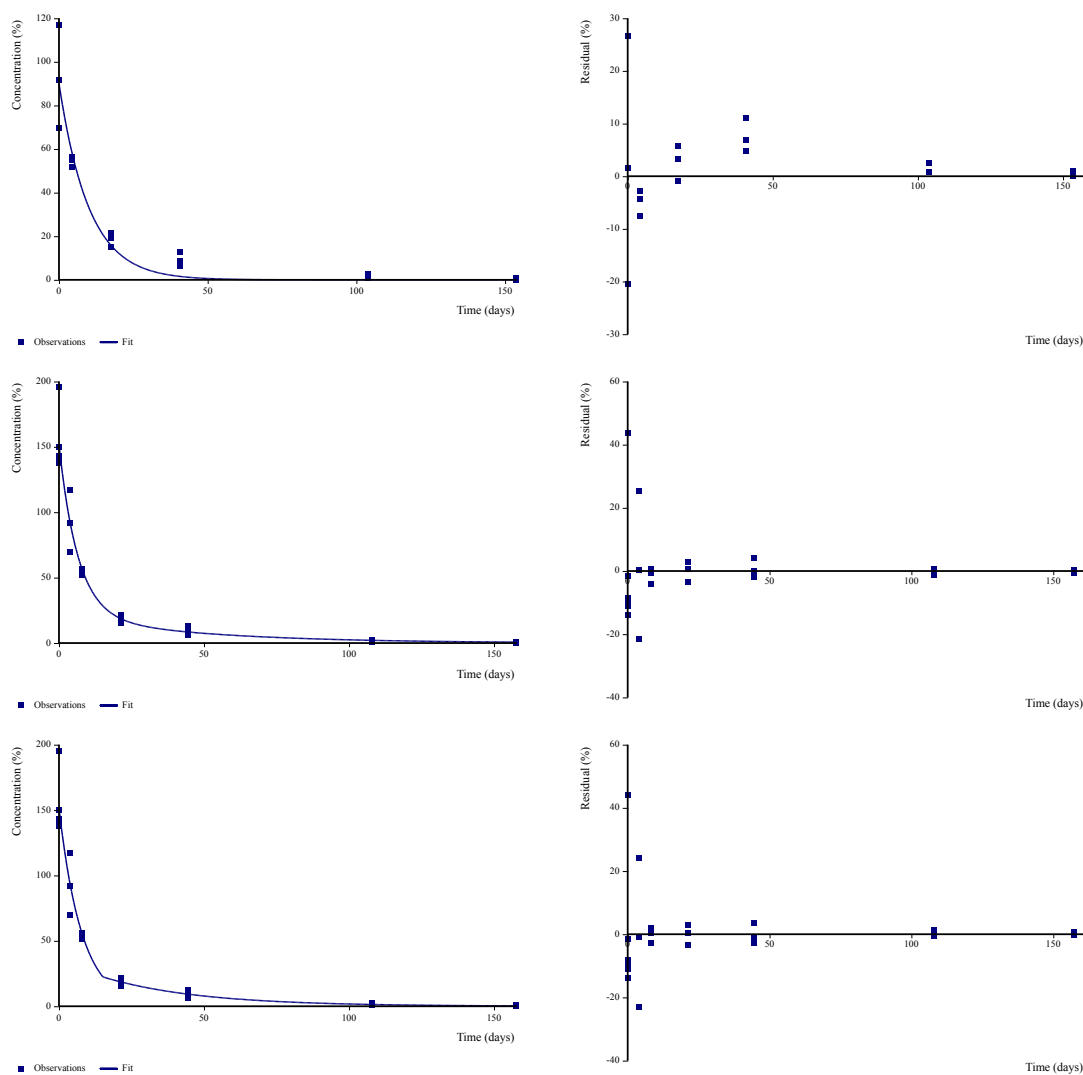


Figure 8.1.2.2.1/5-28: Model fits and residuals for (+)-enantiomer in North Carolina soil. Top row: SFO. Middle row: DFOP. Bottom row: HS. Final model fit: SFO.

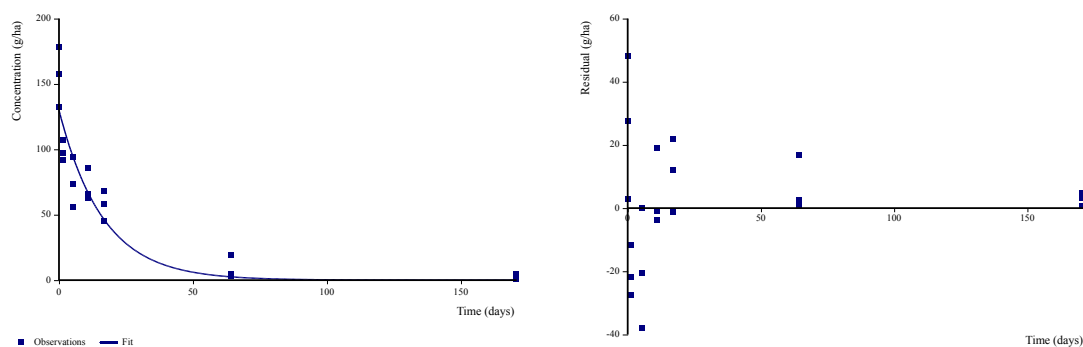


Figure 8.1.2.2.1/5-29: SFO model fit and residuals for (+)-enantiomer in Texas soil.

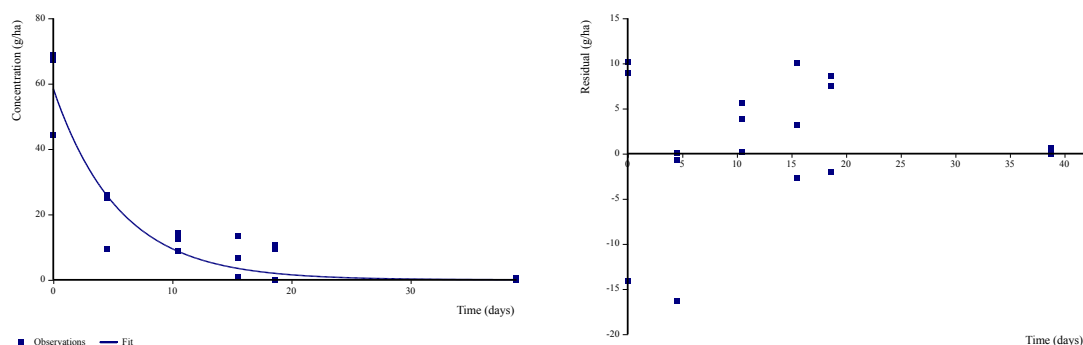


Figure 8.1.2.2.1/5-30: SFO model fit and residuals for (+)-enantiomer in Washington soil.

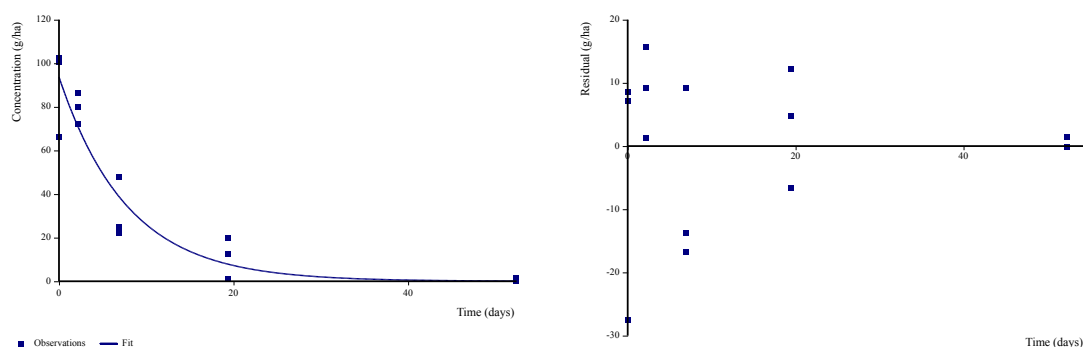


Figure 8.1.2.2.1/5-31: SFO model fit and residuals for (+)-enantiomer in California soil.

Modelling Conclusion

Kinetic evaluations were performed to analyse the degradation kinetics of cinmethylin and its two enantiomers observed in five of the six US field dissipation soils according to the current EFSA guidance for using legacy studies to derive DegT50 values for modelling endpoints. For all models considered appropriate, the visual assessment and goodness-of-fit statistics indicate plausible fit. The t-test was passed for the respective model parameters. Therefore, the resulting endpoints can be considered reliable.

Modelling endpoints are summarised in Tables 8.1.2.2.1/5-46-48 in the Summary section. For cinmethylin overall, DegT50s ranged 3.7 to 19.2 days. The (-)-enantiomer displayed shorter DegT50s than the (+)-enantiomer, with the respective ranges being 3.5 to 17.3 days and 3.8 to 21.1 days.

The HSE evaluator notes that the formal modelling endpoint report was supplied after modelling endpoints were derived for field soils. However, the change in modelling endpoints

for the US soils did not alter the geomean initially derived by the HSE evaluator for the field soil modelling endpoint. As such, the geomean used subsequently for deriving predicted environmental concentrations (PECs) has not changed, and any subsequent conclusions have not changed.

GUIDELINE DEVIATIONS

- The North Carolina field study was terminated at 93 DALA due to severe flooding of the field site caused by Hurricane Matthew. This meant the Applicant had only seven sampling dates including 0 DALA; however, the HSE evaluator concludes this was not a problem due to the fast degradation of cinmethylin in the North Carolina soils;
- For the North Dakota site, 90 DALA soil samples were collected at 180 DALA due to frozen field conditions;
- For the Texas site, analysis of 60 DALA samples from the 3-6 inch (7.6-15.2 cm) depth did not take place due to inadvertent oversight. To handle this, the Applicant assumed the worst-case scenario and applied residue levels detected at the same depth at 30 DALA.

The HSE evaluator accepts the decisions made by the Applicant and concludes these did not significantly affect the results of the field study.

Additionally, there was one noted GLP deviation. Some sample weights that were meant to be collected during soil homogenisation were not able to be recovered from the electronic system used to record them. The Applicant stated this constituted a loss of raw data; however, these data were recorded by personnel during homogenisation and were recovered. The HSE evaluator does not feel that this affected the studies.

CONCLUSIONS

Residues of cinmethylin remained primarily in the 0-15 cm depth throughout the study at all six field sites. The HSE evaluator notes that two replicates (one in New York, one in North Dakota) showed residues at up to 30 cm depth; however, all mean residues (average of three replicates) beyond the 15 cm soil depth were < LOD. Continuous monitoring of soil moisture throughout the sampled soil profile showed generally favourable leaching conditions at all sites; therefore, the Applicant concluded that cinmethylin is not inherently mobile. The Applicant also concluded that leaching did not contribute to dissipation at any site, based on analysing soil until a residue-free depth was observed at every sampling interval. The HSE evaluator agrees with this conclusion.

The degradation of cinmethylin and its two enantiomers was assessed through kinetic evaluation to derive both trigger and modelling endpoints. Table 8.1.2.2.1/5-46 summarises the trigger assessments, while Table 8.1.2.2.1/5-47 summarises the modelling endpoints. The HSE evaluator notes that the summary tables do not include the North Dakota field site; this is because the field site was deemed not relevant to European conditions in an Ecoregion similarity study (see KCA 7.1.2.2.1/9, Jeffries and Warren, 2018a).

The longest DT₉₀ derived from the trigger endpoints was 179.2 days for cinmethylin; therefore, accumulation studies were not triggered for this active substance.

For cinmethylin, DT₅₀s ranged 2.5 – 53.9 days and DT₉₀s ranged 18.2 – 179.2 days. For the (-)-enantiomer, DT₅₀s ranged 2.5 – 47.7 days and DT₉₀s ranged 18.2 – 158.5 days. Dissipation of the (+)-enantiomer was longer than for the (-)-enantiomer, with DT₅₀s ranging 2.6 – 60.2 days and DT₉₀s ranging 18.9 – 200.1 days.

Table 8.1.2.2.1/5-46: Summary of trigger endpoints calculated for the six US soils used to study the dissipation of cinmethylin and its two enantiomers in field conditions.

cinmethylin – Aerobic conditions							
Soil type	Location	pH (CaCl ₂) ^a	Depth (cm)	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Model
Niagara (bare soil)	New York	5.1	0-45	14.9	170.9	9.4	DFOP
Wickham (bare soil)	North Carolina	5.6	0-15	4.2	18.2	3.3	FOMC
Pullman (bare soil)	Texas	6.8	0-30	53.9	179.2	15.7	SFO
Quincy (bare soil)	Washington	7.6	0-15	2.5	20.5	8.4	FOMC
Nord (bare soil)	California	7.7	0-30	12.9	42.7	19.9	SFO
Maximum				53.9			
pH dependence				No			
(-) enantiomer (Reg. No. 5925581) – Aerobic conditions							
Soil type	Location	pH (CaCl ₂) ^a	Depth (cm)	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Model
Niagara (bare soil)	New York	5.1	0-45	12.2	147.1	8.0	DFOP
Wickham (bare soil)	North Carolina	5.6	0-15	4.2	18.2	3.3	FOMC
Pullman (bare soil)	Texas	6.8	0-30	47.7	158.5	15.8	SFO
Quincy (bare soil)	Washington	7.6	0-15	2.5	18.4	7.1	FOMC
Nord (bare soil)	California	7.7	0-30	12.5	41.4	19.2	SFO
Maximum				47.7			
pH dependence				No			
(+) enantiomer (Reg. No. 5925632) – Aerobic conditions							
Soil type	Location	pH (CaCl ₂) ^a	Depth (cm)	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Model
Niagara (bare soil)	New York	5.1	0-45	17.8	193.4	11.2	DFOP
Wickham (bare soil)	North Carolina	5.6	0-15	4.4	18.9	3.0	FOMC
Pullman (bare soil)	Texas	6.8	0-30	60.2	200.1	15.6	SFO
Quincy (bare soil)	Washington	7.6	0-15	2.6	22.9	9.6	FOMC
Nord (bare soil)	California	7.7	0-30	13.2	44.0	17.2	SFO
Maximum				60.2			
pH dependence				No			

^a Soil pH is the mean of the pH measured for all relevant soil depths, converted from pH-H₂O to pH-CaCl₂ using the equation reported in EFSA PECsoil guidance (2017). Relevant soil depths are based upon the depths at which cinmethylin residues were detected, plus the following soil depth.

Table 8.1.2.2.1/5-47: Summary of modelling endpoints calculated for five of the six US soils used to study the dissipation of cinmethylin and its two enantiomers in field conditions. Data were time-step normalised and adjusted to only account for sampling points that occurred after 10 mm of precipitation and irrigation had fallen.

cinmethylin – Aerobic conditions							
Soil type	Location	pH (CaCl ₂) ^a	Depth (cm)	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Model
Niagara (bare soil)	New York	5.1	0-45	19.2	63.8	9.7	SFO
Wickham (bare soil)	North Carolina	5.6	0-15	6.7	22.4	10.5	SFO
Pullman (bare soil)	Texas	6.8	0-30	9.9	33.1	18.4	SFO
Quincy (bare soil)	Washington	7.6	0-15	3.7	12.2	16.0	SFO
Nord (bare soil)	California	7.7	0-30	5.2	17.3	9.9	SFO
Geomean				7.5			
pH dependence				No			
(-) enantiomer (Reg. No. 5925581) – Aerobic conditions							
Soil type	Location	pH (CaCl ₂) ^a	Depth (cm)	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Model
Niagara (bare soil)	New York	5.1	0-45	17.3	57.5	7.9	SFO
Wickham (bare soil)	North Carolina	5.6	0-15	6.5	21.6	10.0	SFO
Pullman (bare soil)	Texas	6.8	0-30	8.7	28.9	18.5	SFO
Quincy (bare soil)	Washington	7.6	0-15	3.5	11.7	15.6	SFO
Nord (bare soil)	California	7.7	0-30	5.0	16.6	9.7	SFO
Geomean				7.0			
pH dependence				No			
(+) enantiomer (Reg. No. 5925632) – Aerobic conditions							
Soil type	Location	pH (CaCl ₂) ^a	Depth (cm)	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Model
Niagara (bare soil)	New York	5.1	0-45	21.1	70.0	11.4	SFO
Wickham (bare soil)	North Carolina	5.6	0-15	7.0	23.2	11.0	SFO
Pullman (bare soil)	Texas	6.8	0-30	11.5	37.6	18.3	SFO
Quincy (bare soil)	Washington	7.6	0-15	3.8	12.7	16.3	SFO
Nord (bare soil)	California	7.7	0-30	5.4	18.0	10.5	SFO
Geomean				8.1			
pH dependence				No			

^a Soil pH is the mean of the pH measured for all relevant soil depths, converted from pH-H₂O to pH-CaCl₂ using the equation reported in EFSA PECsoil guidance (2017). Relevant soil depths are based upon the depths at which cinmethylin residues were detected, plus the following soil depth.

Report:	KCA 7.1.2.2.1/6; Stewart, L. (2016b)
Title	Cinmethylin - Comparison of Extraction Methods to Extract [¹⁴ C]-Cinmethylin (Reg. No. 900202) from Soil.
Document No.:	2016/1134753
Guidelines:	<ul style="list-style-type: none"> • OECD Guidelines for the testing of chemicals, Aerobic Degradation in Soil, Document 307 (April 2002) • US EPA OPPTS Guidelines 835.4100, Anaerobic Soil Metabolism, (October 2008) • GLP of Japanese Ministry of Agriculture, Forestry and Fisheries, 12 Nosan, Notification No.8147, Agriculture Production Bureau, 24 November 2000
GLP:	Yes
Deviations	None
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The aim of this study was to investigate the extractability of cinmethylin residues from soil. Two different extraction procedures were applied: the extraction procedure according to the residue analytical method L0308/01 (KCA 4.1.2/001, Ertunc et al., 2017); and the extraction procedure used in the aerobic soil degradation study (KCA 7.1.1.1/1. Stewart and Abernethy, 2016a).

METHODS

Samples containing residues of cinmethylin were taken from the aerobic soil degradation study in which cinmethylin was applied in two radiolabelled forms ([cyclohexane-4-¹⁴C]-cinmethylin and [benzyl-U-¹⁴C]-cinmethylin; KCA 7.1.1.1/1; Stewart and Abernethy, 2016a). The selection criterion for the soil samples was the occurrence of minor unknown metabolites (< 5% AR) as well as the active substance cinmethylin. All soil samples were derived from soil Lufa 2.2 and stored at -20°C when not in use. Prior to extraction, soil samples were removed from the freezer and allowed to equilibrate to room temperature. Selected soil samples were extracted by applying both extraction procedures, as summarised below.

1. Residue extraction method

Soil samples were sequentially extracted, once with 200 mL acetonitrile and once with a 200 mL mixture of acetonitrile:water (60:40, v/v) on a horizontal shaker at 200 strokes per min for 30 minutes. After each extraction step, samples were centrifuged at 3000 rpm for 15 minutes. The supernatants were decanted into a 500 mL amber jar and the final volume was adjusted to 410 mL. From this, duplicate aliquots of 1 mL each were taken and analysed by liquid scintillation counting (LSC).

2. Aerobic degradation study extraction method

Soil samples were sequentially extracted four times: once using 200 mL acetonitrile, two times with a 200 mL mixture of acetonitrile:water (80:20, v/v), and once with a 200 mL mixture of acetonitrile:water (50:50, v/v) on an end-over-end shaker for 30 minutes. After each extraction step, the sample was centrifuged at 3,000 rpm for 15 minutes. The supernatants from the first and second extraction were decanted into a 500 mL amber jar, made to volume of 450 mL with acetonitrile (Extract 1). The supernatants from the third and fourth extraction were decanted into a 500 mL amber jar, and the final volume was adjusted to 450 mL with acetonitrile (Extract 2). Duplicate aliquots (1 mL) of each extract were analysed by LSC.

HPLC analysis workup

For the samples extracted using method 2, a 50 mL sub-sample of Extract 1 and Extract 2 were combined, and duplicate aliquots were analysed by LSC. Prior to HPLC analysis, combined extracts (method 2) and Extract 1 (method 1) were concentrated. The combined extract (30 mL cyclohexane labelled samples, 40 mL benzyl labelled samples) was concentrated to 5 mL in a centrifuge tube under a stream of nitrogen gas. The sample was thoroughly mixed using a vortex mixer, sonicated, and transferred to an LSC vial. The centrifuge tube was then rinsed with 0.5 mL of acetonitrile, thoroughly mixed using a vortex mixer and sonicated. The rinse liquid was then transferred to the LSC vial containing the sample. Duplicate aliquots (0.1 mL) were analysed by LSC to determine procedural recovery and level of radioactivity. Procedural recoveries ranged from 98-102%. Concentrated extracts were then analysed by radio-HPLC.

The LSC limit of quantification (LOQ) was set to $\leq 0.1\%$ AR and the radio-HPLC LOQ was set to $\leq 0.8\%$ AR.

RESULTS

The extraction efficiency (LSC) and the extracted amount of cinmethylin and its soil metabolites (radio-HPLC) were determined for both extraction methods. One of the methods was applied in the aerobic soil degradation study (method 1) and the other is used for residue analysis of cinmethylin (method 2). Results below provide information on the overall extractability of the radiolabelled material and the quantification of cinmethylin and its potential metabolites in the extracts. In the present study, the measured radioactivity was set in relation to the total applied radioactivity (=100% AR) in the respective soil metabolism/degradation study.

Extractability of radioactive residues

The total extractability of radioactive residues was in the range of 45.5 to 65.6% AR for the different samples and extractions. The extractability of radioactivity was very similar for both methods (Table 8.1.2.2.1/6-1). For both methods, extractability was higher in 59 DAT samples (58.5-65.6%) than in 120 DAT samples (45.2-48.2%). The results are similar to those from the aerobic degradation study, results for which are presented in Table 8.1.2.2.1/6-2. In the aerobic degradation study, the amount of radioactivity extracted from the soil samples was again higher in 59 DAT samples (58.1-63.8%) than in 120 DAT samples (49.4-53.0%).

Table 8.1.2.2.1/6-1: Summary of the extractability of cinmethylin from soil Lufa 2.2 using soil samples derived from the aerobic soil degradation study (KCA 7.1.1.1/1).

Label	DAT ^a	Extraction method	Extract (% AR)	Extraction efficiency ^b (%)	Cinmethylin (% AR)	Sum of minor unknowns ^c (% AR)
Benzyl	59	Residue	58.5	89.2	54.3	4.2
Cyclohexane		Aerobic	65.6	100.0	63.3	2.3
Benzyl	120	Residue	45.5	94.4	43.1	2.4
Cyclohexane		Aerobic	48.2	100.0	45.1	3.1

^a Referring to the original study

^b Extraction efficiency of samples from this study when related to samples from aerobic soil degradation study (mean of replicates)

^c Sum of minor unknown components, none of which individually accounts for >1.5% AR

Table 8.1.2.2.1/6-2: Extractability of cinmethylin from soil Lufa 2.2 as obtained in the soil degradation study (KCA 7.1.1.1/1).

Label	DAT ^a	Extraction method	Extract (% AR)	Extraction efficiency ^b (%)	Cinmethylin (% AR)	Sum of minor unknowns ^c (% AR)
Benzyl	59	Residue	58.5	98.5	54.3	4.2
		Aerobic	60.7		58.5	2.2
			58.1		53.6	4.4
Cyclohexane			Aerobic	65.6	104.8	63.3
		61.4		59.4		2.0
		63.8		62.3		1.5
Benzyl	120	Residue	45.5	90.6	43.1	2.4
		Aerobic	50.9		40.0	10.8
			49.4		45.3	4.1
Cyclohexane			Aerobic	48.2	93.6	45.1
		50.0		43.7		6.3
		53.0		50.9		2.1

^a Referring to the original study

^b Extraction efficiency of samples from this study when related to samples from aerobic soil degradation study (mean of replicates)

^c Sum of minor unknown components, none of which individually accounts for >3.0% AR

Identification and quantification of radioactive residues

The results of the HPLC analyses are presented in Table 8.1.2.2.1/6-1. The Applicant supplied sample chromatograms of concentrated soil extracts. The Applicant stated that the most prominent peak in all extracts consisted of the parent compound (cinmethylin). The identity of cinmethylin was verified by retention time comparison of the ¹⁴C-signals of the quantitative radio-HPLC analyses with those of the unlabelled reference item. The HSE evaluator agrees with this summary.

Cinmethylin was detected in amounts ranging 43.1-63.3% AR in the different samples and extractions. Minor metabolites were detected only in low amounts, accounting for ≤ 1.5% AR. HPLC analysis of the soil extracts revealed very similar results for the two different extraction methods and these results are in accordance with the respective aerobic soil degradation study. Results are presented in Table 8.1.2.2.1/6-2.

CONCLUSION

Both the extraction method used in the aerobic degradation study and the method applied in the soil residue analytical method showed very similar results regarding the extractability of cinmethylin. Extraction efficiency of the residue extraction method (method 2) is in the range 89.2-94.4% when compared to the aerobic degradation method (method 1). When comparing extraction efficiency of the samples extracted using the residue method compared to the original aerobic degradation study samples, the range is 90.6-98.5%. The HSE evaluator agrees that the two extraction methods showed very similar results.

Report:	KCA 7.1.2.2.1/7; Bodsch, 2017a
Title	Determination of the Storage Stability of the BAS 684 H racemate in Soil
Document No.:	2017/1202195
Guidelines:	<ul style="list-style-type: none"> • Chemikaliengesetz, Anhang 1 zu § 19 a Abs. 1 ChemG in the valid version • OECD Principles on Good Laboratory Practice, ENV/MC/CHEM(98)17, Paris 1998 • Storage stability of Residue Samples, EC doc. 7032/VI/95-rev.5, Appendix H, (22/7/97) • Laboratory procedural recovery specimens: SANCO/3029/99 rev. 4 (11/07/00) • OECD 506, OECD Guideline for testing of chemicals, Stability of Pesticide Residues in Stored Commodities • US EPA. Residue Chemistry Test Guidelines. OPPTS 860.1380, Storage Stability Data, Aug. 1996
GLP:	Yes
Deviations	<ul style="list-style-type: none"> • Cinmethylin (+) (Reg. No. 5925632) had a chemical purity of 92.7%. The HSE evaluator does not deem this to have significantly affected the study outcome. • For 32.5 hours of the storage period, the storage temperature increased from an average of -24.6°C to -11.4°C. The Applicant reported that the samples remained “deep frozen” throughout, therefore, no negative impact was expected. The HSE evaluator agrees; • The extract stability for soils from Germany and Italy could not be measured by using 0 DAT specimens due to technical problems. Instead, for Germany the freshly fortified specimens for 14 DAT were remeasured after 17 days, and for Italy the 120 DAT samples were remeasured after 31 days. The Applicant considered this to have had no impact on the study; the HSE evaluator agrees.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The storage stability of cinmethylin (both enantiomers) was determined in soils collected as part of the Europe field dissipation study (KCA 7.1.2.2.1/1; Gut, 2017b). Stability was determined for each enantiomer in six soils: Germany, Italy, Denmark, United Kingdom, Belgium and Spain over a period of 715 or 717 days.

METHODS

Untreated soils were transported under ambient conditions to the test facility where they were stored refrigerated until further processing.

An amount corresponding to a dry weight of approximately 10 g of the untreated control specimens were weighed into 50 mL centrifuge tube. 100 µL of the fortification solution containing both analytes at a concentration of approx. 5 µg/mL in acetonitrile was added. After preparation, the specimens were stored deep frozen at $\leq -18^{\circ}\text{C}$, except the 0 DAT specimens which were prepared for analysis immediately. Control specimens without treatment were also deep frozen and used as control and fortification samples at sampling. Samples were stored at an average of -24.6°C throughout the stability study. The Applicant

notes that for 32.5 hours a temperature deviation occurred where the highest observed storage temperature was -11.4°C; however they reported that the specimens remained deep frozen. As such, the Applicant did not expect a negative impact on the study and the HSE evaluator agrees with this.

The test was carried out in 12 analytical assays per soil at the time intervals of 0, 7, 14, 30, 60, 90, 120, 180, 240, 360, 480 and 720 days after the preparation of the specimens (DAT). The HSE evaluator notes that the study duration is suitable as the longest storage period for a field sample was 545 days.

On the day of analysis, a sample analysis set was prepared comprising two freshly fortified samples per enantiomer (fortified to 0.005 and 0.05 mg/kg_{dry soil}), two previously fortified storage stability samples (fortified to 0.05 mg/kg_{dry soil}), and one control specimen.

Samples were prepared for analysis via LC-MS/MS generally using the procedures described in KCA 4.1.2/001 (Ertunc et al., 2017). The HSE evaluator notes that these methods have been evaluated separately and are the same as those used in the field dissipation study from which these storage stability samples derived (KCA 7.1.2.2.1/2, Gut, 2017a). The Applicant identified the following deviations from the published method; these applied to both the field study and storage stability study:

- Samples comprised 10 g soil + 20 mL extraction solution + 20 mL extraction solution (instead of 5 g + 10 mL + 10 mL);
- Extracts were centrifuged for 5 minutes at 10°C and 15000 rpm (instead of 10 minutes minimum at 20°C at 4000 rpm);
- Injection volume was 25 µL (instead of 50 µL).

The Applicant stated that these method deviations did not impact upon the study as the deviations were validated in the method validation (KCA 4.1.2/1; Ertunc et al., 2017a). The HSE evaluator agrees with this.

The limit of quantitation (LOQ) and method limit of detection (LOD) is 5 and 1.5 µg/kg, respectively. The soil samples were fortified at 50 µg/kg, which is 10 times the aforementioned LOQ.

RESULTS

The HSE evaluator has assessed the representative chromatograms provided by the Applicant and can confirm that the chromatograms do not suggest breakdown of cinmethylin took place while in freezer storage. There was no cinmethylin peak in the representative blank sample chromatograms, and the Applicant stated that no residues of either enantiomer were found above the LOD in untreated samples.

Analytical method validity

The Applicant proved accuracy of the analytical method by simultaneous analysis of two freshly prepared fortified specimens from each matrix on each date of analysis. The fortification level was the same as for the storage stability specimens, except 360 DAT events of trial Denmark and Spain, where a 0.5 mg/kg spiking solution was erroneously used. Results are presented in Table 8.1.2.2.1/7-01; mean recovery rates ranged 92-106% and were well within the SANCO guidance limits of 70-110% (SANCO/3029/99). Relative standard deviations (RSD) ranged 2.7-7.1%. The HSE evaluator concludes the analytical method used is valid.

Table 8.1.2.2.1/7-01: Summary of recoveries for freshly fortified soils from all six field sites and each enantiomer.

	Nominal fortification level (mg/kg)	No. fortified specimens	Mean recovery (%)	Relative standard deviation (%)
Germany				
Reg. No. 5925581 (-)	0.005	12	98	3.5
	0.05	12	101	4.7
Reg. No. 5925632 (+)	0.005	12	99	4.9
	0.05	12	100	4.3
Italy				
Reg. No. 5925581 (-)	0.005	12	103	3.8
	0.05	12	103	3.4
Reg. No. 5925632 (+)	0.005	12	101	4.0
	0.05	12	104	3.2
Denmark				
Reg. No. 5925581 (-)	0.005	12	99	3.8
	0.05	11	101	3.5
	0.5	1	104	N/A
Reg. No. 5925632 (+)	0.005	12	96	5.5
	0.05	11	101	2.8
	0.5	1	106	N/A
United Kingdom				
Reg. No. 5925581 (-)	0.005	12	101	3.4
	0.05	12	103	3.7
Reg. No. 5925632 (+)	0.005	12	100	2.7
	0.05	12	102	3.8
Belgium				
Reg. No. 5925581 (-)	0.005	12	102	3.3
	0.05	12	103	3.5
Reg. No. 5925632 (+)	0.005	12	104	3.3
	0.05	12	102	5.4
Spain				
Reg. No. 5925581 (-)	0.005	12	93	6.9
	0.05	11	92	3.8
	0.5	1	98	N/A
Reg. No. 5925632 (+)	0.005	12	93	7.1
	0.05	11	93	4.1
	0.5	1	95	N/A

N/A = Not applicable due to sample n = 1

Residue stability

The storage stability of (-)-cinmethylin and (+)-cinmethylin in soil at $\leq -18^{\circ}\text{C}$ was determined in spiked specimens which were stored for and analysed at certain time periods.

The uncorrected recovery values in percent of each enantiomer over the whole storage period are presented per field trial site below. All individual sample recoveries were within the required range of 70-120%.

Germany

Following frozen storage, sample recoveries ranged 86-109% with a mean of 98% overall (Table 7.1.2.2.1/7-02). The HSE evaluator confirms there is no trend of declining recoveries over storage time.

Table 8.1.2.2.1/7-02: Stability of residues of cinmethylin in Germany soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Time [days]											
	0	7	14	31	60	90	119	178	238	360	479	717
Reg. No. 5925581	108	103	103	102	100	98	97	91	96	86	95	91
[%]	108	102	100	100	99	101	94	91	93	88	95	88
Mean value [%]	108	102	101	101	100	100	96	91	94	87	95	89
Reg. No. 5925632	105	105	100	103	102	100	98	91	94	92	100	92
[%]	109	104	101	101	99	102	100	91	98	88	102	92
Mean value [%]	107	105	100	102	101	101	99	91	96	90	101	92

Italy

Following frozen storage, sample recoveries ranged 91-110% with a mean of 101% overall (Table 8.1.2.2.1/8-03). The HSE evaluator confirms there is no trend of declining recoveries over storage time.

Table 8.1.2.2.1/7-03: Stability of residues of cinmethylin in Italy soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Time [days]											
	0	7	14	31	60	90	119	178	238	360	479	717
Reg. No. 5925581	110	106	104	102	107	105	98	91	98	93	99	97
[%]	108	104	103	103	102	104	100	92	99	94	99	99
Mean value [%]	109	105	103	103	104	105	99	92	99	94	99	98
Reg. No. 5925632	109	100	106	100	108	103	102	96	98	95	99	98
[%]	106	101	102	101	107	106	103	94	98	94	99	98
Mean value [%]	108	101	104	100	107	104	103	95	98	95	99	98

Denmark

Following frozen storage, sample recoveries ranged 90-105% with a mean of 98% overall (Table 8.1.2.2.1/8-04). The HSE evaluator confirms there is no trend of declining recoveries over storage time.

Table 8.1.2.2.1/7-04: Stability of residues of cinmethylin in Denmark soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Time [days]											
	0	7	14	31	59	90	120	178	237	357	479	715
Reg. No. 5925581	102	103	101	94	101	97	100	95	93	100	94	96
[%]	103	103	100	97	102	96	101	98	94	98	98	90
Mean value [%]	102	103	101	96	101	97	100	96	93	99	96	93
Reg. No. 5925632	100	104	99	98	101	97	98	96	93	99	96	97
[%]	105	101	100	95	104	98	99	96	92	96	97	99
Mean value [%]	103	103	100	96	103	97	99	96	92	97	97	98

United Kingdom

Following frozen storage, sample recoveries ranged 91-108% with a mean of 100% overall (Table 8.1.2.2.1/8-05). The HSE evaluator confirms there is no trend of declining recoveries over storage time.

Table 8.1.2.2.1/7-05: Stability of residues of cinmethylin in United Kingdom soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Time [days]											
	0	7	14	31	59	90	120	178	237	357	479	715
Reg. No. 5925581	102	108	103	107	105	100	98	104	94	95	98	100
[%]	103	104	103	104	98	98	102	101	92	96	100	99
Mean value [%]	103	106	103	106	102	99	100	102	93	95	99	100
Reg. No. 5925632	98	104	105	106	103	99	97	104	93	91	97	99
[%]	104	102	106	106	98	97	98	101	91	99	101	102
Mean value [%]	101	103	105	106	101	98	98	102	92	95	99	101

Belgium

Following frozen storage, sample recoveries ranged 89-109% with a mean of 100% overall (Table 8.1.2.2.1/8-06). The HSE evaluator confirms there is no trend of declining recoveries over storage time.

Table 8.1.2.2.1/7-06: Stability of residues of cinmethylin in Belgium soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Time [days]											
	0	7	14	31	59	90	120	178	237	357	479	715
Reg. No. 5925581	105	106	100	105	103	98	101	98	93	99	98	94
[%]	104	107	104	102	103	100	102	98	96	98	93	94
Mean value [%]	104	106	102	103	103	99	102	98	94	98	96	94
Reg. No. 5925632	108	107	105	108	101	98	99	99	89	97	96	97
[%]	104	104	109	107	101	100	100	102	90	99	101	95
Mean value [%]	106	105	107	107	101	99	100	101	90	98	98	96

Spain

Following frozen storage, sample recoveries ranged 83-95% with a mean of 91% overall (Table 8.1.2.2.1/8-07). The HSE evaluator confirms there is no trend of declining recoveries over storage time.

Table 8.1.2.2.1/7-07: Stability of residues of cinmethylin in Spain soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Time [days]											
	0	7	14	31	59	90	120	178	237	357	479	715
Reg. No. 5925581	92	92	95	95	89	87	91	91	87	92	89	91
[%]	92	93	94	94	91	89	91	93	88	91	91	83
Mean value [%]	92	93	94	95	90	88	91	92	87	92	90	87
Reg. No. 5925632	94	92	94	95	89	88	90	94	85	91	88	90
[%]	94	91	93	95	93	88	92	93	88	91	88	83
Mean value [%]	94	91	93	95	91	88	91	94	87	91	88	86

Stability of cinmethylin in soil extracts

The Applicant also determined the stability of cinmethylin in soil extracts stored as a final volume solution in 80/20 acetonitrile/water. To establish stability, the Applicant stored final soil extracts from each of the six field sites in the dark at 2-8°C for between 7-31 days and analysed these according to the method. Samples were spiked either with 0.005 or 0.05 mg/kg. Table 8.1.2.2.1/7-08 summarises the results. The Applicant concluded that soil extracts are stable for at least 7 days in all soils.

Table 8.1.2.2.1/7-08: Stability of cinmethylin in soil extracts following refrigeration. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Field site	Analyte	Spiked concentration (mg/kg)	Recovery %
Germany (17 days)	Reg. No. 5925581	0.005	95
		0.05	97
	Reg. No. 5925632	0.005	105
		0.05	102
Italy (31 days)	Reg. No. 5925581	0.005	107
		0.05	109
	Reg. No. 5925632	0.005	99
		0.05	107
Denmark (7 days)	Reg. No. 5925581	0.005	96
		0.05	105, 104, 106
	Reg. No. 5925632	0.005	99
		0.05	103, 100, 106
United Kingdom (7 days)	Reg. No. 5925581	0.005	98
		0.05	109, 104, 106
	Reg. No. 5925632	0.005	98
		0.05	106, 99, 107
Belgium (7 days)	Reg. No. 5925581	0.005	104
		0.05	106, 104, 106
	Reg. No. 5925632	0.005	102
		0.05	107, 105, 105
Spain (7 days)	Reg. No. 5925581	0.005	93
		0.05	97, 92, 94
	Reg. No. 5925632	0.005	87
		0.05	91, 93, 93

CONCLUSION

The results from the storage stability study shows that cinmethylin is stable over a period of at least 715 days when stored in the dark at -18°C or below. Table 8.1.2.2.1/7-09 summarises residue recovery rates for both enantiomers at all six Europe field sites. The HSE evaluator highlights that the storage stability test sufficiently covered the sample storage periods reported for the European field dissipation study (KCA 7.1.2.2.1/1, Gut, 2017a). The longest time period from sampling to analysis (date of extraction o) of the field soil specimens was 545 days. The study has demonstrated no significant decline in recoveries related to storage duration, with < 10% reductions in recoveries between 0 and 720 DAT. The Applicant also determined that cinmethylin is stable in final extracts in a refrigerator for at least 7 days.

Table 8.1.2.2.1/7-09: Summary of stability of cinmethylin in six European soils following frozen storage. Recoveries are means (n = 2) and uncorrected for procedural recoveries.

Fortification Level (mg/kg)	Storage interval (days)	Mean Recovery (%)						Overall mean (% ± RSD)
		DE	IT	DK	UK	BE	ES	
(-) Enantiomer (Reg. No. 5925581)								
0.05	0	108	109	102	103	104	92	103 ± 6
	7 ± 1	102	105	103	106	106	93	103 ± 5
	14 ± 1	101	103	101	103	102	94	101 ± 3
	30 ± 2	101	103	96	106	103	95	100 ± 4
	60 ± 5	100	104	101	102	103	90	100 ± 5
	90 ± 2	100	105	97	99	99	88	99 ± 4
	120 ± 3	96	99	100	100	102	91	96 ± 4
	180 ± 3	91	92	96	102	98	92	93 ± 4
	240 ± 3	94	99	93	93	94	87	94 ± 4
	360 ± 5	87	94	99	95	98	92	94 ± 5
	480 ± 5	95	99	96	99	96	90	96 ± 3
720 ± 5	89	98	93	100	94	87	93 ± 5	
Mean		97	100	98	100	100	91	
(+) Enantiomer (Reg. No. 5925632)								
0.05	0	107	108	103	101	106	94	103 ± 5
	7 ± 1	105	101	103	103	105	91	101 ± 5
	14 ± 1	100	104	100	105	107	93	102 ± 5
	30 ± 2	102	100	96	106	107	95	101 ± 5
	60 ± 5	101	107	103	101	101	91	101 ± 5
	90 ± 2	101	104	97	98	99	88	98 ± 4
	120 ± 3	99	103	99	98	100	91	98 ± 4
	180 ± 3	91	95	96	102	101	94	92 ± 4
	240 ± 3	96	98	92	92	90	87	92 ± 5
	360 ± 5	90	95	97	95	98	91	94 ± 3
	480 ± 5	101	99	97	99	98	88	97 ± 5
720 ± 5	92	98	98	101	96	86	95 ± 5	
Mean		99	100	98	100	100	91	

DE = Germany. IT = Italy. DK = Denmark. UK = United Kingdom. BE = Belgium. ES = Spain.

Report:	KCA 7.1.2.2.1/8; Perez, S., and Jones, A. (2018a)
Title	Freezer storage stability of BAS 684 H (both enantiomers, Reg. Nos. 5925632 and 5925581) in soil
Document No.:	2018/7001858
Guidelines:	U.S. EPA Fate, Transport and Transformation Test Guidelines, OPPTS 835.6100 Terrestrial Field Dissipation OECD Guideline 506
GLP:	Yes
Deviations	<ul style="list-style-type: none"> Cinmethylin (-) (Reg. No. 5925581) had a chemical purity of 92.7%. The HSE evaluator does not deem this to have significantly affected the study outcome.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The purpose of this study was to determine the freezer storage stability of cinmethylin (both enantiomers) in soil. The freezer storage stability of these two analytes was studied in untreated control soil samples collected from the six US field locations used in the US field dissipation study (KCA 7.1.2.2.1/5; Mitchell et al., 2018a): New York (silt loam); North Carolina (sandy loam); North Dakota (clay); Texas (Clay loam); Washington (sand); California (sandy loam).

Storage stability was determined over a period of 12 months for all soils except for New York, for which stability was determined over 14 months.

METHODS

Untreated soil was shipped frozen from each of the six field site locations and stored at -25°C at the test facility. The HSE evaluator highlights that this transport and storage procedure is consistent with that used in the field dissipation study.

Untreated soils were weighed (5.0 ± 0.1 g each) and placed into plastic freezer bags. For stored fortified samples, each control soil sample was fortified with 100 µL of a standard solution containing one enantiomer of cinmethylin (-/+) prepared at a concentration of 2.5 ng/µL, giving a fortification level of 50 µg/kg. The other samples remained unfortified to use as control and procedural fortifications at the time of analysis. Procedural recoveries were fortified with 100 µL of a mixed standard solution containing both enantiomers of cinmethylin prepared at a concentration of 2.5 ng/µL, giving a fortification level of 50 µg/kg. Once fortified, soil samples were placed into frozen storage until analysis at the appropriate storage interval (0, 1, 3, 6, 12, (14) months).

On the day of analysis, an analysis set comprising two fortified samples per enantiomer, two procedural mixed fortification samples, and one control was removed from the freezer and allowed to equilibrate to room temperature. Procedural recovery samples were fortified to 50 µg/kg on the day of extraction.

Samples were prepared for analysis using the procedures described in KCA 4.1.2/001 (Ertunc et al., 2017). The HSE evaluator notes that these methods have been evaluated separately and are the same as those used in the US field dissipation study from which these storage stability samples derived. The limit of quantitation (LOQ) and method limit of detection (LOD) are 5 and 1.5 µg/kg, respectively. The soil samples were fortified at 50 µg/kg, which is 10 times the aforementioned LOQ.

RESULTS

The HSE evaluator has assessed the representative chromatograms provided by the Applicant and can confirm that the chromatograms do not suggest breakdown of cinmethylin took place while in freezer storage. There was no cinmethylin peak in the representative blank sample chromatograms, and the Applicant stated that no residues of either enantiomer were found above the LOD in untreated samples.

Concurrent recoveries

Concurrent recoveries were determined from soil samples spiked on the day of extraction and were generally between 70-120% (Table 8.1.2.2.1/8-01). The HSE evaluator notes that overall mean recovery was within an acceptable range.

Table 8.1.2.2.1/8-01: Summary of concurrent recoveries for all six field sites and each enantiomer as supplied by the Applicant.

State	Fortification Level (mg/kg)	n	Range of Recoveries	Overall Mean \pm %RSD
BAS 684 H (-)				
New York	50	10	83-107	97 \pm 8
North Carolina	50	10	82-106	95 \pm 8
North Dakota	50	10	90-(121)	100 \pm 9
Texas	50	10	81-(126)	95 \pm 15
Washington	50	10	77-104	96 \pm 8
California	50	10	88-109	101 \pm 7
BAS 684 H (+)				
New York	50	10	85-105	96 \pm 7
North Carolina	50	10	84-108	95 \pm 7
North Dakota	50	10	90-106	98 \pm 5
Texas	50	10	83-104	91 \pm 9
Washington	50	10	81-105	98 \pm 7
California	50	10	84-107	97 \pm 7

* Recoveries outside of the acceptance criteria are shown in parenthesis

The HSE evaluator notes that the New York soil also demonstrated high recoveries, though these were excluded by the Applicant. The HSE evaluator has included them in Table 8.1.2.2.1/8-02.

Residue stability

The data showed that the two cinmethylin enantiomers were stable in soil from the six field sites for at least 12 months, and in the case of the New York soil, 14 months, when stored frozen at approximately -25°C. The Applicant based their conclusion on stored recoveries corrected based on procedural recoveries; however, the HSE evaluator draws the same conclusion from the uncorrected recoveries for the stored samples. The HSE evaluator notes that one sample out of 120 demonstrated recovery just below 70%. Each field site is discussed in turn below.

New York

Following frozen storage, sample recoveries ranged 73-119.9% with a mean of 90% overall. The Applicant excluded the samples from the 3 month sampling time due to “high and out of trend” recoveries. The HSE evaluator notes that the procedural recoveries were high (exceeding 135%); however, the uncorrected stored sample recoveries were within the acceptable range and so have been included in the summary table below (Table 8.1.2.2.1/8-02). The HSE evaluator confirms there is no trend of declining recoveries over storage time and that the storage stability study covers the maximum storage duration of field dissipation study samples (395 days).

Table 8.1.2.2.1/8-02: Stability of residues of cinmethylin in New York soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Fortification Level (µg/kg)	Storage interval (days)	Storage interval (months)	% Recovery (mean)
(-) enantiomer	50	0	0	80, 79 (80)
		33	1	97, 96 (96)
		97	3	117, 120 (118)
		180	6	91, 93 (92)
		363	12	89, 89 (89)
		448	14	94, 97 (96)
(+) enantiomer	50	0	0	75, 73 (74)
		33	1	85, 82 (84)
		97	3	78, 102 (90)
		180	6	91, 89 (90)
		363	12	85, 88 (86)
		448	14	84, 87 (86)

North Carolina

Following frozen storage, sample recoveries ranged 69-101% with a mean of 85% overall (Table 8.1.2.2.1/8-03). The HSE evaluator confirms there is no trend of declining recoveries over storage time and that the storage stability study covers the maximum storage duration of field dissipation study samples (140 days).

Table 8.1.2.2.1/8-03: Stability of residues of cinmethylin in North Carolina soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Fortification Level (µg/kg)	Storage interval (days)	Storage interval (months)	% Recovery (mean)
(-) enantiomer	50	0	0	82, 81 (81)
		33	1	101, 101 (101)
		97	3	74, 73 (74)
		180	6	90, 93 (91)
		363	12	92, 93 (93)
(+) enantiomer	50	0	0	78, 77 (78)
		33	1	83, 83 (83)
		97	3	69, 77 (83)
		180	6	89, 85 (87)
		363	12	89, 90 (90)

North Dakota

Following frozen storage, sample recoveries ranged 79-100% with a mean of 90% overall (Table 8.1.2.2.1/8-04). The HSE evaluator confirms there is no trend of declining recoveries over storage time and that the storage stability study covers the maximum storage duration of field dissipation study samples (299 days).

Table 8.1.2.2.1/8-04: Stability of residues of cinmethylin in North Dakota soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Fortification Level (µg/kg)	Storage interval (days)	Storage interval (months)	% Recovery (mean)
(-) enantiomer	50	0	0	87, 84 (85)
		32	1	99, 100 (99)
		96	3	87, 85 (86)
		179	6	94, 96 (95)
		362	12	99, 98 (98)
(+) enantiomer	50	0	0	79, 81 (80)
		32	1	86, 86 (86)
		96	3	80, 92 (86)
		179	6	89, 93 (91)
		362	12	94, 95 (94)

Texas

Following frozen storage, sample recoveries ranged 70-93% with a mean of 83% overall (Table 8.1.2.2.1/8-05). The HSE evaluator confirms there is no trend of declining recoveries over storage time and that the storage stability study covers the maximum storage duration of field dissipation study samples (288 days).

Table 8.1.2.2.1/8-05: Stability of residues of cinmethylin in Texas soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Fortification Level (µg/kg)	Storage interval (days)	Storage interval (months)	% Recovery (mean)
(-) enantiomer	50	0	0	80, 81 (80)
		32	1	86, 88 (87)
		96	3	80, 82 (81)
		180	6	86, 89 (88)
		363	12	93, 93 (93)
(+) enantiomer	50	0	0	70, 71 (71)
		32	1	77, 75 (76)
		96	3	76, 78 (77)
		180	6	87, 92 (90)
		363	12	91, 88 (89)

Washington

Following frozen storage, sample recoveries ranged 72-99% with a mean of 85% overall (Table 8.1.2.2.1/8-06). The HSE evaluator confirms there is no trend of declining recoveries over storage time and that the storage stability study covers the maximum storage duration of field dissipation study samples (300 days).

Table 8.1.2.2.1/8-06: Stability of residues of cinmethylin in Washington soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Fortification Level (µg/kg)	Storage interval (days)	Storage interval (months)	% Recovery (mean)
(-) enantiomer	50	0	0	86, 90 (88)
		31	1	99, 93 (96)
		95	3	78, 82 (80)
		179	6	91, 84 (87)
		362	12	95, 94 (94)
(+) enantiomer	50	0	0	75, 77 (76)
		31	1	83, 79 (81)
		95	3	72, 77 (74)
		179	6	84, 85 (85)
		362	12	86, 87 (86)

California

Following frozen storage, sample recoveries ranged 75-99% with a mean of 86% overall (Table 8.1.2.2.1/8-07). The HSE evaluator confirms there is no trend of declining recoveries over storage time and that the storage stability study covers the maximum storage duration of field dissipation study samples (300 days).

Table 8.1.2.2.1/8-07: Stability of residues of cinmethylin in California soils following frozen storage. Recoveries are shown for individual replicates and are uncorrected for procedural recoveries.

Analyte	Fortification Level (µg/kg)	Storage interval (days)	Storage interval (months)	% Recovery (mean)
(-) enantiomer	50	0	0	84, 82 (83)
		31	1	99, 92 (95)
		95	3	81, 79 (80)
		179	6	90, 90 (90)
		362	12	92, 96 (94)
(+) enantiomer	50	0	0	75, 75 (75)
		31	1	88, 88 (88)
		95	3	76, 78 (77)
		179	6	91, 90 (91)
		362	12	87, 92 (90)

Stability of cinmethylin in soil extracts

The Applicant also determined the stability of cinmethylin in soil extracts stored as a final volume solution in 80/20 acetonitrile/water. To establish stability, the Applicant reserved final volume extracts (initial and final volume extracts are considered equivalent) from a control sample and two recovery samples spiked at 50 µg/kg that had been refrigerated were prepared at the final volume stage and analysed according to the method. Quantification of each analyte in the stored samples was performed using only primary ion transition for quantitation. The results showed that cinmethylin is stable in final extracts for at least the time period tested, which was 182 days.

CONCLUSION

The results from freezer stability study shows that cinmethylin is relatively stable (>70%) while

stored in soil samples at a temperature of -25°C for a duration of approximately 12 months, or 14 months for the New York site. Table 8.1.2.2.1/8-08 summarises residue recovery rates for both enantiomers at all six US field sites. The HSE evaluator highlights that the storage stability test sufficiently covered the sample storage periods reported for the US field dissipation study (KCA 7.1.2.2.1/5, Mitchell et al., 2018a). The study has demonstrated no decline in recoveries related to storage duration. The Applicant also determined that cinmethylin is stable in final extracts in a refrigerator for at least 182 days.

Table 8.1.2.2.1/8-08: Summary of stability of cinmethylin in six US soils following frozen storage. Recoveries are means (n = 2) and uncorrected for procedural recoveries.

Fortification Level (µg/kg)	Storage interval (months)	Mean Recovery (%)						Overall mean (% ± RSD)
		NY	NC	ND	TX	WA	CA	
(-) Enantiomer (Reg. No. 5925581)								
50	0	80	81	85	80	88	83	83 ± 4
	1	96	101	99	87	96	95	96 ± 5
	3	118	74	86	81	80	80	87 ± 18
	6	92	91	95	88	87	90	91 ± 3
	12	89	93	98	93	94	94	94 ± 3
	14	96	- ^a	- ^a	- ^a	- ^a	- ^a	96
Mean		95	88	93	86	89	89	
(+) Enantiomer (Reg. No. 5925632)								
50	0	74	78	80	71	76	75	76 ± 4
	1	84	83	86	76	81	88	83 ± 5
	3	90	83	86	77	74	77	80 ± 9
	6	90	87	91	90	85	91	89 ± 3
	12	86	90	94	89	86	90	89 ± 3
	14	86	- ^a	- ^a	- ^a	- ^a	- ^a	86
Mean		85	82	88	81	81	84	

^a Recovery was not determined at this time point for this field soil.

NY = New York. NC = North Carolina. ND = North Dakota. TX = Texas. WA = Washington. CA = California.

Report:	KCA 7.1.2.2.1/9 Jeffries, M., Warren, R. (2018a)
Title	European Ecoregion Similarity to Six BAS 684 H Terrestrial Field Dissipation Sites in North America: A Crosswalk Exercise Using ENASGIPS v3.0 2017/7016807
Guidelines	OPPTS 835.6100 – Supplemental
GLP?	No – not required
Deviations	None
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The objective of this project was to determine if ecoregions exist in Europe that are similar to ecoregions in North American which contain six cinmethylin terrestrial field dissipation trial sites, i.e. the root ecoregions. An ecoregion is a large unit of land or water containing a geographically distinct assemblage of species, natural communities and environmental conditions (WWF, 2017). The terrestrial field dissipation trial sites were in California, New York, North Carolina, North Dakota, Texas, and Washington (KCA 7.1.2.2.1/5; Mitchell et al., 2018a). All similarity analyses were conducted by the Applicant using the OECD Europe – North America Soil Geographic Information for Pesticide Studies application, ENASGIPS v3.0.

ENASGIPS is a component of a harmonisation project that aimed to maximise the use of pesticide field dissipation studies by developing harmonised international guidance for conducting studies and identifying similar North American and European ecoregions. The underlying premise of ENASGIPS is that pesticide field dissipation behaviour depends primarily on environmental factors such as soil and climate. If these environmental factors are similar between ecoregions, then similar pesticide field dissipation of a compound is also expected. Therefore, data generated from a pesticide terrestrial field dissipation trial conducted in a North American ecoregion is presumed to be representative of dissipation in a similar European ecoregion and vice versa.

The HSE evaluator assessed the Applicant's crosswalk exercise by reviewing the methods followed and subsequent conclusions.

METHODS

Terrestrial field dissipation trial sites

The US terrestrial field dissipation trial sites were located in six US states: California, New York, North Carolina, North Dakota, Texas, and Washington (KCA 7.1.2.2.1/5; Mitchell et al., 2018a). Sites were selected by the Applicant in representative areas for cinmethylin use from both geographic and intended crop perspectives.

ENASGIPS Application

The Applicant utilised the Similarity Assessment Tool within ENASGIPS to identify ecoregions with similar soil and climate data. The tool calculates a similarity score between an ecoregion of interest and all other ecoregions. The similarity score is calculated using some or all of the following variables:

- Annual air temperature;
- Annual precipitation;
- Topsoil pH;
- Topsoil organic carbon;

- Topsoil texture.

Two approaches are available: either the holistic approach, or weight of evidence approach. The Applicant utilised the latter approach, where the user can select only the variables that affect the field dissipation of the active substance.

In this case, cinmethylin is stable to hydrolysis between pH 4-9 (KCA 7.2.1.1/1, Hassink, 2017a); additionally, water solubility and octanol-water partitioning remained constant at this pH range (KCA 2.7/1, Daum, 2016b; KCA 2.5/1, Daum 2017a). As a result, the Applicant expected topsoil pH to have negligible influence on the field dissipation and so discounted this variable from the ENASGIPS calculations. As a result, the four remaining variables were equally weighted in the calculations.

Cinmethylin Ecoregion similarity analysis

The Applicant first determined the North American root ecoregions that contained the six North American cinmethylin terrestrial field dissipation trial sites. The ecoregion crosswalk tool was then executed for each root ecoregion with a similarity score of > 80%. This similarity score threshold is the proposed default similarity score for use with the ENASGIPS tool as specified in the draft OECD harmonisation project (OECD, 2012).

ENASGIPS defines 38 unique European ecoregions and quantifies ecoregion land area with ArcGIS v10.2. These are illustrated in Figure 8.1.2.2.1/9-01.

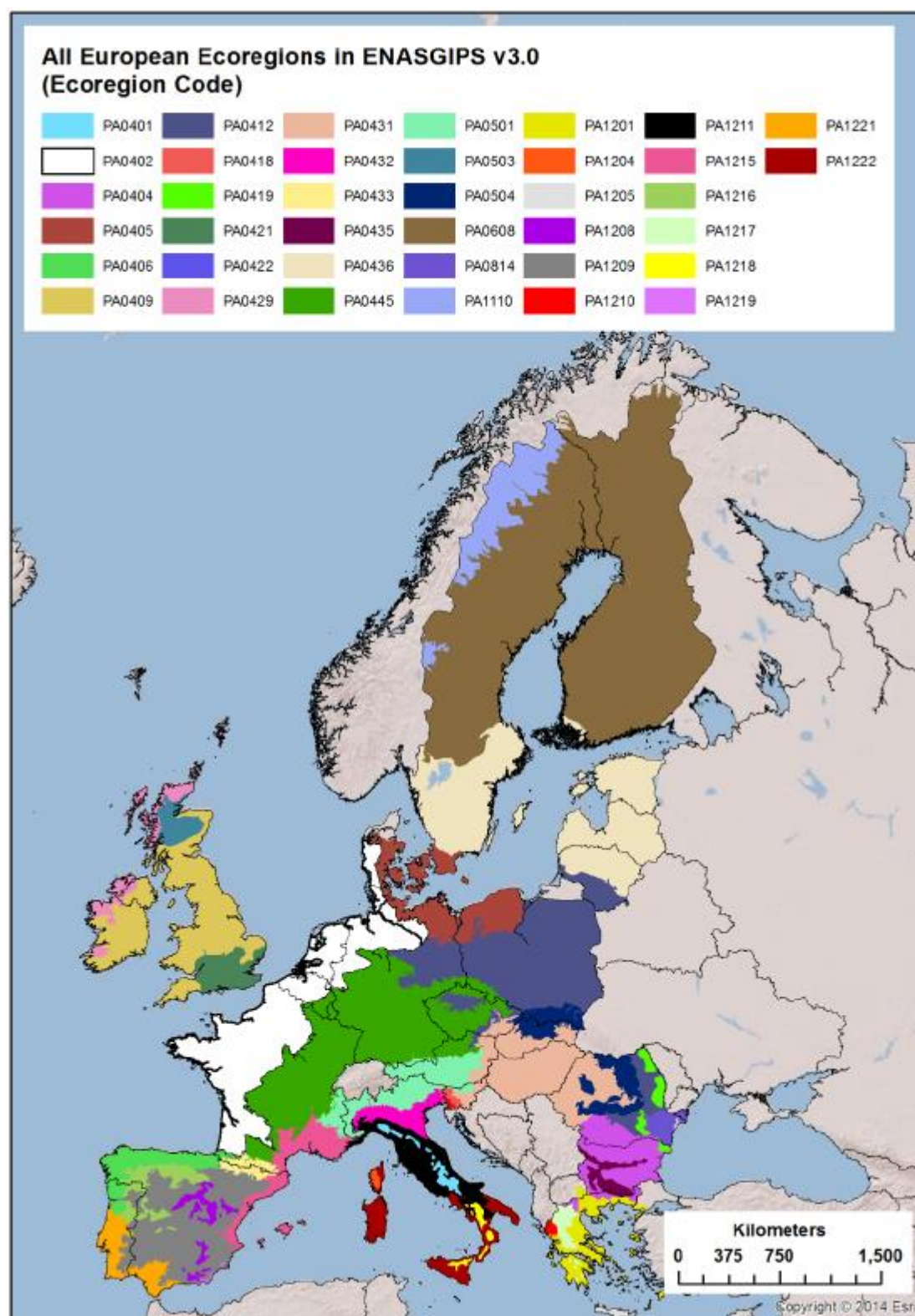


Figure 8.1.2.2.1/9-01: All European ecoregions included in ENASGIPS v3.0.

RESULTS

Root ecoregions containing field trial sites

Figure 8.1.2.2.1/9-02 shows locations of the six North American cinmethylin terrestrial field dissipation sites and the root ecoregions they are located in. Root ecoregions are described below, with their climate and soil properties summarised in Table 8.1.2.2.1/9-01. The HSE evaluator notes that ENASGIPS does not take into account the real conditions observed at the field sites during the field dissipation trials, so has provided a comparison of average climatic data with the climatic conditions recorded for each field site in the US field dissipation study (KCA 7.1.2.2.1/5; Mitchell et al., 2018a). This is also reported in Table 8.1.2.2.1/9-01.

The HSE evaluator calculated the actual precipitation on an annual average basis and compared this and the average temperature for the study duration against the ecoregion averages; this comparison is also presented in Table 8.1.2.2.1/9-01. The HSE evaluator notes that the North Carolina field site was markedly warmer than average at 172%, however, the field study was initiated in June 2016 curtailed in the following September by a hurricane, which skews the comparison.

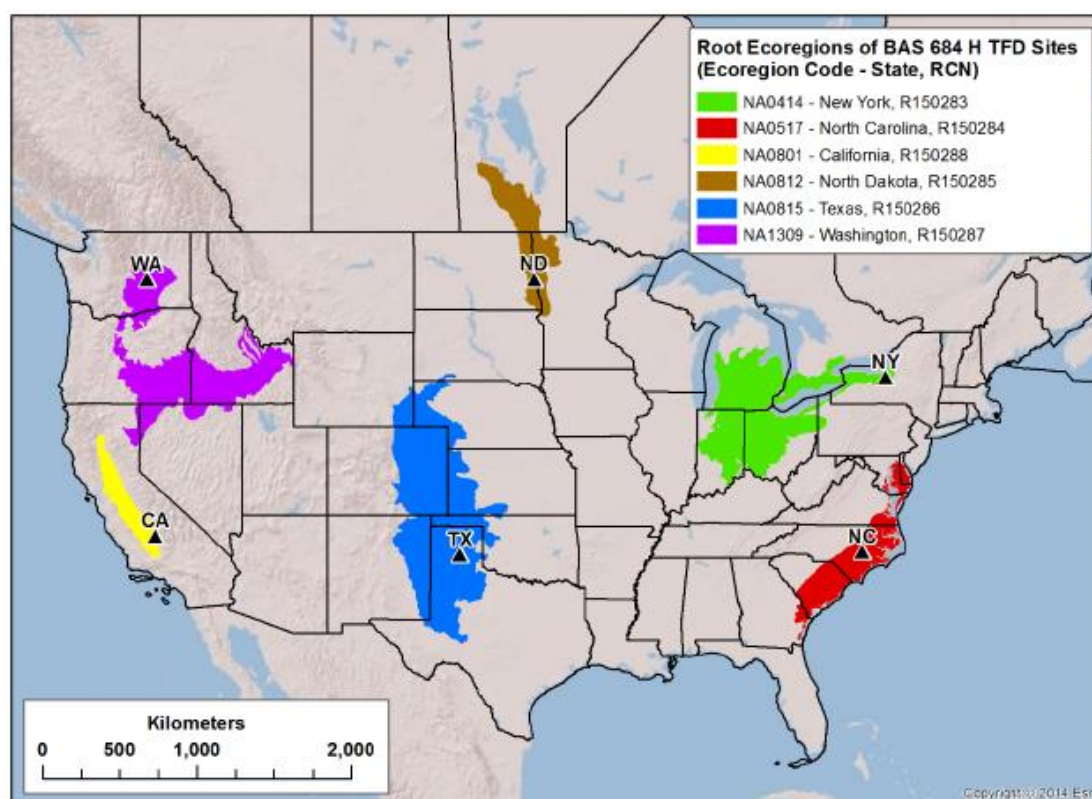


Figure 8.1.2.2.1/9-02:

ENASGIPS output showing the location of the six terrestrial field dissipation sites (noted with the triangle), and the related root ecoregions. CA = California. NC = North Carolina. ND = North Dakota. NY = New York. TX = Texas. WA = Washington.

Table 8.1.2.2.1/9-01: Locations of the six US terrestrial field dissipation sites and characteristics of the root ecoregions in which they are contained.

Field Site	California	New York	North Carolina	North Dakota	Texas	Washington
Latitude	36.00445°	43.19680°	35.26233°	47.12038°	35.11592°	47.13446°
Longitude	-119.07717°	-76.92086°	-77.89098°	-96.98456°	-101.35462°	-119.55504°
Climatic conditions during field dissipation study						
Time period	Apr 2016 – Jul 2017	Oct 2015 – Mar 2017	Jun – Sep 2016	Oct 2015 – Apr 2017	Nov 2015 – May 2017	Oct 2015 – Mar 2017
Temperature (°C) ⁴	17.8	8.0	27.6	4.6	13.2	7.9
Precipitation (mm) ⁵	276.6	1296.4	351.0	668.0	600.7	441.2
Irrigation (mm)	1219.2	342.9	524.8	17.8	341.4	764.8
Root Ecoregion Averages						
Root Ecoregion	NA0801 California Central Valley grasslands	NA0414 Southern Great Lakes forests	NA0517 Middle Atlantic coastal forests	NA0812 Northern tall grasslands	NA0815 Western short grasslands	NA1309 Snake-Columbia shrub steppe
Temperature (°C) ¹	16.5	9.3	16.0	4.1	13.0	8.6
Precipitation (mm) ¹	540	970	1150	620	430	460
Topsoil organic carbon (%) ²	0.90	0.89	0.89	1.79	0.92	1.06
Topsoil pH	6.83	5.95	5.00	6.73	7.41	7.34
Topsoil texture ³	Medium	Medium	Medium	Medium	Medium	Medium
Comparison between average and observed parameters (% difference actual vs average)						
Temperature	107.9%	86.0%	172.5%	69.9%	101.5%	91.9%
Precipitation only	41.0%	89.1%	91.6%	68.0%	88.2%	63.9%
Precipitation + irrigation	221.6%	112.7%	228.5%	112.2%	138.4%	174.8%

¹ Mean annual temperature and precipitation

² Topsoil = 0-30 cm soil depth

³ The dominant topsoil texture of the ecoregion is listed, which is converted to numeric values for the ENASGIPS ecoregion similarity analysis. The HSE evaluator notes that examples include silt, silt loam and loamy soils.

⁴ Mean air temperature for the study duration

⁵ Sum precipitation/irrigation for the study duration

European ecoregion similarity to North American root ecoregions

Overall, the Applicant's crosswalk exercise identified 21 European ecoregions as similar (≥80% similarity) to one or more US field dissipation trial sites, covering approx. 35% of the total European land area as included in ENASGIPS (Table 8.1.2.2.1/9-02). Similarities to each US field trial site are discussed below, as reported by the Applicant. The HSE evaluator accepts these results but notes that no United Kingdom ecoregions are similar to the US field dissipation study root ecoregions.

Table 8.1.2.2.1/9-02: European ecoregions found to be similar to North American root ecoregions containing trial sites from the US field dissipation study.

European ecoregion	Ecoregion area (km ²) ¹	≥ 80% Ecoregion similarity ²
Appenine deciduous montane forests (PA0401)	16119	NY, WA
Dinaric Mountains mixed forests (PA0418)	5506	NY
East European forest steppe (PA0419)	20058	NY, WA
Euxine-Colchic broadleaf forests (PA0422)	190	CA, TX, WA
Po Basin mixed forests (PA0432)	41877	NY
Pyrenees conifer and mixed forests (PA0433)	25886	NY, WA
Rodope montane mixed forests (PA0435)	29059	NY, WA
Western European broadleaf forests (PA0445)	474760	NY
Carpathian montane forests (PA0504)	91554	WA
Aegean and Western Turkey sclerophyllous and mixed forests (PA1201)	83450	CA
Corsican montane broadleaf and mixed forests (PA1204)	3628	TX
Crete Mediterranean forests (PA1205)	8163	TX
Iberian conifer forests (PA1208)	34425	TX, WA
Iberian sclerophyllous and semi-deciduous forests (PA1209)	297601	CA, TX
Illyrian deciduous forests (PA1210)	6600	NY
Italian sclerophyllous and semi-deciduous forests (PA1211)	102050	TX
Northeastern Spain and Southern France Mediterranean forests (PA1215)	90374	TX
South Appenine mixed montane forests (PA1218)	13083	CA, NC, TX, WA
Southeastern Iberian shrubs and woodlands (PA1219)	2719	CA
Southwest Iberian Mediterranean sclerophyllous and mixed forests (PA1221)	70445	CA, TX
Tyrrhenian-Adriatic Sclerophyllous and mixed forests (PA1222)	77543	CA, TX, WA

¹ Area quantified using ArcGIS.

² Similarity determined via weights of evidence analysis, which excluded topsoil pH.

California

Seven European ecoregions are similar to the California root ecoregion (NA0801), with scores

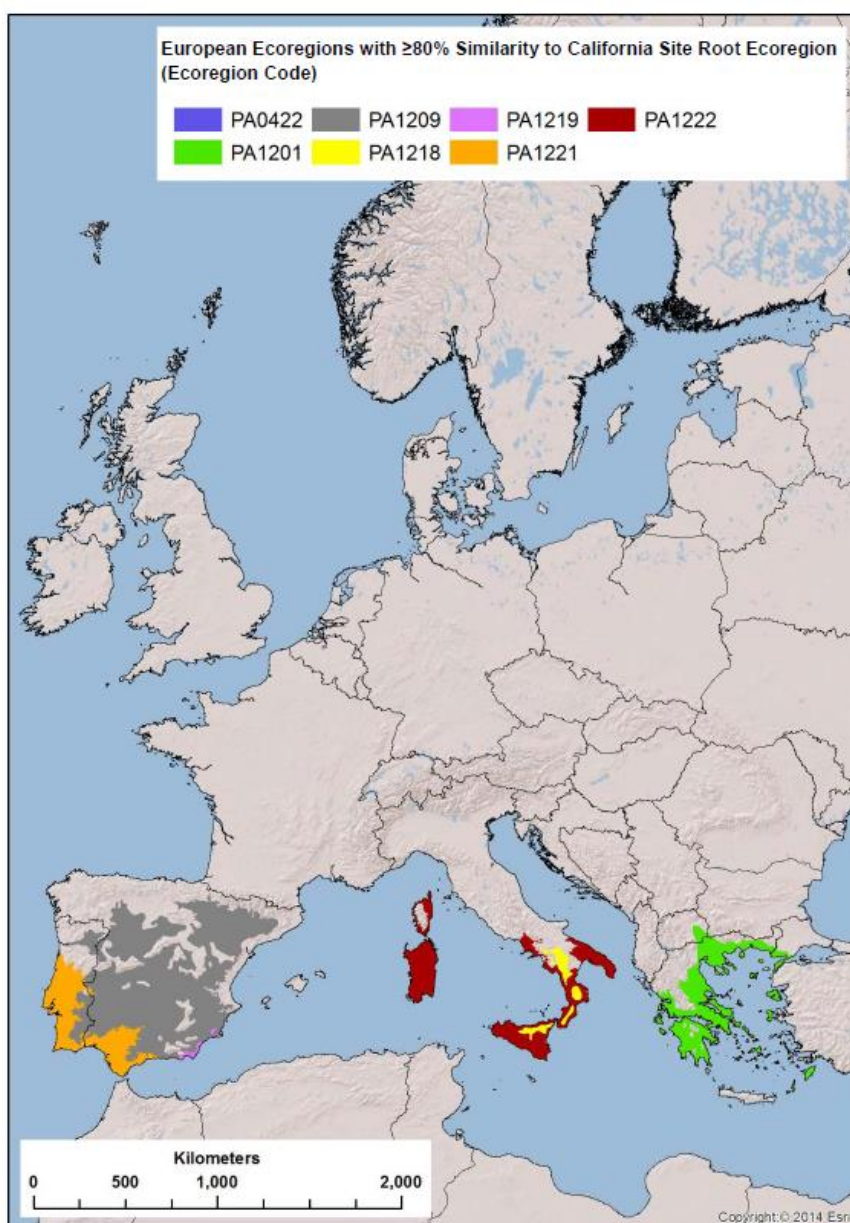
ranging from 81-96% (Table 8.1.2.2.1/9-03). These ecoregions are predominantly located in Greece, Italy, Portugal, and Spain (Figure 8.1.2.2.1/9-03).

Table 8.1.2.2.1/9-03: European ecoregion similarity to the root ecoregion of the California field dissipation trial site, as presented by the Applicant.

European Ecoregions with $\geq 80\%$ Similarity to the Root Ecoregion of the California Trial Site ¹	Similarity (0-100%) ²				
	Overall	Air Temperature	Precipitation	Soil Organic Carbon	Soil Texture
PA0422 - Euxine-Colchic broadleaf forests	84	35	100	100	100
PA1201 - Aegean & Western Turkey sclerophyllous & mixed forests	81	60	100	64	100
PA1209 - Iberian sclerophyllous & semi-deciduous forests	82	44	100	85	100
PA1218 - South Appenine mixed montane forests	88	50	100	100	100
PA1219 - Southeastern Iberian shrubs & woodlands	84	100	71	63	100
PA1221 - Southwest Iberian Mediterranean sclerophyllous & mixed forests	91	100	100	65	100
PA1222 - Tyrrhenian-Adriatic Sclerophyllous & mixed forests	96	100	100	84	100

¹ California root ecoregion: NA0801 – California Central Valley grasslands; RCN R150288.

² Similarity determined via weights of evidence analysis, which excluded topsoil pH.



Note: PA0422 (Euxine-Colchic broadleaf forests) is a 190 km² ecoregion on the southwest coast of the Black Sea which is not visible at this scale.

Figure 8.1.2.2.1/9-03: ENASGIPS output showing European ecoregions similar ($\geq 80\%$ similarity) to the root ecoregion of the California field dissipation trial site.

New York

Eight European ecoregions are similar to the New York root ecoregion (NA0414), with scores ranging from 80-91% (Table 8.1.2.2.1/9-04). These ecoregions are predominantly located in Austria, Bulgaria, Czech Republic, France, Germany, Italy, Romania, and Slovenia (Figure 8.1.2.2.1/9-04).

Table 8.1.2.2.1/9-04: European ecoregion similarity to the root ecoregion of the New York field dissipation trial site, as presented by the Applicant.

European Ecoregions with $\geq 80\%$ Similarity to the Root Ecoregion of the New York Trial Site ¹	Similarity (0-100%) ²				
	Overall	Air Temperature	Precipitation	Soil Organic Carbon	Soil Texture
PA0401 - Appenine deciduous montane forests	80	60	61	100	100
PA0418 - Dinaric Mountains mixed forests	88	100	100	53	100
PA0419 - East European forest steppe	83	100	31	100	100
PA0432 - Po Basin mixed forests	83	41	90	100	100
PA0433 - Pyrenees conifer & mixed forests	84	95	54	88	100
PA0435 - Rodope montane mixed forests	89	100	56	100	100
PA0445 - Western European broadleaf forests	91	100	91	74	100
PA1210 - Illyrian deciduous forests	84	36	100	100	100

¹ New York root ecoregion: NA0414 – Southern Great Lakes forests; RCN R150283.

² Similarity determined via weights of evidence analysis, which excluded topsoil pH.

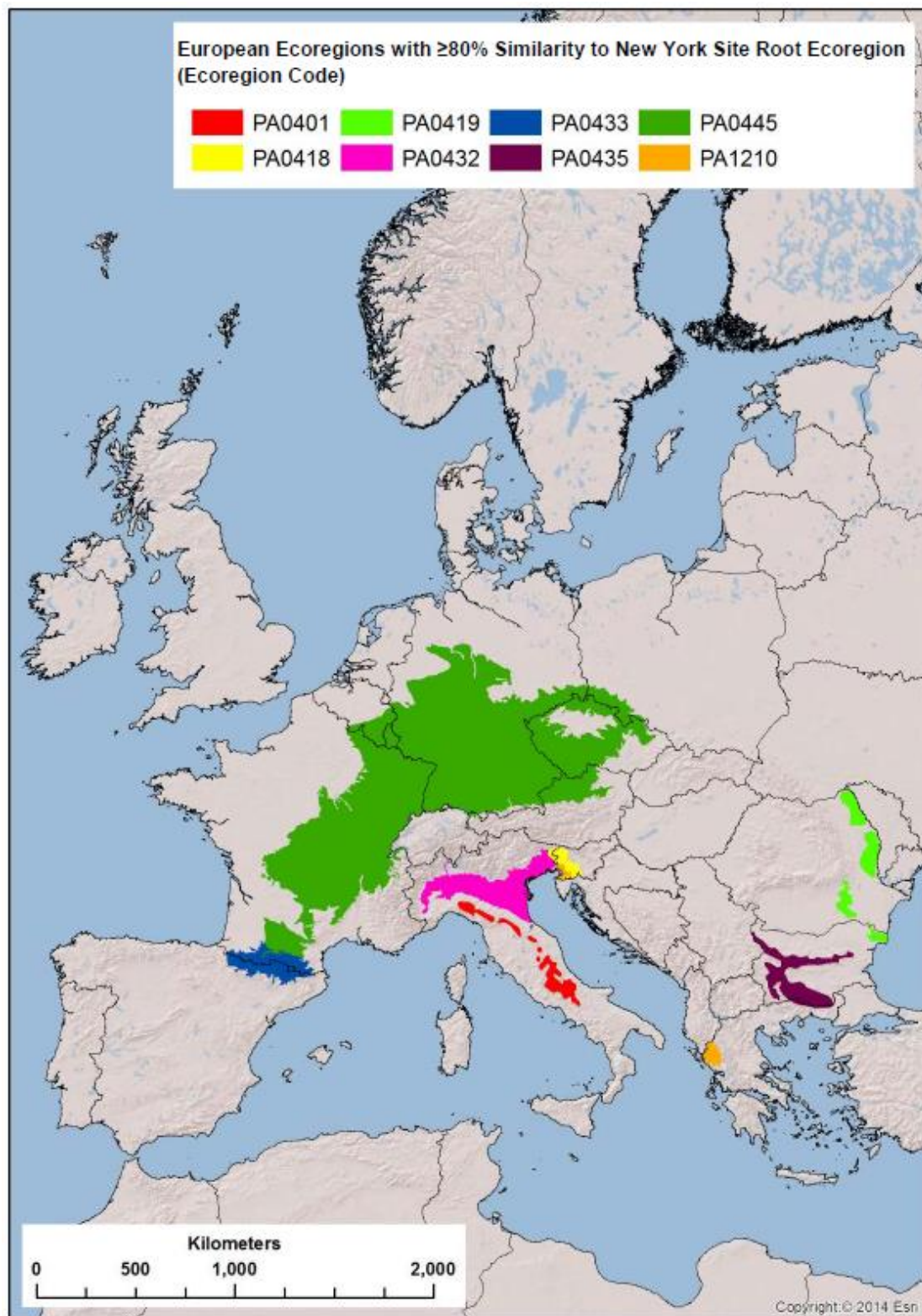


Figure 8.1.2.2.1/9-04: ENASGIPS output showing European ecoregions similar ($\geq 80\%$ similarity) to the root ecoregion of the New York field dissipation trial site.

North Carolina

One European ecoregion, located in southern Italy, is similar to the North Carolina root ecoregion (NA0517) (80% similarity; Table 8.1.2.2.1/9-05; Figure 8.1.2.2.1/9-05).

Table 8.1.2.2.1/9-05: European ecoregion similarity to the root ecoregion of the North Carolina field dissipation trial site, as presented by the Applicant.

European Ecoregions with $\geq 80\%$ Similarity to the Root Ecoregion of the North Carolina Trial Site ¹	Similarity (0-100%) ²				
	Overall	Air Temperature	Precipitation	Soil Organic Carbon	Soil Texture
PA1218 - South Appenine mixed montane forests	80	98	22	100	100

¹ North Carolina root ecoregion: NA0517 – Middle Atlantic coast forests; RCN R150284.

² Similarity determined via weights of evidence analysis, which excluded topsoil pH.



Figure 8.1.2.2.1/9-05: ENASGIPS output showing European ecoregions similar ($\geq 80\%$ similarity) to the root ecoregion of the North Carolina field dissipation trial site.

North Dakota

No European ecoregions are similar to the North Dakota root ecoregion (NA0812).

Texas

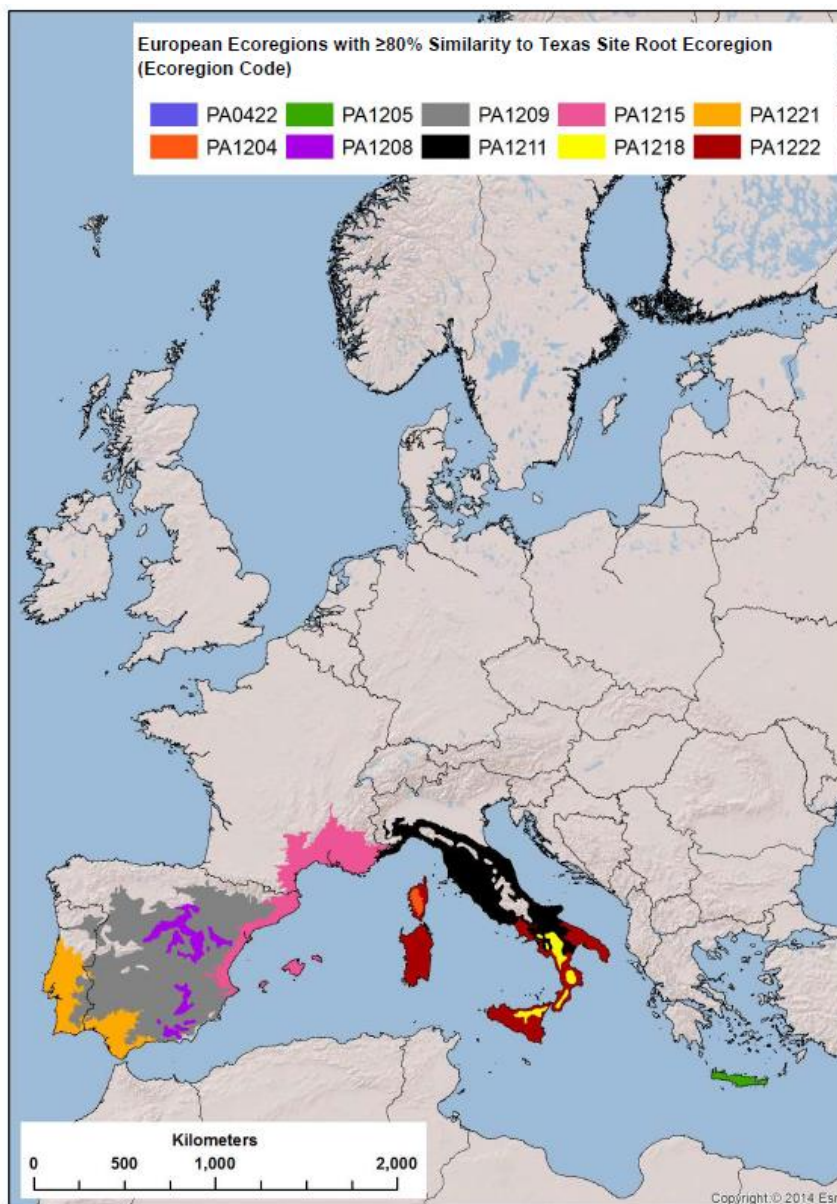
Ten European ecoregions are similar to the Texas root ecoregion (NA0815), with scores ranging from 80-92% (Table 8.1.2.2.1/9-06). These ecoregions are predominantly located in France, Greece, Italy, Portugal, and Spain (Figure 8.1.2.2.1/9-06).

Table 8.1.2.2.1/9-06: European ecoregion similarity to the root ecoregion of the Texas field dissipation trial site, as presented by the Applicant.

European Ecoregions with ≥80% Similarity to the Root Ecoregion of the Texas Trial Site ¹	Similarity (0-100%) ²				
	Overall	Air Temperature	Precipitation	Soil Organic Carbon	Soil Texture
PA0422 - Euxine-Colchic broadleaf forests	84	100	37	100	100
PA1204 - Corsican montane broadleaf & mixed forests	88	100	76	76	100
PA1205 - Crete Mediterranean forests	85	53	100	100	88
PA1208 - Iberian conifer forests	92	100	100	100	67
PA1209 - Iberian sclerophyllous & semi-deciduous forests	90	100	90	100	71
PA1211 - Italian sclerophyllous & semi-deciduous forests	80	100	21	100	100
PA1215 - Northeastern Spain & Southern France Mediterranean forests	81	100	31	92	100
PA1218 - South Appenine mixed montane forests	84	100	37	100	100
PA1221 - Southwest Iberian Mediterranean sclerophyllous & mixed forests	81	95	67	100	63
PA1222 - Tyrrhenian-Adriatic Sclerophyllous & mixed forests	91	100	65	100	100

¹ Texas root ecoregion: NA0815 – Western short grasslands; RCN R150286.

² Similarity determined via weights of evidence analysis, which excluded topsoil pH.



Note: PA0422 (Euxine-Colchic broadleaf forests) is a 190 km² ecoregion on the southwest coast of the Black Sea which is not visible at this scale.

Figure 8.1.2.2.1/9-06: ENASGIPS output showing European ecoregions similar ($\geq 80\%$ similarity) to the root ecoregion of the Texas field dissipation trial site.

Washington

Nine European ecoregions are similar to the Washington root ecoregion (NA1309), with scores

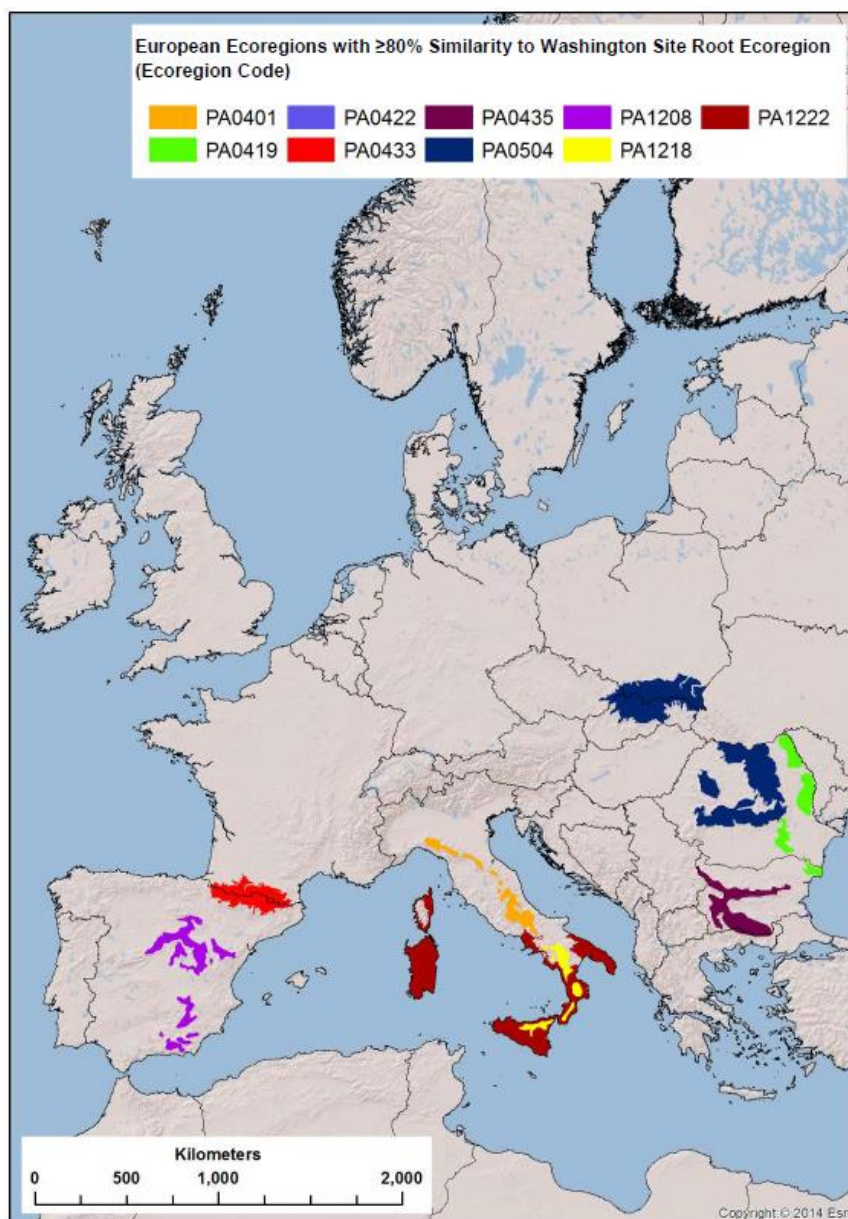
ranging from 80-85% (Table 8.1.2.2.1/9-07). These ecoregions are predominantly located in Bulgaria, France, Italy, Poland, Romania, Slovakia, and Spain (Figure 8.1.2.2.1/9-07).

Table 8.1.2.2.1/9-07: European ecoregion similarity to the root ecoregion of the Washington field dissipation trial site, as presented by the Applicant.

European Ecoregions with $\geq 80\%$ Similarity to the Root Ecoregion of the Washington Trial Site ¹	Similarity (0-100%) ²				
	Overall	Air Temperature	Precipitation	Soil Organic Carbon	Soil Texture
PA0401 - Appenine deciduous montane forests	80	85	35	100	100
PA0419 - East European forest steppe	84	100	100	100	37
PA0422 - Euxine-Colchic broadleaf forests	84	51	84	100	100
PA0433 - Pyrenees conifer & mixed forests	85	100	39	100	100
PA0435 - Rodope montane mixed forests	82	100	38	100	91
PA0504 - Carpathian montane forests	82	100	31	99	96
PA1208 - Iberian conifer forests	82	79	100	100	48
PA1218 - South Appenine mixed montane forests	82	41	85	100	100
PA1222 - Tyrrhenian-Adriatic Sclerophyllous & mixed forests	82	30	100	100	100

¹ Washington root ecoregion: NA1309 – Snake-Columbia shrub steppe; RCN R150287.

² Similarity determined via weights of evidence analysis, which excluded topsoil pH.



Note: PA0422 (Euxine-Colchic broadleaf forests) is a 190 km² ecoregion on the southwest coast of the Black Sea which is not visible at this scale.

Figure 8.1.2.2.1/9-07: ENASGIPS output showing European ecoregions similar ($\geq 80\%$ similarity) to the root ecoregion of the Texas field dissipation trial site.

CONCLUSIONS

The weights of evidence similarity analysis, utilising mean annual air temperature, precipitation, topsoil texture and topsoil organic carbon, determined five of six North American ecoregions containing US field dissipation study trial sites have similar European ecoregions. From a total of 38 European ecoregions, 21 are similar to root ecoregions containing these five field dissipation sites, covering $\sim 35\%$ of the total European land area included in ENASGIPS v3.0. The Applicant found that no European ecoregions were similar to the North Dakota field site; therefore, the North Dakota field site was rejected from further analysis. The HSE evaluator agrees and has not included this field site in geomean modelling endpoint calculations.

The Applicant concluded that results from five US field dissipation sites are applicable to Europe. Table 8.1.2.2.1/9-08 provides a summary of the relevant European countries. The HSE evaluator agrees with the Applicant's conclusion and concludes that results from five of the six field sites contained within the US field dissipation study (KCA 7.1.2.2.1/5, Mitchell et al., 2018a) are relevant to United Kingdom registration considerations based on their relevance to European conditions.

Table 8.1.2.2.1/9-08: US field dissipation trial sites deemed applicable to Europe based on an ENASGIPS crosswalk exercise based on a similarity threshold of $\geq 80\%$ similarity.

US Field Site	Similarity score	Relevant European countries
California	81-96%	Greece, Italy, Portugal, Spain
New York	80-91%	Austria, Bulgaria, Czech Republic, France, Germany, Italy, Romania, Slovenia
North Carolina	80%	Italy
Texas	80-92%	France, Greece, Italy, Portugal, Spain
Washington	80-85%	Bulgaria, France, Italy, Poland, Romania, Slovakia, Spain

B.8.1.2.2. Soil accumulation studies (Data Requirement 7.1.2.2.2)

The field dissipation studies did not trigger the need for soil accumulation studies to be conducted.

B.8.1.3. Adsorption and desorption in soil

B.8.1.3.1. Adsorption and desorption in soil (Data Requirement 7.1.3.1.1 and 7.1.3.1.2)

Report:	KCA 7.1.3.1.1/1; Harder, U., Hegler, F. (2017a)
Title	Adsorption/Desorption – Study with ¹⁴ C-BAS 684 H on eight soils
Document No.:	2016/1171944
Guidelines	OECD Guideline for Testing of Chemicals N. 106 (Jan 2000) US EPA Guideline OPPTS 835.1230 (Nov 2008)
GLP?	Yes
Deviations	<ul style="list-style-type: none"> One batch of the test item, cinmethylin, had a chemical purity of 90.9%. However, the HSE evaluator does not deem this to be significant as the radiochemical purity was 98%. The Applicant did not investigate desorption due to test item volatility. The HSE evaluator accepts this decision. The centrifugation conditions were insufficient for separating particles > 0.1 µm from the aqueous phase. The HSE evaluator concludes this is not a major deviation as the consequence is a potentially more conservative K_{oc} value arising from higher levels of test substance remaining in the aqueous phase.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The Applicant evaluated the adsorption behaviour of cinmethylin on eight soils using a laboratory batch equilibrium test. ¹⁴C-labelled cinmethylin (phenyl-U-¹⁴C) was used for the conduct of the study. The tiered approach utilised by the Applicant (e.g. Tier 2, Tier 3) originates from the experimental procedure recommended in OECD 106.

The HSE evaluator performed quality checks as part of confirming the acceptability of the study conduct and of the endpoints reported by the Applicant. These were based on the evaluator's checklist published by EFSA (2017). Quality checks covered the study conduct, the suitability of analytical methods and data handling.

MATERIALS AND METHODS**Test item**

The Applicant used two batches of phenyl-labelled cinmethylin; the details for these are summarised in Table 8.1.3.1.1/1-01 below. The HSE evaluator notes that the chemical purity of Batch No. 1147-2101 is below 95%; however, this is not seen to be problematic as the radiochemical purity is high at 98% and the Applicant used analytical methods that allowed for correction for potential impurities.

Table 8.1.3.1.1/1-01: Summary of the properties of the test item, cinmethylin, used in this study.

Reg. No.	900202	
Molecular formula	C ₁₈ H ₂₆ O ₂	
Molecular mass (unlabelled; g/mol)	274.4022	
Label	Phenyl-U- ¹⁴ C	
Batch No.	1147-2101	1147-2001
Tests used for	Tiers 2, 3	Tier 1
Concentration a.i. (mg/g)	4.88	4.99
Chemical purity (%)	90.9	97.0
Radiochemical purity (%)	98.0	98.9

Overview of experimental conduct

The study was a batch equilibrium experiment and was conducted following the three tiers as laid out in OECD 106. Figure 8.1.3.1.1/1-01 below provides an overview of the study conduct. Tests will be discussed in greater depth in later sections.

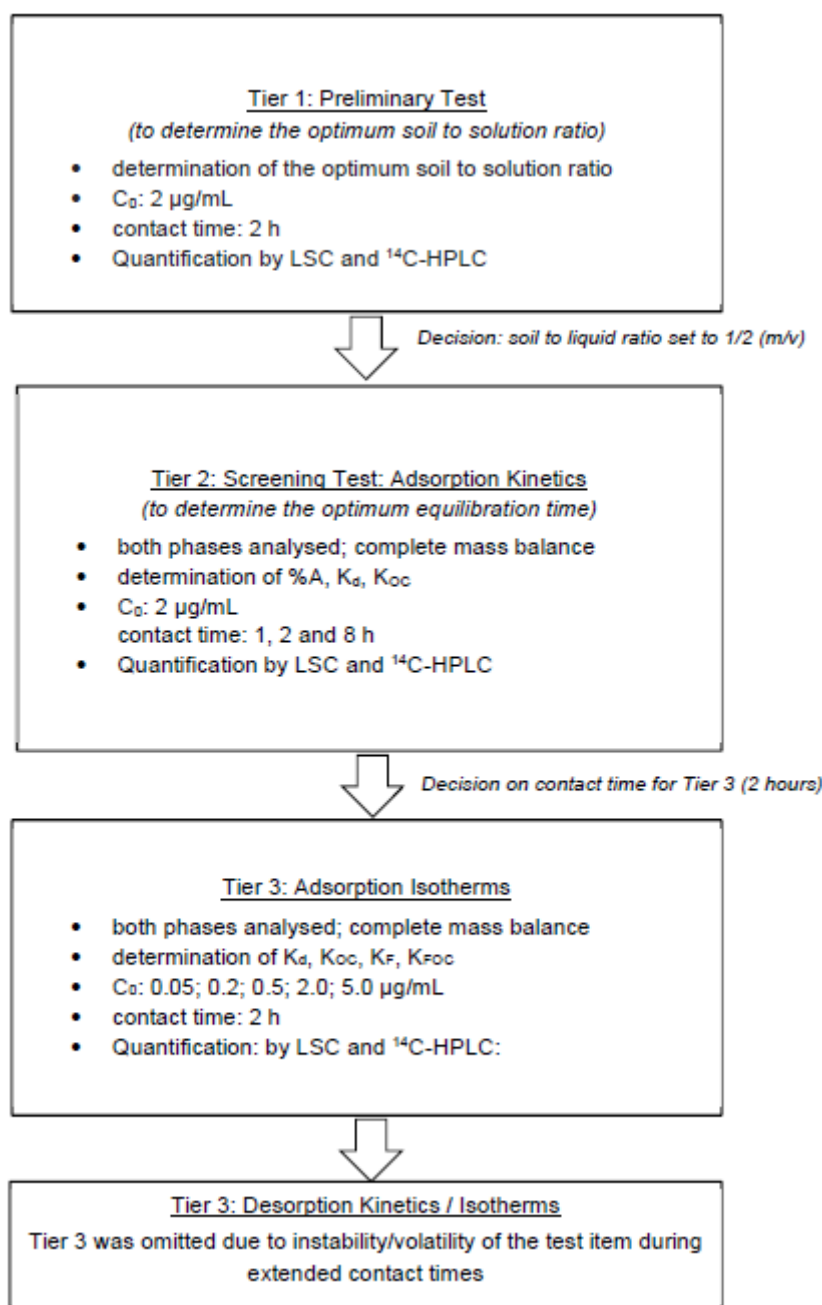


Figure 8.1.3.1.1/1-01: Overview schematic of the study conduct, and process as provided by the Applicant. Decisions made resulting from the previous tier study are in italics.

Soil

The adsorption behaviour of eight soils (five European soils, one soil from Japan and two soils from the USA) was determined in this study. The eight soils covered a pH range (CaCl₂) from 4.4 to 8.1, a range of organic carbon content from 0.66% to 4.34%, and six different USDA textural classes: one sand, one loamy sand, one sandy loam, one clay loam, one silty clay loam and three loams. Details of the physical chemical properties are given in Table 8.1.3.1.1/1-02. The HSE evaluator notes that the cultivation history of the Wyoming site is unknown; however, by checking the origin co-ordinates on Google Map satellite imagery, the HSE evaluator concludes that the soil is likely from an uncultivated grassland. Therefore, the lack of cultivation history is not deemed to have impacted upon the study. Additionally, the HSE evaluator checked the origin co-ordinates for the Gunma soil and notes that the location

shows a wooded river area. The HSE evaluator notes that the soil had a high organic carbon content and low pH and may not be relevant to agricultural soils within Europe; however, the soil provides the example of high organic content/pH that is required by the OECD guidelines, and ultimately retaining the soil does not significantly alter the geometric mean K_{foc} value. Therefore, the HSE evaluator did not reject any of the soils based on their properties.

Table 8.1.3.1.1/1-02: Soil and site characteristics for the eight soils used in the soil adsorption study.

Soil	Origin	USDA classification	Organic Carbon (%)	pH		Particle size distribution (USDA)			CEC (cmol ⁺ /kg)	Cultivation history	Pesticide history
				H ₂ O	CaCl ₂	Clay (< 2 µm)	Silt (2 - 50 µm)	Sand (> 50 µm)			
Li 10	Limburgerhof, Germany 49.408378 / 8.384578	Loamy sand	0.89	6.9	6.1	5.5	12.2	82.3	3.5	Uncultivated for past 5 years	No pesticide use in past 5 years
LUFA 2.1	Dudenhof, Germany 49.318478 / 8.383506	Sand	0.72	6.2	5.6	2.5	7.7	89.8	1.7	Uncultivated for past 5 years	No pesticide use in past 5 years
LUFA 2.3	Offenbach, Germany 49.196194 / 8.172083	Sandy loam	0.66	6.3	5.3	8.5	28.1	63.4	4.5	Uncultivated for past 5 years	No pesticide use in past 5 years
New Jersey	Baptistown, NJ, USA 40.544833 / -74.991833	Loam	1.3	6.8	6.5	22.0	49.0	29.0	8.1	Fallow for past 2 years; unknown prior	No pesticide use in past 2 years; unknown prior
La Gironda	La Gironda, Spain 37.097856 / -4.391144	Silty clay loam	1.92	8.1	7.1	34.6	49.3	16.1	30.7	Fallow for past 5 years	No pesticide use in past 5 years
Poggio Renatico	Poggio Renatico, Italy 44.745869 / 11.518989	Loam	0.82	8.3	7.5	17.3	31.7	51.1	10.2	Uncultivated for past 5 years	2014: 4 apps. ¹ 2013: 3 apps. ² 2012: 3 apps. ³ 2011: 3 apps. ⁴ 2010: 4 apps. ⁵
Gunma	Gunma, Japan 36.38327 / 138.86177	Loam	4.34	5.0	4.4	16.3	36.8	46.9	9.3	Japanese cedar forest	No pesticide use in past 5 years
Wyoming	Wyoming, USA 43.154862 / -108.3393	Clay loam	0.69	8.3	8.1	38.2	38.2	23.6	31.0	Unknown	No pesticide use in past 5 years

¹ In 2014 the soil received Ciclon (glyphosate 360 g/L) at a rate of 10 L/ha and Bi-Fen (MCPA 337 g/L + 2,4D 331 g/L) at a rate of 4 L/ha on 10/3/14, 12/5/14, 17/6/14 and 27/8/14. The soil was sampled on 9/10/14.

² In 2013 the soil received Ciclon (glyphosate 360 g/L) at a rate of 10 L/ha and Bi-Fen (MCPA 337 g/L + 2,4D 331 g/L) at a rate of 4 L/ha on 12/4/13, 11/7/13 and 11/10/13.

³ In 2012 the soil received Ciclon (glyphosate 360 g/L) at a rate of 10 L/ha and Bi-Fen (MCPA 337 g/L + 2,4D 331 g/L) at a rate of 4 L/ha on 27/3/12, 19/7/12 and 5/10/12.

⁴ In 2011 the soil received Ciclon (glyphosate 360 g/L) at a rate of 10 L/ha and Bi-Fen (MCPA 337 g/L + 2,4D 331 g/L) at a rate of 4 L/ha on 24/3/11, 23/6/11 and 15/9/11.

⁵ In 2010 the soil received Ciclon (glyphosate 360 g/L) at a rate of 10 L/ha and Bi-Fen (MCPA 302 g/L + 2,4D 375 g/L) at a rate of 4 L/ha on 9/4/10, 10/6/10, 28/7/10 and 3/9/2010.

Soil preparation

Soils were received air dried and sieved to a particle size < 2 mm prior to the study start. The Applicant determined actual residual water content of the soils prior to starting the Tier 2 and 3 studies, and this ranged from 0.31 to 6.85%. This was accounted for in all subsequent concentration calculations.

Preparation of application solutions

Two batches of the test item cinmethylin were used in the experiments. Batch 1147-2001 was used solely for the Preliminary Test (Tier 1), the determination of the optimum soil to liquid ratio, adsorption to the experimental vessels and the stability of the test substance in 0.01 M CaCl₂ solution. All other Tier 2 and 3 experiments were conducted using batch 1147-2101. Several solutions were prepared for each tier, with each method outlined below. Solution concentrations are summarised in Table 8.1.3.1.1/1-03.

Tier 1 solutions:

During the preliminary test (Tier 1), cinmethylin adsorption to the test vessel was determined as well as its stability in 0.01 M CaCl₂ solution with an additional set of solutions. The Applicant indexed these with an asterisk to discern these from other test solutions. Solutions A*-C* were prepared using batch 1147-2001 of cinmethylin. A* solutions related to a nominal concentration of 5 µg/mL, B* solutions related to a nominal concentration of 2 µg/mL, and C* solutions related to a nominal concentration of 0.5 µg/mL.

- Solution A1* was prepared by adding 1.3 mL of the cinmethylin stock solution in toluene to 1 mL water. The toluene was removed under a constant stream of nitrogen gas. 1 mL acetonitrile (total solvent < 1% in stock solution) and 5 mL distilled water were added. 994 mL of 0.01 M CaCl₂ was added and the mixture was thoroughly shaken.
- App0002* was prepared by diluting 755 mL of A1* in 245 mL of 0.01 M CaCl₂. This solution was made to prepare dilutions.
- B1* was prepared by diluting 515 mL of App0002 with 485 mL 0.01 M CaCl₂.
- A2* was prepared by mixing 0.9 mL of the cinmethylin stock solution in toluene with 1 mL distilled water. The toluene was removed under a constant stream of nitrogen gas. 1 mL acetonitrile and 4 mL distilled water were added. 700 mL of 0.01 M CaCl₂ was added and the mixture was thoroughly shaken.
- A3* was prepared by diluting 343 mL of A2* with 40 mL of 0.01 M CaCl₂.
- B3* was prepared by diluting 200 mL of A2* in a volumetric flask with 0.01 M CaCl₂ to 500 mL.
- C1* was prepared by diluting 125 mL of B3* in a volumetric flask with 0.01 M CaCl₂ to 500 mL.

Tier 2 solutions:

- A1 and A2 were prepared by evaporating 1.2 mL of the cinmethylin stock solution to dryness under a constant stream of nitrogen gas. The pellet was re-dissolved in 1 mL acetonitrile, dissolution was ascertained by sonication.
- B1, B2 and B3 were prepared by diluting 400 µL of A1 with 600 µL acetonitrile and sonicating afterwards. B1 and B2 were diluted in this manner from A1, while B3 was diluted in this manner from A2.

Tier 3 solutions:

Additional to the solutions A1 and A2 prepared for Tier 2, three additional solutions were prepared for Tier 3:

- C1 was prepared by diluting 250 µL of B3 with 750 µL acetonitrile and sonicating afterwards.
- D1 was prepared by diluting 50 µL of B3 with 450 µL acetonitrile and sonicating afterwards.

- E1 was prepared by diluting 12.5 µL of B3 with 487.5 µL acetonitrile and sonicating afterwards.

Concentrations were determined by LSC for total radioactivity and by ^{14}C -HPLC for the test item. HPLC measurements were corrected for any potential impurities. Table 8.1.3.1.1/1-03 summarises nominal and actual concentrations for each test solution used in the three studies. The HSE evaluator notes that the Tier 2 and 3 “test solutions” are utilised as stock solutions, wherein 10 µL of the solution is transferred into each test vessel (containing 5 g soil and 10 mL CaCl_2). The nominal test concentrations within the test vessels were 0.05, 0.2, 0.5, 2 and 5 µg/mL. Further explanation of the Tier 2 and 3 experimental procedures is provided in the following sections.

The HSE evaluator notes that the OECD guidelines state, on solubility, that stock concentrations should be below the known water solubility for the test substance. In the case of cinmethylin, this is 0.058 g/L at pH 7. The “test solutions”, better described as stock solutions that were used for Tiers 2 and 3, exceeded this limit. However, these were diluted to the target concentrations outlined above within the test vessels. The OECD guidelines also stipulate that the initial substance concentration within the test vessels should not exceed 50% of the active substance’s solubility. This guideline was not exceeded by the test concentrations within the test vessels. Although it is not ideal for stock solutions to exceed the solubility limit outlined in the guidance, the HSE evaluator concludes that this did not significantly affect the conduct and outcome of the study.

Table 8.1.3.1.1/1-03: Summary of test solutions used for the adsorption studies.

Solution name	Nominal concentration (µg/mL)	LSC concentration (µg/mL)	HPLC % ROI ³	HPLC-corr. concentration (µg/mL) ⁴
Tier 1 ¹				
A1*	5	4.74	100	4.74
A2*		5.89	100	5.89
A3*		4.96	100	4.96
B1*	2	2.03	n.d.	2.03
B3*		2.30	n.d.	2.30
C1*	0.5	0.53	n.d.	0.53
Tiers 2 and 3 (10 µL added to each test vessel) ²				
A1	5000 (to give 5 µg/mL)	5051.03	100	5051.03
A2		5087.64	100	5087.64
B1	2000 (to give 2 µg/mL)	2021.94	n.d.	2021.93
B2		2105.48	n.d.	2105.48
B3		2124.18	n.d.	2124.18
C1	500 (to give 0.5 µg/mL)	514.52	n.d.	514.52
D1	200 (to give 0.2 µg/mL)	215.19	n.d.	215.19
E1	50 (to give 0.05 µg/mL)	53.79	n.d.	53.79

n.d. = not determined due to solutions being dilutions of previously tested solutions.

¹ cinmethylin batch 1147-2001

² cinmethylin batch 1147-2021. Solutions B1 and B2 were used for Tier 2. Solutions A2, B3, C1, D1 and E1 were used for Tier 3. The HSE evaluator notes that it appears that Solution A1 was not used in the conduct of the final experiments.

³ Proportion of region of interest on chromatogram attributed to cinmethylin

⁴ Corrected for the proportion of the region of interest attributed to cinmethylin to account for any potential impurities.

General experimental procedures (Tiers 2 and 3)

For Tiers 2 and 3, the Applicant noted that the following procedures were consistent for the two tiers. Equilibration and incubation of soils with the test item were accomplished under dark conditions at room temperature. The adsorption kinetic experiments (Tier 2) and

adsorption isotherms (Tier 3) were conducted in triplicate in 12 mL soda-lime-glass culture tubes with a screw cap. The Applicant notes that the headspace of the test vessels was chosen to be as small as possible so that shaking was feasible while minimising test substance evaporation.

Soil was weighed into the test vessels and pre-equilibrated overnight (minimum 14 hours) with 10 mL 0.01 M CaCl_2 solution. Following pre-equilibration, 10 μL of the test item in acetonitrile was added. The solvent concentration was $< 0.1\%$ in the final test setup. The soil weighed in was based on the calculated dry weight of 5 g of the soil. The wet weight of the soil as weighed in was recorded. The total volume of aqueous phase included the CaCl_2 volume, the residual soil (as determined by the dry weight determination) and the weight of the added test item. The soil suspension was agitated at room temperature in the dark with the test vessels being placed horizontally on a shaker. At the respective sampling time the soil and aqueous phase were separated by centrifugation at 2000 rpm for 15 min and the aqueous phase was decanted. The aqueous and solid phases were weighed. The remaining solid soil phase was extracted with 6.5 mL acetonitrile (30 min at 250 rpm on a shaker) and centrifuged at 2000 rpm for 15 min. After two more extraction steps with 6.5 mL acetonitrile, the extracts were combined, and the final volume was adjusted to 20 mL with acetonitrile.

The HSE evaluator notes that the Applicant's centrifugation conditions were insufficient for separating particles $> 0.1 \mu\text{m}$ diameter from the aqueous phase. The eight soils in the present study have soil densities ranging $0.99 - 1.54 \text{ g/cm}^3$. Assuming the midpoint of 1.2 g/cm^3 , suitable centrifugation conditions would be 60 min at 6000 rpm as an example. However, the HSE evaluator does not deem this to be a major deviation as poor separation potentially means more test substance remains in the aqueous phase, thereby giving a more conservative K_{foc} .

Tier 1 – Preliminary test

For testing suitable soil/solution ratios, the soils LUFA 2.1 and La Gironde were chosen by the Applicant since they differed distinctly in pH and organic carbon. For each soil a soil/solution ratio of 1/1, 1/2 and 1/5 was tested to be able to select the appropriate soil/solution ratio for Tier 3. The application solution B1* was used (nominal cinmethylin concentration of 2 $\mu\text{g/mL}$) and a contact time of 2 h was chosen.

Tier 2 – Screening test

The aim of this experiment was to determine the optimal contact time at one concentration level, at which adsorption equilibrium was reached, allowing for complete mass balance and acceptable stability of the test item. Complete parental mass balance was established at each time interval to determine a suitable contact time for Tier 3 at which cinmethylin stability was confirmed.

Test method

All eight soils were used, with the soil/solution ratio set to 1/2 (m/v). The test was conducted with a nominal concentration of 2 $\mu\text{g/mL}$. Three replicates per sampling interval were prepared in parallel. 5 g dry weight soil aliquots (based on the pre-determined wet weight of individual soils) were weighed into the glass centrifuge tubes. Soil aliquots were equilibrated for 14 hours with 10 mL 0.01 M CaCl_2 in the dark at room temperature and with agitation on a horizontal shaker at 150 rpm. After the equilibration time, 10 μL of application solution B1 (sampling time 2 and 8 hours) or B2 (sampling time 1 hour) was added to each sample.

Soils were sampled at 1, 2, 4 and 8 hours to establish adsorption kinetics. The Applicant notes that, due to different experimental conduct for the 4 hour samples, these were not considered further and not included in the adsorption kinetics. Incubation took place at room temperature in the dark using a horizontal shaker at 150 rpm. At the respective sampling time point, the test vessel was removed and centrifuged at 2000 rpm for 15 minutes in a swing-free bucket

rotor. The mass and volume of each phase were determined by weighing. 0.01 mL aliquots of the aqueous phase were quantified by LSC. Analysis for total radioactivity was done in duplicate with the mean values being reported. Cinmethylin specific quantification was accomplished by ^{14}C -HPLC.

Calculation of the adsorption coefficient K_d

Both the aqueous phase as well as the soil extract were subjected to test item specific analysis by ^{14}C -HPLC allowing detection of potential degradation products and determination of total radioactivity by LSC. In addition to the liquid phase and the soil extract, total radioactivity in the soil after extraction (non-extractable residues) was determined.

Parental mass balance was established for each time interval. Mass balance was established on total radioactivity (including non-extractable residues) as well as test item specific as based on the results by ^{14}C -HPLC analysis (sum of test item in the aqueous phase and the soil extract).

Percent adsorption as well as adsorption coefficients were calculated for each time interval. The liquid entrained in the soil pellet after centrifugation and phase separation was considered when calculating soil concentrations of the test item. The percent adsorption (%A) was calculated solely from the soil extract because this value was used as an estimate for the further experimental approach. All adsorption (distribution) coefficients were calculated using the direct method.

Tier 3 – Adsorption isotherms

The aim of this experiment was to assess the influence of cinmethylin concentration on the extent of adsorption.

Test method

All eight soils were used, with the soil/solution ratio set to 1/2 (m/v). Five nominal concentrations were assessed: 0.05, 0.2, 0.5, 2 and 5 $\mu\text{g/mL}$. Soils were prepared as outlined for Tier 2. After two hours, 10 μL of the relevant application solution was added to each sample. Blank samples were included with no application solution to obtain background readings and to assess contamination.

Based on the outcome of the Tier 2 test, a contact time of 2 hours was chosen for determining adsorption isotherms as significantly longer contact time did not lead to a pronounced higher adsorption. The Applicant also noted that longer contact times would have led to lower parental mass balances due to possible volatilisation of the test item. Soils were incubated as previously outlined for Tier 2.

Analysis of aqueous and soil phases was performed as outlined for Tier 2. Non-extractable residues (NERs) were determined via combustion and trapping of the developed $^{14}\text{CO}_2$ for analysis via LSC.

Calculation of the Freundlich Isotherms

Both the aqueous phase as well as the soil extract were subjected to test item specific analysis by ^{14}C -HPLC and determination of total radioactivity by LSC. In addition to the liquid phase and the soil extract, total radioactivity in the soil remaining after extraction (non-extractable residues) was determined.

Mass balance was established for cinmethylin based on the results derived from ^{14}C -HPLC analysis as well as a complete ^{14}C mass balance including the soil NERs. An additional mass balance based on total radioactivity as determined by LSC was done despite isotherms being based on the direct method using test item specific HPLC data. The HSE evaluator notes that

this additional step using LSC was not necessary, but has included it within the study evaluation for completeness.

Adsorption coefficients were calculated for each concentration based on the direct method. The residual aqueous phase remaining in the soil after centrifugation and phase separation was considered when calculating soil concentrations of the test item. The estimation of the Freundlich parameters was conducted by a linear fit of the log transformed data using Microsoft Excel 2016. The adsorption coefficient ($\log K_F^{\text{ads}}$) was derived via the intercept function and the exponent $1/n$ was taken from the slope function. The Applicant also determined the mass adsorbed to the soil and the concentration in the aqueous phase.

The HSE evaluator assessed the Applicant's Freundlich isotherm derivation by inputting the aqueous and soil phase concentrations for all eight soils into a modified version of the Microsoft Excel EFSA OECD 106 Calculation Tool (EFSA, 2017). The tool was modified only to enable handling of triplicate samples, with no other modifications. The HSE evaluator input the same data as those used by the Applicant and found that the EFSA calculator tool produced different log-transformed values for the isotherms, which therefore affected the adsorption kinetic values slightly. The HSE evaluator apportioned this to the Applicant's presentation of data with rounding to two decimal places. The HSE evaluator accepted the data, procedures and subsequent adsorption isotherms and sorption kinetic values presented by the Applicant.

Control samples

Control samples were used to determine the stability of cinmethylin in 0.01 M CaCl₂ solution as well as its potential adsorption to the test vessels. Control samples were prepared using solutions C1* (0.5 µg/mL) and A3* (5 µg/mL). Incubation times were 2 and 8 hours for samples treated with C1, and 8 hours for samples treated with A3.

Limits of detection

The LSC limit of detection (LOD) was set to 0.61 µg/L of cinmethylin concentration. The limit of quantification (LOQ) was set to 0.91 µg/L. The lowest measured sample concentration was 4.34 µg/L. For HPLC, the LOQ was set to 0.89 µg/L, while the lowest measured sample concentration was 1.45 µg/L.

The OECD 106 Evaluator's Checklist (EFSA, 2017) states that LOQs should be at least two orders of magnitude below the lowest nominal concentration tested, which in this case is 0.05 µg/mL, or 50 µg/L. The Applicant stated that the HPLC LOQ was 0.89 µg/L and the lowest measured sample concentration was 62% higher than the LOQ. Additionally, no samples were measured to be below the LOQ. Therefore, the HSE evaluator does not deem this deviation to have significantly affected the study conduct or outcome.

RESULTS

Cinmethylin mass balance was established throughout by the analysis of both the aqueous phase and soil extracts.

Tier 1 – Preliminary test

The Applicant tested three soil/liquid ratios to determine the optimal ratio: 1/1, 1/2 and 1/5. At the 1/1 ratio, the soil adsorption of cinmethylin was 66.4% with LUFA 2.1 soil and 68.9% with La Gironda soil. At the ratios 1/2 and 1/5 the adsorption values decreased respectively to 46.8% and 33.5% for LUFA 2.1 soil and 55.7% and 43.7% with La Gironda soil (Table 8.1.3.1.1/1-04). OECD guidelines stipulate that the adsorbed percentage should be > 20% and preferably > 50%. Therefore, the Applicant chose the soil/solution ratio of 1/2 and applied this to Tiers 2 and 3. The HSE evaluator agrees with this decision, and notes that the Applicant did not supply mass balances for the Tier 1 test.

Table 8.1.3.1.1/1-04: Summary of the adsorption of phenyl-U-labelled cinmethylin to two soils at different soil/liquid ratios over two hours.

Soil	pH	Ratio	Soil (g)	CaCl ₂ (mL)	Adsorption (%)	Mean Adsorption (%)
La Gironda	7.1	1:1	7.0	7.0	69.7	68.9
					N/A ^a	
					68.1	
		1:2	5.0	10.0	63.4	55.7
					57.5	
					46.3	
		1:5	2.0	10.0	46.1	43.7
					44.2	
					40.8	
LUFA 2.1	5.6	1:1	7.0	7.0	66.8	66.4
					66.0	
					66.2	
		1:2	5.0	10.0	45.9	46.8
					48.6	
					45.9	
		1:5	2.0	10.0	37.0	33.5
					32.6	
					30.8	

HPLC analysis was used for the assessment of cinmethylin stability in both phases at the 1:2 ratio. Stability in the aqueous phase was > 88% (ranging 88.0 – 90.5% for La Gironda and 94.0 – 95.1% for LUFA 2.1) and 100% for the soil phase for both soils.

The Applicant provided chromatograms to demonstrate that they did not vary to the chromatogram pattern seen in Tiers 2 and 3. The HSE evaluator examined these chromatograms and agrees that there is no significant difference in the patterns observed.

Tier 2 – Screening test

Cinmethylin stability

The Applicant investigated test item stability after incubation periods of 2 and 8 hours during the test vessel adsorption test. The Applicants found that no metabolite formation occurred after 2 and 8 hours at a cinmethylin concentration of 0.5 µg/mL; however, a peak (7.84% region of interest) was detected after 8 hours at 5 µg/mL, suggesting cinmethylin was not stable at higher concentrations and longer contact times. The HSE evaluator examined the supplied chromatograms and agrees with this conclusion.

Test vessel adsorption

Table 8.1.3.1.1/1-05 summarises the results of the test vessel adsorption experiment. Adsorption to the test vessel ranged 2.2 to 27.6% AR and overall recoveries ranged 40.7 to 91.1% AR. The HSE evaluator examined the chromatograms supplied by the Applicant to show the glass extracts and agrees with the Applicant's conclusion that cinmethylin was the only observed peak in the 0.5 µg/mL samples.

Table 8.1.3.1.1/1-05: Adsorption of cinmethylin to test vessel surfaces after 2 and 8 hours.

Cinmethylin Concentration (µg/mL)	Incubation period (hours)	Test vessel adsorption (% AR)	Aqueous phase recovery (% AR)	Parent (% ROI)	Others (% ROI)	Total recovery (% AR)
0.5	2	2.2	88.8	100.0	0.0	91.1
	8	27.6	27.4	100.0	0.0	54.9
5	8	22.3	18.3	92.16	7.84 ^a	40.7

^a Retention time of 23.2 min.

Due to the high rates of sorption to the test vessel wall, the Applicant opted to conduct the sorption study using the direct method, to ensure losses to test vessel walls did not impact upon the study results.

Incubation time test

The Applicant supplied results from experiments using 1, 2- and 8-hour incubation periods. The Applicant stated the results after 8 hours of incubation showed similar total recoveries and metabolite formation to the results after 1 and 2 hours. Generally, for all soils, the AR proportion adsorbed to soil was similar at 2 and 8 hours; therefore, the Applicant assumed that adsorption equilibrium was reached within 2 hours. The HSE evaluator notes that it is not ideal to conclude that equilibrium is reached with just two time points; however, it is noted that the 8 hour incubation period was not ideal due to volatilisation risk.

Results are discussed per soil below and are summarised in full in Table 8.1.3.1.1/1-06. Where mass balances were below 90%, the Applicant highlighted the negligible test vessel adsorption rates. Therefore, the Applicant suggested that these low mass balances indicated possible volatility of cinmethylin. However, as they applied the direct method, the Applicant stated that possible volatilisation did not lead to overestimation of test item adsorption in these studies. The HSE Evaluator agrees and notes that volatilisation studies have demonstrated that cinmethylin does readily volatilise from soil and plant surfaces (See KCA 7.3.1/2; Hassink, J., 2017b).

Li 10: An increase of adsorption was observed until 2 h, reaching 59.5% parental mass absorbed to soil. Total recovery was between 84.5% (1 h) and 88.0% AR (8 h) while parental recovery without NER was between 81.6% (1 h) and 85.5% (8 h). NER was between 0.2% (2 h) and 1.1% (1 h) TAR.

LUFA 2.1: Adsorption of 47.3% of parental mass to soil was observed after 2 h, with a slight increase to a maximum of 52.9% after 8 h. Total recovery was between 83.8% (8 h) and 89.8% AR (2 h) while parental recovery without NER was between 82.0% (8 h) and 88.8% (2 h). NER was between 0.7% (2 h) and 0.9% (1 h) AR.

LUFA 2.3: Parental mass adsorbed to soil increased to 52.1% after 2 h, with a decrease to 47.8% after 8 h. Total recovery was between 84.9% (1 h) and 93.5% AR (8 h) while parental recovery without NER was between 82.2% (1 h) and 91.3% (8 h). NER was between 0.1% (8 h) and 0.2% (2 h) TAR.

New Jersey: Parental mass adsorbed to soil increased to 65.6% after 2 h, with a decrease to 59.7% after 8 h. Total recovery was between 89.1% (1 h) and 89.9% AR (2 h) while parental recovery without NER was between 86.2% (1 h) and 86.3% (2 h). NER was between 0.3% (1 h) and 0.4% (2 h) TAR.

La Gironda: Parental mass adsorbed to soil was 62.9% after 2 h, with an increase to 67.8% after 8 h. Total recovery was between 90.2% (2 h) and 93.0% AR (8 h) while parental recovery without NER was between 85.8% (2 h) and 89.3% (8 h). NER was between 0.6% (1 h and 2 h) and 0.7% (8 h) TAR.

Poggio Renatico: Parental mass adsorbed to soil was 50.0% after 2 h, with an increase to 57.0% after 8 h. Total recovery was between 86.5% (1 h) and 94.7% AR (2 h) while parental recovery without NER was between 83.2% (1 h) and 91.2% (2 h). NER was between 1.6% (1 h) and 1.7% (2 h and 8 h) TAR.

Gunma: Parental mass adsorbed to soil was 75.4% after 2 h, with an increase to 80.2% after 8 h. Total recovery was between 90.1% (1 h) and 97.9% AR (8 h) while parental recovery without NER was between 85.2% (1 h) and 91.9% (8 h). NER was between 3.4% (2 h) and 6.0% (8 h) TAR.

Wyoming: Parental mass adsorbed to soil was 47.0% after 2 h, with a slight increase to 51.4% after 8 h. Total recovery was between 89.2% (1 h) and 97.3% AR (8 h) while parental recovery without NER was between 82.7% (1 h) and 90.9% (8 h). NER was between 4.2% (1 h) and 4.9% (8 h) TAR.

The HSE evaluator notes that the mean radioactive recovery across all eight soils increased with incubation time, with 87.7% recovered at 1 h, 90.6% at 2 h and 91.7% at 8 h. Mean parent-only recoveries derived from HPLC analysis also increased with time: 84.9% at 1 h, 87.4% at 2 h and 88.5% at 8 h. Non-extractable residues (NER) did not show a time-related trend, with 2 h incubation showing the lowest at 2.0%, followed by 1 h (2.2%) and 8 h (2.5%). The HSE evaluator also calculated the volume of liquid retained by the soil phase, which ranged 11.8 – 40.7% retention (mean 24.9%). The HSE evaluator can confirm that the retained moisture was accounted for in the reported values. Detailed results are shown in Tables 8.1.3.1.1/1-06-08.

The HSE evaluator examined the chromatograms for metabolite patterns for each soil and agrees with the Applicant that the metabolite pattern does not show a trend with increasing incubation time.

Table 8.1.3.1.1/1-06: Tier 2 Adsorption kinetics results arising from eight soils incubated with cinmethylin for 1 hour. Nominal test concentration = 2 µg/mL. Soil to liquid ratio = 1/2 (m/v).

Soil	Rep.	Aqueous phase		Soil phase		Parent recovery		NER (% AR) ²	Radioactive recovery (% AR) ³
		(% parent) ¹	% ROI	(% parent) ¹	% ROI	LSC (% AR)	HPLC (% parent)		
Li 10 (Germany)	1	32.0	93.4	49.5	100.0	83.3	81.5	0.9	84.2
	2	32.7	93.2	48.8		83.5	81.5	1.0	84.4
	3	32.8	93.9	48.9		83.4	81.7	1.5	84.9
	Mean	32.5	93.5	49.1		83.4	81.6	1.1	84.5
LUFA 2.1 (Germany)	1	28.8	94.7	54.7	100.0	84.9	83.6	0.8	85.7
	2	28.8	93.4	53.6		84.1	82.4	0.9	85.0
	3	28.8	93.0	54.6		85.2	83.4	0.9	86.1
	Mean	28.8	93.7	54.3		84.7	83.1	0.9	85.6
LUFA 2.3 (Germany)	1	32.1	93.6	49.8	100.0	83.7	81.9	0.7	84.4
	2	32.4	92.0	48.8		83.5	81.2	0.7	84.2
	3	31.3	93.9	52.2		85.1	83.5	0.8	85.9
	Mean	31.9	93.2	50.3		84.1	82.2	0.7	84.8
New Jersey (USA)	1	25.9	93.1	59.1	100.0	86.5	85.0	1.5	87.9
	2	25.3	91.8	58.9		85.9	84.1	1.4	87.3
	3	37.4	95.6	52.1		90.9	89.6	1.1	92.0
	Mean	29.5	93.5	56.7		87.7	86.2	1.3	89.1
La Gironde (Spain)	1	22.1	91.4	63.8	100.0	87.4	85.9	3.3	90.7
	2	23.4	90.4	60.9		86.1	84.3	2.7	88.7
	3	29.5	92.5	61.4		92.6	90.9	2.4	95.0
	Mean	25.0	91.4	62.0		88.7	87.0	2.8	91.5
Poggio Renatico (Italy)	1	28.8	92.0	53.9	100.0	84.7	82.7	1.5	86.2
	2	28.8	92.8	55.2		85.7	84.0	1.0	86.8
	3	30.0	93.9	52.9		84.4	82.7	2.2	86.6
	Mean	29.2	92.9	54.0		84.9	83.2	1.6	86.5
Gunma (Japan)	1	11.6	100.0	73.5	100.0	85.1	85.1	4.6	89.7
	2	13.9		71.6		85.5	85.5	4.2	89.7
	3	13.6		71.3		84.9	84.9	6.0	90.9
	Mean	13.0		72.1		85.1	85.1	4.9	90.1
Wyoming (USA)	1	30.1	89.9	52.4	100.0	84.9	82.5	5.5	90.4
	2	30.9	91.1	52.1		85.3	83.0	3.7	88.9
	3	30.6	91.5	52.1		84.8	82.7	3.6	88.4
	Mean	30.5	90.8	52.2		85.0	82.7	4.2	89.2

% AR – total applied radioactivity

% ROI – region of interest determined from the HPLC chromatogram

¹ Aqueous and soil phases and parent recovery were determined by ¹⁴C-HPLC analysis

² NER – Non-extractable residues determined by LSC

³ Radioactive recovery derived from LSC analysis

Table 8.1.3.1.1/1-07: Tier 2 Adsorption kinetics results arising from eight soils incubated with cinmethylin for 2 hours. Nominal test concentration = 2 µg/mL. Soil to liquid ratio = 1/2 (m/v).

Soil	Rep.	Aqueous phase		Soil phase		Parent recovery		NER (% AR) ²	Radioactive recovery (% AR) ³
		(% parent) ¹	% ROI	(% parent) ¹	% ROI	LSC (% AR)	HPLC (% parent)		
Li 10 (Germany)	1	26.5	100.0	59.0	100.0	85.5	85.5	0.3	85.7
	2	26.5	100.0	59.4		85.9	85.9	0.2	86.1
	3	24.3	92.0	60.1		86.1	84.4	0.2	86.3
	Mean	25.8	97.3	59.5		85.8	85.3	0.2	86.0
LUFA 2.1 (Germany)	1	49.6	100.0	44.3	100.0	93.9	93.9	0.5	94.5
	2	49.3	100.0	44.4		90.6	90.6	0.6	91.2
	3	28.6	96.0	53.2		82.8	81.8	0.9	83.6
	Mean	41.5	98.7	47.3		89.1	88.8	0.7	89.8
LUFA 2.3 (Germany)	1	25.3	91.4	58.2	100.0	85.4	83.5	0.9	86.4
	2	26.5	91.0	52.3		81.0	78.9	0.9	81.9
	3	48.1	95.6	45.7		95.6	93.7	0.7	96.2
	Mean	33.3	92.7	52.1		87.3	87.3	0.8	87.3
New Jersey (USA)	1	21.3	90.8	66.8	100.0	89.7	88.1	2.0	91.8
	2	21.8	92.5	66.5		89.6	88.3	2.5	92.1
	3	19.2	90.2	63.4		84.1	82.5	1.9	86.1
	Mean	20.7	91.2	65.6		87.8	86.3	2.2	90.0
La Gironda (Spain)	1	18.1	88.2	67.2	100.0	87.0	85.3	3.4	90.4
	2	25.7	92.5	61.0		88.2	86.7	2.7	90.9
	3	25.1	93.5	60.3		86.6	85.4	2.6	89.2
	Mean	25.0	91.4	62.9		87.2	85.8	2.9	90.2
Poggio Renatico (Italy)	1	41.5	94.8	53.4	100.0	96.5	94.9	1.9	98.4
	2	39.5	94.3	49.5		90.8	89.0	1.9	92.7
	3	42.6	94.4	47.2		91.7	89.8	1.4	93.1
	Mean	41.2	94.5	50.0		93.0	91.2	1.7	94.7
Gunma (Japan)	1	14.5	100.0	78.5	100.0	92.9	92.9	3.4	96.3
	2	16.7		75.7		92.4	92.4	3.4	95.7
	3	15.3		72.0		87.3	87.3	3.4	90.7
	Mean	15.5		75.4		90.9	90.9	3.4	94.3
Wyoming (USA)	1	34.8	92.9	50.2	100.0	86.7	85.1	4.7	91.4
	2	39.1	93.7	48.4		89.1	87.5	4.4	93.6
	3	41.8	95.3	42.4		85.6	84.3	3.8	89.4
	Mean	38.6	94.0	47.0		87.1	85.6	4.3	91.4

% AR – total applied radioactivity

% ROI – region of interest taken from HPLC chromatogram

¹ Aqueous and soil phases and parent recovery were determined by ¹⁴C-HPLC analysis

² NER – Non-extractable residues determined by LSC

³ Radioactive recovery derived from LSC analysis

Table 8.1.3.1.1/1-08: Tier 2 Adsorption kinetics results arising from eight soils incubated with cinmethylin for 8 hours. Nominal test concentration = 2 µg/mL. Soil to liquid ratio = 1/2 (m/v).

Soil	Rep.	Aqueous phase		Soil phase		Parent recovery		NER (% AR) ²	Radioactive recovery (% AR) ³
		(% parent) ¹	% ROI	(% parent) ¹	% ROI	LSC (% AR)	HPLC (% parent)		
Li 10 (Germany)	1	28.6	92.7	52.5	100.0	82.9	81.0	1.0	83.8
	2	31.4	94.9	57.3		90.0	88.7	0.9	90.9
	3	30.7	94.3	56.0		88.2	86.7	1.0	89.1
	Mean	30.2	94.0	55.2		87.0	85.5	0.9	88.0
LUFA 2.1 (Germany)	1	32.8	96.8	54.6	100.0	88.3	87.4	0.5	88.9
	2	34.6	96.9	52.7		88.1	87.2	0.6	88.7
	3	20.0	92.7	51.5		72.8	71.5	1.2	73.9
	Mean	29.1	95.5	52.9		83.1	82.0	0.8	83.8
LUFA 2.3 (Germany)	1	44.7	96.3	45.5	100.0	91.6	90.2	0.6	92.2
	2	41.7	95.5	48.1		91.5	89.9	0.6	92.1
	3	44.1	95.5	49.7		95.5	93.7	0.6	96.1
	Mean	43.5	95.8	47.8		92.8	91.3	0.6	93.5
New Jersey (USA)	1	23.2	95.3	57.4	100.0	81.4	80.5	2.2	83.6
	2	28.4	94.7	61.1		90.7	89.5	1.8	92.5
	3	28.0	95.1	60.6		89.7	88.6	1.9	91.6
	Mean	26.5	95.0	59.7		87.3	86.2	2.0	89.2
La Gironde (Spain)	1	20.1	97.0	64.4	100.0	84.9	84.4	3.0	87.9
	2	22.0	95.5	68.1		90.9	90.1	3.5	94.3
	3	22.4	97.6	70.9		93.7	93.3	3.1	96.9
	Mean	21.5	96.7	67.8		89.8	89.3	3.2	93.0
Poggio Renatico (Italy)	1	36.0	94.5	56.5	100.0	94.2	92.5	1.3	95.5
	2	35.5	93.9	56.1		93.4	91.6	2.2	95.6
	3	29.9	93.3	58.3		89.8	88.2	1.6	91.4
	Mean	33.8	93.9	57.0		92.5	90.8	1.7	94.2
Gunma (Japan)	1	11.2	100.0	80.4	100.0	91.6	91.6	6.5	98.1
	2	11.7		77.1		88.9	88.9	3.8	92.7
	3	12.2		83.0		95.2	95.2	7.7	102.8
	Mean	11.7		80.2		91.9	91.9	6.0	97.9
Wyoming (USA)	1	38.2	94.6	50.6	100.0	90.3	88.8	5.9	96.2
	2	38.9	92.6	50.9		92.0	89.9	3.7	95.8
	3	41.5	96.6	52.5		95.0	94.0	5.0	100.0
	Mean	39.5	94.6	51.3		92.5	90.9	4.8	97.3

% AR – total applied radioactivity

% ROI – region of interest taken from HPLC chromatogram

¹ Aqueous and soil phases and parent recovery were determined by ¹⁴C-HPLC analysis

² NER – Non-extractable residues determined by LSC

³ Radioactive recovery derived from LSC analysis

The Applicant calculated the distribution co-efficient (K_d) and the organic carbon normalised adsorption co-efficient (K_{oc}) based on the concentration of cinmethylin in the soil and aqueous phase extracts. The following equations were used; these are derived from the OECD 106 guidelines.

$$K_d = \frac{C_s^{ads}(eq)}{C_{aq}^{ads}(eq)} = \frac{m_s^{ads}(eq)}{m_{aq}^{ads}(eq)} \frac{V_0}{m_{soil}} (cm^3 g^{-1})$$

Where:

$C_s^{ads}(eq)$ = content of the substance adsorbed on the soil at adsorption equilibrium ($\mu g g^{-1}$);

$C_{aq}^{ads}(eq)$ = mass concentration of the substance in the aqueous phase at adsorption equilibrium ($\mu g cm^{-3}$); this concentration is analytically determined considering the values given by the blanks.

$m_s^{ads}(eq)$ = mass of the test substance adsorbed on the soil at adsorption equilibrium (μg);

$m_{aq}^{ads}(eq)$ = mass of the test substance in the solution at adsorption equilibrium (μg);

m_{soil} = quantity of the soil phase expressed in dry mass of soil (g);

V_0 = initial volume of the aqueous phase in contact with the soil (cm^3).

$$K_{oc} = K_d \cdot \frac{100}{\% oc} (cm^3 g^{-1})$$

Where:

% oc = percentage of organic carbon in the soil sample ($g g^{-1}$).

Table 8.1.3.1.1/1-09 summarises the cinmethylin concentrations and resulting K_d and K_{oc} values following 1, 2 and 8 hours of equilibration.

Table 8.1.3.1.1/1-09: Tier 2 Distribution co-efficient for adsorption (K_d) and organic carbon normalised adsorption co-efficient (K_{oc}) for eight soils. Nominal test concentration = 2 µg/mL. Soil to liquid ratio = 1/2 (m/v).

Soil	Replicate	1 Hour				2 Hours				8 Hours			
		Aq. Conc. (µg/mL)	Soil Conc. (µg/g)	K_d (mL/g)	K_{oc} (mL/g)	Aq. Conc. (µg/mL)	Soil Conc. (µg/g)	K_d (mL/g)	K_{oc} (mL/g)	Aq. Conc. (µg/mL)	Soil Conc. (µg/g)	K_d (mL/g)	K_{oc} (mL/g)
Li 10 (Germany)	1	0.67	2.09	3.11	349.63	0.53	2.39	4.47	502.35	0.58	2.12	3.69	414.08
	2	0.69	2.06	3.00	336.88	0.53	2.41	4.50	506.11	0.63	2.32	3.66	410.99
	3	0.69	2.06	2.99	336.10	0.49	2.43	4.95	556.64	0.61	2.27	3.67	412.19
	Mean	0.68	2.07	3.03	340.87	0.52	2.41	4.64	521.70	0.61	2.24	3.67	412.42
LUFA 2.1 (Germany)	1	0.61	2.30	3.80	528.21	1.00	1.79	1.79	248.59	0.66	2.21	3.34	463.50
	2	0.60	2.25	3.73	518.17	0.93	1.79	1.92	266.83	0.70	2.13	3.05	423.93
	3	0.60	2.30	3.81	528.56	0.58	2.15	3.73	518.19	0.40	2.08	5.16	716.03
	Mean	0.60	2.29	3.78	524.98	0.84	1.91	2.48	344.54	0.59	2.14	3.85	534.49
LUFA 2.3 (Germany)	1	0.67	2.10	3.11	471.48	0.51	2.35	4.63	701.05	0.90	1.84	2.04	309.73
	2	0.68	2.06	3.03	458.43	0.53	2.12	3.96	599.63	0.84	1.95	2.31	350.75
	3	0.66	2.20	3.35	508.22	0.97	1.85	1.91	289.27	0.89	2.01	2.26	342.66
	Mean	0.67	2.12	3.16	479.38	0.67	2.11	3.50	529.98	0.88	1.93	2.21	334.38
New Jersey (USA)	1	0.54	2.49	4.60	353.87	0.43	2.70	6.33	486.81	0.46	2.32	4.99	383.95
	2	0.53	2.48	4.69	361.11	0.44	2.69	6.16	473.48	0.57	2.47	4.33	333.36
	3	0.78	2.20	2.81	215.97	0.38	2.56	6.67	512.89	0.56	2.45	4.37	335.94
	Mean	0.62	2.39	4.03	310.32	0.42	2.65	6.38	491.06	0.53	2.41	4.56	351.08

Note: Cinmethylin concentrations are derived from HPLC analysis. All values have been calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted from the soil phase.

Table 8.1.3.1.1/1-09 continued

Soil	Replicate	1 Hour				2 Hours				8 Hours			
		Aq. Conc. (µg/mL)	Soil Conc. (µg/g)	K _d (mL/g)	K _{oc} (mL/g)	Aq. Conc. (µg/mL)	Soil Conc. (µg/g)	K _d (mL/g)	K _{oc} (mL/g)	Aq. Conc. (µg/mL)	Soil Conc. (µg/g)	K _d (mL/g)	K _{oc} (mL/g)
La Gironde (Spain)	1	0.46	2.69	5.89	306.90	0.36	2.72	7.58	394.71	0.40	2.60	6.54	340.50
	2	0.48	2.56	5.31	276.81	0.51	2.47	4.85	252.55	0.44	2.75	6.32	328.92
	3	0.61	2.59	4.25	221.42	0.50	2.44	4.91	255.71	0.44	2.87	6.46	336.32
	Mean	0.52	2.61	5.15	268.38	0.45	2.54	5.78	300.99	0.43	2.74	6.44	335.25
Poggio Renatico (Italy)	1	0.60	2.27	3.77	460.06	0.83	2.16	2.59	316.39	0.72	2.29	3.17	385.99
	2	0.60	2.32	3.86	470.98	0.79	2.00	2.52	307.71	0.71	2.27	3.19	388.75
	3	0.63	2.23	3.56	433.94	0.85	1.91	2.24	272.66	0.60	2.36	3.92	478.38
	Mean	0.61	2.27	3.73	454.99	0.83	2.02	2.45	298.92	0.68	2.30	3.43	417.71
Gunma (Japan)	1	0.24	3.09	12.88	296.74	0.29	3.17	11.02	253.97	0.22	3.25	14.61	336.74
	2	0.29	3.01	10.43	240.40	0.33	3.06	9.21	212.29	0.23	3.12	13.35	307.52
	3	0.28	3.00	10.65	245.39	0.30	2.91	9.54	219.81	0.24	3.35	13.80	317.93
	Mean	0.27	3.03	11.32	260.84	0.31	3.05	9.93	228.69	0.23	3.24	13.92	320.73
Wyoming (USA)	1	0.61	2.17	3.62	524.10	0.68	2.03	2.99	433.70	0.74	2.05	2.75	398.36
	2	0.63	2.16	3.50	507.88	0.76	1.96	2.57	372.02	0.76	2.06	2.71	393.29
	3	0.62	2.16	3.53	511.26	0.82	1.71	2.10	304.86	0.81	2.12	2.63	380.54
	Mean	0.62	2.16	3.55	514.41	0.75	1.90	2.55	370.19	0.77	2.08	2.70	390.73

Note: Cinmethylin concentrations are derived from HPLC analysis. All values have been calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted from the soil phase.

Based on the instability of cinmethylin, the high levels of sorption to the test vessel walls and the equilibration time, the Applicant concluded that an incubation time of 2 hours was optimal. The HSE evaluator agrees.

Tier 3 – Adsorption isotherms

The Applicant stated that adsorption isotherms were established based on the direct method, hence analysis of the aqueous phase as well as the soil phase. Furthermore, isotherms were established based on test item specific analysis of both phases and not based on total radioactivity. For this purpose, all application solutions as well as samples (aqueous phases and soil extracts) were quantified by ^{14}C -HPLC as well. This approach was chosen as cinmethylin was not completely stable for 8 h in CaCl_2 -solution.

As discussed in the Methods section, the HSE evaluator accepted the data and procedures of the Applicant and the subsequent adsorption isotherms and sorption kinetics values. The values and isotherms reported below are as reported by the Applicant. The HSE evaluator notes that there were small differences in the kinetics values when comparing the Applicant's values with those derived from the EFSA OECD 106 Excel calculator tool. The HSE evaluator investigated this and has apportioned this to the effect of rounding of aqueous and soil phase concentration values and the subsequent effect of this on the log-transformed values used for the Freundlich isotherms.

Adsorption study results are summarised for each soil in Tables 8.1.3.1.1/1-10-17. Associated adsorption isotherms are shown in Figures 7.1.3.1.1/1-02-09, with isotherms derived from the Applicant and residuals derived from the HSE evaluator's own assessment of the data. The Freundlich adsorption coefficients K_F covered a range from 1.88 mL/g to 13.49 mL/g for the eight soils, being lowest for the sandy loam (LUFA 2.3) and highest for the loam (Gunma). The K_{FOC} values ranged from 266.45 mL/g to 645.70 mL/g. The Freundlich adsorption exponent ($1/n$) indicated a slight non-linearity of the adsorption for 7 out of 8 soils. Six soils showed a slightly more pronounced adsorption behaviour of the test item at lower concentrations.

Table 8.1.3.1.1/1-10: Tier 3 summary results for Li 10 soil. Contact time = 2 hours, soil to liquid ratio = 1/2 (m/v).

Nominal conc. (µg/mL)	Actual conc. (µg/mL)	Aqueous conc. (µg/mL)	Soil conc. (µg/g)	Parental recovery (without NER) (% applied)	NER (% AR)	Total recovery (% AR)	K _d (mL/g) ¹	K _{oc} (mL/g) ¹
0.05	0.05	0.01	0.06	82.8	1.3	84.1	4.64	521.47
		0.01	0.06	83.6	0.9	84.5	4.71	529.11
		0.01	0.06	85.5	1.0	86.4	4.57	513.73
Mean		0.01	0.06	84.0	0.9	85.0	4.64	521.44
0.2	0.21	0.05	0.25	82.7	1.0	85.4	5.00	562.32
		0.05	0.24	80.0	0.9	82.4	4.47	501.82
		0.05	0.24	80.2	0.8	82.8	4.68	526.12
Mean		0.05	0.24	80.9	0.9	83.6	4.72	530.09
0.5	0.51	0.13	0.61	85.4	0.9	88.0	4.59	515.56
		0.14	0.61	86.8	0.8	89.3	4.22	474.43
		0.14	0.68	93.9	1.1	97.1	4.77	536.27
Mean		0.14	0.63	88.7	0.9	91.4	4.53	508.75
2	2.12	0.59	2.38	84.0	0.8	86.5	3.99	448.86
		0.56	2.40	82.8	0.9	85.5	4.28	480.63
		0.55	2.36	81.2	1.0	84.1	4.31	484.65
Mean		0.57	2.38	82.7	0.9	85.3	4.20	471.38
5	5.07	1.26	5.91	82.8	1.1	85.7	4.70	527.78
		1.11	5.76	78.5	1.0	81.6	5.17	580.61
		1.24	5.89	82.4	0.9	85.4	4.73	531.71
Mean		1.21	5.85	81.2	1.0	84.2	4.87	546.70

¹ Calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted.

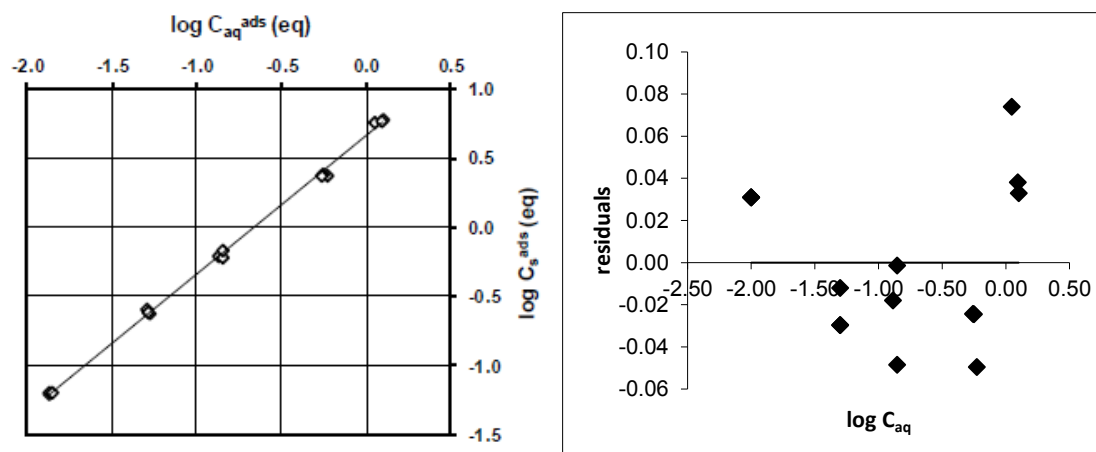


Figure 8.1.3.1.1/1-02: Left: Adsorption isotherm of cinmethylin to soil Li 10 over 2 hours. Nominal test concentrations range from 0.05 to 5 µg/mL. $1/n = 1.00$. $K_r = 4.54$. $K_{oc} = 510.13$. $R^2 = 0.998$. Right: Residuals plot for the adsorption isotherm.

Table 8.1.3.1.1/1-11: Tier 3 summary results for LUFA 2.1 soil. Contact time = 2 hours, soil to liquid ratio = 1/2 (m/v).

Nominal conc. (µg/mL)	Actual conc. (µg/mL)	Aqueous conc. (µg/mL)	Soil conc. (µg/g)	Parental recovery (without NER) (% applied)	NER (% AR)	Total recovery (% AR)	K _d (mL/g) ¹	K _{oc} (mL/g) ¹
0.05	0.05	0.01	0.06	86.1	1.6	87.7	4.28	594.82
		0.03	0.05	98.4	0.5	98.9	2.03	282.34
		0.01	0.06	85.2	1.3	86.4	4.60	638.84
Mean		0.02	0.06	89.9	1.1	91.0	3.64	505.33
0.2	0.21	0.05	0.25	82.9	1.2	85.0	4.69	650.93
		0.05	0.25	81.4	1.0	84.0	4.93	685.30
		0.11	0.23	102.0	1.0	104.6	2.16	300.23
Mean		0.07	0.24	88.8	1.0	91.2	3.93	545.48
0.5	0.51	0.13	0.59	83.3	0.9	86.5	4.49	623.17
		0.24	0.54	100.0	0.7	103.0	2.22	308.80
		0.13	0.61	85.2	1.3	88.5	4.72	655.50
Mean		0.17	0.58	89.5	1.0	92.6	3.81	529.16
2	2.12	1.15	1.81	96.7	0.5	99.8	1.58	219.52
		1.01	2.00	94.6	0.5	97.7	1.98	275.17
		1.04	2.03	96.9	0.7	100.0	1.95	270.31
Mean		1.06	1.94	96.1	0.6	99.2	1.84	255.00
5	5.07	1.45	5.80	85.7	1.9	91.1	4.00	555.27
		1.40	6.15	88.0	2.0	93.5	4.40	610.87
		1.21	5.92	82.1	1.0	86.2	4.87	676.56
Mean		1.35	5.96	85.3	1.6	90.2	4.42	614.23

¹ Calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted.

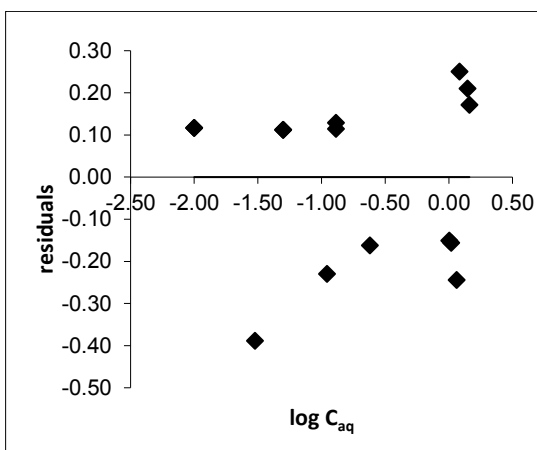
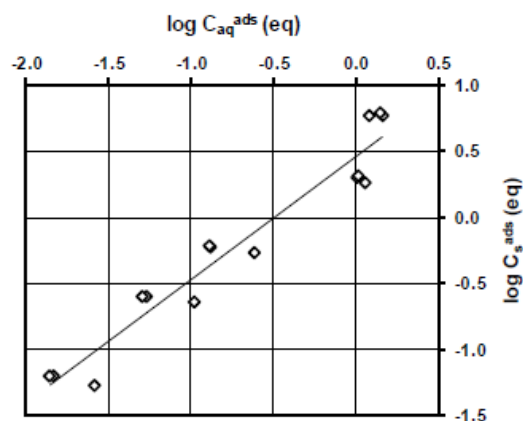


Figure 8.1.3.1.1/1-03: Left: Adsorption isotherm of cinmethylin to soil Lufa 2.1 over 2 hours. Nominal test concentrations range from 0.05 to 5 µg/mL. $1/n = 0.93$. $K_f = 2.89$. $K_{foc} = 401.43$. $R^2 = 0.938$. Right: Residuals plot for the adsorption isotherm.

Table 8.1.3.1.1/1-12: Tier 3 summary results for LUFA 2.3 soil. Contact time = 2 hours, soil to liquid ratio = 1/2 (m/v).

Nominal conc. (µg/mL)	Actual conc. (µg/mL)	Aqueous conc. (µg/mL)	Soil conc. (µg/g)	Parental recovery (without NER) (% applied)	NER (% AR)	Total recovery (% AR)	K _d (mL/g) ¹	K _{oc} (mL/g) ¹
0.05	0.05	0.02	0.05	90.9	1.0	90.9	2.24	339.59
		0.03	0.05	93.4	0.9	93.4	2.01	303.80
		0.02	0.05	93.1	0.7	93.1	2.11	320.04
Mean		0.02	0.05	92.5	0.9	92.5	2.12	321.14
0.2	0.21	0.10	0.20	91.2	0.8	91.2	2.06	312.23
		0.09	0.20	90.7	0.7	90.7	2.12	321.25
		0.10	0.20	91.3	0.8	91.3	2.09	317.16
Mean		0.10	0.20	91.1	0.7	91.1	2.09	316.88
0.5	0.51	0.24	0.50	94.8	0.7	94.8	2.09	315.96
		0.24	0.50	95.5	0.7	95.5	2.06	311.81
		0.27	0.50	100.8	0.9	100.8	1.86	281.90
Mean		0.25	0.50	97.0	0.8	97.0	2.00	303.22
2	2.12	1.05	1.90	94.6	0.8	94.6	1.80	273.41
		1.02	1.87	92.0	0.7	92.0	1.83	277.88
		1.02	1.94	93.8	0.7	93.8	1.90	287.57
Mean		1.03	1.90	93.5	0.7	93.5	1.85	279.62
5	5.07	2.18	4.57	87.9	0.7	87.9	2.10	317.55
		2.54	4.39	93.4	0.6	93.4	1.73	261.63
		2.53	4.23	91.6	0.9	91.6	1.67	253.16
Mean		2.42	4.40	91.0	0.7	91.0	1.83	277.45

¹ Calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted.

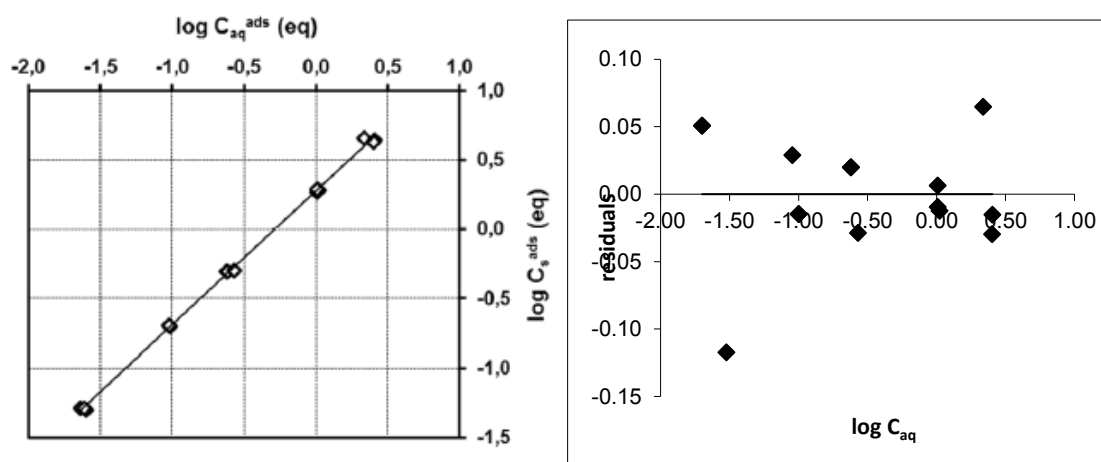


Figure 8.1.3.1.1/1-04: Left: Adsorption isotherm of cinmethylin to soil Lufa 2.3 over 2 hours. Nominal test concentrations range from 0.05 to 5 µg/mL. $1/n = 0.96$. $K_f = 1.88$. $K_{foc} = 284.29$. $R^2 = 0.999$. Right: Residuals plot for the adsorption isotherm.

Table 8.1.3.1.1/1-13: Tier 3 summary results for New Jersey soil. Contact time = 2 hours, soil to liquid ratio = 1/2 (m/v).

Nominal conc. (µg/mL)	Actual conc. (µg/mL)	Aqueous conc. (µg/mL)	Soil conc. (µg/g)	Parental recovery (without NER) (% applied)	NER (% AR)	Total recovery (% AR)	K _d (mL/g) ¹	K _{oc} (mL/g) ¹
0.05	0.05	0.02	0.07	91.8	1.7	93.4	4.45	341.93
		0.02	0.07	93.4	2.6	96.0	4.29	329.92
		0.02	0.07	95.2	2.5	97.7	4.36	335.60
Mean		0.02	0.07	93.5	2.3	95.7	4.37	335.82
0.2	0.21	0.06	0.26	88.4	2.3	92.9	4.31	331.53
		0.06	0.26	91.5	3.4	96.1	4.09	314.70
		0.06	0.27	92.2	2.6	96.1	4.17	320.89
Mean		0.06	0.26	90.7	2.8	95.0	4.19	322.37
0.5	0.51	0.17	0.63	93.7	2.4	98.1	3.73	287.17
		0.16	0.63	92.5	2.6	97.1	3.90	300.22
		0.17	0.62	94.4	2.6	99.0	3.59	276.02
Mean		0.17	0.63	93.5	2.6	98.1	3.74	287.80
2	2.11	0.42	2.60	81.3	4.0	87.2	6.15	473.28
		0.74	2.34	90.2	2.4	94.7	3.16	243.31
		0.69	2.38	88.5	2.9	93.6	3.46	266.16
Mean		0.62	2.44	86.6	3.1	91.8	4.26	327.58
5	5.05	1.70	5.00	82.8	2.4	87.4	2.93	225.52
		1.60	5.05	81.2	1.6	84.9	3.17	243.47
		1.54	5.09	80.4	0.9	83.2	3.32	255.15
Mean		1.61	5.05	81.5	1.6	85.2	3.14	241.38

¹ Calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted.

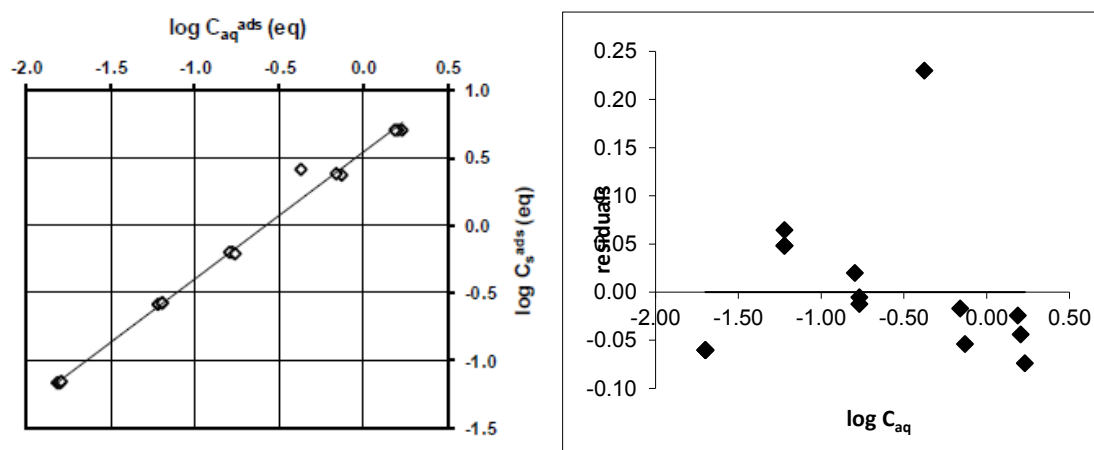


Figure 8.1.3.1.1/1-05: Left: Adsorption isotherm of cinmethylin to soil New Jersey over 2 hours. Nominal test concentrations range from 0.05 to 5 µg/mL. $1/n = 0.94$. $K_f = 3.46$. $K_{foc} = 266.45$. $R^2 = 0.991$. Right: Residuals plot for the adsorption isotherm.

Table 8.1.3.1.1/1-14: Tier 3 summary results for La Gironda soil. Contact time = 2 hours, soil to liquid ratio = 1/2 (m/v).

Nominal conc. (µg/mL)	Actual conc. (µg/mL)	Aqueous conc. (µg/mL)	Soil conc. (µg/g)	Parental recovery (without NER) (% applied)	NER (% AR)	Total recovery (% AR)	K _d (mL/g) ¹	K _{oc} (mL/g) ¹
0.05	0.05	0.01	0.076	92.3	10.6	106.8	6.66	347.07
		0.01	0.074	95.5	7.9	105.1	5.37	279.69
		0.01	0.073	89.9	6.2	96.0	6.39	332.90
Mean		0.01	0.074	92.5	8.2	102.7	6.14	319.89
0.2	0.21	0.06	0.274	90.0	13.8	105.5	4.96	258.10
		0.04	0.269	83.8	4.1	89.3	6.03	314.13
		0.06	0.274	90.1	9.2	101.1	4.91	255.85
Mean		0.05	0.272	88.0	9.1	98.6	5.30	276.03
0.5	0.50	0.13	0.589	82.8	3.2	88.7	4.57	237.89
		0.15	0.69	96.8	11.3	110.1	4.61	240.07
		0.15	0.688	96.5	7.1	105.6	4.61	239.89
Mean		0.14	0.656	92.0	7.2	101.5	4.59	239.29
2	2.08	0.46	2.428	79.4	3.5	85.8	5.23	272.45
		0.45	2.344	76.7	4.8	84.0	5.24	272.96
		0.61	2.577	89.8	10.8	103.1	4.24	221.08
Mean		0.51	2.450	82.0	6.4	91.0	4.91	255.49
5	4.99	0.88	6.916	85.6	10.1	99.0	7.85	408.79
		1.66	6.463	96.8	7.3	107.6	3.89	202.59
		0.92	7.313	90.3	6.0	99.9	7.96	414.40
Mean		1.15	6.897	90.9	7.8	102.1	6.56	341.93

¹ Calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted.

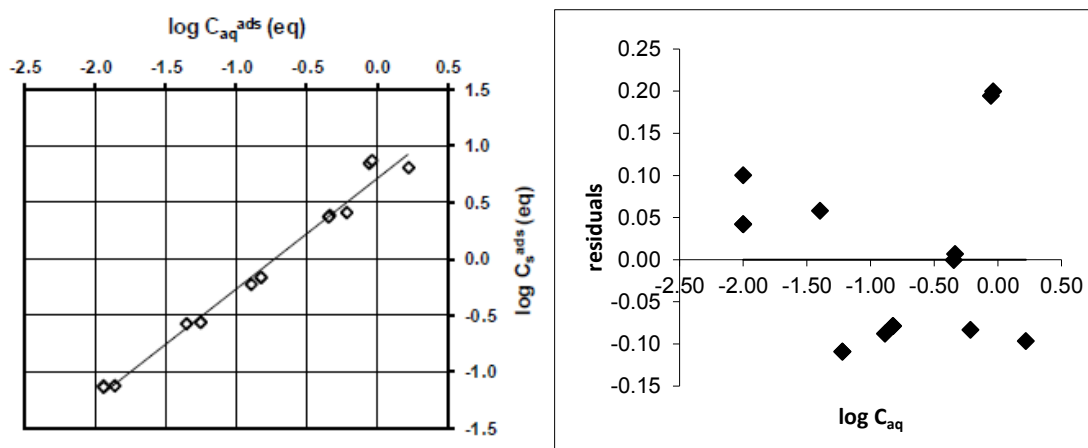


Figure 8.1.3.1.1/1-06: Left: Adsorption isotherm of cinmethylin to soil La Gironda over 2 hours. Nominal test concentrations range from 0.05 to 5 µg/mL. 1/n = 0.98. K_f = 5.19. K_{foc} = 270.15. R² = 0.984. Right: Residuals plot for the adsorption isotherm.

Table 8.1.3.1.1/1-15: Tier 3 summary results for Poggio Renatico soil. Contact time = 2 hours, soil to liquid ratio = 1/2 (m/v).

Nominal conc. (µg/mL)	Actual conc. (µg/mL)	Aqueous conc. (µg/mL)	Soil conc. (µg/g)	Parental recovery (without NER) (% applied)	NER (% AR)	Total recovery (% AR)	K _d (mL/g) ¹	K _{oc} (mL/g) ¹
0.05	0.05	0.02	0.06	92.6	1.7	94.4	3.19	388.76
		0.02	0.06	95.0	1.6	96.6	3.13	381.10
		0.02	0.06	89.7	1.1	94.2	3.65	445.29
Mean		0.02	0.06	92.4	1.5	95.0	3.32	405.05
0.2	0.21	0.09	0.26	101.2	1.7	104.9	2.97	361.74
		0.04	0.30	89.1	1.6	93.0	7.79	949.94
		0.09	0.26	101.0	1.5	104.6	2.96	361.12
Mean		0.07	0.27	97.1	1.6	100.8	4.57	557.60
0.5	0.51	0.08	0.65	79.8	1.4	83.3	7.76	945.77
		0.09	0.71	86.2	1.3	89.9	7.86	957.93
		0.09	0.70	86.4	1.5	89.8	7.52	916.54
Mean		0.09	0.69	84.1	1.4	87.7	7.71	940.08
2	2.11	0.34	2.57	76.4	2.3	81.8	7.65	932.71
		0.38	2.52	77.7	1.4	81.4	6.56	800.42
		0.37	2.53	77.2	2.0	81.8	6.86	837.01
Mean		0.36	2.54	77.1	1.9	81.7	7.03	856.71
5	5.05	2.36	4.72	93.1	1.1	97.4	2.00	244.05
		1.08	6.24	82.7	1.8	88.6	5.79	705.62
		1.00	6.53	84.0	1.9	90.2	6.55	799.24
Mean		1.48	5.83	86.6	1.6	92.1	4.78	582.97

¹ Calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted.

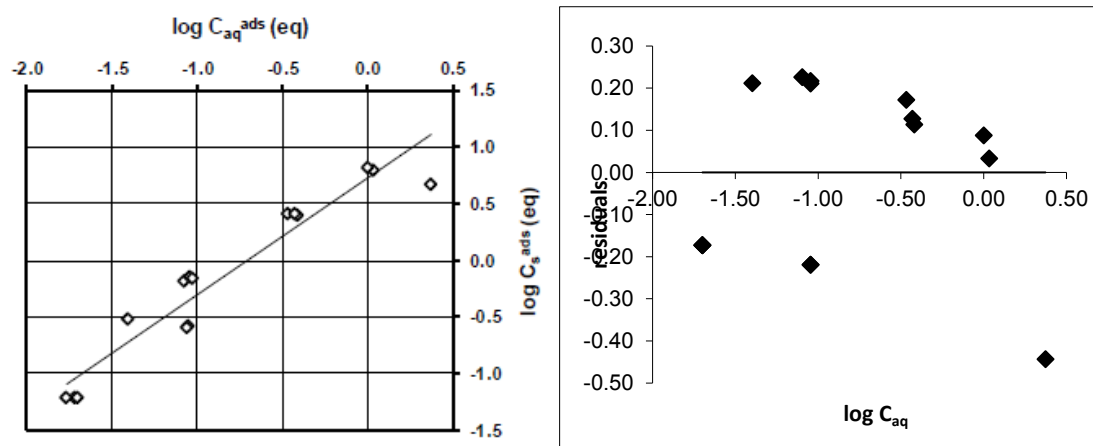


Figure 8.1.3.1.1/1-07: Left: Adsorption isotherm of cinmethylin to soil Poggio Renatico over 2 hours. Nominal test concentrations range from 0.05 to 5 µg/mL. 1/n = 1.03. K_r = 5.29. K_{loc} = 645.70. R² = 0.920. Right: Residuals plot for the adsorption isotherm.

Table 8.1.3.1.1/1-16: Tier 3 summary results for Gunma soil. Contact time = 2 hours, soil to liquid ratio = 1/2 (m/v).

Nominal conc. (µg/mL)	Actual conc. (µg/mL)	Aqueous conc. (µg/mL)	Soil conc. (µg/g)	Parental recovery (without NER) (% applied)	NER (% AR)	Total recovery (% AR)	K _d (mL/g) ¹	K _{oc} (mL/g) ¹
0.05	0.05	0.00	0.09	88.9	5.4	94.2	19.99	460.68
		0.01	0.09	93.3	5.0	98.3	13.67	314.97
		0.01	0.08	86.9	4.6	91.5	16.22	373.73
Mean		0.01	0.09	89.7	5.0	94.7	16.63	383.13
0.2	0.21	0.02	0.36	93.4	4.5	97.9	15.81	364.19
		0.02	0.37	95.9	4.8	100.7	16.84	387.92
		0.02	0.36	94.7	4.8	99.5	17.29	398.44
Mean		0.02	0.36	94.7	4.7	99.4	16.64	383.52
0.5	0.51	0.05	0.84	91.8	5.1	96.8	16.29	375.38
		0.07	0.85	97.2	5.3	102.5	11.44	263.62
		0.05	0.86	93.7	5.9	99.6	16.67	384.09
Mean		0.06	0.85	94.2	5.4	99.7	14.80	341.03
2	2.09	0.22	3.14	84.6	4.1	88.7	14.20	327.28
		0.21	3.26	87.0	6.9	94.0	15.27	351.80
		0.23	3.15	85.1	5.1	90.2	13.91	320.46
Mean		0.22	3.19	85.6	5.4	91.0	14.46	333.18
5	5.00	0.54	8.78	97.0	6.8	103.8	16.40	377.81
		0.86	9.22	107.8	6.9	114.7	10.74	247.43
		0.55	8.74	96.8	6.2	103.4	15.97	367.97
Mean		0.65	8.91	100.5	6.6	107.3	14.37	331.07

¹ Calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted.

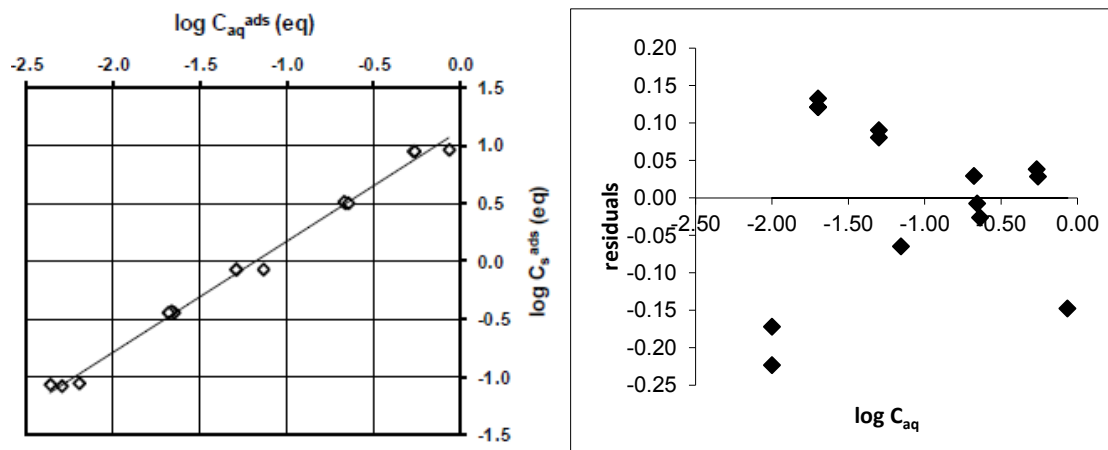


Figure 8.1.3.1.1/1-08: Left: Adsorption isotherm of cinmethylin to soil Gunma over 2 hours. Nominal test concentrations range from 0.05 to 5 µg/mL. $1/n = 0.96$. $K_f = 13.49$. $K_{loc} = 310.77$. $R^2 = 0.993$. Right: Residuals plot for the adsorption isotherm.

Table 8.1.3.1.1/1-17: Tier 3 summary results for Wyoming soil. Contact time = 2 hours, soil to liquid ratio = 1/2 (m/v).

Nominal conc. (µg/mL)	Actual conc. (µg/mL)	Aqueous conc. (µg/mL)	Soil conc. (µg/g)	Parental recovery (without NER) (% applied)	NER (% AR)	Total recovery (% AR)	K _d (mL/g) ¹	K _{oc} (mL/g) ¹
0.05	0.05	0.02	0.07	105.4	15.0	120.4	2.90	420.12
		0.02	0.07	104.6	13.9	120.3	3.45	499.36
		0.01	0.07	81.8	11.6	95.4	7.64	1107.55
Mean		0.02	0.07	97.3	13.5	112.0	4.66	675.68
0.2	0.21	0.09	0.22	96.7	15.4	114.0	2.31	334.53
		0.05	0.28	86.9	14.0	103.1	5.92	858.58
		0.10	0.22	99.6	6.5	108.1	2.18	315.40
Mean		0.08	0.24	94.4	12.0	108.4	3.47	502.84
0.5	0.50	0.23	0.46	90.4	5.5	98.0	2.02	292.55
		0.24	0.51	97.4	17.7	116.9	2.15	311.49
		0.13	0.58	83.1	10.1	95.1	4.42	640.77
Mean		0.20	0.52	90.3	11.1	103.3	2.86	414.94
2	2.05	0.90	1.92	89.0	6.2	98.0	2.13	309.26
		0.38	2.46	76.6	7.3	87.2	6.46	935.52
		0.89	1.86	87.2	10.4	100.5	2.09	302.81
Mean		0.72	2.08	84.3	8.0	95.2	3.56	515.86
5	4.90	1.09	6.30	84.1	7.7	96.2	5.79	839.04
		1.22	6.88	92.6	5.0	102.5	5.62	815.17
		2.39	6.05	108.3	8.4	120.7	2.53	367.30
Mean		1.57	6.41	95.0	7.0	106.5	4.65	673.84

¹ Calculated based on the amount adsorbed onto the soil, with the cinmethylin associated with the residual liquid in the soil pellet subtracted.

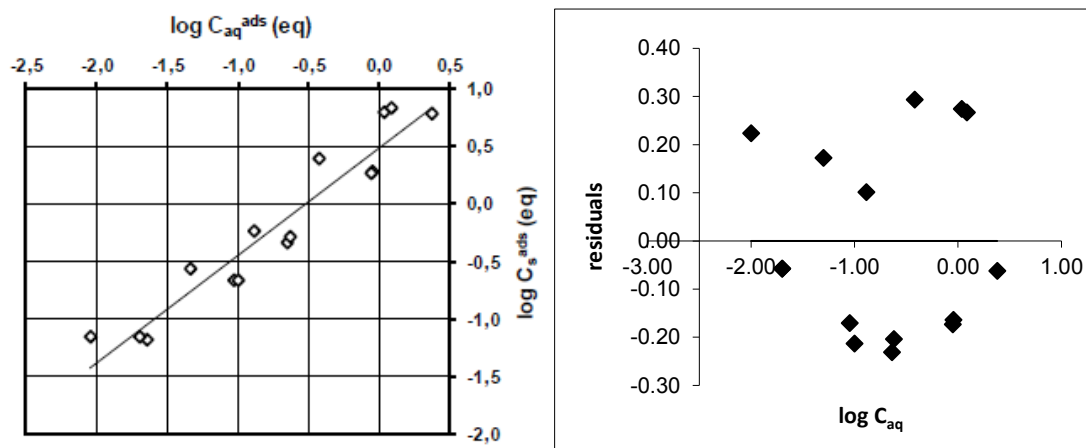


Figure 8.1.3.1.1/1-09: Left: Adsorption isotherm of cinmethylin to soil Wyoming over 2 hours. Nominal test concentrations range from 0.05 to 5 µg/mL. $1/n = 0.94$. $K_f = 3.07$. $K_{foc} = 445.32$. $R^2 = 0.916$. Right: Residuals plot for the adsorption isotherm.

Table 8.1.3.1.1/1-18 summarises the sorption kinetics values for the eight studied soils. Based on the goodness-of-fit criteria outlined in the EFSA OECD 106 checklist (EFSA, 2017), the HSE evaluator reviewed the isotherm for each soil through visual analysis of the isotherm and residuals, and through checking the R^2 and $1/n$ values. Three soils had unacceptable visual fits and R^2 values, all markedly below the recommended value of 0.975: LUFA 2.1, Poggio Renatico, and Wyoming. The HSE evaluator deemed the Freundlich isotherms for these three soils to be unsuitable for predicting sorption, and so these have been excluded from the following conclusions.

Table 8.1.3.1.1/1-18: Summary of adsorption kinetics for cinmethylin in eight soils. Greyed out columns represent soils that were rejected due to poor R^2 values (< 0.95).

Soil	Units	Li 10	LUFA 2.1	LUFA 2.3	New Jersey	La Gironde	Poggio Renatico	Gunma	Wyoming
Adsorption method	-	Direct	Direct	Direct	Direct	Direct	Direct	Direct	Direct
Soil/solution ratio	(g dw/mL)	1/2	1/2	1/2	1/2	1/2	1/2	1/2	1/2
Parental recovery (withought NER) at highest concentration	%	81.2	85.3	91.0	81.5	90.9	86.6	100.5	95.0
Adsorbed percentage (range)	%	58.0 (55.2-66.1)	54.6 (42.6-60.5)	46.1 (41.6-48.5)	58.6 (49.1-65.1)	64.4 (55.2-71.9)	61.0 (46.4-70.8)	81.8 (74.0-90.6)	56.3 (43.8-67.7)
$K_D \times$ soil/solution ratio	-	2.02-3.00	0.79-3.00	0.83-1.25	1.48-3.11	1.98-4.07	1.01-4.02	4.06-9.39	1.03-3.62
$K_{F,ads}$ (95% CIs)	L/kg dw	4.54 (4.28-4.82)	2.89 (2.07-4.04)	1.87 (1.80-1.96)	3.46 (3.05-3.93)	5.19 (4.27-6.30)	5.29 (3.38-8.29)	13.49 (11.54-15.76)	3.07 (2.07-4.57)
1/n (95% CIs)	-	1.00 (0.97-1.02)	0.93 (0.78-1.07)	0.96 (0.94-0.98)	0.94 (0.88-0.99)	0.98 (0.91-1.06)	1.03 (0.85-1.21)	0.96 (0.91-1.00)	0.94 (0.77-1.11)
R^2	-	0.998	0.938	0.999	0.991	0.984	0.920	0.993	0.916
Visual fit ¹	-	Good	Poor	Good	Good	Moderate	Poor	Good	Poor
K_{Foc}	L/kg OC	510.13	401.43	284.29	266.45	270.15	645.70	310.77	445.32

¹ Visual fit assessed the visual goodness-of-fit of the trendline to the measured data, with “good” describing a very close fit to almost all measured data points, “moderate” describing a relatively close fit to the measured data, and “poor” describing a fit where most measured data is not close to the line due to a high degree of scatter.

pH dependence

The HSE evaluator investigated pH dependence by conducting linear regression analysis, plotting soil pH for five soils against K_{foc} (Figure 8.1.3.1.1/1-10). The linear regression showed that sorption of cinmethylin is not dependent upon soil pH ($R^2 = 0.0429$; $p = 0.738$).

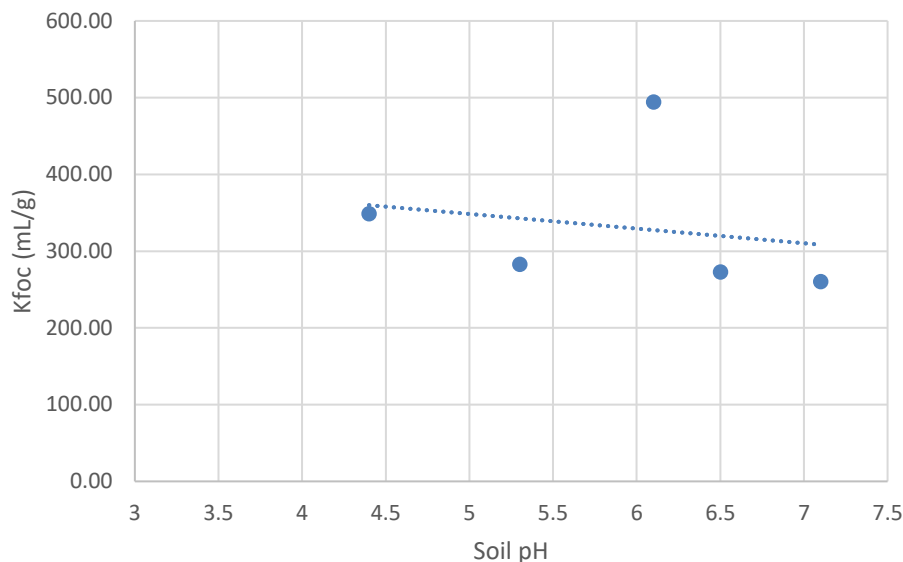


Figure 8.1.3.1.1/1-10: Linear regression investigating the pH dependence of cinmethylin sorption to five soils. $R^2 = 0.0429$; $p = 0.738$.

Organic carbon dependence

The HSE evaluator investigated the organic carbon dependence of cinmethylin sorption by conducting linear regression analysis, plotting soil organic carbon for five soils against K_f (Figure 8.1.3.1.1/1-11). The linear regression showed that sorption of cinmethylin is dependent upon soil organic carbon ($R^2 = 0.9539$; $p = 0.004$).

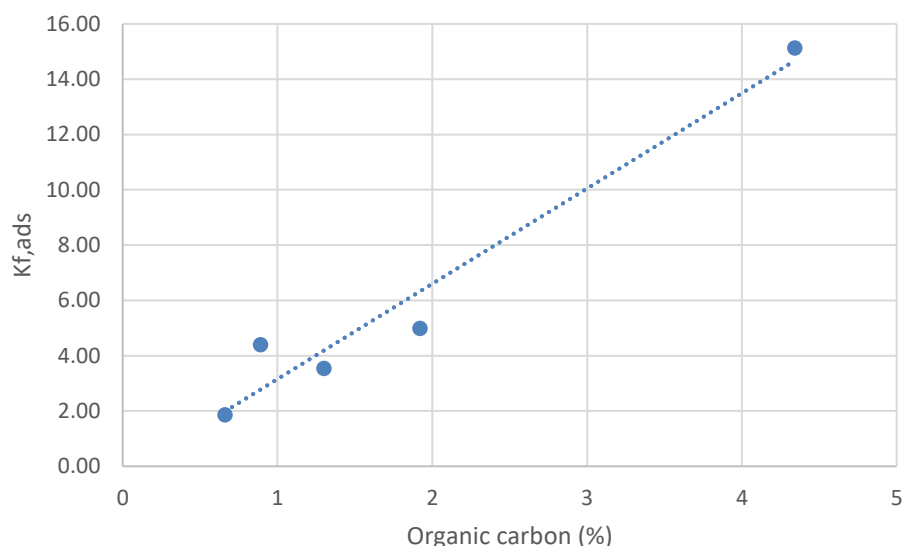


Figure 8.1.3.1.1/1-11: Linear regression investigating the organic carbon dependence of cinmethylin sorption to five soils. $R^2 = 0.9539$; $p = 0.004$.

CONCLUSIONS

The Applicant determined the adsorption behaviour of cinmethylin on eight soils. The test item was shown to be stable in CaCl_2 for 2 hours at $0.5 \mu\text{g/mL}$, yielding a recovery of 91.1% AR. HPLC injection confirmed no metabolite formation. However, for incubation times of 8 hours, the recovery was between 40.7% and 54.9% AR, indicating volatilisation or degradation of the test substance. At $5 \mu\text{g/mL}$ (the highest concentration) and 8 hours of incubation, the test item was shown to form an unidentified metabolite with approx. 7.84% AR (retention time 23.2 min). Therefore, experiments at Tier 3 were conducted with 2 h of incubation time.

The HSE evaluator performed all relevant quality checks as part of confirming the study's acceptability and the reported endpoints. These checks confirmed that the mass balance of 84.2 to 107.3% and adsorption of 46.1 to 81.8% were acceptable due to the use of the direct method. The acceptability of the analytical method was confirmed over the entire range of concentrations measured, with a reported HPLC LOQ of $0.89 \mu\text{g/L}$.

The HSE evaluator accepted five soils out of the eight supplied for determining sorption behaviour. Three soils were rejected due to poor visual fits and R^2 values below 0.975. The remaining five soils had R^2 values ranging 0.984 to 0.999 and the visual fit of both the regressions and residual plots were acceptable. The Freundlich adsorption coefficients K_F of the five accepted soils ranged 1.88 to 13.49 mL/g and the K_{FOC} values ranged from 266.45 mL/g to 510.13 mL/g . An overview of the adsorption values for the five soils accepted by the HSE evaluator is in Table 8.1.3.1.1/1-19.

The HSE evaluator concluded that there was no pH dependence for cinmethylin sorption. There was a strong trend showing organic carbon dependence.

Table 8.1.3.1.1/1-19: Overview of adsorption isotherms for cinmethylin on five soils.

Soil	Soil type (USDA)	C_{org} (%)	pH (CaCl_2)	K_F (mL/g)	K_{FOC} (mL/g)	1/n	R^2
Li 10	Loamy sand	0.89	6.1	4.54	510.13	1.00	0.998
Lufa 2.3	Sandy loam	0.66	5.3	1.88	284.29	0.96	0.999
New Jersey	Loam	1.30	6.5	3.46	266.45	0.94	0.991
La Gironda	Silty clay loam	1.92	7.1	5.19	270.15	0.98	0.984
Gunma	Loam	4.34	4.4	13.49	310.77	0.96	0.993

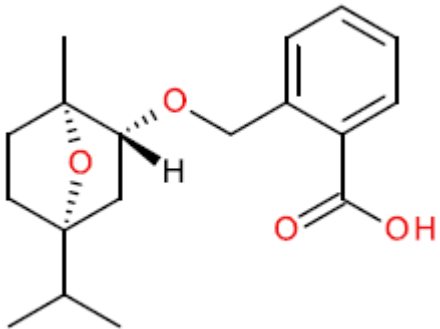
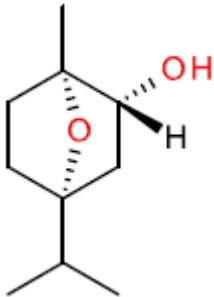
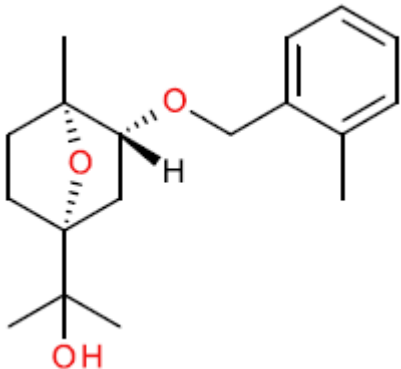
Report:	KCA 7.1.3.1.2/1; Platz, K., 2017a
Title	QSAR estimation of adsorption coefficients of M684H001, M684H003 and M684H004 metabolites of BAS 684 H
Document No.:	2017/1200466
Guidelines:	None
GLP:	No – this is a QSAR estimation of parameters
Deviations	None

Previous evaluations:	None – report submitted as part of a new active substance registration.
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INTRODUCTION

The Applicant estimated adsorption coefficients (K_{oc}) for the metabolites M684H001, M684H003 and M684H004 that occurred in studies with cinmethylin in aqueous systems. The QSAR method implemented in the EPISuite KocWIN tool were used. Table 8.1.3.1.2/1-01 summarises details of the three studied metabolites.

Table 8.1.3.1.2/1-01: Summary of metabolites of cinmethylin in aqueous systems.

Metabolite	Mass (g/mol)	Structural formula	Relevant studies
M684H001	304.4		Aerobic mineralisation in surface water (KCA 7.2.2.2/1) Aerobic aquatic metabolism (KCA 7.2.2.3/1)
	SMILES	<chem>C(C)C12CCC(C)(O1)C(C2)OCc3ccccc3C(=O)O</chem>	
M684H003	170.2		Aqueous photolysis (KCA 7.2.1.2/1) Photolysis in sterile natural water (KCA 7.2.1.3/1)
	SMILES	<chem>CC(C)C12CCC(C)(O1)C(O)C2</chem>	
M684H004	290.4		Aerobic aquatic metabolism (KCA 7.2.2.3/1)
	SMILES	<chem>C(C)(C)(O)C12CC(OCc3c(C)ccc3)C(C)(CC1)O2</chem>	

METHODS

The Applicant used KocWIN v.2.00 within the EPISuite tool to estimate K_{oc} values, using SMILES codes for metabolite identification. Values were obtained without a known $\log K_{ow}$ value, and the Applicant reported values obtained using both the molecular connectivity index (MCI) and the $\log K_{ow}$ methods.

The HSE evaluator assessed the Applicant's QSAR estimation by also using KocWIN v.2.00 to estimate values. The HSE evaluator agreed with the Applicant's processes and input values; as such, the obtained values presented in the following sections are those provided by the Applicant.

RESULTS

Table 8.1.3.1.2/1-02 summarises the obtained K_{oc} values estimated by the Applicant using KocWIN.

Table 8.1.3.1.2/1-02: Estimated K_{oc} values for metabolites of cinmethylin arising in aqueous studies.

Metabolite	Log K _{ow} ¹	K _{oc} (mL/g) MCI Method	K _{oc} (mL/g) Log K _{ow} method
M684H001	3.54	430.2	85.63
M684H003	1.59	18.61	20.07
M684H004	3.05	422.4	104.6

¹ Log K_{ow} estimated by KowWIN.

CONCLUSION

The Applicant stated that predicted values reported in Table 8.1.3.1.2/1-02 were in the range of experimental K_{oc} values observed for several similar structures, and thus deemed appropriate for further use in exposure assessments. The HSE evaluator notes that the Applicant did not provide the information to confirm that the values were in the range of similar structures, but accepts the reported K_{oc} values.

B.8.1.3.2. Aged sorption (Data Requirement 7.1.3.2)

Aged sorption data were not required for this active substance.

B.8.1.4. Mobility in soil

The study of mobility in soil is triggered when it is not possible to obtain reliable adsorption coefficient values for four soils from laboratory adsorption studies. As cinmethylin consistently demonstrated K_{oc} values greater than 25 mL/g, the study of mobility in soils was not triggered. Therefore, the data requirements 7.1.4.1.1, 7.1.4.1.2, 7.1.4.2 and 7.1.4.3 were not required for this active substance.

B.8.1.5. Persistence of cinmethylin in soil

The Applicant considered whether cinmethylin fulfils the persistence (P) or very persistent (vP) criteria within the PBT and vPvB assessments, which are defined according to Section 3.7.2.1. and 3.7.3.1, respectively, of Annex II of Regulation 1107/2009 as follows:

An active substance, safener or synergist fulfils the persistence criterion where:

- *The half-life in soil is higher than 120 days.*

An active substance, safener or synergist fulfils the 'very persistent' criterion where:

- *the half-life in soil is higher than 180 days.*

The relevant endpoints for the persistence assessment were identified based on the DG SANCO working document on "Evidence Needed to Identify POP, PBT and vPvB Properties for Pesticides" [SANCO 2012. DG SANCO Working Document on "Evidence Needed to Identify POP, PBT and vPvB Properties for Pesticides". Brussels: European Commission Health and Consumers Directorate-General. Report 25.09.2012 - rev. 3.]. According to this document, when available, field degradation half-lives are relevant for the P and vP assessment.

The degradation of cinmethylin was investigated in a laboratory soil degradation study in four aerobic soils [see KCA 7.1.1.1/1]. Additionally, the degradation of cinmethylin was investigated under field conditions, with field plots established in representative growing regions of Europe [see KCA 7.1.2.2.1/1]. Cinmethylin was incorporated into soil to exclude surface processes and to enable a straightforward generation of modeling DegT₅₀ as input for calculation of predicted environmental concentrations as recommended by EFSA [EFSA (2014)]. A kinetic evaluation was performed to

derive degradation parameters that can be used as input for modeling according to the EFSA (2014) guidance [see LCA 7.1.2.1.1/1]. The Applicant also submitted a US field dissipation study that was not designed for derivation of DegT_{50s}; however, the EFSA guidance for deriving DegT_{50s} from legacy studies was applied to the field data to allow derivation of DegT₅₀ values for modelling endpoints. The geometric mean normalized DegT₅₀ of cinmethylin was calculated from 11 soils (six from Europe and five from the United States) and was determined to be 11.1 days. This half-life describes the degradation rate in bulk soil: degradation due to surface processes is not included. Details were presented in Section CA 8.1.2.

Due to the exclusion of surface processes, the DegT₅₀ derived from data collected in European field studies are appropriate for an initial conservative assessment of persistence of cinmethylin in soil. Considering the geomean DegT₅₀ of 11.1 days derived from these studies, cinmethylin does not meet the requirements set forth for classification as P and vP in soil.

B.8.2. FATE AND BEHAVIOUR IN WATER AND SEDIMENT

The Applicant investigated the fate and behaviour of cinmethylin in the aquatic environment through a series of studies that investigated the chemical and photochemical degradation [see B.8.2.1], and biological degradation [see B.8.2.2]. Additionally, the Applicant investigated the potential effects of water treatment procedures on cinmethylin and its metabolites [see B.8.2.3]. Furthermore, the persistence of cinmethylin in the aquatic environment is assessed.

Two major metabolites, defined as breakdown products reaching 10% or more of the applied radioactivity, were observed in aquatic system studies. Table CA 8.2-01 summarises these; however, the HSE evaluator notes that they do not trigger further work.

Table CA 8.2-01 Metabolites identified in aquatic degradation studies.

Metabolite identity	Relevant studies	Peak formation (% AR)
M684H001	Aerobic mineralisation Water-sediment	13.1% 11.4% water / 3.8% sediment
M684H003	Indirect photolysis	11.5%

Route and rate of chemical and photochemical degradation in aquatic systems

The Applicant investigated the route and rate of chemical and photochemical degradation in the aquatic environment in three studies covering aqueous hydrolysis, and direct and indirect aqueous photolysis. Table CA 8.2-02 summarises the relevant studies. Kinetic evaluations were performed for the photolysis studies to derive trigger endpoints in both cases. One major metabolite was identified to be a product of indirect photochemical degradation, peaking at 11.5% AR after 15 days of irradiation.

Table CA 8.2-02 Laboratory studies investigating the chemical and photochemical degradation of cinmethylin in aquatic systems.

Laboratory study	Study type	Endpoints calculated?
Hassink, J., 2017a KCA 7.2.1.1/1	Aqueous hydrolysis	None
Hassink, J., 2017d KCA 7.2.1.2/1	Direct aqueous photolysis	Trigger
Hassink, J., 2017f KCA 7.2.1.3/1	Indirect aqueous photolysis	Trigger

The aqueous hydrolysis of cinmethylin was investigated at four pH levels (4, 5, 7 and 9) over 31 days [see KCA 7.2.1.1/1]. The Applicant also investigated the enantiomer ratio for any changes through the duration of the study. Cinmethylin was hydrolytically stable in aqueous solution at all four pH levels, with all samples measuring above 96.2% AR after 31 days. It was not possible to calculate degradation rates, and as a result it is concluded that hydrolysis is not a route of degradation for cinmethylin.

The aqueous photolysis of cinmethylin was explored in two studies, both using three labelled positions: [cyclohexane-4-¹⁴C]-, [phenyl-U-¹⁴C]- and [benzyl-¹³C]-cinmethylin, with the latter two combined to form one treatment. The first study investigated cinmethylin in a sterile aqueous buffer solution under 15 days of continuous artificial irradiation (equivalent to 17.4 days of natural sunlight at 40°N) [see KCA 7.2.1.2/1]. After 15 days, cinmethylin levels decreased from an average of 100% AR to 77% AR in the photolysis samples, and 96% in the dark control samples. The DT₅₀ was determined to be 41.8 days in artificial light, or 48.5 days in natural sunlight. A photolysis-only degradation rate could not be determined due to there being no reliable endpoints for the dark control samples. With the hydrolysis study showing no notable hydrolytic degradation, the HSE evaluator

notes that the degradation observed can be attributed to photolytic processes. Additionally, it was not possible to calculate the quantum yield as the UV spectrum of cinmethylin showed no absorption above 290 nm and hence no overlap with the spectrum of sunlight. Therefore, it was concluded that the degradation observed was due to indirect photolysis, such as by OH radicals in the water phase.

The Applicant also submitted an indirect photolysis study, investigating the degradation of cinmethylin in a sterile natural water collected from a pond in Germany and deriving modelling endpoints [see KCA 7.2.1.3/1]. After 15 days of irradiation, cinmethylin levels decreased from an average of 100% AR to 70% AR in the cyclohexane-labelled samples, and 66% AR in phenyl/benzyl-labelled samples. In dark controls, cinmethylin levels decreased to 96% and 94% AR respectively. One major metabolite, M684H003, was identified in the cyclohexane-labelled photolysis samples only. Levels increased steadily through the duration of the study, peaking at 11.0% AR after 15 days and showing no decline pattern. Individual metabolite peaks did not exceed 2.9% AR in the phenyl/benzyl-labelled samples. The DT₅₀ for indirect photolysis was determined to be 30.0 days in artificial light, or 34.8 days in natural sunlight. A photolysis-only degradation rate could not be determined due to no reliable endpoints for the dark control samples, though as before, this degradation can likely be attributed to photolytic processes.

Overall, the radiolabelling was adequate for following the metabolism of cinmethylin in these studies.

In conclusion, indirect photolysis appears to be a major route of the degradation of cinmethylin, while also forming the photolysis metabolite M684H003. Tables 8.2-03 – 04 summarise the endpoints derived from the photochemical degradation studies.

Table CA 8.2-03 Summary of trigger endpoints for the direct photolysis of cinmethylin following 15 days of continuous irradiation.

Study	DT ₅₀ (d)	DT ₉₀ (d)	χ ² error (%)	Method of calculation	DT ₅₀ natural sunlight (d)
Photolysis	41.8	139.0	2.4	SFO	48.5
Dark	> 1000	> 1000	1.4	SFO	> 1000

Table CA 8.2-04 Summary of trigger endpoints for the indirect photolysis of cinmethylin following 15 days of continuous irradiation in sterile natural water.

Study	Parent/ metabolite	DT ₅₀ (d)	DT ₉₀ (d)	χ ² error (%)	Method of calculation	DT ₅₀ natural sunlight (d)
Photolysis	Cinmethylin	30.0 ^a	99.6 ^a	-	SFO	34.8
	M684H003 ^b	> 1000	> 1000	14.6	SFO	> 1000
Dark	Cinmethylin	> 1000	> 1000	1.4	SFO	> 1000

^a Degradation rates are geomeans derived from two radiolabel experiments.

^b Metabolite was present only in the cyclohexane-labelled experiment.

Route and rate of biological degradation in aquatic systems

The Applicant submitted three laboratory studies to investigate the route and rate of biological degradation of cinmethylin in aquatic systems, plus one modelling study to supplement these. Studies were performed using [cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]- cinmethylin. Table CA 8.2-05 summarises the relevant studies.

Table CA 8.2-05 Laboratory studies investigating biological degradation of cinmethylin in aquatic systems.

Laboratory aquatic study	Study type	Endpoints calculated?
Schwarz, H., 2017a KCA 7.2.2.1/1	Ready biodegradability (CO ₂ evolution)	None
Mueller-Werthwein, M., Hegler, F., 2018a KCA 7.2.2.2/1	Aerobic mineralisation	Trigger
Mueller-Werthwein, M., Freundlich, B., 2017a KCA 7.2.2.3/1	Water/sediment	Trigger
He, W., Pape, L., 2017a KCA 7.2.2.3/2	Kinetic evaluation of water/sediment study	Modelling

The ready biodegradability of cinmethylin was studied by measuring the formed carbon dioxide (OECD 301 B: CO₂ evolution test) [see KCA 7.2.2.1/1]. The study passed all validity criteria. Cinmethylin did not biodegrade, demonstrating < 5% biodegradation over the course of 28 days at a test concentration of 20 mg/L in an inoculum derived from municipal activated sludge. Therefore, cinmethylin would be classed as not readily biodegradable. Cinmethylin was also found to not be inhibitory, with 38% biodegradation taking place after 14 days.

The aerobic mineralisation of cinmethylin was investigated in a pure water environment in a pelagic test [See KCA 7.2.2.2/1]. The Applicant studied two radiolabels ([cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]- cinmethylin) at two concentrations: 10 µg/L and 50 µg/L. Cinmethylin was slowly degraded in a pure water environment, with 62% AR (cyclohexane-label) and 85% AR (phenyl-label) remaining in water at the low concentration, and 81% AR and 91% AR remaining at the high concentration after 63 days. Volatiles peaked at 2.9 – 5% AR at 63 days depending on the label, with volatiles measuring higher in the cyclohexane-labelled samples. One metabolite exceeded 10% AR, with M684H001 peaking at 13.1% AR after 63 days. It was not possible to derive endpoints for the metabolite due to it only being present in three sampling points and showing no decline phase during the study; as a result, the HSE evaluator has included a default DT₅₀ of 1000 days.

The aerobic aquatic metabolism of cinmethylin was investigated in two aerobic water/sediment systems in dark conditions, with one system taken from a pond-like side-arm of a river, and one taken from a small stream [see KCA 7.2.2.3/1]. The Applicant conducted kinetic evaluation for deriving trigger endpoints within this study, with a supplementary study provided for derived modelling endpoints [see KCA 7.2.2.3/2]. For both systems, total radioactive residues in the water decreased from initial levels of 80 – 92% AR to 2.6 – 9.6% AR after 100 days. The residues in sediment increased correspondingly, reaching 45 – 62% AR after 100 days, of which 19 – 35% AR was still extractable. Cinmethylin peaked in sediment at 51 – 56% AR after 14 or 56 days, with levels declining to 16 – 30% AR by 100 days. One major metabolite, M684H001, was identified by the Applicant, with levels in water peaking at 6.5 – 11.4% AR after 28 days in water, and at 1.8 – 3.8% AR in sediment after 28 – 56 days. NER levels peaked in sediment at 26 – 37% AR after 78 – 100 days.

Overall, the radiolabelling was adequate for following the metabolism of cinmethylin in these studies.

In conclusion, aerobic metabolism appears to be a major route of the degradation of cinmethylin in aquatic systems, while also forming the metabolite M684H001. Mineralisation and biodegradability were not important routes of degradation.

Table CA 8.2-06 reports the trigger endpoints from the aerobic mineralisation study. Table CA 8.2-07 reports the modelling endpoints arising from the water-sediment study, and Table CA 8.2-08 reports the trigger endpoints. Table CA 8.2-09 provides a summary of the peak formations for both cinmethylin and its metabolites.

Table CA 8.2-06 Trigger endpoints derived from the aqueous aerobic mineralisation study.

Parent	63 day study				
Concentration	pH	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ^2)	Method of calculation
10 µg/L	7.3	138	457	1.4	SFO
50 µg/L		334	1110	1.8	SFO
M684H001	Max. 13.1% AR at 63 DAT				
	7.3	1000 ^a	-	-	-

^a Endpoints could not be derived as the metabolite concentration was still rising at 63 DAT, hence default DT₅₀ of 1000 days.

Table CA 8.2-07 Modelling endpoints for cinmethylin derived from the water-sediment study.

Parent	Distribution (Max. in sediment 55.9 % after 56 d)					
Whole system degradation rates						
Water / sediment system	pH water	pH sed (CaCl ₂)	Temp. °C	DegT ₅₀ /DegT ₉₀ whole system	St. (χ ² %)	Method of calculation
Berghäuser Altrhein, Germany	7.58	6.90	20 ± 2	38.7 / 128.4	11.8	SFO
Ranschgraben, Germany	7.30	5.90	20 ± 2	39.7 / 131.8	6.3	SFO
Geometric mean DegT ₅₀ whole system				39.2		
Water compartment dissipation rates (for UK surface water assessment)						
Water / sediment system	pH water	pH sed (CaCl ₂)	Temp. °C	DisT ₅₀ /DisT ₉₀ water	St. (χ ² %)	Method of calculation
Berghäuser Altrhein, Germany	7.58	6.90	20 ± 2	5.1 / 17.0	11.5	SFO
Ranschgraben, Germany	7.30	5.90	20 ± 2	8.8 / 25.2	4.4	DFOP
Maximum DisT ₅₀				8.8		

Table CA 8.2-08

Trigger endpoints for cinmethylin and its enantiomers derived from the water-sediment study.

Parent (Max. in sediment 55.9% after 56 d) – Trigger endpoints							
System	Phase	pH ^a	Temp. °C	DT ₅₀ (d) ^a	DT ₉₀ (d) ^a	St. (χ ²)	Method of calculation
Berghäuser Altrhein	Total		20 ± 2	38.7	128.4	11.8	SFO
	Water	7.58		5.2 ^b	21.5	3.6	DFOP
	Sediment	6.9		81.3	270.1	22.9	SFO
Ranschgraben	Total			39.7	131.8	6.3	SFO
	Water	7.30		4.8 ^b	25.2	4.4	DFOP
	Sediment	5.9		56.1	>1000	0.5	FOMC
Maximum	Total			39.7	131.8		
	Water			5.2	25.2		
	Sediment			81.3	>1000		
(-)-enantiomer (Reg. No. 5925581) – Trigger endpoints							
Berghäuser Altrhein	Total		20 ± 2	57.9	192.4	19.9	SFO
Ranschgraben	Total			49.2	163.5	8.8	SFO
Maximum	Total			57.9	192.4		
(+) -enantiomer (Reg. No. 5925632) – Trigger endpoints							
Berghäuser Altrhein	Total		20 ± 2	29.2	96.9	21.9	SFO
Ranschgraben	Total			30.0	99.6	11.6	SFO
Maximum	Total			30.0	99.6		

^a For total system, degradation rates (DegT_{50/90}) are shown. For water and sediment systems, dissipation rates (DisT_{50/90}) are shown.

^b Overall DT₅₀ shown

Table CA 8.2-09

Peak formation (as % AR) of cinmethylin and relevant metabolites in water and sediment. Note peak formations listed here are the greatest of all aquatic studies and are therefore suitable for use in modelling.

Compartment	Peak Formation (%AR)	
	Cinmethylin	M684H001
Water	-	11.4 % (Berghäuser Altrhein, 28d)
Sediment	55.9 % (Berghäuser Altrhein, 56d)	3.8 % (Ranschgraben, 28d)

Enantiomeric ratio changes

The Applicant investigated the enantiomeric ratio throughout the course of most of the aquatic degradation studies. In the hydrolysis study there was no change from the 50:50 enantiomer ratio at any pH after 31 days (KCA 7.2.1.1/1). There was also no significant change in the ratio after 15 days in the direct photolysis study (KCA 7.2.1.2/1) or in the indirect photolysis study (KCA 7.2.1.3/1). The HSE evaluator concludes that chemical degradation of cinmethylin does not alter the enantiomer ratio.

Regarding biological degradation, the Applicant did not explore the enantiomer ratio in relation to ready biodegradability (KCA 7.2.2.1/1); however, no biodegradation was observed. The enantiomer ratio did not change significantly due to aerobic mineralisation (KCA 7.2.2.2/1), with a ratio of 48:52 observed in the cyclohexane-labelled low concentration (10 µg/L) study and phenyl-labelled high concentration (50 µg/L) study at 63 days. However, large changes in the enantiomer ratio were observed in the water-sediment study, with the ratio shifting towards the (-)-enantiomer (KCA 7.2.2.3/1). In the Berghäuser Altrhein system, changes were observed in both the water and sediment

portions, with water shifting to 60:40 (cyclohexane label) and 58:42 (phenyl label) after 14 days, and ratios in the sediment shifting from 57:43 and 56:44 at 14 DAT to 71:29 and 76:24 at 100 DAT with 30% and 24% of the initially applied cinmethylin remaining in the sediment respectively. Enantiomeric shifts were less pronounced in the Ranschgraben system, with ratios observed in the water at approximately 55:45 at 14 DAT. In the sediment, initial ratios of 55:45 at 14 DAT shifted to 67:33 by 100 DAT in both radiolabels.

The HSE evaluator concludes that changes in the enantiomeric ratio in aquatic systems are driven by the aerobic degradation, with more rapid degradation of the (+)-enantiomer. In the water-sediment study, the (-)-enantiomer DT_{50} (57.9 days) is almost twice as long as the (+)-enantiomer DT_{50} (30.0 days). This contrasts with the degradation of the enantiomers in the soil, where the (-)-enantiomer degrades more rapidly than the (+)-enantiomer.

pH dependence

As previously mentioned, the partition co-efficient ($\log P_{ow}$) for cinmethylin was 4.5 at pH 5.8 and 20°C (see KCA 2.7/001). Additionally, cinmethylin demonstrated no dissociation between pH 3.2 – 10.9 (see KCA 2.8/001). Therefore, no influence of pH on cinmethylin degradation rates was anticipated. As the hydrolytic degradation study showed no hydrolysis or influence of pH on hydrolysis, the HSE evaluator concluded that there is no pH dependence of cinmethylin degradation in aquatic systems.

Persistence

Cinmethylin was found to be neither persistent (P) nor very persistent (vP) in the water or sediment compartments, in line with the DG SANCO definitions. See Section B.8.2.4 for further discussion.

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

B.8.2.1.1. Hydrolytic degradation (Data Requirement 7.2.1.1)

Report:	KCA 7.2.1.1/1; Hassink, J. (2017a)
Title	BAS 684 H: Aqueous hydrolysis at four different pH values
Document No.:	2016/1330118
Guidelines	OECD Guideline 111 – Hydrolysis as a function of pH (Apr 2004) US EPA Guideline OPPTS 835.2120 JMAFF Guideline 2-6-1, Notification No. 12 Nouan 8147 (Nov 2000)
GLP?	Yes
Deviations	<ul style="list-style-type: none"> • The study design appears to be based on single replicates for each pH level when the guidelines recommend samples to be in duplicate; • The test was conducted at 25°C instead of 50°C as required by the guidelines for the Tier 1 study; • The test was conducted over 31 days with no 5 DAT sampling time when the guidelines for the Tier 1 study require the test duration to be 5 days. <p>The HSE evaluator notes that deviations are discussed further throughout the evaluation; however, the deviations were not considered to invalidate the study.</p>
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The degradation of ¹⁴C-labelled cinmethylin in aqueous solutions was studied over 31 days at four pH levels: 4, 5, 7, and 9. The Applicant conducted the study to both OECD and EPA guidelines, though the HSE evaluator notes that there were several deviations from these guidelines.

MATERIALS AND METHODS

Test items

Two labelled test items were used in this study: [cyclohexane-4-¹⁴C]- and [cyclohexane-4-¹³C]-cinmethylin with respective chemical purities of 99.4% and 98.1%. Three unlabelled reference items were also used for identification purposes: cinmethylin, Reg. No. 5925581 ((-)-cinmethylin) and Reg. No. 5925632 ((+)-cinmethylin). The HSE evaluator notes that the chemical purity of one of the unlabelled reference items, (+)-cinmethylin, was low at 92.7%. The HSE evaluator does not deem this to have impacted upon the study conduct.

Stock solutions and application solutions

Prior to application solution creation, ¹⁴C-labelled test items were dried under nitrogen and dissolved with 5 mL acetonitrile, while ¹³C-labelled test items were transferred into flasks and diluted with 10 mL acetonitrile.

To create application solutions, 4 mL of the ¹³C stock solution and 5 mL of the ¹⁴C stock solution were made up to 10 mL volume with acetonitrile. The final application solution concentration was 1.08 mg/mL and the ¹⁴C/¹³C ratio was confirmed by mass spectrometry to be 1:1 (w/w). The radiochemical purity of the test item was checked by radio-HPLC and measured 97.8%.

All buffer solutions were prepared with commercially available buffers (Titrisol, Merck) according to the manufacturer's instructions. Thereafter, the solutions were diluted by the factor 10 in double distilled water to avoid interactions with the test item. The following buffer concentrates were used:

- pH 4: Titrisol 1.09884 (citrate/HCl)
- pH 5: Titrisol 1.09885 (citrate/NaOH)
- pH 7: Titrisol 1.09887 (phosphate)
- pH 9: Titrisol 1.09889 (boric acid/KCl/NaOH)

0.924 mL of the application solution (containing about 1.0 mg BAS 684 H) was transferred into 500 mL of the diluted buffer, corresponding to a final concentration of about 2.0 mg/L a.s. Subsets of 50 mL were used for hydrolysis.

All material used during the study and all buffer solutions were sterilised prior to the experiments. All solutions were prepared under a laminar bench.

Study conduct

The sterile samples (50 mL subsets) were stored in a climatic chamber at the required temperature of 25°C for 31 days. Prior to analysis, the sterility of solutions was checked at each sampling time. The pH was checked for each sample after analysis. The HSE evaluator notes that the OECD 111 guideline states, as a preliminary test, to undertake the test at a temperature of 50°C, and that this was not conducted in this case.

The sampling times were 0, 3, 10, 15, 20, 24 and 31 days after treatment. The HSE evaluator notes that OECD 111 recommends conducting the test with duplicate samples, however, the Applicant appears to have tested one sample at each time point. The HSE evaluator concludes that, since mass balances were consistently high throughout (> 97%), this has not impacted upon the study on this occasion.

All samples of the test solutions were directly analysed without a work-up. All samples were measured for radioactivity (LSC) and were analysed by HPLC to determine the amount of test item and potential metabolites. The Applicant additionally conducted chiral HPLC analysis to determine the enantiomer ratio throughout the study. The Applicant stated that all samples were analysed as soon as possible, and if necessary, samples were stored in a refrigerator before analysis. The HSE evaluator notes that there is no mention of the storage duration where samples were refrigerated; however, the experiment mass balance data is acceptable and HPLC analysis does not indicate that samples degraded during storage.

The LSC limit of detection (LOD) was 0.009% of total applied radioactivity (TAR) and the limit of quantification (LOQ) was 0.014% with a background of 0.005% AR. For HPLC, the LOQ was 0.378% AR.

RESULTS

Mass balance and sample sterility

Mass balances are presented in Table 8.2.1.1/1-01 and show that mass balance ranged 97 – 102% AR over 31 days. No loss of radioactivity occurred.

All samples were checked for sterility by the plate count technique and proved to be sterile.

Table 8.2.1.1/1-01: Recovery of radioactivity after treatment with $^{14}\text{C}/^{13}\text{C}$ -labelled cinmethylin incubated at pH 4 – 9 and 25°C. Data are presented as supplied by the Applicant.

DAT	pH 4 % TAR	pH 5 % TAR	pH 7 % TAR	pH 9 % TAR
0	100.0	100.0	100.0	100.0
3	101.5	100.8	97.3	98.6
10	100.5	100.1	99.9	97.3
15	100.2	99.9	98.9	98.7
20	100.7	99.2	97.4	97.5
24	100.5	98.9	99.5	98.4
31	100.4	98.6	98.7	97.8

Hydrolysis

Table 8.2.1.1/1-02 provides an overview for the radio-HPLC analysis of the treated samples across the four pH levels. No significant degradation was observed at any pH level, with cinmethylin levels ranging 96.2 – 97.9% AR after 31 days. No significant metabolites were formed.

Table 8.2.1.1/1-02: Radio-HPLC analysis of cinmethylin hydrolysis at pH 4 – 9 and 25°C after 31 days incubation.

DAT	pH 4 (% AR)			pH 5 (% AR)		
	Parent	Unknown ¹	Sum	Parent	Sum others ²	Sum
0	97.8	2.2	100.0	97.4	2.6	100.0
3	99.0	2.5	101.5	98.5	2.2	100.8
10	98.2	2.3	100.5	98.0	2.1	100.1
15	97.4	2.8	100.2	97.1	1.9	99.9
20	98.1	2.6	100.7	96.7	2.5	99.2
24	98.2	2.4	100.5	96.1	2.7	98.9
31	97.9	2.5	100.4	96.6	2.0	98.6
DAT	pH 7 (% AR)			pH 9 (% AR)		
	Parent	Sum others ³	Sum	Parent	Sum others ⁴	Sum
0	97.5	2.5	100.0	97.9	2.1	100.0
3	95.3	2.0	97.3	96.8	1.8	98.6
10	97.9	2.0	99.9	95.6	1.8	97.3
15	97.2	1.7	98.9	97.0	1.7	98.7
20	95.5	1.9	97.4	95.5	2.0	97.5
24	97.8	1.7	99.5	96.4	2.0	98.4
31	97.6	1.2	98.7	96.2	1.6	97.8

DAT = days after treatment. AR = total applied radioactivity.

¹ Retention time of 20.1 min

² Each individual peak < 2.8% AR

³ Each individual peak < 2.0% AR

⁴ Each individual peak < 2.0% AR

Enantiomer ratio

The Applicant investigated the enantiomer ratio in 0 and 31 DAT samples; there was no significant shift in the ratio over the course of the hydrolysis study (Table 8.2.1.1/1-03).

Table 8.2.1.1/1-03: Enantiomer ratio of $^{14}\text{C}/^{13}\text{C}$ -cinmethylin at 0 and 31 DAT at 4 pH levels. Results derived from chiral HPLC analysis.

Test	(-) enantiomer (% ROI)	(+) enantiomer (% ROI)	Cinmethylin (% AR) ¹
0 DAT			
pH 4	50.0	50.0	97.8
pH 5	50.5	49.5	97.4
pH 7	50.6	49.4	97.5
pH 9	49.4	50.6	97.9
31 DAT			
pH 4	50.0	50.0	97.9
pH 5	50.0	50.0	96.6
pH 7	50.2	49.8	97.6
pH 9	49.2	50.8	96.2

ROI = region of interest.

¹ Derived from radio-HPLC analysis

The HSE evaluator notes that the Applicant did not submit any further hydrolytic results. OECD 111 states that a Tier 1 preliminary test should be undertaken at 50°C unless the test item is known to be hydrolytically unstable; this study was undertaken at 25°C. However, the HSE evaluator notes that hydrolytic degradation was minor (< 5%) at all studied pH levels; this demonstrates that cinmethylin is hydrolytically stable at environmentally relevant conditions and temperatures. Therefore, the HSE evaluator concludes that this study is sufficient and no further hydrolysis studies are necessary.

It was not possible to calculate degradation rates due to insufficient degradation occurring over 31 days.

CONCLUSION

Cinmethylin was stable in sterile aqueous solution at pH 4, 5, 7 and 9 for 31 days at 25°C. No degradation products were detected at levels $\geq 3\%$ AR; additionally, there was no change in the enantiomer ratio during the study.

B.8.2.1.2. Direct photochemical degradation (Data Requirement 7.2.1.2)

Report:	KCA 7.2.1.2/1; Hassink, J. (2017d)
Title	Aqueous photolysis of BAS 684 H
Document No.:	2017/1066632
Guidelines	OECD Guideline 316 – Phototransformation of chemicals in water – direct photolysis (Oct 2008) US EPA Guideline OPPTS 835.2240 – Photodegradation in water (Oct 2008) FOCUS Kinetics guidance (2006; 2014)
GLP?	Yes
Deviations	<ul style="list-style-type: none"> One non-labelled reference test item, Reg. No. 5925632 ((+)-enantiomer) had a chemical purity below 95%. The HSE evaluator does not deem this to be a major issue as the item was not used in the actual photolysis study.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The investigation of photolytic degradation of cinmethylin in water was conducted according to OECD guidelines and US EPA guidelines using four labelled cinmethylin compounds (and two radiolabelled test items). Two cyclohexane-labelled compounds were combined, and two phenyl/benzyl-labelled compounds were also combined, creating two treatments. The study was conducted over 15 days of continuous artificial irradiation. The Applicant also provided a kinetic evaluation conducted to FOCUS Kinetics guidance to derive trigger endpoints (2006; 2014).

MATERIALS AND METHODS**Test items**

Four labelled test items, two of which were radiolabelled, and three unlabelled reference items were used in this study. The radiolabelled items were [cyclohexane-4-¹⁴C]-cinmethylin, [cyclohexane-4-¹³C]-cinmethylin, [phenyl-U-¹⁴C]-cinmethylin and [benzyl-¹³C]-cinmethylin⁴. The unlabelled reference items were cinmethylin, Reg. No. 5925581 ((-)-enantiomer) and Reg. No. 5925632 ((+)-enantiomer). The HSE evaluator confirms that the chemical purity of all four radiolabelled test items, and two of the three unlabelled reference items were > 95%. However, one unlabelled reference item, (+)-cinmethylin, was low at 92.7%. The HSE evaluator does not deem this to have impacted upon the study conduct.

Stock solutions and application solutions

Prior to application solution creation, ¹⁴C-labelled test items were dried under nitrogen and dissolved with 5 mL acetonitrile, while ¹³C-labelled test items were transferred into flasks and diluted with 10 mL acetonitrile. The Applicant created two application solutions: cyclohexane-labelled and phenyl/benzyl-labelled, each using a combination of ¹⁴C- and ¹³C-labelled test items.

To prepare the cyclohexane-labelled cinmethylin application solution, the Applicant mixed the whole [cyclohexane-4-¹⁴C]-labelled stock with 4 mL of the [cyclohexane-4-¹³C]-labelled stock with 1 mL acetonitrile. To prepare the phenyl/benzyl-labelled application solution, the Applicant mixed the

⁴ The UK evaluator notes that the Applicant has referred to “non-extractable residues” (NER) throughout the assessment presented here. A more accurate term for these residues would be “unextracted residues”, as the proportion of unextracted residues varies based upon the extraction used. For consistency, the UK evaluator has retained the use of “NER” throughout this assessment report but has made this note for clarity.

whole [phenyl- ^{14}C]-labelled stock with 3.894 mL of the [benzyl- ^{13}C]-labelled stock and 1 mL acetonitrile.

The Applicant determined exact concentrations by taking 10 μL aliquot of each application solution, evaporating each one to dryness under a stream of nitrogen and re-dissolving these in 1 mL acetonitrile. Aliquots were measured by LSC; actual concentrations were determined to be 1.101 mg/mL (cyclohexane-labelled) and 1.024 mg/mL (phenyl/benzyl-labelled). Aliquots were also analysed by HPLC for radiochemical purity; from a mean of three measurements the radiochemical purity was 97.8% (cyclohexane-labelled) and 95.3% (phenyl/benzyl-labelled). The $^{14}\text{C}/^{13}\text{C}$ ratio for both application solutions was 1:1 (w/w) and was confirmed by mass spectrometry.

Photolysis test system and procedure

The test item was dissolved in a sterile aqueous buffer solution. The buffer solution was prepared from Titrisol-solution by 10-fold dilution and sterile filtration (Merck 1.09887; phosphate buffer pH 7). Test solution nominal concentrations were 2 mg/L; to achieve this the Applicant brought 0.908 mL of the cyclohexane-labelled solution to 500 mL with the buffer, and 0.977 mL of the phenyl/benzyl-labelled solution to 500 mL with the buffer. These solutions were both used for dark control and photolysis samples.

The test item was dissolved in a sterile aqueous buffer solution at pH 7 (phosphate buffer). Twelve glass vessels (volume approx. 18 mL) with a quartz glass covering were situated in rectangular thermostatic controlled blocks and were filled with the test solution. Each vessel had an air inlet and outlet; the incoming air was sterilised with a sterile filter, moistened, and CO_2 was removed by 0.5 M NaOH. Volatiles (including $^{14}\text{CO}_2$) were trapped in four different trapping solutions set across five traps: 0.5 M NaOH; 0.5 M NaOH; distilled H_2O ; ethylene glycol; and 0.5 M H_2SO_4 .

For the irradiated samples, the Applicant used a SUNTEST CPS device fitted with a xenon lamp running at an intensity of approx. 3 mW/cm^2 , simulating a clear summer day at 40°N. A UV filter was fitted to cut off wavelengths < 290 nm to simulate natural sunlight. Irradiation was constant for 15 days, and incubation was at $25 \pm 1^\circ\text{C}$. This equates to 17.4 days of natural sunlight at 40°N.

For the dark control samples, the Applicant stored these in Erlenmeyer flasks in a climatic chamber set at $25 \pm 1^\circ\text{C}$.

For both irradiated and dark control samples, the Applicant sterilised all glassware by autoclaving before sample workup. Buffer sample sterility was checked for every sampling time.

Photolysis test samples

Samples were taken in duplicate at 0, 1, 3, 7, 9, 11 and 15 days after treatment (DAT). At each sampling time an aliquot was analysed by LSC for total radioactivity and HPLC for sufficient separation of test item and potential degradation products. The respective trapping solutions were analysed on total radioactive material by LSC. The Applicant noted that the 15 d samples of the H_2SO_4 trap were analysed by HPLC and showed cinmethylin as the only compound.

All samples were analysed directly where possible. Where necessary, samples were refrigerated before analysis. The HSE evaluator notes that the Applicant did not describe the storage conditions or duration, however, material balances were high for all samples at 0 DAT, leading the HSE evaluator to conclude that sample storage conditions were appropriate.

Analytical methods

All samples were measured for radioactivity by LSC and HPLC. LSC was used for quantifying radioactivity; HPLC was used to quantify the test item and potential degradation products. Chiral analysis was also performed by HPLC. Main metabolites were identified by MS analysis.

Limits of detection (LOD) and quantification (LOQ) for cinmethylin (all labels) were 0.011% total applied radioactivity (TAR) and 0.017% AR respectively for LSC analysis, and the HPLC LOQ was 0.075% AR.

Determination of quantum yield (Φ)

The Applicant determined the quantum yield of cinmethylin by using a chemical actinometer solution made up according to Dulin and Mill (1982). Two sample vessels were filled with approx. 18 mL of this solution to give the actinometer-mixture of PNAP (2×10^{-5} M) and pyridine (7.8×10^{-2} M). These vessels were irradiated together with the test solutions in the SUNTEST device. The spectra of the actinometer (1:200 dilution) and the test item were measured in the range 290–800 nm. Volatiles were not collected for these samples. The test item did not show any absorption above 290 nm; therefore, the Applicant concluded the quantum yield of cinmethylin is zero and did not pursue further testing. The HSE evaluator checked the UV spectrum supplied by the Applicant and confirms this conclusion.

Kinetic evaluation

The Applicant conducted a kinetic evaluation to derive trigger endpoints for cinmethylin and its metabolite M684H003 in aquatic hydrolysis samples. The Applicant conducted the evaluation to FOCUS kinetic guidance (2006; 2014) and used the software package KinGUI version 2 with an error tolerance set to $1\text{E-}03$ and the number of iterations of the optimisation tool (IRLS) set to 10. Trigger endpoints were derived from the kinetic models that provided the best fit to the measured data. Goodness-of-fit was compared for SFO and FOMC models. Model appropriateness was tested through detailed statistical analysis including visual assessment of the goodness of fit, Chi^2 scaled-error criterion and t-test significance.

Data were derived from HPLC analysis. The Applicant investigated the cyclohexane-labelled and phenyl/benzyl-labelled experiments separately due to the metabolite M684H003 only appearing in the cyclohexane-labelled samples; this gave two separate kinetic evaluations with two replicates each. The 0 DAT values of the parent and metabolite were left unchanged as the values are close to the values observed in the purity check of the application solution. The Applicant calculated geometric mean DegT_{50} and DegT_{90} values based on the two radiolabel positions for the parent. The Applicant also investigated the formation and degradation behaviour of the major metabolite.

The HSE evaluator assessed the supplied kinetic evaluation by deriving trigger endpoints in CAKE version 3.2, with the evaluation also following FOCUS guidance on deriving trigger endpoints. The degradation data reported in the Kinetic Evaluation section were used to derive endpoints for both photolysis and dark control samples. The HSE evaluator evaluated the decisions made by the Applicant and disagreed with their data handling. Firstly, the Applicant did not use full material balance data for the 0 DAT sampling point as required by FOCUS kinetics guidance, instead using parent- and metabolite-specific data from HPLC analysis. Secondly, the metabolite M684H003 did not trigger consideration in kinetic evaluation as it was consistently observed at levels $< 10\%$ AR and did not display a clear degradation phase. The HSE evaluator has therefore rejected the Applicant's kinetic evaluation and subsequent endpoints, instead presenting their own evaluation.

RESULTS**Mass balance and sample sterility**

A summary of both the LSC analysis for mass balance and volatiles, and HPLC analysis for separation of parent and metabolites are reported in Tables 8.2.1.2/1-01 – 02 for photolysis samples. Tables 8.2.1.2/1-03 – 04 summarise the HPLC analysis for dark control samples. LSC derived mass balances ranged 91.5 – 105.2% AR and 95.4 – 102.3% AR for the photolysis and dark control samples

respectively. Cinmethylin was the only trapped volatile product found in the trapping solutions. After 15 days of irradiation the volatiles reached a mean of 6.9% AR in cyclohexane-labelled samples, and 2.5% AR in phenyl/benzyl-labelled samples. The HSE evaluator notes that, due to the level of volatilisation observed, the kinetic evaluations reported in the following section generated dissipation rates rather than degradation rates.

HPLC analysis showed that cinmethylin accounted for 75.6% AR at 15 DAT in the cyclohexane-labelled samples, and 84.3% AR in the phenyl/benzyl-labelled samples. In the dark control samples, the mean cinmethylin concentration was 97.7% AR and 95.9% AR in the cyclohexane- and phenyl/benzyl-labelled samples respectively.

One major metabolite was observed in the cyclohexane-labelled samples. The metabolite, identified by MS analysis to be M684H003, peaked at 8.9% AR at 11 DAT and was at 6.8% AR at 15 DAT in photolysis samples. The metabolite was also present in dark control samples, but peaked at 2.3% AR at 9 DAT and was measured at 2.1% AR at 15 DAT. Several minor degradation products also occurred, but none of them with > 5% AR. The HSE evaluator notes that this is a novel metabolite for the aquatic photolysis study.

A polar fraction with a peak of 11.2% AR was detected in the 15 DAT sample of the phenyl/benzyl-labelled photolysis samples. This was fractionated and reanalysed by the Applicant; the reanalysis showed a pattern of unknown fractions individually ranging 0.52 – 4.98% AR.

All samples were checked for sterility by the plate count technique and proved to be sterile.

Table 8.2.1.2/1-01: HPLC and LSC analysis for the photolysis of cyclohexane-labelled cinmethylin in water following 15 days continuous UV irradiation, expressed in % applied radioactivity (% AR).

DAT	Replicate	HPLC analysis				LSC analysis		
		Cinmethylin	M684H003 ¹	Sum Others ²	Total	Water	Volatiles	Total
0	I	97.1	1.1	1.1	99.4	99.4	n.a.	99.4
	II	98.2	1.1	1.3	100.6	100.6	n.a.	100.6
	Mean	97.7	1.1	1.2	100.0	100.0	n.a.	100.0
1	I	101.4	1.4	0.7	103.6	103.6	n.d.	103.6
	II	100.8	1.5	0.7	103.0	103.0	n.d.	103.0
	Mean	101.1	1.5	0.7	103.3	103.3	n.d.	103.3
3	I	95.5	2.1	0.9	98.5	98.5	n.d.	98.5
	II	92.9	2.3	1.1	96.3	96.3	0.5	96.8
	Mean	94.2	2.2	1.0	97.4	97.4	0.3	97.7
7	I	95.8	2.1	n.d.	97.9	97.9	0.5	98.5
	II	96.2	2.6	0.5	99.3	99.3	n.d.	99.3
	Mean	96.0	2.4	0.3	98.6	98.6	0.3	98.9
9	I	92.4	2.1	0.4	94.9	94.9	2.0	96.8
	II	87.1	1.6	0.4	89.2	89.2	2.2	91.5
	Mean	90.0	1.9	0.4	92.0	92.0	2.1	94.1
11	I	84.6	5.2	3.7	93.4	93.4	2.2	95.5
	II	68.5	8.4	14.6	91.5	91.5	5.6	97.0
	Mean	76.6	6.8	9.2	92.4	92.4	3.9	96.3
15	I	75.6	6.8	5.5	87.9	87.9	5.6	93.5
	II	75.6	5.0	3.6	84.1	84.1	8.1	92.3
	Mean	75.6	5.9	4.5	86.0	86.0	6.9	92.9

Note: the rounding to one decimal place means that totals do not always reflect the sum of the values as presented.

n.a. = not analysed; n.d. = not detected.

¹ HPLC retention time of 20.3 min. Identified by MS analysis.

² Each individual peak measured < 6.0% AR.

Table 8.2.1.2/1-02: HPLC analysis for the dark control samples of cyclohexane-labelled cinmethylin in water, expressed in % applied radioactivity (% AR).

DAT	Replicate	HPLC analysis			
		Cinmethylin	M684H003 ¹	Sum Others ²	Total
1	I	97.1	1.1	0.6	98.7
	II	95.3	2.0	0.9	98.1
	Mean	96.2	1.6	0.8	98.4
3	I	96.7	1.6	0.7	99.0
	II	96.5	1.7	0.4	98.6
	Mean	96.6	1.7	0.6	98.8
7	I	97.1	1.9	n.d.	99.0
	II	97.3	1.5	n.d.	98.8
	Mean	97.2	1.7	n.d.	98.9
9	I	98.6	2.3	0.3	101.2
	II	96.5	1.7	0.3	98.6
	Mean	97.6	2.0	0.3	99.9
11	I	101.1	1.2	n.d.	102.3
	II	96.3	1.6	n.d.	97.9
	Mean	98.7	1.4	n.d.	100.1
15	I	97.1	2.1	n.d.	99.2
	II	96.5	1.8	n.d.	98.2
	Mean	97.7	2.0	n.d.	98.7

Note: the rounding to one decimal place means that totals do not always reflect the sum of the values as presented.

n.a. = not analysed; n.d. = not detected.

¹ HPLC retention time of 20.3 min. Identified by MS analysis.

² Each individual peak measured < 6.0% AR.

Table 8.2.1.2/1-03: HPLC and LSC analysis for the photolysis of phenyl/benzyl-labelled cinmethylin in water following 15 days continuous UV irradiation, expressed in % applied radioactivity (% AR).

DAT	Replicate	HPLC analysis				LSC analysis		
		Cinmethylin	Unknown polar fraction ¹	Sum Others ²	Total	Water	Volatiles	Total
0	I	95.1	n.d.	4.4	99.5	99.5	n.a.	99.5
	II	92.9	n.d.	7.6	100.5	100.5	n.a.	100.5
	Mean	94.0	n.d.	6.0	100.0	100.0	n.a.	100.0
1	I	95.4	0.8	7.3	103.5	103.5	0.1	103.6
	II	94.4	1.6	9.1	105.1	105.1	0.1	105.2
	Mean	94.9	1.2	8.2	104.3	104.3	0.1	104.4
3	I	95.4	1.2	3.2	99.8	99.8	0.3	100.1
	II	95.2	1.6	2.9	99.7	99.7	n.d.	99.7
	Mean	95.3	1.4	3.0	99.8	99.8	0.2	99.9
7	I	91.4	2.2	2.3	95.8	95.8	0.9	96.8
	II	90.5	2.0	2.2	94.7	94.7	0.5	95.2
	Mean	90.9	2.1	2.3	95.3	95.3	0.7	96.0
9	I	93.6	2.4	2.3	98.2	98.2	0.1	98.4
	II	91.9	2.3	2.7	96.9	96.9	1.0	97.9
	Mean	92.7	2.4	2.5	97.6	97.5	0.6	98.1
11	I	81.6	5.5 ³	4.5	91.6	91.6	2.1	93.8
	II	87.0	6.6 ³	3.8	97.5	97.5	0.1	97.6
	Mean	84.3	6.1	4.2	94.6	94.5	1.2	95.7
15	I	72.4	11.2 ³	4.9	88.5	88.5	3.5	92.0
	II	83.0	8.9 ³	4.0	96.0	96.0	1.3	97.3
	Mean	77.7	10.1	4.5	92.3	92.2	2.5	94.6

Note: the rounding to one decimal place means that totals do not always reflect the sum of the values as presented.

n.a. = not analysed; n.d. = not detected.

¹ HPLC retention time of 4.4 min.

² Each individual peak measured < 3.2% AR.

³ Further characterised by fractionation and analysis by HPLC. The reanalysis of samples showed a pattern of unknown fractions, each < 5% AR.

Table 8.2.1.2/1-04: HPLC and LSC analysis for the dark control samples of phenyl/benzyl-labelled cinmethylin in water, expressed in % applied radioactivity (% AR).

DAT	Replicate	HPLC analysis				LSC analysis
		Cinmethylin	Unknown polar fraction ¹	Sum Others ²	Total	Total in water
1	I	89.4	0.3	5.8	95.4	95.4
	II	94.7	n.d.	4.1	98.8	98.8
	Mean	92.0	0.2	4.9	97.1	97.1
3	I	94.3	0.3	5.0	99.7	99.7
	II	93.4	0.2	4.7	98.3	98.3
	Mean	93.9	0.3	4.9	99.0	99.0
7	I	95.8	0.4	3.9	100.1	100.1
	II	95.9	0.7	3.8	100.4	100.4
	Mean	95.9	0.6	3.9	100.2	100.2
9	I	94.7	0.3	3.7	98.7	98.7
	II	96.3	0.4	3.3	100.0	100.0
	Mean	95.5	0.4	3.5	99.4	99.4
11	I	94.5	0.4	3.5	98.4	98.4
	II	93.4	0.3	4.1	97.8	97.8
	Mean	94.0	0.4	3.8	98.1	98.1
15	I	94.6	0.3	3.4	98.3	98.3
	II	97.2	0.4	3.3	100.9	100.9
	Mean	95.9	0.4	3.4	99.6	99.6

Note: the rounding to one decimal place means that totals do not always reflect the sum of the values as presented.

n.a. = not analysed; n.d. = not detected.

¹ HPLC retention time of 4.3 min.

² Each individual peak measured < 0.9% AR.

Chiral analysis of enantiomer ratio

The Applicant investigated the enantiomeric ratio over time via qualitative chiral HPLC analysis of samples at 0 and 15 DAT. Results are summarised in Table 8.2.1.2/1-05 for the cyclohexane-label, and Table 8.2.1.2/1-06 for the phenyl/benzyl-label. The results obtained showed that the enantiomeric ratio remained at around 50:50 in both photolysis and dark control samples for both label positions.

Table 8.2.1.2/1-05: Determination of enantiomeric ratios in photolysis and dark control samples treated with the cyclohexane-labelled cinmethylin.

DAT	Replicate	Cinmethylin (% AR) ¹	(-)-enantiomer (% cinmethylin)	(+)-enantiomer (% cinmethylin)
0	I	97.1	49.8	50.2
	II	98.2	49.2	50.8
	Mean	97.7	49.5	50.5
15	I	75.6	48.6	51.4
	II	75.6	48.2	51.8
	Mean	75.6	48.4	51.6
Dark 15	I	97.1	50.1	49.9
	II	96.5	50.7	49.3
	Mean	97.7	50.4	49.6

¹ Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

Table 8.2.1.2/1-06: Determination of enantiomeric ratios in photolysis and dark control samples treated with the phenyl/benzyl-labelled cinmethylin.

DAT	Replicate	Cinmethylin (% AR) ¹	(-)-enantiomer (% cinmethylin)	(+)-enantiomer (% cinmethylin)
0	I	95.1	51.2	48.8
	II	92.9	50.7	49.3
	Mean	94.0	50.9	49.1
15	I	72.4	49.5	50.5
	II	83.0	48.3	51.7
	Mean	77.7	48.9	51.1
Dark 15	I	94.6	52.1	47.9
	II	97.2	51.0	49.0
	Mean	95.9	51.6	48.4

¹ Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

KINETIC EVALUATION

A kinetics study was undertaken by the Applicant to investigate the degradation behaviour of cinmethylin in both irradiated and dark conditions. The kinetic evaluation was conducted to determine degradation parameters for trigger endpoints according to the FOCUS degradation kinetics guidance (2006; 2014). The HSE evaluator rejected the Applicant's kinetic evaluation for reasons outlined in the Methods section.

The HSE evaluator evaluated the degradation of cinmethylin in the photolysis experiment and in the dark control separately. Measurements from the two radiolabels were combined, giving four replicates per time point. Table 8.2.1.2/1-07 summarises the data used for the following kinetic evaluations. The HSE evaluator notes that it was not possible to derive degradation rates for the individual enantiomers as only two sampling points, 0 and 15 DAT were analysed by chiral HPLC.

Table 8.2.1.2/1-07: Experimental data used for the kinetic evaluation of cinmethylin degradation in photolysis and dark control samples.

Photolysis		Dark control	
DAT	Cinmethylin (% AR)	DAT	Cinmethylin (% AR)
0	99.4	0	99.4
0	100.6	0	100.6
0	99.5	0	99.5
0	100.5	0	100.5
1	101.4	1	97.1
1	100.8	1	95.3
1	95.4	1	89.4
1	94.4	1	94.7
3	95.5	3	96.7
3	92.9	3	96.5
3	95.4	3	94.3
3	95.2	3	93.4
7	95.8	7	97.1
7	96.2	7	97.3
7	91.4	7	95.8
7	90.5	7	95.9
9	92.4	9	98.6
9	87.1	9	96.5
9	93.6	9	94.7
9	91.9	9	96.3
11	84.6	11	101.1
11	68.5	11	96.3
11	81.6	11	94.5
11	87.0	11	93.4
15	75.6	15	97.1
15	75.6	15	96.5
15	72.4	15	94.6
15	83.0	15	97.2

The HSE evaluator followed the recommended procedure for deriving trigger endpoints and compared the SFO and FOMC models. Appropriateness of a distinct kinetic model to describe photolytic degradation was tested based on visual assessment of goodness-of-fit, the χ^2 error rate, and the t-test to determine whether estimated degradation parameters differ from zero. In this case, there was no need to explore other biphasic models.

Results

The kinetic evaluations for photolysis and dark control samples are summarised in Tables 8.2.1.2/1-08 – 09 respectively. For the photolysis samples, the visual fit was good for both SFO and FOMC with randomly scattered residuals (Figure 8.2.1.2/1-01). SFO was chosen for the lowest error rate. For the dark control samples, SFO gave a good visual model fit with randomly scattered residuals, but it was not possible to fit an FOMC model (Figure 8.2.1.2/1-02). The slope derived for the SFO model was not significantly different to zero; therefore, no reliable endpoints can be derived for the dark control data, though the evaluation is included here for information. Table 8.2.1.2/1-11 summarises the kinetic models, estimated parameters decision process for both the photolysis and dark control samples.

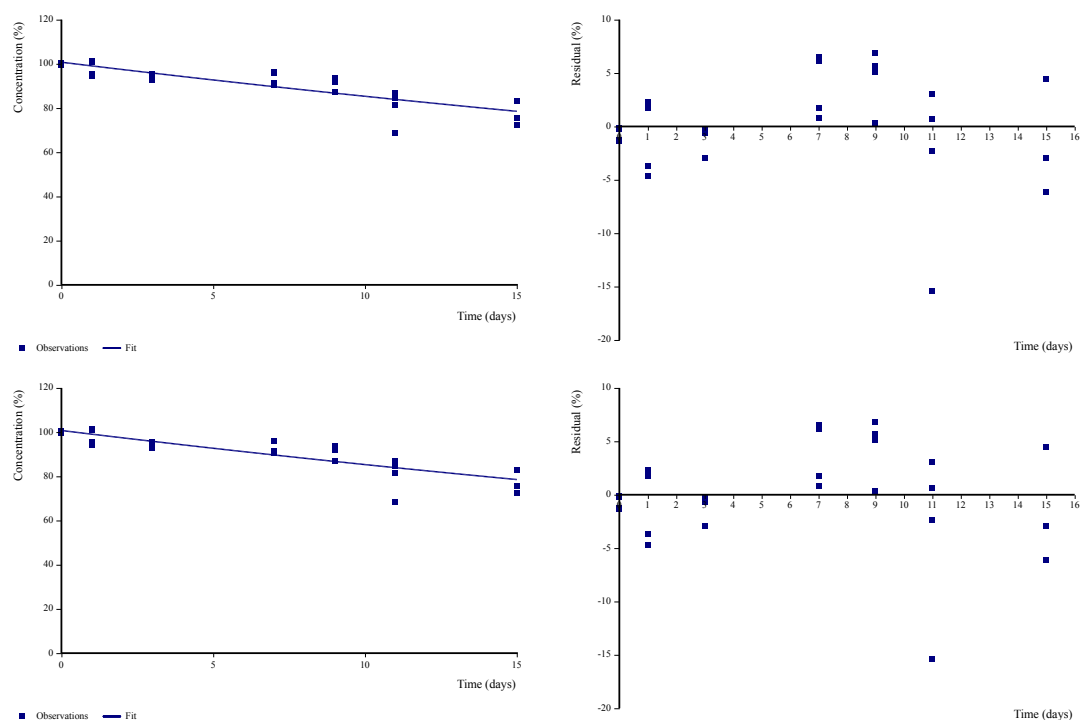


Figure 8.2.1.2/1-01: Model fits and residuals for the photolysis experiment. Top row: SFO. Bottom row: FOMC. Final fit: SFO. DegT₅₀ = 41.8 d. DegT₉₀ = 139 d. Chi² error = 2.42%.

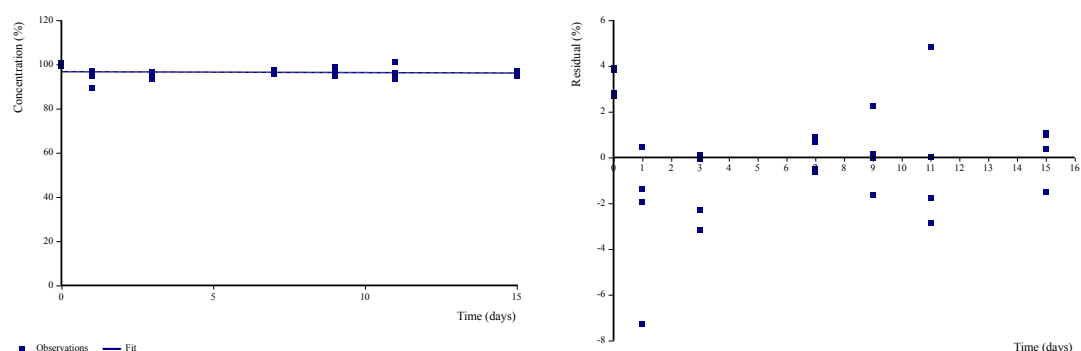


Figure 8.2.1.2/1-02: SFO model fit and residuals for the dark control experiment. DegT₅₀ > 1000 d. DegT₉₀ > 1000 d. Chi² error = 1.37%.

Table 8.2.1.2/1-08: Summary of the kinetic evaluation of cinmethylin (photolysis samples). The evaluation was conducted to derive trigger endpoints.

Experiment	Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ ² error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Photolysis	SFO	Good	100.7	k (d): 0.0166	0.013 – 0.021	< 0.0001	2.42	41.8	139
	FOMC	Good	100.7	α: 27.99 β: 1680	10.09 – 45.89 684.40 – 2680.0	- -	2.62	42.1	144
HSE evaluator decision: SFO and FOMC display similarly good fits to the measured data with scattered residuals. Both models demonstrate low error rates, but SFO has the lowest error. Use SFO to derive trigger endpoints.									

Table 8.2.1.2/1-09: Summary of the kinetic evaluation of cinmethylin (dark control). The evaluation was conducted to derive trigger endpoints.

Experiment	Kinetic	Visual	Initial	Estimated	95%	t-test	χ ²	DT ₅₀	DT ₉₀
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	model	fit	value (M ₀)	parameters	Confidence Intervals		error (%)	(d)	(d)
Dark Control	SFO	Good	96.7	k (d): 4.1E-4	-0.002 – 0.002	0.339	1.37	> 1000	> 1000
	FOMC	Could not derive a model fit							
	HSE evaluator decision: HSE evaluator decision: SFO offered a good visual fit with a very low χ^2 error rate. The rate constant is not estimated to be significantly different to zero. An FOMC model could not be fitted to the data. Therefore, no reliable endpoints can be derived for cinmethylin.								

n.d. – not derived

CONCLUSION

It was demonstrated that cinmethylin degrades in water under the influence of light. The HSE evaluator notes that there were losses observed as a result of the volatilisation of cinmethylin; as a result, the kinetic evaluation endpoints will be reported as dissipation rates and not degradation rates.

The DisT₅₀ in the artificial light test system was determined to be 41.8 days by kinetic evaluation, or 48.5 days in natural sunlight at 40°N. The HSE evaluator has not calculated an explicit photolysis-only degradation rate due to there being no reliable endpoints derived for the dark control samples, though the lack of hydrolytic degradation in the hydrolysis study (see KCA 7.2.1.1/01) indicates that the degradation observed is attributable to photolytic processes or volatilisation.

One metabolite, M684H003 was detected at levels > 5% AR, with 6% AR measured at the study end in the photolysis samples. This was detected only in the cyclohexane-labelled samples in both the light and dark samples, indicating that formation is not driven by photolytic processes. The metabolite displayed a slight decrease in levels by the study end; as a result, it was unlikely that robust kinetic parameters could be derived. Therefore, the HSE evaluator did not attempt kinetic evaluation on this metabolite.

The UV spectrum of cinmethylin showed no absorption above 290 nm and therefore no overlap with the spectrum of sunlight, hence, the quantum yield is zero and no direct photolytic degradation occurred. The Applicant concluded that the degradation of cinmethylin under light is assumed to be due to indirect photolysis e.g. by OH radicals in the water phase.

Reference:

Dulin, D., Mill, T., 1982. Development and evaluation of sunlight actinometers. Environmental Science and Technology, 16 (11), 815-820.

B.8.2.1.3. Indirect photochemical degradation (Data Requirement 7.2.1.3)

Report:	KCA 7.2.1.3/1; Hassink, J. (2017f)
Title	Photolysis of BAS 684 H in sterile natural water
Document No.:	2017/1066631
Guidelines	No specific guidelines
GLP?	Yes
Deviations	Due to a technical failure after 14 days, the 15 DAT samples of the cyclohexane-labelled experiment had to be repeated. The Applicant provided additional 0 and 15 DAT analyses for these samples.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The Applicant investigated the indirect photolytic degradation of cinmethylin in a sterile natural water over a period of 15 days of continuous artificial irradiation. Two cyclohexane-labelled compounds were combined, and two phenyl/benzyl-labelled compounds were also combined, creating two treatments. The Applicant also provided a kinetic evaluation conducted to FOCUS Kinetics guidance to derive trigger endpoints (2006; 2014).

MATERIALS AND METHODS**Test items**

Four radiolabelled test items and three unlabelled reference items were used in this study; these are summarised in Table 8.2.1.3/1-01. Three unlabelled reference items were also used; these are summarised in Table 8.2.1.3/1-02. The HSE evaluator confirms that the chemical purity of all four radiolabelled test items, and two of the three unlabelled reference items were > 95%. However, one unlabelled reference item, the (+)-enantiomer, was low at 92.7%. The HSE evaluator does not deem this to have impacted upon the study conduct. The HSE evaluator also notes that the radiochemical purity was not provided for the two ¹³C-labelled substances; however, inspection of the mass spectrometry analysis reports showed that each radiolabel contained one peak, identified as cinmethylin.

Table 8.2.1.3/1-01: Summary of radiolabelled test items used in the present study.

Substance name	Cinmethylin			
Reg. No.	900202			
Internal code	BAS 684 H			
Molecular formula	C ₁₈ H ₂₆ O ₂			
Molecular mass	274.4 g/mol			
Radiolabel position	Cyclohexane-4- ¹⁴ C	Phenyl-U- ¹⁴ C	Benzyl- ¹³ C	Cyclohexane-4- ¹³ C
Batch No.	1146-1001	1147-2001	1159-1012	1165-2001
Radiochemical purity	99.4%	98.9%	Not provided	Not provided
Chemical purity	99.3%	97.0%	99.6%	98.1%

Table 8.2.1.3/1-02: Summary of unlabelled reference items used in the present study.

Substance name	Cinmethylin	(-)-enantiomer	(+)-enantiomer
Internal code	BAS 684 H	-	-
Reg. No.	900202	5925581	5925632
Batch No.	L87-84	L87-20	L87-18
Chemical purity	99.0%	95.4%	92.7%
Noted impurities	0.5% cyclohexane	2.2% cyclohexane	4.5% cyclohexane

Stock solutions and application solutions

Stock and application solutions were prepared as part of the direct photolysis study (KCA 7.2.1.2/1; Hassink, J., 2017d). Prior to application solution creation, ^{14}C -labelled test items were dried under nitrogen and dissolved with 5 mL acetonitrile, while ^{13}C -labelled test items were transferred into flasks and diluted with 10 mL acetonitrile. The Applicant created two application solutions: cyclohexane-labelled and phenyl/benzyl-labelled, each using a combination of ^{14}C - and ^{13}C -labelled test items.

To prepare the cyclohexane-labelled cinmethylin application solution, the Applicant mixed the whole [cyclohexane-4- ^{14}C]-labelled stock with 4 mL of the [cyclohexane-4- ^{13}C]-labelled stock with 1 mL acetonitrile. The phenyl/benzyl-labelled application solution was the same as prepared for the direct photolysis study. The application solution was created by mixing the whole [phenyl- ^{14}C]-labelled stock with 3.894 mL of the [benzyl- ^{13}C]-labelled stock and 1 mL acetonitrile.

The Applicant determined exact concentrations by taking 10 μL aliquot of each application solution, evaporating each one to dryness under a stream of nitrogen and re-dissolving these in 1 mL acetonitrile. Aliquots were measured by LSC; actual concentrations were determined to be 1.125 mg/mL (cyclohexane-labelled) and 1.059 mg/mL (phenyl/benzyl-labelled). Aliquots were also analysed by HPLC for radiochemical purity; from a mean of three measurements the radiochemical purity was 97.8% (cyclohexane-labelled) and 95.3% (phenyl/benzyl-labelled). The $^{14}\text{C}/^{13}\text{C}$ ratio for both application solutions was 1:1 (w/w) and was confirmed by mass spectrometry.

Photolysis test system and procedure

The test system was s a natural pond water. It was sampled from pond “Kleiner Waldsee”, Kastenberghede, west of the town Schifferstadt, Germany. The water characteristics are given in Table 8.2.1.3/1-03.

Table 8.2.1.3/1-03: Characteristics of the pond water used to study indirect photolysis of cinmethylin.

Parameter	Measurement
Suspended particles (mg/L)	7.0
Total organic carbon (mg/L)	16.0
Nitrate content (mg/L)	< 1.0
Conductivity at 25°C ($\mu\text{S}/\text{cm}$)	262.0

The test item was dissolved in the sterile natural water (sterilisation method not provided). Test solution nominal concentrations were 2 mg/L; to achieve this the Applicant brought 0.89 mL of the cyclohexane-labelled solution to 500 mL with the natural water, and 0.944 mL of the phenyl/benzyl-labelled solution to 500 mL with the natural water. These solutions were both used for dark control and photolysis samples.

Twelve glass vessels (volume approx. 18 mL) with a quartz glass covering were situated in rectangular thermostatic controlled blocks and were filled with the test solution. Each vessel had an air inlet and outlet; the incoming air was sterilised with a sterile filter, moistened, and CO_2 was removed by 0.5 M

NaOH. Volatiles (including $^{14}\text{CO}_2$) were trapped in four different trapping solutions set across five traps: 0.5 M NaOH; 0.5 M NaOH; distilled H_2O ; ethylene glycol; and 0.5 M H_2SO_4 .

For the irradiated samples, the Applicant used a SUNTEST CPS device fitted with a xenon lamp running at an intensity of approx. 3 mW/cm^2 , simulating a clear summer day at 40°N . A UV filter was fitted to cut off wavelengths $< 290 \text{ nm}$ to simulate natural sunlight. Irradiation was constant for 15 days, and incubation was at $25 \pm 1^\circ\text{C}$. This equates to 17.4 days of natural sunlight at 40°N .

For the dark control samples, the Applicant stored these in Erlenmeyer flasks in a climatic chamber set at $25 \pm 1^\circ\text{C}$. For each label, two 0 DAT samples with volumes of approx. 18 mL were maintained separately without incubation and were analysed directly.

For both irradiated and dark control samples, the Applicant sterilised all glassware by autoclaving before sample workup. Buffer sample sterility was checked for every sampling time.

Photolysis test samples

Samples were taken in duplicate at 0, 1, 3, 7, 9, 11 and 15 days after treatment (DAT). The Applicant noted that the 15 DAT sample of the cyclohexane-label had to be repeated due to a technical failure after day 14. Therefore 0 DAT and 15 DAT were analysed additionally. The amount of applied test item was identical.

At each sampling time an aliquot was analysed by LSC for total radioactivity and HPLC for sufficient separation of test item and potential degradation products. The respective trapping solutions were analysed on total radioactive material by LSC.

All samples were analysed directly where possible. Where necessary, samples were refrigerated before analysis. The HSE evaluator notes that the Applicant did not describe the storage conditions or duration, however, material balances were high for all samples at 0 DAT, the hydrolysis study showed no hydrolytic degradation (see KCA 7.2.1.1/01), and there was very little aerobic mineralisation of cinmethylin over 63 days (see KCA 7.2.2.2/01). Therefore, the HSE evaluator concludes that sample storage conditions were appropriate.

Analytical methods

All samples were measured for radioactivity by LSC and HPLC. LSC was used for quantifying radioactivity; HPLC was used to quantify the test item and potential degradation products. Chiral analysis was also performed by HPLC. Main metabolites were identified by MS analysis.

Limits of detection (LOD) and quantification (LOQ) for cinmethylin (all labels) were 0.026% total applied radioactivity (TAR) and 0.038% AR respectively for LSC analysis, and the HPLC LOQ was 0.309% AR.

Kinetic evaluation

The Applicant conducted a kinetic evaluation to derive trigger endpoints for cinmethylin and its metabolite M684H003 following photolysis in sterile natural water samples. The Applicant conducted the evaluation to FOCUS kinetic guidance (2006; 2014) and used the software package KinGUI version 2 with an error tolerance set to $1\text{E-}03$ and the number of iterations of the optimisation tool (IRLS) set to 10. Trigger endpoints were derived from the kinetic models that provided the best fit to the measured data. Goodness-of-fit was compared for SFO and FOMC models. Model appropriateness was tested through detailed statistical analysis including visual assessment of the goodness of fit, Chi^2 scaled-error criterion and t-test significance.

Data were derived from HPLC analysis. The Applicant investigated the cyclohexane-labelled and phenyl/benzyl-labelled experiments separately due to the metabolite M684H003 only appearing in the cyclohexane-labelled samples; this gave two separate kinetic evaluations with two replicates each. The

0 DAT values of the parent and metabolite were left unchanged as the values are close to the values observed in the purity check of the application solution. The Applicant calculated geometric mean DegT₅₀ and DegT₉₀ values based on the two radiolabels. The Applicant also investigated the formation and degradation behaviour of the major metabolite.

The HSE evaluator assessed the supplied kinetic evaluation by deriving trigger endpoints in CAKE version 3.2, with the evaluation also following FOCUS guidance on deriving trigger endpoints. The degradation data reported in the Kinetic Evaluation section were used to derive endpoints for both photolysis and dark control samples. The HSE evaluator evaluated the decisions made by the Applicant and disagreed with their data handling: the Applicant did not use full material balance data for the 0 DAT sampling point as required by FOCUS kinetics guidance, instead using parent- and metabolite-specific data from HPLC analysis. Additionally, the Applicant conducted kinetic evaluation on both the parent and the metabolite M684H003 when the metabolite did not show a decline phase. However, the HSE evaluator has retained the pathway fit in the evaluation.

The HSE evaluator has therefore rejected the Applicant's kinetic evaluation and subsequent endpoints, instead presenting the HSE evaluator's own evaluation.

RESULTS

Mass balance and sample sterility

A summary of both the LSC analysis for mass balance and volatiles, and HPLC analysis for separation of parent and metabolites are reported in Table 8.2.1.3/1-04 – 05 for photolysis samples. Table 8.2.1.3/1-05 – 06 summarise the HPLC analysis for dark control samples. LSC derived mass balances ranged 91 – 101% AR and 97 – 99% AR for the photolysis and dark control samples respectively. Cinmethylin was the only trapped volatile product found in the trapping solutions. After 15 days of irradiation the volatiles reached a mean of 0.5% AR in cyclohexane-labelled samples, and 5.7% AR in phenyl/benzyl-labelled samples.

All samples were checked for sterility by the plate count method and were found to be sterile.

HPLC analysis showed that cinmethylin accounted for 69.7% AR at 15 DAT in the cyclohexane-labelled samples, and 66.3% AR in the phenyl/benzyl-labelled samples. In the dark control samples, the mean cinmethylin concentration was 95.7% AR and 93.7% AR in the cyclohexane- and phenyl/benzyl-labelled samples respectively.

One major metabolite was observed in the cyclohexane-labelled samples. The metabolite, identified by MS analysis to be M684H003, was already present at 0 DAT at 1.8% AR and peaked at 11.5% AR (mean 11.0%) at 15 DAT in photolysis samples, with no degradation observed. Several minor degradation products also occurred, but none of them with > 3.7% AR. The HSE evaluator notes that this metabolite is unique to the aquatic photolysis studies.

No distinct metabolites were observed in the phenyl/benzyl-labelled photolysis samples, but a polar fraction with no distinct HPLC peak greater than 5% AR was detected. This was fractionated and reanalysed by the Applicant; the reanalysis showed a pattern of unknown fractions individually ranging 0.06 – 4.68% AR.

Table 8.2.1.3/1-05: HPLC and LSC analysis for the photolysis of cyclohexane-labelled cinmethylin in water following 15 days continuous UV irradiation, expressed in % applied radioactivity (% AR).

DAT	Replicate	HPLC analysis				LSC analysis		
		Cinmethylin	M684H003 ¹	Sum Others ²	Total	Water	Volatiles	Total
0	I	96.8	1.8	1.0	99.5	99.5	n.a.	99.5
	II	97.5	1.8	1.1	100.5	100.5	n.a.	100.5
	Mean	97.2	1.8	1.0	100.0	100.0	n.a.	100.0
1	I	100.1	2.3	n.d.	102.4	102.4	n.d.	102.4
	II	94.6	2.3	n.d.	96.9	96.9	n.d.	96.9
	Mean	97.3	2.3	n.d.	99.7	99.7	n.d.	99.7
3	I	96.4	2.8	1.0	100.2	100.2	n.d.	100.2
	II	94.6	3.3	0.7	98.6	98.6	0.1	98.7
	Mean	95.5	3.1	0.9	99.4	99.4	< 0.1	99.5
7	I	91.1	5.0	3.1	99.1	99.1	0.1	99.3
	II	85.3	7.0	3.7	96.0	96.0	0.6	96.6
	Mean	88.2	6.0	3.4	97.5	97.5	0.4	97.9
9	I	83.9	7.5	5.4	96.7	96.7	0.1	96.9
	II	83.0	6.5	6.1	95.5	95.5	1.0	96.5
	Mean	83.4	7.0	5.7	96.1	96.1	0.5	96.7
11	I	83.4	6.1	3.9	93.4	93.4	1.0	94.4
	II	81.4	6.1	5.8	93.4	93.4	1.3	94.7
	Mean	82.4	6.1	4.9	93.4	93.4	1.1	94.5
0 *	I	96.6	1.7	0.9	99.3	99.3	n.a.	99.3
	II	98.5	2.2	n.d.	100.7	100.7	n.a.	100.7
	Mean	97.6	2.0	0.5	100.0	100.0	n.a.	100.0
15 *	I	69.4	10.6	8.9	88.9	88.9	0.6	89.5
	II	69.9	11.5	9.7	91.1	91.1	0.4	91.5
	Mean	69.7	11.0	9.3	90.0	90.0	0.5	90.5

Note: the rounding to one decimal place means that totals do not always reflect the sum of the values as presented.

n.a. = not analysed; n.d. = not detected.

¹ HPLC retention time of 20.1 min. Identified by MS analysis.

² Each individual peak measured < 3.7% AR.

* Separate incubation for 15 day analysis due to instrument failure.

Table 8.2.1.3/1-06: HPLC analysis for the dark control samples of cyclohexane-labelled cinmethylin in water, expressed in % applied radioactivity (% AR).

DAT	Replicate	HPLC analysis			
		Cinmethylin	M684H003 ¹	Sum Others ²	Total
1	I	95.5	2.0	0.7	98.2
	II	96.7	1.6	0.6	98.9
	Mean	96.1	1.8	0.7	98.5
3	I	97.0	2.2	n.d.	99.2
	II	96.6	2.5	n.d.	99.1
	Mean	96.8	2.4	n.d.	99.2
7	I	94.8	2.7	n.d.	97.5
	II	96.0	2.2	n.d.	98.2
	Mean	95.4	2.5	n.d.	97.9
9	I	96.6	1.9	n.d.	98.4
	II	97.0	2.0	n.d.	99.0
	Mean	96.8	1.9	n.d.	98.7
11	I	95.9	2.1	n.d.	98.0
	II	95.7	2.7	n.d.	98.4
	Mean	95.8	2.4	n.d.	98.2
15	I	96.6	2.7	n.d.	99.3
	II	94.9	2.0	n.d.	96.8
	Mean	95.7	2.3	n.d.	98.1

Note: the rounding to one decimal place means that totals do not always reflect the sum of the values as presented.

n.a. = not analysed; n.d. = not detected.

¹ HPLC retention time of 20.1 min. Identified by MS analysis.

² Each individual peak measured < 0.7% AR.

Table 8.2.1.3/1-07: HPLC and LSC analysis for the photolysis of phenyl/benzyl-labelled cinmethylin in water following 15 days continuous UV irradiation, expressed in % applied radioactivity (% AR).

DAT	Replicate	HPLC analysis				LSC analysis		
		Cinmethylin	Unknown polar fraction ¹	Sum Others ²	Total	Water	Volatiles	Total
0	I	94.3	0.3	5.8	100.3	100.3	n.a.	100.3
	II	94.5	n.d.	5.2	99.7	99.7	n.a.	99.7
	Mean	94.4	0.1	5.5	100.0	100.0	n.a.	100.0
1	I	95.8	0.6	5.0	101.4	101.4	0.0	101.4
	II	96.2	0.6	4.5	101.3	101.3	0.2	101.5
	Mean	96.0	0.6	4.7	101.4	101.3	0.1	101.4
3	I	93.5	2.9	4.6	101.1	101.1	0.3	101.5
	II	92.3	3.6	4.3	100.2	100.2	0.2	100.4
	Mean	92.9	3.3	4.5	100.7	100.7	0.3	100.9
7	I	85.2	7.2	5.1	97.4	97.4	1.3	98.8
	II	82.4	7.2	5.8	95.4	95.4	1.0	96.4
	Mean	83.8	7.2	5.4	96.4	96.4	1.2	97.6
9	I	79.9	8.5	5.9	94.3	94.3	2.7	96.9
	II	84.1	9.0	5.4	98.5	98.5	0.0	98.5
	Mean	82.0	8.8	5.7	96.4	96.4	1.4	97.7
11	I	75.6	11.5	6.3	93.4	93.4	1.4	94.8
	II	77.6	8.5	4.7	90.8	90.8	2.5	93.3
	Mean	76.6	10.0	5.5	92.1	92.1	2.0	94.1
15	I	65.9	12.9	5.3	84.0	84.0	6.5	90.5
	II	66.7	13.3	7.4	87.5	87.5	4.9	92.4
	Mean	66.3	13.1	6.3	85.7	85.7	5.7	91.4

Note: the rounding to one decimal place means that totals do not always reflect the sum of the values as presented.

n.a. = not analysed; n.d. = not detected.

¹ HPLC retention time of 4.2 min.

² Each individual peak measured < 2.9% AR.

Table 8.2.1.3/1-08: HPLC and LSC analysis for the dark control samples of phenyl/benzyl-labelled cinmethylin in water, expressed in % applied radioactivity (% AR).

DAT	Replicate	HPLC analysis				LSC analysis
		Cinmethylin	Unknown polar fraction ¹	Sum Others ²	Total	Total in water
1	I	92.6	n.d.	4.6	97.2	97.2
	II	94.0	n.d.	5.1	99.1	99.1
	Mean	93.3	n.d.	4.8	98.1	98.1
3	I	93.5	n.d.	4.3	97.8	97.8
	II	92.6	0.4	3.9	96.9	96.9
	Mean	93.0	0.2	4.1	97.3	97.3
7	I	91.3	0.5	4.0	95.8	95.8
	II	92.3	0.4	4.5	97.1	97.1
	Mean	91.8	0.5	4.2	96.5	96.5
9	I	92.8	0.6	4.0	97.4	97.4
	II	93.0	n.d.	4.3	97.3	97.3
	Mean	92.9	0.3	4.2	97.4	97.4
11	I	94.8	3.7	n.d.	98.5	98.5
	II	92.8	1.3	2.1	96.2	96.2
	Mean	93.8	2.5	1.1	97.4	97.4
15	I	93.4	0.6	4.3	98.4	98.4
	II	94.0	0.5	3.9	98.4	98.4
	Mean	93.7	0.6	4.1	98.4	98.4

Note: the rounding to one decimal place means that totals do not always reflect the sum of the values as presented.

n.a. = not analysed; n.d. = not detected.

¹ HPLC retention time of 4.3 min.

² Each individual peak measured < 2.9% AR.

Chiral analysis of enantiomer ratio

The Applicant investigated the enantiomeric ratio over time via qualitative chiral HPLC analysis of samples at 0 and 15 DAT. Results are summarised in Table 8.2.1.3/1-09 for the cyclohexane-label, and Table 8.2.1.3/1-10 for the phenyl/benzyl-label. The results obtained showed that the enantiomeric ratio remained at around 50:50 in both photolysis and dark control samples for both label positions.

Table 8.2.1.3/1-09: Determination of enantiomeric ratios in photolysis and dark control samples treated with the cyclohexane-labelled cinmethylin.

DAT	Replicate	Cinmethylin (% AR) ¹	(-)-enantiomer (% cinmethylin)	(+)-enantiomer (% cinmethylin)
0	I	96.8	50.0	50.0
	II	97.5	49.3	50.7
	Mean	97.2	49.6	50.4
15	I	69.4	49.6	50.4
	II	69.9	47.5	52.5
	Mean	69.7	48.6	51.4
Dark 15	I	96.6	50.9	49.1
	II	94.9	50.5	49.5
	Mean	95.7	50.7	49.3

¹ Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

Table 8.2.1.3/1-10: Determination of enantiomeric ratios in photolysis and dark control samples treated with the phenyl/benzyl-labelled cinmethylin.

DAT	Replicate	Cinmethylin (% AR) ¹	(-)-enantiomer (% cinmethylin)	(+)-enantiomer (% cinmethylin)
0	I	94.3	51.9	48.1
	II	94.5	51.2	48.8
	Mean	94.4	51.5	48.5
15	I	65.9	51.6	48.4
	II	66.7	51.3	48.7
	Mean	66.3	51.5	48.5
Dark 15	I	93.4	51.5	48.5
	II	94.0	50.8	49.2
	Mean	93.7	51.2	48.8

¹ Cinmethylin value derived from radio-HPLC analysis of cinmethylin extracts showing the parent and metabolites. Value shown is for the parent only.

KINETIC EVALUATION

A kinetics study was undertaken by the Applicant to investigate the degradation behaviour of cinmethylin in both irradiated and dark conditions. The kinetic evaluation was conducted to determine degradation parameters for trigger endpoints according to the FOCUS degradation kinetics guidance (2006; 2014).

Due to the presence of the metabolite M684H003 in the cyclohexane-labelled photolysis samples, the Applicant treated each radiolabel as a separate experiment, leading to four distinct kinetic evaluations: cyclohexane- and phenyl/benzyl-labelled samples, each with photolysis and dark control. The Applicant performed parent-only kinetic evaluations in the cyclohexane-labelled dark control and both phenyl/benzyl-labelled experiments, and a compartment modelling approach for the kinetic evaluation of cinmethylin and M684H003 in cyclohexane-labelled photolysis samples. The Applicant assessed the goodness-of-fit of SFO and FOMC in the first instance; if FOMC offered the best fit then the biphasic models DFOP and HS were additionally explored.

The Applicant tested the model appropriateness through detailed statistical analysis including visual assessment of the goodness of fit, χ^2 scaled-error criterion and t-test significance. The visual fit was categorised as follows:

- Poor fit = the fit does not follow the pattern of the measured residues, not acceptable to derive modelling endpoints;
- Acceptable fit = the fit mainly follows the pattern of the measured residues with small deviations, acceptable to derive modelling endpoints;
- Good fit = the fit follows the pattern of the measured residues well, residuals are randomly scattered around zero, acceptable to derive modelling endpoints.

The Applicant used KINGUI version 2 using IRLS optimisation; error tolerance was set to 10^{-3} and maximum iterations of the optimisation tool was set to 100. Each experiment was considered as a separate dataset due to the presence of the metabolite M684H003 in cyclohexane-labelled samples only. As such, there were four distinct experiments for kinetic evaluation.

The HSE evaluator checked the data sets used by the Applicant for the kinetic evaluation and notes that the 0 DAT values reflect parent-only concentrations at 0 DAT as derived from HPLC analysis and are not the full mass balance measured by LSC. Additionally, the Applicant used measured values for the metabolite at 0 DAT when these should have been set to 0% AR. As a result, the HSE evaluator rejected the Applicant's kinetic evaluations due to the initial differing. The following kinetic evaluation is the HSE evaluator's own.

The HSE evaluator conducted the kinetic evaluation using CAKE version 3.2 to derive trigger endpoints following FOCUS kinetics guidance. A model's appropriateness was tested as outlined previously. Table 8.2.1.3/1-11-12 summarises the data used to derive trigger endpoints, derived from LSC mass balance for 0 DAT and cinmethylin and M684H003 concentrations derived from HPLC for all other time points. The HSE evaluator notes that, due to a clear decline phase, it was not possible to determine a degradation rate for M684H003; however the metabolite evaluation was retained to determine a formation fraction and to provide a pathway fit. The HSE evaluator also notes that it was not possible to derive degradation rates for the individual enantiomers as only two sampling points, 0 and 15 DAT, were analysed by chiral HPLC.

Table 8.2.1.3/1-11: Experimental data used for the kinetic evaluation of cinmethylin degradation in cyclohexane-labelled photolysis and dark control samples.

Photolysis			Dark control	
DAT	Cinmethylin (% AR)	M684H003 (% AR)	DAT	Cinmethylin (% AR)
0	99.5	0	0	99.5
0	100.5	0	0	100.5
0	99.3	0	0	99.3
0	100.7	0	0	100.7
1	100.1	2.3	1	95.5
1	94.6	2.3	1	96.7
3	96.4	2.8	3	97.0
3	94.6	3.3	3	96.6
7	91.1	5.0	7	94.8
7	85.3	7.0	7	96.0
9	83.9	7.5	9	96.6
9	83	6.5	9	97.0
11	83.4	6.1	11	95.9
11	81.4	6.1	11	95.7
15	69.4	10.6	15	96.6
15	69.9	11.5	15	94.9

Table 8.2.1.3/1-12: Experimental data used for the kinetic evaluation of cinmethylin degradation in phenyl/benzyl-labelled photolysis and dark control samples.

Photolysis		Dark control	
DAT	Cinmethylin (% AR)	DAT	Cinmethylin (% AR)
0	100.3	0	100.3
0	99.7	0	99.7
1	95.8	1	92.6
1	96.2	1	94.0
3	93.5	3	93.5
3	92.3	3	92.6
7	85.2	7	91.3
7	82.4	7	92.3
9	79.9	9	92.8
9	84.1	9	93.0
11	75.6	11	94.8
11	77.6	11	92.8
15	65.9	15	93.4
15	66.7	15	94.0

The HSE evaluator followed the recommended procedure for deriving trigger endpoints and compared the SFO and FOMC models. Appropriateness of a distinct kinetic model to describe photolytic degradation was tested based on visual assessment of goodness-of-fit, the χ^2 error rate, and the t-test to determine whether estimated degradation parameters differ from zero. In this case, there was no need to explore other biphasic models.

Results

The kinetic evaluations for photolysis and dark control samples are summarised in Table 8.2.1.3/1-13-14 respectively. For the photolysis samples, the visual fit was good for both SFO and FOMC with randomly scattered residuals (Figure 8.2.1.3/1-01). SFO was chosen for the lowest error rate. For the dark control samples, SFO gave a good visual model fit with randomly scattered residuals, but it was not possible to fit an FOMC model (Figure 8.2.1.3/1-02). The slope derived for the SFO model was not significantly different to zero; therefore, no reliable endpoints can be derived for the dark control data, though the evaluation is included here for information. Table 8.2.1.3/1-13 – 14 summarise the kinetic models, estimated parameters decision process for both the photolysis and dark control samples.

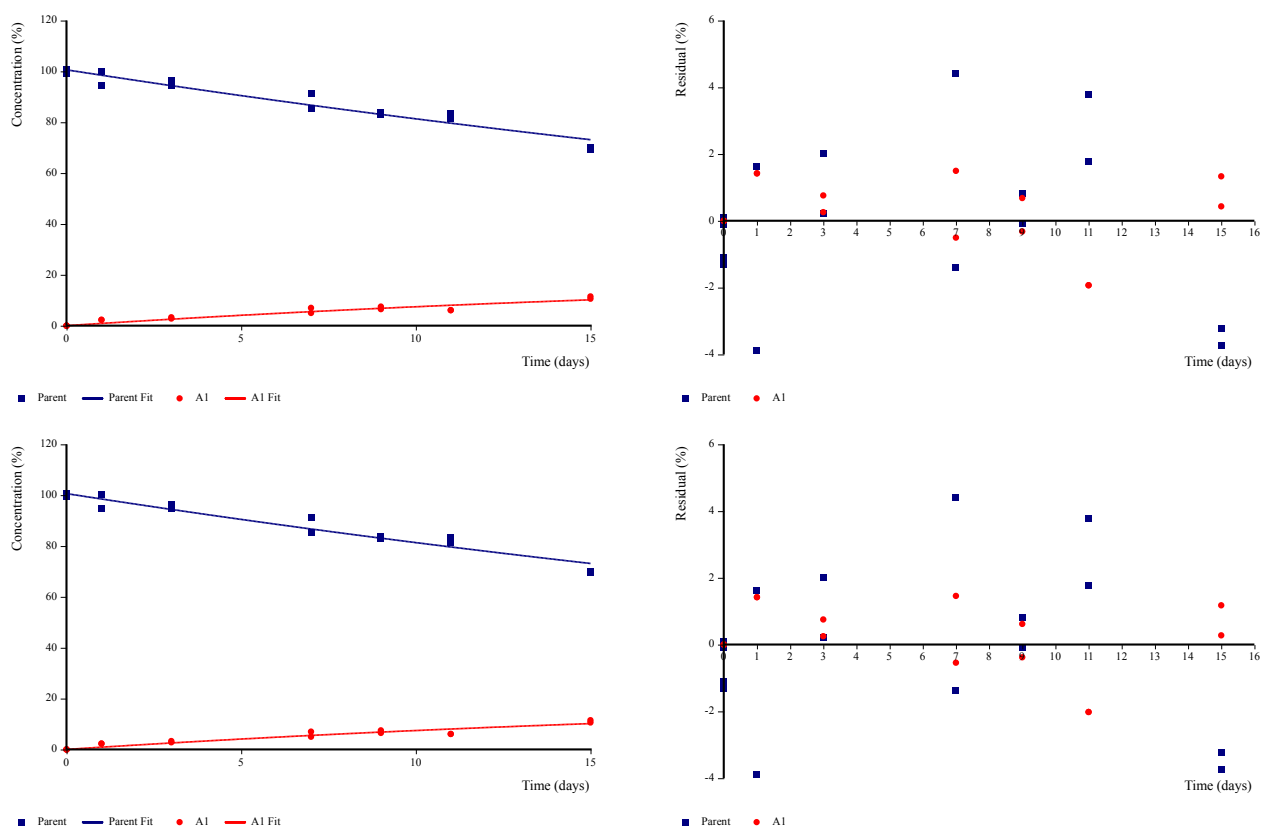


Figure 8.2.1.3/1-01: Combined model fits and residuals for the photolysis experiment, cyclohexane-labelled cinmethylin (blue) plus metabolite M684H003 (red). Top row: parent SFO; metabolite SFO. Bottom row: parent FOMC; metabolite SFO. Final fit: SFO-SFO. Parent $\text{DegT}_{50} = 32.6$ d. Parent $\text{DegT}_{90} = 108$ d. Metabolite degradation rates could not be reliably derived. Chi^2 error = 1.71%.

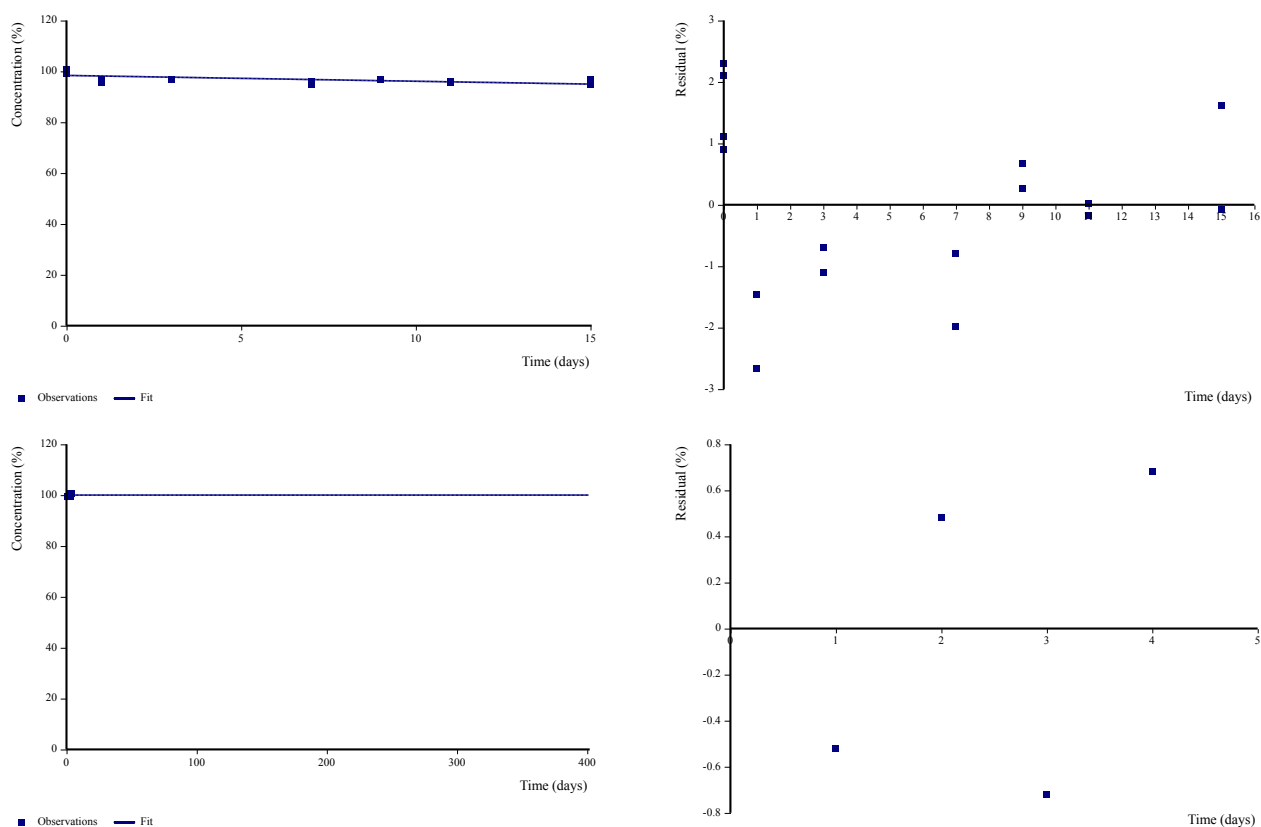


Figure 8.2.1.3/1-02: Model fit and residuals for the dark control experiment, cyclohexane-labelled cinmethylin. Top row: SFO. Bottom row: FOMC. Final fit: SFO. $\text{DegT}_{50} = 295$ d. $\text{DegT}_{90} = 979$ d. Chi^2 error = 1.0%.

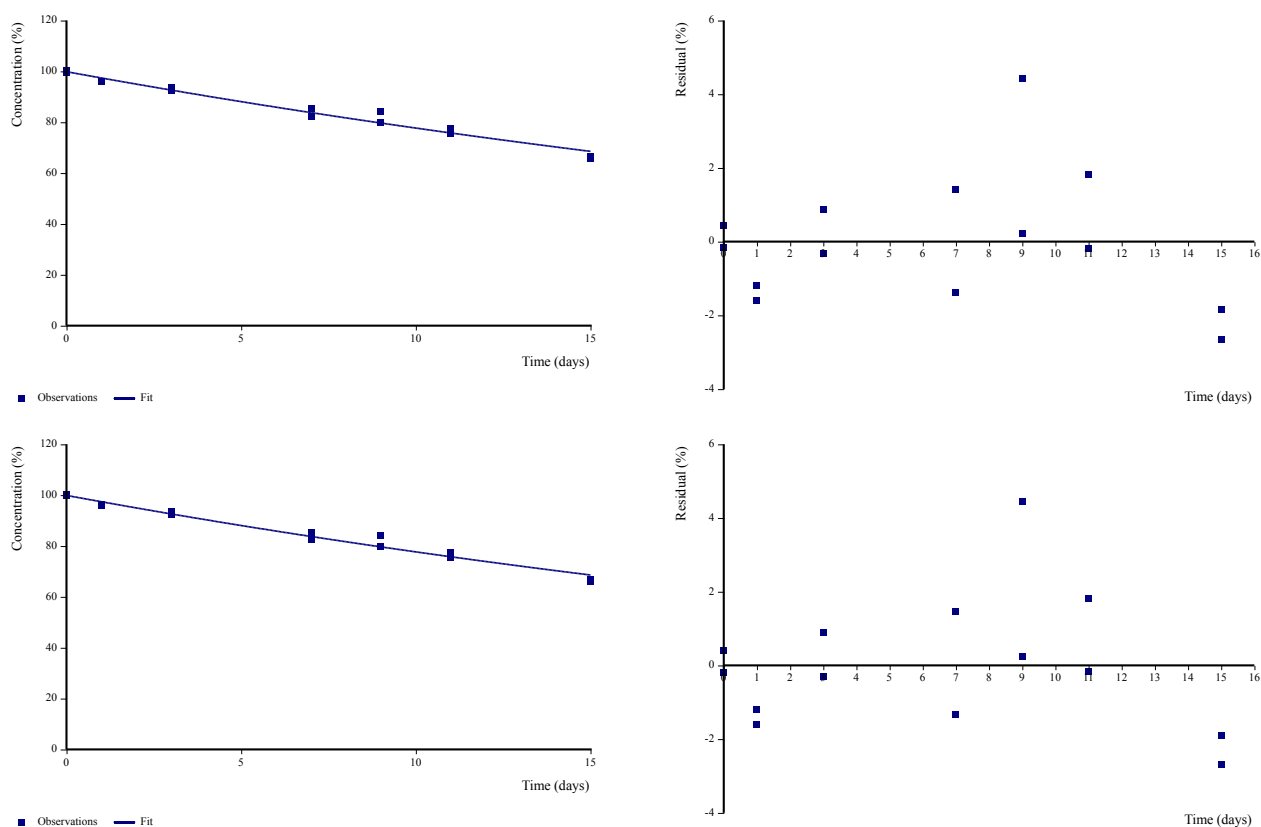


Figure 8.2.1.3/1-03: Model fit and residuals for the photolysis experiment, phenyl/benzyl-labelled cinmethylin. Top row: SFO. Bottom row: FOMC. Final fit: SFO. $\text{DegT}_{50} = 27.6$ d. $\text{DegT}_{90} = 91.8$ d. Chi^2 error = 1.28%.

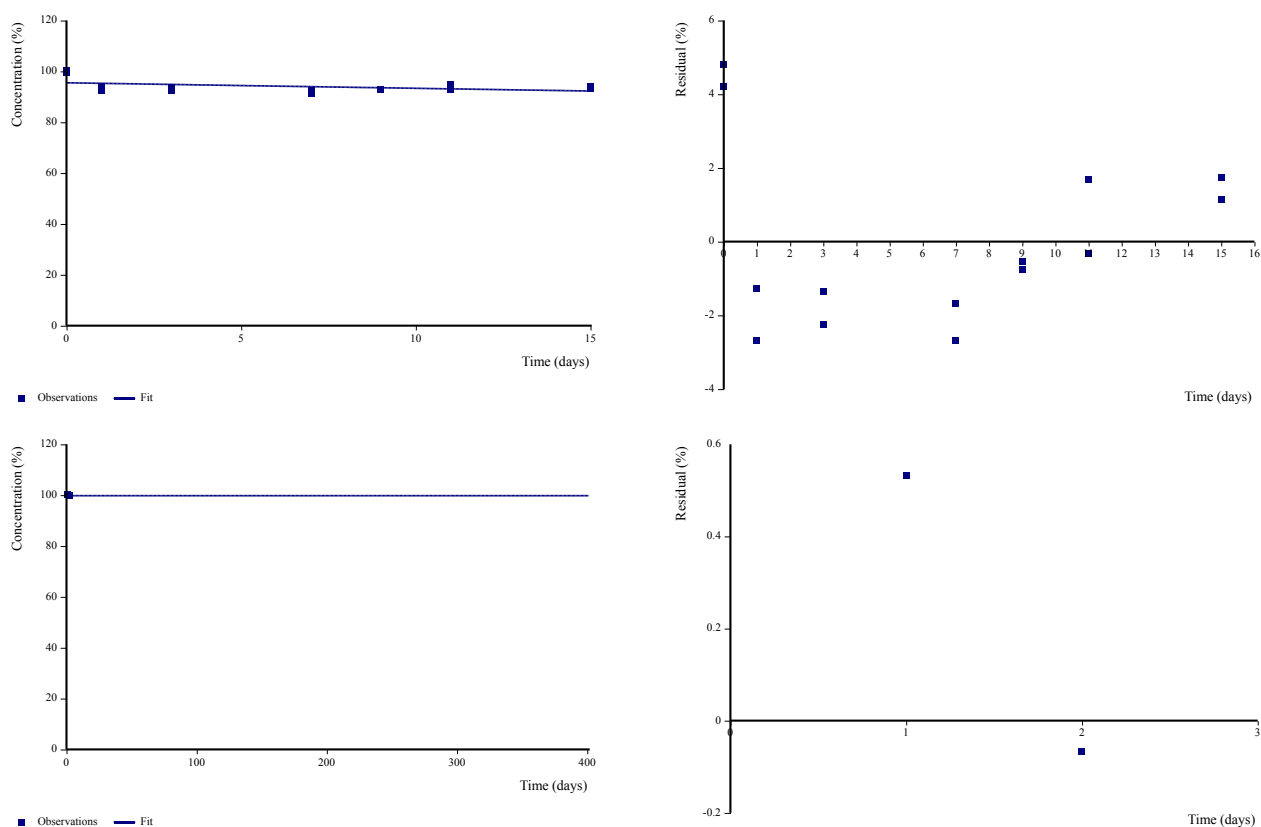


Figure 8.2.1.3/1-04: Model fit and residuals for the dark control experiment, phenyl/benzyl-labelled cinmethylin. Top row: SFO. Bottom row: FOMC. Final fit: SFO. DegT₅₀ = 302 d. DegT₉₀ = 1000 d. Chi² error = 1.37%.

Table 8.2.1.3/1-13: Summary of the kinetic evaluation of cyclohexane-labelled cinmethylin. The evaluation was conducted to derive trigger endpoints.

Experiment	Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Photolysis	Step 1: Run parent SFO and FOMC								
	SFO	Good	100.6	k: 0.02126	0.0182 – 0.0240	< 0.0001	1.71	32.6	108
	FOMC	Good	101.5	α : 11.36 β : 486.2	-364.9 – 387.6 n.d.	- -	1.85	30.6	109
	HSE evaluator decision: SFO and FOMC display similarly good fits to the measured data with randomly scattered residuals. Both models demonstrate low error rates, but SFO has the lowest error. Use SFO to derive combined fit.								
	Parent SFO	Good	100.6	k: 0.02126	0.0182 – 0.0240	< 0.0001	1.71	32.6	108
	Metabolite SFO	Good	0	k: 0.01588	-0.0496 – 0.0810	0.311	14.60	43.7	145
	HSE evaluator decision: Residues are well described by SFO combined fit. Due to the lack of decline phase, the metabolite degradation rate constant could not be estimated significantly different from zero. Use SFO-SFO for deriving parent degradation.								
Dark control	SFO	Good	100.6	k: 0.00235	7.96E-4 – 0.0040	0.00295	1.0	295	979
	FOMC	Good	100.0	α : 0.00254 β : 7.77E-7	0.0020 – 0.0030 n.d.	- -	n.d.	> 1000	> 1000
	HSE evaluator decision: SFO describes residues well with a low error rate. An FOMC model could not be fitted to these data. The estimated DegT50 is significantly longer than the 15 day study duration; therefore, even though the P value is acceptable, it can be concluded that there was no significant observed degradation.								

n.d. – not derived

Table 8.2.1.3/1-14: Summary of the kinetic evaluation of phenyl/benzyl-labelled cinmethylin. The evaluation was conducted to derive trigger endpoints.

Experiment	Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Photolysis	SFO	Good	99.86	k: 0.02509	0.0225 – 0.0280	< 0.0001	1.28	27.6	91.8
	FOMC	Good	99.89	α : 19.27 β : 761.6	-3.765 – 42.30 -152.7 – 1680	- -	1.40	27.9	96.7
	HSE evaluator decision: SFO describes the residues well with a low error rate and FOMC does not improve on this. Use SFO to derive trigger endpoints.								
Dark Control	SFO	Good	95.50	k: 0.0023	-0.0007 – 0.0050	0.0614	1.89	302	1000
	FOMC	Poor	99.77	α : 0.0039 β : 8.79E-8	0.0034 – 0.004 n.d.	- -	n.d.	> 1000	> 1000
	HSE evaluator decision: SFO offered a good visual fit with a low χ^2 error rate. The rate constant is not estimated to be significantly different to zero. An FOMC model could not be fitted to these data. Therefore, no significant degradation of cinmethylin was observed.								

n.d. – not derived

CONCLUSION

It was demonstrated that cinmethylin degrades in sterile natural water under the influence of light. Table 8.2.1.3/1-15 summarises the estimated endpoints. The HSE evaluator notes that, due to volatilisation of the parent, the resulting endpoints are dissipation rates as opposed to degradation rates. The geomean DisT₅₀ for both radiolabels was determined by kinetic evaluation to be 30.0 days under study conditions, equivalent to 34.8 days in natural sunlight at 40°N. The HSE evaluator has not calculated a photolysis-only degradation rate due to there being no reliable endpoints derived for the dark control samples; however, the lack of dissipation in the dark control indicates that the losses are driven by photolytic processes and volatilisation.

One metabolite, M684H003 was observed in the cyclohexane-labelled experiment, with a peak of 11% AR being achieved at 15 DAT. No decline pattern was observed, and no other metabolites were observed at levels > 5% AR.

Table 8.2.1.3/1-15: Trigger endpoints for cinmethylin and its metabolite M684H003 following photolysis in sterile natural water.

	Label	Compound	Formation fraction	Model	DisT ₅₀ (d)	DisT ₉₀ (d)	χ^2 error (%)
Photolysis	Cyclohexane-4- ¹⁴ C	Cinmethylin	-	SFO	32.6	108	1.7
		M684H003	0.4186	SFO	No significant degradation derived		14.6
	Phenyl-U- ¹⁴ C / Benzyl- ¹³ C	Cinmethylin	-	SFO	27.6	91.8	1.3
		Cinmethylin geometric mean			30.0	99.6	
Dark control	Cyclohexane-4- ¹⁴ C	Cinmethylin	-	SFO	No significant degradation derived		
	Phenyl-U- ¹⁴ C / Benzyl- ¹³ C	Cinmethylin	-	SFO			

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

B.8.2.2.1. Ready biodegradability (Data Requirement 7.2.2.1)

Report:	KCA 7.2.2.1/1; Schwarz, H. (2017a)
Title	BAS 684 H (Cinmethylin): Determination of the ready biodegradability in the CO ₂ -evolution test.
Document No.:	2017/1077282
Guidelines	OECD 301B – Ready Biodegradability International Standard ISO 9439, US EPA OPPTS 835.3110, Commission Regulation (EC) No 440/2008 C.4-C
GLP?	Yes
Deviations	None
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The Applicant studied the ready biodegradability of cinmethylin (BAS 684 H) by measurement of the formed carbon dioxide (OECD 301 B: CO₂ evolution test). The Applicant used aniline as the reference item.

MATERIALS AND METHODS

Test items

Table 8.2.2.1/1-01 summarises the information for the two test materials used in this study. The HSE evaluator notes that the chemical purity of cinmethylin was low at 93%; however, this has not impacted upon the study. The selected nominal test concentration was 20 mg TOC/L, corresponding to approximately 25 mg/L cinmethylin. The Applicant noted that the selected test concentration caused no toxic effects to the microorganisms. The selected test concentration was tested in an additional inhibition control test assay and no toxic effects to the microorganisms were observed. For the reference substance, a stock solution containing 401.1 mg/L aniline was prepared.

Table 8.2.2.1/1-01: Test material information for the study of the ready biodegradability of cinmethylin.

Name	Cinmethylin	Aniline
Registration number	14/0066-5	01/0298-23
Molecular formula	C ₁₈ H ₂₆ O ₂	C ₆ H ₇ N
Molecular mass	274.4 g/mol	93 g/mol
Batch identity	COD-002038	STBF7930V
Water solubility	63 mg/L (20°C)	Not given
Total organic carbon ¹	787 mg/g	Not given
Chemical Purity	93.0%	Not given

¹ The content of TOC was calculated by the Applicant for a purity of 100%, using the molecular formula of the test item.

Test system and procedure

The Applicant utilised municipal activated sludge from the wastewater treatment plant of Mannheim, Germany. The inoculum was collected on 22 March 2017 from the aeration tank of the plant. A suitable aliquot of the activated sludge suspension was sieved by a finely woven mesh (mesh size approx. 1 mm). To reduce the content of inorganic carbon in the blank controls the activated sludge was aerated with carbon dioxide free air for about 24 hours at 22 ± 2°C.

On the day of exposure, the suspension was washed one time with drinking water. Aeration was stopped, and the sludge was allowed to settle. After settling the supernatant was discarded and the remaining sludge suspension was filled up with drinking water and the concentration of the sludge was adjusted to 6.0 g/L dry weight. Aliquots of 7.5 mL were added to the test vessels to obtain an activated sludge concentration of 30 mg/L dry weight.

The mineral medium was prepared in compliance with the OECD 301 B guidelines, and was prepared from the following four solutions:

- Solution A: 8.50 g KH_2PO_4 + 21.75 g K_2HPO_4 + 33.40 g $\text{Na}_2\text{HPO}_4 \times 2 \text{ H}_2\text{O}$ + 0.50 g NH_4Cl in 1000 mL deionised water. The pH value was adjusted to 7.4.
Solution B: 36.40 g $\text{CaCl}_2 \times 2 \text{ H}_2\text{O}$ in 1000 mL deionised water.
Solution C: 22.50 g $\text{MgSO}_4 \times 7 \text{ H}_2\text{O}$ in 1000 mL deionised water.
Solution D: 0.25 g $\text{FeCl}_3 \times 6 \text{ H}_2\text{O}$ in 1000 mL deionised water.

15 mL Solution A, 1.5 mL Solution B, 1.5 mL Solution C and 1.5 mL Solution D was used for the preparation of the test assays, which were performed in 2 L incubation bottles filled to a volume of 1.5 L.

The bottles were connected to two serial scrubbing bottles (total volume 250 mL) filled with 100 mL 0.05 mol sodium hydroxide solution for the adsorption of carbon dioxide from biodegradation processes. Incubation bottles were stirred on magnetic stirrers; the aeration was performed with carbon dioxide free air at a flow rate of approx. 800 mL per hour.

The test assays were prepared on the day of exposure. The required volumes of deionised water and mineral salt solutions were applied to all test vessels. For preparation of the test substance and inhibition control samples, the required amounts of the test substance aliquots for a test concentration of 20 mg/L TOC were weighed onto small glass plates and completely added with the glass plates to the vessels of the test substance assays and to the vessel of the inhibition control. Due to poor cinmethylin solubility, these were sonicated for several minutes to dissolve the test substance in the test medium. The HSE evaluator notes that solution homogeneity was not tested; however, little variability was observed over the course of the test, suggesting test substance was sufficiently distributed.

For the reference substance assays, the aniline stock solution was added to achieve 20 mg TOC/L in the reference substance assay and 20 mg TOC/L in the inhibition control.

The test vessel pH values were measured and adjusted to 7.4 ± 0.2 , if necessary. Aliquots of activated sludge suspension were added to all test vessels to adjust the concentration of activated sludge to 30 mg/L dry weight. Samples for the measurement of dissolved inorganic carbon (DIC) were taken from blank control assays.

Twice a week, the total inorganic carbon (TIC) values of the adsorption solutions of the first trap were determined and used for the calculation of the produced carbon dioxide. After each sampling, the second trap was moved forward and the new trap with fresh sodium hydroxide solution was placed into the second position. Each trap was analysed separately.

At the end of exposure, the pH values were measured in each test vessel. For stripping of carbon dioxide dissolved in the test medium, each test vessel was acidified by adding 2 mL of concentrated hydrochloric acid. The concentration of dissolved organic carbon (DOC) in the blank controls and reference substance assays were determined. The Applicant stated that DOC measurements could not be performed from the inhibition control and test substance assays due to poor solubility of cinmethylin in water.

The aeration was continued for about 24 hours and the released carbon dioxide amounts in both traps of each test vessel were determined and added to the calculated amount of the previous day.

Analytical methods

Analyses of TIC and DOC were performed as repeat determination using a TOC analyser with autosampler. The system was calibrated before the start of sample measurements using standard samples. TIC samples were measured without any additional treatment. DOC samples were centrifuged for 15 minutes at 4000 rpm prior to analysis. All samples were analysed on the day of sampling.

The measured amount of carbon dioxide at the end of the test was compared with the calculated maximal theoretical production (ThCO_2) and reported as a percentage of biodegradation.

RESULTS

The degree of cinmethylin biodegradation after 28 days was $< 5\% \text{ CO}_2/\text{ThCO}_2$, while it was 98% for aniline and 44% in the inhibition control test (Table 8.2.2.1/1-02). OECD guidelines state that a test substance is required to degrade by $> 60\%$ for the substance to be classified as readily biodegradable. Additionally, for a substance to be classed as inhibitory, the inhibition control sample needs to show $< 25\% \text{ ThCO}_2$. As cinmethylin demonstrated $< 5\%$ biodegradation after 28 days, and 38% biodegradation in the inhibition control after 14 days, cinmethylin is neither readily biodegradable nor inhibitory.

Table 8.2.2.1/1-02: Degree of biodegradation, expressed as $\% \text{ CO}_2/\text{ThCO}_2$.

Test duration (days)	Reference substance	Inhibition control	Cinmethylin		
			Replicate 1	Replicate 2	Mean
0	0	0	0	0	0
1	-1	0	0	0	0
4	31	13	4	3	4
7	57	24	3	2	3
11	80	34	1	1	1
14	87	38	0	-1	-1
18	93	42	-1	0	-1
21	95	43	-1	0	-1
26	97	43	-1	-1	-1
28	98	44	-1	-1	-1

The Applicant assessed the present study against the validity criteria defined in the OECD 301 B guidelines. Reference substance biodegradation was $> 60\% \text{ CO}_2/\text{ThCO}_2$ after 14 days; inhibition control biodegradation was $> 25\% \text{ CO}_2/\text{ThCO}_2$ after 14 days; and the dissolved inorganic carbon (DIC) was $< 1 \text{ mg/L}$ at the test concentration of 20 mg/L at the study start. As there was no plateau phase in the cinmethylin samples, it was not necessary to assess variance between samples. The Applicant concluded the test was valid; the HSE evaluator agreed.

CONCLUSION

Cinmethylin was not readily biodegradable in this CO_2 evolution test over 28 days at a test concentration of 20 mg/L in an inoculum derived from municipal activated sludge. Cinmethylin was also not found to be inhibitory.

B.8.2.2.2. Aerobic mineralisation in surface water (Data Requirement 7.2.2.2)

Report:	KCA 7.2.2.2/1; Mueller-Werthwein, M., and Hegler, F. (2018a)
Title	14C-BAS 684 H: Aerobic mineralisation in surface water
Document No.:	2017/1156778
Guidelines	OECD 309: Aerobic mineralisation in surface water – simulation biodegradation test FOCUS Kinetics (2006; 2014)
GLP?	Yes
Deviations	<ul style="list-style-type: none"> One radiolabelled test substance (phenyl-labelled cinmethylin) and several reference item chemical purities were below 95%. The HSE evaluator did not deem this to be a major issue as the radiochemical purity was high for the test substance, and the reference items were used for identification purposes and not in the actual study; One metabolite reference item was a non-GLP substance. The HSE evaluator acknowledges that this was only used for metabolite identification purposes and does not deem this to be a significant deviation.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The Applicant determined the mineralisation and degradation rate of cinmethylin in an aquatic system under dark conditions in a laboratory according to OECD 309 guidelines. Metabolites forming in the water were also determined. The pelagic test system was chosen for the present study and was performed with two concentrations: 10 µg/L (“low” concentration) and 50 µg/L (“high” concentration). Two radiolabel positions were studied: cyclohexane-4-¹⁴C and phenyl-U-¹⁴C. The Applicant also investigated the enantiomeric ratio during the study. Kinetic evaluation was conducted to derive trigger endpoints following FOCUS Kinetics guidance (2006; 2014).

MATERIALS AND METHODS**Test materials and reference items**

The Applicant studied the mineralisation of cinmethylin using two labelled forms; in addition, the control item, benzoic acid, was radiolabelled (ring-U-¹⁴C). Table 8.2.2.2/1-01 summarises the details for the test materials. Additionally, the Applicant used three unlabelled cinmethylin reference items (Table 8.2.2.2/1-02) and six unlabelled metabolites as reference items (Table 8.2.2.2/1-03). The HSE evaluator notes that the chemical purity of the phenyl-labelled test item is low at 90.9%, though this is not a concern as radiochemical purity is high at 98.0%. Additionally, the chemical purity of the reference items for (+)-enantiomer, M684H002 and M684H014 are also low, though again this is not a concern as these items were not used in the main study. The HSE evaluator notes that the Applicant also supplied details for a reference item for the metabolite M684H018; however, since this metabolite was not observed in the present study, the HSE evaluator has not included details of this reference item.

Table 8.2.2.2/1-01: ¹⁴C-labelled test material details for the study of the aquatic mineralisation of cinmethylin.

Substance name	Cinmethylin		Benzoic acid
Reg. No.	900202		4005129
Internal code	BAS 684 H		-
Molecular formula	C ₁₈ H ₂₆ O ₂		C ₇ H ₆ O ₂
Molecular mass	274.4 g/mol		126.1 g/mol
Radiolabel position	Cyclohexane-4- ¹⁴ C	Phenyl-U- ¹⁴ C	Ring-U- ¹⁴ C
Batch No.	1146-2001	1147-2101	-
Radiochemical purity	97.9%	98.0%	98.4%
Chemical purity	95.9%	90.9%	-

Table 8.2.2.2/1-02: Unlabelled cinmethylin reference item details for the study of the aquatic mineralisation.

Substance name	Cinmethylin	(-)-enantiomer	(+)-enantiomer
Internal code	BAS 684 H	-	-
Reg. No.	900202	5925581	5925632
Batch No.	L87-84	L87-20	L87-18
Chemical purity	99.0%	95.0%	92.7%
Noted impurities	0.5% cyclohexane	1.7% cyclohexane	4.4% cyclohexane

Table 8.2.2.2/1-03: Unlabelled metabolite reference item details for the study of the aquatic mineralisation of cinmethylin.

Internal code	M684H001	M684H002	M684H004	M684H014	M684H019
Reg. No.	6055521	6055479	6055480	6055477	6066766
Batch No.	L87-226	L87-106	L87-146	L87-124	L2017-013
Chemical purity	99.9%	94.4%	97.8%	91.8%	99.1%
Noted impurities	None	None	None	0.1% hexane	0.1% hexane

Water sampling

Water was collected on 26th April 2017 from Ranschgraben, a small stream surrounded by forest east of Schifferstadt, Rhineland-Palatinate, south-western Germany. The water was filtered through a 100 µm sieve at the field sampling site. Water was stored covered, but with access to the atmosphere at 4°C under dark conditions until test vessels were filled. The water's pH, O₂ content, redox potential and temperature were all measured immediately on arrival at the laboratory; these measurements were repeated prior to filling test vessels at the study start (0 DAT) and were measured regularly throughout the study. Table 8.2.2.2/1-04 summarises the physicochemical properties of the test system. The HSE evaluator notes that the microbial plate count was low by 63 days, having reduced by over 97%. However, benzoic acid degraded rapidly, confirming that the water samples were sufficiently microbially active during the study. The HSE evaluator notes that the guidelines only require the Applicant to demonstrate sufficient microbial populations in the reference substance samples; therefore, the HSE evaluator concluded that the low microbial counts at the study end indicated issues with microbial activity.

Table 8.2.2.2/1-04: Characterisation of the test system water used in the present study.

04. Characterisation of the test system water used in the present study		
Water sample origin	Ranschgraben, Rhineland-Palatinate, Germany	
Water characterisation parameters		
Total nitrogen (mg/L)	0.01	
Total phosphorus (mg/L)	0.205	
Total organic carbon (mg/L)	< 0.5	
Dissolved organic carbon (mg/L)	< 0.5	
Carbonate hardness (mmol/L)	0.80	
Hardness (mmol/L)	0.95	
Parameters measured on sampling day		
Temperature (°C)	10.4	
pH	7.53	
O ₂ concentration (mg/L)	10.4	
Redox potential (mV)	155	
Parameters measured at study start (0 DAT) ¹		
Temperature (°C)	9.1	
pH	7.33	
O ₂ concentration (mg/L)	10.5	
Redox potential (mV)	206	
Parameters measured at study end (63 DAT) ²		
Temperature (°C)	21.2 (20.8 – 21.4)	
pH	7.70 (7.42 – 7.82)	
O ₂ concentration (mg/L)	8.91 (8.87 – 8.97)	
Redox potential (mV)	154.5 (147 – 161)	
Microbial plate count		
(colony forming units/mL)	Sampling day	63 DAT
Bacteria	4380	112
Fungi	94	4
Actinomycetes	130	0

¹ Parameters were measured prior to the study starting, before test vessels were filled.

² Parameters reported are a mean of eight samples with the range in parentheses. Values are derived from duplicate samples of the low and high concentrations of cyclohexane- and phenyl-labelled cinmethylin.

Experimental set up

Ninety-six test vessels were prepared for incubation in total. Each 500 mL glass flask was filled with 400 mL water. For the sterile controls, 16 test vessels were sterilised in an autoclave (30 min at 121°C), tightly closed and incubated without aeration at $20 \pm 2^\circ\text{C}$ under dark conditions. Table 8.2.2.2/1-05 summarises the test vessel set up.

Table 8.2.2.2/1-05: Summary of test vessels

System		Test concentration (µg/L)	Number of vessels
Test vessels			
Cinmethylin	Cyclohexane-4- ¹⁴ C	10	18
		50	18
	Phenyl-U- ¹⁴ C	10	18
		50	18
Controls			
¹⁴ C-benzoic acid		10	3
¹⁴ C-benzoic acid + 20 µL acetonitrile		10	3
Sterile	Cyclohexane-4- ¹⁴ C	50	8
	Phenyl-U- ¹⁴ C	50	8
Untreated (for water characterisation)		-	2

Test vessels were placed on multi-plate magnetic stirrers in an incubator providing the test vessels with a continuous flow of fresh air. Magnetic stir bars were used to maintain oxygen saturation at a sufficiently high level.

Each test vessel (except sterile control flasks) was connected to the air stream leading to a trapping system of two gas washing bottles for collection of $^{14}\text{CO}_2$: for test vessels, the flasks contained 35 mL ethylene glycol and 45 mL 1 M NaOH; for the benzoic acid vessels, both flasks contained 45 mL 1 M NaOH. Traps containing NaOH were amended with a coloured pH indicator after 14 days. The incubator operated at a temperature that kept the water phase in the test vessels at $20 \pm 2^\circ\text{C}$.

Test item application

Both test items were provided in toluene. The Applicant evaporated off the toluene before the test item was redissolved in 1 mL acetonitrile to form the stock solutions with a final concentration of 2.208 mg/mL (cyclohexane-labelled cinmethylin), and 2.104 mg/mL (phenyl-labelled cinmethylin), as determined by LSC. For the benzoic acid stock solution, 1.19 mg ^{14}C -benzoic acid was dissolved in 2.5 mL sterile water, giving a final measured concentration of 0.297 mg/mL.

Nominal application solution concentrations were 10 $\mu\text{g/L}$ (low) and 50 $\mu\text{g/L}$ (high). To achieve these, the Applicant pipetted 85 μL of the cyclohexane-labelled stock into 915 μL acetonitrile for the low concentration, and 550 μL acetonitrile was added to 450 μL of stock solution for the high concentration. For the phenyl-labelled application solutions, 90 μL of stock was pipetted into 910 μL acetonitrile for the low concentration, and 524 μL acetonitrile was added to 476 μL of stock solution for the high concentration. For benzoic acid, 612 μL of stock solution were made up to 10 mL with sterile water.

All application solution concentrations were determined by LSC. Cyclohexane-labelled application solution concentrations measured 0.186 mg/mL (low) and 0.979 mg/mL (high). Phenyl-labelled application solution concentrations measured 0.195 mg/mL (low) and 1.037 mg/mL (high). The actual benzoic acid application solution concentration was 0.018 mg/mL.

Nominal application rates of 10 $\mu\text{g/L}$ and 50 $\mu\text{g/L}$ were achieved by pipetting 20 μL of the corresponding application solutions into the upper water layer of the test vessels. For the cyclohexane-labelled samples this corresponded to 3.716 μg and 19.575 μg for low and high concentrations respectively; for the phenyl-labelled samples this corresponded to 3.898 μg and 20.739 μg respectively.

For the viability controls, three vessels were treated with 220 μL ^{14}C -benzoic acid, to achieve a nominal rate of 10 $\mu\text{g/L}$. To test for the potential influence of acetonitrile on the viability, three additional test vessels were treated with 220 μL ^{14}C -benzoic acid and 20 μL acetonitrile. Sterilised test vessels were treated under sterile conditions to achieve a nominal application rate of 50 $\mu\text{g/L}$.

Sampling and work-up

Duplicate test vessels were sampled at 0, 3, 7, 14, 28, 42 and 63 days for both test concentrations and both labels. Sterile vessels were sampled at the same intervals, except day 0. Benzoic acid vessels were taken at 0, 1, 3, 7, 15, 30, 41 and 64 days after treatment (DAT), with the volatile traps sampled at the same intervals except for day 0. Untreated control vessels were sampled after 63 days.

For sampling, the respective flasks were removed from the incubator and the parameters temperature, O_2 content, pH and redox potential were recorded. Volatile traps were disconnected from the air stream and stored at room temperature until analysis. The water volume was determined, then the contents were transferred into graduated cylinders and the test vessels were rinsed three times with approx. 20 mL acetonitrile. The acetonitrile was added to the corresponding sample and the total volume was determined. For the untreated test vessels, following parameter determination (as above)

the two vessels were combined, and aliquots were taken for microbial plate counts. Processed samples were either analysed immediately or stored in a freezer prior to analysis.

The Applicant noted that, on day 15, one of the air tubes connected to one benzoic acid vessel had a leak, leading to a reduced air flow through the connected trapping system and thus a reduced $^{14}\text{CO}_2$ amount in the volatile trap. The connection was fixed, however, the reduced $^{14}\text{CO}_2$ amounts measured in the first 15 days led to reduced cumulative values for the following sampling times compared to the other two replicates.

Analytical method

For determination of the ^{14}C -concentration, three aliquots were taken from each test vessel for quantification by LSC. For the high concentration, aliquots were 1 mL; for the low concentration, aliquots were 4 mL for the 0 – 14 days samples, and 1 mL for the subsequent samples. Additionally, 5 mL subsamples from each replicate were transferred to HPLC vials for analysis by radio-HPLC.

Selected samples were also analysed by chiral-HPLC to investigate the enantiomer ratio. To prevent cinmethylin loss due to volatilisation during sample workup, the test item was extracted by liquid/liquid partition from the water sample, concentrated and re-dissolved.

To quantify volatiles, the trapping solutions were transferred into 50 mL volumetric flasks and filled up to volume with either 1 mol/L NaOH for the NaOH trapping solution, or distilled water for the ethylene glycol trapping solution. Three aliquots (amounts not given) were added to scintillation cocktail and measured by LSC. A $^{14}\text{CO}_2$ verification was performed by expelling the $^{14}\text{CO}_2$ after acidification of the NaOH trapping solution and re-measuring the radioactivity by LSC.

Cinmethylin and its metabolites M684H001, M684H004, M684H014 and M684H019 were identified and confirmed by HPLC-MS and by comparison of the retention times with those of authentic reference items, considering the delay between UV- and radio-detectors.

The limit of detection (LOD) and limit of quantification (LOQ) were calculated for each label position at both low and high concentrations for LSC and HPLC analysis. These values are summarised in Table 8.2.2.2/1-06. The HSE evaluator notes that all LODs and LOQs were acceptable.

Table 8.2.2.2/1-06: Summary of LODs and LOQs for ^{14}C -labelled cinmethylin at low and high concentrations when measured by LSC and radio-HPLC.

	Cyclohexane-label (% AR)		Phenyl-label (% AR)	
	LOD	LOQ	LOD	LOQ
LSC				
Low concentration (10 µg/L)	0.35	0.52	0.16	0.24
High concentration (50 µg/L)	0.27	0.40	0.12	0.18
HPLC				
Low concentration (10 µg/L)	0.14	0.28	0.08	0.15
High concentration (50 µg/L)	0.06	0.12	0.06	0.12

RESULTS

Physicochemical parameters of test systems

The HSE evaluator examined the water parameter measurements taken throughout the study and confirms that air temperature remained stable, ranging 20 – 21.8°C and the oxygen content consistently remained above 8 mg/L, or > 89%. Redox potential fluctuated throughout the study but remained between 124 – 219 mV and showed a small decline by the study end, therefore showing

conditions remained aerobic throughout. The pH values measured in the range of 7.33 (0 DAT) – 8.30 for treated test vessels, and 8.23 – 9.06 for treated sterile systems.

Mass balance

The actual applied amounts of test item per test vessel containing 400 mL water were 3.716 µg (low concentration) and 19.575 µg (high concentration) for the cyclohexane-labelled cinmethylin samples and 3.898 µg (low) and 20.739 µg (high) for the phenyl-labelled cinmethylin samples. Mass balances are presented in Table 8.2.2.2/1-07-10; in summary, these ranged 93.2 – 101.0% AR in the viable test vessels, and 96.3 – 101.5% AR in the sterile vessels. The amount of radioactivity in the water remained almost constant over the incubation period, ranging 88.3 – 93.9% AR after 63 days across both labels and concentrations. Radioactivity detected in volatile traps did not exceed 5.2% AR in any of the cinmethylin-treated test vessels, indicating a low rate of mineralisation.

Table 8.2.2.2/1-07: Material balance (% AR) and distribution of radioactivity after application of cyclohexane-labelled cinmethylin, low concentration (10 µg/L), as presented by the Applicant.

Days after treatment	Test container	%TAR			
		Water	Volatiles ethylene glycol	Volatiles NaOH (CO ₂)	Material balance
0	TC01	99.0	n.p.	n.p.	99.0
	TC02	99.4	n.p.	n.p.	99.4
	mean	99.2	n.p.	n.p.	99.2
3	TC03	99.1	0.0	0.0	99.1
	TC04	99.8	0.0	0.0	99.8
	mean	99.5	0.0	0.0	99.5
7	TC05	97.1	0.0	0.0	97.1
	TC06	99.1	0.0	0.1	99.2
	mean	98.1	0.0	0.1	98.2
14	TC07	100.1	0.0	0.3	100.3
	TC08	101.1	0.0	0.3	101.4
	mean	100.6	0.0	0.3	100.9
28	TC09	93.9	0.0	1.7	95.6
	TC10	96.7	0.0	0.8	97.5
	mean	95.3	0.0	1.2	96.6
42	TC11	91.4	0.0	4.2	95.6
	TC12	91.3	0.1	4.0	95.4
	mean	91.3	0.1	4.1	95.5
63	TC13	88.1	0.1	4.4	92.6
	TC14	88.5	0.2	5.2	93.9
	mean	88.3	0.1	4.8	93.2

n.p. = not performed

TAR = total applied radioactivity

Table 8.2.2.2/1-08: Material balance and distribution of radioactivity after application of cyclohexane-labelled cinmethylin, high concentration (50 µg/L), as presented by the Applicant.

Days after treatment	Test container	%TAR			
		Water	Volatiles ethylene glycol	Volatiles NaOH (CO ₂)	Material balance
0	TC19	100.9	n.p.	n.p.	100.9
	TC20	101.2	n.p.	n.p.	101.2
	mean	101.0	n.p.	n.p.	101.0
3	TC21	99.8	0.0	0.0	99.8
	TC22	100.7	0.0	0.0	100.7
	mean	100.3	0.0	0.0	100.3
7	TC23	99.0	0.0	0.1	99.1
	TC24	98.4	0.0	0.1	98.5
	mean	98.7	0.0	0.1	98.8
14	TC25	96.5	0.0	0.6	97.1
	TC26	96.2	0.0	0.6	96.7
	mean	96.3	0.0	0.6	96.9
28	TC27	92.5	0.0	3.0	95.5
	TC28	95.4	0.1	2.5	97.9
	mean	94.0	0.0	2.7	96.7
42	TC29	94.3	0.0	1.7	95.9
	TC30	92.2	0.1	3.0	95.3
	mean	93.3	0.0	2.3	95.6
63	TC31	91.3	0.2	5.1	96.6
	TC32	91.8	0.1	4.5	96.5
	mean	91.6	0.2	4.8	96.6

n.p. = not performed

TAR = total applied radioactivity

Table 8.2.2.2/1-09: Material balance and distribution of radioactivity after application of phenyl-labelled cinmethylin, low concentration (10 µg/L), as presented by the Applicant.

Days after treatment	Test container	%TAR			
		Water	Volatiles ethylene glycol	Volatiles NaOH (CO ₂)	Material balance
0	TC45	98.9	n.p.	n.p.	98.9
	TC46	101.0	n.p.	n.p.	101.0
	mean	100.0	n.p.	n.p.	100.0
3	TC47	99.3	0.0	0.0	99.3
	TC48	98.2	0.0	0.0	98.2
	mean	98.7	0.0	0.0	98.8
7	TC49	100.4	0.0	0.2	100.6
	TC50	99.5	0.0	0.2	99.7
	mean	99.9	0.0	0.2	100.1
14	TC51	100.8	0.0	0.5	101.3
	TC52	97.5	0.0	0.7	98.2
	mean	99.2	0.0	0.6	99.7
28	TC53	91.4	0.0	1.6	93.0
	TC54	94.2	0.0	2.0	96.1
	mean	92.8	0.0	1.8	94.6
42	TC55	93.7	0.1	2.6	96.5
	TC56	92.4	0.0	3.2	95.5
	mean	93.1	0.0	2.9	96.0
63	TC57	90.4	0.1	3.4	93.9
	TC58	91.5	0.1	3.3	94.8
	mean	90.9	0.1	3.3	94.4

n.p. = not performed

TAR = total applied radioactivity

Table 8.2.2.2/1-10: Material balance and distribution of radioactivity after application of phenyl-labelled cinmethylin, high concentration (50 µg/L), as presented by the Applicant.

Days after treatment	Test container	%TAR			
		Water	Volatiles ethylene glycol	Volatiles NaOH (CO ₂)	Material balance
0	TC63	100.6	n.p.	n.p.	100.6
	TC64	101.0	n.p.	n.p.	101.0
	mean	100.8	n.p.	n.p.	100.8
3	TC65	98.9	0.0	0.0	98.9
	TC66	98.8	0.0	0.0	98.8
	mean	98.8	0.0	0.0	98.8
7	TC67	96.7	0.0	0.1	96.9
	TC68	98.3	0.0	0.0	98.4
	mean	97.5	0.0	0.1	97.6
14	TC69	96.7	0.0	0.5	97.2
	TC70	96.4	0.0	0.1	96.5
	mean	96.6	0.0	0.3	96.8
28	TC71	95.5	0.0	1.0	96.6
	TC72	93.5	0.0	1.8	95.3
	mean	94.5	0.0	1.4	95.9
42	TC73	93.5	0.1	2.2	95.8
	TC74	94.2	0.1	2.8	97.0
	mean	93.8	0.1	2.5	96.4
63	TC75	93.9	0.2	3.0	97.1
	TC76	94.0	0.0	2.5	96.5
	mean	93.9	0.1	2.8	96.8

n.p. = not performed

TAR = total applied radioactivity

The Applicant provided data for the sterile controls and ¹⁴C-benzoic acid samples. The sterile samples demonstrated that the test system remained sterile, with % AR detected in the water samples ranging 96.8 – 100.0% in the cyclohexane-labelled samples and 96.3 – 101.5% in the phenyl-labelled samples. Volatiles were not quantified for the sterile controls as these were not connected to a volatile trap. The benzoic acid samples demonstrated that the Ranschgraben test system was microbially active, with 80.3 – 85.2% of the applied substance evolved as ¹⁴CO₂ after 64 days in the benzoic acid samples, and 78.8 – 85.9% evolved in the benzoic acid + 20 mL acetonitrile samples. There was no notable difference in CO₂ evolution between the benzoic acid samples and benzoic acid + 20 mL acetonitrile samples, demonstrating the additional solvent did not affect microbial activity. Overall, mean mass balances ranged 83.6 – 99.1% AR (Table 8.2.2.2/1-11).

Table 8.2.2.2/1-11: Mean material balances and distribution of radioactivity after application of ^{14}C -benzoic acid or ^{14}C -benzoic acid + 20 mL acetonitrile. Data are expressed as % AR; mean of 3 replicates.

Days after treatment	Benzoic acid			Benzoic acid + 20 mL ACN		
	Water	Volatiles	Total	Water	Volatiles	Total
0	98.5	n.p.	98.5	99.1	n.p.	99.1
1	90.4	4.2	94.6	89.5	4.4	93.8
3	74.5	12.4	86.8	70.4	13.2	83.6
7	63.6	26.5	90.1	54.6	31.8	86.4
15	40.2	48.7	88.9	38.8	46.8 ¹	85.6
30	19.8	68.9	88.7	8.0	77.1	85.1
41	16.2	73.7	89.9	5.3	80.9	86.2
64	6.2	83.4	89.7	4.4	83.5	87.9

n.p. – not performed.

¹ One replicate experienced a leaky gas tube, with individual replicates measuring 30.3, 55.7 and 54.5% AR. This affected the mean at 15 DAT and all subsequent time points due to lower cumulative CO₂ values.

Characterisation of residues in water

The results show that the microbial degradation of cinmethylin in water under dark conditions was very slow overall. After 63 days, 62.2% AR (cyclohexane-label) and 80.7% AR (phenyl-label) remained as unchanged parent for the 10 µg/L concentration; for the 50 µg/L concentration, cinmethylin amounted to 85.0% AR (cyclohexane-label) and 91.2% AR (phenyl-label). Results are summarised below and in Table 8.2.2.2/1-12-13 for the cyclohexane- and phenyl-labelled samples respectively.

Four metabolites appeared in the chromatograms which could be identified. The Applicant stated that all metabolites were formed by various oxidation and hydroxylation reactions.

M684H001 was formed to maximum amounts of 5.8% AR in phenyl-labelled samples and 13.1% AR in cyclohexane-labelled samples at the low concentration. In high concentration vessels, it reached respective amounts of 1.9 and 2.3% AR.

M684H004 was detected at both concentrations and labels; however, it did not exceed 1.3% AR at any sampling time.

M684H014 was detected in all incubations from day 0, with levels of 1.2 – 2.0% AR. It remained in the range of 1.2 – 2.7% AR during the incubation period.

M684H019 was also detected at both concentrations and labels and did not exceed 2.4% AR during the experiment. The Applicant highlighted that M684H019 has the same mass and fragmentation pattern in mass spectrometry as the potential metabolite M684H018, which has a different hydroxylation position at the phenyl ring. The HPLC retention time of the reference item revealed with high certainty that the peak in the water samples consisted of M684H019 and not of M684H018. The HSE evaluator assessed the supplied chromatogram and agrees with the Applicant's assessment. The HSE evaluator also notes that the Applicant has proposed a combined metabolite identity for all metabolites formed by hydroxylation of the phenyl ring, M684H043. This includes both M684H018 and M684H019.

Several unknown peaks were also detected, however, none of them exceeded 4% AR, with the highest percentage, 4.0% AR, reached at one time point in one cyclohexane-labelled sample at the low concentration. The Applicant attempted to identify this peak with a retention time of 18.3 min; the fragmentation pattern suggested a cineol plus acetate fragment, but the Applicant could not propose an unequivocal structure. Unknown peaks that occurred sporadically and below 2% AR are summarised as “others” in results tables.

Table 8.2.2.2/1-12: Metabolite overview for water after application of cyclohexane-labelled cinmethylin (Cin.) to the pelagic test system and incubation under dark conditions. Values are expressed as % AR.

Days after treatment	Total	Unknown	Unknown	Unknown	M684 H004	M684 H001	M684 H019	M684 H014	Cin.	Sum others ¹
	t _{Ret} ~	9.7	10.5	18.3	68.5	70.0	74.6	90.2	91.2	
Low concentration (10 µg/L)										
0	I	99.0	-	-	-	-	-	1.9	94.9	2.1
	II	99.4	-	-	-	-	-	1.8	96.3	1.3
	Mean	99.2	-	-	-	-	-	1.9	95.6	1.7
3	I	99.1	-	-	-	-	-	1.7	96.5	0.9
	II	99.8	-	-	-	-	-	2.0	97.4	0.4
	Mean	99.5	-	-	-	-	-	1.9	97.0	0.7
7	I	97.1	-	0.5	-	-	-	1.9	94.3	0.4
	II	99.1	-	-	-	-	-	2.4	95.6	1.1
	Mean	98.1	-	0.2	-	-	-	2.2	95.0	0.7
14	I	100.1	-	0.6	-	-	-	2.2	97.3	0.0
	II	101.1	-	-	-	-	-	3.2	97.0	0.9
	Mean	100.6	-	0.3	-	-	-	2.7	97.1	0.4
28	I	93.9	-	-	0.5	3.0	0.9	2.9	86.6	0.0
	II	96.7	2.1	-	-	1.2	-	1.7	91.7	0.0
	Mean	95.3	1.1	-	0.3	2.1	0.4	2.3	89.1	0.0
42	I	91.4	-	3.6	0.7	1.5	6.1	0.6	1.6	1.5
	II	91.3	-	-	-	1.0	5.3	1.3	1.9	0.0
	Mean	91.3	-	1.8	0.3	1.3	5.7	1.0	1.7	0.7
63	I	88.1	1.2	3.0	3.2	-	12.8	3.0	2.0	1.9
	II	88.5	1.6	1.2	4.7	-	13.5	1.9	2.3	0.0
	Mean	88.3	1.4	2.1	4.0	-	13.1	2.4	2.1	0.9
High concentration (50 µg/L)										
0	I	100.9	-	-	-	-	-	2.1	96.7	2.1
	II	101.2	-	-	-	-	-	2.0	97.7	1.6
	Mean	101.0	-	-	-	-	-	2.0	97.2	1.8
3	I	99.8	-	-	-	-	-	2.1	95.9	1.7
	II	100.7	-	-	-	-	-	2.2	96.6	1.9
	Mean	100.3	-	-	-	-	-	2.2	96.2	1.8
7	I	99.0	-	-	-	-	-	2.2	95.5	1.3
	II	98.4	-	-	-	-	-	2.2	95.3	0.8
	Mean	98.7	-	-	-	-	-	2.2	95.4	1.1
14	I	96.5	-	-	-	-	-	2.1	93.1	1.4
	II	96.2	-	-	-	0.6	0.7	2.0	90.9	1.9
	Mean	96.3	-	-	-	0.3	0.3	2.1	92.0	1.7
28	I	92.5	-	-	-	2.5	1.4	2.1	85.5	1.0
	II	95.4	-	-	-	0.9	1.2	2.3	91.1	0.0
	Mean	94.0	-	-	-	1.7	1.3	2.2	88.3	0.5
42	I	94.3	-	-	-	0.6	1.6	1.5	87.7	0.8
	II	92.2	-	-	-	0.6	1.9	0.7	86.6	0.4
	Mean	93.3	-	-	-	0.6	1.8	1.1	87.1	0.6
63	I	91.3	-	-	-	3.0	2.1	2.2	83.5	0.6
	II	91.8	-	-	-	1.6	1.0	2.3	86.6	0.4
	Mean	91.6	-	-	-	2.3	1.6	2.2	85.0	0.5

t_{Ret} = retention time (min)

- = not detected

¹ Sum of several peaks; each individual peak ≤ 1.3% AR in 10 µg/L samples and ≤ 1.6% AR in 50 µg/L samples)

Table 8.2.2.2/1-13: Metabolite overview for water after application of phenyl-labelled cinmethylin to the pelagic test system and incubation under dark conditions. Values are expressed as % AR.

Days after treatment		Total	M684H004	M684H001	M684H019	M684H014	Cinmethylin	Sum others ¹
		t _{Ret} ~	68.5	70.0	74.6	90.2	91.2	
Low concentration (10 µg/L)								
0	I	98.9	-	-	-	1.1	97.4	0.5
	II	101.0	-	-	-	1.6	98.6	0.7
	Mean	100.0	-	-	-	1.3	98.0	0.6
3	I	99.3	-	-	-	1.2	96.8	1.2
	II	98.2	-	-	-	1.6	96.6	0.0
	Mean	98.7	-	-	-	1.4	96.7	0.6
7	I	100.4	-	-	-	1.3	99.0	0.0
	II	99.5	-	-	-	1.3	97.9	0.3
	Mean	99.9	-	-	-	1.3	98.5	0.1
14	I	100.8	-	0.7	-	1.6	97.5	1.0
	II	97.5	-	0.7	-	1.1	95.0	0.7
	Mean	99.2	-	0.7	-	1.3	96.3	0.8
28	I	91.4	1.0	4.3	0.7	1.0	82.3	2.2
	II	94.2	-	2.4	0.9	1.5	89.1	0.3
	Mean	92.8	0.5	3.3	0.8	1.2	85.7	1.2
42	I	93.7	0.2	1.4	-	1.4	90.7	0.0
	II	92.4	-	3.9	3.2	1.0	79.9	4.2
	Mean	93.0	0.1	2.7	1.6	1.2	85.3	2.1
63	I	90.4	0.8	6.2	2.1	1.2	79.4	0.6
	II	91.5	0.7	5.4	1.8	1.5	82.0	0.0
	Mean	90.9	0.8	5.8	2.0	1.3	80.7	0.3
High concentration (50 µg/L)								
0	I	100.6	-	-	-	1.2	97.9	1.5
	II	101.0	-	-	-	1.2	98.4	1.5
	Mean	100.8	-	-	-	1.2	98.1	1.5
3	I	98.9	-	-	-	1.3	96.5	1.0
	II	98.8	-	-	-	1.3	96.5	1.0
	Mean	98.8	-	-	-	1.3	96.5	1.0
7	I	96.7	-	-	-	1.3	94.8	0.6
	II	98.3	-	-	-	1.4	96.0	0.9
	Mean	97.5	-	-	-	1.3	95.4	0.7
14	I	96.7	-	0.3	-	1.4	94.1	0.9
	II	96.4	-	0.2	0.1	1.3	93.9	1.0
	Mean	96.6	-	0.2	0.1	1.3	94.0	1.0
28	I	95.5	-	1.4	-	1.3	92.1	0.7
	II	93.5	1.1	2.0	0.6	1.3	88.5	0.0
	Mean	94.5	0.6	1.7	0.3	1.3	90.3	0.4
42	I	93.5	0.2	0.8	1.0	1.3	89.7	0.5
	II	94.2	0.6	2.9	2.0	1.4	86.3	0.8
	Mean	93.8	0.4	1.9	1.5	1.4	88.0	0.7
63	I	93.9	-	0.7	0.5	1.3	91.3	0.0
	II	94.0	-	1.0	0.5	1.4	91.1	0.0
	Mean	93.9	-	0.9	0.5	1.4	91.2	0.0

t_{Ret} = retention time (min)

- = not detected

¹ Sum of several peaks; each individual peak ≤ 1.6% AR in 10 µg/L samples and ≤ 1.1% AR in 50 µg/L samples)

Three metabolites were detected in the sterile water samples treated with 50 µg/L cinmethylin: two unknowns with retention times unique to the sterile samples, and M684H014. No metabolites exceeded 1.4% AR (Table 8.2.2.2/1-14). The Applicant notes that M684H014 was present in flasks from 0 DAT, consistent with the non-sterile flasks. The Applicant attempted to identify the unknown with a 12.5 min retention time in the cyclohexane-labelled samples, however it was not possible. The Applicant suggested this was a small cleavage product due to low mass (186 u).

Table 8.2.2.2/1-14: Metabolite overview for the sterile water samples following application of 50 µg/L cinmethylin (cyclohexane- and phenyl-labelled) and incubation under dark conditions. Values are expressed as % AR.

Days after treatment	Total $t_{Ret} \sim$	Unknown	Unknown	M684H014	Cinmethylin	Sum others ¹
Cyclohexane-label						
3	98.9	1.7	-	1.4	94.6	1.1
7	97.9	2.7	-	1.2	94.0	0.0
14	99.6	3.3	-	1.0	94.6	0.6
28	98.6	3.1	-	1.3	94.2	0.0
42	100.0	3.3	-	1.2	95.3	0.2
63	96.8	3.4	-	1.3	92.1	0.0
Phenyl-label						
3	101.5	-	1.3	0.6	98.7	0.9
7	96.3	-	1.6	0.4	94.3	0.0
14	97.4	-	1.9	0.7	94.6	0.2
28	98.1	-	2.2	0.6	95.4	0.0
42	96.6	-	2.1	0.5	93.8	0.2
63	97.8	-	2.3	0.6	94.9	0.0

t_{Ret} = retention time (min)

- = not detected

¹ Sum of several peaks; each individual peak $\leq 0.7\%$ AR

Enantiomer ratio

Over 63 days, there was no notable difference in the enantiomer ratio in either the cyclohexane- or phenyl-labelled cinmethylin samples. Table 8.2.2.2/1-15 and 7.2.2.2/1-16 summarise the results of the chiral HPLC analysis for the cyclohexane label and phenyl label respectively.

Table 8.2.2.2/1-15: Investigation of the enantiomer ratio in the water phase following application of cyclohexane-labelled cinmethylin and incubation under dark conditions.

Days after treatment		% AR	Cinmethylin	% AR		Ratio	
				(-)-enant.	(+)-enant.	(-)-enant.	(+)-enant.
Stock solution		n.p.	n.p.	n.p.	n.p.	50.3	49.7
Low concentration (10 µg/L)							
0 ¹	I	99.0	94.9	47.7	47.2	50.3	49.7
	II	99.4	96.3	48.4	47.9	50.3	49.7
	Mean	99.2	95.6	48.1	47.5	50.3	49.7
28	I	93.9	86.6	44.2	42.4	51.0	49.0
	II	96.7	91.7	46.2	45.5	50.4	49.6
	Mean	95.3	89.1	45.2	44.0	50.7	49.3
63	I	88.1	61.1	31.3	29.7	51.3	48.7
	II	88.5	63.3	33.8	29.6	53.3	46.7
	Mean	88.3	62.2	32.6	29.6	52.4	47.6
High concentration (50 µg/L)							
0 ¹	I	100.9	96.7	48.6	48.0	50.3	49.7
	II	101.2	97.7	49.1	48.5	50.3	49.7
	Mean	101.0	97.2	48.9	48.3	50.3	49.7
28	I	92.5	85.5	41.9	43.6	49.0	51.0
	II	95.4	91.1	43.9	47.2	48.2	51.8
	Mean	94.0	88.3	42.9	45.4	48.6	51.4
63	I	91.3	83.5	41.0	42.5	49.1	50.9
	II	91.8	86.6	43.5	43.1	50.2	49.8
	Mean	91.6	85.0	42.3	42.8	49.7	50.3

n.p. not performed

¹ Calculation based on total cinmethylin at 0 DAT and the enantiomeric ratio in stock solution.

Table 8.2.2.2/1-16: Investigation of the enantiomer ratio in the water phase following application of phenyl-labelled cinmethylin and incubation under dark conditions.

Days after treatment		% AR	Cinmethylin	% AR		Ratio	
				(-)-enant.	(+)-enant.	(-)-enant.	(+)-enant.
Stock solution		n.p.	n.p.	n.p.	n.p.	51.4	48.6
Low concentration (10 µg/L)							
0 ¹	I	98.9	97.4	50.1	47.3	51.4	48.6
	II	101.0	98.6	50.7	47.9	51.4	48.6
	Mean	100.0	98.0	50.4	47.6	51.4	48.6
28	I	91.4	82.3	42.9	39.4	52.1	47.9
	II	94.2	89.1	44.5	44.6	49.9	50.1
	Mean	92.8	85.7	43.7	42.0	51.0	49.0
63	I	90.4	79.4	39.3	40.1	49.5	50.5
	II	91.5	82.0	41.1	41.0	50.1	49.9
	Mean	90.9	80.7	40.2	40.5	49.8	50.2
High concentration (50 µg/L)							
0 ¹	I	100.6	97.9	50.3	47.6	51.4	48.6
	II	101.0	98.4	50.6	47.8	51.4	48.6
	Mean	100.8	98.1	50.4	47.7	51.4	48.6
28	I	95.5	92.1	48.2	43.9	52.3	47.7
	II	93.5	88.5	46.7	41.8	52.8	47.2
	Mean	94.5	90.3	47.5	42.8	52.6	47.4
63	I	93.9	91.3	41.9	49.4	45.9	54.1
	II	94.0	91.1	45.0	46.1	49.4	50.6
	Mean	93.9	91.2	43.4	47.8	47.6	52.4

n.p. not performed

¹ Calculation based on total cinmethylin at 0 DAT and the enantiomeric ratio in stock solution.

KINETIC EVALUATION

The Applicant investigated the degradation kinetics of cinmethylin via aerobic mineralisation according to FOCUS kinetics guidance (2006; 2014) to derive trigger endpoints.

Test procedure

The Applicant conducted two kinetic evaluations, one each for cinmethylin only at the low- and high test concentrations used in the present study. In line with EFSA guidance, the Applicant did not perform kinetic evaluation on metabolites; the HSE evaluator accepts this decision.

The Applicant tested the model appropriateness through detailed statistical analysis including visual assessment of the goodness of fit, Chi² scaled-error criterion and t-test significance. The visual fit was categorised as follows:

- Poor fit = the fit does not follow the pattern of the measured residues, not acceptable to derive modelling endpoints;
- Acceptable fit = the fit mainly follows the pattern of the measured residues with small deviations, acceptable to derive modelling endpoints;
- Good fit = the fit follows the pattern of the measured residues well, residuals are randomly scattered around zero, acceptable to derive modelling endpoints.

The Applicant used KINGUI version 2 using IRLS optimisation; error tolerance was set to 10⁻⁶ and maximum iterations of the optimisation tool was set to 100. The results obtained from the experiments treated with the two differently labelled test items were considered as replicates for kinetic evaluation, giving two distinct kinetic evaluations with four replicates at each time point.

The HSE evaluator checked the data sets used by the Applicant for the kinetic evaluation and notes that the 0 DAT values reflect parent concentrations at 0 DAT as derived from HPLC analysis and are not the full mass balance measured by LSC. As a result, the HSE evaluator rejects the Applicant's kinetic evaluations due to the initial concentrations differing. The following kinetic evaluation is the HSE evaluator's own.

The HSE evaluator conducted the kinetic evaluation using CAKE version 3.2 to derive trigger endpoints following FOCUS kinetics guidance. A model's appropriateness was tested as outlined previously. Table 8.2.2.2/1-17 summarises the data used to derive trigger endpoints, derived from LSC mass balance for 0 DAT and cinmethylin concentrations derived from HPLC for all other time points.

Table 8.2.2.2/1-17: Experimental data used for the kinetic evaluation of the degradation of cinmethylin through aerobic mineralisation.

Days after treatment	Label	% AR	
		Low concentration	High concentration
0	Cyclohexane	99.0	100.9
0	Cyclohexane	99.4	101.2
0	Phenyl	98.9	100.6
0	Phenyl	101.0	101.0
3	Cyclohexane	96.5	95.9
3	Cyclohexane	97.4	96.6
3	Phenyl	96.8	96.5
3	Phenyl	96.6	96.5
7	Cyclohexane	94.3	95.5
7	Cyclohexane	95.6	95.3
7	Phenyl	99.0	94.8
7	Phenyl	97.9	96.0
14	Cyclohexane	97.3	93.1
14	Cyclohexane	97.0	90.9
14	Phenyl	97.5	94.1
14	Phenyl	95.0	93.9
28	Cyclohexane	86.6	85.5
28	Cyclohexane	91.7	91.1
28	Phenyl	82.3	92.1
28	Phenyl	89.1	88.5
42	Cyclohexane	75.8	87.7
42	Cyclohexane	81.9	86.6
42	Phenyl	90.7	89.7
42	Phenyl	79.9	86.3
63	Cyclohexane	61.1	83.5
63	Cyclohexane	63.3	86.6
63	Phenyl	79.4	91.3
63	Phenyl	82.0	91.1

Results

Table 8.2.2.2/1-18 summarises the statistical assessment of kinetic models for cinmethylin at both concentrations. For the low concentration, both SFO and FOMC provided low χ^2 error rates of < 2%, however, SFO provided the lowest error rate and offered a good visual fit (Figure 8.2.2.2/1-01). Therefore, SFO was chosen for deriving trigger endpoints. For the high concentration, SFO offered low error rates, however there was a trend to the residuals with the model fit both underestimating and overestimating observations (Figure 8.2.2.2/1-02). FOMC offered a better fit overall so DFOP and HS were explored; however, the confidence intervals for the parameters included zero; additionally DFOP and HS parameters failed the t test. The HSE evaluator considered this and concluded that SFO offered the most reliable fit of the three models.

Table 8.2.2.2/1-18: Summary of kinetic model evaluation for deriving trigger endpoints for cinmethylin. Final models are highlighted in bold.

Conc.	Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Low	SFO	Good	100.3	k: 0.0050	0.0040 – 0.0060	< 0.0001	1.43	138	457
	FOMC	Good	100.4	α : 5.7290 β : 1110	-67.45 – 78.91 -	- -	1.54	143	549
High	SFO	Good	97.28	k: 0.0021	0.0015 – 0.0030	< 0.0001	1.84	334	1110
	FOMC	Good	100.8	α : 0.0416 β : 1.9520	0.0252 – 0.0580 -0.7330 – 4.6370	- -	0.68	> 10000	> 10000
	DFOP	Good	100.2	k1: 0.0709 k2: 2.1E-9 g: 0.1254	-0.0164 – 0.1580 -0.0022 – 0.0020 0.0109 – 0.240	0.0533 0.50 -	0.74	> 10000 k1: 9.77 k2: > 10000	> 10000
	HS	Good	99.49	k1: 0.0053 k2: 3.3E-4 tb: 21.07	0.0031 – 0.0070 -0.0007 – 0.0010 -42.440 – 84.590	< 0.0001 0.2513 -	0.95	1790 k1: 131 k2: 2110	6700

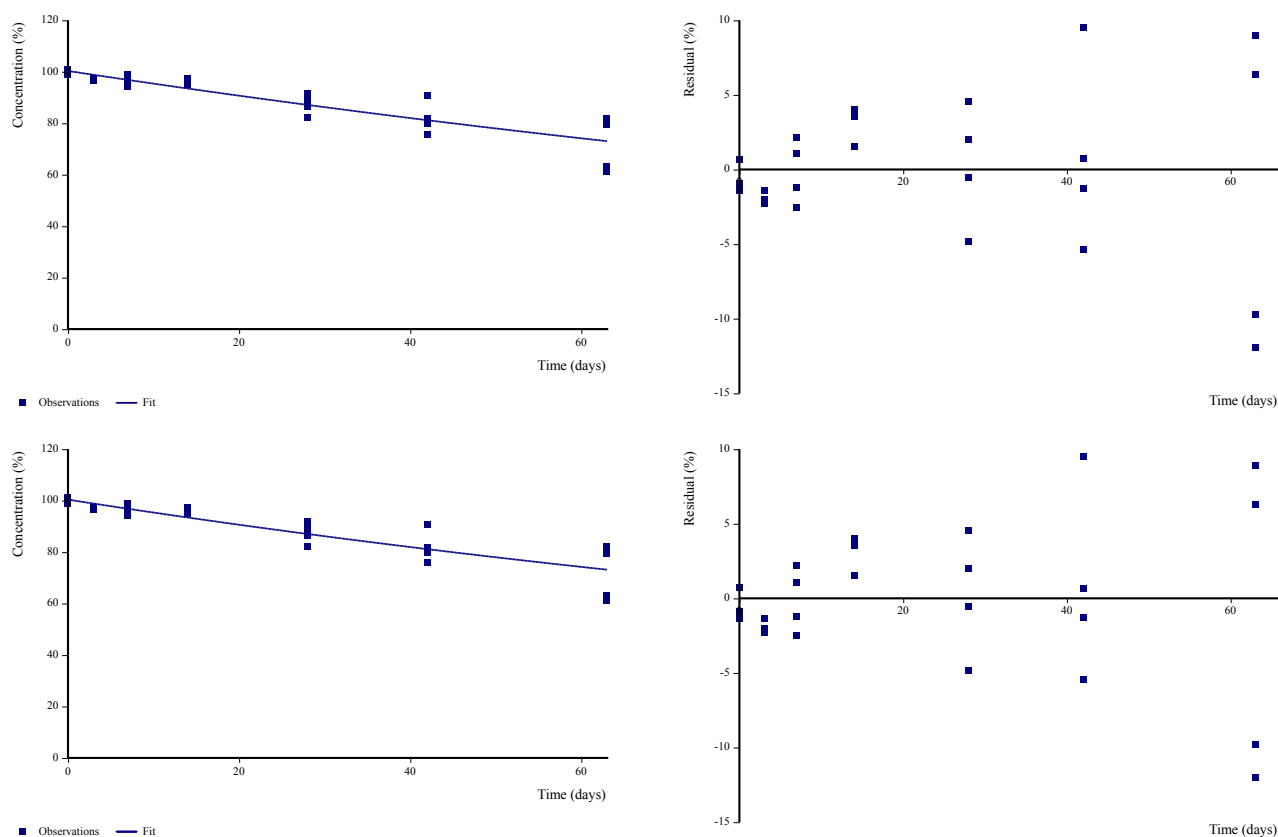


Figure 8.2.2.2/1-01: Model fits and residuals for cinmethylin in water, low concentration. Top row: SFO. Bottom row: FOMC. Final model fit: SFO. χ^2 error = 1.4%. DT₅₀ = 138 days. DT₉₀ = 457 days.

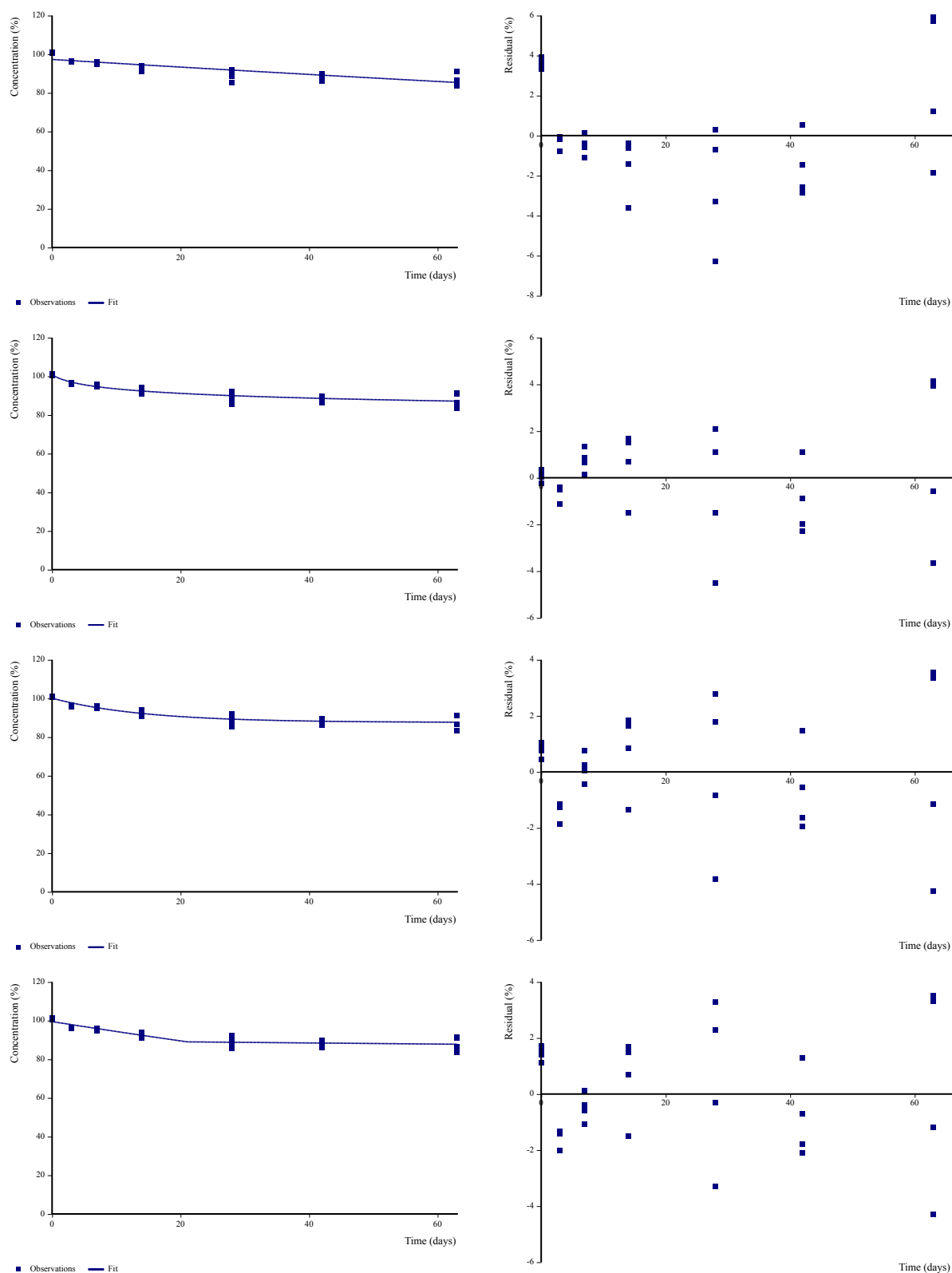


Figure 8.2.2.2/1-02: Model fits and residuals for cinmethylin in water, high concentration. Top row: SFO. Second row: FOMC. Third row: DFOP. Bottom row: HS. Final model fit: SFO. χ^2 error = 1.8%. DT_{50} = 334 days. DT_{90} = 1110 days.

CONCLUSION

From the obtained results, it can be concluded that cinmethylin is only very slowly degraded in a natural water environment in the absence of sediment, as provided in the pelagic test. For the low concentration (10 µg/L), 62.2 – 80.7% AR could be recovered as unchanged parent for the two radiolabels; for the high concentration (50 µg/L), 85.0 – 91.2% AR was still detected as cinmethylin after 63 days.

Several peaks were detected for metabolites, though only one, M684H001, exceeded 5% AR with a maximum amount of 13.1% AR reached in the low concentration study at 63 days. Kinetic evaluation was not necessary for this study.

The kinetic evaluation conducted by the HSE evaluator determined a cinmethylin DT₅₀ of 138 days for the low concentration. The high concentration DT₅₀ was 334 days. Table 8.2.2.2/1-19 summarises these endpoints.

Table 8.2.2.2/1-19: Summary of trigger endpoints for cinmethylin in water following dark incubation for 63 days.

	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Parameters	Method of calculation
Low concentration	138	457	1.4	k: 0.0050	SFO
High concentration	334	1110	1.8	k: 0.0021	SFO

B.8.2.2.3. Water/sediment study (Data Requirement 7.2.2.3)

Report:	CA 7.2.2.3/01 Mueller-Werthwein M. and Freundlich B., 2017
Title	Aerobic aquatic metabolism of BAS 684 H (Reg.No. 900202)
Document No.:	2016/1119819
Guidelines:	<ul style="list-style-type: none"> • OECD 308: Aerobic and anaerobic transformation in aquatic sediment systems (April 2002) • OPPTS 835.4300: Aerobic aquatic metabolism (Oct. 2008)
GLP:	Yes
Deviations	None

SUMMARY

The degradation of cinmethylin was investigated in two aerobic water/sediment systems under dark conditions. One system was taken from a pond like side-arm of a river (Berghäuser Altrhein), the second system was taken from a small stream (Ranschgraben). Each of the systems was treated separately with [cyclohexane-4-¹⁴C]-cinmethylin and [phenyl-U-¹⁴C]-cinmethylin.

The influence of microbial activity was tested during the experiment by applying the test substance to sterilized vessels.

The test vessels were attached to a flow-through system for continuous aeration and incubated at a temperature of 20 ± 2°C in the dark.

Samples for the cyclohexane- and phenyl-label experiments were taken at 0, 0.25, 1, 3, 7, 14, 28, 56, 78 and 100 days after treatment. The sterile vessels were worked up after 101 days.

Water and sediment were worked up separately. Water samples and sediment extracts were analysed by radio-HPLC. The amount of non-extractable residues was determined by combustion and liquid scintillation counting (LSC). Volatiles were trapped in appropriate trapping solutions and analysed by LSC. Metabolites were identified by comparison of retention times to those of reference items and by mass spectrometry. Chiral analysis was applied to selected samples to check a potential enantiomeric shift during incubation.

For both systems and radio-labels, the total radioactive residues in the water decreased from initially 80.4 % - 91.9 % of the total applied radioactivity (TAR) to 2.6 % - 9.6 % AR after 100 days. Correspondingly, the radioactive residues in the sediment increased in both systems, reaching 44.8 % - 62.3 % AR at the end of the incubation of which 19.2 to 35.4 % of the radioactive residues in sediment was still extractable with acetonitrile and acetonitrile/water.

Metabolite M684H001 was the only major metabolite detected in this study (>10 %, 5-10 % at two consecutive sample time points or > 5 % but not yet reached maximum at study end). M684H001 was detected in water samples treated with [cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]-cinmethylin at a maximum concentration of 6.5-11.4 % AR after 28 days. Metabolite M684H001 was detected in sediment treated with [cyclohexane-4-¹⁴C]-cinmethylin or [phenyl-U-¹⁴C]-cinmethylin at a maximum concentration of 1.8 % - 3.8 % AR after 28 - 56 days.

Metabolite M684H004 was not detected in water or sediment samples treated with [cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]-cinmethylin at more than 5 % AR at any time point. Several further peaks were observed in water samples, however, most of them occurring only sporadically and not exceeding 3.4 % AR at any sampling time.

The analyses of sediment extracts showed that cinmethylin reached its highest amount in sediment after 14 or 56 days with 51.1 % - 55.9 % AR, followed by a decrease to 16.2 % - 30.3 % AR after 100 days.

The non-extractable residues in sediment of both systems reached maximum amounts of 25.6 - 37.3 % AR after 78 - 100 days. They were further characterized in selected sediment samples by humic substance fractionation. Despite slight differences between the two labels, the radioactivity is roughly equally distributed between fulvic acids, humic acids and humins.

Cinmethylin showed a rather high mineralisation rate in both systems with both labels. Volatile radioactivity recovered from trapping solutions accounted for 42.5 - 47.0 % AR for [cyclohexane-4-¹⁴C]-cinmethylin and up to 27.8 - 30.5 % AR for [phenyl-U-¹⁴C]-cinmethylin after 78-100 days. By acidifying aliquots of the NaOH trapping solutions and subsequent LSC measurements it could be confirmed that the radioactivity in the trapping solutions consisted of dissolved ¹⁴CO₂.

For both test systems and labels, the sterilized test vessels showed higher cinmethylin concentrations in water (10.3 % - 11.5 % AR) and sediment (77.7 - 79.9 % AR) at the end of incubation than the viable vessels. Nearly all radioactive residues recovered in the water phases or sediment extracts consisted of unchanged parent. The non-extractable residues in the sterilized test vessels were significantly lower (2.4 % - 3.1 % AR) than those of the biological active incubations (21.2 % - 30.8 % AR) indicating that degradation of cinmethylin in sediment is depending on the presence of an active microbial population. From this it can be concluded that both ring moieties of the molecule are microbially degradable and prone to mineralisation.

The ratio between the two enantiomers in both test systems and with both labels was slightly shifted towards the (-)-enantiomer over time. In system Berghäuser Altrhein, the ratio (-)-enantiomer: (+)-enantiomer changed to 70:30 ([cyclohexane-4-¹⁴C]-cinmethylin) and 75:25 ([phenyl-U-¹⁴C]-cinmethylin) after 100 days. In system Ranschgraben, the ratio was 67:33 (both labels). From the results expressed as % AR it is obvious that the possible change in the enantiomeric ratio is caused by different degradation rates of the two enantiomers.

I. MATERIAL AND METHODS

A. MATERIALS

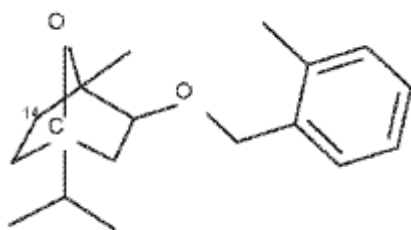
1. Test material

The test item cinmethylin was used in two ¹⁴C-labeled forms.

Reg. No.: 900202
Internal code: BAS 684 H
Chemical name: (1RS,2SR,4SR)-1,4-epoxy-p-menth-2-yl 2-methylbenzyl ether
Molecular mass: 274.4 g mol⁻¹ (unlabeled)
Molecular formula: C₁₈H₂₆O₂

1. [Cyclohexane-4-¹⁴C]-cinmethylin

Batch No.: 1146-1001
Specific radioactivity: 7.75 MBq mg⁻¹ (465000 dpm/μg)
Radiochemical purity: 99.4 %, see certificate of analysis in the final report
Chemical purity: 99.3 %
Chemical structure:



2. [Phenyl-U-¹⁴C]-cinmethylin

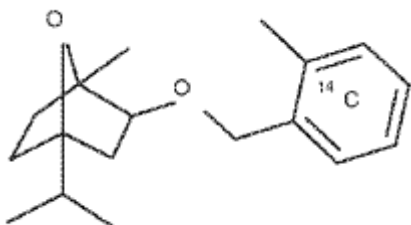
Batch No.: 1147-2001

Specific radioactivity: 17.1 MBq mg⁻¹ (1026000 dpm/μg)

Radiochemical purity: 98.9 %, see certificate of analysis in the final report

Chemical purity: 97.0 %

Chemical structure:



2. Test system

Two natural water/sediment systems were collected on August 25, 2015. Both sampling sites are located at the South-Western part of Germany. One system is designated as “Berghäuser Altrhein”, a pond-like side arm of the river Rhine south of Speyer surrounded by a forest. The second system is designated as “Ranschgraben”, a small stream east of Schifferstadt, running several kilometers through forest upstream of the sampling site.

The water was passed through a 200 μm filter direct at the sampling site. Sediment and water were transported to the laboratory, the sediment was passed through a 2 mm sieve and water and sediment were stored at 20°C. Sediment and water were filled into the test vessels 1 day after collection from the field sites.

The physico-chemical properties of the systems are summarised in Table 8.2.2.3/01-01.

Table 8.2.2.3/01-01: Characterization of the water/sediment systems

Water			Berghäuser Altrhein		Ranschgraben	
Temperature*	[°C]		21.4		17.3	
pH*			7.58		7.30	
Redox potential*	[mV]		142		136	
O2 content*	[mg L ⁻¹]		9.6		8.5	
Total N	[mg L ⁻¹]	beginning	1.62		0.10	
		end	0.80		0.43	
Total P	[mg L ⁻¹]	beginning	0.454		0.234	
		end	0.117		0.165	
TOC / org. C	[mg L ⁻¹]	beginning	10.1		4.5	
		end	17.4		18.7	
Water hardness	[mmol L ⁻¹]		1.50		0.78	
Bacteria	[cfu mL ⁻¹]	beginning	1.58 x 10 ³		1.21 x 10 ⁴	
		end	3.72 x 10 ²		3.96 x 10 ²	
Fungi	[cfu mL ⁻¹]	beginning	20		1.08 x 10 ²	
		end	0		0	
Actinomycetes	[cfu mL ⁻¹]	beginning	32		2.70 x 10 ³	
		end	6		8	
Sediment			Berghäuser Altrhein		Ranschgraben	
Sampling depth*	[cm]		0 - 20		0 - 10	
pH	(CaCl ₂)		6.9		5.9	
	(H ₂ O)		7.3		6.3	
Redox potential*	[mV]		-232		-276	
Total N	%	beginning	0.57		0.29	
		end	0.53		0.27	
Total P	[mg/kg]	beginning	859		1360	
		end	755		1330	
TOC / org. C	[%]	beginning	6.11		4.05	
		end	6.22		3.70	
CEC	[cmol+ kg ⁻¹]		28.7		12.9	
Particle size distribution			USDA	DIN 4220	USDA	DIN 4220
Clay	[%]		36.4	38.4	16.0	16.3
Silt	[%]		59.5	57.9	23.2	24.7
Sand	[%]		4.1	3.7	60.8	58.9
Soil type			Silty clay loam	Silty clay	Sandy loam	Loamy sand
Bacteria	[cfu g ⁻¹]	beginning	5.09 x 10 ⁷		9.94 x 10 ⁶	
		end	1.95 x 10 ⁷		4.52 x 10 ⁶	
Fungi	[cfu g ⁻¹]	beginning	9.16 x 10 ⁴		6.85 x 10 ³	
		end	4.18 x 10 ⁴		6.21 x 10 ³	
Actinomycetes	[cfu g ⁻¹]	beginning	2.57 x 10 ⁵		3.27 x 10 ⁶	
		end	2.59 x 10 ⁵		7.10 x 10 ⁴	

* measured directly at sampling site

CEC = cation exchange capacity

cfu = colony forming unit

TOC = total organic carbon

B. STUDY DESIGN

1. Experimental conditions

A total of 31 test vessels was prepared for each water/sediment system: 13 flasks per radiolabel (10 sampling + 3 reserve samples) + 1 flask per radiolabel for incubation under sterile conditions. In addition, 3 untreated flasks were prepared for system characterization at the end of the incubation.

For system Berghäuser Altrhein, the test vessels were filled with about 120 g of wet sediment and about 300 mL of water (water:sediment ratio of 2.5:1). For system Ranschgraben, the test vessels were filled with about 145 g of wet sediment and about 300 mL of water (water:sediment ratio of 2.07:1). This corresponded to a sediment layer of about 2 cm and a water layer of about 7 cm for both systems. These experimental conditions are a minor deviation from the OECD 308 guidance which states a water:sediment ratio between 3:1 and 4:1 should be used, however the HSE evaluator does not consider that these deviations would influence the outcome of the experiment.

After being filled with sediment and water, the test vessels could equilibrate for 13 days before treatment. The equilibration was monitored by measuring redox potential of water and sediment, temperature, O₂-content and pH of randomly selected test vessels in intervals of a few days.

For application, appropriate amounts (20 µL) of the respective application solutions (prepared in acetonitrile) were pipetted to the water surface to achieve a nominal amount of about 15 µg test item per test vessel. This corresponded to a field application rate of about 500 g active substance per ha assuming overspray over a 1 m deep water body. The amount of test item per test vessel was calculated for a 300-mL water volume. The test vessels for the 0 and 0.25-day samplings were treated 6 or 7 days later than the 1 – 100 (101) day samples and kept in the incubator until treatment. One test vessel per system and label was heat sterilized (121 °C, 30 min) prior to application of the test item. After treatment, the same parameters as during the pre-equilibration period were measured in each sample before workup.

During incubation, the test vessels were continuously aerated, and the upper water layer was slightly agitated to keep the oxygen saturation on a sufficiently high level. Each test vessel was connected to a volatile trapping system consisting of a sequence of three gas washing bottles containing different trapping solutions for potential ¹⁴C-volatiles (ethylene glycol, 2 x 1 M NaOH). The HSE evaluator notes that the aqueous photolysis study (KCA 7.2.1.2/1; Hassink, J. 2017d) also used H₂SO₄ (0.5M) as a trapping solution. The raw data from the aqueous photolysis study suggests that H₂SO₄ was the only trapping solution that trapped measurable quantities of the active substance. The lack of H₂SO₄ used as a trapping solution in this study is likely why the mass balances are low for some time points.

The test vessels sterilized after the equilibration period were not connected to the air flow system but closed and only opened for a short moment to be treated with test item under sterile conditions.

Equilibration and subsequent incubation were carried out in an incubator at a temperature of 20 ± 2 °C in the dark.

2. Sampling

Single samples for [cyclohexane-4-¹⁴C]-cinmethylin and [phenyl-U-¹⁴C]-cinmethylin experiments were taken at 0, 0.25, 1, 3, 7, 14, 28, 56, 78, and 100 days after treatment (DAT). The results obtained with [cyclohexane-4-¹⁴C]-cinmethylin and [phenyl-U-¹⁴C]-cinmethylin are considered as duplicates per water/sediment system for test item and common metabolites. The sterile vessels were worked up after 101 days. The HSE evaluator notes that true replicate samples were not collected, and the Applicant has used the two radio-labelled positions as replicates.

The volatile traps were disconnected from the air stream, the content transferred into volumetric flasks, filled up to the calibration mark, closed, and stored at room temperature until LSC measurement. During the incubation period, they were replaced as required by new traps containing fresh trapping solutions.

The control vessels for determination of the microbial activity (untreated) were sampled 100 days after treatment.

3. Description of analytical procedures

Water

The water was decanted carefully from the test vessels into a 500 mL round-bottom flask and its volume determined by weighing. For the 0 DAT samples the walls of the test vessels were additionally rinsed with acetonitrile. The acetonitrile was added to the water sample and the total weight was determined. The samples were homogenised by shaking before taking 4 x 1 mL subsamples for LSC measurement. Subsamples of each sample were transferred to HPLC vials and aliquots were subjected to HPLC analysis. A modified HPLC method was used to separate the components of a prominent peak occurring at approximately 34.3 min.

Polar peaks occurring in the HPLC chromatograms of the water samples were assumed to be caused by dissolved $^{14}\text{CO}_2$. Thus, additional analyses were carried out. Water samples from 14 DAT onwards were acidified with formic acid and homogenised by ultrasonication to release dissolved $^{14}\text{CO}_2$ from the water. Aliquots were measured by LSC and radio-HPLC.

Sediment

After carefully decanting the water, the sediment was transferred into a centrifuge tube. The test vessel was rinsed with pure acetonitrile and the rinsing solution added to the sediment. For extraction, the centrifuge tube was then placed on a rotary shaker (270 rpm) for 20 min. Since the sediment still contained a high portion of water, this first extraction can be considered as acetonitrile/water extraction.

After centrifugation (8,000 rpm, 5 min), the supernatant was decanted, made up to volume with respective extraction solvent, and aliquots measured by LSC. The extraction was repeated twice with 95 mL acetonitrile/water (1:1, v:v) and once with 95 mL pure acetonitrile, respectively.

The four-corresponding acetonitrile/water and acetonitrile extracts per sample were combined and aliquots of the combined extracts were measured for radioactivity by LSC. The recoveries were always > 90 % AR. For HPLC analysis, 5 mL of the pooled extracts were transferred into HPLC vials, respectively, and aliquots subjected to HPLC analysis. A modified HPLC method was used to separate the components of a prominent peak occurring at about 34.3 min with the first method.

The extracted sediment residues were dried at room temperature under a stream of nitrogen and samples homogenised using an analytical mill. The amount of non-extractable radioactive residues (NER) was determined by combustion of three to five aliquots in an oxidizer and analysis of the evolved ^{14}C by LSC.

Deviations of extraction procedure for the 14 - 100 day samplings

Since it was noticed that the dissolved CO_2 in the water phase increased (especially in system Berghäuser Altrhein), attempts were made to investigate, if the remaining water in the sediment also

contained dissolved CO₂. This was considered a risk potentially leading to mass balance losses during work-up.

To capture potentially escaping CO₂ from sediment during the first extraction step, the first extraction was performed directly in the test vessel before transfer into a centrifuge tube. The solvent volume of the first extraction had to be increased to up to 120 mL in order to later transfer the slurry into the centrifuge tube. After adding the acetonitrile/water mixture, the test vessel was then closed with a screw cap and placed on a rotary shaker for 20 min. Then the test vessel was connected to a series of two gas washing flasks filled with 1 M NaOH, and the head space was flushed with air for 30 min through the NaOH traps. Aliquots of the NaOH trapping solutions were then analysed for radioactivity by LSC. After expelling the CO₂, the sediment slurry was transferred into centrifuge tubes. The supernatant after centrifugation was collected in volumetric flasks and aliquots measured by LSC.

Additional extractions

To check if the NERs potentially consist of very unpolar, strong sorbing metabolites at later time points, the extraction procedure was continued for the sediments of 56- and 100-day samples using ethylacetate and cyclohexane. For this, the sediment residue after the last acetonitrile extraction was weighed, homogenised and then divided into two portions. About 20 % of the sediment was weighed into a centrifuge vessel for further extraction, the rest was dried, homogenised in a mill and aliquots combusted for the usual NER quantification.

The additional extractions were done first with 22 mL ethylacetate followed by 22 mL cyclohexane. Each extraction step was performed for 20 min on a rotary shaker (270 rpm). The extracts were separated by centrifugation (8,000 rpm, 5 min). The organic extracts were collected in 25 mL volumetric flasks, respectively and made up to volume by the respective extraction solvent prior to analysis for radioactivity by LSC. Since the amounts of radioactivity were negligible in both extracts, they were not further analysed.

Characterisation of non-extractable residues

The non-extractable radioactive residues in sediment were further characterised in 28, 78 and 100 day samples for both systems and radiolabels by separation into fulvic acids, humic acids and humins.

For each of the selected dry sediment samples, about 25 g was weighed into a 250 mL centrifuge tube and extracted three times with 0.5 M NaOH. The headspace of the centrifuge tube was purged with nitrogen before closing and placing the vessel on a rotary shaker. Each solubilization step lasted between 8 and 15 hours. After each solubilisation, the samples were centrifuged and the supernatants were collected in volumetric flasks. The solutions were made up to volume and aliquots were measured by LSC. The corresponding NaOH-supernatants were combined for each sample, the volumetric flasks rinsed with 0.5 M NaOH and the rinsing solution added to the combined extracts. The combined sample was acidified with conc. HCl to pH 1.5 ± 0.1 and stored for 3 days in a refrigerator to precipitate the acid-insoluble humic acids. After centrifugation (9,000 rpm, 10 min), the volume of the supernatant was determined and the radioactive residues in the supernatant (fulvic acids) measured by LSC.

The precipitate (humic acids) was re-dissolved in 0.5 M NaOH and transferred to a volumetric flask. The centrifuge tube was rinsed with NaOH, added to the dissolved precipitate and made up to volume, and the solution was measured for radioactivity.

After drying the sediment at room temperature under a stream of nitrogen (one sample only at room temperature) and homogenising using an analytical mill, the remaining radioactivity in sediment (humins) was determined by combustion.

The fulvic acid fraction of the selected samples was further investigated by HPLC.

Volatiles

Radioactive residues in the volatile trapping solutions (ethylene glycol and NaOH) were determined by LSC.

All trapping solutions with radioactivity > 5 % AR (all first of the two NaOH traps from 28 – 100 DAT) were further analysed to confirm that the observed radioactivity in the trapping solutions resulted from dissolved $^{14}\text{CO}_2$. Aliquots of the NaOH trapping solutions were acidified with concentrated HCl, shaken and ultrasonicated, followed by aeration with a stream of nitrogen for approximately 10 minutes. LSC results of radioactive residues < 50 dpm mL⁻¹ demonstrate that the radioactivity in the NaOH trapping solutions originally consisted of $^{14}\text{CO}_2$. The HSE evaluator notes a trapping solution specifically for trapping the active substance was not used. The aqueous photolysis study (KCA 7.2.1.2/1; Hassink, J. 2017d) used H₂SO₄ (0.5M) as a trapping solution for the active substance. The lack of H₂SO₄ used as a trapping solution in this study is likely why the mass balances are low for some time points.

Chiral analysis

Cinmethylin is a racemic mixture of two enantiomers (Reg. No. 5925581 and Reg. No. 5925632). To investigate the ratio of the two enantiomers over time, a chiral HPLC method was used to analyse application solutions as well as water samples and sediment extracts containing more than 10 % AR, i.e. 14-100 DAT samples.

For this, in order to prevent losses of cinmethylin due to volatilization during sample workup, the test item was extracted by liquid/liquid partition from the water sample, concentrated and re-dissolved. To concentrate the sediment extracts, a SPE (solid phase extraction) with a Backerbond C18 column and acetonitrile was performed. A concentration step was needed prior to the chiral analysis to achieve a sufficient signal.

Limit of quantification (LOQ) / limit of detection (LOD)

Within the study report, values below 0.1 % of the total applied radioactivity are not reported due to lack of significance. The following LOD and LOQ values have been reported for each radio-label position:

Cyclohexane-labelled cinmethylin

LSC, water, LOD = 0.242 % AR, LOQ = 0.363 % AR

LSC, sediment, LOD = 0.040 % AR, LOQ = 0.060 % AR

HPLC, water, LOQ = 0.040 % AR

HPLC, sediment, LOQ (Berghäuser Altrhein) = 0.369 % AR, LOQ (Ranschgraben) = 0.295 % AR

Phenyl-labelling cinmethylin

LSC, water, LOD = 0.109 % AR, LOQ = 0.164 % AR

LSC, sediment, LOD = 0.018 % AR, LOQ = 0.027 % AR

HPLC, water, LOQ = 0.032 % AR

HPLC, sediment, LOQ (Berghäuser Altrhein) = 0.093 % AR, LOQ (Ranschgraben) = 0.088 % AR

Microbial activity of the water sediment systems

The Berghäuser Altrhein and Ranschgraben water and sediment were measured for microbial activity at the start and end of the study. The sediment and water for both water/sediment types were microbially active throughout the study (Table 8.2.2.3/01-01).

II. RESULTS AND DISCUSSION

A. MASS BALANCE

The material balance in the test vessels ranged from 90.4 to 98.1 % AR (system Berghäuser Altrhein) and from 88.9 to 99.1 % AR (system Ranschgraben). Results of the distribution of radioactivity are presented in Table 8.2.2.3/01-02 and Table 8.2.2.3/01-03. The HSE evaluator notes that the material balance fell below the required 90% AR in system Ranschgraben for one sample. The HSE evaluator does not deem this to have affected the study outcome.

System Berghäuser Altrhein

The total radioactive residues in the water layer declined from 80.4 – 89.6 at day 0 to 6.9 – 9.6 % AR after 100 days. Corresponding to the decline of radioactive residues in the water phase the radioactive residues in the sediment increased in both labels, reaching levels of 53.5 – 60.0 % AR during the 100-day experiment. The non-extractable radioactivity in the sediment (NER) increased to 21.2 – 30.8 % AR at the end of the incubation period. Volatile radioactivity recovered from trapping solutions was $^{14}\text{CO}_2$ and accounted for 26.0 – 28.3 % after 100 days.

System Ranschgraben

Dissipation of radioactive residues from the water phase followed a similar pattern as in system Berghäuser Altrhein. Total radioactive residues in the water phase declined during the incubation period with both labels from 91.7 - 91.9 at day 0 to 2.6 – 6.9 % AR after 100 days, resulting in increased amounts of radioactive residues in the sediment phase of 44.8 – 62.3 % AR at the end of incubation. Maximum amount measured in sediment was 60 and 53.5 % AR. Non-extractable radioactive residues in the sediment accounted for 25.6 – 26.9 % AR after 100 days. Volatile radioactive residues recovered from trapping solutions were assigned to $^{14}\text{CO}_2$ and accounted for 27.8 – 47.0 % after 100 days.

Two further extractions were performed for two selected sampling dates for each label (56 and 100 DAT) using ethyl acetate and subsequently cyclohexane. The additional extracts did not contain significant amounts of radioactivity (< 1.0 % AR in any extract).

Table 8.2.2.3/01-02: Material balance and distribution of radioactive residues after application of [cyclohexane-

DAT	Vessel	[% AR]		
		Water	Acidified water HCOOH	Sediment
				Total extractable
Berghäuser Altrhein; [cyclohexane-4- ¹⁴ C]-cinmethylin				
0	VG01	80.4	n.p.	9.9
0.25	VG02	80.7	n.p.	9.9
1	VG03	71.7	n.p.	23.5
3	VG04	57.9	n.p.	35.8
7	VG05	42.9	n.p.	49.4
14	VG06	33.8	28.5	51.4
28	VG07	27.4	18.6	33.7
56	VG08	11.0	10.6	60.0
78	VG11	6.5	4.9	13.6
100	VG12	9.6	8.5	34.7
101(s)	VG14	12.9	n.p.	78.9
Berghäuser Altrhein; [phenyl-U- ¹⁴ C]-cinmethylin				
0	VG15	89.6	n.p.	4.1
0.25	VG16	78.7	n.p.	13.1
1	VG17	74.4	n.p.	22.1
3	VG18	58.2	n.p.	35.2
7	VG19	40.5	n.p.	49.9
14	VG20	31.5	30.2	53.5
28	VG21	21.8	16.8	37.4
56	VG22	11.7	10.3	37.9
78	VG26	6.7	4.6	16.3
100	VG23	6.9	6.1	28.8
101(s)	VG28	12.5	n.p.	81.0

DAT = Days after treatment

TAR = Total applied radioactivity

NER = Non-extractable radioactive residues

n.p. = Not performed

(s) = Sterile vessel

0.0 = Value < LOQ (LOQ = 0.1 % AR)

a = Results from acidified water analyses not considered for material balance

Table 8.2.2.3/01-03: Material balance and distribution of radioactive residues after application of [cyclohexane-4-¹⁴C]-cinmethylin and [phenyl-U-¹⁴C]-cinmethylin to water/sediment system Ranschgraben and incubation under dark conditions [% AR]

DAT	Vessel	[% AR]								
		Water	Acidified water HCOOH	Sediment				Volatiles / mineralisation		Material balance ^a
				Total extractable	NER	Volatiles during extraction (NaOH total)	Total	Ethylene-glycol	NaOH total (CO2)	
Ranschgraben; [cyclohexane-4- ¹⁴ C]-cinmethylin										
0	VG29	91.9	n.p.	5.4	0.1	n.p.	5.5	n.p.	n.p.	97.4
0.25	VG30	79.3	n.p.	10.9	0.3	n.p.	11.2	0.0	0.0	90.5
1	VG31	69.9	n.p.	25.9	0.9	n.p.	26.8	0.0	0.1	96.8
3	VG32	52.5	n.p.	42.7	1.8	n.p.	44.5	0.0	0.5	97.4
7	VG33	41.3	n.p.	51.3	3.3	n.p.	54.5	0.2	1.2	97.2
14	VG34	32.2	31.5	55.4	5.2	0.0	60.7	0.5	2.9	96.3
28	VG35	20.0	19.0	37.8	19.7	0.2	57.7	0.3	16.8	94.8
56	VG36	5.7	5.7	27.8	25.2	0.1	53.1	0.2	35.8	94.8
78	VG37	2.8	2.8	20.0	25.5	0.0	45.5	0.6	40.1	88.9
100	VG38	2.6	2.7	19.2	25.6	0.0	44.8	0.7	47.0	95.1
101(s)	VG42	11.6	n.p.	78.2	2.4	0.0	80.5	n.p.	n.p.	92.1
Ranschgraben; [phenyl-U- ¹⁴ C]-cinmethylin										
0	VG43	91.7	n.p.	5.8	0.1	n.p.	5.9	n.p.	n.p.	97.6
0.25	VG44	78.4	n.p.	12.9	0.4	n.p.	13.2	0.1	0.0	91.8
1	VG45	70.2	n.p.	24.4	1.0	n.p.	25.4	0.0	0.2	95.9
3	VG46	56.3	n.p.	40.1	2.0	n.p.	42.1	0.1	0.7	99.1
7	VG47	41.0	n.p.	51.6	3.0	n.p.	54.6	0.2	1.2	97.0
14	VG49	29.3	28.7	55.0	6.6	0.0	61.7	0.0	0.0	91.0
28	VG50	21.7	21.1	51.8	13.7	0.1	65.6	0.2	8.7	96.2
56	VG51	11.5	11.6	41.7	22.3	0.1	64.1	0.5	19.6	95.7
78	VG52	10.3	10.3	41.3	22.5	0.1	63.9	0.5	18.7	93.4
100	VG54	6.9	6.9	35.4	26.9	0.0	62.3	0.7	27.8	97.7
101(s)	VG56	11.1	n.p.	80.3	3.1	0.0	83.4	n.p.	n.p.	94.5

DAT = Days after treatment

NER = Non-extractable radioactive residues

n.p. = Not performed

(s) = Sterile vessel

TAR = Total applied radioactivity

0.0 = Value < LOQ (LOQ = 0.1 % AR)

a = Results from acidified water analyses not considered for material balance

B. TRANSFORMATION OF PARENT COMPOUND

Characterisation and identification of residues in water and sediment extracts

An overview of active ingredient and metabolites for the water samples and sediment extracts is presented in Table 8.2.2.3/01-04 to Table 8.2.2.3/01-15. First the cyclohexane-4-¹⁴C label in the Berghäuser Altrhein system is presented; using HPLC for peak separation, then modified HPLC for peak separation and then acidification of selected water samples. Next the phenyl-U-¹⁴C label in the Berghäuser Altrhein system is presented; using HPLC for peak separation, then modified HPLC for peak separation and then acidification of selected water samples. Next the cyclohexane-4-¹⁴C label in the Ranschgraben system is presented; using HPLC for peak separation, then modified HPLC for peak separation and then acidification of selected water samples. Finally, the phenyl-U-¹⁴C label in the Ranschgraben system is presented; using HPLC for peak separation, then modified HPLC for peak separation and then acidification of selected water samples.

One prominent peak occurred at a retention time of 34.4 min during original HPLC analysis in water samples from Berghäuser Altrhein ([cyclohexane-4-¹⁴C]-cinmethylin). MS analysis confirmed the presence of two molecular ions with similar retention times. Thus, a modified HPLC method with a slower gradient was developed for better peak separation and all samples containing this peak were re-analysed. The separated metabolite peaks could be assigned by co-chromatography with reference items as well as by MS analysis to the known metabolites M684H001 and M684H004.

Table 8.2.2.3/01-04: Metabolite overview for the water and sediment phase after application and incubation of [cyclohexane-4-¹⁴C]-cinmethylin to the water/sediment system Berghäuser Altrhein [% AR], HPLC system for peak separation.

DAT	Vessel	[% AR]									
		¹⁴ C total	Unknown 8.1 min	Unknown 9.8 min	Unknown 10.1 min	Unknown 26.4 min	Unknown 27.4 min	M684H001 / M684H004	M684H014	cinnethylin	Sum others ^a
Water											
0	VG01	80.4	-	-	-	0.4	-	-	0.6	79.3	-
0.25	VG02	80.7	-	-	-	0.5	-	-	0.8	79.5	-
1	VG03	71.7	-	-	-	0.5	-	0.5	0.8	69.9	-
3	VG04	57.9	-	-	-	-	-	1.0	0.6	56.3	-
7	VG05	42.9	1.2	0.7	-	-	0.2	2.8	0.6	37.5	-
14	VG06	33.8	3.1	1.1	1.2	-	0.6	6.6	-	20.7	0.6
28	VG07	27.4	6.9	5.9	-	-	0.8	10.7	-	2.4	0.7
56	VG08	11.0	-	-	-	-	-	7.3	-	3.3	0.5
78	VG11	6.5	1.6	1.7	0.1	-	-	2.0	0.3	0.0	0.8
100	VG12	9.6	0.9	0.7	0.2	0.1	-	4.9	-	1.2	1.5
101 (s)	VG14	12.9	-	-	-	1.2	-	-	-	11.5	0.2
Sediment											
0	VG01	9.9	-	-	-	-	-	-	-	9.9	-
0.25	VG02	9.9	-	-	-	-	-	-	-	9.9	-
1	VG03	23.5	-	-	-	-	-	-	-	23.5	-
3	VG04	35.8	-	-	-	-	-	-	0.8	35.1	-
7	VG05	49.4	-	-	-	-	-	0.5	1.0	47.9	-
14	VG06	51.4	-	-	-	-	-	1.7	0.8	48.9	-
28	VG07	33.7	-	-	-	-	-	3.4	0.6	29.7	-
56	VG08	60.0	-	-	-	-	-	4.0	-	55.9	-
78	VG11	13.6	-	-	-	-	-	1.6	-	12.1	-
100	VG12	34.7	-	-	-	-	-	3.5	-	30.3	0.8
101 (s)	VG14	78.9	-	-	-	0.7	-	-	-	78.2	-

DAT Days after treatment

TAR Total applied radioactivity

(s) Sterile vessel

- Not detected

a sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-05: Metabolite overview for the water and sediment phase after application and incubation of [cyclohexane-4-¹⁴C]-cinmethylin to the water/sediment system Berghäuser Altrhein [% AR], modified HPLC system for peak separation

DAT	Vessel	[% AR]							
		¹⁴ C total	Unknown 7.9 min	Unknown 8.5 min	Unknown 16.6 min / 17.1 min	M684H004	M684H001	cinmethylin	Sum others ^a
Water									
1	VG03	71.7	-	-	-	-	-	70.6	1.1
3	VG04	57.9	-	-	-	-	0.8	56.5	0.6
7	VG05	42.9	0.4	0.8	-	0.6	2.1	37.6	1.4
14	VG06	33.8	1.2	2.9	0.7	0.6	6.7	21.0	0.7
28	VG07	27.4	5.4	6.1	1.1	0.3	11.4	2.8	0.1
56	VG08	11.0	1.0	-	-	0.5	6.6	2.9	-
78	VG11	6.5	1.7	1.8	-	-	2.4	0.4	0.2
100	VG12	9.6	0.8	1.3	-	0.3	5.4	1.4	0.5
Sediment									
7	VG05	49.4	-	-	-	-	-	49.4	-
14	VG06	51.4	-	-	-	0.7	0.6	50.0	-
28	VG07	33.7	-	-	-	2.5	1.3	29.9	-
56	VG08	60.0	-	-	0.3	1.4	2.6	54.4	1.2
78	VG11	13.6	-	-	-	-	1.1	12.6	-
100	VG12	34.7	-	-	-	-	2.1	31.9	0.6

DAT Days after treatment

TAR Total applied radioactivity

- Not detected

^a sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-06: Metabolite overview for the water phase after application and incubation of [cyclohexane-4-¹⁴C]-cinmethylin to the water/sediment system Berghäuser Altrhein [% AR] after acidification of selected water samples

DAT	Vessel	[% AR]									
		¹⁴ C total	Unknown 8.1 min	Unknown 9.8 min	Unknown 10.1 min	Unknown 26.4min	Unknown 27.4 min	M684H001 / M684H004	M684H014	cinnethylin	Sum others ^a
Water											
14	VG06	33.8	3.1	1.1	1.2	-	0.6	6.6	-	20.7	0.6
28	VG07	27.4	6.9	5.9	-	-	0.8	10.7	-	2.4	0.7
56	VG08	11.0	-	-	-	-	-	7.3	-	3.3	0.5
78	VG11	6.5	1.6	1.7	0.1	-	-	2.0	0.3	0.0	0.8
100	VG12	9.6	0.9	0.7	0.2	0.1	-	4.9	-	1.2	1.5
Water; HCOOH											
14	VG06	28.5	-	0.3	-	-	0.6	6.4	0.2	20.0	1.0
28	VG07	18.6	0.8	0.4	-	0.2	1.1	12.4	-	2.7	1.1
56	VG08	10.6	-	-	-	-	-	6.6	-	2.8	1.2
78	VG11	4.9	-	-	0.4	0.1	0.2	2.1	-	0.5	1.6
100	VG12	8.5	-	0.4	-	-	-	5.0	-	1.1	2.0

DAT Days after treatment

TAR Total applied radioactivity

- Not detected

a Sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-07: Metabolite overview for the water and sediment phase after application and incubation of [phenyl-U-¹⁴C]-cinmethylin to the water/sediment system Berghäuser Altrhein [% AR], HPLC system for peak separation.

DAT	Vessel	[% AR]					
		¹⁴ C total	Unknown 7.6 min	Unknown 9.8 min	M684H001 / M684H004	cinnethylin	Sum others ^a
Water							
0	VG15	89.6	-	-	-	88.8	0.8
0.25	VG16	78.7	-	-	-	77.3	1.4
1	VG17	74.4	-	-	0.3	72.7	1.4
3	VG18	58.2	-	-	1.3	56.5	0.5
7	VG19	40.5	-	-	2.9	35.5	2.1
14	VG20	31.5	1.3	0.7	5.3	23.3	0.9
28	VG21	21.8	4.0	2.6	9.4	5.3	0.5
56	VG22	11.7	1.0	0.6	6.8	1.9	1.3
78	VG26	6.7	2.5	1.8	1.0	0.4	1.0
100	VG23	6.9	-	-	3.5	1.0	2.5
101 (s)	VG28	12.5	-	-	-	11.4	1.1
Sediment							
0	VG15	4.1	-	-	-	4.0	0.2
0.25	VG16	13.1	-	-	-	13.1	-
1	VG17	22.1	-	-	-	22.1	-
3	VG18	35.2	-	-	-	34.8	0.5
7	VG19	49.9	-	-	0.6	49.0	0.3
14	VG20	53.5	-	-	1.9	51.1	0.6
28	VG21	37.4	-	-	4.0	32.6	0.8
56	VG22	37.9	-	-	3.9	33.1	0.9
78	VG26	16.3	-	-	1.0	15.3	-
100	VG23	28.8	-	-	2.8	24.2	1.8
101 (s)	VG28	81.0	-	-	-	79.9	1.1

DAT Days after treatment

TAR Total applied radioactivity

(s) Sterile vessel

- Not detected

a Sum of several peaks; each individual peak < 1.1 % AR

Table 8.2.2.3/01-08: Metabolite overview for the water and sediment phase after application and incubation of [phenyl-U-¹⁴C]-cinmethylin to the water/sediment system Berghäuser Altrhein [% AR], modified HPLC system for peak separation

DAT	Vessel	[% AR]						
		¹⁴ C total	Unknown 7.6 min	Unknown 8.6 min	M684H004	M684H001	cinnethylin	Sum others ^a
Water								
1	VG17	74.4	-	-	-	-	73.1	1.3
3	VG18	58.2	0.4	0.6	0.3	0.8	55.4	0.7
7	VG19	40.5	1.7	-	0.3	2.8	34.8	0.9
14	VG20	31.5	0.9	1.0	0.3	5.0	24.2	0.1
28	VG21	21.8	3.0	2.8	0.8	9.4	5.0	0.9
56	VG22	11.7	1.3	0.9	0.7	6.5	2.3	-
78	VG26	6.7	2.4	2.0	0.4	0.9	0.4	0.5
100	VG23	6.9	0.4	1.0	0.4	3.2	1.1	0.8
Sediment								
7	VG19	49.9	-	-	0.1	1.0	47.7	1.1
14	VG20	53.5	-	-	-	0.8	51.8	0.9
28	VG21	37.4	-	-	0.6	3.4	32.4	0.9
56	VG22	37.9	-	-	1.2	3.2	32.5	1.0
78	VG26	16.3	-	-	0.6	0.3	14.6	0.8
100	VG23	28.8	-	-	0.6	2.1	24.7	1.3

DAT Days after treatment

TAR Total applied radioactivity

- Not detected

a Sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-09: Metabolite overview for the water phase after application and incubation of [phenyl-U-¹⁴C]-cinmethylin to the water/sediment system Berghäuser Altrhein [% AR] after acidification of selected water samples

DAT	Vessel	[% AR]					
		¹⁴ C total	Unknown 7.6 min	Unknown 9.8 min	M684H001 / M684H004	cinnethylin	Sum others ^a
Water							
14	VG20	31.5	1.3	0.7	5.3	23.3	0.9
28	VG21	21.8	4.0	2.6	9.4	5.3	0.5
56	VG22	11.7	1.0	0.6	6.8	1.9	1.3
78	VG26	6.7	2.5	1.8	1.0	0.4	1.0
100	VG23	6.9	-	-	3.5	1.0	2.5
Water; HCOOH							
14	VG20	30.2	-	0.5	5.4	23.7	0.6
28	VG21	16.8	-	0.4	10.7	5.2	0.5
56	VG22	10.3	-	-	6.5	2.1	1.6
78	VG26	4.6	-	0.4	1.6	0.5	2.2
100	VG23	6.1	-	0.2	3.2	0.3	2.3

DAT Days after treatment

TAR Total applied radioactivity

- Not detected

^a a sum of several peaks; each individual peak < 1.1 % AR

Table 8.2.2.3/01-10: Metabolite overview for the water and sediment phase after application and incubation of [cyclohexane-4-¹⁴C]-cinmethylin to the water/sediment system Ranschgraben [% AR], HPLC system for peak separation.

DAT	Vessel	[% AR]							
		¹⁴ C total	Unknown 25.3 min	Unknown 26.4 min	Unknown 27.4 min	M684H001 / M684H004	M684H014	cinmethylin	Sum others ^a
Water									
0	VG29	91.9	-	0.7	-	-	1.1	90.1	-
0.25	VG30	79.3	-	0.6	-	-	0.8	77.9	-
1	VG31	69.9	-	-	-	-	0.7	69.2	-
3	VG32	52.5	-	-	0.2	0.4	0.4	51.4	-
7	VG33	41.3	-	-	0.8	1.8	0.5	38.2	-
14	VG34	32.2	-	-	1.5	4.5	0.5	25.5	0.3
28	VG35	20.0	1.3	-	3.4	10.5	0.5	3.4	0.9
56	VG36	5.7	-	0.2	-	3.9	-	1.6	-
78	VG37	2.8	-	0.2	-	1.4	0.1	0.6	0.4
100	VG38	2.6	-	0.1	-	1.7	0.1	0.7	0.0
101 (s)	VG42	11.6	-	1.3	-	-	0.1	10.3	-
Sediment									
0	VG29	5.4	-	-	-	-	-	5.4	-
0.25	VG30	10.9	-	-	-	-	-	10.9	-
1	VG31	25.9	-	-	-	-	-	25.9	-
3	VG32	42.7	-	-	-	-	0.7	42.0	-
7	VG33	51.3	-	-	0.3	0.4	0.4	50.2	-
14	VG34	55.4	-	-	-	1.6	0.4	53.4	-
28	VG35	37.8	-	0.9	-	2.8	2.0	32.1	-
56	VG36	27.8	-	-	-	2.6	1.3	23.5	0.4
78	VG37	20.0	-	-	-	2.6	1.7	15.7	-
100	VG38	19.2	-	-	-	2.5	0.5	16.2	-
101 (s)	VG42	78.2	-	-	-	-	0.4	77.7	-

DAT Days after treatment

TAR Total applied radioactivity

(s) Sterile vessel

- Not detected

a sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-11: Metabolite overview for the water and sediment phase after application and incubation of [cyclohexane-4-¹⁴C]-cinmethylin to the water/sediment system Ranschgraben [% AR], modified HPLC system for peak separation

DAT	Vessel	[% AR]						
		¹⁴ C total	Unknown 16.0 min	M684H004	M684H001	cinnmethylin	Unknown	Sum others ^a
Water								
3	VG32	52.5	-	-		51.3	-	1.2
7	VG33	41.3	0.3	0.5	1.4	37.3	-	2.0
14	VG34	32.2	2.1	0.9	3.5	24.5	-	1.3
28	VG35	20.0	3.3	1.5	9.8	2.6	-	2.8
56	VG36	5.7	-	1.5	1.7	1.4	-	1.1
78	VG37	2.8	-	0.2	1.6	0.7	-	0.3
100	VG38	2.6	-	0.2	1.5	0.5	-	0.4
Sediment								
7	VG33	51.3	-	-	-	51.3	-	-
14	VG34	55.4	-	-	1.2	54.3	-	-
28	VG35	37.8	-	-	3.8	32.9	-	1.1
56	VG36	27.8	-	-	2.9	24.9	-	-
78	VG37	20.0	-	-	2.0	17.6	0.4	-
100	VG38	19.2	-	-	1.4	17.7	-	-

DAT Days after treatment

TAR Total applied radioactivity

- Not detected

^a a sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-12: Metabolite overview for the water phase after application and incubation of [cyclohexane-4-¹⁴C]-cinmethylin to the water/sediment system Ranschgraben [% AR] after acidification of selected water samples

DAT	Vessel	[% AR]							
		¹⁴ C total	Unknown 25.3 min	Unknown 26.4 min	Unknown 27.4 min	M684H001 / M684H004	M684H014	cinnmethylin	Sum others ^a
Water									
14	VG34	32.2	-	-	1.5	4.5	0.5	25.5	0.3
28	VG35	20.0	1.3	-	3.4	10.5	0.5	3.4	0.9
56	VG36	5.7	-	0.2	-	3.9	-	1.6	-
78	VG37	2.8	-	0.2	-	1.4	0.1	0.6	0.4
100	VG38	2.6	-	0.1	-	1.7	0.1	0.7	0.0
Water; HCOOH									
14	VG34	31.5	-	-	2.1	4.2	0.2	24.3	0.6
28	VG35	19.0	1.1	-	3.6	10.6	-	2.2	1.5
56	VG36	5.7	-	-	-	4.5	-	1.3	-
78	VG37	2.8	-	0.2	-	1.8	0.2	0.5	0.1
100	VG38	2.7	-	-	-	1.9	-	0.8	-

DAT Days after treatment

TAR Total applied radioactivity

- Not detected

a Sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-13: Metabolite overview for the water and sediment phase after application and incubation of [phenyl-U-¹⁴C]-cinmethylin to the water/sediment system Ranschgraben [% AR], HPLC system for peak separation.

DAT	Vessel	[% AR]				
		¹⁴ C total	M684H001 / M684H004	M684H014	cinnethylin	Sum others ^a
Water						
0	VG43	91.7	-	1.2	89.6	0.8
0.25	VG44	78.4	-	0.7	77.1	0.6
1	VG45	70.2	-	0.9	68.3	1.0
3	VG46	56.3	0.3	0.5	55.4	-
7	VG47	41.0	1.0	0.4	39.5	-
14	VG49	29.3	3.5	0.3	25.1	0.4
28	VG50	21.7	7.9	0.3	13.0	0.5
56	VG51	11.5	6.4	0.3	4.9	-
78	VG52	10.3	6.1	0.1	3.6	0.5
100	VG54	6.9	3.9	0.1	2.1	0.9
101 (s)	VG56	11.1	-	0.1	10.3	0.7
Sediment						
0	VG43	5.8	-	-	5.8	-
0.25	VG44	12.9	-	-	12.9	-
1	VG45	24.4	-	0.3	24.1	-
3	VG46	40.1	-	0.6	39.4	-
7	VG47	51.6	0.3	1.2	50.1	-
14	VG49	55.0	1.5	0.9	52.6	-
28	VG50	51.8	2.7	2.0	46.7	0.4
56	VG51	41.7	5.5	1.4	34.8	-
78	VG52	41.3	5.0	1.9	34.3	0.1
100	VG54	35.4	4.8	0.6	29.9	-
101 (s)	VG56	80.3	-	0.6	78.9	0.8

DAT Days after treatment

TAR Total applied radioactivity

(s) Sterile vessel

- Not detected

a Sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-14: Metabolite overview for the water and sediment phase after application and incubation of [phenyl-U-¹⁴C]-cinmethylin to the water/sediment system Ranschgraben [% AR], modified HPLC system for peak separation

DAT	Vessel	[% AR]					
		¹⁴ C total	M684H004	M684H001	M684H014	cinnethylin	Sum others ^a
Water							
0.25	VG45	78.4	-	-	0.8	77.6	-
3	VG46	56.3	-	-	0.6	55.7	-
7	VG47	41.0	0.2	0.6	0.4	39.8	-
14	VG49	29.3	0.8	2.8	0.4	25.0	0.3
28	VG50	21.7	2.1	6.5	0.3	12.4	0.6
56	VG51	11.5	3.1	3.2	0.3	4.9	-
78	VG52	10.3	3.7	2.5	0.2	3.8	0.1
100	VG54	6.9	3.0	1.1	0.3	2.3	0.2
Sediment							
7	VG47	51.6	-	0.3	0.7	50.7	-
14	VG49	55.0	0.3	0.8	1.5	52.5	-
28	VG50	51.8	0.6	1.8	1.5	47.8	-
56	VG51	41.7	3.3	1.5	1.9	35.0	-
78	VG52	41.3	3.7	1.5	2.1	34.0	-
100	VG54	35.4	3.8	1.1	2.5	28.0	-

DAT Days after treatment

TAR Total applied radioactivity

- Not detected

a Sum of several peaks; each individual peak < 1.0 % AR

Table 8.2.2.3/01-15: Metabolite overview for the water phase after application and incubation of [phenyl-U-¹⁴C]-cinmethylin to the water/sediment system Ranschgraben [% AR] after acidification of selected water samples

DAT	Vessel	[% AR]				
		¹⁴ C total	M684H001 / M684H004	M684H014	cinnemethylin	Sum others ^a
Water						
14	VG49	29.3	3.5	0.3	25.1	0.4
28	VG50	21.7	7.9	0.3	13.0	0.5
56	VG51	11.5	6.4	0.3	4.9	-
78	VG52	10.3	6.1	0.1	3.6	0.5
100	VG54	6.9	3.9	0.1	2.1	0.9
Water; HCOOH						
14	VG49	28.7	3.7	0.2	24.3	0.4
28	VG50	21.1	7.6	0.2	12.6	0.7
56	VG51	11.6	6.3	0.1	5.2	-
78	VG52	10.3	6.2	0.1	3.4	0.5
100	VG54	6.9	4.0	-	2.2	0.7

DAT Days after treatment

TAR Total applied radioactivity

- Not detected

a Sum of several peaks; each individual peak < 1.0 % AR

Water

System Berghäuser Altrhein

[cyclohexane-4-¹⁴C]-cinmethylin

The portion of [cyclohexane-4-¹⁴C]-cinmethylin in the water phase declined from 79.3 % AR at time zero to 1.2 % AR after 100 days.

The peak occurring at the retention time of 34.4 min was further separated by the modified HPLC method. The two peaks were identified as metabolites M684H001 and M684H004, reaching maximum amounts of 11.4 % after 28 DAT and 0.6 % AR after 7/14 DAT, respectively.

Two very polar peaks reaching amounts of 6.9 % AR can most likely be attributed to ¹⁴CO₂ as concluded after acidification of the respective water samples. None of the unidentified peaks exceeded 1.1 % AR at any sampling time.

[phenyl-U-¹⁴C]-cinmethylin

The portion of [phenyl-U-¹⁴C]-cinmethylin in the water phase declined from 88.8 % AR at day 0 to 1.0 % AR after 100 days.

Again, the peak occurring at the retention time of 34.4 min was further separated by the modified HPLC method. The two separated metabolite peaks (M684H001 and M684H004) reached maximum amounts after of 9.4 % and 0.8 % AR after 28 days, respectively.

As with [cyclohexane-4- ^{14}C]-cinmethylin, very polar peaks were detected in water in amounts of up to 4.0 % AR in the time period between 14 – 78 days. After acidification of the water samples, if at all, only small peaks <1 % AR were left. Thus, the polar peaks can be most likely attributed to $^{14}\text{CO}_2$. None of the unidentified peaks exceeded 0.5 % AR at any sampling time.

System Ranschgraben

[cyclohexane-4- ^{14}C]-cinmethylin

The portion of [cyclohexane-4- ^{14}C]-cinmethylin in the water phase declined from 90.1 % AR at day 0 to 0.7 % AR after 100 days.

The peak with the retention time of 34.9 min was further separated by the modified HPLC method. Metabolites M684H001 and M684H004 reached maximum amounts of 9.8 % and 1.5 % AR after 28 days, respectively.

Several further peaks were detected in amounts up to 3.4 % AR, most of them occurred only sporadically. Different from system Berghäuser Altrhein, no peaks were observed at early retention times, and no noticeable difference was observed in the HPLC results/chromatograms of original and acidified samples. This might be explained by a generally lower mineralisation rate in this system with less or no dissolved CO_2 in the water phase. Also, the slightly lower pH of the Ranschgraben water might have contributed to a general lower $^{14}\text{CO}_2$ dissolution.

No further degradates were assigned to known metabolites by co-chromatography with reference items. None of the unidentified peaks exceeded 3.4 % AR at any sampling time.

[phenyl-U- ^{14}C]-cinmethylin

The portion of [phenyl-U- ^{14}C]-cinmethylin in the water phase declined from 89.6 % AR at day 0 to 2.1 % AR after 100 days.

Metabolites M684H001 and M684H004 reached maximum amounts of 6.5 % AR after 28 days and 3.7 % AR after 78 days, respectively.

Further peaks were detected in amounts up to 1.2 % AR. As described for [cyclohexane-4- ^{14}C]-cinmethylin, no peaks were observed at early retention times, but for comparison the samples from DAT 14 on were acidified to release potentially dissolved carbonates/ $^{14}\text{CO}_2$ from the water phase. Again, no noticeable difference was observed in the HPLC results/chromatograms of original and acidified samples.

Sediment**System Berghäuser Altrhein***[cyclohexane-4-¹⁴C]-cinmethylin*

Detected amounts of [cyclohexane-4-¹⁴C]-cinmethylin extracted from the sediment phase reached a maximum of 55.9 % AR after 56 DAT, followed by a decrease to 30.3 % AR after 100 DAT.

One prominent peak occurring at a retention time of 34.4 min was further separated by the modified HPLC method with a slower gradient. The separated metabolite peaks were assigned to the known metabolites M684H001 and M684H004, reaching maximum amounts of 2.6 % AR after 56 DAT and 2.5 % AR after 28 DAT, respectively. Few unknown metabolites were detected, occurring only sporadically after 3 – 56 DAT. None of those metabolites exceeded 1.0 % AR at any sampling time.

[phenyl-U-¹⁴C]-cinmethylin

Detected amounts of [phenyl-U-¹⁴C]-cinmethylin extracted from the sediment phase reached a maximum of 51.1 % AR after 14 DAT, followed by a decrease to 24.2 % AR after 100 DAT.

The peak with the retention time of 34.9 min was further separated by the modified HPLC method. The separated metabolite peaks were assigned to the known metabolites M684H001 and M684H004, reaching maxima of 3.4 % AR after 28 DAT and 1.2 % AR after 56 DAT, respectively. Few unknown metabolites were detected sporadically. None of those metabolites exceeded 1.1 % AR at any sampling time.

System Ranschgraben*[cyclohexane-4-¹⁴C]-cinmethylin*

Detected amounts of [cyclohexane-4-¹⁴C]-cinmethylin extracted from the sediment phase reached a transient maximum of 53.4 % AR after 14 DAT, followed by a decrease to 16.2 % AR after 100 DAT.

The peak with the retention time of 34.9 min was further analysed using the modified HPLC method. The metabolite peak was solely assigned to metabolite M684H001, reaching a maximum amount of 3.8 % AR after 28 DAT. Few unknown metabolites were detected, occurring only very sporadically. None of these unknown metabolites exceeded 2.0 % AR at any sampling time.

[phenyl-U-¹⁴C]-cinmethylin

Detected amounts of [phenyl-U-¹⁴C]-cinmethylin extracted from the sediment phase reached a maximum of 52.6 % AR after 14 DAT, followed by a decrease to 29.9 % AR after 100 DAT.

The peak with the retention time of 34.9 min was further separated by the modified HPLC method. The separated metabolite peaks were assigned to the known metabolites M684H001 and M684H004, reaching maximum amounts of 1.8 % AR after 28 DAT and 2.5 % AR after 100 DAT, respectively. Several unknown metabolites were detected, most of them occurring only sporadically. None of these unknown metabolites exceeded 3.8 % AR at any sampling time.

Sterilised assays

All results of the analysis of the sterilized test vessels are presented in the same tables as the results of the viable test vessels.

The sterilised incubations (101 days) showed higher concentrations of cinmethylin in water and sediment as the 100 day samples of the viable vessels. Nearly all radioactive residues recovered in the water phases or sediment extracts consisted of unchanged parent. In system Berghäuser Altrhein, cinmethylin was detected in portions of 11.5 % ([cyclohexane-4-¹⁴C]-cinmethylin) and 11.4 % AR ([phenyl-U-¹⁴C]-cinmethylin) in the water samples, and portions of 78.2 % ([cyclohexane-4-¹⁴C]-cinmethylin) and 79.9 % AR ([phenyl-U-¹⁴C]-cinmethylin) were detected in the combined sediment extracts of the sterilised test vessels. In system Ranschgraben, cinmethylin was detected in amounts of 10.3 % ([cyclohexane-4-¹⁴C]-cinmethylin) and 10.3 % AR ([phenyl-U-¹⁴C]-cinmethylin) in the water samples, and 77.7 % ([cyclohexane-4-¹⁴C]-cinmethylin) and 78.9 % AR ([phenyl-U-¹⁴C]-cinmethylin) in the combined sediment extracts.

The non-extractable residues in sediment of the sterilised test vessels were significantly lower (2.4 – 3.1 % AR, 101 DAT) than those of the biologically active incubations (21.2 – 30.8 % AR, 100 DAT), indicating that the degradation/biotransformation of cinmethylin in the water/sediment systems depends on the presence of an active microbial population. This is observed with [cyclohexane-4-¹⁴C]-cinmethylin and [phenyl-U-¹⁴C]-cinmethylin, demonstrating that both rings of the molecule are microbially degradable and prone to mineralisation.

Chiral HPLC

Results of the chiral radio-HPLC analyses are summarised in Table 8.2.2.3/01-16 and Table 8.2.2.3/01-17.

Table 8.2.2.3/01-16: Chiral radio-HPLC analysis (LC081, system 17) of selected water samples and sediment extracts of system Berghäuser Altrhein after incubation with ¹⁴C-cinmethylin

Matrix	DAT	Total ERR [% AR]	Total cinmethylin [% AR]	E(-) [% ROI]	E(+) [% ROI]	E(-) [% AR]	E(+) [% AR]	Enantiomer ratio (- : +) [%ROI]
System Berghäuser Altrhein, [cyclohexane-4- ¹⁴ C]-cinmethylin								
Application solution		n.p.	n.p.	53.3	46.7	n.p.	n.p.	53:47
Water	0 a)	n.p.	79.3	n.p.	n.p.	42.3	37.1	n.p.
	14	33.8	20.7	59.6	40.4	12.3	8.4	60:40
Sediment extract	14	51.4	48.9	56.6	43.4	27.7	21.2	57:43
	28	33.7	29.7	64.0	36.0	19.0	10.7	64:36
	56	60.0	55.9	58.8	41.2	32.9	23.0	59:41
	78	13.6	12.1	61.1	38.9	7.4	4.7	61:39
	100	34.7	30.3	70.7	29.3	21.4	8.9	71:29
System Berghäuser Altrhein, [phenyl-U- ¹⁴ C]-cinmethylin								
Application solution		n.r.	n.r.	50.8	49.2	n.p.	n.p.	51:49
Water	0 a)	n.p.	88.8	n.p.	n.p.	45.1	43.7	n.p.
	14	31.5	23.3	57.8	42.2	13.5	9.9	58:42
Sediment extract	14	53.5	51.1	56.2	43.8	28.7	22.4	56:44
	28	37.4	32.6	67.5	32.5	22.0	10.6	68:32
	56	37.9	33.1	68.9	31.1	22.8	10.3	69:31
	78	16.3	15.3	69.0	31.0	10.6	4.8	69:31
	100	28.8	24.2	76.4	23.6	18.5	5.7	76:24

DAT Days after treatment

ERR Extractable Radioactive Residues

n.p. Not performed

E(-)/E(+) (-)-enantiomer, Reg. No. 5925581 / (+)-enantiomer, Reg. No. 5925632

AR Total applied radioactivity

ROI "Region of interest" = peak area with regard to the total integrated peak area in a chromatogram

a) Calculation based on total cinmethylin at DAT 0 and enantiomeric ratio (% ROI) in application solution

Table 8.2.2.3/01-17: Chiral radio-HPLC analysis (LC081, system 17) of selected water samples and sediment extracts of system Ranschgraben after incubation with ^{14}C -cinmethylin

Matrix	DAT	Total ERR [% AR]	Total cinmethylin [% AR]	E(-) [% ROI]	E(+) [% ROI]	E(-) [% AR]	E(+) [% AR]	Enantiomer ratio (- : +) [%TAR]
System Ranschgraben, [cyclohexane-4- ^{14}C]-cinmethylin								
Application solution		n.p.	n.p.	53.3	46.7	n.p.	n.p.	53:47
Water	0 a)	91.9	90.1	n.p.	n.p.	48.0	42.1	n.p.
	14	32.2	25.5	54.9	45.1	14.0	11.5	55:45
Sediment extract	14	55.4	53.4	56.2	43.8	30.1	23.4	56:44
	28	37.8	32.1	61.9	38.1	19.9	12.2	62:38
	56	27.8	23.5	60.8	39.2	14.3	9.2	61:39
	78	20.0	15.7	62.5	37.5	9.8	5.9	63:38
	100	19.2	16.2	67.2	32.8	10.9	5.3	67:33
System Ranschgraben, [phenyl-U- ^{14}C]-cinmethylin								
Application solution		n.p.	n.p.	50.8	49.2	n.p.	n.p.	51:49
Water	0 a)	91.7	89.6	n.p.	n.p.	45.6	44.1	n.p.
	14	29.3	25.1	55.8	44.2	14.0	11.1	56:44
	28	21.7	13.0	66.9	33.1	8.7	4.3	67:33
Sediment extract	14	55.0	52.6	54.7	45.3	28.8	23.8	55:45
	28	51.8	46.7	59.6	40.4	27.9	18.9	60:40
	56	41.7	34.8	65.4	34.6	22.8	12.0	65:35
	78	41.3	34.3	64.7	35.3	22.2	12.1	65:35
	100	35.4	29.9	67.0	33.0	20.0	9.9	67:33

DAT Days after treatment

ERR Extractable radioactive residues

n.p. Not performed

E(-)/E(+) (-)-enantiomer, Reg. No. 5925581 / (+)-enantiomer, Reg. No. 5925632

AR Total applied radioactivity

ROI "Region of interest" = peak area with regard to the total integrated peak area in a chromatogram

a) Calculation based on total cinmethylin at DAT 0 and enantiomeric ratio (% ROI) in application solution

The enantiomeric ratio in the application solutions was 53:47 (- : +) for [cyclohexane-4- ^{14}C]-cinmethylin, and 51:49 (- : +) for [phenyl-U- ^{14}C]-cinmethylin. The ratio between the two enantiomers in both test systems and with both labels was shifted towards the (-)-enantiomer (Reg. No. 5925581) over time. In system Berghäuser Altrhein, the ratio (-)-enantiomer : (+)-enantiomer changed to 71:29 ([cyclohexane-4- ^{14}C]-cinmethylin) and 76:24 ([phenyl-U- ^{14}C]-cinmethylin) after 100 days. In system Ranschgraben, the ratio was 67:33 (both labels).

From the results expressed as % AR it is the Applicants opinion that the possible change in the enantiomeric ratio is caused by different degradation rates of the two enantiomers and not by enantiomeric conversion, i.e. no formation of one enantiomer from the other. In both test systems, both enantiomers were degraded throughout the incubation period.

C. CHARACTERISATION OF NON-EXTRACTABLE RESIDUES (NER)

Results of the humic substance fractionation are summarised in Table 8.2.2.3/01-18.

System Berghäuser Altrhein

The non-extractable residues (NER) reached maximum portions of 27.7 % AR and 37.3 % AR in system Berghäuser Altrhein ([cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]-cinmethylin, respectively).

With both labels and at all sampling dates, most of the radioactive residues found in the NER fraction was associated with the humin fraction (8.3 to 18.5 % AR), accounting for about 40 – 50 % of the NER. The remaining radioactivity was distributed between fulvic and humic acids.

System Ranschgraben

The non-extractable residues (NER) reached maximum amounts of 25.6 % AR and 26.9 % AR in system Ranschgraben ([cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]-cinmethylin, respectively). With both labels, at the end of incubation the radioactive residues after solvent extraction were about equally distributed between the fractions fulvic acids, humic acids and humins.

The fulvic acid fractions were further investigated by HPLC. Peaks obtained were found in the medium polar and polar region of the chromatogram for both test systems and labels. However, none of the peaks could be reliably assigned to known metabolites.

Table 8.2.2.3/01-18: Distribution of radioactive residues between fulvic acids, humic acids and humins in sediment samples after application of ¹⁴C-cinmethylin to water/sediment systems and incubation

Sediment sample	DAT	Vessel No.	[% AR]					Recovery %
			Total NER	Fulvic acids	Humic acids	Humins	Sum	
Berghäuser Altrhein (cyclohexane-4- ¹⁴ C]-cinmethylin)	28	VG07	20.9	7.6	4.4	8.3	20.2	96.8
	78	VG11	27.7	8.9	6.3	11.5	26.7	96.4
	100	VG12	21.2	6.8	4.6	8.8	20.2	95.1
Berghäuser Altrhein ([phenyl-U- ¹⁴ C]-cinmethylin)	28	VG21	24.7	5.6	5.9	11.4	22.9	92.8
	78	VG26	37.3	8.1	8.6	18.5	35.2	94.5
	100	VG23	30.8	7.1	7.1	14.3	28.5	92.7
Ranschgraben (cyclohexane-4- ¹⁴ C]-cinmethylin)	28	VG35	19.7	9.5	4.4	5.2	19.0	96.9
	78	VG37	25.5	9.6	7.9	7.4	24.9	97.8
	100	VG38	25.6	6.9	6.3	6.8	19.9	77.8 ^a
Ranschgraben ([phenyl-U- ¹⁴ C]-cinmethylin)	28	VG50	13.7	4.3	4.2	4.5	12.9	94.5
	78	VG52	22.5	7.1	7.1	8.3	22.6	100.2
	100	VG54	26.9	7.5	8.1	8.1	23.8	88.4

DAT Days after treatment

NER Non-extractable radioactive residues

TAR Total applied radioactivity

^a The low recovery can be apportioned to the loss of a sample

D. KINETIC EVALUATION

1. Introduction

The degradation behaviour of cinmethylin has been investigated in two natural water/sediment systems in Germany (Berghäuser Altrhein, Ranschgraben), each treated separately with cyclohexane-¹⁴C and phenyl-¹⁴C-labeled test substance. The test systems were incubated in the dark for up to 100 days.

The purpose of this evaluation was to analyse the dissipation and degradation kinetics of cinmethylin, its two enantiomers and its metabolites according to FOCUS degradation kinetics guidance (2006; 2014), to derive degradation parameters as triggers for additional work (trigger endpoints). A separate study was submitted to derive modelling endpoints (He and Pape, 2017; KCA 7.2.2.3/002).

The Applicant performed kinetic evaluations for the parent substance cinmethylin, its two enantiomers Reg. No. 5925581 ((-)-enantiomer) and Reg. No. 5925632 ((+)-enantiomer) and its metabolites M684H001 and M684H004. The evaluation was performed at the following levels recommended by FOCUS:

Parent substance and its enantiomers: Level P-I: one-compartment approach, assessment of parent degradation in the total system (applied for parent and its enantiomers, separately) as well as dissipation from the water and sediment phase of the test systems (parent only).

Metabolites: Level M-I dissipation: one-compartment approach, assessment of metabolite dissipation from the maximum observed concentration in the total system, the water and sediment phase of the test systems.

The HSE evaluator notes that dissipation and degradation DT₅₀s are not required for metabolites in a UK only application because the surface water exposure assessment for metabolites utilises a “total dose” approach. Therefore, the HSE evaluator has also not assessed the Applicant’s Level M-I evaluations.

The Applicant used KINGUI version 2 using IRLS optimisation; error tolerance was set to 10⁻⁶ and maximum iterations of the optimisation tool was set to 100. Trigger endpoints were derived from the kinetic models that provided the best fit to the measured data. Initially, goodness-of-fit was compared for SFO and FOMC models. If FOMC resulted in a better fit or no clear decision could be made, then the Applicant tested the biphasic DFOP and HS models. Model appropriateness was tested through detailed statistical analysis including visual assessment of the goodness of fit, Chi² scaled-error criterion and t-test significance.

The results obtained from the experiments with the same test systems treated with the two differently labelled test items were considered as replicates for kinetic evaluation.

At Level P-I for total system and water phase, the kinetic evaluation started on the day of treatment (i.e. 0 DAT). The initial concentration of the test substance in the total system or in water was set to the material balance recovered at 0 DAT as recommended by FOCUS (2006; 2014); for enantiomers the measured data at 0 DAT was used.

The assessment of dissipation in sediment at Level P-I dissipation only requires kinetics to be fitted to the corresponding decline data, starting from the maximum observed concentration in the compartment. The dissipation of the respective compound was thus evaluated starting at the day of maximum occurrence that was defined as 0 days after maximum concentration. All later time points were adjusted accordingly as days after maximum concentrations. Values below the detection limit

(LOD) for parent compound and degradation products were treated as recommended by FOCUS (2006; 2014).

The HSE evaluator assessed the supplied kinetic evaluation for the parent and the two enantiomers by deriving trigger endpoints for the parent and two enantiomers in CAKE version 3.2, with this evaluation also following FOCUS guidance on deriving trigger endpoints. The HSE evaluator agreed with the procedures and data handling undertaken by the Applicant in the supplied kinetic evaluation, though did not agree with all decisions. The Applicant's kinetic evaluations are presented below, apart from the instances where the HSE evaluator disagreed; in these cases, the HSE evaluator's kinetic evaluation and derived endpoints are presented.

2. Kinetic fits

The HSE evaluator has evaluated the decisions made by the Applicant and the resulting trigger endpoints and has accepted most of these. Therefore, the results presented are derived from the Applicant's assessment except where the HSE evaluator disagreed, in which case the HSE evaluator's own assessments are presented.

System Berghäuser Altrhein (BA)

Level P-I – Cinmethylin

Table 8.2.2.3/01-19 summarises the kinetic models and derived endpoints for the total system, water and sediment phases in turn, as supplied by the Applicant. The kinetic models and decisions taken are discussed in turn below.

Total system

The SFO visual fit was acceptable with a χ^2 below 15%. The FOMC model did not improve the visual fit but did offer a slightly lower χ^2 error value, though the standard deviation of β was greater than β . DFOP and HS did not improve the visual fit compared to SFO. The Applicant concluded SFO was the most appropriate model; the HSE evaluator agrees with this. Figure 8.2.2.3/01-01 displays the model fits and residuals for cinmethylin degradation in the total system.

Water phase

The initial, unconstrained SFO fit led to an underestimated M_0 of 83.95%. The Applicant then repeated the SFO fit with M_0 fixed to the mean of the residue data at 0 DAT (92.35%). The revised SFO visual fit was acceptable with a χ^2 below 15%. The FOMC model improved the visual fit and provided a lower χ^2 error value. DFOP further improved the visual fit and provided the lowest χ^2 error value; additionally, all model parameters were significantly different from zero. The HS model fit did not further improve the visual fit and provided a higher χ^2 error value. The Applicant concluded DFOP was the most appropriate model. The HSE evaluator notes the inconsistent treatment of underestimated M_0 values, but this does not change the outcome of the decision made by the Applicant. The HSE evaluator agrees DFOP is the best model fit. Figure 8.2.2.3/01-02 displays the model fits and residuals for cinmethylin dissipation from the water phase.

Sediment phase

The SFO visual fit was acceptable. The χ^2 error value was above 15% but is acceptable as the visual fit was acceptable with a clear decline of residues. The k parameter was also significantly different to zero. The FOMC model did not improve the visual fit and offered a higher χ^2 error value. The Applicant concluded SFO was the most appropriate model; the HSE evaluator agrees with this. Figure 8.2.2.3/01-03 displays the model fits and residuals for cinmethylin dissipation from the sediment phase.

Table 8.2.2.3/01-19: Summary of kinetic model evaluation for cinmethylin in System Berghäuser Altrhein, Level P-I (trigger endpoints). Final kinetic models are highlighted in bold.

Phase	Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Total System	SFO	Acceptable	92.35	k: 0.01793	0.0132 – 0.023	<0.0001	11.8	38.7	128.4
	FOMC	Acceptable	95.24	α : 1.2386 β : 42.6584	-0.5404 – 3.018 -47.482 – 132.799	- -	11.2	32.0	231.1
	DFOP	Acceptable	95.25	k1 (d): 0.0348 k2 (d): 2.3E-14 g: 0.773	-0.034 – 0.103 -0.059 – 0.059 -0.662 – 2.209	0.167 0.500	11.6	29.9	>1000
	HS	Acceptable	91.54	k1 (d): 0.00358 k2 (d): 0.01811 tb: 1.0	-0.388 – 0.395 0.012 – 0.024 -25.506 – 27.506	0.493 <0.0001	13.0	39.1	127.9
Water Phase	SFO ^a	Acceptable	92.1	k: 0.1353	0.115 – 0.156	<0.0001	11.5	5.1	17.0
	FOMC	Good	86.05	α : 2.3032 β : 14.9789	0.784 – 3.822 2.136 – 27.822	- -	7.0	5.3	25.7
	DFOP	Good	92.09	k1 (d): 6.2859 k2 (d): 0.0991 g: 0.1611	1.454 – 11.117 0.090 – 0.108 0.119 – 0.203	0.0107 <0.0001	3.6	5.2 ^b	21.5
	HS	Good	86.35	k1 (d): 0.1532 k2 (d): 0.0857 tb: 3.6456	0.121 – 0.185 0.059 – 0.113 0.572 – 6.719	<0.0001 <0.0001	6.9	5.2	24.0
Sediment Phase	SFO	Acceptable	45.65	k: 0.0085	0.001 – 0.016	0.0334	22.9	81.3	270.1
	FOMC	Acceptable	49.82	α : 0.191 β : 2.704	-0.407 – 0.790 -23.701 – 29.11	- -	25.5	98.7	>1000

^a Values presented are from the revised SFO visual fit with an M_0 fixed at the mean 0 DAT concentration level.

^b Overall DT₅₀ presented.

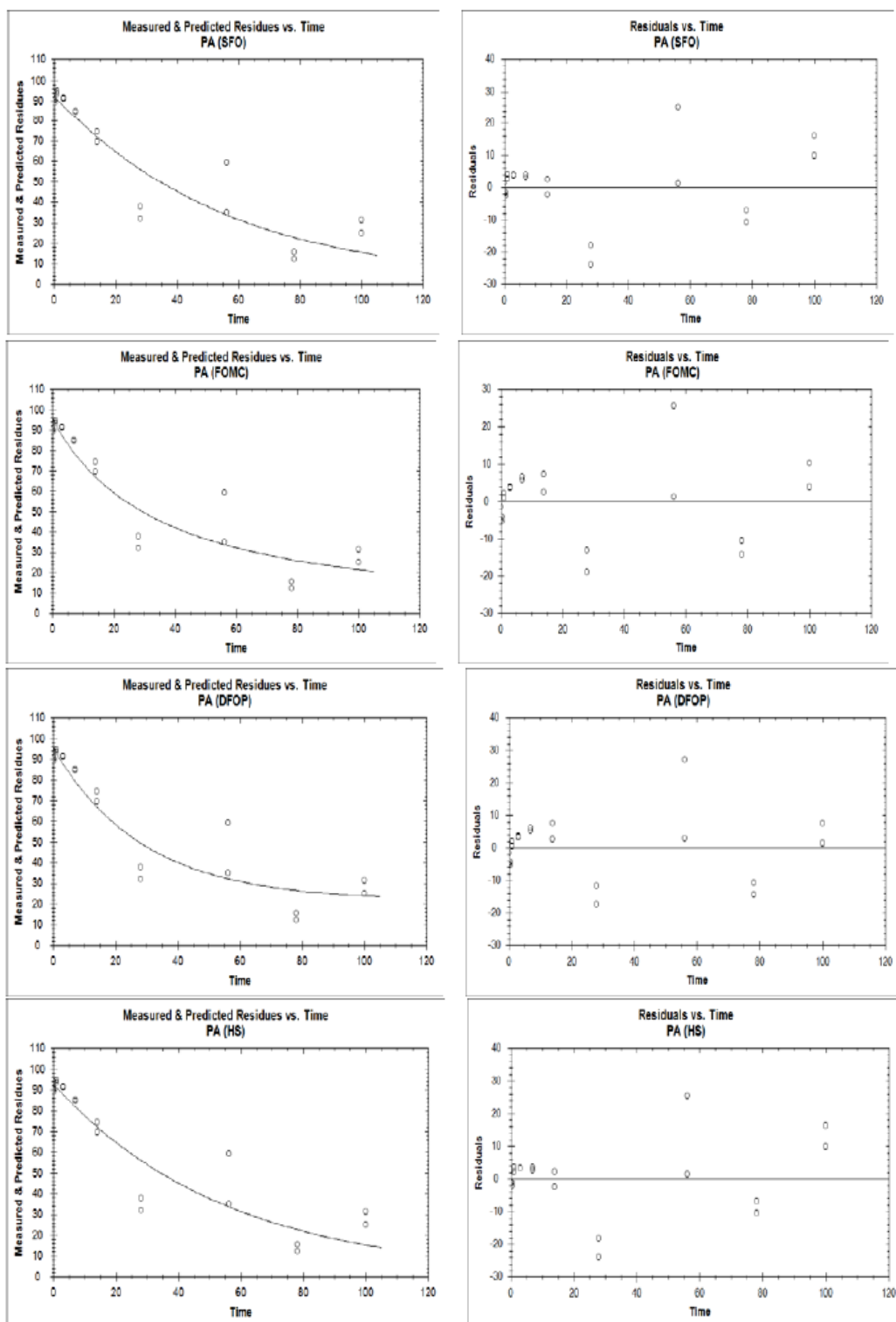


Figure 8.2.2.3/01-01: Model fits and residuals for cinmethylin in the System Berghäuser Altrhein, Level P-I, total system. First row: SFO. Second row: FOMC. Third row: DFOP. Fourth row: HS. Final model fit: SFO. χ^2 error = 11.8%. DegT₅₀ = 38.7 days. DegT₉₀ = 128.4 days.

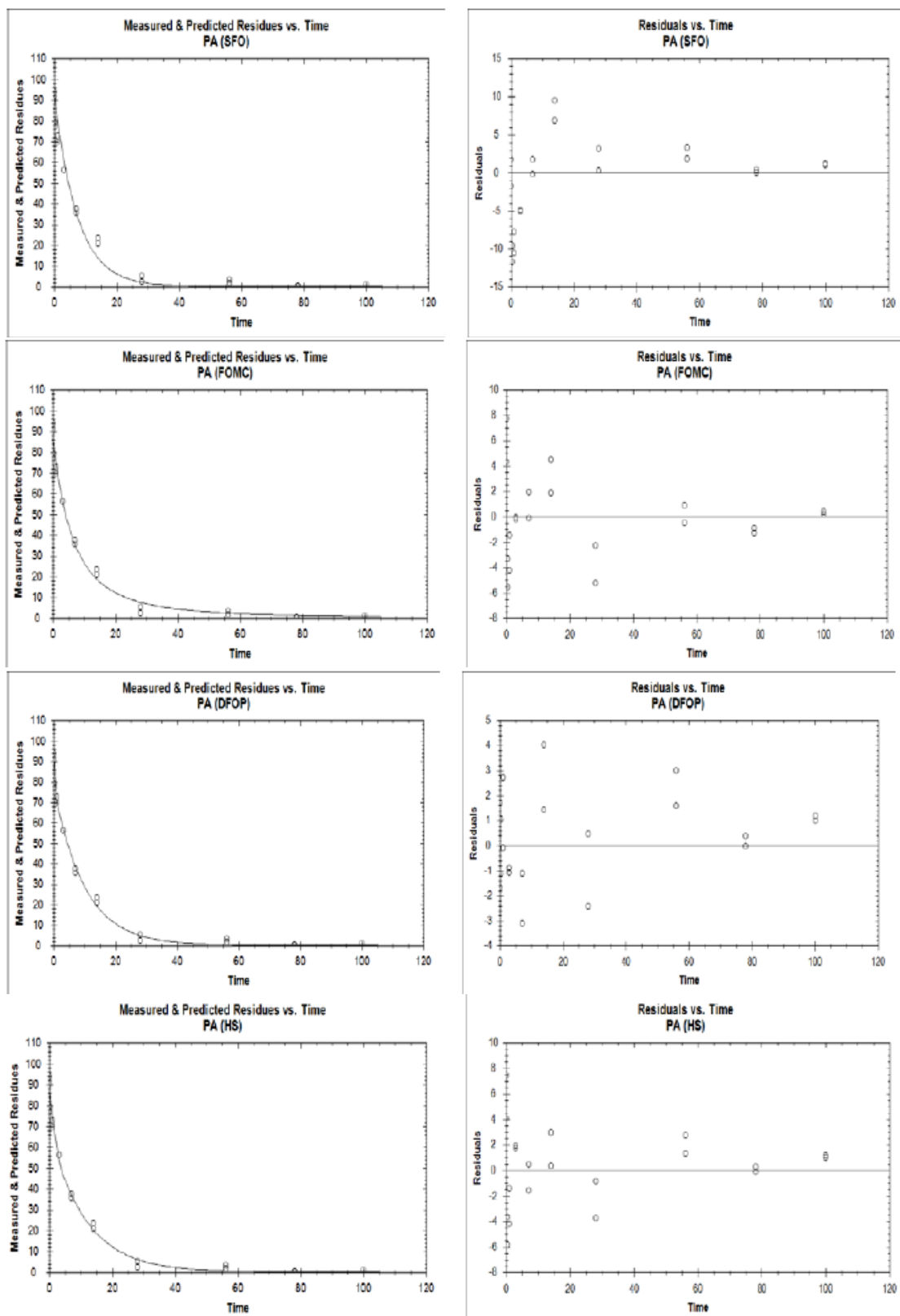


Figure 8.2.2.3/01-02: Model fits and residuals for cinmethylin in the System Berghäuser Altrhein water phase. First row: SFO. Second row: FOMC. Third row: DFOP. Fourth row: HS. Final model fit: DFOP. χ^2 error = 3.6%. DisT_{50} = 5.2 days. DisT_{90} = 21.5 days.

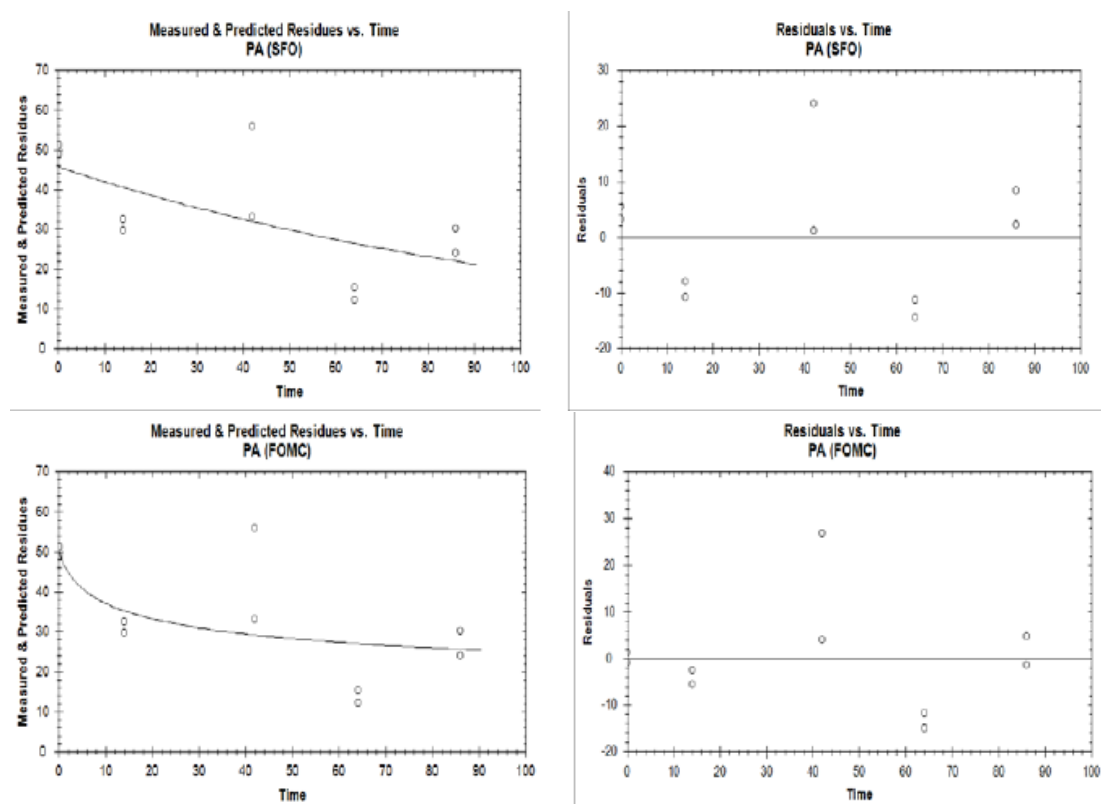


Figure 8.2.2.3/01-03: Model fits and residuals for cinmethylin in the System Berghäuser Altrhein sediment phase. First row: SFO. Second row: FOMC. Final model fit: SFO. χ^2 error = 22.9%. DisT₅₀ = 81.3 days. DisT₉₀ = 270.1 days.

System Ranschgraben (RG)

Level P-I – Cinmethylin

Table 8.2.2.3/01-20 summarises the kinetic models and derived endpoints for the total system, water and sediment phases in turn, as supplied by the Applicant. The kinetic models and decisions taken are discussed in turn below.

Total system

The SFO visual fit was good with a χ^2 below 7%. The FOMC model did not improve the visual fit but did offer a slightly lower χ^2 error value, though the standard deviation of β was greater than β and the confidence intervals included zero for both α and β . DFOP and HS improved the visual fit compared to SFO; however, both models failed the t test so these were rejected. The Applicant concluded SFO was the most appropriate model; the HSE evaluator agrees with this. Figure 8.2.2.3/01-04 displays the model fits and residuals for cinmethylin degradation in the total system.

Water phase

The initial, unconstrained SFO fit led to an underestimated M_0 of 83.6%. The Applicant then repeated the SFO fit with M_0 fixed to the mean of the residue data at 0 DAT (97.5%). The revised SFO visual fit was acceptable with a χ^2 above 15%. The FOMC model improved the visual fit and provided a lower χ^2 error value. DFOP further improved the visual fit and provided the lowest χ^2 error value; additionally, all model parameters were significantly different from zero. The HS model fit did not further improve the visual fit and provided a higher χ^2 error value. The Applicant concluded DFOP was the most appropriate model. The HSE evaluator notes the inconsistent treatment of underestimated M_0 values as the Applicant only adjusted this for SFO and not for subsequent kinetic

fits, but this does not change the outcome of the decision made by the Applicant. The HSE evaluator agrees DFOP is the best model fit. Figure 8.2.2.3/01-05 displays the model fits and residuals for cinmethylin dissipation from the water phase.

Sediment phase

The SFO visual fit was good with a χ^2 error value below 7%. The k parameter was also significantly different to zero. The FOMC model improved the visual fit and offered a lower χ^2 error value. DFOP and HS did not further improve the visual fit compared to FOMC, and both models provided higher χ^2 values. The Applicant concluded FOMC was the most appropriate model; the HSE evaluator agrees with this. Figure 8.2.2.3/01-06 displays the model fits and residuals for cinmethylin dissipation from the sediment phase.

Table 8.2.2.3/01-20: Summary of kinetic model evaluation for cinmethylin in System Ranschgraben, Level P-I (trigger endpoints). Final kinetic models are highlighted in bold.

Phase	Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Total System	SFO	Good	97.571	k: 0.0175	0.014 – 0.021	5.74E-9	6.3	39.7	131.8
	FOMC	Good	97.095	α : 2.191 β : 96.616	-1.975 – 6.357 -135.417 – 328.649	- -	5.9	36.0	179.8
	DFOP	Good	97.310	k1 (d): 0.027 k2 (d): 2.3E-14 g: 0.823	-0.0316 – 0.086 -0.0877 – 0.088 -1.094 – 2.740	0.189 0.500	5.8	34.3	> 1000
	HS	Good	96.879	k1 (d): 0.020 k2 (d): 0.005 tb: 58.265	0.0153 – 0.025 -0.0240 – 0.0330 -2.1728 – 118.704	3.25E-7 0.377	5.4	34.2	297.9
Water Phase	SFO ^a	Acceptable	97.50	k: 0.146	0.110 – 0.182	8.74E-8	18.7	4.7	15.8
	FOMC	Acceptable	88.683	α : 1.146 β : 5.556	0.578 – 1.713 0.964 – 10.149	- -	10.1	4.6	35.9
	DFOP	Acceptable	97.409	k1 (d): 4.594 k2 (d): 0.079 g: 0.273	2.119 – 7.068 0.068 – 0.089 0.220 – 0.325	0.001 7.61E-11	4.4	4.8 ^b	25.2
	HS	Acceptable	92.320	k1 (d): 0.330 k2 (d): 0.070 tb: 1.337	0.226 – 0.435 0.053 – 0.087 0.719 – 1.954	6.57E-6 2.64E-7	7.5	4.9	27.9
Sediment Phase	SFO	Good	49.712	k: 0.011	0.005 – 0.016	0.0021	6.6	64.8	215.1
	FOMC	Good	53.019	α: 0.428 β: 13.818	-0.412 – 1.267 -41.620 – 69.256	- -	0.5	56.1	> 1000
	DFOP	Good	52.98	k1 (d): 0.059 k2 (d): 0.004 g: 0.393	-0.224 – 0.342 -0.027 – 0.036 -1.138 – 1.923	0.348 0.405	0.7	55.7	448.8
	HS	Good	53.0	k1 (d): 0.114 k2 (d): 0.008 tb: 1.950	-0.103 – 0.332 0.0002 – 0.016 1.938 – 1.962	0.171 0.045	3.7	60.4	260.5

^a Values presented are from the revised SFO visual fit with an M₀ fixed at the mean 0 DAT concentration level.

^b Overall DT₅₀ presented.

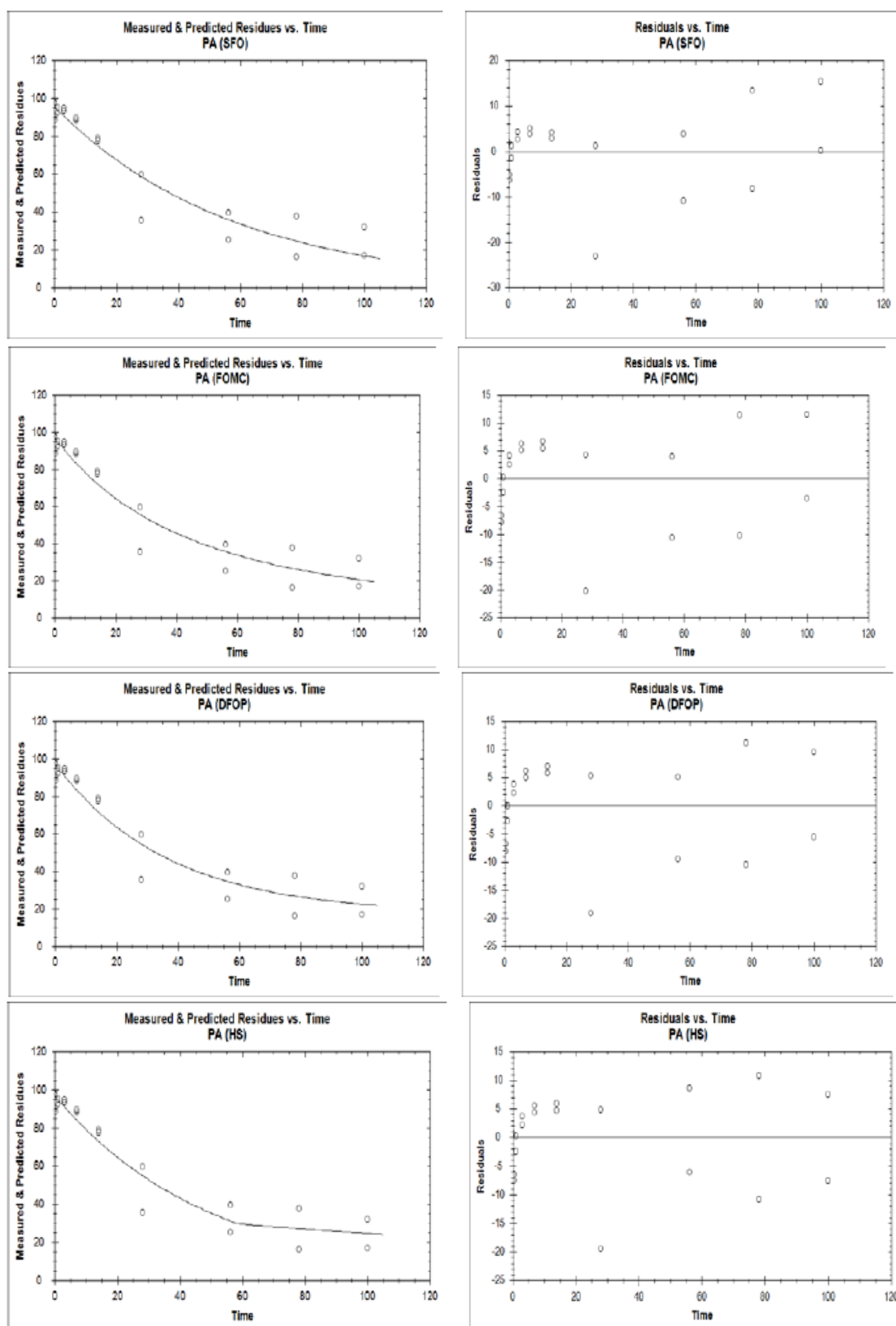


Figure 8.2.2.3/01-04: Model fits and residuals for cinmethylin in the System Ranschgraben, Level P-I, total system. First row: SFO. Second row: FOMC. Third row: DFOP. Fourth row: HS. Final model fit: SFO. χ^2 error = 6.3%. DegT₅₀ = 39.7 days. DegT₉₀ = 131.8 days.

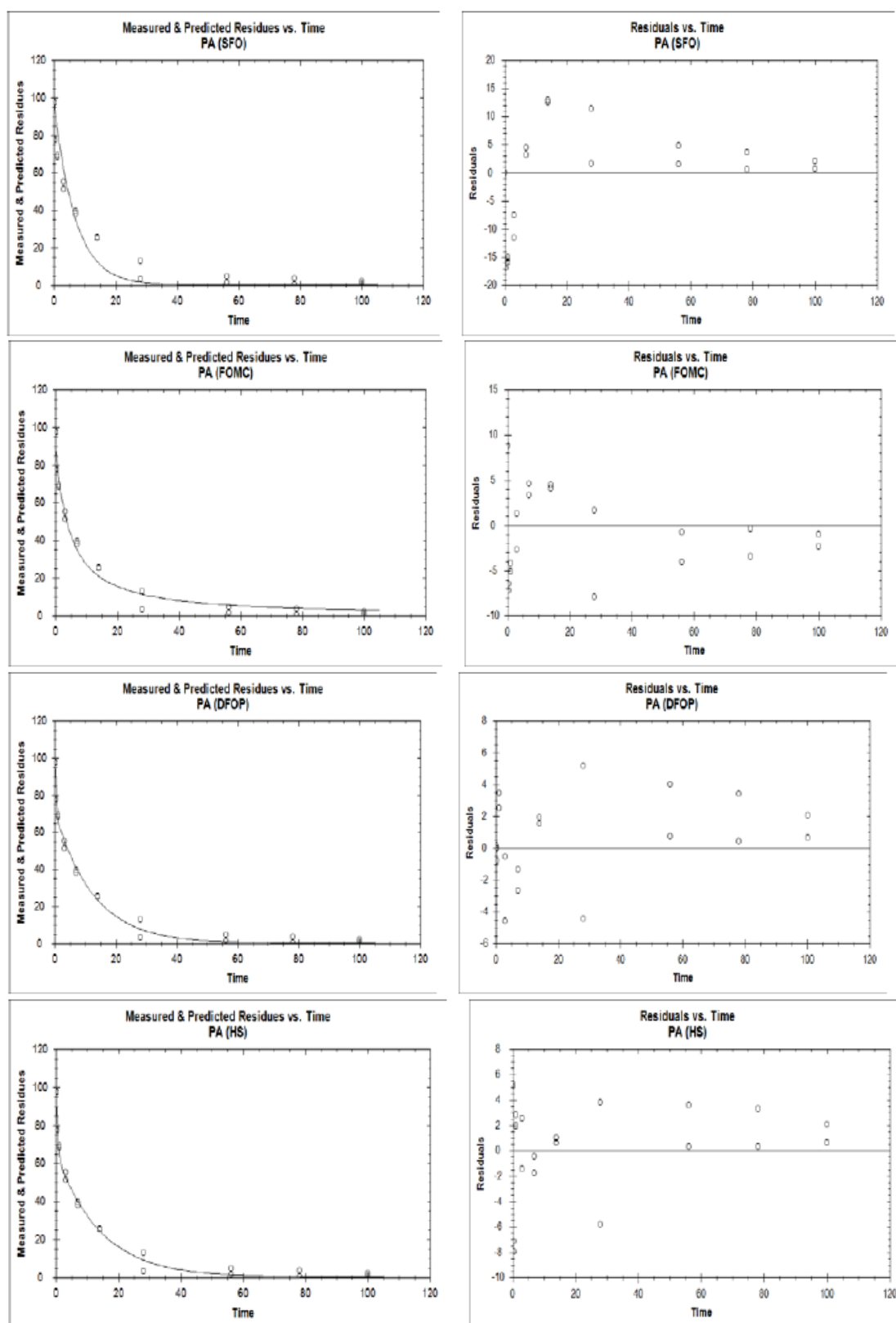


Figure 8.2.2.3/01-05: Model fits and residuals for cinmethylin in the System Ranschgraben water phase. First row: SFO. Second row: FOMC. Third row: DFOP. Fourth row: HS. Final model fit: DFOP. χ^2 error = 4.4%. DisT_{50} = 4.8 days. DisT_{90} = 25.2 days.

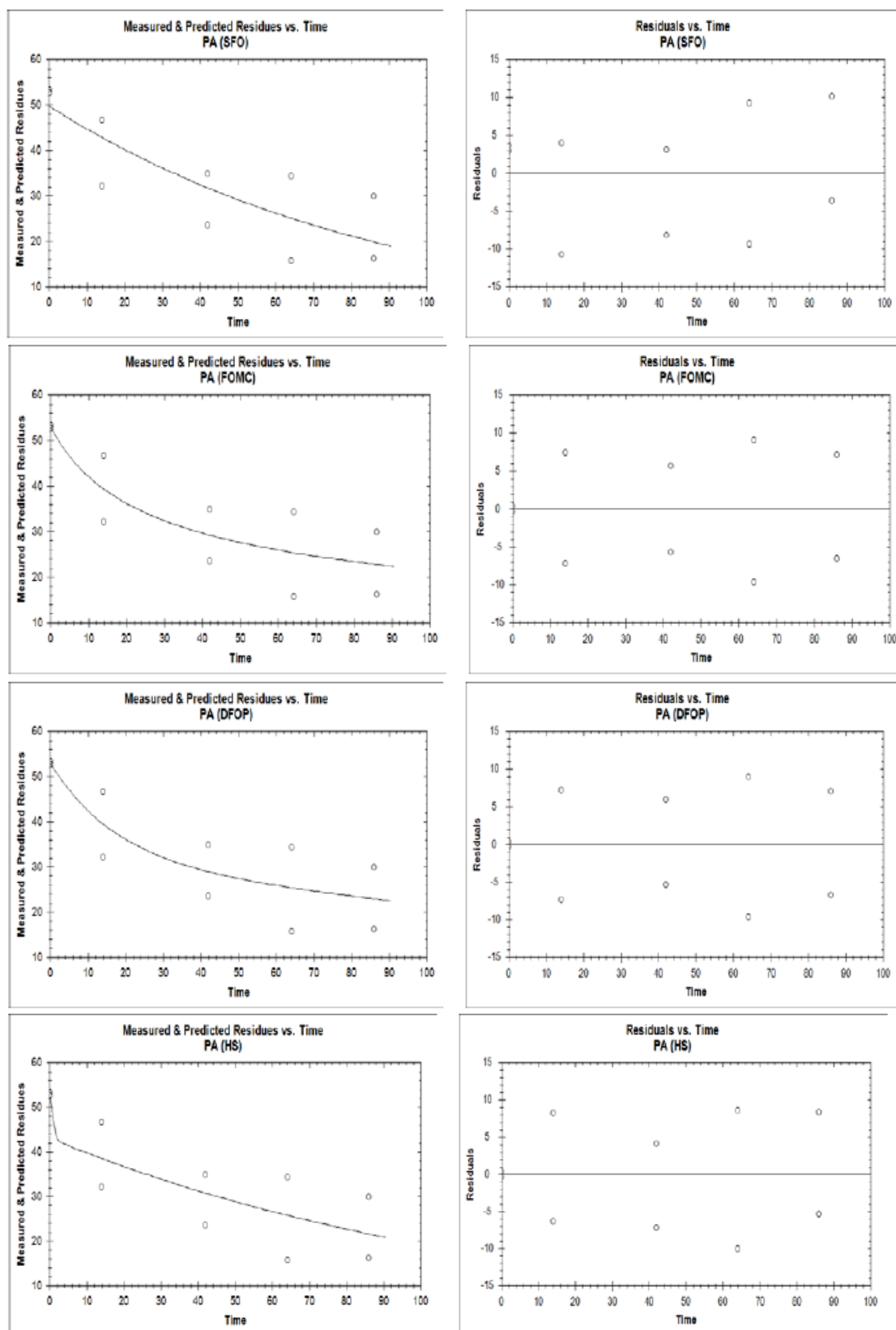


Figure 8.2.2.3/01-06: Model fits and residuals for cinmethylin in the System Ranschgraben sediment phase. First row: SFO. Second row: FOMC. Third row: DFOP. Fourth row: HS. Final model fit: FOMC. χ^2 error = 0.5%. DisT_{50} = 56.1 days. DisT_{90} > 1000 days.

Kinetic evaluation of enantiomers

The Applicant supplied kinetic evaluations to derive trigger endpoints for the degradation of the two enantiomers Reg. No. 5925581 ((-)-cinmethylin) and Reg. No. 5925632 ((+)-cinmethylin) in the total system. The Applicant followed the P-I kinetics process for the two enantiomers. The HSE evaluator agreed with the processes followed by the Applicant and their overall decisions; therefore, the kinetic evaluations presented below are as provided by the Applicant.

System Berghäuser Altrhein

Table 8.2.2.3/01-21 summarises the kinetic fits for both enantiomers in the total system. For Reg. No. 5925581, the Applicant described the SFO visual fit as acceptable. The χ^2 error value was above 15% but was deemed as acceptable as there was a clear decline of measured residue; the parameter k was also significantly different from zero. The FOMC model did not improve the visual fit and provided a higher χ^2 error value. The Applicant concluded that SFO was the most appropriate kinetic model; the HSE evaluator agreed with this conclusion. Figure 8.2.2.3/01-07 shows the model fits and residuals for the degradation of Reg. No. 5925581 from the total system.

For Reg. No. 5925632, the Applicant described the SFO fit as acceptable, though the χ^2 error value was over 20%. However, there was a clear decline in residues and the k parameter was significantly different from zero. The FOMC model did not improve the visual fit and provided a higher χ^2 error value. Therefore, the Applicant concluded that SFO was the most appropriate kinetic model; the HSE evaluator agreed with this conclusion. Figure 8.2.2.3/01-08 shows the model fits and residuals for the degradation of Reg. No. 5925632 from the total system.

Table 8.2.2.3/01-21: Summary of kinetic model evaluation for the two enantiomers Reg. No. 5925581 and 5925632 in System Berghäuser Altrhein. Final kinetic models are highlighted in bold.

	Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test (σ for FOMC)	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Reg. No. 5925581	SFO	Acceptable	42.761	k: 0.012	0.006 – 0.018	0.001	19.9	57.9	192.4
	FOMC	Acceptable	45.028	α : 0.888 β : 41.364	-1.541 – 3.317 -136.736 – 219.464	1.239 90.869	20.9	48.9	511.6
Reg. No. 5925632	SFO	Acceptable	39.250	k: 0.024	0.014 – 0.034	0.0005	21.9	29.2	96.9
	FOMC	Acceptable	41.148	α : 1.508 β : 39.442	-1.743 – 4.758 -85.160 – 164.043	1.659 63.574	22.0	23.0	142.2

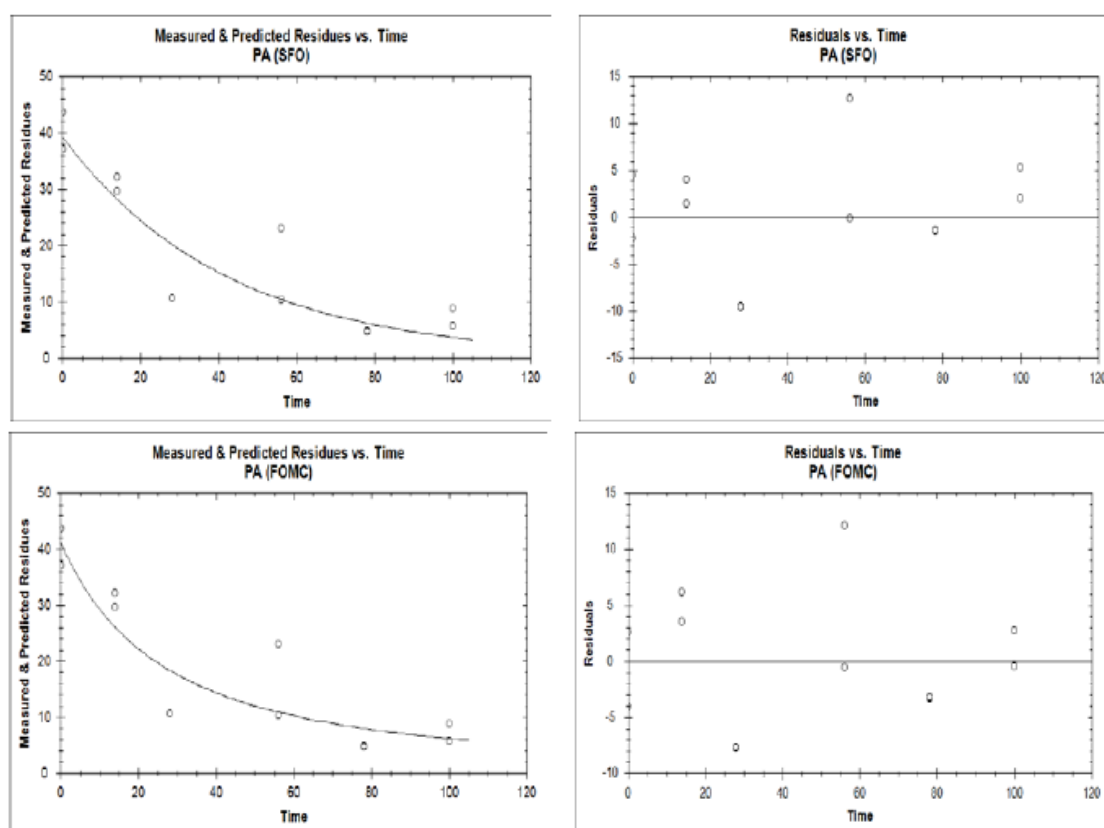


Figure 8.2.2.3/01-08: Model fits and residuals for enantiomer Reg. No. 5925632 in the System Berghäuser Altrhein total system. First row: SFO. Second row: FOMC. Final model fit: SFO. χ^2 error = 21.9%. DegT₅₀ = 29.2 days. DegT₉₀ = 96.9 days.

System Ranschgraben

Table 8.2.2.3/01-22 summarises the kinetic fits for both enantiomers in the total system. For Reg. No. 5925581, the Applicant described the SFO visual fit as good, with a χ^2 error value below 15% and k parameter significantly different from zero. The FOMC model did not improve the visual fit and provided a higher χ^2 error value. The Applicant concluded that SFO was the most appropriate kinetic model; the HSE evaluator agreed with this conclusion. Figure 8.2.2.3/01-09 shows the model fits and residuals for the degradation of Reg. No. 5925581 from the total system.

For Reg. No. 5925632, the Applicant described the SFO fit as good, with a χ^2 error value below 15% and k parameter significantly different from zero. The FOMC model did not improve the visual fit and provided a similar χ^2 error value. Therefore, the Applicant concluded that SFO was the most appropriate kinetic model; the HSE evaluator agreed with this conclusion. Figure 8.2.2.3/01-10 shows the mode fits and residuals for the degradation of Reg. No. 5925632 from the total system.

Table 8.2.2.3/01-22: Summary of kinetic model evaluation for the two enantiomers Reg. No. 5925581 and 5925632 in System Ranschgraben. Final kinetic models are highlighted in bold.

	Kinetic model	Visual fit	Initial value (M ₀)	Estimated parameters	95% Confidence Intervals	t-test (σ for FOMC)	χ ² error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Reg. No. 5925581	SFO	Good	47.506	k: 0.014	0.009 – 0.019	0.0001	8.8	49.2	163.5
	FOMC	Good	48.646	α: 2.132 β: 117.184	-6.157 – 10.420 -456.598 – 690.970	4.229 292.751	9.0	45.0	227.9
Reg. No. 5925632	SFO	Good	43.341	k: 0.023	0.017 – 0.029	<0.0001	11.6	30.0	99.6
	FOMC	Good	44.329	α: 2.902 β: 99.463	-4.237 – 10.040 -203.959 – 402.880	3.642 154.810	11.6	26.8	120.5

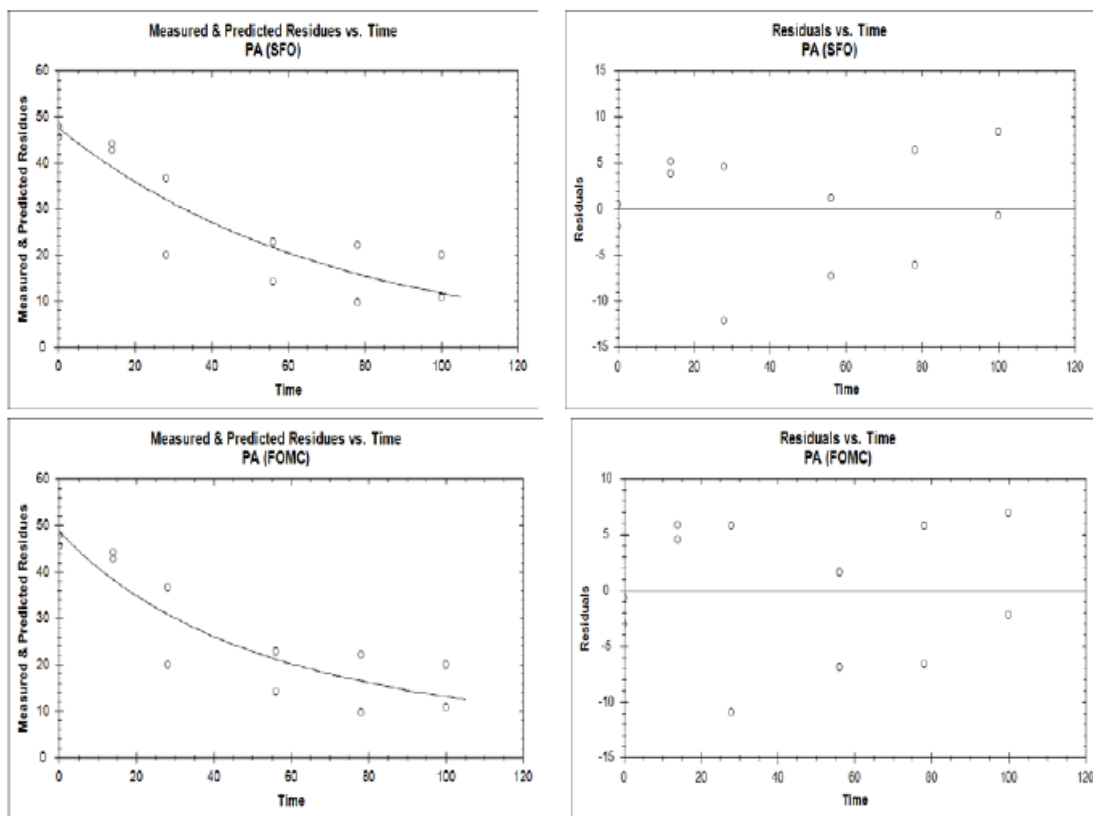


Figure 8.2.2.3/01-09: Model fits and residuals for enantiomer Reg. No. 5925581 in the System Ranschgraben total system. First row: SFO. Second row: FOMC. Final model fit: SFO. χ^2 error = 8.8%. DegT₅₀ = 49.2 days. DegT₉₀ = 163.5 days.

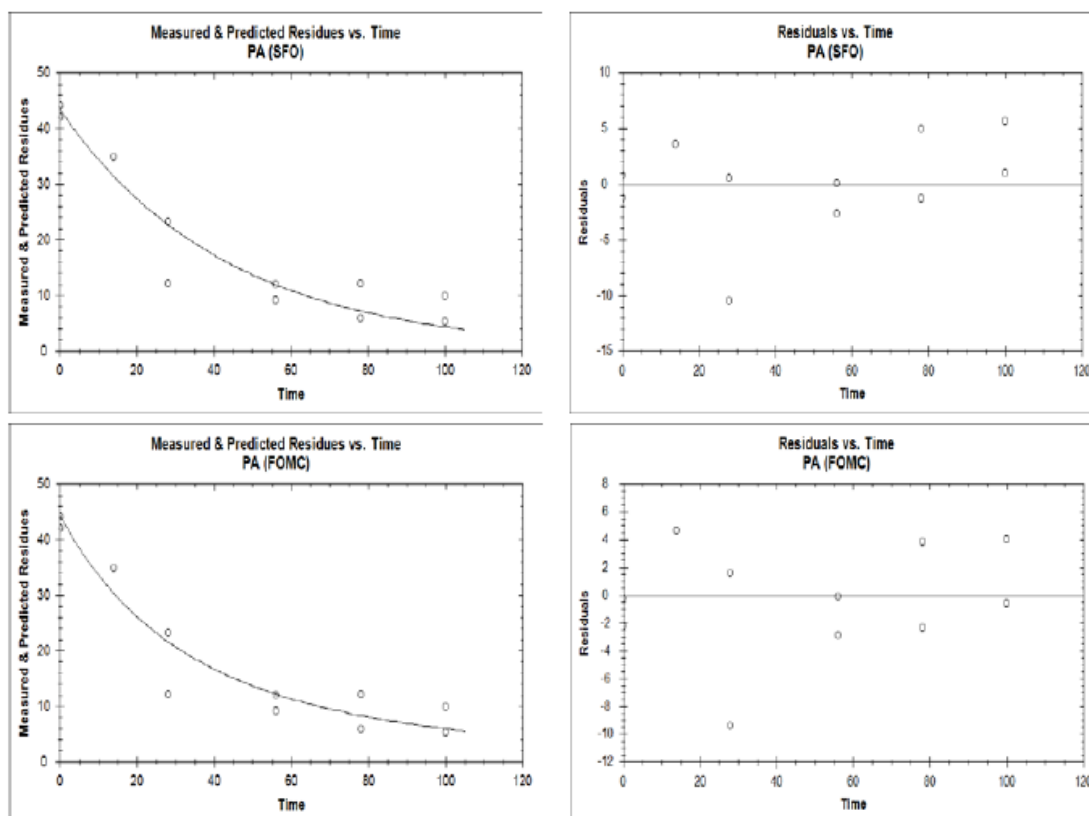


Figure 8.2.2.3/01-10: Model fits and residuals for enantiomer Reg. No. 5925632 in the System Ranschgraben total system. First row: SFO. Second row: FOMC. Final model fit: SFO. χ^2 error = 11.6%. DegT₅₀ = 30.0 days. DegT₉₀ = 99.6 days.

III. CONCLUSION

Overall, it can be concluded that cinmethylin dissipates at a fast rate from the water phase and degrades at a moderate rate in the sediment when incubated in water/sediment systems under dark conditions.

Metabolite M684H001 was the only major metabolite detected in this study (>10 %, 5-10 % at two consecutive sample time points or > 5 % but not yet reached maximum at study end). M684H001 was detected in water samples treated with [cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]-cinmethylin at a maximum concentration of 6.5-11.4 % AR after 28 days. M684H001 was detected in sediment samples treated with [cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]-cinmethylin at a maximum concentration of 1.8-3.8 % AR after 28 days.

Metabolite M684H004 was detected in water and sediment samples treated with [cyclohexane-4-¹⁴C]- and [phenyl-U-¹⁴C]-cinmethylin at less than 5 % AR at all time points. Several further peaks were observed in water samples, however, most of them occurring only sporadically and not exceeding 3.4 % AR at any sampling time.

Table 8.2.2.3/01-23 Peak formation (as % AR) of cinmethylin and relevant metabolites in total system, water and sediment. Note peak formations listed here are the greatest of all aquatic studies and are therefore suitable for use in modelling

Compartment	Peak Formation (%AR)			
	cinmethylin	M684H001	M684H004	M684H014
Water	-	11.4 % (Berghäuser Altrhein, 28d)	3.7 % (Ranschgraben, 78d)	0.8 % (Berghäuser Altrhein, 1d)
Sediment	55.9 % (Berghäuser Altrhein, 56d)	3.8 % (Ranschgraben, 28d)	3.8 % (Ranschgraben, 100d)	2.5 % (Ranschgraben, 100d)

The Applicant evaluated the dissipation and degradation kinetics of cinmethylin, and its two enantiomers Reg. No. 5925581 and Reg. No. 5925632. For all models considered appropriate to derive kinetic endpoints, the visual assessment and goodness-of-fit statistics indicate plausible fit. For some fits χ^2 error values above 15% were obtained but according to FOCUS, the χ^2 error of 15% should not be considered as an absolute cut-off criterion. As the visual fits were acceptable and a clear decline of the measured residues was observed the high χ^2 error values are acceptable. The t-test was passed for the respective model parameters. Therefore, the resulting endpoints can be considered reliable. The HSE evaluator accepts this summary. The accepted trigger endpoints are summarised in Table 8.2.2.3/01-24.

Table 8.2.2.3/01-24: Calculated trigger endpoints for cinmethylin and its two enantiomers (Reg. Nos. 5925581 and 5925632) in two water-sediment systems in laboratory conditions.

Cinmethylin								
System	Phase	pH ^a	Temp. °C	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ ²)	Parameters	Method of calculation
Berghäuser Altrhein	Total		20 ± 2	38.7	128.4	11.8	k: 0.0179	SFO
	Water	7.58		5.2 ^b	21.5	3.6	k1: 6.2859 k2: 0.0991 g: 0.1611	DFOP
	Sediment	6.9		81.3	270.1	22.9	k: 0.0085	SFO
Ranschgraben	Total			39.7	131.8	6.3	k: 0.0175	SFO
	Water	7.30		4.8 ^b	25.2	4.4	k1: 4.594 k2: 0.079 g: 0.273	DFOP
	Sediment	5.9		56.1	>1000	0.5	α: 0.428 β: 13.818	FOMC
Maximum	Total			39.7	131.8			
	Water			8.8	25.2			
	Sediment			81.3	>1000			
Reg. No. 5925581 ((-)-cinmethylin)								
Berghäuser Altrhein	Total		20 ± 2	57.9	192.4	19.9	k: 0.012	SFO
	Total			49.2	163.5	8.8	k: 0.014	SFO
Maximum	Total			57.9	192.4			
Reg. No. 5925632 ((+)-cinmethylin)								
Berghäuser Altrhein	Total		20 ± 2	29.2	96.9	21.9	k: 0.024	SFO
Ranschgraben	Total			30.0	99.6	11.6	k: 0.023	SFO
Maximum	Total			30.0	99.6			

^a pH for the water phase was measured at the time of sampling. pH for the sediment phase was measured in CaCl₂.

^b Overall DT₅₀ shown.

Report:	KCA 7.2.2.3/02 He, W., and Pape, L., 2017
Title	Kinetic evaluation of degradation of BAS 684 H in water/sediment systems: Determination of modelling endpoints according to FOCUS Degradation Kinetics
Document No.:	2017/1021064
Guidelines	FOCUS Degradation kinetics (2006) FOCUS Degradation kinetics (2014)
GLP?	No – kinetic modelling conducted in compliance with the Codex of Good Modelling Practices.
Deviations	None

INTRODUCTION

The Applicant investigated the degradation behaviour of cinmethylin in two water/sediment systems (Berghäuser Altrhein and Ranschgraben), each treated separately with cyclohexane-¹⁴C- and phenyl-¹⁴C-labeled test substance (KCA 7.2.2.3/01, Mueller-Werthwein and Freundlich, 2017). The test systems were incubated in the dark for up to 100 days.

The purpose of the current evaluation was to derive degradation parameters of cinmethylin for modelling purposes (modelling endpoints) according to current guidance of the FOCUS workgroup on degradation kinetics (2006; 2014). Degradation parameters as triggers for additional work (trigger endpoints) for cinmethylin were evaluated in the original study report (KCA 7.2.2.3/01, Mueller-Werthwein and Freundlich, 2017).

TEST PROCEDURE

The Applicant performed kinetic evaluation for the parent substance cinmethylin and its metabolites M684H001 and M684H004. The evaluation was performed at the following levels recommended by FOCUS:

Parent substance:

- Level P-I: one-compartment approach, assessment of parent degradation in the total system (applied for parent and its enantiomers, separately) as well as dissipation from the water and sediment phase of the test systems;
- Level P-II: two-compartment approach: water and sediment, assessment of parent degradation in water and sediment phase and the partitioning between both phases of the test systems.

Metabolites:

- Level M-I dissipation: one-compartment approach, assessment of metabolite dissipation from the maximum observed concentration in the total system as well as in the water and sediment phase of the test systems;
- Level M-I degradation: multi-compartment approach, assessment of metabolite degradation in a combined fit of parent and metabolite in the total system.

At Level P-I and Level M-I dissipation, the data from the kinetic evaluation for derivation of trigger endpoints as given in the original study report were directly used to derive modelling endpoints (KCA 7.2.2.3/01, Mueller-Werthwein and Freundlich, 2017). The HSE evaluator has not assessed the Applicant's Level P-II assessment because DegT₅₀ values for water and sediment are not required for a UK only assessment. The Applicant also provided kinetic evaluation for the metabolites M684H001 and M684H004. However, dissipation and degradation DT_{50s} are not required for metabolites in a UK only application because the surface water exposure assessment for metabolites utilises a "total dose" approach. Therefore, the HSE evaluator has also not assessed the Applicant's Level M-I evaluations.

The kinetic models employed for this evaluation were described by the FOCUS workgroup on degradation kinetics. Level P-I dissipation modelling endpoints were derived preferably from the SFO model. If the SFO model was not appropriate, pragmatic procedures were used to derive conservative pseudo-SFO degradation rates from the appropriate bi-phasic model.

The Applicant tested the model appropriateness through detailed statistical analysis including visual assessment of the goodness of fit, χ^2 scaled-error criterion and t-test significance. The visual fit was categorised as follows:

- Poor fit = the fit does not follow the pattern of the measured residues, not acceptable to derive modelling endpoints;
- Acceptable fit = the fit mainly follows the pattern of the measured residues with small deviations, acceptable to derive modelling endpoints;
- Good fit = the fit follows the pattern of the measured residues well, residuals are randomly scattered around zero, acceptable to derive modelling endpoints.

Furthermore, a kinetic model is considered appropriate for deriving modelling endpoints if the χ^2 error value is low (ideally below 15%) and the t-test for the degradation parameters is passed at 10% error level ($P < 0.1$). The Applicant used KINGUI version 2 using IRLS optimisation; error tolerance was set to 10^{-6} and maximum iterations of the optimisation tool was set to 100. The results obtained from the experiments with the same test systems treated with the two differently labelled test items were considered as replicates for kinetic evaluation.

At Level P-I for total system and water phase, the kinetic evaluation started on the day of treatment (i.e. 0 DAT). The initial concentration of the test substance in the total system or in water was set to the material balance recovered at 0 DAT as recommended by FOCUS (2006; 2014); for enantiomers the measured data at 0 DAT was used.

The assessment of dissipation in sediment at Level P-I only requires kinetics to be fitted to the corresponding decline data, starting from the maximum observed concentration in the compartment. The dissipation of the respective compound was thus evaluated starting at the day of maximum occurrence that was defined as 0 days after maximum concentration. All later time points were adjusted accordingly as days after maximum concentrations. Values below the detection limit (LOD) for parent compound and degradation products were treated as recommended by FOCUS (2006; 2014).

The HSE evaluator assessed the supplied kinetic evaluation by deriving modelling endpoints for the cinmethylin in CAKE version 3.2, with this evaluation also following FOCUS guidance on deriving modelling endpoints. The HSE evaluator agreed with the data handling and procedures undertaken by the Applicant in the supplied kinetic evaluation, though did not agree with all decisions. Where the HSE evaluator agrees, the Applicant's kinetic evaluations are presented below. Where the HSE evaluator disagreed, the HSE evaluator's kinetic evaluation and derived endpoints are presented instead.

RESULTS AND DISCUSSION

The datasets for each water/sediment system were analysed considering the procedures and kinetic models for derivation of modelling endpoints proposed by FOCUS workgroup on degradation kinetics (2006, 2014). For some fits error values above 15% were obtained. The Applicant attributed these to the scattering of the measured data. As the observations were generally well described by the fitted curves the high error values are acceptable. Kinetic evaluations are covered in turn below, organised by test system. All references to "initial kinetic evaluations" refer to the decisions made for deriving trigger endpoints (KCA 7.2.2.3/01, Mueller-Werthwein and Freundlich, 2017).

*System Berghäuser Altrhein (BA)***Level P-I – Cinmethylin**

Table 8.2.2.3/02-01 summarises the statistical assessment of kinetic models for cinmethylin in System Berghäuser Altrhein. Visual assessment is discussed in turn below.

Total system

In the initial kinetic evaluation, the SFO model was selected as best-fit model as the visual fit was acceptable, the χ^2 error rate was below 15% and the k parameter was significantly different to zero. Hence, the SFO model is also appropriate to derive modelling endpoints (Figure 8.2.2.3/02-01). The HSE evaluator agrees with this decision.

Water phase

In the initial kinetic evaluation, DFOP provided the best fit. For SFO, the model underestimated the initial concentration (M_0) at 86.35%. Therefore, the initial concentration of the parent compound was fixed to the mean residue data at 0 DAT (92.1%). The corresponding SFO model was deemed appropriate as the visual fit was acceptable, the χ^2 error rate was below 15% and the k parameter was significantly different to zero. Hence, the SFO model is also appropriate to derive modelling endpoints (Figure 8.2.2.3/02-02). The HSE evaluator agrees with this decision.

Sediment phase

In the initial kinetic evaluation, the SFO model was selected as best-fit model as the visual fit was acceptable, the χ^2 error rate was below 15% and the k parameter was significantly different to zero. Hence, the SFO model is also appropriate to derive modelling endpoints (Figure 8.2.2.3/02-03). The HSE evaluator agrees with this decision.

Table 8.2.2.3/02-01: Summary of kinetic model evaluation for deriving modelling endpoints for cinmethylin in System Berghäuser Altrhein, Level P-I.

Phase	Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Total System	SFO	Acceptable	92.347	k: 0.01793	0.0132 – 0.023	<0.0001	11.8	38.7	128.4
Water Phase	SFO ^a	Acceptable	92.1	k: 0.1353	0.115 – 0.156	<0.0001	11.5	5.1	17.0
Sediment Phase	SFO	Acceptable	45.652	k: 0.0085	0.001 – 0.016	0.0334	22.9	81.3	270.1

^a Values presented are from the revised SFO visual fit with an M_0 fixed at the mean 0 DAT concentration level.

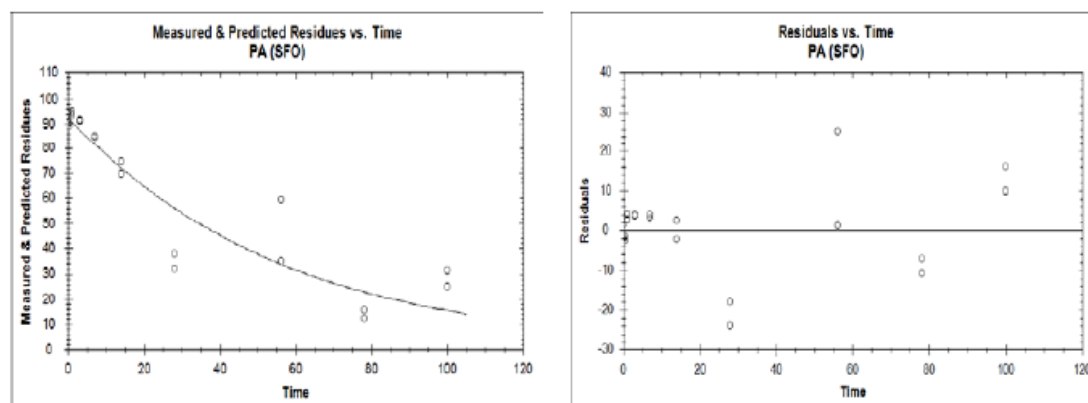


Figure 8.2.2.3/02-01: SFO model fit and residuals for cinmethylin in the System Berghäuser Altrhein, Level P-I, total system.

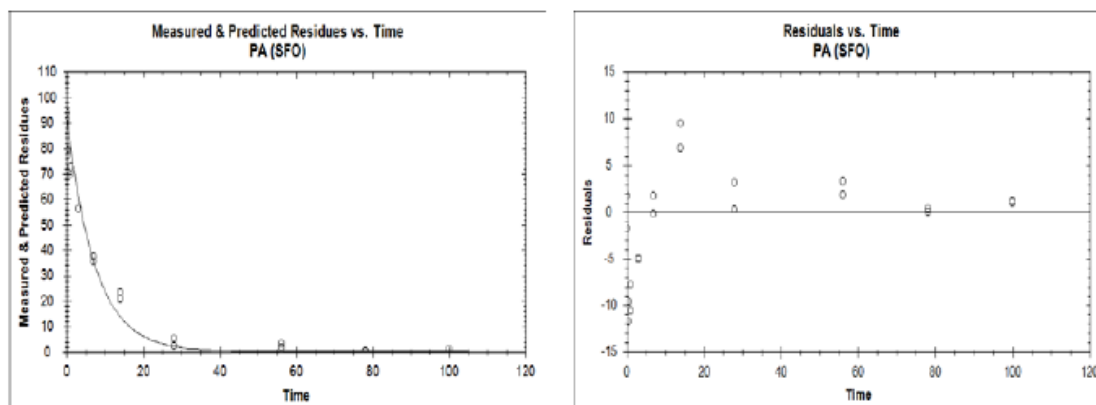


Figure 8.2.2.3/02-02: SFO model fit and residuals for cinmethylin in the System Berghäuser Altrhein, Level P-I, water phase.

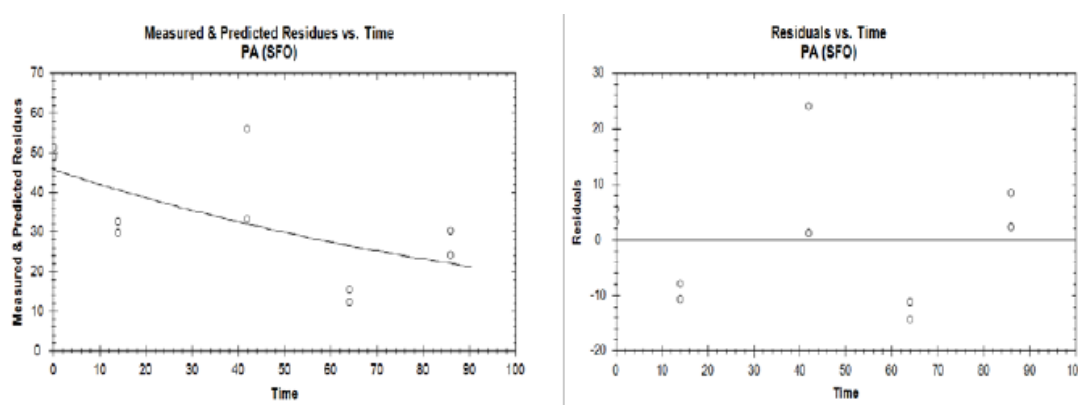


Figure 8.2.2.3/02-03: SFO model fit and residuals for cinmethylin in the System Berghäuser Altrhein, Level P-I, sediment phase.

System Ranschgraben (RG)

Level P-I – Cinmethylin

Table 8.2.2.3/02-02 summarises the statistical assessment of kinetic models for cinmethylin in System Ranschgraben. Visual assessment is discussed in turn below.

Total system

In the initial kinetic evaluation, the SFO model was selected as best-fit model as the visual fit was acceptable, the χ^2 error rate was below 7% and the k parameter was significantly different to zero. Hence, the SFO model is also appropriate to derive modelling endpoints (Figure 8.2.2.3/02-04). The HSE evaluator agrees with this decision.

Water phase

In the initial kinetic evaluation, DFOP provided the best fit. For SFO, the initial concentration of the parent compound was fixed to the mean residue data at 0 DAT. The Applicant deemed the corresponding SFO model appropriate as the visual fit was acceptable; the χ^2 error rate was above 15% but a clear decline in residues was apparent. The k parameter was also significantly different to zero. The HSE evaluator disagrees with the Applicant's conclusion that SFO is acceptable as the visual fit shows clear underestimation of cinmethylin from 15 DAT onwards, and rejects this modelling endpoint. The HSE evaluator's own evaluation is presented below.

For SFO, the χ^2 error rate is unacceptably high and the visual fit is poor as the model fit underestimates concentrations for five time points and displays systematic deviations in residuals (Figure 8.2.2.3/02-05); therefore, the HSE evaluator proceeded to explore biphasic models according

to FOCUS kinetics guidance (2006; 2014). As < 10% of initial activity remained at 100 DAT, the guidance suggests applying FOMC, hockey stick and/or DFOP for deriving modelling endpoints. Of the three biphasic models, DFOP offered an accurate initial value (M_0), an acceptable visual fit, and the lowest χ^2 error rate (< 5%). Additionally, k_1 and k_2 parameters passed the t test. The HSE evaluator concluded the DFOP model fit was appropriate for deriving modelling endpoints.

Sediment phase

In the initial kinetic evaluation, the SFO model was selected as best-fit model as the visual fit was acceptable, the χ^2 error rate was below 15% and the k parameter was significantly different to zero. Hence, the SFO model is also appropriate for deriving modelling endpoints (Figure 8.2.2.3/02-06). The HSE evaluator accepts this decision.

Table 8.2.2.3/02-02: Summary of kinetic model evaluation for deriving modelling endpoints for cinmethylin in System Ranschgraben, Level P-I.

Phase	Kinetic model	Visual fit	Initial value (M_0)	Estimated parameters	95% Confidence Intervals	t-test	χ^2 error (%)	DT ₅₀ (d)	DT ₉₀ (d)
Total System	SFO	Good	95.57	k: 0.017	0.014 – 0.021	<0.0001	6.3	39.7	131.8
Water Phase ^a	SFO ^b	Poor	97.5	k: 0.146	0.105 – 0.187	<0.0001	23.7	4.74	15.8
	FOMC	Good	88.68	α : 1.146 β : 5.556	0.535 – 1.756 0.613 – 10.50	-	10.1	4.62 (10.8) ^c	35.9
	DFOP	Acceptable	97.41	k_1 (d): 4.594 k_2 (d): 0.079 g: 0.273	2.119 – 7.068 0.068 – 0.089 0.220 – 0.325	0.001 7.61E-11	4.4	8.8 ^d	25.2
	HS	Acceptable	92.32	k_1 (d): 0.330 k_2 (d): 0.070 tb: 1.337	0.226 – 0.435 0.053 – 0.087 0.719 – 1.954	6.57E-6 2.64E-7	7.5	4.9 (8.4) ^c	27.9
Sediment Phase	SFO	Acceptable	49.71	k: 0.011	0.005 – 0.016	0.002	6.6	64.8	215.1

^a HSE evaluator's evaluation

^b Values presented are from the revised SFO visual fit with an M_0 fixed at the mean 0 DAT concentration level.

^c Pseudo-SFO DT₅₀ calculated as follows: DT₉₀ / 3.32

^d Slow phase DT₅₀ calculated as follows: $\ln(2) / k_2$

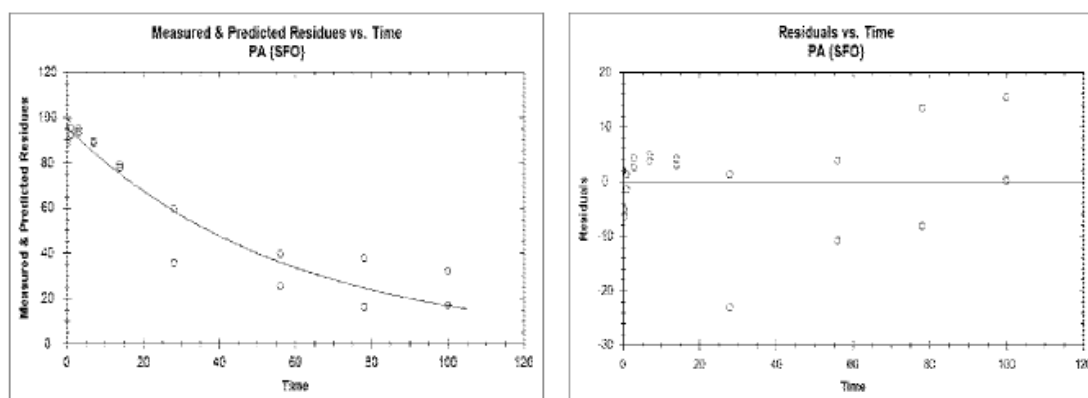


Figure 8.2.2.3/02-04: SFO model fit and residuals for cinmethylin in the System Ranschgraben, Level P-I, total system.

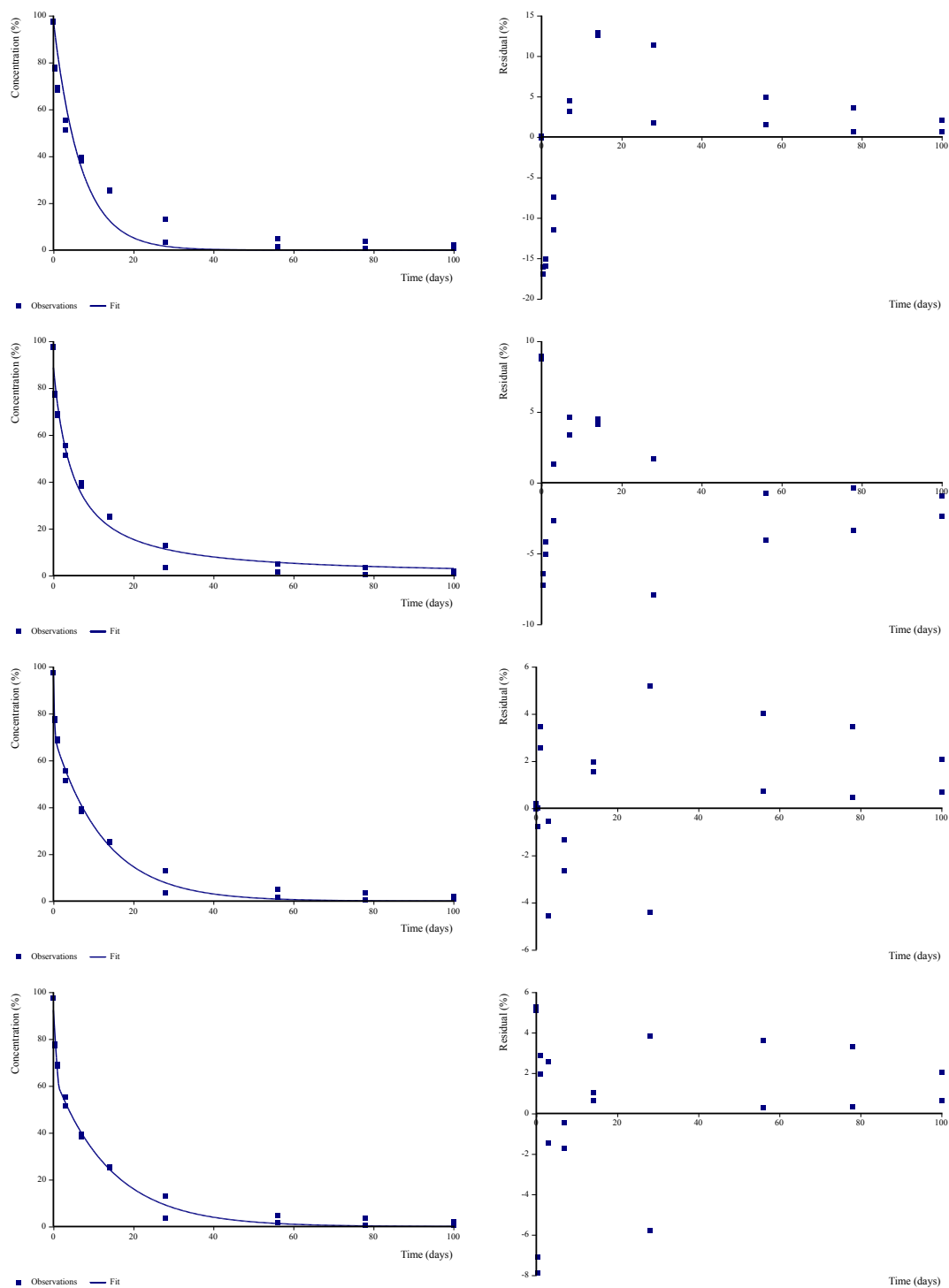


Figure 8.2.2.3/02-05: Model fits and residuals for cinmethylin in the System Ranschgraben, Level P-I, water phase. Top row: SFO. Second row: FOMC. Third row: DFOP. Bottom row: HS. Final model fit: DFOP. χ^2 error = 4.4%. DisT₅₀ = 8.8 days. DisT₉₀ = 25.2 days.

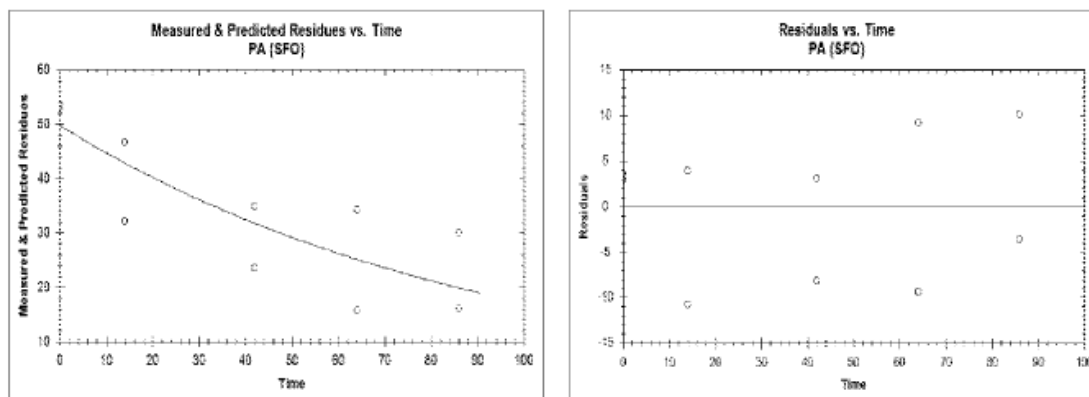


Figure 8.2.2.3/02-06: SFO model fit and residuals for cinmethylin in the System Ranschgraben, Level P-I, sediment phase.

CONCLUSIONS

The dissipation and degradation kinetics of cinmethylin in two water/sediment systems were evaluated according to FOCUS kinetics guidance (2006; 2014) to derive modelling endpoints. Table 8.2.2.3/02-03 summarise these endpoints. For all models considered appropriate, the visual assessment and goodness-of-fit statistics indicated plausible fits. For some fits, χ^2 error rates were above the recommended 15% level; the Applicant attributed this to scatter of the measured data and the HSE evaluator agrees with this. The resulting endpoints summarised below can be considered reliable.

Table 8.2.2.3/02-03: Summary of modelling endpoints for cinmethylin, Level P-I degradation.

Cinmethylin								
System	Phase	pH ^a	Temp. °C	DT ₅₀ (d)	DT ₉₀ (d)	St. (χ^2)	Parameters	Method of calculation
Berghäuser Altrhein	Total		20 ± 2	38.7	128.4	11.8	k: 0.0179	SFO
	Water	7.58		5.1	17.0	11.5	k: 0.1353	SFO
	Sediment	6.9		81.3	270.1	22.9	k: 0.0085	SFO
Ranschgraben	Total			39.7	131.8	6.3	k: 0.0175	SFO
	Water	7.30		8.8 ^b	25.2	4.4	k1: 4.594 k2: 0.079 g: 0.273	DFOP
	Sediment	5.9		64.8	215.1	6.6	k: 0.011	SFO
Maximum	Total			39.7	131.8			
	Water			8.8	25.2			
	Sediment			81.3	>1000			

^a pH for the water phase was measured at the time of sampling. pH for the sediment phase was measured in CaCl₂.

^b Slow phase DT₅₀ calculated as follows: $\ln(2) / k_2$

B.8.2.2.4. Irradiated water/sediment study (Data Requirement 7.2.2.4)

The Applicant did not submit an irradiated water/sediment study as this was not a mandatory data requirement for cinmethylin.

B.8.2.3. Degradation in the saturated zone

One calculation-based study was submitted by the Applicant to investigate the effect of ozone and chlorination treatment on cinmethylin. This is summarised below.

B.8.2.3.1. Ozone and chlorination treatment

Report:	KCA 7.2.3/1; Salzmann, S., Cirpus, P. (2018a)
Title	Estimation of reactivity of BAS 684 H in aqueous solution upon ozone and chlorination treatment
Document No.:	2017/1224113
Guidelines	No specific guidelines
GLP?	No
Deviations	Not applicable
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The risk of the formation of by-products from cinmethylin and its metabolites M684H001, M684H003 and M684H004 during the ozonation and/or chlorination of drinking water was investigated based on literature analysis and by quantum chemical calculations.

The HSE evaluator has considered the points discussed by the Applicant in the following sections and has deemed their procedures to be valid.

METHODS**Test Material**

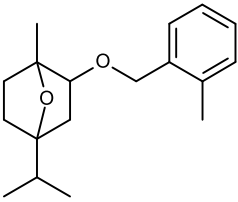
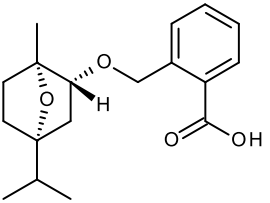
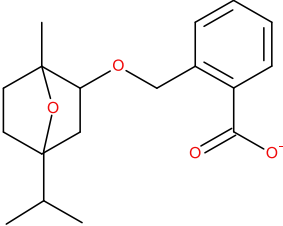
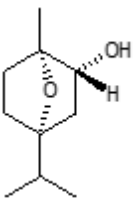
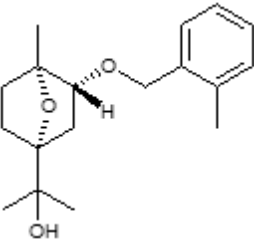
Name:	Cinmethylin
BAS-Code:	BAS 684 H
Reg. No.:	900202
CAS-No.:	87818-31-3
Chemical name (IUPAC):	(1RS, 2SR, 4SR)-1,4-epoxy-p-menth-2-yl 2-methylbenzyl ether
Molecular formula:	C ₁₈ H ₂₆ O ₂
Molecular weight:	274.4 g/mol (unlabeled)

Calculation Methods

The Applicant built cinmethylin and its metabolites in 3D using the Maestro user interface. To get as consistent as possible sampling of all relevant conformers of a given compound, a combination of 3 different generation methods was employed. Quantum chemical calculations were performed with the Turbomole software package (v. 7.2).

The Applicant evaluated relevant protonation states of cinmethylin and its metabolites using a BASF internal protocol. All hypothetical structures resulting from (de)protonation at N, O, S hetero atoms were generated. For each of these structures, 50 conformers were generated and scored for their energetic relevance. In a subsequent step the pK_a values were computed and only protonation states relevant under experimental conditions, comprising a pK_a range for 5-9, are reported in Table 8.2.3/1-01. Populations of the respective species have been roughly approximated with the Henderson-Hasselbach equation for a pH of 7.

Table 8.2.3/1-01: Protonation states relevant under experimental conditions.

ID	Chemical Structure	Calculated pK _a	Population at pH 7
Cinmethylin			
		-	100%
M684H001			
M684H001		-	0%
M684H001 anion		4.1	100%
M684H003			
		-	100%
M684H004			
		-	100%

Reactions with Chlorination agent HOCl

The Applicant evaluated the potential reactivity of cinmethylin and its metabolites with the chlorination agent HOCl through transition state searches. Benzene was used as reference for comparison. Nuclear arrangements of the educt cluster are depicted in the bottom left of Figure 8.2.3/1-01, which were used as starting point for the transition state search. Two starting clusters were constructed via superposition for each aromatic C-H moiety of cinmethylin and its metabolite M684H001 in order to probe the susceptibility of the aromatic rings to electrophilic attack by HOCl. As the structural variation between cinmethylin and M684H004 does not occur at or close to the benzene ring, no change in the reactivity of this metabolite's aromatic moiety, as compared to cinmethylin, is expected. Due to the lack of an aromatic moiety, M684H003 will not show such reactivity towards HOCl.

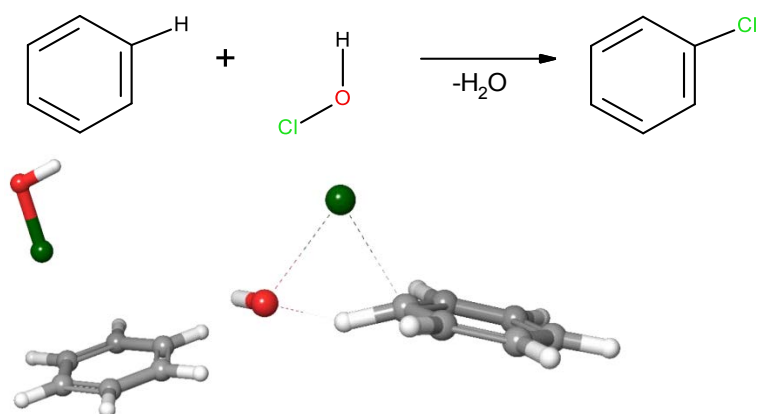


Figure 8.2.3/1-01: Reaction scheme of benzene representing the phenyl residue of cinmethylin and its metabolites M684H001, M684H003 and M684H004, respectively, and HClO.

RESULTS**Quantum chemical calculations**

M684H001 shows a protonation state different from what is depicted in Table 8.2.3/1-01. At neutral pH, M684H001 is predicted to exist purely in its anionic form (Figure 8.2.3/1-01), in perfect agreement to benzoic acid (pK_a = 4.202).

Reactivity with Ozone

Cinmethylin does not contain any nitrogen. As such, the formation of nitrosamine and other nitrogenous by-products is not possible.

There are no unsaturated olefins bonds. Therefore, no Criegee intermediates are expected in cinmethylin or its metabolites.

Reactivity with OH radicals

OH radicals are formed as secondary oxidants from ozone and HOCl decomposition in water. Their reactivity is found to be very high, which is corroborated in the calculations. For all hydrogens contained in cinmethylin, the abstraction of *H by *OH in order to form water was found to be (nearly) barrierless, leading to the conclusion that *OH will react with cinmethylin whenever and wherever they come close. Depending on the concentration of *OH, this reaction can repeat various times, eventually leading to the complete fragmentation of cinmethylin. Prominent places for breakage are the C-O bonds.

Reactivity with HOCl – chlorination

The transition state searches have estimated the reaction barrier heights for the attack of the aromatic CH moieties of benzene, cinmethylin (M684H004) and M684H001 by HOCl. Cinmethylin (and by inference M684H004) shows reaction barriers that are in the same energy range or slightly higher as compared to benzene. Hence, it can be concluded that their reactivity is comparable to that of benzene. Due to the electron-withdrawing effect of the carboxyl group, M684H001 is a worse candidate for electrophilic attack by HOCl.

CONCLUSION

The Applicant estimated the risk of cinmethylin and its metabolites M684H001, M684H003 and M684H004 forming transformation products during the ozonation or chlorination of drinking water based on literature analysis and by quantum chemical calculations.

The results show that cinmethylin and its metabolites react with the secondary oxidant OH. The OH radical is formed by decomposition of ozone and HOCl in water. The reaction with OH radicals leads to a successive fragmentation of the molecules. Based on calculations, the susceptibility of the aromatic CH moieties of cinmethylin and the metabolites M684H004 and M684H001 towards electrophilic attack by HOCl is estimated to be similar to benzene and benzoic acid, respectively.

Due to the absence of nitrogen in the molecular structures of cinmethylin and its metabolites M684H001, M684H003 and M684H004, a conversion into nitrosamines or other nitrogenous disinfection by-products is not possible. As there are no unsaturated bonds present in cinmethylin and its metabolites, no Criegee intermediates are expected.

The HSE Evaluator agrees with these conclusions.

B.8.2.4. Assessment of persistence of cinmethylin in water

The Applicant considered whether cinmethylin fulfils the persistence or very persistent criteria within the PBT and vPvB assessments, which are defined according to Section 3.7.2.1. and 3.7.3.1, respectively, of Annex II of Regulation 1107/2009 as follows:

An active substance, safener or synergist fulfils the persistence criterion where:

- *The half-life in marine water is higher than 60 days,*
- *The half-life in fresh or estuarine water is higher than 40 days,*
- *The half-life in marine sediment is higher than 180 days,*
- *The half-life in fresh or estuarine water sediment is higher than 120 days*

An active substance, safener or synergist fulfils the 'very persistent' criterion where:

- *the half-life in marine, fresh- or estuarine water is higher than 60 days,*
- *the half-life in marine, fresh- or estuarine water sediment is higher than 180 days*

The relevant endpoints for the persistence assessment were identified based on the DG SANCO working document on "Evidence Needed to Identify POP, PBT and vPvB Properties for Pesticides" [SANCO 2012. DG SANCO Working Document on "Evidence Needed to Identify POP, PBT and vPvB Properties for Pesticides". Brussels: European Commission Health and Consumers Directorate-General. Report 25.09.2012 - rev. 3.]. According to this document, degradation half-lives in the whole system of aerobic aquatic studies shall be compared with trigger values relevant for P and vP assessment for the degrading compartment. Additionally, data on aquatic photolysis should also be considered when relevant.

Cinmethylin was found to be hydrolytically stable at all pH values tested (pH 4-9) at 25°C [see KCA 7.2.1.1/1]. In the direct photolysis study, cinmethylin was observed to degrade with a DegT₅₀ of 41.8

days (continuous irradiation). In the indirect photolysis study, degradation was faster with a DT_{50} calculated to be 30.0 days [see KCA 7.2.1.2/1 and KCA 7.2.1.3/1].

In an aerobic water/sediment study under dark conditions, cinmethylin was observed to quickly partition from the water phase to the sediment phase [see KCA 7.2.2.3/1]. The maximum dissipation half-life of cinmethylin from the water phase is 5.2 days, which is related to the sorption to sediment. Considering the rapid dissipation from water, the sediment compartment can be assumed to be the degrading compartment.

The degradation half-life of cinmethylin in the whole system was found to be 39.2 days (geomean dissipation half-life, Level P-I).

According to the DG SANCO working document, degradation half-lives in the whole system should be compared with trigger values relevant for P and vP assessment for the degrading compartment. Considering the geomean $DisT_{50}$ of 39.2 days and the trigger values of 120 and 180 days for the sediment compartment, cinmethylin does not fulfil the criterion for P nor for vP.

Furthermore, the aqueous photolysis studies demonstrated that photolysis in the water phase is an additional dissipation pathway for cinmethylin from the aquatic environment.

B.8.3. FATE AND BEHAVIOUR IN AIR

To investigate the fate and behaviour of cinmethylin in air, the Applicant submitted one laboratory study, one semi-field study, and one QSAR estimation study. Details of these studies are summarised in Table CA 8.3-01 below.

Table CA 8.3-01 Summary of studies investigating the route and rate of cinmethylin degradation in the air.

Air study	Study type
Hassink, J., 2015a KCA 7.3.1/1	Photochemical oxidative degradation (QSAR estimate)
Hassink, J., 2017b KCA 7.3.1/2	Volatilisation on soil and plant surfaces
Wallace, D., 2017a KCA 7.3.2/1	Wind tunnel study measuring the transport of cinmethylin via air

The route and rate of degradation for reactions of cinmethylin in the atmosphere were investigated via QSAR estimation [see KCA 7.3.1/1]. The Applicant explored photochemical oxidative degradation and derived a hydroxyl radical degradation rate of 0.178 days, assuming 12 hours of daylight. The QSAR estimation could not calculate an ozone attack degradation rate, even though the cinmethylin molecule contains sites vulnerable to ozone attack.

The Applicant also investigated the volatilisation of cinmethylin in formulation (BAS 684 02 H; EC formulation) from soil and plant surfaces [see KCA 7.3.1/2]. After 24 hours, volatilisation from the soil surface was 73% and 89% from the plant surface, indicating a high degree of volatility and providing context to some of the methodological issues observed in soil sorption and photolysis studies. Table KCA 8.3-02 summarises the derived endpoints for the route and rate of degradation in air.

Table CA 8.3-02 Summary of endpoints for the route and rate of cinmethylin degradation in the air.

Study	Endpoint	
Photochemical oxidative degradation	Hydroxyl radical degradation rate	0.178 d (12 h day)
	Ozone attack degradation rate	Could not be derived
Volatilisation	Volatilisation rate: soil	73% (24 h)
	Volatilisation rate: plant	89% (24 h)

Due to the high rates of volatilisation, the Applicant also provided a semi-field study to investigate the transport of cinmethylin via air in a semi-outdoor large wind tunnel study [see KCA 7.3.2/1]. Cinmethylin was applied in formulation (BAS 684 03 H; emulsifiable concentrate) on summer barley at a target application rate of 500 g (a.i.)/ha. Maximum deposition was observed at 1 m 48 hours after application, with 0.82% of the applied amount measured. 0.14 – 0.17% was measured at 20 m.

The HSE evaluator concludes that volatilisation is a major route of dissipation for cinmethylin, and that it is short lived in the air. Additionally, there are no concerns relating to local and global effects, such as tropospheric accumulation.

B.8.3.1. Route and rate of degradation in air (Data Requirement 7.3.1)

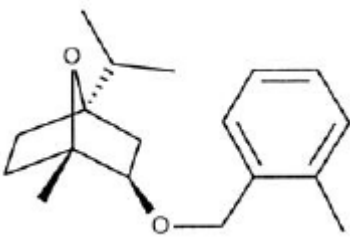
B.8.3.1.1. Photochemical oxidative degradation

Report:	KCA 7.3.1/1; Hassink, J (2015a)
Title	Photochemical oxidative degradation of BAS 684 H (QSAR estimates)
Document No.:	2015/1005045
Guidelines	None
GLP?	No – this is a QSAR estimation of parameters
Deviations	None
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The Applicant estimated the degradation rates for reactions of cinmethylin with hydroxyl radicals and ozone in the atmosphere. These were calculated using the AOPWIN tool based on Atkinson's increment method. Table 8.3.1/1-01 summarises details related to the active substance.

Table 8.3.1/1-01: Summary of the active substance.

Common name	Cinmethylin
Internal code	BAS 684 H
SMILE notation	<chem>Cc1ccccc1COC2CC3(CCC2(O3)C)C(C)C</chem>
Molar mass	274.4 g/mol
Empirical formula	C ₁₈ H ₂₆ O ₂
Structure	

METHODS

The Applicant used AOPWIN v.2.00 within the EPISuite tool to estimate the degradation rate for reactions of cinmethylin with hydroxyl radicals based on the structural formula. Assuming a pseudo-first order reaction, the degradation half-life via this reaction route is calculated by accounting for the diurnally and seasonally averaged concentration of hydroxyl radicals in the troposphere. The degradation rate resulting from ozone attack could also be estimated, with the half-life for this process accounting for the ozone concentration in the air.

The HSE evaluator assessed the Applicant's QSAR estimation by also using AOPWIN to estimate values. The HSE evaluator agreed with the Applicant's processes and input values; as such, the obtained values presented in the following sections are those provided by the Applicant.

RESULTS

The overall hydroxyl rate constant was determined to be $59.961 \times 10^{-12} \text{ cm}^3/\text{molecule/s}$. The weighted global average tropospheric hydroxyl radical concentration is $1.5 \times 10^6 \text{ mol/cm}^3$ for a 12-hour period. This gives a half life of 0.178 days (12 hour day).

For ozone attack degradation, cinmethylin contains reactive sites for an ozone attack; however, AOPWIN could not approximate a degradation rate.

CONCLUSION

The half life for cinmethylin degradation by hydroxyl radicals is 0.178 days (12 hour day). The HSE evaluator agrees and accepts the Applicant's calculated half life. It can be concluded that cinmethylin will be degraded by photochemical processes in the troposphere. Due to this degradation in air, it can be concluded that there is a low risk of long-range transport of cinmethylin.

B.8.3.1.1. Volatilisation from soil and plant surfaces

Report:	KCA 7.3.1/2; Hassink, J. (2017b)
Title	Volatilisation of BAS 684 H after Application of BAS 684 02 H on Soil and Plant Surfaces
Document No.:	2016/1331921
Guidelines	BBA (Biologische Bundesanstalt für Land- und Forstwirtschaft) BRD: Richtlinien für die amtliche Prüfung von Pflanzenschutzmitteln, Teil IV, 6-1, Juli 1990
GLP?	Yes
Deviations	None
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The Applicant investigated the volatilisation behavior of cinmethylin for a time period of 24 hours after application of the emulsifiable concentrate formulation BAS 684 02 H on soil and plant surfaces in a circulation chamber using a blank formulation spiked with ¹⁴C-cinmethylin.

MATERIAL AND METHODS

Test Material

The Applicant used one radiolabeled test item, phenyl-U-¹⁴C cinmethylin (batch number 1147-2001; chemical purity 97%; radiochemical purity 98.9%), and the cinmethylin formulation BAS 684 02 H containing a nominal content of 750 g/L cinmethylin (batch number FD-150416-0012; actual content 750.2 g/L).

Soil

The soil Lufa 5M was used for the soil volatilisation study. Prior to the study the soil was sieved through a fine, 2 mm mesh sieve. Table 8.3.1/2-01 summarises the soil properties.

Table 8.3.1/2-01: Soil properties for the soil used for the volatilisation study.

Soil name		Lufa 5M
Origin		Rheinland Pfalz, Germany
Soil texture	Sand	57.7%
	Silt	28.4%
	Clay	13.9%
Textural class (USDA)		Sandy loam
Organic carbon		0.9%
pH (CaCl₂)		7.3
Maximum WHC		31.5 g/100 g dry soil
Pesticide history		No pesticides used in the past 5 years

Plant

The Applicant used Bush bean (*Phaseolus spp*) with a growth stage of before the first blossom.

Experimental conditions

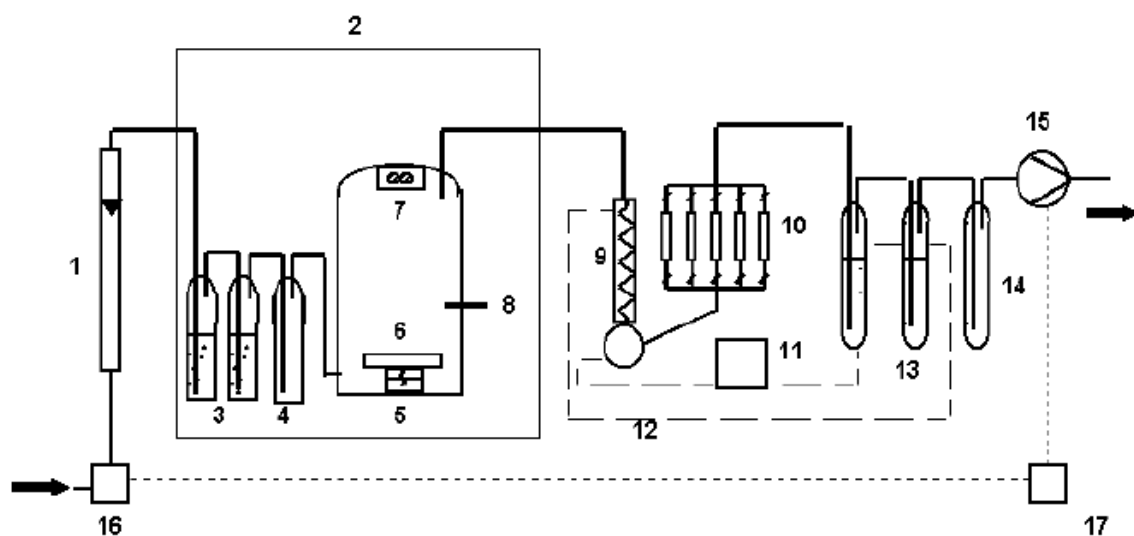
For each volatilisation experiment the application solution was freshly prepared. Based on a nominal field application rate of 500 g/ha cinmethylin, the resulting nominal application rate was 565.5 µg active ingredient on a treated area of 113.1 cm². About 28.2 mg of the BAS 684 02 H formulation (EC formulation) and 350 µL labelled cinmethylin (0.398 mg/mL) were diluted with water to a total of 20 mL. Based on the actual LSC measurement of the application solutions, soil and plant were treated with 602 µg and 636 µg cinmethylin, corresponding to 533 g/ha and 563 g/ha respectively.

The soil and the plant were treated via a FullCone TG 0.5 nozzle (Spraying Systems Co.) in a closed application chamber made of glass.

Volatilisation from plant surfaces:

A bush bean planted in a soil-containing glass tray was used for the experiment. For the application, the soil was covered with Teflon shields and a filter paper. The Teflon shields prevent contamination of the soil surface. The filter paper is used for the adsorption of application solution which might be stripped off during removing the plant from the application chamber. During the application process the filter paper is covered with Teflon sheets.

Immediately after application, the plant was introduced into the circulation chamber, contained within a climatic chamber. Figure 8.3.1/2-01 illustrates the chamber. The circulation chamber consists of a 3 L flat flange beaker with a flat flange lid. A fan, mounted in the centre of the lid, produced an air flow rate of 1 m/s which is directed perpendicular to the test system. Fresh air is sucked through the circulation chamber exchanging the atmosphere in the apparatus at a rate of about 200 L/h (about 60 times per hour). The flow was automatically adjusted by an electronic flow controller. Items volatilised from the test system were trapped by an adsorber filled with charcoal and PU foam after passing a cryotrap for removing the water from the moistened air. Possibly evolved products were trapped by ethylene-glycol located at the end of the sampling device.



1 Flowmeter

2 Incubator (21°C)

3 conc./sat. K_2CO_3

4 Safety Bottle

5 Circulation Chamber

6 Test System

7 Fan

8 Temperature/Humidity Probe

9 Cryotrap

10 Charcoal Adsorbers & PU-foam

11 Thermostat (5°C)

12 Cooling Circuit

13 Ethylene-glycol

14 Safety Bottle

15 Adjustable Pump

16 Flow Probe

17 Flow Controller

K_2CO_3 (3) was not used in this study, the air humidity was sufficient.

Figure 8.3.1/2-01: Schematic diagram of the circulation chamber used for the volatilisation study.

A diurnal cycle was simulated in the climatic chamber with a lamp for 24 hours (7.5 h light, 15 h dark, 1.5 hr light). The temperature during the volatilisation experiment ranged 20.1 – 21.5°C. The relative humidity of the incoming air was on average 49.7%.

Volatilisation from the soil surface

For determination of volatilisation from the soil surface, the soil was adjusted to 60% of the maximum water holding capacity (MWC).

The basic procedure for this volatilisation experiment was the same as in the plant trial. The soil moisture was adjusted to 60% MWHC and 100 g of the moistened soil was weighed into each Petri dish. During the application the border of the Petri dish was covered with a Teflon sheet with a circular opening to avoid contamination of the glass. After application, the Teflon sheet was removed and plant and/or the soil were removed from the application chamber and transferred directly to the circulation chamber.

The temperature during the volatilisation experiment ranged 20.1 – 20.2°C. Evaporation of water from the soil surfaces led to an average relative humidity of 45.9%. One diurnal cycles was simulated for 24 hours (8 h light, 14 h dark, 2 h light). Moisture losses were compensated throughout the experiment by using a wick immersed in a water reservoir. The water content of the soil on the petri dish remained constant during the experiment.

Sampling

Samples were taken at 1, 3, 6, and 24 h after application. At each sampling time the condensate of the cryotrap was removed, the ethylene-glycol traps were replaced, and new charcoal and PU-traps were connected.

At the end of each experiment, both the circulation chamber and the tubes were rinsed twice and the rinsate was analysed. The remaining radioactivity in soil and plant was determined.

The HSE evaluator notes that the study was conducted using single replicates. The HSE evaluator concludes that, while the study is valid, the reproducibility, accuracy and precision of this study are not known. Therefore, the HSE evaluator concludes that the results arising from this study may not be robust.

Plant experiment:

After removing the plant, the application device was thoroughly rinsed with acetonitrile. The application chamber was rinsed twice. Three aliquots (volume not known) of all resulting solutions (nozzle, loop, application chamber, transfer equipment, cryo-trap wash) were measured by LSC to determine the application losses.

The Applicant classed radioactivity in the soil as part of the volatilised item; therefore, they included the soil in this portion. The HSE evaluator notes that this would potentially include cinmethylin that has dripped off the plant surface and onto the soil, potentially increasing the apparent volatilisation levels. The soil was successively extracted three times, first with 150 mL acetonitrile followed by 150 mL acetonitrile/water (50/50), centrifuged and filtered. Finally, the residue was extracted for the third time with 150 mL water. After centrifugation and filtering, all extracts were combined. The soil residue was homogenised after drying.

Three aliquots of the combined extract were analysed by LSC, nine aliquots of the soil (each about 0.5 g) were combusted before LSC measurement. The plant was entirely combusted together with the filter and the total radioactivity measured by LSC.

At the end of the experiment, the subsurface parts of the plant were macerated in 150 mL acetonitrile using an Ultraturrax and the mixture was shaken for 10 min. The resulting suspension was centrifuged and filtered by suction through a filter paper. Next, the residue was shaken for 10 min with 150 mL 50/50 acetonitrile/water, centrifuged and filtered. Finally, the residue was extracted for the third time with 150 mL water. The extracts were combined. The plant residues and filter paper were dried overnight. Three plant extract aliquots (volume not known) were measured by LSC. The plant residues including the filter paper from filtering (divided into 9 aliquots) were measured by LSC after combustion.

Soil experiment:

The basic procedure was the same as in the plant trial, only the nine combusted aliquots of soil consisted 1 g soil each.

Volatiles

Each PU-foam was extracted once with 80 mL acetonitrile, collected in a 100 mL volumetric flask and brought up to volume with acetonitrile.

The charcoal was divided into five small portions. These portions were measured by LSC after combustion. The cotton wool plugs were also combusted and measured by LSC. The LSC results for the individual charcoal portions were summarised and the value for the cotton wool plugs was added, resulting in the total amount of parent equivalent.

Volatilisation kinetics

In order to obtain the kinetics of the volatilisation process, the activities measured in the condensates and in the charcoal (including the tubewash) were added up and plotted as cumulated values against sampling time. The result was not the absolute volatilisation curve of the test item because the circulation chamber walls were rinsed only at the end of the trial. To have comparable values, the value for the circulation chamber wash solution was not included in the 24 h value. Therefore, kinetics of the volatilisation in terms of percent of applied test item were not reported. However, it is assumed by the Applicant that the amounts found in the condensate and in the charcoal are approximately proportional to the total volatilised amount. The HSE evaluator agrees.

The Applicant calculated the volatilisation rate in three ways:

1. Via traps and applied item (TAS):

The sum of the amounts of cinmethylin detected in the condensate, in the charcoal traps and the tube wash, the fan wash, and the circulation chamber wash (and for the plant experiment: the amount of a.s. in the soil) were defined as the volatile part. This value is related to the total amount of a.s. applied to the test system.

2. Via residues and applied item (RAS):

The item in the test system (i.e. either sum of plant extract and plant residues or sum of soil extract and soil residue) plus the a.s. equivalents in the CO₂ traps are the non-volatile part. The difference between this value and the amount applied to the test system is related to the total amount of a.s. applied to the test system.

3. Via residues and the recovery rate of the volatilisation experiment (RRV):

The non-volatile part was calculated as RAS but corrected with the recovery of the volatilisation experiment.

Limits of detection

The Applicant did not supply limits of detection for this experiment.

RESULTS AND DISCUSSION

Recovery rates were calculated both for the complete experiment (i.e. all solutions, extracts, combusted samples vs. loop content) and for the respective volatilisation experiment (i.e. traps at every sampling time, circulation chamber wash and test system after 24 h vs. item applied to the test system). For clarity, the HSE evaluator notes that the volatilisation experiment would have generated data based on directly measured volatilisation rates, and that the Applicant would preferably have used these values to draw conclusions. Table 8.3.1/2-01 summarises the obtained recoveries and volatilisation rates for both experiment types.

The Applicant noted that residues in the adsorption traps (“TAS” in the table below) were low due to the loss of cinmethylin in the experimental set up, which led to poor total recovery for the volatilisation experiment (ranging 25.7 – 36.1% cinmethylin after 24 hours). Therefore, the Applicant

could not conclude based on directly measured volatilisation rates, and instead used the indirect measurement values to inform discussion and conclusions, calculated using the remaining, non-volatile amount of cinmethylin (“RAS” in the table below). The HSE evaluator agrees with the Applicant’s approach of disregarding the direct measurements due to the low recoveries, and using indirect measurements to determine volatilisation instead.

From the indirectly calculated values, volatilisation rates were deemed to be high – 73.3% volatilisation from the soil surface, and 89.2% volatilisation from the plant surface. The HSE evaluator agrees that these rates demonstrate significant volatilisation.

Table 8.3.1/2-01: Recovery of radioactivity (expressed as % cinmethylin) during plant and soil volatilisation experiments. The Applicant drew their conclusions based upon the “RAS” line in the table below due to poor recovery of cinmethylin during the volatilisation experiment that would have generated directly measured volatilisation rates.

	Soil	Plant
Recovery rates (%)		
Complete experiment	83.7	86.2
Volatilisation experiment	36.1	25.7
Volatilisation rate (%)		
Traps and applied substance (TAS)	9.4	14.9
Residue and applied substance (RAS) ^a	73.3	89.2
Residue and recovery in volatilisation experiment (RRV)	26.2	58.1

^a Indirect measurement, i.e. including eventual degradation and/or adsorption processes

CONCLUSION

The volatilisation of cinmethylin from plant surfaces and soil is significant within the first 24 hours following application of BAS 684 02 H (EC formulation), even from a soil surface with less than 60% sand.

The recovery rates for the direct volatilisation experiments were poor and unreliable, therefore the Applicant and HSE evaluator rejected these from further consideration. Based upon the indirect measurement derived from the calculation of the remaining, non-volatile amount of the applied cinmethylin, the Applicant concluded that the volatilisation rate of cinmethylin from soil and plant surfaces was 73% and 89% respectively. The Applicant concluded that the high rates demonstrate significant volatilisation of cinmethylin from plant or soil surfaces.

The HSE evaluator notes that the study was conducted with single replicates and as such, the results arising from the study may not be robust due to the lack of insight into accuracy, precision and reproducibility. The HSE evaluator agrees with the Applicant’s conclusion and notes that the conclusion of this study led to a wind tunnel study investigating potential off-site movement of cinmethylin via short range transport (see KCA 7.3.2/1). The HSE evaluator also notes that, due to the use of the indirect measurement of volatilisation, these volatilisation rates could be considered as worst case values.

B.8.3.2. Transport via air (Data Requirement 7.3.2)

B.8.3.2.1. Wind tunnel study

Report:	KCA 7.3.2/1; Wallace, D. (2017a)
Title	Large outdoor wind tunnel study to evaluate volatilisation, short range transport and deposition of volatilised BAS 684 H (applied as EC formulated product) as a function of distance from the treated area (0-20 m)
Document No.:	2017/1192649
Guidelines	None
GLP?	Yes
Deviations	The test item and reference item were applied to the treated area in the wrong order. However, because the two spray applications happened almost immediately after one another, the HSE evaluator takes the view that this had no impact on the study outcome.
Previous evaluations:	None – report submitted as part of a new active substance registration.

INTRODUCTION

The Applicant conducted an outdoor wind tunnel study to investigate the worst-case aqueous deposition values of volatilised cinmethylin into surface water bodies.

STUDY DESIGN

Cinmethylin was applied as an emulsifiable concentrate formulation (BAS 684 03 H) on a target area grown with summer barley at a target application rate of 500 g (a.i.)/ha. The HSE evaluator confirms that this application rate is consistent with the proposed application rate on winter wheat at BBCH stages 00-29. To ensure the absence of spray drift, the Applicant applied the test and reference substances with 90% drift reducing nozzles.

To demonstrate proper functioning of the wind tunnel test system, the Applicant applied Lindane SC as an internal standard at a target application rate of 200 g (a.i.)/ha in the same treatment area. At the time of application to the plot, the summer barley was in BBCH stage 14-23, with a spray solution interception of approx. 66.6%.

The test and reference items were applied using a 4 m portable boom sprayer fitted with eight 90% drift reducing spray nozzles at a pressure of 2.0 bar. Approximately 3 L of spray solution was applied to the target plot, corresponding to 300 L/ha. The Applicant noted that the study design involved spraying cinmethylin first, followed by spraying the reference item. However, these were applied in the wrong order, meaning the reference item was sprayed first. The HSE evaluator takes the view that, because the spray applications occurred seven minutes apart, this error did not impact upon the study outcome.

The study was carried out under controlled conditions in a wind tunnel approximately 55 m long, 6.5 m wide and 3.1 m high. At one end of the tunnel a wind engine comprising 26 simultaneously working fans was installed; the other end was open. A 5 m air equilibrium distance was established between the wind engine and target spray area.

Stainless steel trays containing 25 L tap water (dimensions 50 cm long, 100 cm wide, 12 cm high) were placed at 1, 3, 5, 10, 15 and 20 m downwind, to represent artificial water bodies with an initial

depth of 5 cm. An additional background steel tray was set up between the wind engine and target area. The steel trays were placed in position five minutes after the reference item was applied to avoid contamination via spray drift. The wind engine was started following the placement of the steel trays.

Air sampling devices were established at 1, 10 and 20 m downwind, and at the background control area (two per position). Sorbent tubes made of glass filled with three polyurethane foam plugs were fitted after the wind engine was started. The air flow was set to 2 L/min and this was checked visually at every sampling time.

Figure 8.3.2/1-01 illustrates the experimental set up.

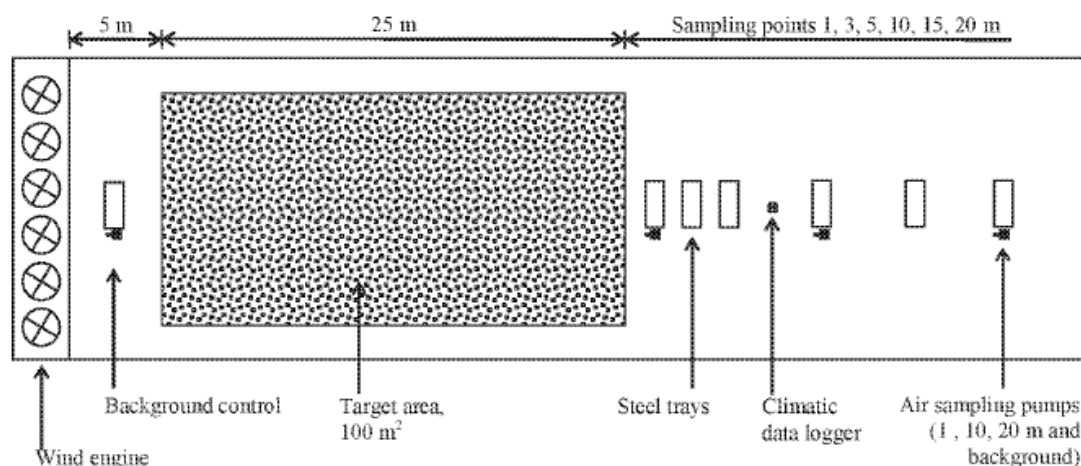


Figure 8.3.2/1-01: Sketch of the test system used in the present wind tunnel study.

Meteorological parameters were recorded within the wind tunnel during the experiment including wind speed, wind direction, relative air humidity and air temperature. Global irradiation data was recorded from a meteorological data station approximately 50 m from the wind tunnel. The wind engine was set to provide a constant wind speed of 2 m/s. The HSE evaluator notes that the Applicant does not claim GLP compliance for the meteorological parameters.

Water sampling intervals were 12, 24, 48, 72 and 96 hours after treatment. The HSE evaluator notes that the water was not replaced at each time interval, with aliquots being taken from each tray. At all sampling distances, the water within the steel trays was homogenised by stirring before two 0.5 L specimens were taken from each steel tray. The Applicant determined the weight of each sample, and also weighed the remaining water at the study end to be able to account for evaporation losses. Air sampling tubes were also taken at each sampling time, with new tubes put into position.

Water and air samples were frozen directly after sampling and were stored frozen ($\leq 18^{\circ}\text{C}$). Water samples were stored for a maximum of 15 days before analysis while air samples were stored for a maximum of approx. 2 months. Concentrations of cinmethylin and Lindane were determined by LC-MS/MS or GC-ECD analysis of extracts.

Table 8.3.2/1-01 summarises the limits of detection and quantitation for cinmethylin and lindane in air and water specimens.

Table 8.3.2/1-01: Limits of detection and quantitation for air and water samples.

	Water samples		Air samples	
	Water concentration (µg/L)	Proportion of applied spray (%)	Extract concentration (µg/L)	Resulting air concentration (µg/m ³)
Cinmethylin				
LOD	0.025	0.002	0.05	0.0002
LOQ	0.1	0.008	1.0	0.003
Lindane				
LOQ	0.1	0.021	1.5	0.003

Two reference solutions containing 100 mL of the analytical standard of the test item and reference item (concentration 1 µg/L) were incubated in quartz glass vessels for the same time as the experiment (96 hours) and exposed to the same meteorological conditions as the water samples in the steel trays to determine if any hydrolysis or photolysis occurred. Results indicated that no hydrolysis or photolysis occurred.

In the view of the Applicant, five minutes was an appropriate time to wait to exclude spray drift. Additionally, the Applicant is of the view that volatilisation is also not likely to occur at distances greater than 20 m; however, the HSE evaluator notes that there have been cases where herbicide damage as a result of volatilisation have likely occurred at distances greater than 20 m.

Spray application

The cinmethylin spray application took place at on 6 April 2017 at 8:35 am, with the lindane application occurring seven minutes later, and the Applicant states that the applications took place in accordance with good agricultural practice (GAP) using a 4 m portable boom sprayer fitted with eight 90% drift reducing nozzles at a pressure of 2.0 bar.

RESULTS

Climatic conditions

During the 96 hour test period, wind speed ranged 1.77 – 2.37 m/s (mean 2.2 m/s), air temperature ranged 4.0 – 24.3°C (mean 11.9°C), and humidity ranged 32.2 – 95.5% (mean 62.1%). The HSE evaluator concludes that meteorological conditions were not extreme during the study.

Aqueous deposition after volatilisation

Deposition of cinmethylin into water trays following volatilisation ranged 0.14 – 0.82% of the applied amount, with a fast decline as a function of distance from the spray event. The highest deposition was recorded at 48 hours after the spray event. The Applicant noted that 1 m deposition decreased due to declining deposition and re-volatilisation from the water surface; the HSE evaluator notes that this offers a part justification for why deposition values reduce over time after 48 hours.

Relative deposition of cinmethylin and lindane in the background samples were consistently below LOD or LOQ in the background samples. Table 8.3.2/1-01 summarises the deposition results for cinmethylin and lindane.

Table 8.3.2/1-01: Relative and absolute deposition of cinmethylin (formulated as BAS 684 03 H) and Lindane over 96 hours and 20 m distance (mean, n = 2).

Distance (m)	Deposition relative to the amount applied to the target area (%)					Absolute deposition on water (µg/m ²)				
	12 hours	24 hours	48 hours	72 hours	96 hours	12 hours	24 hours	48 hours	72 hours	96 hours
Cinmethylin (test item)										
1	0.59	0.71	0.82	0.71	0.67	293.55	357.21	408.11	357.35	333.02
3	0.42	0.47	0.56	0.50	0.41	211.24	235.87	279.28	248.09	206.73
5	0.34	0.38	0.43	0.38	0.35	172.02	191.68	214.34	190.59	174.02
10	0.22	0.26	0.29	0.26	0.22	112.25	131.56	146.64	130.48	108.45
15	0.16	0.20	0.22	0.21	0.17	80.36	99.71	109.14	104.21	86.92
20	0.14	0.14	0.17	0.14	0.14	69.32	72.02	84.78	72.29	68.58
Background	<LOD	<LOD	<LOD	<LOD	<LOQ	<LOD	<LOD	<LOD	<LOD	<LOQ
Lindane (reference item)										
1	0.73	0.70	0.69	0.58	0.37	136.27	130.32	128.17	107.99	68.13
3	0.54	0.50	0.53	0.46	0.37	99.58	92.11	98.03	86.17	67.95
5	0.48	0.44	0.46	0.42	0.33	89.51	81.83	84.80	77.91	61.68
10	0.25	0.24	0.22	0.23	0.14	46.97	43.78	41.26	42.56	25.72
15	0.20	0.21	0.24	0.19	0.16	37.05	38.77	43.58	35.34	29.69
20	0.17	0.19	0.18	0.15	0.14	32.01	35.90	33.60	28.32	26.70
Background	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD

LOQ = 0.008% applied amount or 3.84 µg/cm² for cinmethylin, and 0.021% or 3.84 µg/cm² for lindane.

LOD = 0.002% applied amount or 0.96 µg/cm² for cinmethylin.

Air concentration after volatilisation

Air concentrations of cinmethylin ranged 0.01 – 3.01 µg/m³ during the 96 hour study, with rapid declines associated with both distance and time. The highest air concentrations were observed at 1 m distance 12 hours after treatment. The HSE evaluator notes that, at 12 hours, a reading of 0.01 µg/m³ was measured in the background sample; additionally, no lindane measurement was reported for the background sample. The Applicant has not offered a reason for this. All other background measurements were below LOQ. Air concentrations are summarised in Table 8.3.2/1-02; the HSE evaluator notes that there were no values showing air concentrations relative to the amount applied for direct comparison of air concentrations.

The HSE evaluator also notes that there is a 2.8 times difference in concentrations of the application solutions (wherein cinmethylin was applied at a higher concentration). Cinmethylin deposited at over four times the rate of lindane at 1 m distance after 12 hours, and over 2.2 times the rate of lindane at 20 m after 12 hours. Therefore, the HSE evaluator concludes that cinmethylin could be volatilising at approximately the same, or a higher rate, than lindane.

Table 8.3.2/1-02: Air concentrations of cinmethylin (formulated as BAS 684 03 H) and Lindane over 96 hours and 20 m distance (mean, n = 2).

Distance (m)	Air concentration (µg/m ³)				
	0-12 hours	12-24 hours	24-48 hours	48-72 hours	72-96 hours
Cinmethylin (test item)					
1	3.01	0.53	0.29	0.14	0.07
10	0.80	0.16	0.08	0.03	0.02
20	0.47	0.09	0.06	0.02	0.01
Background	0.01	<LOQ	<LOQ	<LOQ	<LOQ
Lindane (reference item)					
1	0.74	0.29	0.16	0.10	0.07
10	0.32	0.15	0.09	0.06	0.04
20	0.21	0.08	0.05	0.03	0.02

CONCLUSION

The maximum deposition within the experiment accounted for about 0.82% of the applied amount at the 1 m distance 48 hours after application. Deposition decreased with increasing distance and was in the range from 0.14 and 0.17% of the applied amount at the 20 m sampling distance. Lindane air concentrations and aqueous deposition were in a typical range in terms of distance from the treated area and time after treatment, indicating valid study conduct.

Air samples were also taken to quantify volatilised cinmethylin. Air concentrations decreased rapidly from the 1 m to the 10 m sampling distance. The maximum air concentration was measured at the first sampling period at 12 hours after application and measured $3.01 \mu\text{g}/\text{m}^3$ at 1 m. At this sampling point, air concentration decreased with increasing time after treatment and accounted for $0.07 \mu\text{g m}^{-3}$ at the 72-96 hours after application point. Air concentrations of cinmethylin also decreased with increasing distance and time after application: at the 20 m sampling point, cinmethylin levels peaked at $0.47 \mu\text{g}/\text{m}^3$ at 0-12 hours and decreased to $0.01 \mu\text{g}/\text{m}^3$ after 96 hours.

The HSE evaluator notes that the deposition values are significant when placed in the context of the Rautmann spray drift values. When considering drift and deposition at 1 m, 0.82% due to volatilisation equates to an additional 30% of cinmethylin deposition after 48 hours when considering the Rautmann drift value of 2.77% at 1 m. At 5 m, 0.43% of deposition was observed at 48 hours; on top of the Rautmann drift value of 0.57% this would account for an additional 75% of cinmethylin being deposited at this distance due to volatilisation. Therefore, the HSE evaluator considers the impact of deposition because of volatilisation to be significant.

B.8.3.3. Local and global effects (Data Requirement 7.3.3)

Local and global effects must be considered for substances that are to be applied in high amounts. This data requirement was not triggered by cinmethylin.

B.8.4. DEFINITION OF THE RESIDUE**B.8.4.1. Definition of the residue for risk assessment (Data Requirement 7.4.1)**

According to the results presented in the sections CA 8.1-8.3, the following compounds are to be considered for the environmental risk assessment.

Soil:

Cinmethylin (parent only)

Groundwater:

Cinmethylin (parent only)

Surface Water:

Cinmethylin

M684H001

M684H003

Sediment

Cinmethylin (parent only)

Air:

Cinmethylin (parent only)

B.8.4.2. Definition of the residue for monitoring

According to the results presented in the sections CA 8.1-8.3, the following compounds are to be provisionally considered for monitoring:

Soil:

Cinmethylin (parent only)

Groundwater:

Cinmethylin (parent only)

Surface Water:

Cinmethylin (parent only)

Sediment:

Cinmethylin (parent only)

Air:

Cinmethylin (parent only)

B.8.5. MONITORING DATA CONCERNING FATE AND BEHAVIOUR OF THE ACTIVE SUBSTANCE, METABOLITES, DEGRADATION AND REACTION PRODUCTS

As a new active substance, there are no monitoring data available at present for cinmethylin in the environment.

B.8.6. REFERENCES RELIED ON**B.8.6.1. Literature Search**

A literature review has been carried out for the active substance BAS 684 H (cinmethylin). The literature review has been conducted in accordance with Article 8(5) of Regulation No. 1107/2009 and is based on the EFSA guidance document as published in EFSA Journal 2011; 9(2):2092.

The key objective of the submitted literature review was to establish whether any scientific peer-reviewed open literature published within the last ten years before the date of submission of the dossier would be relevant for the risk assessment of BAS 684 H and its metabolites. In this section the conduct of the literature search methods in relation to fate and behaviour studies has been evaluated; the conclusions of which are presented here. Key information from this report has been summarised below.

Submitted data:	Studies submitted for the purpose of renewal: - CA 8.6.1/01 Esswein, U. 2018
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Report:	CA 8.6.1/01 Esswein, U., (2018)
Title	Literature search report - Cinmethylin
Guidelines:	Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation No 1107/2009 (EFSA Journal 2011;9(2):2092)
GLP:	No
Deviations	None specified

One literature search was submitted to address all areas of the RAR. The HSE evaluator has assessed the suitability of the mechanics of the literature search in line with EFSA guidance on conducting literature searches (EFSA, 2011). The HSE evaluator can confirm that the process used was acceptable (discussed in further detail below). With regards to the relevance and reliability of the literature identified, only the area of environmental fate and behaviour is commented on here. All other areas of the assessment will be covered within the relevant section. No references identified impacted on the fate evaluation.

The process of selection of relevant scientific peer-reviewed open literature was done in two steps: The *First Selection step* for relevance was based on summary records (e.g. titles, abstracts, index terms, keywords).

- Irrelevant records were tagged as “Ballast” and not further processed.
- Summary records which appear to be relevant and those of unclear relevance were tagged as “Hit” and went to the next level of evaluation.

The *Second Detailed Assessment* was done by the scientific experts in the corresponding areas. Records tagged as “Hit” were further evaluated in depth, with three typical registers, namely:

- "no relevant endpoint"
- "evaluated - not-relevant"
- "used for dossier"

The "Hits" were reviewed based on the information given in the title and the abstract with regard to relevance for the regulatory endpoints in the respective regulatory area. Those records which were clearly judged as not assignable to any regulatory endpoint were shifted into the register "no relevant endpoint" with an explanation of rationale.

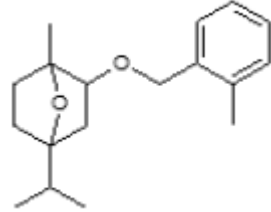
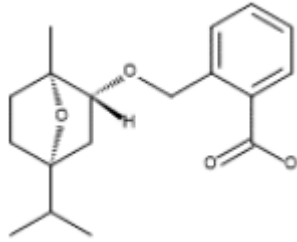
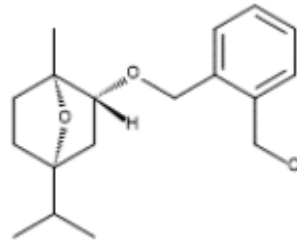
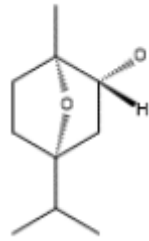
All remaining records were assessed in detail based on the complete report and thus, separated into relevant reports for further discussion and those clearly not relevant.

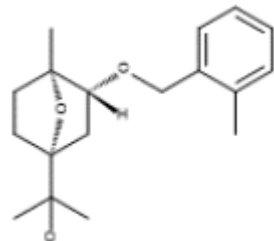
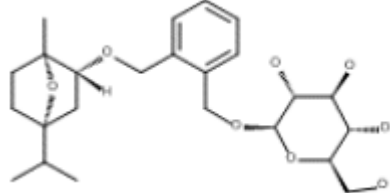
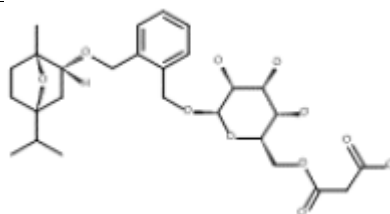
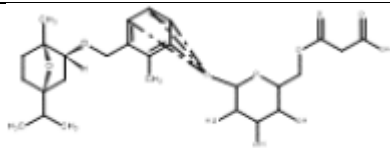
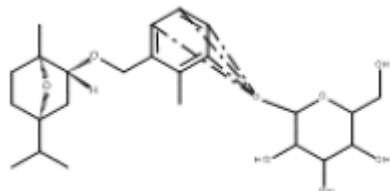
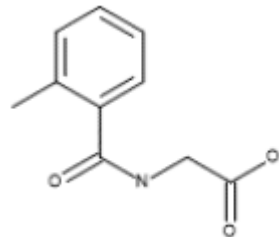
Criteria to assign a record to the register "used for dossier" were:

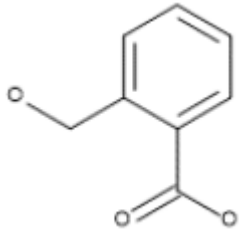
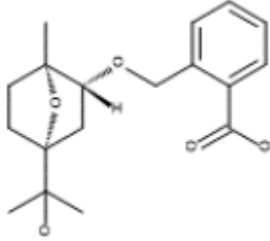
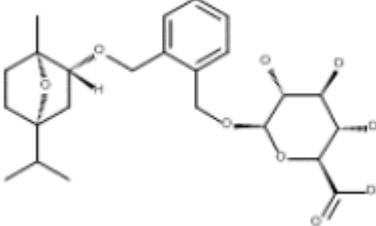
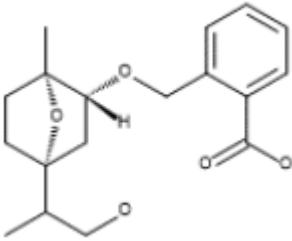
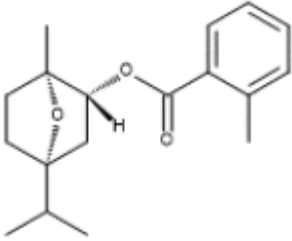
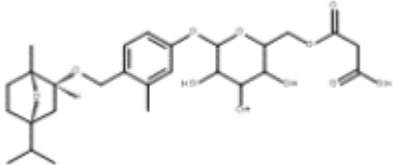
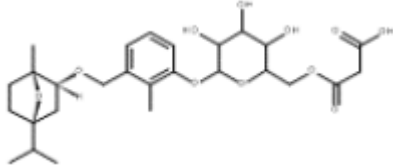
- Records providing information about additional/new/unknown/potentially contradictory effects or data which might impact the hazard assessment endpoints or the risk assessments parameters and which, in addition, have a high grade of reliability, i.e., grade 1 or 2 based on the 'Klimisch' scoring system.

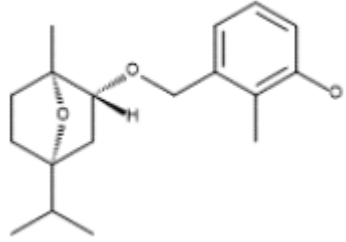
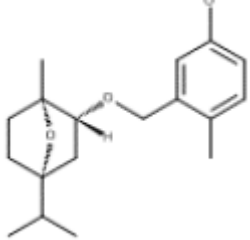
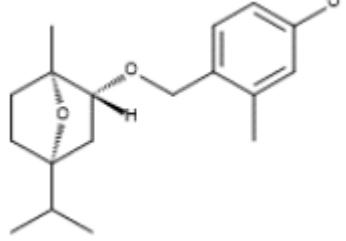
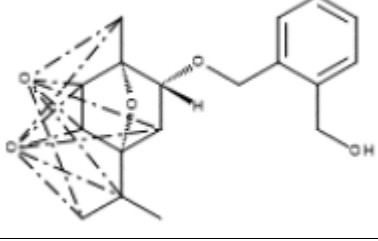
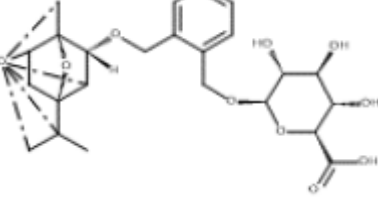
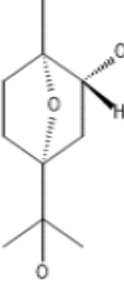
All available CAS numbers of stereoisomers of cinmethylin and metabolites have been included in the search profile.

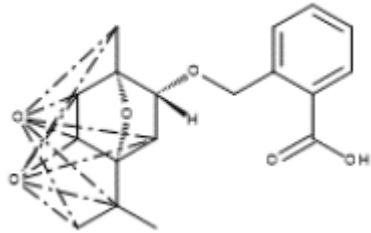
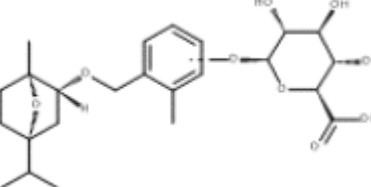
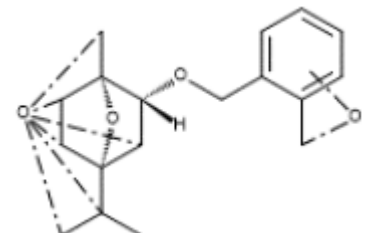
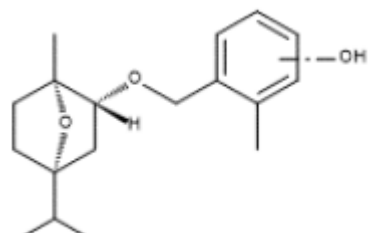
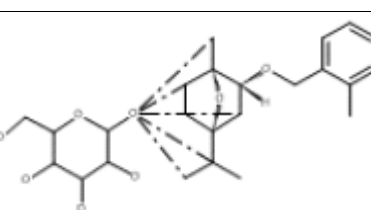
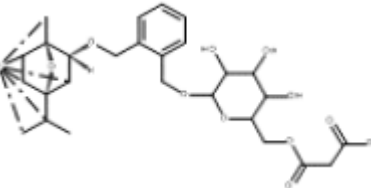
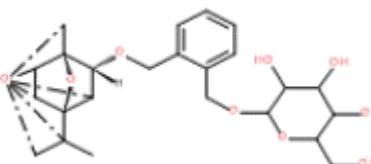
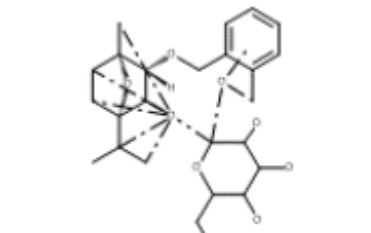
Table CA 8.6.1/01-01 List of input parameters for the database search on BAS 684 H and its metabolites

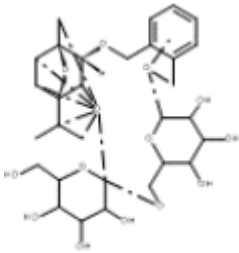
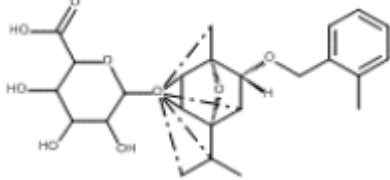
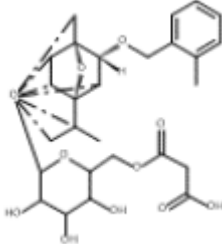
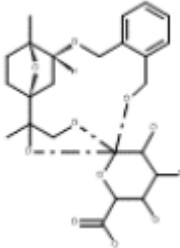
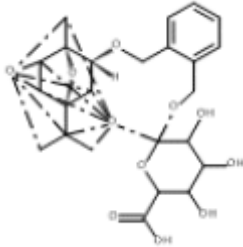
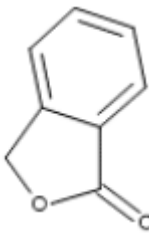
Internal Code	IUPAC Name	Molecular Structure	CAS Number
BAS 684 H			
BAS 684 H	(1R,2SR,4SR)-1,4-epoxy-p-menth-2-yl 2-methylbenzyl ether		87818-31-3 87819-60-1 87818-61-9 Stereo-Isomer: 112502-84-8 99827-45-9 87818-68-6 1245807-70-8
Metabolites			
M684H001 (60555521)	2-({[(1SR,2RS,4RS)-1-methyl-4-(propan-2-yl)-7-oxabicyclo[2.2.1]hept-2-yl]oxy}methyl)benzoic acid		87819-14-5
M684H002 (60554479)	[2-({[(1SR,2RS,4RS)-1-methyl-4-(propan-2-yl)-7-oxabicyclo[2.2.1]hept-2-yl]oxy}methyl)phenyl]methanol		99765-53-4
M684H003 (45395586)	(1SR,2RS,4RS)-1-methyl-4-(propan-2-yl)-7-oxabicyclo[2.2.1]heptan-2-ol		22555-57-3 22621-68-7 38630-76-1 50302-07-3 87172-89-2 96645-97-5 103834-29-3 134461-72-6 134461-73-7 134527-97-2

			134527-98-3 134527-99-4 134528-00-0 134528-01-1 134528-02-2 152453-46-8 152453-51-5 152453-52-6 152453-53-7 152519-96-5 152519-97-6 152519-98-7 152519-99-8 1933681-69-6
M684H004 (60554480)	2-{{(1RS,3RS,4SR)-4-methyl-3-[(2-methylbenzyl)oxy]-7-oxabicyclo[2.2.1]hept-1-yl}propan-2-ol		119973-51-2
M684H005 (60672256)	[2-({[(1SR,2RS,4RS)-1-methyl-4-(propan-2-yl)-7-oxabicyclo[2.2.1]heptan-2-yl]oxy}methyl)phenyl)methyl beta-D-glucopyranoside		no CAS
M684H006 (60672258)	[2-({[(1SR,2RS,4RS)-1-methyl-4-(propan-2-yl)-7-oxabicyclo[2.2.1]heptan-2-yl]oxy}methyl)phenyl)methyl 6-O-(carboxyacetyl)-beta-D-glucopyranoside		no CAS
M684H007			no CAS
M684H008			no CAS
M684H009 (730322)	N-(2-methylbenzoyl)glycine		42013-20-7

M684H010 (1116009)	2-(hydroxymethyl)benzoic acid		612-20-4
M684H011 (60554478)	2-({[(1SR,2RS,4RS)-4-(2-hydroxypropan-2-yl)-1-methyl-7-oxabicyclo[2.2.1]hept-2-yl]oxy}methyl)benzoic acid		99765-60-3
M684H012 (60747715)	[2-({[(1SR,2RS,4RS)-1-methyl-4-(propan-2-yl)-7-oxabicyclo[2.2.1]heptan-2-yl]oxy}methyl)phenyl]methyl beta-D-glucopyranosiduronic acid		no CAS
M684H013 (60554481)	2-({[(1SR,2RS,4RS)-4-(1-hydroxypropan-2-yl)-1-methyl-7-oxabicyclo[2.2.1]hept-2-yl]oxy}methyl)benzoic acid		110901-97-8 120053-26-1 120053-27-2
M684H014 (60554477)	(1SR,2RS,4RS)-1-methyl-4-(propan-2-yl)-7-oxabicyclo[2.2.1]hept-2-yl 2-methylbenzoate		130772-87-1 1334643-80-9
M684H015			no CAS
M684H016			no CAS

M684H017 (60667765)	2-methyl-3- ({[(1SR,2RS,4RS)-1-methyl- 4-(propan-2-yl)-7- oxabicyclo[2.2.1]heptan-2- yl]oxy}methyl)phenol		119973-33-0
M684H018 (60672259)	4-methyl-3- ({[(1SR,2RS,4RS)-1-methyl- 4-(propan-2-yl)-7- oxabicyclo[2.2.1]heptan-2- yl]oxy}methyl)phenol		119973-35-2
M684H019 (60667766)	3-methyl-4- ({[(1SR,2RS,4RS)-1-methyl- 4-(propan-2-yl)-7- oxabicyclo[2.2.1]heptan-2- yl]oxy}methyl)phenol		119973-34-1
M684H021			119973-46-5
M684H022			no CAS
M684H026 (60590081)	(1SR,2RS,4RS)-4-(2- hydroxypropan-2-yl)-1- methyl-7- oxabicyclo[2.2.1]heptan-2-ol		87129-26-8 98857-39-7 161168-84-9 176896-66-5 1932066-49-3 1932367-62-8 1932534-82-1 1932543-20-8

M684H027			119973-50-1
M684H034			no CAS
M684H039			119973-44-3 119973-52-3 119997-23-8 119973-42-1
M684H043			see M684H017, M684H018, M684 H019
M684H046			no CAS
M684H047			no CAS
M684H048			no CAS
M684H050			no CAS

M684H051			no CAS
M684H052			no CAS
M684H055			no CAS
M684H056			no CAS
M684H057			no CAS
M684H059 (188511)	2-benzofuran-1(3H)-one		87-41-2

The search terms included were used to establish relevant literature. It was noted that the Applicant also considered fate and behaviour specific terms as well as substance specific terms.

Table CA 8.6.1/01-02 summarises the databases searched by the Applicant. The Applicant confirmed that the search started as early as the respective database started, which is considered acceptable by the HSE evaluator.

Table CA 8.6.1/01-02 Databases searched

List of databases used in the literature review	Main Search	Update Search
1. CAPLUS	2017-07-27	2018-04-22
2. BIOSIS	2017-07-26	2018-04-18
3. CAB Abstracts	2017-07-26	2018-04-18
Total number of databases searched: 3		

An overview of the results is provided in Table KCA 8.6.1/01-03; details of the irrelevant studies are provided in Table KCA 8.6.1/01-04; studies potentially relevant for the Efate dossier are provided in Table KCA 8.6.1/01-05; and studies fully evaluated for relevance to the Efate dossier are provided in Table 8.6.1/01-06. No studies were considered relevant for the Efate dossier.

Table KCA 8.6.1/01-03 Results of the study selection process, for each data requirement or group of data requirements searched.

Summary of the review	CAPLUS	BIOSIS	CAB Abstracts
Total number of summary records retrieved	59	23	47
Total number of summary records after removing duplicates	59	11	28
Total number of summary records retrieved after first selection step	29	3	11

Updated search on 2018-04-23 (BIOSIS: 20180418/UP; CAB Abstracts: 20180418/UP; CAPLUS: 20180422/UP) retrieved 2 additional results after duplicate removal (1 from CAPLUS, 1 from BIOSIS).

Studies which were performed by Shell Agriculture in the 1980s to investigate the metabolic fate of BAS 684 H were considered. However, none of the studies were performed according to GLP and all studies have major deviations to current test guidelines. Furthermore, a detailed documentation is missing, the studies were performed with phenyl-labelled BAS 684 H only and the behaviour of the enantiomers was not investigated. None of the studies are considered relevant for regulatory purposes. None of the results obtained in these non-GLP studies is in contradiction with the new GLP data generated for the current submission. The HSE evaluator requested that all available abstracts for the studies performed by Shell Agriculture be submitted and can confirm that they are not of higher enough quality to be considered relevant for regulatory purposes.

Table KCA 8.6.1/01-04 Irrelevant records tagged as “Ballast” and not further processed

Title	Author	Source/Patent No	Ballast	Comment
A time for herbicide discovery.	Duke, Stephen O. [Reprint Author]	Pest Management Science, (APR 2012) Vol. 68, No. 4, pp. 493. http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1526-4998 . ISSN: 1526-498X. E-ISSN: 1526-4998.	yes	not Efate
Effect of buckwheat (<i>Fagopyrum esculentum</i> meonch) leaf extract on weeds	Choudhury, P. P. Dureja, Prem [Reprint Author]	Pesticide Research Journal, (JUN 2007) Vol. 19, No. 1, pp. 7-8. ISSN: 0970-6763.	yes	not Efate

grown in winter rice under north bengal conditions.				
Natural products as sources of herbicides: Current status and future trends.	Duke, S. O. [Reprint author] Dayan, F. E. Romagni, J. G. Rimando, A. M.	Weed Research, (Feb., 2000) Vol. 40, No. 1, pp. 99-111. print. CODEN: WEREAT. ISSN: 0043-1737.	yes	not Efate
Weed management in transplanted, lowland rice (Oryza sativa).	Gogoi, A. K.	Indian Journal of Agronomy, (1995) Vol. 40, No. 3, pp. 415-419. CODEN: IJAGAZ. ISSN: 0537-197X.	yes	not Efate
Downy brome (Bromus tectorum) control in winter wheat and winter rye.	Blackshaw, R. E.	Canadian Journal of Plant Science, (1994) Vol. 74, No. 1, pp. 185-191. CODEN: CPLSAY. ISSN: 0008-4220.	yes	not Efate
WEED CONTROL IN RICE SEEDLING NURSERIES AND ITS EFFECT ON THE TRANSPLANTED CROP.	FAJARDO F F [Reprint author] RAO A N MOODY K	Journal of Plant Protection in the Tropics, (1990) Vol. 7, No. 3, pp. 165-172. ISSN: 0127-6883.	yes	not Efate
CULTIVATION AND HERBICIDES FOR WEED CONTROL IN SWEET POTATO IPOMOEA-BATATAS.	GLAZE N C [Reprint author] HALL M R	Weed Technology, (1990) Vol. 4, No. 3, pp. 518-523. CODEN: WETEE9. ISSN: 0890-037X.	yes	not Efate
ARTEMISININ A CONSTITUENT OF ANNUAL WORMWOOD ARTEMISIA-ANNUA IS A SELECTIVE PHYTOTOXIN.	DUKE S O [Reprint author] VAUGHN K C CROOM E M JR ELSOHLY H N	Weed Science, (1987) Vol. 35, No. 4, pp. 499-505. CODEN: WEESA6. ISSN: 0043-1745.	yes	not Efate
Effect of chemical weed-control methods on productivity of transplanted rice (Oryza sativa).	Halder, J. Patra, A. K.	Indian Journal of Agronomy (2007), Volume 52, Number 3, pp. 111-113, 5 refs. ISSN: 0537-197X Published by: Indian Society of Agronomy, New Delhi	yes	not Efate
Effect of puddling, water	Subramanyam, D.	Journal of Research ANGRAU (2007), Volume 35, Number 2, pp. 9-	yes	not Efate

and weed management on yield and nutrient uptake in transplanted rice and associated weeds.	Reddy, C. R. Reddy, D. S.	15, 6 refs. ISSN: 0970-0226 Published by: Acharya N G Ranga Agricultural University, Hyderabad		
Influence of integrated weed management practices on growth and yield of transplanted rice (<i>Oryza sativa</i> L.).	Subramanyam, D. Reddy, D. S. Reddy, C. R.	Crop Research (Hisar) (2007), Volume 34, Number 1/3, pp. 1-5, 6 refs. ISSN: 0970-4884 Published by: Agricultural Research Information Centre, Hisar	yes	not Efate
Effect of sequential application of herbicides on weed control in transplanted rice (<i>Oryza sativa</i> L.).	Rao, A. S.	Crop Research (Hisar) (1995), Volume 9, Number 2, pp. 203-210, 6 refs. ISSN: 0970-4884	yes	not Efate
Argold: a new rice herbicide.	Jones, G.	Shell Agriculture (1989), Number 3, pp. 10-11 ISSN: 0953-9026	yes	not Efate
Performance of cinmethylin and FMC-57020 as herbicides for direct seeded cucumbers.	Chase, W. R. Putnam, A. R.	Proceedings, North Central Weed Control Conference. (1986), Number Vol.41, 26 p. Conference: Proceedings, North Central Weed Control Conference.	yes	not Efate
Line source herbigation of cinmethylin (SD-95481) for grass control in pinto beans.	Arnold, R. N. Gregory, E. J. Smeal, D.	Proceedings of the Western Society of Weed Science. (1987), Number Vol.40, pp. 133-140 Conference: Proceedings of the Western Society of Weed Science.	yes	not Efate
Influence of ethalfluralin and cinmethylin on cucumbers and sweet potatoes grown sequentially.	Bonanno, A. R.	Proceedings, Southern Weed Science Society, 39th annual meeting. (1986), 173 p. Conference: Proceedings, Southern Weed Science Society, 39th annual meeting.	yes	not Efate
Influence of sequential herbicide application on cucurbit growth and development.	Boucounis, T. G. Whitwell, T.	Proceedings, Southern Weed Science Society, 39th annual meeting. (1986), 180 p. Conference: Proceedings, Southern Weed Science Society, 39th annual meeting.	yes	not Efate

The influence of cinmethylin on the growth and yield of muskmelons grown with polyethylene mulches and row covers.	Motsenbocker, C. E. Bonanno, A. R.	Proceedings, Southern Weed Science Society, 39th annual meeting. (1986), 179 p. Conference: Proceedings, Southern Weed Science Society, 39th annual meeting.	yes	not Efate
Performance of cinmethylin (Cinch herbicide) in soybeans.	Forney, D. R. May, J. W. Bozarth, G. A.	Proceedings, Southern Weed Science Society, 38th annual meeting. (1985), 497 p. Conference: Proceedings, Southern Weed Science Society, 38th annual meeting.	yes	not Efate
Evaluation of herbicides for weed control in gardens and the effect of these on the growth of the crop.	Mattson, M. P.	Proceedings, North Central Weed Control Conference. (1985), Number Vol. 40, 114 p. Published by: USA, St. Louis, Missouri Conference: Proceedings, North Central Weed Control Conference.	yes	not Efate
Response of soyabeans and hard red winter wheat to herbicide treatments of imazaquin, AC 263, 499, FMC 57020, cinmethylin, DPX-R6025 and RL 8347.	Sommers, B. K. Russ, O. G. Claassen, M. M. Janssen, K. A. Maddux, L. D.	Proceedings, North Central Weed Control Conference. (1985), Number Vol. 40, pp. 87-88 Conference: Proceedings, North Central Weed Control Conference.	yes	not Efate
Metabolic fate of cinmethylin in rats.	Lee, P. W. Stearns, S. M. Powell, W. R. Burton, W. B.	Abstracts of papers, 191st ACS national meeting. (1986), AGRO 38 p. Published by: American Chemical Society, Washington DC Conference: Abstracts of papers, 191st ACS national meeting.	yes	not Efate
Cinmethylin (Cinch herbicide) for use in vegetable, vine, tree and ornamental crops.	May, J. W. Goss, J. R.	Proceedings, Southern Weed Science Society, 38th annual meeting. (1985), 121 p. Conference: Proceedings, Southern Weed Science Society, 38th annual meeting.	yes	not Efate
Influence of mechanical incorporation on the herbicidal behaviour of SD 95481.	Wittsell, L. E. May, J. W.	Proceedings, North Central Weed Control Conference. (1983), 156 p. Conference: Proceedings, North Central Weed Control Conference.	yes	not Efate
Impact of rainfall on the performance of	Wittsell, L. E. May, J. W.	Proceedings, North Central Weed Control Conference. (1983), pp. 154-155 Conference: Proceedings, North	yes	not Efate

SD 95481.		Central Weed Control Conference.		
Risk-based high-throughput chemical screening and prioritization using exposure models and in vitro bioactivity assays	Shin, Hyeong-Moo Ernststoff, Alexi Arnot, Jon A. Wetmore, Barbara A. Csiszar, Susan A. Fantke, Peter Zhang, Xianming McKone, Thomas E. Joliet, Olivier Bennett, Deborah H.	Environmental Science + Technology (2015), 49(11), 6760-6771 CODEN: ESTHAG; ISSN: 0013-936X	yes	not Efate
Predictive Endocrine Testing in the 21st Century Using in Vitro Assays of Estrogen Receptor Signaling Responses	Rotroff, Daniel M. Martin, Matt T. Dix, David J. Filer, Dayne L. Houck, Keith A. Knudsen, Thomas B. Sipes, Nisha S. Reif, David M. Xia, Menghang Huang, Ruili Judson, Richard S.	Environmental Science + Technology (2014), 48(15), 8706-8716 CODEN: ESTHAG; ISSN: 0013-936X	yes	not Efate
High-Throughput Models for Exposure-Based Chemical Prioritization in the ExpoCast Project	Wambaugh, John F. Setzer, R. Woodrow Reif, David M. Gangwal, Sumit Mitchell-Blackwood, Jade Arnot, Jon A. Joliet, Olivier Frame, Alicia Rabinowitz, James Knudsen, Thomas B. Judson, Richard S. Egeghy, Peter Vallero, Daniel Cohen Hubal, Elaine A.	Environmental Science + Technology (2013), 47(15), 8479-8488 CODEN: ESTHAG; ISSN: 0013-936X	yes	not Efate

Validation study on a method for multiresidue analysis of pesticides in cereals and pulses with supercritical fluid extraction	Uranishi, Katsushige Yamashita, Hirokazu Olayama, Akiko Yamamoto, Keigo	Shokuhin Eiseigaku Zasshi (2012), 53(6), 278-290 CODEN: SKEZAP; ISSN: 0015-6426	yes	not Efate
Plant cell membrane as a marker for light-dependent and light-independent herbicide mechanisms of action	Dayan, Franck E. Watson, Susan B.	Pesticide Biochemistry and Physiology (2011), 101(3), 182-190 CODEN: PCBPBS; ISSN: 0048-3575	yes	not Efate
Predictive Models of Prenatal Developmental Toxicity from ToxCast High-Throughput Screening Data	Sipes, Nisha S. Martin, Matthew T. Reif, David M. Kleinstreuer, Nicole C. Judson, Richard S. Singh, Amar V. Chandler, Kelly J. Dix, David J. Kavlock, Robert J. Knudsen, Thomas B.	Toxicological Sciences (2011), 124(1), 109-127 CODEN: TOSCF2; ISSN: 1096-0929	yes	not Efate
The potential for pyroxasulfone to selectively control resistant and susceptible rigid ryegrass (<i>Lolium rigidum</i>) biotypes in Australian grain crop production systems	Walsh, Michael J. Fowler, Tarnya M. Crowe, Bronwyn Ambe, Toshihiro Powles, Stephen B.	Weed Technology (2011), 25(1), 30-37 CODEN: WETEE9; ISSN: 0890-037X	yes	not Efate
Using nuclear receptor activity to stratify hepatocarcinogens	Shah, Imran Houck, Keith Judson, Richard S. Kavlock, Robert J. Martin, Matthew T. Reif, David M. Wambaugh,	PLoS One (2011), 6(2), e14584 CODEN: POLNCL; ISSN: 1932-6203 URL: http://www.plosone.org/article/fetchObjectAttachment.action?uri=info%3Adoi%2F10.1371%2Fjournal.pone.0014584+representation=PDF	yes	not Efate

	John Dix, David J.			
Endocrine profiling and prioritization of environmental chemicals using ToxCast data	Reif, David M. Martin, Matthew T. Tan, Shirlee W. Houck, Keith A. Judson, Richard S. Richard, Ann M. Knudsen, Thomas B. Dix, David J. Kavlock, Robert J.	Environmental Health Perspectives (2010), 118(12), 1714-1720 CODEN: EVHPAZ; ISSN: 0091- 6765	yes	not Efate
Xenobiotic- Metabolizing Enzyme and Transporter Gene Expression in Primary Cultures of Human Hepatocytes Modulated by Toxcast Chemicals	Rotroff, Daniel M. Beam, Andrew L. Dix, David J. Farmer, Adam Freeman, Kimberly M. Houck, Keith A. Judson, Richard S. LeCluyse, Edward L. Martin, Matthew T. Reif, David M. Ferguson, Stephen S.	Journal of Toxicology and Environmental Health, Part B: Critical Reviews (2010), 13(2-4), 329-346 CODEN: JTECFR; ISSN: 1093-7404	yes	not Efate
In Vitro Screening of Environmental Chemicals for Targeted Testing Prioritization: The ToxCast Project	Judson, Richard S. Houck, Keith A. Kavlock, Robert J. Knudsen, Thomas B. Martin, Matthew T. Mortensen, Holly M. Reif, David M. Rotroff, Daniel M. Shah, Imran Richard, Ann	Environmental Health Perspectives (2010), 118(4), 485-492 CODEN: EVHPAZ; ISSN: 0091-6765	yes	not Efate

	M. Dix, David J.			
Screening Rules for Leads of Fungicides, Herbicides, and Insecticides	Liu, Bin Zhu, Fucheng Huang, Ying Wang, Yuhui Yu, Fei Fan, Botao Yao, Jianhua	Journal of Agricultural and Food Chemistry (2010), 58(5), 2673-2684 CODEN: JAFCAU; ISSN: 0021-8561	yes	not Efate
Evaluation of high-throughput genotoxicity assays used in profiling the US EPA ToxCast chemicals	Knight, Andrew W. Little, Stephen Houck, Keith Dix, David Judson, Richard Richard, Ann McCarroll, Nancy Akerman, Gregory Yang, Chihai Birrell, Louise Walmsley, Richard M.	Regulatory Toxicology and Pharmacology (2009), 55(2), 188-199 CODEN: RTOPDW; ISSN: 0273-2300	yes	not Efate
Profiling chemical based on chronic toxicity results from the U.S. EPA ToxRef Database	Martin, Matthew T. Judson, Richard S. Reif, David M. Kavlock, Robert J. Dix, David J.	Environmental Health Perspectives (2009), 117(3), 392-399 CODEN: EVHPAZ; ISSN: 0091-6765	yes	not Efate
Effect of chemical weed-control methods on productivity of transplanted rice (<i>Oryza sativa</i>)	Halder, J. Patra, A. K.	Indian Journal of Agronomy (2007), 52(2), 111-113 CODEN: IJAGAZ; ISSN: 0537-197X	yes	not Efate
Pesticide residue monitoring method in agricultural products with GC/MS and LC/MS/MS	Nishina, Takeshi Murakawa, Hiroshi Fukushima, Kouhei Tobino, Toshiaki	Kumamoto-ken Hoken Kankyo Kagaku Kenkyushoho (2006), Volume Date 2005, 35, 78-85 CODEN: KHKKF8; ISSN: 1341-6480	yes	not Efate
Pesticide residue monitoring method in agricultural products with supercritical fluid extraction and	Nishina, Takeshi Fukushima, Kouhei Murakawa, Hiroshi Tobino,	Kumamoto-ken Hoken Kankyo Kagaku Kenkyushoho (2006), Volume Date 2005, 35, 57-63 CODEN: KHKKF8; ISSN: 1341-6480	yes	not Efate

GC/MS. (3)	Toshiaki			
Comparison of supercritical fluid extraction (SFE)-GC/MS method and acetonitrile extraction. GC/MS method for simultaneous analysis of pesticide residue in mini-tomato	Murakawa, Hiroshi Fukushima, Kouhei Nishina, Takeshi Araki, Seishi Tobino, Toshiaki	Kumamoto-ken Hoken Kankyo Kagaku Kenkyushoho (2006), Volume Date 2005, 35, 45-50 CODEN: KHKKF8; ISSN: 1341-6480	yes	not Efate
Analysis of simultaneous screening for 277 pesticides in malt and beer by liquid chromatography with tandem mass spectrometry	Omote, M. Harayama, K. Sasaki, T. Mochizuki, N. Yamashita, H.	Journal of the American Society of Brewing Chemists (2006), 64(3), 139-150 CODEN: JSBCD3; ISSN: 0361-0470	yes	not Efate
Multiresidue analysis of pesticides in agricultural products. Part II. Application of combination column of macroporous diatomaceous earth and graphitized carbon black for pesticide residue analysis	Iijima, Kazuaki Saka, Machiko Odanaka, Yoshitsugu Kato, Yasuhiro Takada, Makoto Hosomi, Masaaki	Journal of Pesticide Science (Tokyo, Japan) (2006), 31(2), 190-202 CODEN: JPSTCF; ISSN: 1348-589X	yes	not Efate
Growth and yield of irrigated cotton (<i>Gossypium hirsutum</i>) as influenced by different chemical and non-chemical weed-management practices	Sivakumar, C. Subbian, P.	Indian Journal of Agronomy (2002), 47(1), 123-129 CODEN: IJAGAZ; ISSN: 0537-197X	yes	not Efate
Estimated intakes of pesticides from box lunches and related commercial foods	Ogawa, Masahiko Sakamoto, Akiko Ohkuma, Kazuyuki Sato, Makoto Shimura, Kyoko	Mie-ken Eisei Kenkyusho Nenpo (1999), Volume Date 1997, 43, 79-91 CODEN: MKENDS; ISSN: 0912-5752	yes	not Efate

Extraction, Analysis, and Study on the Volatiles in Roselle Tea	Chen, Shyh-Hung Huang, Tzou-Chi Ho, Chi-Tang Tsai, Pi-Jen	Journal of Agricultural and Food Chemistry (1998), 46(3), 1101-1105 CODEN: JAFCAU; ISSN: 0021-8561	yes	not Efate
Effect of herbicide mixtures and sequential application on weed control in transplanted rice (<i>Oryza sativa</i>)	Rao, A. S. Singh, R. P.	Indian Journal of Agronomy (1997), 42(1), 77-81 CODEN: IJAGAZ; ISSN: 0537-197X	yes	not Efate
Influence of soil moisture on phytotoxicity of cinmethylin to various crops	Russell, Steven G. Monaco, Thomas J. Weber, Jerome B.	Weed Science (1991), 39(3), 402-7 CODEN: WEESA6; ISSN: 0043-1745	yes	not Efate
Factors affecting the performance and crop phytotoxicity of a new rice herbicide, cinmethylin. I. Effects of water depth and soil type on the distribution and uptake of cinmethylin by transplanted and direct-seeded rice	Grayson, B. Terence Webb, James D.	Pesticide Science (1991), 32(2), 207-18 CODEN: PSSCBG; ISSN: 0031-613X	yes	not Efate
Influence of simulated rainfall and soil moisture on herbicidal activity of cinmethylin	Russell, Steven G. Monaco, Thomas J. Weber, Jerome B.	Weed Science (1990), 38(3), 267-72 CODEN: WEESA6; ISSN: 0043-1745	yes	not Efate
Natural products phytotoxicity: a bioassay suitable for small quantities of slightly water-soluble compounds	Dornbos, D. L., Jr. Spencer, G. F.	Journal of Chemical Ecology (1990), 16(2), 339-52 CODEN: JCECD8; ISSN: 0098-0331	yes	not Efate
Seedling volunteer asparagus, <i>Asparagus</i>	Boydston, Rick A.	Weed Technology (1988), 2(3), 294-8 CODEN: WETEE9; ISSN: 0890-037X	yes	not Efate

officinalis, control with herbicides				
Metabolic fate of cinmethylin in rats	Lee, Philip W. Stearns, Stephen M. Powell, Walter R. Stoutamire, Donald W. Payne, George B. Woodward, Michael D. Burton, William B. Silveira, Edward J. Ehmann, Axel	Journal of Agricultural and Food Chemistry (1986), 34(2), 162-70 CODEN: JAFCAU; ISSN: 0021- 8561	yes	not Efate

Table KCA 8.6.1/01-05 References evaluated as potentially relevant for Efate dossier

Title	Author	Source/Patent No	Reference further evaluated as potentially relevant for Efate dossier	Comments / Justification
AMMONIUM THIOSULFATE EFFECT ON HERBICIDE LONGEVITY IN SOIL.	GOOS R J [Reprint author] AHRENS W H	Agronomy Journal, (1992) Vol. 84, No. 3, pp. 459-463. CODEN: AGJOAT. ISSN: 0002-1962.	yes	See Table KCA 8.6.1/01-06. Further evaluated
SOIL BIOACTIVITY PERSISTENCE AND LEACHING OF CINMETHYLIN IMAZAQUIN AND METAZACHLO R.	LOLAS P C [Reprint author] GALOPOULOS A	Zizaniology, (1985) Vol. 1, No. 4, pp. 221-228. CODEN: ZIZADJ. ISSN: 0255-7940.	yes	See Table KCA 8.6.1/01-06. Further evaluated
AEROBIC SOIL METABOLISM AND SOIL SORPTION OF CINMETHYLIN.	WOODWARD M D [Reprint author] STOUTAMIRE D W SILVEIRA E J	Abstracts of Papers American Chemical Society, (1986) Vol. 191, No. 9. Meeting Info.: 191ST AMERICAN CHEMICAL SOCIETY NATIONAL MEETING, NEW YORK, N.Y., USA, APR. 13-18, 1986. ABSTR PAP AM CHEM SOC. CODEN: ACSRAL. ISSN: 0065-7727.	yes	See Table KCA 8.6.1/01-06. Further evaluated
Acute toxicity assessment of 20 herbicides to the green alga <i>Scenedesmus quadricauda</i> (Turp.) Breb.	Ma, J. Lin, F. Wang, S. Xu, L.	Bulletin of Environmental Contamination and Toxicology (2004), Volume 72, Number 6, pp. 1164-1171, 19 refs. ISSN: 0007-4861 DOI: 10.1007/s00128-004-0366-4 Published by: Springer-Verlag New York Inc., New York	no	Ecotoxicology. No relevant endpoint.
Cinmethylin - a	Jones, R. G.	Pest management in	no	Herbicidal

new herbicide developed for use in rice.	Editor(s): Grayson, B.T. Green, M.B. Copping, L.G.	rice (conference held by the Society of Chemical Industry, London, UK, 4-7 June 1990). (1990), pp. 349-357, 2 refs. Published by: Elsevier Applied Science Publishers Ltd., Barking Conference: Pest management in rice (conference held by the Society of Chemical Industry, London, UK, 4-7 June 1990).		activity. No relevant endpoint.
Retention and mobility of AC 252,214, chlorsulfuron, prometryn, and SD 95481 in soils.	Liu, S. L. Weber, J. B.	Proceedings, Southern Weed Science Society, 38th annual meeting. (1985), pp. 465-474, 4 refs. Conference: Proceedings, Southern Weed Science Society, 38th annual meeting.	yes	See Table KCA 8.6.1/01-06. Further evaluated
Persistence of cynmethylin activity in soil.	Price, T. P. Forney, D. R.	Proceedings, North Central Weed Control Conference. (1985), Number Vol.40, 16 p. Conference: Proceedings, North Central Weed Control Conference.	no	Herbicidal activity. No relevant endpoint.
The activity, pre-emergence selectivity and persistence of some recently developed herbicides: DOWCO 453, quizalofop-ethyl, BAS 517 OOH, cinmethylin, AC 263,499 and RST 20024 H.	Richardson, W. G. West, T. M.	Technical Report, Agricultural and Food Research Council, Long Ashton Research Station, Weed Research Division (1986), Number 91, 62 p., 4 refs.	no	Herbicidal activity. No relevant endpoint.
Aerobic soil metabolism and soil sorption of cinmethylin.	Woodward, M. D. Stoutamire, D. W. Silveira, E. J.	Abstracts of papers, 191st ACS national meeting. (1986), AGRO 62 p. Published by: American Chemical Society, Washington DC Conference: Abstracts	no	Duplicate.

		of papers, 191st ACS national meeting.		
Cinch herbicide (SD 95481): a new soil applied herbicide for use in broadleaved crops.	Bozarth, G. A. May, J. W. Goss, J. R. Long, J. H.	Proceedings, Southern Weed Science Society, 37th annual meeting. (1984), 390 p. Conference: Proceedings, Southern Weed Science Society, 37th annual meeting.	yes	See Table KCA 8.6.1/01-06. Further evaluated
Yellow foxtail life cycle and germination potential in an established alfalfa hay environment.	Wallace, R. W.	Proceedings, 37th annual California weed conference., pp. 12-13 Conference: Proceedings, 37th annual California weed conference.	no	Herbicidal activity. No relevant endpoint.
SD 95481, a new soil applied herbicide for use in soybeans.	Goss, J. R. Long, J. H.	Proceedings, North Central Weed Control Conference. (1983), 155 p. Conference: Proceedings, North Central Weed Control Conference.	yes	See Table KCA 8.6.1/01-06. Further evaluated
Today's herbicide: Cinch herbicide.	May, J. W.	Weeds Today (1984), Volume 15, Number 4, pp. 7-8	yes	See Table KCA 8.6.1/01-06. Further evaluated
SD 95481 - a new soil-applied herbicide for use in broadleaved crops.	May, J. W. Long, J. H., Jr. Goss, J. R.	Proceedings of the Western Society of Weed Science. (1984), pp. 93-94 Conference: Proceedings of the Western Society of Weed Science.	yes	See Table KCA 8.6.1/01-06. Further evaluated
Effect-Directed Analysis of Toxicants in Sediment with Combined Passive Dosing and in Vivo Toxicity Testing	Qi, Hongxue Li, Huizhen Wei, Yanli Mehler, W. Tyler Zeng, Eddy Y. You, Jing	Environmental Science + Technology (2017), 51(11), 6414-6421 CODEN: ESTHAG; ISSN: 0013-936X	no	Analysis of sediments of the Pearl River (China). Cinmethylin detected in sediments between 4.20 and 39.6 ng/g dry weight. Non-EU monitoring;

				No relevant endpoints.
Mineralising urban net-zero water treatment: Phase II field results and design recommendations	Gassie, Lucien W. Englehardt, James D. Wang, Jian Brinkman, Nichole Garland, Jay Gardinali, Piero Guo, Tianjiao	Water Research (2016), 105, 496-506 CODEN: WATRAG; ISSN: 0043-1354	no	The paper describes the performance of a water management system. No relevant endpoints.
Toxicokinetic triage for environmental chemicals	Wambaugh, John F. Wetmore, Barbara A. Pearce, Robert Strope, Cory Goldsmith, Rocky Sluka, James P. Sedykh, Alexander Tropsha, Alex Bosgra, Sieto Shah, Imran Judson, Richard Thomas, Russell S. Setzer, R. Woodrow	Toxicological Sciences (2015), 147(1), 55-67 CODEN: TOSCF2; ISSN: 1096-0929	no	The paper investigates the applicability/ reliability of high-throughput toxicokinetic models. No relevant endpoints.
Application of organic matter screening software in environmental warning	Jia, Liming Chen, Xin Jiang, Bo Du, Yingqiu	Huanjing Huaxue (2015), 34(5), 1022-1024 CODEN: HUHADB; ISSN: 0254-6108	no	Not English. Non-EU monitoring; No relevant endpoints.
A pilot survey of 39 Victorian WWTP effluents using a high speed luminescent umu test in conjunction with a novel GC-MS-database technique for automatic identification of micropollutants	Allinson, Mayumi Kageyama, Shiho Nakajima, Daisuke Kamata, Ryo Shiraishi, Fujio Goto, Sumio Salzman, Scott Andrew Allinson, Graeme	Water Science and Technology (2012), 66(4), 768-774 CODEN: WSTED4; ISSN: 0273-1223	no	Monitoring of pesticides in Australian wastewater treatment plant effluents. Non-EU monitoring; No relevant endpoints.

Zebrafish developmental screening of the ToxCast Phase I chemical library	Padilla, S. Corum, D. Padnos, B. Hunter, D. L. Beam, A. Houck, K. A. Sipes, N. Kleinstreuer, N. Knudsen, T. Dix, D. J. Reif, D. M.	Reproductive Toxicology (2012), 33(2), 174-187 CODEN: REPTED; ISSN: 0890-6238	no	Ecotoxicology. No relevant endpoint.
Herbicidal Activity of Cineole Derivatives	Barton, Allan F. M. Dell, Bernard Knight, Allan R.	Journal of Agricultural and Food Chemistry (2010), 58(18), 10147-10155 CODEN: JAFCAU; ISSN: 0021-8561	no	Herbicidal activity. No relevant endpoint.
Pesticide residue monitoring method in agricultural products with shaking and salting-out extraction	Yoshida, Tatsuo Murakawa, Hiroshi Hukushima, Kouhei Yoshimoto, Hidekazu Tobino, Toshiaki	Kumamoto-ken Hoken Kankyo Kagaku Kenkyushoho (2009), Volume Date 2008, 38, 40-50 CODEN: KHKKF8; ISSN: 1341-6480	no	Analytics/ Consumer Safety. No relevant endpoints.
Pesticide persistence in the environment - collected data and structure-based analysis	Alikhanidi, Sokratis Takahashi, Yoshimasa	Journal of Computer Chemistry, Japan (2004), 3(2), 59-70 CODEN: JCCJAG; ISSN: 1347-1767	no	No data generated in this study.
Calculating pesticide sorption coefficients (Kd) using selected soil properties	Weber, Jerome B. Wilkerson, Gail G. Reinhardt, Carl F.	Chemosphere (2004), 55(2), 157-166 CODEN: CMSHAF; ISSN: 0045-6535	no	No data generated in this study.
Prediction of Soil Sorption Coefficient of a Diverse Set of Organic Chemicals From Molecular Structure	Huuskonen, Jarmo	Journal of Chemical Information and Computer Sciences (2003), 43(5), 1457-1462 CODEN: JCISD8; ISSN: 0095-2338	no	No data generated in this study.
Simultaneous determination of pesticides and their seasonal variation in Ishikari River basin	Kondoh, Hideharu Fukuyama, Ryuji Liu, Ai-Min	Kankyo Kagaku (2001), 11(2), 253-266 CODEN: KKAGEY; ISSN: 0917-2408	no	81 compounds (pesticides and transformation products) were monitored between

				1998 and 2000 in the Ishikari River (Japan). Non-EU monitoring; No relevant endpoints.
Inhibition of plant asparagine synthetase by monoterpene cineoles	Romagni, Joanne G. Duke, Stephen O. Dayan, Franck E.	Plant Physiology (2000), 123(2), 725-732 CODEN: PLPHAY; ISSN: 0032-0889	no	Herbicidal activity. No relevant endpoint.
Survey of pesticide residues in health tea and herbal tea	Ogawa, Masahiko Sakamoto, Akiko Ohkuma, Kazuyuki Nakayama, Osamu	Nippon Shokuhin Kagaku Gakkaishi (1999), 6(2), 140-145 CODEN: NSKGF4; ISSN: 1341-2094	no	Consumer safety. No relevant endpoints.
Compounds with selective toxicity towards the off-flavor metabolite-producing cyanobacterium <i>Oscillatoria</i> cf. <i>chalybea</i>	Schrader, Kevin K. de Regt, Marjan Q. Tidwell, Paula D. Tucker, Craig S. Duke, Stephen O.	Aquaculture (1998), 163(1,2), 85-99 CODEN: AQCLAL; ISSN: 0044-8486	no	The study investigates the toxicity of several compounds (including Cinmethylin) towards the cyanobacterium <i>O. cf. chalybea</i> and the green alga <i>Selenastrum capricornutum</i> . No relevant endpoints.
Adsorptivity of pesticides to suspended soil particles in water	Matsuki, Tsukasa Takashima, Kumiko Konaka, Yukari Nohara, Kenji Yano, Yasumasa Kamei, Katsuhiro Okinishi, Norio	Hiroshima-shi Eisei Kenkyusho Nenpo (1996), Volume Date 1995, 15, 54-58 CODEN: HEKNEU; ISSN: 0911-2073	no	In Japanese and no translation is available to BASF.

Significance and application of microbial toxicity tests in assessing ecotoxicological risks of contaminants in soil and sediment	van Beelen, P. Doelman, P.	Chemosphere (1997), 34(3), 455-499 CODEN: CSMHAF; ISSN: 0045-6535	no	The study evaluates different microbial toxicity tests and proposes a novel method to derive soil and sediment quality guidelines using microbial toxicity tests. No relevant endpoints.
Microbial models of soil metabolism: biotransformations of prosulfuron, fludioxonil, and Cinch by soil and soil microorganisms (<i>Streptomyces griseolus</i>)	Kulowski, Kerry	(1996) 132 pp. Avail.: From degree-granting institution From: Diss. Abstr. Int., B 1996, 57(5), 3173	yes	See Table KCA 8.6.1/01-06. Further evaluated
Validation of models of uptake of organic chemicals by plant roots	Polder, Marieke D. Hulzebos, Etje M. Jager, D. Tjalling	Environmental Toxicology and Chemistry (1995), 14(9), 1615-23 CODEN: ETOCDK; ISSN: 0730-7268	yes	See Table KCA 8.6.1/01-06. Further evaluated
Effects of preemergence and postemergence herbicides on urea hydrolysis and nitrification of urea nitrogen in soil	Martens, D.A. Bremner, J.M.	Biology and Fertility of Soils (1994), 17(4), 309-13 CODEN: BFSOEE; ISSN: 0178-2762	no	Not relevant to Efate. No relevant endpoints.
Efficacy of downy brome herbicides as influenced by soil properties	Blackshaw, R. E. Moyer, J. R. Kozub, G. C.	Canadian Journal of Plant Science (1994), 74(1), 177-83 CODEN: CPLSAY; ISSN: 0008-4220	no	Herbicidal activity. No relevant endpoint.
Study of root uptake and xylem translocation of cinmethylin and related	Hsu, Francis C. Marxmillier, Ronald L. Yang, Alex Y. S.	Plant Physiology (1990), 93(4), 1573-8 CODEN: PLPHAY; ISSN: 0032-0889	no	Describe the root uptake and the xylem translocation

compounds in detopped soybean roots using a pressure chamber technique				of cinmethylin. No relevant endpoints.
Bioaccumulation of cinmethylin in bluegill sunfish	Lee, Philip W. Forbis, Alan D. Franklin, Larry	Journal of Agricultural and Food Chemistry (1990), 38(1), 323-7 CODEN: JAFCAU; ISSN: 0021-8561	no	Ecotoxicology. No relevant endpoint.
Metabolic fate of cinmethylin in goat	Woodward, Michael D. Stearns, Stephen M. Lee, Philip W.	Journal of Agricultural and Food Chemistry (1989), 37(3), 787-91 CODEN: JAFCAU; ISSN: 0021-8561	no	Consumer Safety No relevant endpoints.
The use of WL95481 in transplanted paddy rice	Moncorge, J. M. Murphy, M. W.	Proceedings - British Crop Protection Conference--Weeds (1987), (1), 197-204 CODEN: PBCWDF; ISSN: 0144-1604	yes	See Table KCA 8.6.1/01-06. Further evaluated
The physical and chemical properties of the herbicide cinmethylin (SD 95481)	Grayson, B. Terence Williams, Karen S. Freehauf, Paul A. Pease, Rodney R. Ziesel, William T. Sereno, Richard L. Reinsfelder, Ronald E.	Pesticide Science (1987), 21(2), 143-53 CODEN: PSSCBG; ISSN: 0031-613X	yes	See Table KCA 8.6.1/01-06. Further evaluated
Synthesis of radiolabeled herbicides for environmental fate studies	Burton, W. B. Hoewing, T. D. Naidu, Motupalli V.	Synth. Appl. Isot. Labeled Compd. Proc. Int. Symp., 2nd (1986), Meeting Date 1985, 317-18. Editor(s): Muccino, Richard Robert. Publisher: Elsevier, Amsterdam, Neth. CODEN: 55BUAT	no	Describes the synthesis route for the production of 14C-labeled cinmethylin. No relevant endpoints.
Cinmethylin, imazaquin and metazachlor performance for weed control in tobacco	Lolas, P. C.	Proceedings - British Crop Protection Conference--Weeds (1985), (3), 841-8 CODEN: PBCWDF; ISSN: 0144-1604	yes	See Table KCA 8.6.1/01-06. Further evaluated
SD 95481 a versatile new herbicide with wide spectrum crop use	May, J. W. Goss, J. R. Moncorge, J. M. Murphy, M. W.	Proceedings - British Crop Protection Conference--Weeds (1985), (1), 265-70 CODEN: PBCWDF; ISSN: 0144-1604	yes	See Table KCA 8.6.1/01-06. Further evaluated

Table KCA 8.6.1/01-06 References evaluated in detail for relevance for the Efate dossier

Title	Author	Source/Patent No	To be used for dossier: yes/no	Comments / Justification for non-relevance
AMMONIUM THIOSULFATE EFFECT ON HERBICIDE LONGEVITY IN SOIL.	GOOS R J [Reprint author] AHRENS W H	Agronomy Journal, (1992) Vol. 84, No. 3, pp. 459-463. CODEN: AGJOAT. ISSN: 0002-1962.	no	<p>The study investigates the effect of a fertilizer (ammonium thiosulfate) on the persistence of several herbicides (including cinmethylin) in soil. No specific analysis of the residues of cinmethylin in soil over time was performed. Only the residual herbicidal activity was monitored, by observing the plant fresh weight reduction of foxtail millet (bioassay).</p> <p>Study not suitable to derive Efate endpoints. No relevance for EU risk assessment.</p>
SOIL BIOACTIVITY PERSISTENCE AND LEACHING OF CINMETHYLIN IMAZAQUIN AND METAZACHLOR.	LOLAS P C [Reprint author] GALOPOULOS A	Zizaniology, (1985) Vol. 1, No. 4, pp. 221-228. CODEN: ZIZADJ. ISSN: 0255-7940.	no	<p>The persistence and the leaching potential of three herbicides (including cinmethylin) were evaluated in greenhouse and in field studies. No specific analysis of the residues of cinmethylin in soil was performed. The residues present in soil were evaluated by monitoring the reduction of oat growth (bioassay).</p> <p>Study not suitable to derive Efate endpoints. No relevance for EU risk assessment.</p>

AEROBIC SOIL METABOLISM AND SOIL SORPTION OF CINMETHYLIN.	WOODWARD M D [Reprint author] STOUTAMIRE D W SILVEIRA E J	Abstracts of Papers American Chemical Society, (1986) Vol. 191, No. 9. Meeting Info.: 191ST AMERICAN CHEMICAL SOCIETY NATIONAL MEETING, NEW YORK, N.Y., USA, APR. 13-18, 1986. ABSTR PAP AM CHEM SOC. CODEN: ACSRAL. ISSN: 0065-7727.	no	The reference is only a short abstract.
Retention and mobility of AC 252,214, chlorsulfuron, prometryn, and SD 95481 in soils.	Liu, S. L. Weber, J. B.	Proceedings, Southern Weed Science Society, 38th annual meeting. (1985), pp. 465-474, 4 refs. Conference: Proceedings, Southern Weed Science Society, 38th annual meeting.	no	<p>The mobility of several herbicides, including cinmethylin, was investigated in an adsorption/desorption study and in a soil column study.</p> <p>Non-guideline conditions.</p> <p>Adsorption/desorption experiments: Only the amount of radioactivity in the aqueous phase is determined. The missing radioactivity is assumed to be sorbed to the soil. But no information is provided on the mass balance and on the stability of the test substance. Only reported percentages of adsorption. No sorption coefficients were reported.</p> <p>Study not suitable to derive E fate endpoints. No relevance for EU risk assessment.</p>

Cinch herbicide (SD 95481): a new soil applied herbicide for use in broadleaved crops.	Bozarth, G. A. May, J. W. Goss, J. R. Long, J. H.	Proceedings, Southern Weed Science Society, 37th annual meeting. (1984), 390 p. Conference: Proceedings, Southern Weed Science Society, 37th annual meeting.	no	The reference is a short abstract and only describes broadly the environmental fate profile of cinmethylin. Contains no relevant endpoints. No relevance for EU risk assessment.
SD 95481, a new soil applied herbicide for use in soybeans.	Goss, J. R. Long, J. H.	Proceedings, North Central Weed Control Conference. (1983), 155 p. Conference: Proceedings, North Central Weed Control Conference.	no	The reference is a short abstract and only describes broadly the environmental fate profile of cinmethylin. Contains no relevant endpoints. No relevance for EU risk assessment.
Today's herbicide: Cinch herbicide.	May, J. W.	Weeds Today (1984), Volume 15, Number 4, pp. 7-8	no	The reference is a short abstract and only describes broadly the environmental fate profile of cinmethylin. Contains no relevant endpoints. No relevance for EU risk assessment.
SD 95481 - a new soil-applied herbicide for use in broadleaved crops.	May, J. W. Long, J. H., Jr. Goss, J. R.	Proceedings of the Western Society of Weed Science. (1984), pp. 93-94 Conference: Proceedings of the Western Society of Weed Science.	no	The reference is a short abstract and only describes broadly the environmental fate profile of cinmethylin. Contains no relevant endpoints. No relevance for EU risk assessment.
Microbial models of soil metabolism: biotransformations of prosulfuron, fludioxonil, and Cinch by soil and soil microorganisms (Streptomyces	Kulowski, Kerry	(1996) 132 pp. Avail.: From degree-granting institution From: Diss. Abstr. Int., B 1996, 57(5), 3173	no	Pure cultures of representative soil microorganisms cultivated in the laboratory were used as models to predict the metabolism of several xenobiotics (including cinmethylin) in soil. The metabolic pathway obtained

griseolus)				<p>with the model microorganisms was compared to the metabolic pathway observed when cinmethylin is incubated with a soil suspension.</p> <p>The study is not performed according to guideline and cannot be used to derive endpoints.</p> <p>No relevant endpoints.</p> <p>The findings are similar to those derived from the regulatory studies; there were no metabolites measured >5 %.</p>
Validation of models of uptake of organic chemicals by plant roots	Polder, Marieke D. Hulzebos, Etje M. Jager, D. Tjalling	Environmental Toxicology and Chemistry (1995), 14(9), 1615-23 CODEN: ETOCDK; ISSN: 0730-7268	no	<p>Not relevant to Efate.</p> <p>No relevant endpoints.</p>
The use of WL95481 in transplanted paddy rice	Moncorge, J. M. Murphy, M. W.	Proceedings - British Crop Protection Conference--Weeds (1987), (1), 197-204 CODEN: PBCWDF; ISSN: 0144-1604	no	<p>Not relevant to Efate. No relevant endpoints.</p>
The physical and chemical properties of the herbicide cinmethylin (SD 95481)	Grayson, B. Terence Williams, Karen S. Freehauf, Paul A. Pease, Rodney R. Ziesel, William T. Serenio, Richard L. Reinsfelder, Ronald E.	Pesticide Science (1987), 21(2), 143-53 CODEN: PSSCBG; ISSN: 0031-613X	no	<p>The reference mainly contains information on the physico-chemical properties of cinmethylin. Soil organic matter / water sorption coefficient (K_{om}) are mentioned. The conduct of the sorption experiment is only briefly described.</p>
Cinmethylin,	Lolas, P. C.	Proceedings -	no	<p>The study focuses on the</p>

imazaquin and metazachlor performance for weed control in tobacco		British Crop Protection Conference-- Weeds (1985), (3), 841-8 CODEN: PBCWDF; ISSN: 0144-1604		herbicidal activity. The soil persistence is also addressed but no specific analytical method was used to determine the residues of cinmethylin in the soil samples. The residues present at a given time and a given soil depth were evaluated using a bioassay (reduction of oat growth). The study cannot be used to derive degradation endpoints. No relevant endpoints.
SD 95481 a versatile new herbicide with wide spectrum crop use	May, J. W. Goss, J. R. Moncorge, J. M. Murphy, M. W.	Proceedings - British Crop Protection Conference-- Weeds (1985), (1), 265-70 CODEN: PBCWDF; ISSN: 0144-1604	no	The reference describes the herbicidal activity. General comments on the environmental fate profile of cinmethylin are included but no relevant endpoints are mentioned. No relevant for risk assessment.

In conclusion, the HSE evaluator agrees that no studies identified in the literature review were considered relevant for the Environmental Fate dossier.

REFERENCES RELIED ON

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCA 7.1.1.1/1	Stewart L., Abernethy A.	2016 a	Cinmethylin - Aerobic degradation of [14C]- Cinmethylin (Reg.No. 900202) in soil 2015/1186904 Charles River Laboratories Edinburgh Ltd., Tranent East Lothian EH33 2NE, United Kingdom yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.1.1.2/1	Staudenmaier H., Pape L.	2017 a	Anaerobic soil metabolism of Cinmethylin (BAS 684 H) 2016/1053970 BASF SE, Limburgerhof, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.1.1.3/1	Hassink J.	2017 c	Soil photolysis of BAS 684 H 2016/1333357 BASF SE, Limburgerhof, Germany	No	Yes	Data for first approval	BASF	None – data for first approval

			Fed.Rep. yes Unpublished					
KCA 7.1.2.1.1/1	He W.	2018 a	Kinetic evaluation of laboratory aerobic soil degradation studies with BAS 684 H: Determination of modeling endpoints according to FOCUS 2017/1217117 Dr. Knoell Consult GmbH, Mannheim, Germany Fed.Rep. no Unpublished	No	No	Not applicable	BASF	None – data for first approval
KCA 7.1.2.2.1/1	Gut T.	2017 a	Field soil dissipation study of BAS 684 H in the formulation BAS 684 02 H on bare soil at 6 different sites in Northern and Southern Europe, 2015-2017 2017/1190305 SGS Institut Fresenius GmbH, Taunusstein, Germany Fed. Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.1.2.2.1/2	Gut T.	2017 b	Amendment 1: Field soil dissipation study of BAS 684 H in the formulation BAS 684 02 H on bare soil at 6	No	Yes	Data for first approval	BASF	None – data for first approval

			<p>different sites in Northern and Southern Europe, 2015-2017</p> <p>2017/1217703</p> <p>SGS Institut Fresenius GmbH, Taunusstein, Germany Fed. Rep.</p> <p>yes</p> <p>Unpublished</p>					
KCA 7.1.2.2.1/3	He W., Pape L.	2018 a	<p>Kinetic evaluation of a field dissipation study with BAS 684 H conducted in 2015 to 2017: Determination of trigger endpoints for the racemate and its enantiomers (Reg.No. 5925581 and Reg.No. 5925632) according to FOCUS</p> <p>2017/1199007</p> <p>Dr. Knoell Consult GmbH, Mannheim, Germany Fed.Rep.</p> <p>no</p> <p>Unpublished</p>	No	No	Not applicable	BASF	None – data for first approval
KCA 7.1.2.2.1/4	He W., Pape L.	2018 a	<p>Kinetic evaluation of a field dissipation study with BAS 684 H conducted in 2015 to 2017: Determination of modeling endpoints for the racemate and its enantiomers (Reg.No.</p>	No	No	Not applicable	BASF	None – data for first approval

			5925581 and Reg.No. 5925632) according to FOCUS 2017/1199008 Dr. Knoell Consult GmbH, Mannheim, Germany Fed.Rep. no Unpublished					
KCA 7.1.2.2.1/5	Mitchell J. et al.	2018 a	Terrestrial field dissipation of the herbicide BAS 684 H following broadcast applications of BAS 684 02 H (EC) 2017/7017329 Waterborne Environmental Inc., Leesburg VA, United States of America yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.1.2.2.1/6	Stewart L.	2016 b	Cinmethylin - Comparison of extraction methods to extract [14C]- Cinmethylin (Reg.No. 900202) from soil 2016/1134753 Charles River Laboratories Edinburgh Ltd., Tranent East Lothian EH33 2NE, United	No	Yes	Data for first approval	BASF	None – data for first approval

			Kingdom yes Unpublished					
KCA 7.1.2.2.1/7	Bodsch J.	2017 a	Determination of the storage stability of the BAS 684 H racemate in soil 2017/1202195 SGS Institut Fresenius GmbH, Taunusstein, Germany Fed. Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.1.2.2.1/8	Perez S., Jones A.	2018 a	Freezer storage stability of BAS 684 H (both enantiomers, Reg. No. 5925632 and 5925581) in soil 2018/7001858 ADPEN Laboratories Inc., Jacksonville FL, United States of America yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.1.2.2.1/9	Jeffries M., Warren R.	2018 a	European ecoregion similarity to six BAS 684 H terrestrial field dissipation sites in North America: A crosswalk exercise using ENASGIPS v3.0	No	No	Not applicable	BASF	None – data for first approval

			2017/7016807 BASF Corp., Research Triangle Park NC, United States of America no Unpublished					
KCA 7.1.2.2.1/ XX	Donaldson, F.P.	2020	Kinetic evaluation of a field dissipation study with BAS 684 H conducted in the USA from 2015 to 2017; Determination of modelling endpoints according to FOCUS 2019/2052931 BASF Corp., Research Triangle Park NC, United States of America no Unpublished	No	No	N/A	BASF	None – data for first approval
KCA 7.1.3.1.1/1	Harder U., Hegler F.	2017 a	Adsorption/desorption - Study with 14C-BAS 684 H on eight soils 2016/1171944 BASF SE, Limburgerhof, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.1.3.1.2/1	Platz K.	2017 a	QSAR estimation of adsorption	No	No	Not applicable	BASF	None – data for first approval

			coefficients of M684H001, M684H003 and M684H004 metabolites of BAS 684 H 2017/1200466 BASF SE, Limburgerhof, Germany Fed.Rep. no Unpublished					
KCA 7.2.1.1/1	Hassink J.	2017 a	BAS 684 H: Aqueous hydrolysis at four different pH values 2016/1330118 BASF SE, Limburgerhof, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.2.1.2/1	Hassink J.	2017 d	Aqueous photolysis of BAS 684 H 2017/1066632 BASF SE, Limburgerhof, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.2.1.3/1	Hassink J.	2017 f	Photolysis of BAS 684 H in sterile natural water 2017/1066631 BASF SE, Limburgerhof, Germany	No	Yes	Data for first approval	BASF	None – data for first approval

			Fed.Rep. yes Unpublished					
KCA 7.2.2.1/1	Schwarz H.	2017 a	BAS 684 H (Cinmethylin) - Determination of the ready biodegradability in the CO2- Evolution test 2017/1077282 BASF SE, Ludwigshafen/R hein, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.2.2.2/1	Mueller- Werthwein M., Hegler F.	2018 a	14C-BAS 684 H - Aerobic mineralization in surface water 2017/1156778 BASF SE, Limburgerhof, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.2.2.3/1	Mueller- Werthwein M., Freundlich B.	2017 a	Aerobic aquatic metabolism of BAS 684 H (Reg.No. 900202) 2016/1119819 BASF SE, Limburgerhof, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.2.2.3/2	He W., Pape L.	2017 a	Kinetic evaluation of	No	No	Not applicable	BASF	None – data for first

			<p>degradation of BAS 684 H in water/sediment systems: Determination of modeling endpoints according to FOCUS degradation kinetics</p> <p>2017/1021064</p> <p>Dr. Knoell Consult GmbH, Mannheim, Germany Fed.Rep.</p> <p>no</p> <p>Unpublished</p>					approval
KCA 7.2.3/1	Salzmann S., Cirpus P.	2018 a	<p>Estimation of reactivity of BAS 684 H in aqueous solution upon ozone and chlorination treatment</p> <p>2017/1224113</p> <p>BASF SE, Limburgerhof, Germany Fed.Rep.</p> <p>no</p> <p>Unpublished</p>	No	No	Not applicable	BASF	None – data for first approval
KCA 7.3.1/1	Hassink J.	2015 a	<p>Photochemical oxidative degradation of BAS 684 H (QSAR estimates)</p> <p>2015/1005045</p> <p>BASF SE, Limburgerhof, Germany Fed.Rep.</p> <p>no</p>	No	No	Not applicable	BASF	None – data for first approval

			Unpublished					
KCA 7.3.1/2	Hassink J.	2017 b	<p>Volatilisation of BAS 684 H after application of BAS 684 02 H on soil and plant surfaces</p> <p>2016/1331921</p> <p>BASF SE, Limburgerhof, Germany Fed.Rep.</p> <p>yes</p> <p>Unpublished</p>	No	Yes	Data for first approval	BASF	None – data for first approval
KCA 7.3.2/1	Wallace D.	2017 a	<p>Large outdoor wind tunnel study to evaluate volatilisation, short range transport and deposition of volatilised BAS 684 H (applied as EC formulated product) as a function of distance from the treated area (0-20 m)</p> <p>2017/1192649</p> <p>RLP AgroScience GmbH, Neustadt/Weinstrasse, Germany Fed.Rep.</p> <p>yes</p> <p>Unpublished</p>	No	Yes	Data for first approval	BASF	None – data for first approval