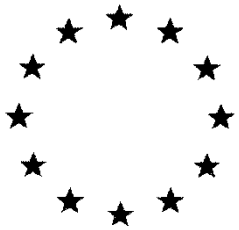
European Commission



Draft Assessment Report prepared according to the Commission Regulation (EU) N° 1107/2009

Napropamide-M

Volume 3 – B.8 (AS)

Rapporteur Member State: United Kingdom

Version History

When	What
June 2017	Initial DAR

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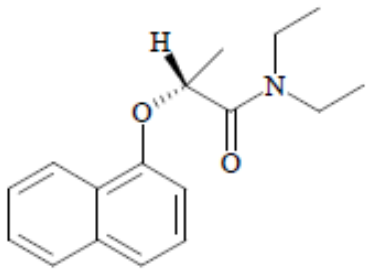
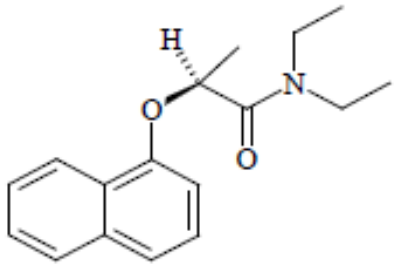
B.8. ENVIRONMENTAL FATE AND BEHAVIOUR

Data on the fate and behaviour of the new active substance, napropamide-M were submitted for first approval under Regulation 1107/2009. Napropamide-M is the resolved isomer of the existing active substance and racemate, napropamide. Figure B.8-1 below shows the two isomers, napropamide-M (D form) and napropamide-L (L form) that form the racemic mixture. All fate and behaviour studies evaluated here are newly submitted studies that concern the isomer napropamide-M exclusively. Chiral purity of the supplied test substance was reported as 99.9% of the D-isomer for all radiolabelled studies with radiochemical purity of napropamide-M stated as 99.10% and the specific activity as 56.10 mCi/mmol. The chemical purity of napropamide-M was reported as 99.5% at 280 nm. Chiral HPLC analysis was performed for all radiolabelled studies. The RMS has confirmed that napropamide-M remained as the D-isomer throughout all environmental fate radiolabelled studies and no isomerisation to the L-form occurred.

Figure B.8-1 Test substance, napropamide-M and its isomer L-napropamide



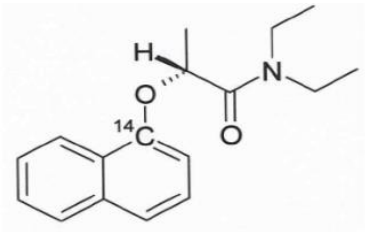
Napropamide-M
(D-isomer)



L-Napropamide
(L-isomer)

All radiolabelled studies in this section used [naphthyl-1-^{14}C] labelled napropamide-M. Figure B.8-2 below shows this radiolabel on the most stable part of the molecule, the ring structure. The RMS does not believe the non-labelled part of napropamide-M is likely to form metabolites or degradation products that have a greater stability. The RMS considers napropamide-M to be appropriately labelled for environmental fate and behaviour studies. All studies were conducted with test material of minimum radiochemical purity of 99.10%, unless stated otherwise. Specific radioactivity of the test substance was 56.10 µCi/ mg in all studies.

Figure B.8-2 The radiolabel [naphthyl-1-^{14}C] used in environmental fate and behaviour studies of napropamide-M



The recommended maximum annual rate of napropamide-M (formulated as D-Devrinol, code HBW03) is 765 g a.s/ ha, to be used as described in table B.8-1 below. The herbicide is intended for use as a pre-emergent broadcast spray on oilseed rape and brassica crops in all zones.

B.8-1 Intended GAP uses for the product D-Devrinol containing the active substance, napropamide-M

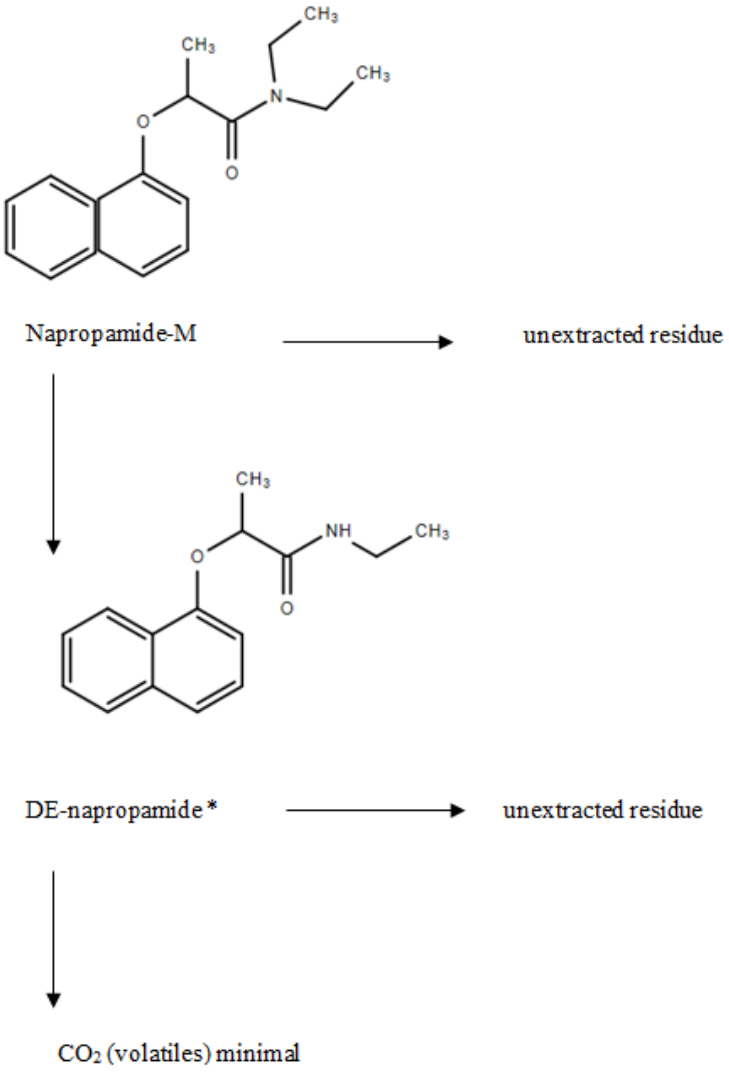
Crop	Member state or country	Method	Timing of application BBCH	Maximum number of applications	Maximum individual application rate (Kg a.s./ ha)	Comments
Winter oilseed rape	All zones	Broadcast spray and incorporation	Pre-sowing; summer-autumn	1	0.765	
Winter oilseed rape	All zones	Broadcast spray and no incorporation	Pre-sowing; summer-autumn	1	0.765	
Brassica vegetables	All zones	Broadcast spray and incorporation	Pre-planting/ pre-sowing; spring-summer	1	0.765	Treatment is made to soil prior to sowing or transplanting of crops
Brassica vegetables	All zones	Broadcast spray and no incorporation	Pre-planting/ pre-sowing; spring-summer	1	0.765	Treatment is made to soil prior to sowing or transplanting of crops
Winter oilseed rape	All zones	Broadcast spray and no incorporation	Post-sowing, pre-emergence/ BBCH 00-08, summer-autumn	1	0.765	
Brassica vegetables	All zones	Broadcast spray and no incorporation	Post-sowing, pre-emergence/ BBCH 00-08, summer-autumn	1	0.765	Treatment is made to soil post-sowing but not post-transplanting of crops

Unless stated otherwise, all studies were conducted according to GLP and are considered to be acceptable by the RMS.

B.8.1. FATE AND BEHAVIOUR IN SOIL

B.8.1.1. Route and rate of degradation in soil

Figure B.8.1.1-1 Proposed degradation pathway of napropamide-M in soil provided by the test facility



*and several other minor metabolites. The true degradation pathway cannot be confirmed but no major metabolites were observed in either laboratory or field soil studies.

B.8.1.1.1 Aerobic degradation in soil

Study author	Ahmad, S. (2015a)
Study title	[Naphthyl-1-^{14}C] Napropamide-M: Aerobic Soil Metabolism and Transformation
Study date	21/05/2015
Annex point	CA 7.1.1.1-01
Previous evaluation	New active substance, no previous studies submitted.

Study design

An aerobic soil degradation study was conducted with napropamide-M according to OECD: Guideline 307; Aerobic and Anaerobic Transformation in Soil, April 24, 2002. It was conducted in compliance with US GLP except for the one deviation: reference standards, with the exception of napropamide-M, were not GLP characterised. Since no major metabolites are formed in this study, accurate identification is not considered to be critical in this case.

Mass balances reported (75.7-154.1% AR) were significantly outside the range considered acceptable by the OECD guidelines for a radiolabelled study (i.e. 90- 110% AR). The RMS notes that dosing solution appears to have exceeded solubility of the test material in water. Napropamide-M has water solubility of 39 mg/l at neutral pH and 20°C. The dosing solution contained 25 mg active substance in a volume of 107 ml (92 ml water and 15 ml methanol to aid dissolution). Furthermore, a failure to perform a homogeneity and quantification check of the final dosing solution resulted in the potential for individual vessels to receive different amounts of the test substance, which may have led to the variable data. Consequently, the study author has normalised the results to percentage recovered radioactivity.

Radiolabelled [naphthyl-1-^{14}C] napropamide-M was applied at a target rate of 2.5 mg/kg soil, equivalent to a field application rate of 1.875 kg a.s./ha based on 5 cm soil depth (twice the proposed dose, 0.765 kg a.s./ha). Approximately 25 mg test substance (*ca* 30:70 % radiolabelled to non-radiolabelled) was dissolved in water (92 ml) and methanol (15 ml) before application to soil samples. The RMS notes that a high percentage of methanol (>10%) was used to prepare the dosing solution, but accepts that the water solubility of this compound is low.

Degradation of napropamide-M was studied in five soils, two from the UK, two from France and one from Spain, characterised as clay, loamy sand, sandy loam, clay loam, and loam respectively, (range 2-3.7 % O.M, pH 6.6-7.6). Details of the soil properties are given in Table B.8.1.1.1-1. No information was submitted regarding the pesticide history of the sites. Soils arrived at the laboratory within two to three days of sampling and were stored at *ca* 4ºC for 35 days until use.

Table B.8. 1.1.1-1 Physicochemical properties of test soils used in the aerobic laboratory degradation study

Soil (JRFA ID no.[1])	Classification[2]	pH (H_2O)	OM (%)	OC (%)	Sand[2] (%)	Silt[2] (%)	Clay[2] (%)	CEC (meq/ 100g)	Moisture content at 1/3 bar (%)
UK (102083)	Clay	7.3	3.7	2.15	37	11	52	32.6	35.4
UK (102168)	Loamy sand	7.5	2.3	1.34	85	9	6	7.4	10.5
France (102169)	Sandy loam	6.6	2.0	1.16	63	23	14	10.0	16.3
France (102170)	Clay loam	7.6	2.0	1.16	39	27	34	21.5	27.3
Spain (102171)	Loam	7.4	2.2	1.28	29	47	24	11.8	28.6

[1] JRFA ID= Test facility soil identification number
[2] USDA textural class

Soil samples (50 g dry weight equivalent, 2 mm sieved) were placed into individual incubation vessels fitted with traps. Equipment consisted of glass incubation vessels, ground glass connectors, and PVC tubing providing a moist air flow through system. Pre-study checks confirmed that the test substance did not adsorb to the glass vessels. A total of five traps consisted of three to collect volatile compounds and $^{14}CO_2$, with 1:1 ethylene glycol: water, 0.05 M sulphuric acid and 1 M potassium hydroxide respectively and two safety traps. Treated samples were incubated for 180 days under aerobic conditions in the dark at 20 ±2°C. Soil moisture was adjusted periodically by weight, every two weeks. Soil samples were analysed at 0, 1, 3, 7, 14, 21, 30, 60, 90, 120 and 180 days after treatment. No trapping media was associated with zero day samples.

The OECD 307 guidance recommends using controls for the measurement of microbial biomass initially, during and at the end of the studies: one with untreated soil and one with solvent only. A control with sterile soil should also be performed. The study author reported that 14 control vessels were prepared for each soil type plus one contingency control, but the nature of these control samples was not described. It was also reported in the study that a blank solution of methanol: water (1:3 v/v) was applied to the soil of control test vessels, to be used for measurement of microbial biomass at the end of the incubation period. However, the RMS was unable to determine from the study report whether the 14 control samples initially mentioned, were the same ones referred to as being treated with solvent blank solution. The microbial biomass measured via fumigation extraction methods at the start of the study (reported as "around the time of test substance application") and at the end of the incubation period, was provided in a table of soil characterisation (determined by another test facility). Again it was not clear if those biomass measurements given (table B.8.1.1.1-2) were from the solvent-spiked control samples. No other results were reported for any control samples.

Table B.8.1.1.1-2 Microbial biomass of soils used in the aerobic laboratory degradation study of napropamide-M

Soil (JRFA ID no.[1])	Classification[2]	Microbial Biomass	
		Initial (µg OC/ g sediment)	Final (µg OC/ g sediment)
UK (102083)	Clay	684.0	894.5
UK (102168)	Loamy sand	395.5	405.9
France (102169)	Sandy loam	337.5	364.1
France (102170)	Clay loam	538.6	573.6
Spain (102171)	Loam	360.8	409.0

1 JRFA ID= Test facility soil identification number
2 USDA textural class

Samples were extracted five times in total. Three times with acetonitrile, once with acetonitrile: water (1:1, v:v), once with methanol: 1N hydrochloric acid (1:1, v:v). Samples were shaken on an end-over-end shaker for one hour and then centrifuged after each extraction. It was suspected that certain samples had not been adequately shaken; therefore further extractions were deemed necessary. These extractions were done with 1:1 acetonitrile: water, 0.5% acetic acid in acetonitrile, and another 1:1 acetonitrile: water (samples marked in tables B.8.1.1.1-3 to -12 footnotes. Results of the original extractions were not provided in these cases). The RMS notes that a total of five extractions usually provides adequate extraction and any additional extractions should be a procedural step with original results transparently reported. Therefore the RMS is not able to confirm if the additional extractions were justified or what the impact on the results of those extra extractions is.

Radioactivity in the extracts was quantified by LSC prior to analysis to identify napropamide-M and its metabolites via reversed phase HPLC with on-line radio-detection. The identity of napropamide-M and its metabolites were confirmed using mass spectral analysis of representative samples. The average LOD and LOQ values for extracts were 11.5 and 44.9 dpm respectively. All sample extracts were analysed within five days of extraction.

Due to suspected non-homogenous dosing solution causing variability in the material balances, the material balances were normalised to the replicates (see Tables B.8.1.1.1-3 to -12).

Chiral HPLC analysis was performed on selected samples to confirm the ratio of D- and L-isomers in the sample. Pooled extracts from Day 0, 60 and 180 samples were concentrated and analysed for D- and L-isomers.

Unextracted residue was quantified by combustion with LSC and for the 120 day sample was fractionated into fulvic, humic and humin components for each soil type (see Table B.8.1.1.1-23). Combustion was performed using the R.J. Harvey Biological Oxidiser (OX 501) in triplicate. Combustion and trapping efficiencies were tested at the beginning of each session by combusting ^{14}C mannitol (^{14}-C standard). Combustion efficiencies were >95% or a correction was made to the calculation. The average LOD and LOQ values for combustions were 13.2 and 49.7 dpm respectively.

Results and Conclusion

Tables B.8.1.1.1-3 to -12 show material balances of radioactivity across all five soil types. Mass balance for all soils ranged from 75.7 – 154.1% AR (individual replicates), however there was no obvious decline of mass balance with time and it was considered that the variation may have been due to the dosing solution not being homogeneous. The results from the study were presented normalised to the total recovered radioactivity (RR) obtained for each replicate sample. The RMS has presented the results both in terms of original applied radioactivity (AR) and as RR, for transparency.

Mean extracted radioactivity decreased from 98.0 – 99.2% RR at day 0 to 71.2- 86.4% RR at 120 days, with no clear pattern of decline. Unextracted residues reached a maximum mean 34% AR (or 28.4% RR) at 120 days. CO_2/volatile levels were <4%AR or %RR. It was not specified in the study how much was CO_2 as opposed to other volatile compounds.

Table B.8.1.1.1-3 Material balances in clay soil (102083) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	0.43	<0.	<0.1	<0.1	0.6	1.6	<0.1	<0.1	0.1	<0.1
	R2	N/A	0.26	<0.	<0.1	<0.1	1.0	0.2	0.1	0.9	0.1	0.24
	Mean	N/A	0.3	<0.	<0.1	<0.1	0.8	0.9	<0.1	0.5	0.1	0.1
Extractions	R1	78.3	102.4	147	86.6	90.1	91.9	91.2	89.1	79.8[+]	83.6	77.7
	R2	74.5	94.8	84.	104.2[+]	92.8	87.4	99.6	86.3	64.1	78.5	70.5
	Mean	76.4	98.6	115	95.4	91.5	89.7	95.4	87.7	72.0	81.1	74.1
Unextracted residues	R1	1.8	2.9	7.0	7.6	12.1	16.2	19.7	15.5	22.0	18.9	9.4
	R2	1.2	2.5	6.1	11.7	11.1	14.7	14.0	14.7	22.2	18.8	15.4
	Mean	1.5	2.7	6.6	9.7	11.6	15.5	16.9	15.1	22.1	18.9	12.4
Material balance	R1	80.1	105.7	154[++]	94.2	102.2	108.7	112.5	104.6	101.8	102.6	87.1
	R2	75.7	97.6	90.	115.9	103.9	103.1	113.8	101.1	87.2	97.4	86.1
	Mean	77.9	101.6	122	105.1	103.1	105.9	113.2	102.9	94.5	100.0	86.6

[+] extra extractions done on replicate due to possible inadequate shaking.
[++] samples were reanalyzed for verification.
[+++] variable recoveries may be due to non-homogenous dosing solution
N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B.8.1.1.1-4. Material balances in clay soil (102083) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	0.4	<0.1	<0.1	<0.1	0.6	1.4	<0.1	<0.1	0.1	<0.1
	R2	N/A	0.3	<0.1	<0.1	<0.1	1.0	0.2	0.1	1.0	0.1	0.3
	Mean	N/A	0.3	<0.1	<0.1	<0.1	0.8	0.8	<0.1	0.5	0.1	0.1
Extractions	R1	97.8	96.9	95.5	91.9	88.2	84.5	81.1	85.2	78.4	81.5	89.3
	R2	98.4	97.2	93.3	89.9	89.3	84.8	87.5	85.4	73.5	80.6	81.9
	Mean	98.1	97.0	94.4	90.9	88.7	84.6	84.3	85.3	75.9	81.0	85.6
Unextracted residues	R1	2.2	2.7	4.5	8.1	11.8	14.9	17.5	14.8	21.6	18.4	10.7
	R2	1.6	2.6	6.7	10.1	10.7	14.3	12.3	14.5	25.5	19.3	17.9
	Mean	1.9	2.6	5.6	9.1	11.3	14.6	14.9	14.7	23.5	18.9	14.3
Material balance	R1	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	R2	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Mean	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B. 8.1.1.1-5 Material balances in loamy sand soil (102168) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	0.5	<0.1	<0.1	<0.1	<0.1	0.1	0.2	0.15	1.8	0.67
	R2	N/A	0.4	<0.1	<0.1	<0.1	1.2	0.2	0.1	0.25	0.4	0.66
	Mean	N/A	0.5	<0.1	<0.1	<0.1	0.6	0.2	0.2	0.2	1.1	0.7
Extractions	R1	81.7	104.3	89.0	98.1[+]	78.0	84.8	103.3	84.5	73.2	78.6	94.0
	R2	84.2	93.8	93.7	89.6	81.3[++]	85.7	100.3	93.3	77.2	82.5	95.7
	Mean	83.0	99.1	91.4	93.9	79.7	85.3	101.8	88.9	75.2	80.6	94.8
Unextracted residues	R1	1.8	1.1	3.0	6.0	5.6	5.5	6.8	7.6	9.6	13.2	9.6
	R2	1.7	1.1	4.1	2.4	3.3	6.2	9.7	8.3	9.2	11.2	8.0
	Mean	1.8	1.1	3.6	4.2	4.5	5.9	8.3	8.0	9.4	12.2	8.8
Material balance[+++]	R1	83.5	105.9	92.0	104.1	83.6	90.3	110.2	92.3	83.0	93.6	104.3
	R2	85.9	95.3	97.8	92.0	84.6	93.1	110.2	101.7	86.7	94.1	104.3
	Mean	84.7 [+++]	100.6	94.9	98.1	84.1	91.7	110.2	97.0	84.9	93.9	104.3

[+] 5th extraction was inadvertently done with 0.5% acetic acid instead of 1:1 acetonitrile:water
[++] Extra extraction done on replicate due to possible inadequate shaking.
[+++] variable recoveries may be due to non-homogenous dosing solution
N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B. 8.1.1.1-6 Material balances in loamy sand soil (102168) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	0.5	<0.1	<0.1	<0.1	<0.1	0.1	0.2	0.2	1.9	0.6
	R2	N/A	0.4	<0.1	<0.1	<0.1	1.3	0.2	0.1	0.3	0.4	0.6
	Mean	N/A	0.4	<0.1	<0.1	<0.1	0.6	0.1	0.2	0.2	1.2	0.6
Extractions	R1	97.9	98.5	96.7	94.2	93.3	93.9	93.7	91.5	88.2	84.0	90.1
	R2	98.1	98.5	95.8	97.4	96.1	92.1	91.0	91.7	89.1	87.7	91.7
	Mean	98.0	98.5	96.3	95.8	94.7	93.0	92.4	91.6	88.7	85.8	90.9
Unextracted residues	R1	2.1	1.0	3.3	5.8	6.7	6.1	6.2	8.2	11.6	14.1	9.2
	R2	1.9	1.1	4.2	2.6	3.9	6.7	8.8	8.2	10.7	11.9	7.7
	Mean	2.0	1.1	3.7	4.2	5.3	6.4	7.5	8.2	11.1	13.0	8.4
Material balance	R1	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	R2	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Mean	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B. 8.1.1.1-7 Material balances in sandy loam soil (102169) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	<0.1	<0.1	<0.1	<0.1	<0.1	0.4	4.9	0.2	0.1	0.37
	R2	N/A	<0.1	<0.1	<0.1	<0.1	<0.1	1.2	1.0	<0.1	<0.1	0.25
	Mean	N/A	<0.1	<0.1	<0.1	<0.1	<0.1	0.8	3.0	0.1	<0.1	0.3
Extractions	R1	82.1	95.9	83.9	80.0	82.2[+]	86.0	80.8	76.0	72.3	80.4	78.6[+]
	R2	78.8	87.0	84.1	81.3	84.0	81.8	72.8	97.5	75.7	86.2	72.2
	Mean	80.5	91.5	84.0	80.7	83.1	83.9	76.8	86.7	74.0	83.3	75.4
Unextracted residues	R1	1.0	1.84	4.47	6.5	15.7	20.6	13.8	29.6	19.3	22.5	15.05
	R2	0.9	1.33	5.79	5.6	16.3	21.1	15.2	26.1	19.2	22.0	16.1
	Mean	1.0	1.6	5.1	6.1	16.0	20.9	14.5	27.9	19.3	22.3	15.6
Material balance[+++]	R1	83.1	97.7	88.4	86.5	97.9	106.6	95.0	110.5	91.8	103.0	94.0
	R2	79.7	88.3	89.9	86.9	100.3	102.9	89.2	124.5	94.9	108.2	88.5
	Mean	81.4	93.0	89.1	86.7	99.1	104.8	92.1	117.5	93.4	105.6	91.3

[+] Extra extraction done on replicate due to possible inadequate shaking.
[+++] variable recoveries may be due to non-homogenous dosing solution
N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B. 8.1.1.1-8 Material balances in sandy loam soil (102169) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	<0.1	<0.1	<0.1	<0.1	<0.1	0.4	4.4	0.2	0.1	0.4
	R2	N/A	<0.1	<0.1	<0.1	<0.1	<0.1	1.3	0.8	<0.1	<0.1	0.3
	Mean	N/A	<0.1	<0.1	<0.1	<0.1	<0.1	0.9	2.6	0.1	0.1	0.3
Extractions	R1	98.8	98.1	94.9	92.5	84.0	80.7	85.1	68.8	78.8	78.1	83.6
	R2	98.9	98.5	93.6	93.6	83.7	79.5	81.6	78.3	79.8	79.7	81.5
	Mean	98.8	98.3	94.3	93.0	83.9	80.1	83.3	73.5	79.3	78.9	82.6
Unextracted residues	R1	1.2	1.9	5.1	7.5	16.0	19.3	14.5	26.8	21.0	21.8	16.0
	R2	1.1	1.5	6.4	6.4	16.3	20.5	17.0	20.9	20.2	20.3	18.2
	Mean	1.2	1.7	5.7	7.0	16.1	19.9	15.8	23.9	20.6	21.1	17.1
Material balance	R1	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	R2	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Mean	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B. 8.1.1.1-9 Material balances in clay loam soil (102170) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	0.1	<0.1	<0.1	<0.1	1.1	6.2	0.5	0.3	0.4	0.1
	R2	N/A	0.3	<0.1	<0.1	<0.1	4.9	1.0	0.3	0.1	0.4	0.2
	Mean	N/A	0.2	<0.1	<0.1	<0.1	3.0	3.6	0.4	0.2	0.4	0.2
Extractions	R1	94.0	97.0	91.8	81.9	86.4[+]	80.6	60.3	81.4	65.3	83.5	78.9
	R2	87.9	90.9	85.9	85.2	88.0	72.5	84.4	95.1	77.5	82.4	76.9[+]
	Mean	91.0	94.0	88.9	83.6	87.2	76.6	72.4	88.3	71.4	83.0	77.9
Unextracted residues	R1	1.0	2.2	4.8	4.7	12.2	11.5	24.7	25.6	21.0	23.9	17.5
	R2	1.2	2.1	4.7	6.8	11.1	17.3	16.1	23.6	11.3	44.0	17.2
	Mean	1.1	2.2	4.8	5.8	11.7	14.4	20.4	24.6	16.2	34.0	17.4
Material balance[+++]	R1	95.1	99.3	96.6	86.6	98.6	93.2	91.2	107.5	86.6	107.8	96.5
	R2	89.1	93.3	90.6	92.0	99.1	94.7	101.5	118.9	88.9	126.8	94.2
	Mean	92.1	96.3	93.6	89.3	98.9	94.0	96.3	113.2	87.8	117.3	95.4

[+] Extra extraction done on replicate due to possible inadequate shaking.
[+++] variable recoveries may be due to non-homogenous dosing solution
N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B. 8.1.1.1-10 Material balances in clay loam soil (102170) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	0.1	<0.1	<0.1	<0.1	1.2	6.8	0.5	0.3	0.4	0.1
	R2	N/A	0.3	<0.1	<0.1	<0.1	5.2	1.0	0.3	0.1	0.3	0.2
	Mean	N/A	0.2	<0.1	<0.1	<0.1	3.2	3.9	0.4	0.2	0.3	0.2
Extractions	R1	98.9	97.6	95.1	94.6	87.6	86.5	66.1	75.7	75.4	77.5	81.7
	R2	98.7	97.4	94.8	92.6	88.8	76.6	83.2	79.9	87.2	65.0	81.6
	Mean	98.8	97.5	95.0	93.6	88.2	81.5	74.6	77.8	81.3	71.2	81.7
Unextracted residues	R1	1.1	2.3	4.9	5.4	12.4	12.3	27.1	23.9	24.2	22.2	18.1
	R2	1.3	2.3	5.2	7.4	11.2	18.3	15.8	19.8	12.7	34.7	18.2
	Mean	1.2	2.3	50	6.4	11.8	15.3	21.5	21.8	18.5	28.4	18.2
Material balance	R1	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	R2	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Mean	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B. 8.1.1.1-11 Material balances in loam soil (102171) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	<0.1	<0.1	<0.1	<0.1	0.4	0.3	0.2	0.1	0.1	0.1
	R2	N/A	<0.1	<0.1	<0.1	<0.1	0.2	<0.1	0.2	0.9	0.1	0.1
	Mean	N/A	<0.1	<0.1	<0.1	<0.1	0.3	0.2	0.2	0.5	0.1	0.1
Extractions	R1	99.7	95.4	86.1	86.7	88.3	88.3	96.4	114.4	88.3	93.7	87.9
	R2	100.4	97.3	89.6	90.5	85.1	84.5	101.4	103.6	91.3	91.0	97.7
	Mean	100.1	96.4	87.9	88.6	86.7	86.4	98.9	109.0	89.8	92.4	92.8
Unextracted residues	R1	0.7	1.2	3.0	2.5	2.8	3.9	5.1	16.1	9.6	15.9	5.8
	R2	0.9	1.6	3.4	3.0	2.6	3.8	3.8	16.0	9.9	13.0	5.8
	Mean	0.8	1.4	3.2	2.8	2.7	3.9	4.5	16.1	9.8	14.5	5.8
Material balance[+++]	R1	100.4	96.6	89.1	89.2	91.1	92.6	101.8	130.7	98.0	109.7	93.8
	R2	101.3	98.9	93.0	93.5	87.7	88.5	105.2	119.8	102.1	104.1	103.6
	Mean	100.8	97.7	91.1	91.4	89.4	90.6	103.5	125.2	100.1	106.9	98.7

[+++] variable recoveries may be due to non-homogenous dosing solution
N/A = not applicable- no volatile trapping media were associated with zero day samples

Table B.8.1.1.1-12 Material balances in loam soil (102171) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
$^{14}CO_2$/ Volatiles	R1	N/A	<0.1	<0.1	<0.1	<0.1	0.4	0.3	0.2	0.1	0.1	0.1
	R2	N/A	<0.1	<0.1	<0.1	<0.1	0.2	<0.1	0.2	0.9	0.1	0.1
	Mean	N/A	<0.1	<0.1	<0.1	<0.1	0.3	0.2	0.2	0.5	0.1	0.1
Extractions	R1	99.4	98.8	96.6	97.2	96.9	95.4	94.7	87.5	90.1	85.4	93.7
	R2	99.1	98.4	96.3	96.8	97.0	95.5	96.4	86.5	89.4	87.4	94.3
	Mean	99.2	98.6	96.5	97.0	97.0	95.4	95.5	87.0	89.8	86.4	94.0
Unextracted residues	R1	0.6	1.2	3.4	2.8	3.1	4.2	5.0	12.3	9.8	14.5	6.2
	R2	0.9	1.6	3.7	3.2	3.0	4.3	3.6	13.3	9.7	12.5	5.6
	Mean	0.8	1.4	3.5	3.0	3.0	4.3	4.3	12.8	9.7	13.5	5.9
Material balance	R1	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	R2	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Mean	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

N/A = not applicable- no volatile trapping media were associated with zero day samples

Tables 8.1.1.1-13 to -22 show the distribution of the radioactivity between the parent compound and metabolites identified across all five soils presented as %AR and %RR values. Three minor metabolites were detected at low levels. No metabolites exceeded 5% AR or % RR at two time-points, 10% at any time-point or were at 5% and increasing at study termination.

DE-napropamide (reached a maximum mean 8.9% AR or 8.2% RR), 1,4 naphthoquinone (maximum mean 5.85% AR or 5.56% RR) and 1-naphthol (<5% AR or RR at all sampling intervals). DE-napropamide was the only metabolite detected in the clay and loamy sand soils.

Table B. 8.1.1.1-13 Distribution of radioactivity in clay soil (102083) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	76.4	98.6	115.9	95.4	91.5	89.7	95.4	87.7	71.9	81.1	74.1
napropamide-M	R1	78.3	102.4	147.1	86.6	90.1	91.9	90.8	89.1	79.8	83.0	77.7
	R2	74.5	94.8	84.6	104.2	92.8	87.4	99.2	86.3	64.1	77.7	70.4
	Mean	76.4	98.6	115.9	95.4	91.5	89.7	95.0	87.7	71.9	80.3	74.1
DE-Nap	R1	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.7	0.0
	R2	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.9	0.1
	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.8	0.1

Table B. 8.1.1.1-14 Distribution of radioactivity in clay soil (102083) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	98.1	97.0	94.4	90.9	88.7	84.6	84.3	85.3	76.0	81.0	85.6
napropamide-M	R1	97.8	96.9	95.5	91.9	88.2	84.5	80.8	85.2	78.4	80.8	89.3
	R2	98.4	97.2	93.3	89.9	89.3	84.8	87.2	85.4	73.5	79.7	81.8
	Mean	98.1	97.0	94.4	90.9	88.7	84.6	84.0	85.3	76.0	80.3	85.5
DE-Nap	R1	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.7	0.0
	R2	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.9	0.1
	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.8	0.1

Table B.8.1.1.1- 15 Distribution of radioactivity in loamy sand soil (102168) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	82.9	99.0	91.4	93.8	79.7	85.3	101.8	88.9	75.2	80.6	94.8
napropamide-M	R1	81.7	104.3	89.0	98.1	78.0	84.8	101.7	82.4	71.4	75.1	94.0
	R2	84.2	93.8	93.7	89.6	79.0	84.5	98.0	92.2	75.1	80.7	95.0
	Mean	82.9	99.0	91.4	93.8	78.5	84.7	99.8	87.3	73.3	77.9	94.5
DE-Nap	R1	0.0	0.0	0.0	0.0	0.0	0.0	1.6	2.2	1.8	3.6	0.0
	R2	0.0	0.0	0.0	0.0	1.4	1.2	2.3	1.1	2.1	1.8	0.7
	Mean	0.0	0.0	0.0	0.0	0.7	0.6	1.9	1.6	2.0	2.7	0.4

Table B.8.1.1.1- 16 Distribution of radioactivity in loamy sand soil (102168) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	98.0	98.5	96.3	95.8	94.7	93.0	92.4	91.6	88.7	85.8	90.9
napropamide-M	R1	97.9	98.5	96.7	94.2	93.3	93.9	92.3	89.2	86.1	80.2	90.1
	R2	98.1	98.5	95.8	97.4	93.4	90.7	88.9	90.7	86.6	85.8	91.0
	Mean	98.0	98.5	96.3	95.8	93.4	92.3	90.6	90.0	86.3	83.0	90.6
DE-Nap	R1	0	0	0	0	0	0	1.4	2.3	2.2	3.8	0
	R2	0	0	0	0	1.7	1.3	2.1	1.0	2.5	1.9	0.7
	Mean	0	0	0	0	0.8	0.7	1.8	1.7	2.3	2.9	0.3

Table B.8.1.1.1- 17 Distribution of radioactivity in sandy loam soil (102169) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	80.5	91.4	84.0	80.7	83.1	83.9	76.8	86.7	74.0	83.3	75.4
napropamide-M	R1	82.1	95.9	83.9	80.0	80.4	86.0	79.1	75.4	71.6	69.3	78.4
	R2	78.8	87.0	84.1	81.4	81.9	81.8	71.6	95.0	73.6	78.8	71.8
	Mean	80.5	91.4	84.0	80.7	81.2	83.9	75.4	85.2	72.6	74.0	75.1
DE-Nap	R1	0.0	0.0	0.0	0.0	1.8	0.0	1.6	0.7	0.7	4.6	0.1
	R2	0.0	0.0	0.0	0.0	2.1	0.0	1.2	2.5	2.1	2.2	0.4
	Mean	0.0	0.0	0.0	0.0	2.0	0.0	1.4	1.6	1.4	3.4	0.3
1, 4-NQ	R1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	6.5	0.0
	R2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.2	0.0
	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	5.9	0.0

Table B.8.1.1.1- 18 Distribution of radioactivity in sandy loam soil (102169) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	98.8	98.3	94.3	93.0	83.9	80.1	83.3	73.5	79.3	78.9	82.6
napropamide-M	R1	98.8	98.1	94.9	92.5	82.1	80.7	83.3	68.2	78.0	67.3	83.4
	R2	98.9	98.5	93.6	93.6	81.7	79.5	80.3	76.3	77.5	72.8	81.1
	Mean	98.8	98.3	94.3	93.0	81.9	80.1	81.8	72.2	77.7	70.0	82.3
DE-Nap	R1	0.0	0.0	0.0	0.0	1.9	0.0	1.7	0.6	0.8	4.5	0.2
	R2	0.0	0.0	0.0	0.0	2.1	0.0	1.3	2.0	2.3	2.1	0.4
	Mean	0.0	0.0	0.0	0.0	2.0	0.0	1.5	1.3	1.5	3.3	0.3
1, 4-NQ	R1	0	0	0	0	0	0	0	0	0	6.3	0
	R2	0	0	0	0	0	0	0	0	0	4.8	0
	Mean	0	0	0	0	0	0	0	0	0	5.6	0

Table B. 8.1.1.1-19 Distribution of radioactivity in clay loam soil (102170) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	91.0	94.0	88.8	83.6	87.2	76.6	72.3	88.2	71.4	82.9	77.9
napropamide-M	R1	94.0	97.0	91.8	81.9	84.6	79.8	58.9	80.0	65.3	78.5	78.9
	R2	87.9	90.9	85.9	85.2	86.2	72.5	83.2	94.7	77.0	82.4	76.6
	Mean	91.0	94.0	88.8	83.6	85.4	76.2	71.0	87.3	71.1	80.4	77.8
DE-Nap	R1	0.0	0.0	0.0	0.0	1.8	0.8	1.3	1.4	0.0	3.9	0.0
	R2	0.0	0.0	0.0	0.0	1.7	0.0	1.3	0.4	0.6	0.0	0.2
	Mean	0.0	0.0	0.0	0.0	1.8	0.4	1.3	0.9	0.3	1.9	0.1
1-Naphthol	R1	0	0	0	0	0	0	0	0	0	1.2	0
	R2	0	0	0	0	0	0	0	0	0	0	0
	Mean	0	0	0	0	0	0	0	0	0	0.6	0

Table B. 8.1.1.1-20 Distribution of radioactivity in clay loam soil (102170) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	98.8	97.5	95.0	93.6	88.2	81.5	74.6	77.8	81.3	71.2	81.7
napropamide-M	R1	98.9	97.6	95.1	94.6	85.8	85.6	64.6	74.4	75.4	72.8	81.7
	R2	98.7	97.4	94.9	92.6	87.0	76.6	81.9	79.6	86.5	65.0	81.3
	Mean	98.8	97.5	95.0	93.6	86.4	81.1	73.3	77.0	81.0	68.9	81.5
DE-Nap	R1	0.0	0.0	0.0	0.0	1.8	0.9	1.5	1.3	0.0	3.6	0.0
	R2	0.0	0.0	0.0	0.0	1.8	0.0	1.2	0.3	0.7	0.0	0.2
	Mean	0.0	0.0	0.0	0.0	1.8	0.4	1.4	0.8	0.3	1.8	0.1
1-Naphthol	R1	0	0	0	0	0	0	0	0	0	1.1	0
	R2	0	0	0	0	0	0	0	0	0	0	0
	Mean	0	0	0	0	0	0	0	0	0	0.5	0

Table B. 8.1.1.1-21 Distribution of radioactivity in loam soil (102171) expressed as applied radioactivity (%AR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	100.0	96.3	87.9	88.6	86.7	86.4	98.9	109.0	89.8	92.4	92.8
napropamide-M	R1	99.7	95.4	86.1	86.7	88.3	87.1	95.5	113.1	84.2	79.7	87.9
	R2	100.4	97.3	89.6	90.5	85.1	83.5	101.0	102.6	88.3	87.2	97.6
	Mean	100.0	96.3	87.9	88.6	86.7	85.3	98.3	107.9	86.3	83.5	92.7
DE-Nap	R1	0.0	0.0	0.0	0.0	0.0	1.2	0.8	1.3	0.9	14.0	0.0
	R2	0.0	0.0	0.0	0.0	0.0	1.0	0.5	1.0	1.8	3.8	0.2
	Mean	0.0	0.0	0.0	0.0	0.0	1.1	0.7	1.1	1.3	8.9	0.1
1, 4-NQ	R1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.2	0.0	0.0
	R2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.3	0.0	0.0
	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.2	0.0	0.0

Table B. 8.1.1.1-22 Distribution of radioactivity in loam soil (102171) expressed as recovered radioactivity (%RR) for the aerobic laboratory study

Description		Sampling interval (days)										
		0	1	3	7	14	21	30	60	90	120	180
Total extractable	Mean	99.2	98.6	96.5	97.0	97.0	95.4	95.5	87.0	89.8	86.4	94.0
napropamide-M	R1	99.4	98.8	96.6	97.2	96.9	94.1	93.9	86.6	85.9	72.7	93.7
	R2	99.1	98.4	96.3	96.8	97.0	94.4	95.9	85.7	86.5	83.7	94.1
	Mean	99.2	98.6	96.5	97.0	97.0	94.3	94.9	86.1	86.2	78.2	93.9
DE-Nap	R1	0.0	0.0	0.0	0.0	0.0	1.2	0.8	1.0	0.9	12.7	0.0
	R2	0.0	0.0	0.0	0.0	0.0	1.1	0.5	0.8	1.7	3.7	0.2
	Mean	0.0	0.0	0.0	0.0	0.0	1.2	0.6	0.9	1.3	8.2	0.1
1, 4-NQ	R1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.3	0.0	0.0
	R2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.2	0.0	0.0
	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.2	0.0	0.0

Results from the chiral HPLC analysis confirm that Napropamide-M remained in the D- form with no indication of isomerization to the L- form. The RMS notes that no pre-dose chiral analysis was undertaken to assess the potential for isomeric instability during storage. However, the supplied test material was reported as 99.9% of the desired isomer and there was no detection of the L isomer in any of the zero day samples or the samples taken at 60 and 180 days. On balance, the RMS views the possibility of the L-form appearing prior to the study start as unlikely.

Table B.8.1.1.1-23 shows the results of the organic matter fractionation. AR% was most strongly associated with humin across all five soil types.

Table B.8.1.1.1-23 Characterisation of unextracted radioactivity at 120 days for soils used in the aerobic laboratory degradation studies of ^{14}C napropamide-M

Soil (JRFA ID no.[1])	%AR Characterised		
	Fulvic	Humic	Humin
UK(102083) Clay	0.4	2.1	6.2
UK (102168) Loamy sand	1.7	4.3	5.8
France(102169) Sandy loam	3.3	5.8	9.7
France (102170) Clay Loam	3.2	0.6	13.4
Spain (102171) Loam	2.3	1.0	10.2

[1] JRFA ID= Test facility soil identification number

The study author calculated degradation rates (DT_{50}, DT_{75} and DT_{90}) for both the %AR and %RR datasets for napropamide-M (0-120 days), using the individual replicate values and linear regression analysis of log transformed data. Under FOCUS degradation kinetics guidance it is no longer recommended to use linear regression analysis for this purpose.

The RMS repeated the calculations using non-linear regression in the DegKin v.2 spreadsheet, (SFO, 2 reps). Table B.8.1.1.1-24 shows the DT_{50} values based on both 0- 120 day and 0- 180 day datasets. The RMS calculated the geometric mean DT_{50} as 353.40 %RR (0-120 days). As all results were extrapolated well beyond the study duration and are therefore uncertain, the RMS has subsequently not reported the DT_{90} values, which were all in excess of 900 days. The results show that napropamide-M degrades slowly across several contrasting soil types under aerobic laboratory conditions. A kinetic reassessment was performed according to FOCUS guidelines, which is presented in the section below (study by Croucher, A. & Ford, S. (2015b)).

Table B.8.1.1.1-24 RMS' DT_{50} and χ^2 values for the aerobic laboratory degradation of [naphthyl-1-^{14}C] napropamide-M for 0-120 day and 0-180 day datasets

Soil (JRFA ID no.[1])	Classification[2]	Using %AR data		Using %RR data	
		DT_{50}	χ^2	DT_{50}	χ^2
UK (102083)	Clay	345.3 (411.6)	8.6 (8.5)	394.5 (755.5)	3.3 (4.6)
UK (102168)	Loamy sand	471.1 (>1000)	10.8 (11.5)	537.2 (>1000)	1.1 (2.7)
France (102169)	Sandy loam	619.0 (869.5)	4.1 (4.2)	254.3 (500.3)	5.0 (7.0)
France (102170)	Clay loam	562.7 (859.8)	6.3 (6.3)	267.4 (501.6)	5.6 (7.1)
Spain (102171)	Loam	1513.0 (>1000)	6.5 (6.3)	382.5 (875.0)	1.2 (4.2)
Arithmetic mean		702.22 (828.18)	-	367.18	-
Geometric mean		611.82 (790.00)	-	353.40	-

[1] JRFA ID= Test facility soil identification number
[2] USDA textural class
Values reported in parenthesis are calculated including the 180 day samples

Kinetic assessment of the aerobic degradation in soil

Study author	Croucher, A. & Ford, S. (2015b)
Study title	Napropamide-M: kinetic assessment for laboratory aerobic soil degradation study
Study date	August 2015
Annex point	CA 7.1.2.1.1-02
Previous evaluation	New active substance, no previous studies submitted.

The degradation of radiolabelled [napthyl-1-^{14}C] napropamide-M was studied in five European soils under aerobic conditions in the laboratory (see above section B.8.1.1.1). The kinetic degradation rate of napropamide-M was reassessed using the modelling software package CAKE (v 3.1) in accordance with guidance provided by FOCUS (2006) and EFSA (2014). The report used the recovered radioactivity values (i.e. %AR normalised). Initially the models were run including all sampling points up to 180 days, unweighted and using an unconstrained initial value (M0). The acceptability of kinetic fits was judged both visually and statistically (according to the $\chi 2$ error and the t-test functions for SFO or for FOMC the confidence intervals for the α and β parameter estimates were assessed, and a fit was considered acceptable if the intervals did not include zero). The 180 day samples were considered visual and statistical outliers and so the data was reassessed without those values. Persistence endpoints were selected according to the "best fit" kinetic models (summarised in Table B.8.1.1.1-32, see end of section).

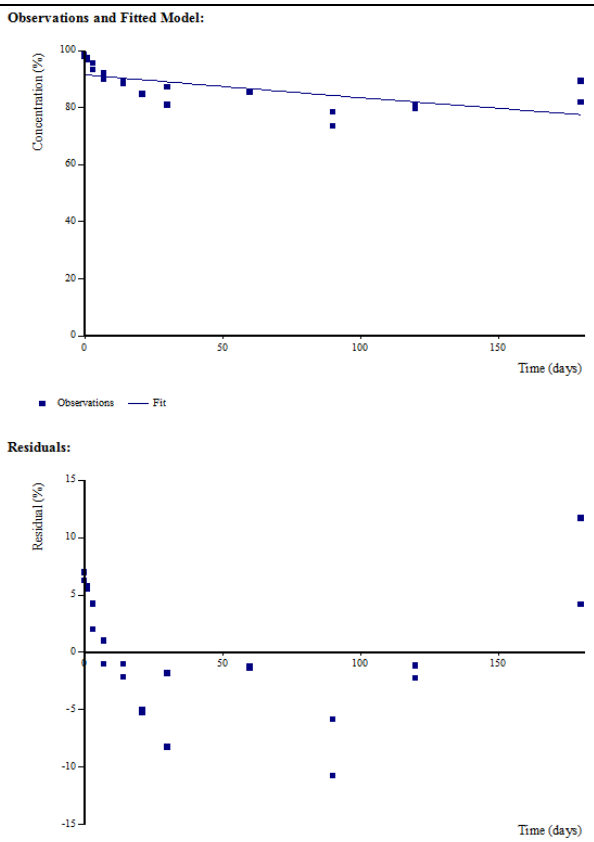
The RMS independently verified the Applicant's kinetic assessment using CAKE software according to the FOCUS guidance, summarised in Tables B.8.1.1.1-25 to-29, with corresponding figures B.8.1.1.1-1 to B.8.1.1.1-5. The Applicant used the default weighting method of IRLS (iteratively reweighted least squares) not OLS (non-linear least squares) but the RMS noted that it made no difference to the results on this occasion. For all soil types, the RMS agreed with the Applicant's visual assessments, statistical results, DT_{50} values and the chosen models to represent best fit.

Table B.8.1.1.1-25 RMS' kinetic evaluation of napropamide-M under aerobic laboratory conditions in clay soil

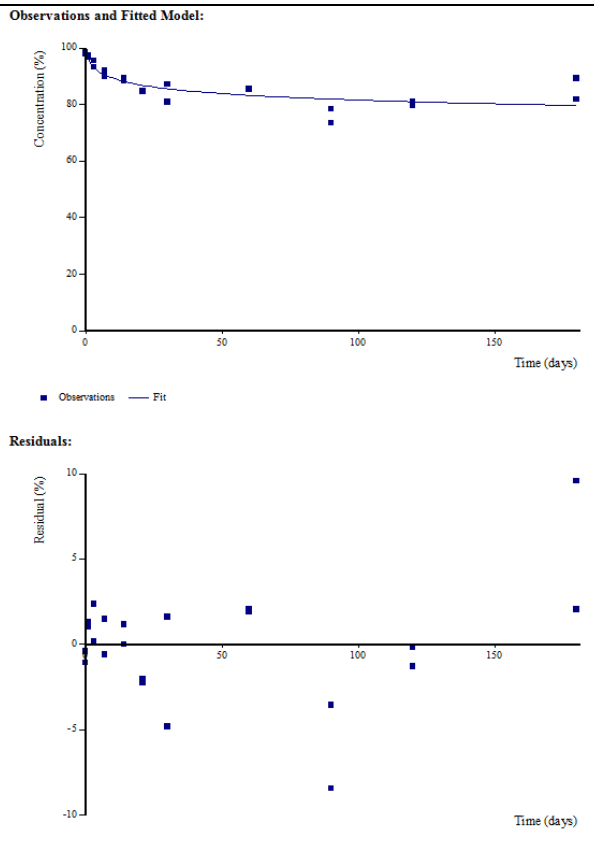
Data	Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50}
0- 180 days	SFO	4.60	Intermediate	p<0.01	755
	FOMC	2.68	Intermediate	α Both 90th and 95th %ile C.I. s do not include zero. β Both 90th and 95th %ile C.I.s include zero.	>10,000
Conclusions: SFO under-predicted time zero values and the initial concentration, residual plots were not scattered randomly and initially under-predicted observed residues, then over-predicted mid points, then under-predicted the last time point. FOMC fit was closer to the initial concentration. FOMC residual plots were closer to the zero line and more evenly distributed above and below it, although the last time point 180d was under-predicted. 180 day values were high and did not fit with the rest of the data. These values were removed and the data reassessed.					
0- 120 days	SFO	3.33	Intermediate	p<0.01	394
	FOMC	1.81	Good	α Both 90th and 95th %ile C.I.s do not include zero. β Both 90th and 95th %ile C.I.s include zero.	>10,000
	DFOP	1.89	Good	K1 90th ile C.I. does not include zero, 95th %ile C.I. includes zero. K2 90th ile C.I. does not include zero, 95th %ile C.I. includes zero.	727
	HS	3.16	Intermediate	K1 90th %ile C.I. does not include zero; 95th %ile C.I. does include zero. K2 Both 90th and 95th %ile C.I. include zero.	>10,000
Conclusions: Although SFO and FOMC fit resulted in acceptable χ2 error, FOMC gave an improved visual fit over SFO. Therefore, other biphasic models were also considered. DFOP has a similar χ^2 err% and visual fit to FOMC. The RMS accepts the Applicant's choice of DFOP based on acceptable 90th %ile confidence intervals. .					

All DT_{90} values were >1000, often >10, 000.

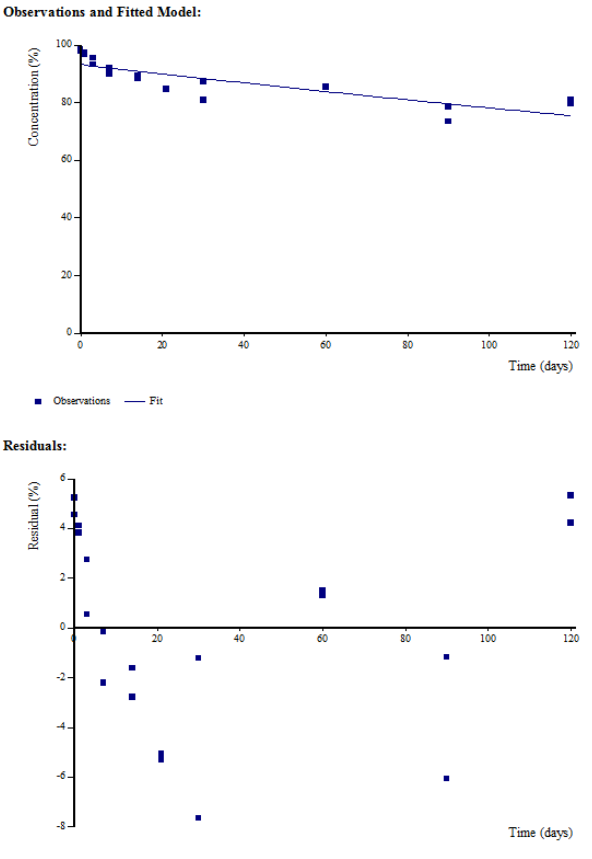
Figure B.8.1.1.1-1 RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in clay soil



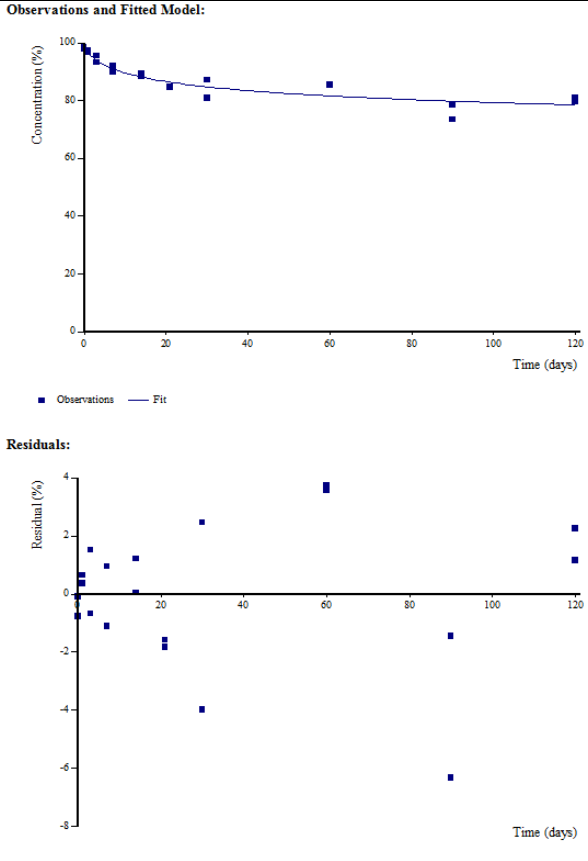
SFO all data



FOMC all data

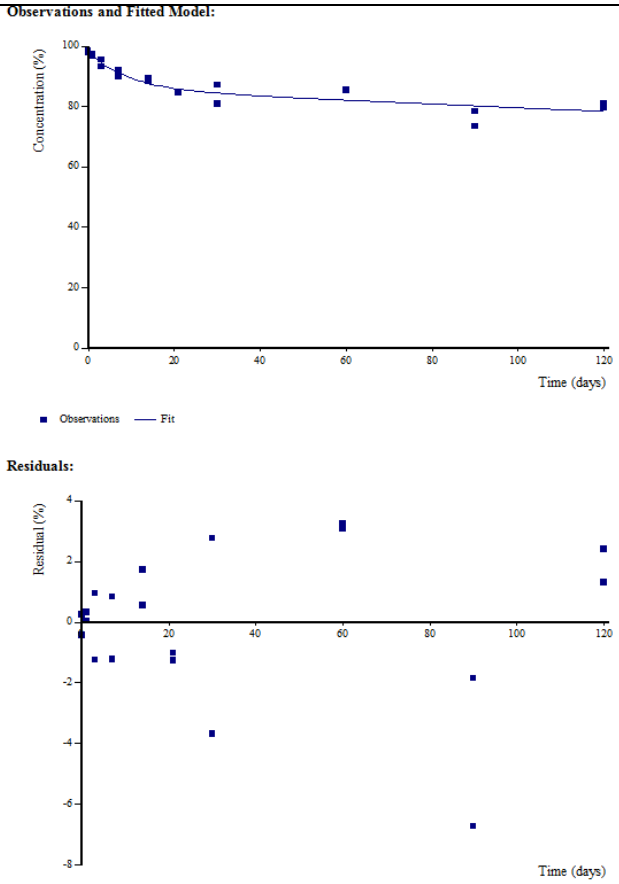


SFO outliers removed

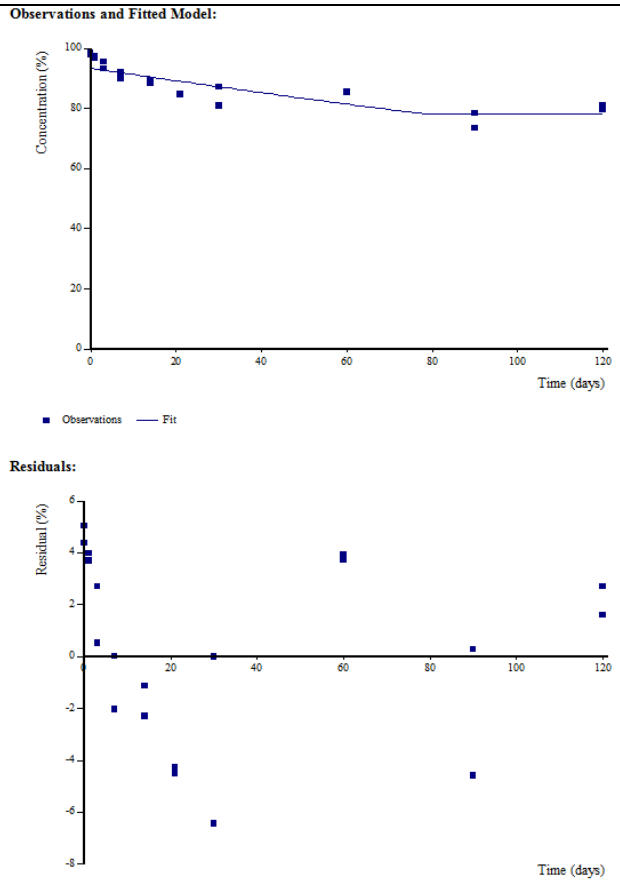


FOMC outliers removed

Figure B.8.1.1.1-1 (continued) RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in clay soil



DFOP outliers removed



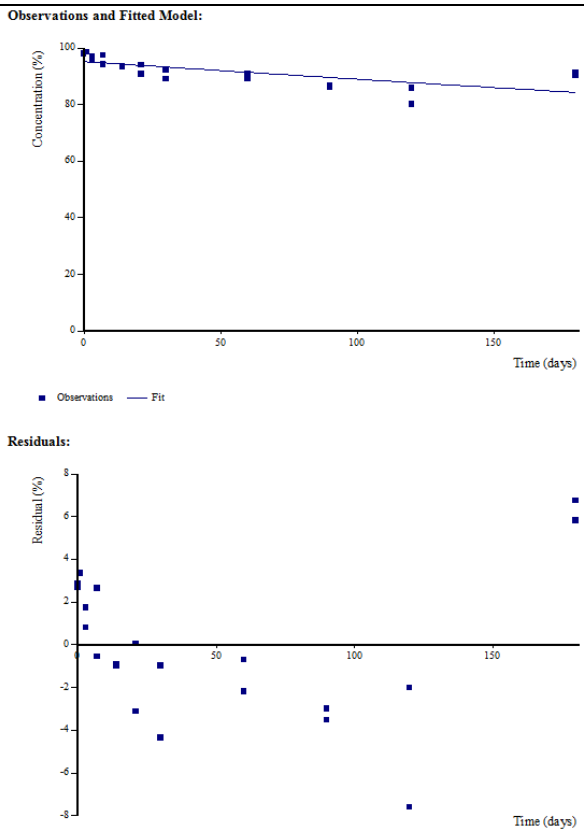
HS outliers removed

Table B.8.1.1.1-26 RMS' kinetic evaluation of napropamide-M under aerobic laboratory conditions in loamy sand soil

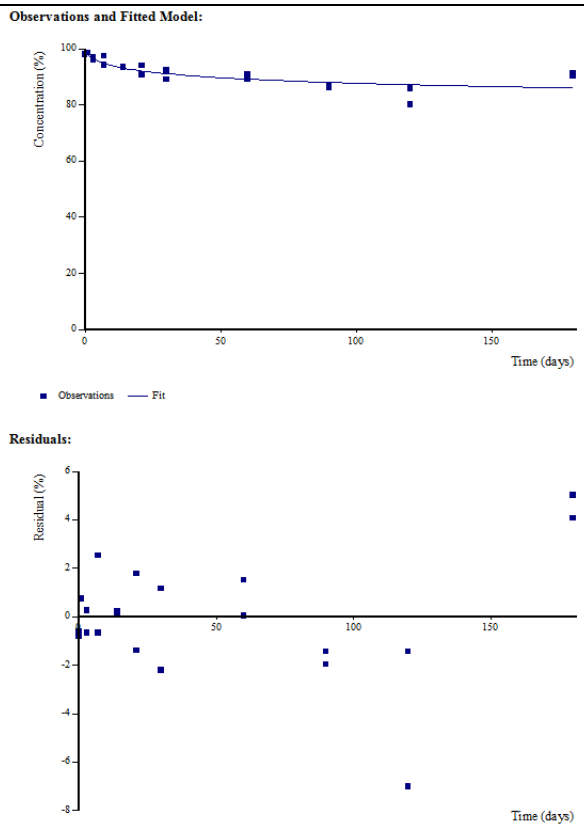
Data	Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50}
0- 180 days	SFO	2.73	Intermediate fit; poor residual	p<0.001	1020
	FOMC	1.83	Good	α Both 90th and 95th %ile C.I.s do not include zero. β Both 90th and 95th %ile C.I.s include zero	>10,000
Conclusions: Better prediction of time zero values and residual scattering with FOMC than SFO. For both models, 180 day values were high and did not fit with the rest of the data. These values were removed and the data reassessed.					
0- 120 days	SFO	1.13	Good	p<0.01	533
	FOMC	0.813	Good	α 95th %ile C.I. does not include zero β 95th %ile C.I. includes zero	>10,000
	DFOP	0.611	Good	K1 Both 90th and 95th ile C.I.s include zero. K2 Both 90th and 95th %ile C.I.s do not include zero.	652
	HS	0.598	Good	K1 90th %ile C.I. does not include zero but 95th %ile C.I does include zero. K2 90th and 95th C.I.s do not include zero.	636
Improved visual fit and residuals with removal of outliers. FOMC better predicts the initial concentration than SFO. Applicant selected HS as best fit. Though the failure of the statistical parameters for DFOP are probably due to the slow degradation rate, given the extrapolation so far beyond the study duration and the closeness of $\chi 2$ error% there is not much to distinguish the two model fits. DFOP could potentially have been accepted in accordance with the FOCUS degradation kinetics guidance that HS should only be considered in exceptional cases but as the regulatory decision is the same either way in this case, the RMS has accepted the Applicant's choice.					

All DT_{90} values were >1000, sometimes >10, 000.

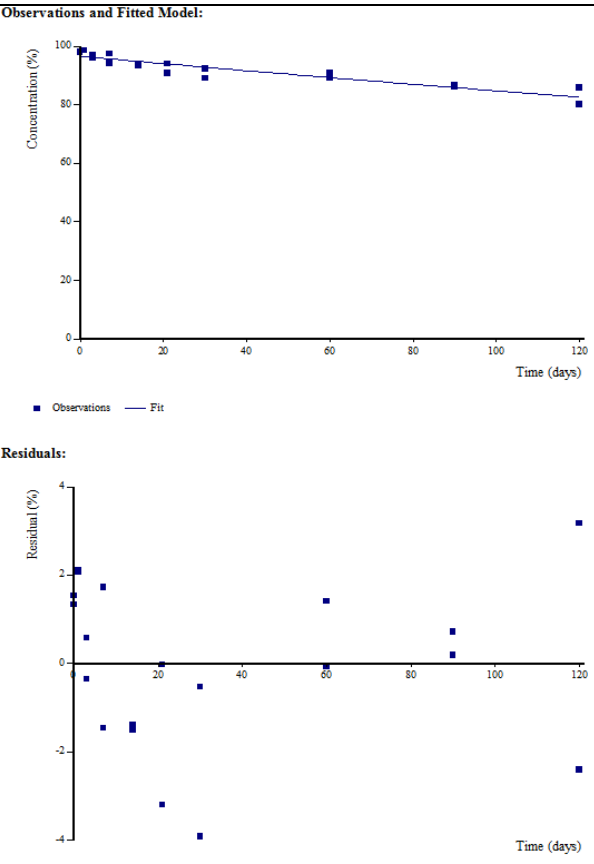
Figure B.8.1.1.1-2 RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in loamy sand soil



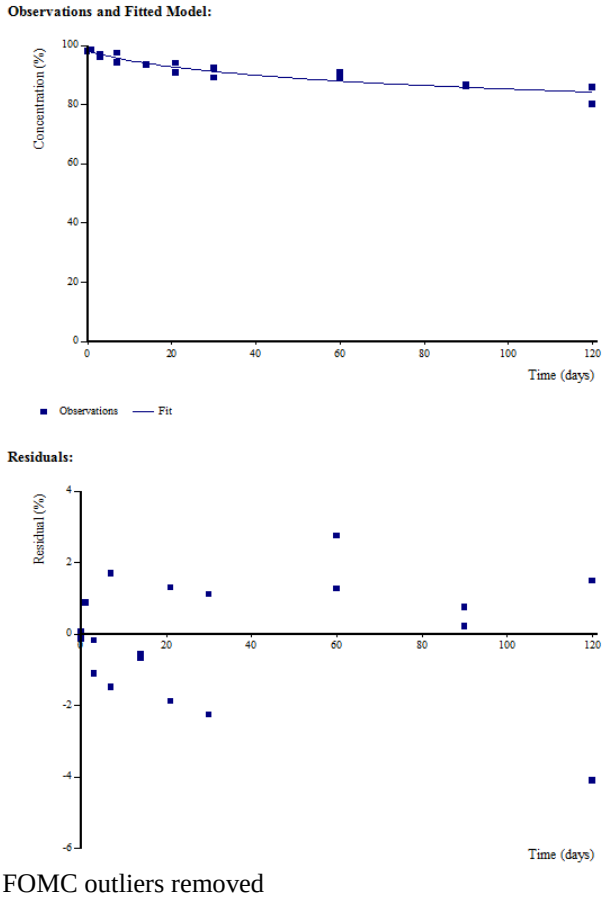
SFO all data



FOMC all data

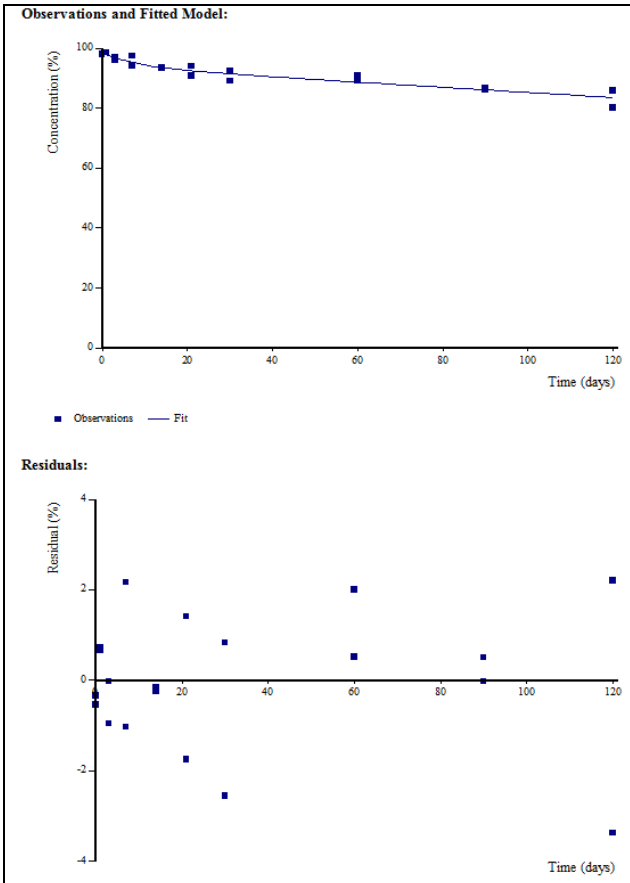


SFO outliers removed

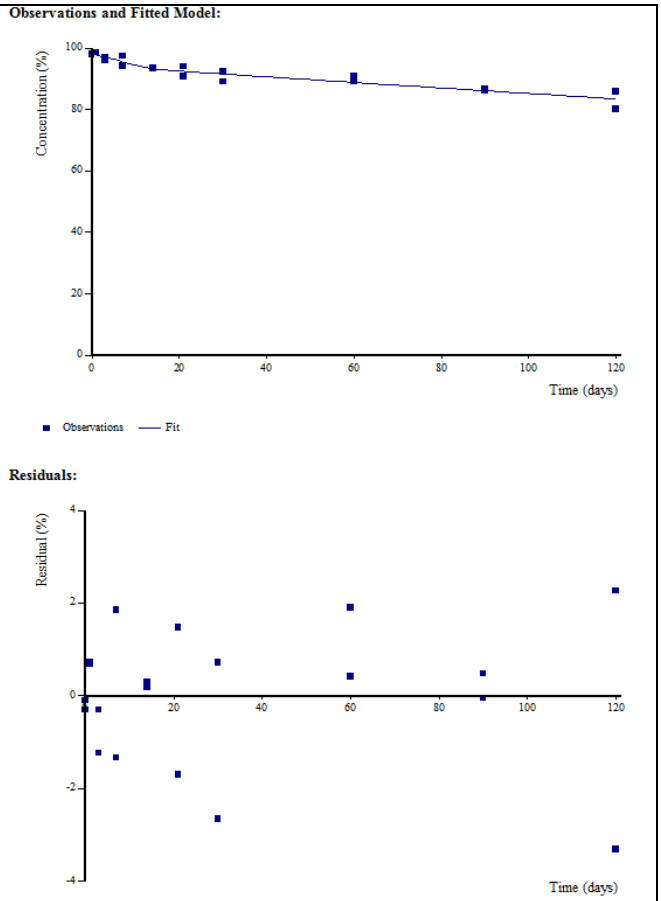


FOMC outliers removed

Figure B.8.1.1.1-2 (continued) RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in loamy sand soil



DFOP outliers removed



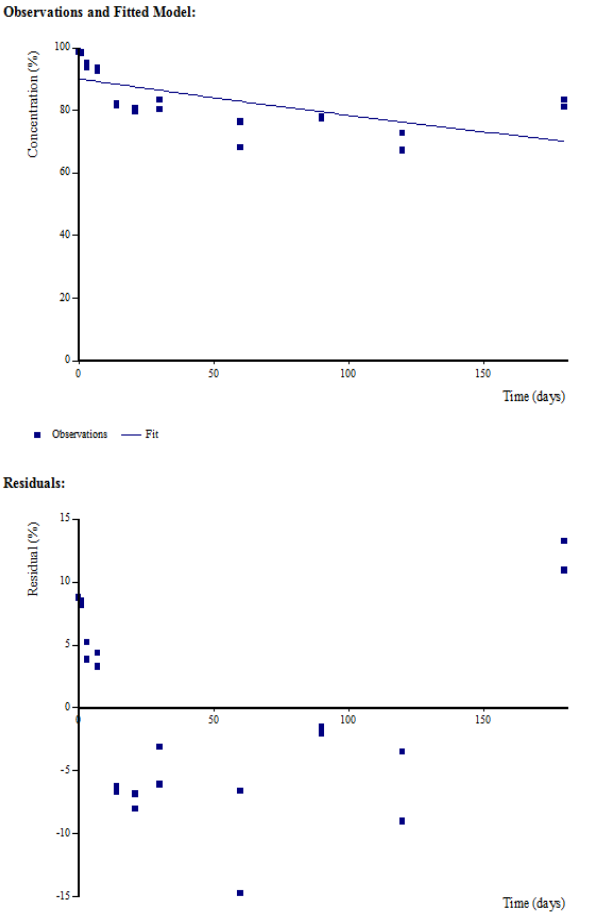
HS outliers removed

Table B.8.1.1.1-27 RMS' kinetic evaluation of napropamide-M under aerobic laboratory conditions in sandy loam soil

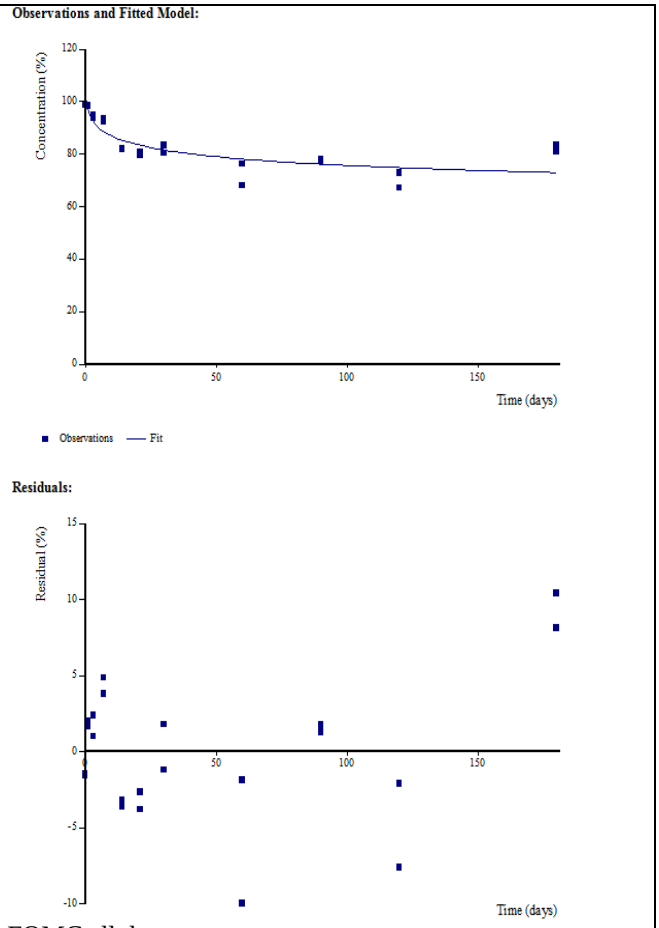
Data	Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50}
0- 180 days	SFO	7.05	Poor	p<0.01	500
	FOMC	4.21	Intermediate	α both 90th and 95th %ile C.I.s do not include zero. β both 90th and 95th %ile C.I.s include zero.	>10,000
Conclusions: Although the χ2 error was acceptable for both SFO and FOMC, the latter improved the visual fit, more closely describing the initial concentration and with residuals more evenly distributed above and below zero line. Both fits underestimated the 180 day values, which were high and did not fit with the rest of the data. These values were removed and the data reassessed, resulting in improved fit for both SFO and FOMC.					
0- 120 days	SFO	5.04	Intermediate	p<0.01	254
	FOMC	2.64	Good	α both 90th and 95th %ile C.I.s do not include zero. β both 90th and 95th %ile C.I.s include zero.	5660
	DFOP	2.54	Good	K1,both 90th and 95th %ile C.I.s do not include zero. K2, both 90th and 95th %ile C.I. include zero.	579
	HS	2.34	Good	K1 both 90th and 95th %ile C.I.s do not include zero. K2 both 90th and 95th %ile C.I.s do not include zero.	408
Conclusions: Although the χ^2 error was acceptable for both SFO and FOMC, as the visual fit was improved by FOMC and χ^2 err% lower, other bi-phasic models were tested. All the biphasic models show a good visual fit, however the χ^2 err% and other statistical parameters were more favourable with the HS model. The RMS notes that the DFOP could potentially have been accepted in accordance with the FOCUS degradation kinetics guidance that HS should only be considered in exceptional cases but as the regulatory decision is the same either way in this case, the RMS has accepted the Applicant's choice of HS as best fit.					

All DT_{90} values were >800, sometimes >10, 000.

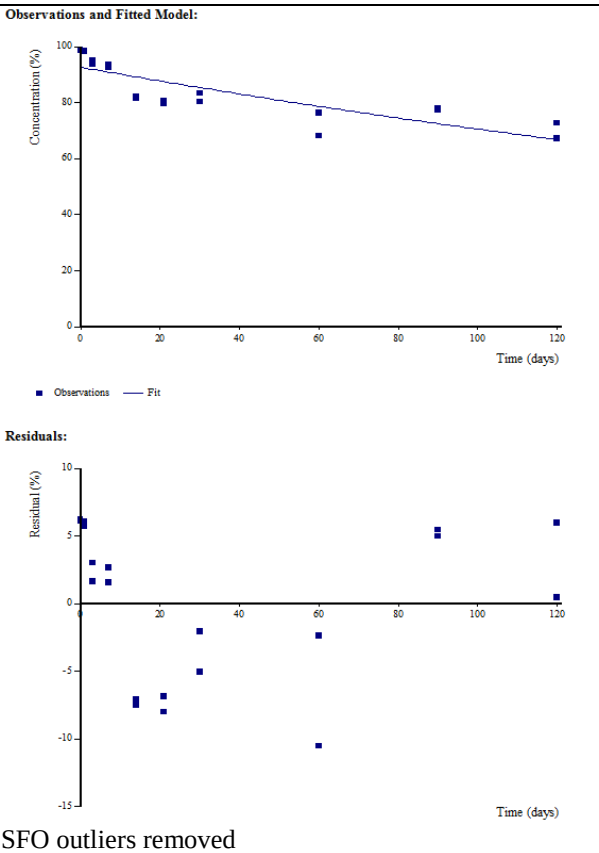
Figure B.8.1.1.1-3 RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in sandy loam soil



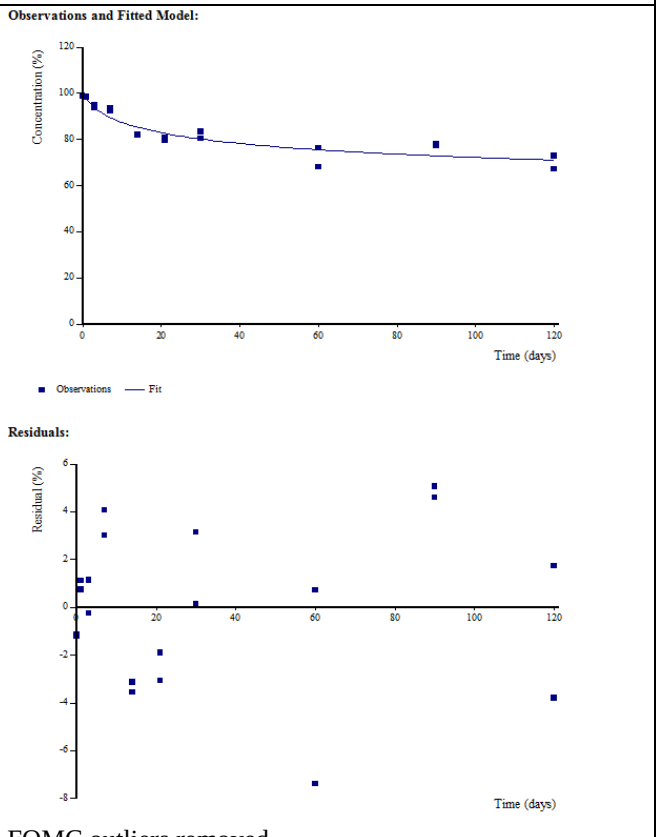
SFO all data



FOMC all data

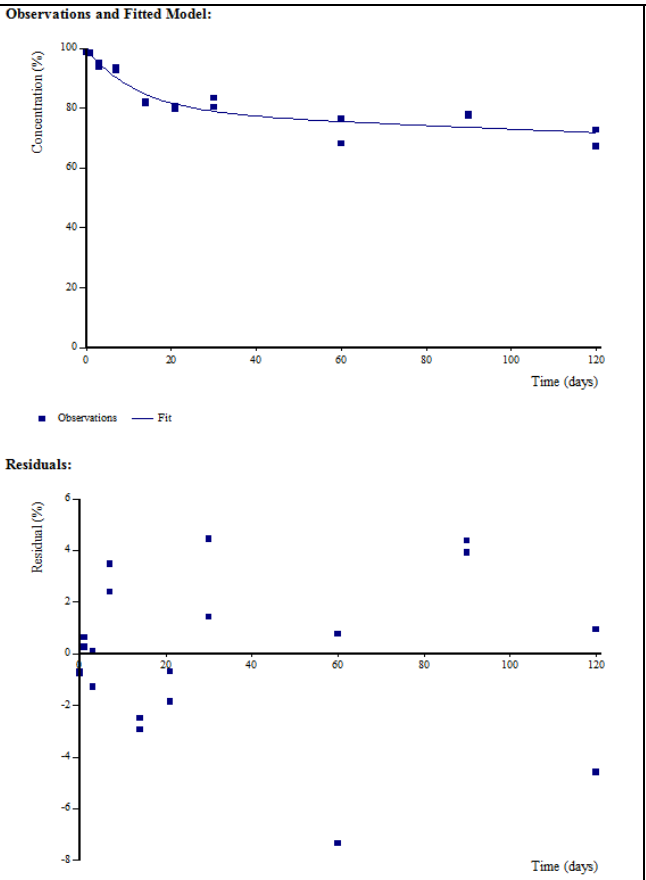


SFO outliers removed

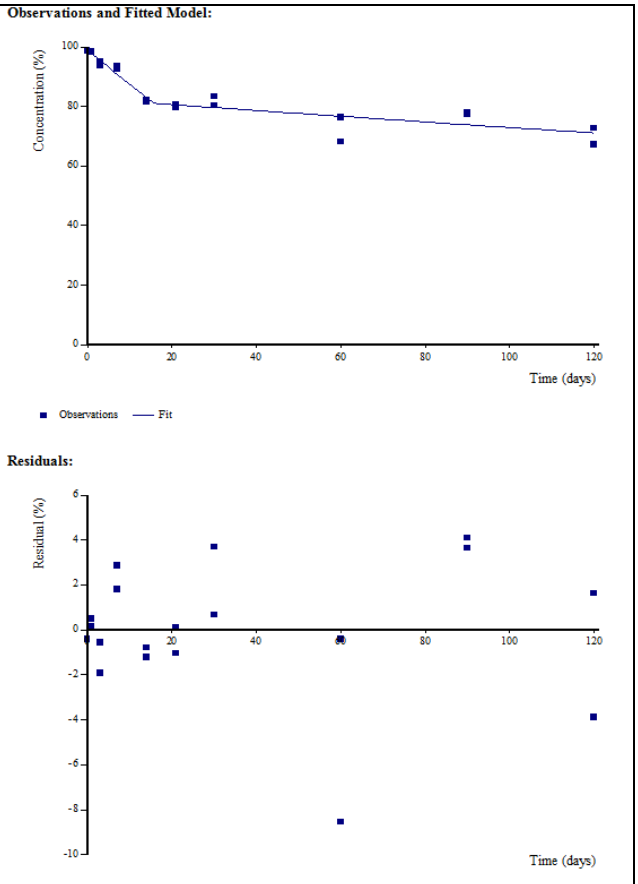


FOMC outliers removed

Figure B.8.1.1.1-3 (continued) RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in sandy loam soil



DFOP outliers removed



HS outliers removed

Table B.8.1.1.1-28 RMS' kinetic evaluation of napropamide-M under aerobic laboratory conditions in clay loam soil

Data	Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50}
0- 180 days	SFO	7.11	Poor	p<0.01	501
	FOMC	4.62	Intermediate-poor	α both 90th and 95th %ile C.I.s do not include zero. β both 90th and 95th %ile C.I.s include zero	>10,000
Conclusions: The SFO model under-predicted the time zero values and over-predicted most of the mid values. The FOMC residual plot showed better scattering. The180 day values were high and did not fit with the rest of the data for either model. These values were removed and the data reassessed, giving some improvement to visual and statistical fits.					
0- 120 days	SFO	5.59	Poor	p<0.01	267
	FOMC	3.7	Intermediate	α both 90th and 95th %ile C.I.s do not include zero. β both 90th and 95th %ile C.I.s include zero.	7220
	DFOP	3.46	Intermediate-good	K1 both 90th and 95th %ile C.I.s include zero K2 both 90th and 95th %ile C.I.s include zero	893
	HS	2.92	Good	K1 both 90th and 95th %ile C.I.s do not include zero. K2 both 90th and 95th %ile C.I.s include zero.	1150
Conclusion: No model had ideal visual or statistical parameters. Residual plots showed wider scattering than compared with other soils studies. The biphasic models were more favourable statistically and visually over SFO. The HS model χ^2 err%, statistical parameters and visual fit were slightly better than DFOP. DFOP could potentially have been accepted in accordance with the FOCUS degradation kinetics guidance that HS should only be considered in exceptional cases but as the DT_{50} provides a more worst case value, the RMS has accepted the Applicant's choice of HS as best fit.					

All DT_{90} values were >800, sometimes >10, 000.

Figure B.8.1.1.1-4 RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in clay loam soil

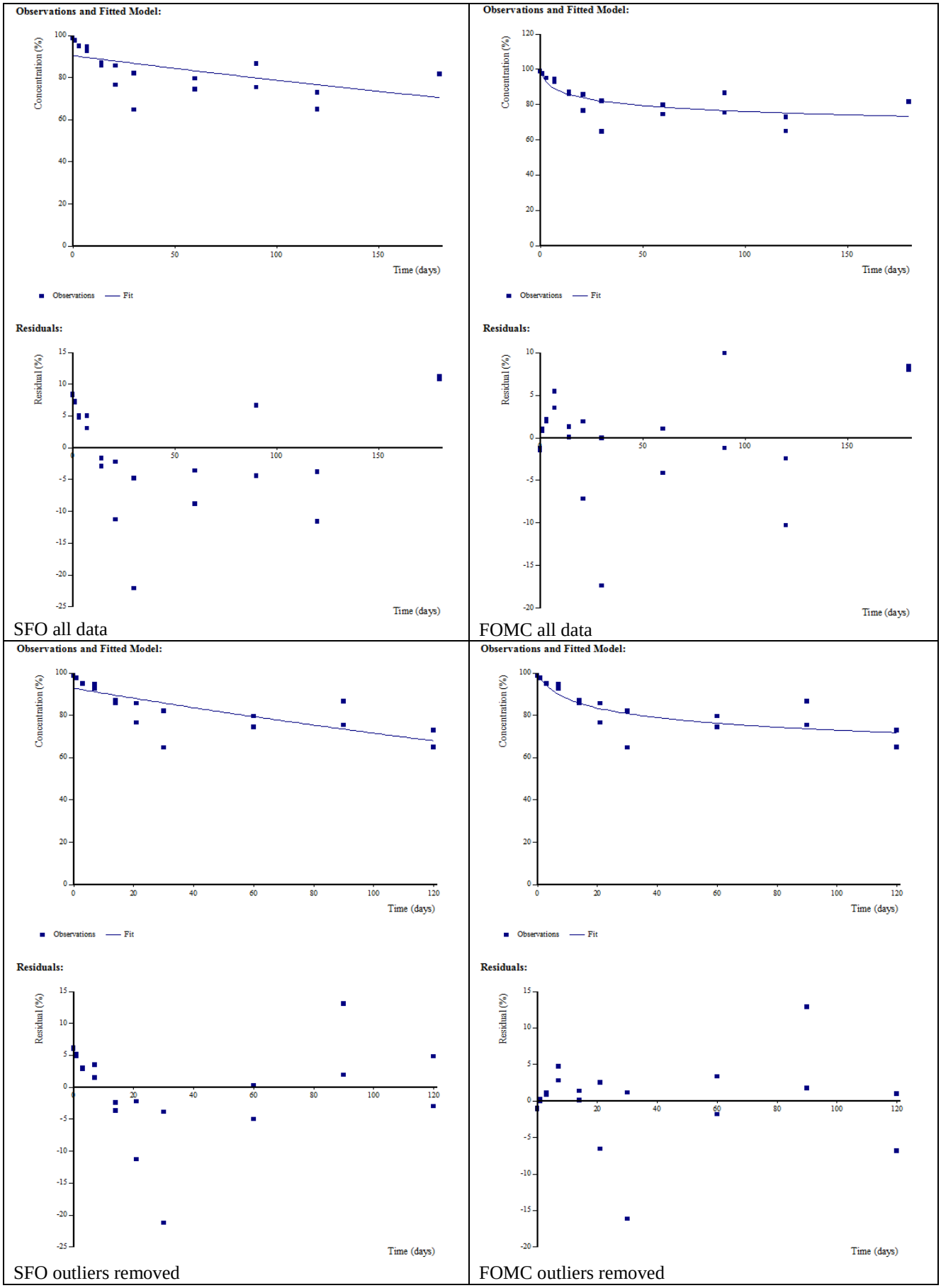
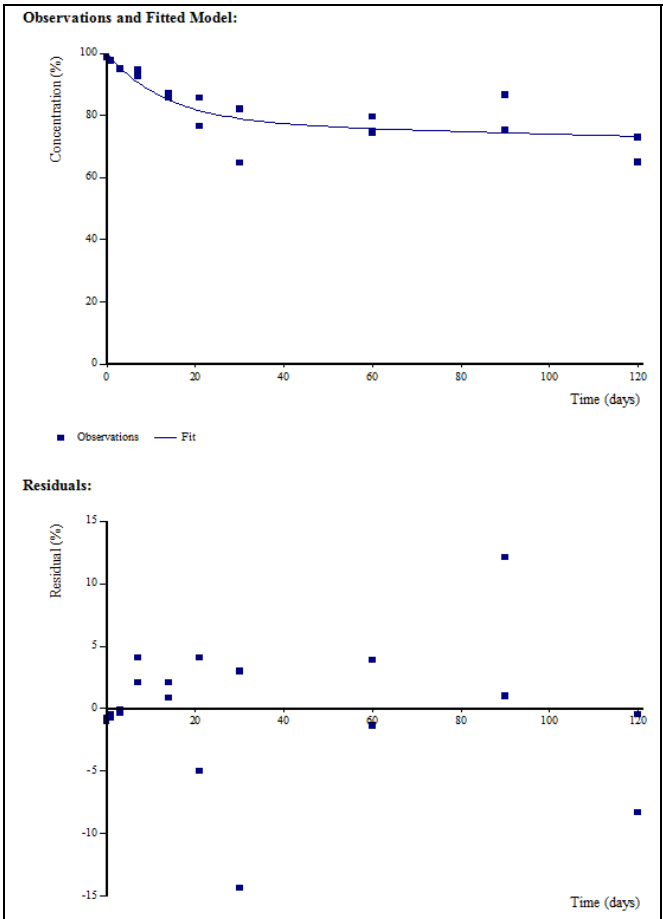
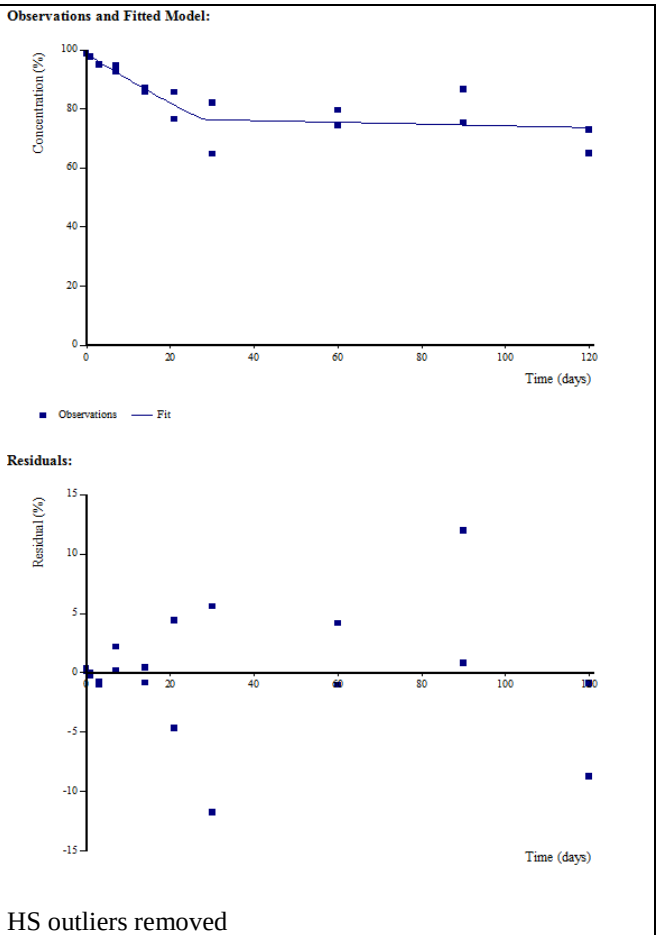


Figure B.8.1.1.1-4 (continued) RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in clay loam soil



DFOP outliers removed



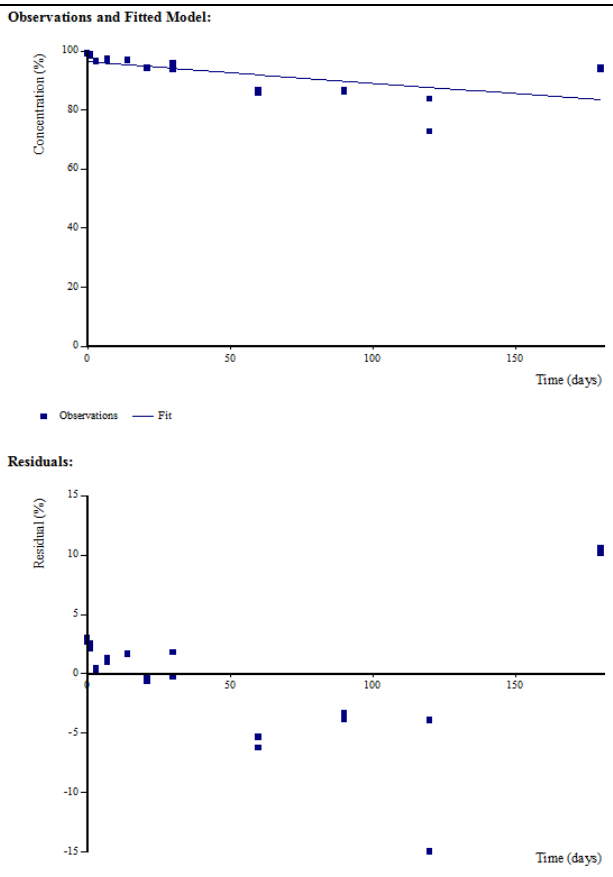
HS outliers removed

Table B.8.1.1.1-29 RMS' kinetic evaluation of napropamide-M under aerobic laboratory conditions in loam soil

Data	Model	χ^2 err%	Visuals	Comments on parameters	DT_{50}
0- 180 days	SFO	4.22	Intermediate	p<0.01	875
	FOMC	3.68	Intermediate	α 95th %ile C.I. includes zero β 95th %ile C.I. includes zero	>10, 000
Conclusions: Good estimation of initial concentration for both models. The 180 day values were high and did not fit with the rest of the data. These values were removed and the data reassessed, giving better statistical and visual fits.					
0- 120 days	SFO	1.19	Good	p<0.01	383
	FOMC	1.26	Good	α both 90th and 95th %ile C.I.s include zero β both 90th and 95th %ile C.I.s include zero	412
	DFOP	Models not assessed.			
	HS				
Both SFO and FOMC showed good visual fits and good scattering for residual plots, however SFO had more favourable statistical parameters. Therefore the RMS agrees with Applicant on their chosen "best fit" model of SFO.					

All DT_{90} values were >1000, sometimes >10, 000.

Figure B.8.1.1.1-5 RMS' graphs and residual plots showing degradation of napropamide-M under aerobic laboratory conditions in loam soil



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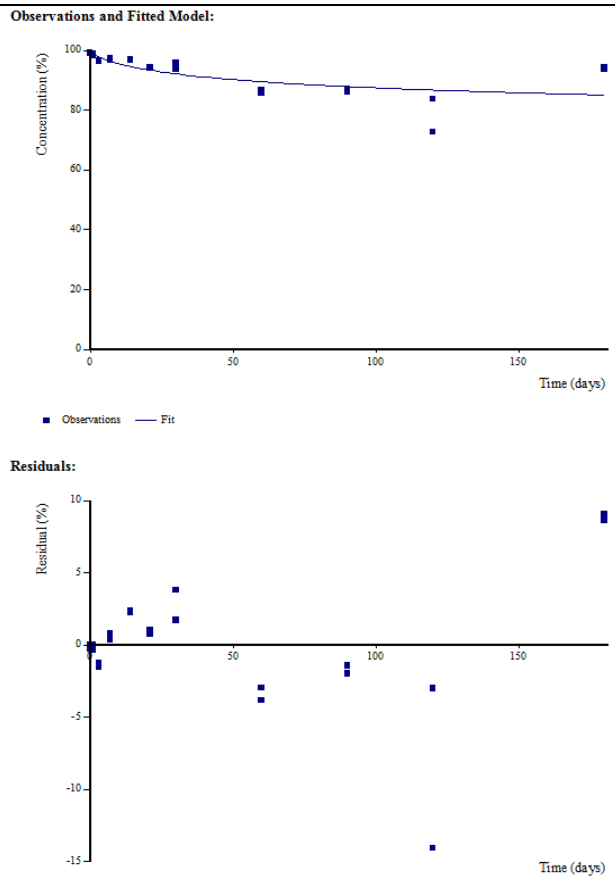
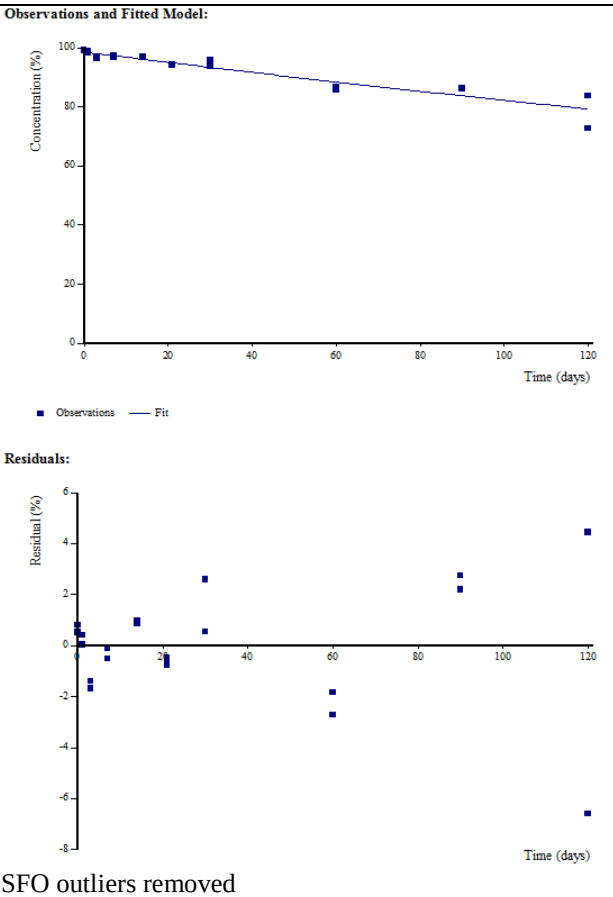
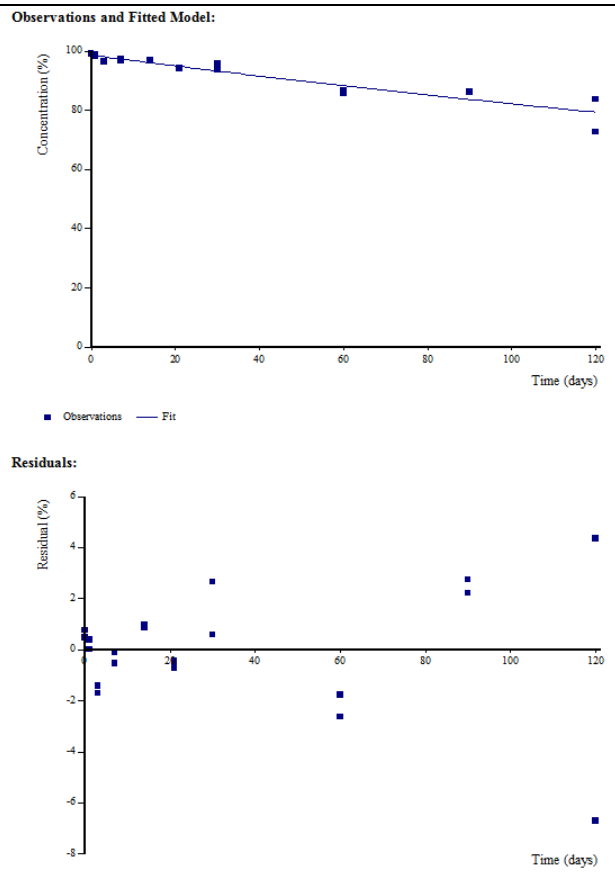


FOMC all data



SFO outliers removed



FOMC outliers removed

For best practice and to assess whether any difference in DT_{50} values would arise between different models used, the RMS also performed the same kinetic assessment for napropamide-M in the KINGUI model software package. There was no discernible difference in visual or statistical assessment between the CAKE and KINGUI results. For loamy sand KINGUI also showed very similar fit and results for DFOP and HS, except slightly higher χ2 error for HS (0.76%) than DFOP (0.612%) compared to in CAKE where it was HS (0.598%) and DFOP (0.611%). For clay loam KINGUI showed similar results to CAKE in that the visual fit for SFO was poor and the best fit visually and in terms of lowest χ^2 error (2.924%) was HS. However, it was not possible to calculate a reliable DT_{50} for this soil in KINGUI, this is unsurprising given the value estimated in CAKE was extrapolated well beyond study duration (>1000d). The RMS has accepted the results derived using CAKE.

Table B.8.1.1.1-30 provides a summary of the "best fit" kinetic models chosen by the Applicant and agreed by the RMS to represent the aerobic degradation of napropamide-M for each soil type. The DT_{50} values reported ranged from 382 to 1150 days, with a geometric mean of 608, indicating that napropamide-M is persistent under laboratory conditions in all the soil types used. All half-life values were based on the 0- 120 day dataset, not the full 0-180 day dataset.

Table B.8.1.1.1-30 Summary of persistence endpoints derived from the kinetic assessment of degradation of napropamide-M under aerobic laboratory conditions

Soil	Kinetic model	χ^2 err%	DT_{50}	DT_{90}
Clay	DFOP	1.89	727	2820
Loamy Sand	HS	0.598	636	2200
Sandy Loam	HS	2.34	408	1690
Clay Loam	HS	2.92	1150	5250
Loam	SFO	1.19	383	1270
Average			661	2646
Geometric mean			608	2338

B.8.1.1.2 **Anaerobic degradation in soil**

Study author	Ahmad, S. (2015b)
Study title	[Naphthyl-1-^{14}C] Napropamide-M: Anaerobic Soil Metabolism and Transformation
Study date	08/05/2015
Annex point	CA 7.1.1.2-01
Previous evaluation	New active substance, no previous studies submitted.

Study Design

An anaerobic soil degradation study was conducted with napropamide-M according to OECD: Guideline 307; Aerobic and Anaerobic Transformation in Soil, April 24, 2002. It was conducted in compliance with US GLP except for following deviation: reference standards, with the exception of napropamide-M, were not GLP characterised. Since no major metabolites are formed in this study, accurate identification is not considered to be critical in this case.

Mass balances reported (97.2 to 139.6%AR) were outside the range considered acceptable by the OECD guidelines for a radiolabelled study (i.e. 90- 110% AR). The RMS notes that dosing solution appears to have exceeded solubility of the test material in water. Napropamide-M has a solubility in water of 39 mg/l at neutral pH and 20°C. The dosing solution contained 25 mg active substance in a volume of 107 ml, 92 ml of which was water. 15 ml of methanol was added to aid dissolution. Furthermore, a failure to perform a homogeneity and quantification check of the final dosing solution resulted in the potential for individual vessels to receive different amounts of the test substance, which may have led to the variable data. Consequently, the study author has normalised the results to percentage recovered radioactivity.

Radiolabelled [naphthyl-1-^{14}C] napropamide-M was applied at a rate of 2.5 mg/kg dry weight of soil, equivalent to 1.875 kg/ha (assuming 5 cm soil depth and soil density of 1.5 g/cm^3).Test substance was dissolved in 92 mL water and 15 mL methanol, applied drop-wise to soil and mixed thoroughly with a glass rod.

Degradation of napropamide-M was studied in a single clay soil from the UK, (3.7% OM, 7.3 pH). Details of the soil properties are given in Table B.8.1.1.2-1. No information was submitted regarding the pesticide history of the site. The soil arrived at the laboratory within three days of sampling and was stored at *ca* 4ºC for 26 days until use.

Table B.8.1.1.2-1 Physicochemical properties of test soil used in the anaerobic laboratory degradation study

Soil (JRFA ID no.[1])	pH (H_2O)	OM (%)	OC (%)	Sand[1] (%)	Silt[1] (%)	Clay[1] (%)	CEC (meq/100g)	Classification[2]	Moisture content at 1/3 bar (%)
UK (102083)	7.3	3.7	2.15	37	11	52	32.6	Clay	35.4

[1] JRFA ID= Test facility soil identification number
[2] USDA textural class

Soil samples (50 g dry weight equivalent, 2 mm sieved) were in individual incubation vessels fitted with traps. All vessels were incorporated into air flow-through systems and acclimatised for one week prior to test substance application. Following application, the test vessels were incubated under aerobic conditions at 20 ± 2°C (monitored continuously) under darkness for 30 days. Thirty days after treatment, the air lines were switched to nitrogen and the soils were flooded with distilled water (1-3 cm above the soil surface). Samples were analysed immediately following test substance application (zero time), and at 30 (end of aerobic phase) 37, 44, 58, 79, 100, 121, 150 and 210 days after treatment. A total of five traps consisted of three to collect volatile compounds and $^{14}CO_2$, (1:1 ethylene glycol: water, 0.05 M sulphuric acid and 1 M potassium hydroxide) and two safety traps. No trapping media for volatiles was associated with zero day samples. Soil moisture was maintained periodically throughout the aerobic phase. Pre-study checks confirmed that the test substance did not adsorb to the glass vessels.

The study author reported that 10 control vessels were prepared for the soil and that biomass was determined at the beginning and end of the study. The nature of these controls was not specified, though later in the study reference was made to a blank solution of methanol: water (1:3 v/v) being applied to the soil of control test vessels, to be used for measurement of microbial biomass at the end of the incubation period. The RMS asked the Applicant to clarify the ratio of methanol to water used. The Applicant claims there was no record in the raw data of a methanol: water solution being used for the control samples. The RMS was unable to determine from the study report whether the microbial biomass, given in the table of soil characterisation, from the start and end of the study (table B.8.1.1.2-2) was from these control samples, and whether or not these were treated with solvent. Measurements of % oxygen from a control soil sample were reported for each sampling interval; again it is not clear if this was a control with or without solvent. No other results were reported for the controls.

Table B.8.1.1.2-2 Microbial biomass of soil used in the anaerobic route and rate degradation study of ^{14}C napropamide-M

Soil (JRFA ID no.[1])	Microbial Biomass	
	Initial (µg OC/ g sediment)	Final (µg OC/ g sediment)
UK (102083)	684.0	616.6

[1] JRFA ID= Test facility soil identification number

Values for redox potential were not reported. Oxygen levels were monitored in a control sample and measured at sampling intervals after day 30, (days 37-210). Levels of % oxygen ranged from 1.01-12.15% and were mostly ≤4%, indicating anaerobic conditions were likely maintained from day 30 for the study duration.

Samples were drawn in duplicate and extracted five times, three times with acetonitrile and once each with acetonitrile: water (1:1; v/v) and methanol: 1N hydrochloric acid (1:1; v/v), by shaking for *ca* 1 hour on an end over-end shaker. Each extract was removed by centrifugation. The extractable soil radioactivity was quantified by LSC. The soil extracts were combined, for each sampling interval, concentrated under nitrogen, centrifuged and analysed by reversed phase HPLC with on-line radio-detection. The identity of napropamide-M and its metabolites were confirmed using mass spectral analysis of representative samples. At each sampling point during the anaerobic phase the water layer was removed from the soil prior to analysis by LSC. Due to suspected non-homogenous dosing solution causing variability in the material balances, the material balances were normalised to the replicates. The average LOD and LOQ values for extracts were 11.5 and 44.9 dpm respectively. All extracts were stored at *ca* -20°C prior to HPLC analysis.

The radioactivity remaining in the soil was quantified by combustion with LSC. The unextracted radioactivity remaining in the soil from the 210 day samples, was characterised by fractionation into fulvic and humic acid, and humin fractions. Samples underwent Soxhlet extraction with hydrochloric acid and subsequently with base. Approximately 30 g ground air-dried soil was extracted with *ca* 150 mL 0.01 M HCl overnight followed by *ca* 150 mL 0.5 M NaOH. Triplicate aliquots were analysed using LSC. The LOD and LOQ values for combustions were 13.2 and 49.7 dpm respectively.

Chiral HPLC analysis to confirm the ratio of D and L isomers was not performed in this study as it had been conducted under the aerobic study. The results of which confirmed that napropamide-M remained in the D- form with no indication of isomerization to the L- form.

Results and Conclusions

Tables B.8.1.1.2-3 and B.8.1.1.2-4 show the material balance of radioactivity in the clay soil. Mass balance ranged from 97.2 to 139.6% AR (individual replicates). The variable results are believed to be due to the improper preparation of the application solution resulting in the possibility that the application solution may not have been homogeneous and test vessels may have received varying amounts of test material. The results from the study were presented normalised to the total recovered radioactivity (RR) obtained for each replicate sample. The RMS has presented the results both in terms of original applied radioactivity (AR) and as RR, for transparency. Mean extractable recovery ranged from 126.9 to 67.3 %AR (or 97.1-56.9 %RR) over 0-210 days.

Unextracted residue reached a maximum mean 44.3 %AR (35.7 % RR) at 121 days. CO_2/volatile levels reached a maximum mean 8.61 %AR (6.57% RR) at day 210. It was not specified in the study how much was CO_2 as opposed to other volatile compounds. The RMS believes that a large proportion of this value is likely to be CO_2 but cannot rule out the possibility of an unidentified volatile metabolite. No volatile metabolites were observed in any other environmental fate study of napropamide-M, making the possibility of an anaerobic soil volatile metabolite unlikely.

Table B.8.1.1.2-3. Material balance in clay soil (102083) expressed as %AR for the anaerobic soil laboratory study

Description		Sampling intervals (days)									
		0	30	37	44	58	79	100	121	150	210
$^{14}CO_2$/ Volatiles	R1	*	0.28	0.19	6.42	0.49	<0.1	10.59	6.16	1.45	9.67
	R2	*	0.80	0.71	4.09	0.52	0.13	4.24	9.36	9.77	7.54
	Mean	*	0.54	0.45	5.26	0.51	0.07	7.42	7.76	5.61	8.61
Extractions	R1	126.3	103.9	87.5	103.5	92.5	86.2	64.0	69.4	65.0	93.3
	R2	127.4	95.8	86.9	93.2	81.3	96.3	81.7	71.5	69.5	83.6
	Mean	126.9	99.9	87.2	98.4	86.9	91.3	72.9	70.5	67.3	88.5
Unextracted residue	R1	3.8	15.8	22.3	15.0	20.0	29.4	21.2	44.4	29.3	34.9
	R2	3.8	16.7	25.7	22.5	30.7	31.2	32.6	44.1	40.8	28.
	Mean	3.8	16.3	24.0	18.8	25.4	30.3	26.9	44.3	35.1	31.8
Water	R1	+	+	0.7	0.8	0.5	0.8	1.5	1.2	1.4	1.7
	R2	+	+	1.8	1.0	2.0	0.7	2.1	1.7	1.1	1.5
	Mean	+	+	1.3	0.9	1.3	0.8	1.8	1.5	1.3	1.6
Material balance $^{+++}$	R1	130.1	120.0	110.7	125.7	113.5	116.4	97.3	121.2	97.2	139.6
	R2	131.2	113.3	115.1	120.8	114.5	128.3	120.6	126.7	121.2	121.3
	Mean	130.7	116.6	112.9	123.3	114.0	122.4	109.0	123.9	109.2	130.5

*No trapping media associated with the zero day sampling interval

\+ No associated test water for these sampling intervals. Soil samples submerged with water after the 30 day sampling interval.

$^{+++}$ variable recoveries may be due to non-homogenous dosing solution

Table B.8.1.1.2-4 Material balance in clay soil (102083) expressed as %RR for the anaerobic soil laboratory study

Description		Sampling intervals (days)									
		0	30	37	44	58	79	100	121	150	210
$^{14}CO_2$/ Volatiles	R1	*	0.2	0.2	5.1	0.4	<0.1	10.9	5.1	1.5	6.9
	R2	*	0.7	0.6	3.4	0.5	0.1	3.5	7.4	8.1	6.2
	Mean	*	0.47	0.39	4.25	0.44	0.1	7.20	6.24	4.78	6.57
Extractions	R1	97.1	86.6	79.0	82.3	81.5	74.1	65.8	57.3	66.9	66.8
	R2	97.1	84.6	75.5	77.2	71.0	75.0	67.7	56.5	57.4	68.9
	Mean	97.1	85.6	77.3	79.7	76.2	74.5	66.8	56.9	62.1	67.9
Unextracted residues	R1	2.9	13.2	20.1	11.9	17.6	25.3	21.8	36.6	30.2	25.0
	R2	2.9	14.7	22.3	18.6	26.8	24.3	27.0	34.8	33.7	23.7
	Mean	2.9	14.0	21.2	15.3	22.2	24.8	24.4	35.7	31.9	24.3
Water	R1	+	+	0.6	0.6	0.4	0.7	1.5	1.0	1.4	1.2
	R2	+	+	1.6	0.8	1.7	0.5	1.7	1.3	0.9	1.2
	Mean	+	+	1.1	0.7	1.1	0.6	1.6	1.2	1.2	1.2
Material Balance^{+++}	R1	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	R2	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
	Mean	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

*No trapping media associated with the zero day sampling interval

+ No associated test water for these sampling intervals. Soil samples submerged with water after the 30 day sampling interval.

$^{+++}$ variable recoveries may be due to non-homogenous dosing solution

Tables B.8.1.1.2-5 and B.8.1.1.2-6 show the distribution of radioactivity between the parent compound and metabolites in clay soil and the associated water phase presented as %AR and %RR values respectively. Napropamide-M degraded in soil under anaerobic conditions to a single minor metabolite DE-napropamide, radiolabelled volatile compounds and unextracted residues. DE-napropamide was detected <2 %AR or RR for all replicates at all sampling intervals. Most extractable radioactivity was associated with the parent compound which represented a mean value of 88.47 %AR (67.84 %RR) at the study end. Both the parent compound and metabolite were strongly associated with the soil extract rather than the overlying water. The unextracted residue was characterised by fractionation for the 210 day samples. Table B.8.1.1.2-7 shows that more OM was associated with fulvic acid than other fractions.

Table B.8.1.1.2-5 Distribution of Radioactivity in Clay Soil (102083) Expressed as AR%

Sampling interval (days)	Compartment	Replicate	Total extractable (AR%)	Parent (%AR)	De-Nap (%AR)
0	soil	1	126.3	125.9	0.4
		2	127.4	125.5	1.9
		mean	126.8	125.7	1.1
30	soil	1	103.9	102.7	1.3
		2	95.8	94.0	1.8
		mean	99.9	98.3	1.5
37	water	1	0.7	0.0	0.0
		2	1.8	0.0	0.0
		mean	1.3	0.0	0.0
	soil	1	87.5	86.7	0.8
		2	86.9	86.2	0.7
		mean	87.2	86.4	0.8
	Total water + soil		88.5	86.4	
44	water	1	0.8	0.0	0.0
		2	1.0	1.0	0.0
		mean	0.9	0.5	0.0
	soil	1	103.5	102.1	1.4
		2	93.2	91.7	1.5
		mean	98.4	96.9	1.5
	Total water + soil		99.2	97.4	
58	water	1	0.5	0.0	0.0
		2	2.0	0.0	0.0
		mean	1.3	0.0	0.0
	soil	1	92.5	91.9	0.6
		2	81.3	80.7	0.6
		mean	86.9	86.3	0.6
	Total water + soil		88.2	86.3	
79	water	1	0.8	0.8	0.0
		2	0.7	0.0	0.0
		mean	0.8	0.4	0.0
	soil	1	86.2	85.3	1.0
		2	96.3	95.2	1.1
		mean	91.3	90.2	1.1
	Total water + soil		92.0	90.6	
100	water	1	1.5	0.0	0.0
		2	2.1	0.0	0.0
		mean	1.8	0.0	0.0
	soil	1	64.0	63.0	1.0
		2	81.7	81.1	0.7
		mean	72.9	72.1	0.8
	Total water + soil		74.6	72.1	
121	water	1	1.2	1.2	0.0
		2	1.7	0.0	0.0
		mean	1.5	0.6	0.0
	soil	1	69.4	69.4	0.0
		2	71.5	71.5	0.0
		mean	70.4	70.4	0.0
	Total water + soil		71.9	71.0	
150	water	1	1.4	0.0	0.0
		2	1.1	0.0	0.0
		mean	1.3	0.0	0.0
	soil	1	65.0	64.6	0.4
		2	69.5	69.1	0.4
		mean	67.2	66.8	0.4
	Total water + soil		68.5	66.8	
	water	1	1.7	0.0	0.0
		2	1.5	0.0	0.0

Sampling interval (days)	Compartment	Replicate	Total extractable (AR%)	Parent (%AR)	De-Nap (%AR)
210		mean	1.6	0.0	0.0
	soil	1	93.4	93.4	0.0
		2	83.6	83.6	0.0
		mean	88.5	88.5	0.0
	Total water + soil		90.1	88.5	

Table B.8.1.1.2-6 Distribution of Radioactivity in Clay Soil (102083) Expressed as RR%

Sampling interval (days)	Compartment	Replicate	Total extractable (%RR)	Parent (%RR)	De-Nap (%RR)
0	soil	1	97.1	96.8	0.3
		2	97.1	95.7	1.4
		mean	97.1	96.2	0.9
30	soil	1	86.6	85.6	1.0
		2	84.6	83.0	1.6
		mean	85.6	84.3	1.3
37	water	1	0.7	0.0	0.0
		2	1.6	0.0	0.0
		mean	1.1	0.0	0.0
	soil	1	79.0	78.3	0.8
		2	75.5	74.9	0.6
		mean	77.3	76.6	0.7
	Total water + soil		78.4	76.6	
44	water	1	0.6	0.0	0.0
		2	0.8	0.8	0.0
		mean	0.7	0.4	0.0
	soil	1	82.4	81.3	1.1
		2	77.2	75.9	1.3
		mean	79.8	78.6	1.2
	Total water + soil		80.5	79.0	
58	water	1	0.5	0.0	0.0
		2	1.7	0.0	0.0
		mean	1.1	0.0	0.0
	soil	1	81.4	81.0	0.5
		2	71.0	70.5	0.5
		mean	76.3	75.7	0.5
	Total water + soil		77.3	75.7	
79	water	1	0.7	0.7	0.0
		2	0.6	0.0	0.0
		mean	0.7	0.4	0.0
	soil	1	74.1	73.2	0.8
		2	75.0	74.2	0.9
		mean	74.6	73.7	0.9
	Total water + soil		75.2	74.1	
100	water	1	1.5	0.0	0.0
		2	1.7	0.0	0.0
		mean	1.6	0.0	0.0
	soil	1	65.8	64.8	1.0
		2	67.8	67.2	0.5
		mean	66.8	66.0	0.8
	Total water + soil		68.4	66.0	
121	water	1	1.0	1.0	0.0
		2	1.3	0.0	0.0
		mean	1.2	0.5	0.0
	soil	1	57.3	57.3	0.0
		2	56.5	56.5	0.0

Sampling interval (days)	Compartment	Replicate	Total extractable (%RR)	Parent (%RR)	De-Nap (%RR)
		mean	56.9	56.9	0.0
	Total water + soil		58.0	57.4	
150	water	1	1.5	0.0	0.0
		2	0.9	0.0	0.0
		mean	1.2	0.0	0.0
	soil	1	66.9	66.5	0.4
		2	57.4	57.0	0.3
		mean	62.1	61.7	0.4
	Total water + soil		63.3	61.7	
210	water	1	1.2	0.0	0.0
		2	1.3	0.0	0.0
		mean	1.3	0.0	0.0
	soil	1	66.8	66.8	0.0
		2	68.9	68.9	0.0
		mean	67.8	67.8	0.0
	Total water + soil		69.1	67.8	

Table B.8.1.1.2-7 Characterisation of unextracted radioactivity at 210 days for soils used in the anaerobic route and rate degradation studies of ^{14}C napropamide-M

210 day samples	% AR Characterised	
	Fulvic Acid	Humic Acid
Clay Soil, UK (102083)	0.04	<0.01

The first order dissipation DT_{50} was recorded in the study report as 239 days (based on %RR, 216.6 based on %AR). For calculation of the DT_{50s}, only the anaerobic phase was taken into consideration (i.e. day 30 to day 150) and calculations combined both the soil and water phases. The study author calculated degradation rates for both the %AR and %RR datasets for napropamide-M, using the individual replicate values and linear regression analysis of log transformed data. Under FOCUS degradation kinetics guidance it is no longer recommended to use linear regression analysis for this purpose.

The RMS repeated the calculations using non-linear regression in the DegKin v.2 spreadsheet, (SFO, 2 reps). Results are shown in table B.1.1.2-8. As these results were extrapolated well beyond the study duration and are therefore uncertain, the RMS has subsequently not reported DT_{90} values. These results are superseded by the kinetic reassessment according to FOCUS guidelines, presented below (study by Croucher, A. & Ford, S. (2015c)). In conclusion, napropamide-M degrades slowly under anaerobic conditions in clay soil.

B.8.1.1.2-8 RMS' DT_{50} and χ^2 values for combined soil and water used in the anaerobic route and rate degradation studies of ^{14}C napropamide-M over 120 days

Soil (JRFA ID no.[1])	Classification[2]	%AR		%RR	
		DT_{50}	χ^2	DT_{50}	χ^2
UK (102083)	Clay	219.6 (535.1)	4.6 (8.8)	239.6 (418.0)	4.2 (6.0)

[1] JRFA ID= Test facility soil identification number
[2] USDA textural class
Values reported in parenthesis represent those calculated including the 210 day sampling interval

Kinetic assessment for anaerobic degradation in soil

Study author	Croucher, A. & Ford, S. (2015c)
Study title	Napropamide-M: kinetic assessment for laboratory anaerobic soil degradation study
Study date	August 2015
Annex point	CA 7.1.2.1.3-02
Previous evaluation	New active substance, no previous studies submitted.

The degradation of [naphthyl-1-^{14}C] radiolabelled napropamide-M was studied in a single European clay soil under anaerobic laboratory conditions (see 3CA B.8.1.1.2). The degradation kinetics were reassessed using the CAKE modelling software package (v 3.1) in accordance with FOCUS (2006) and EFSA (2014). The report used the recovered radioactivity values (i.e. %AR normalised). Initially the models were run including all sampling points up to 180 days, unweighted and using an unconstrained initial value (M0). The acceptability of kinetic fits was judged both visually and statistically (according to the $\chi 2$ error and the t-test functions for SFO or for FOMC the confidence intervals for the α and β parameter estimates were assessed, and a fit was considered acceptable if the intervals did not include zero). The 180 day samples were considered visual and statistical outliers and so the data was reassessed without those values. The Applicant selected SFO as the best fit kinetic model for the persistence endpoint.

The RMS independently verified the Applicant's kinetic assessment using both CAKE and KINGUI modelling packages and found the difference in results between model types to be negligible. Therefore, table B.8.1.1.2-9 below reports the results derived from the CAKE software only.

Table B.8.1.1.2-9 RMS' kinetic assessment of the degradation of napropamide-M under anaerobic conditions in clay soil

Data	Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50}
0-180 days	SFO	6.01 (6.0)	Intermediate	p<0.01	418
	FOMC	4.97 (4.92)	Intermediate	α 90th %ile C.I. does not include zero but 95th %ile does. β both 90th%ile and 95th %ile C.I.s include zero.	6450 (6630)
Conclusions: The SFO model under-predicted the initial concentration and the residual plot showed some over-prediction of the mid-points. The FOMC model better predicted the initial time zero value. The 180 day values were high and did not fit with the rest of the data. These values were removed and the data reassessed.					
0-120 days	SFO	3.39 (3.33)	Good	p<0.01	241
	FOMC	3.55 (3.47)	Good	α & β both 90th %ile and 95th %ile C.I.s include zero	326 (339)
Conclusions: The removal of the 180 day values improved the visual and statistical fits for both models. The initial concentration was better predicted for the modified SFO model and residual scattering was more randomly distributed. The χ^2 error values were acceptable for both models yet the confidence intervals included zero for the FOMC model. The FOMC did not significantly improve visual or statistical fit over SFO therefore SFO accepted. The RMS agrees with the Applicant's results for the kinetic anaerobic assessment.					

All DT_{90} values were >800, often >10, 000.

Values in parenthesis represent the Applicant's results. These are slightly different due to the incorrect value used for the 1st replicate of the 49 day sample which is shown in the Applicant kinetic report as 72.94. The RMS notes that the correct value should be 73.94.

Figure B.8.1.1.2-1 below shows the model graphical outputs for the kinetic assessment in CAKE modelling package. Graphs a) and b) represent the initial assessments which included all the sampling intervals, whereas c) and d) represent the refined models after the removal of the 180 day outliers. Graph c) represents the "best fit" SFO model.

Figure B.8.1.1.2-1 RMS' graphs and residual plots showing the degradation of napropamide-M under anaerobic conditions in clay soil

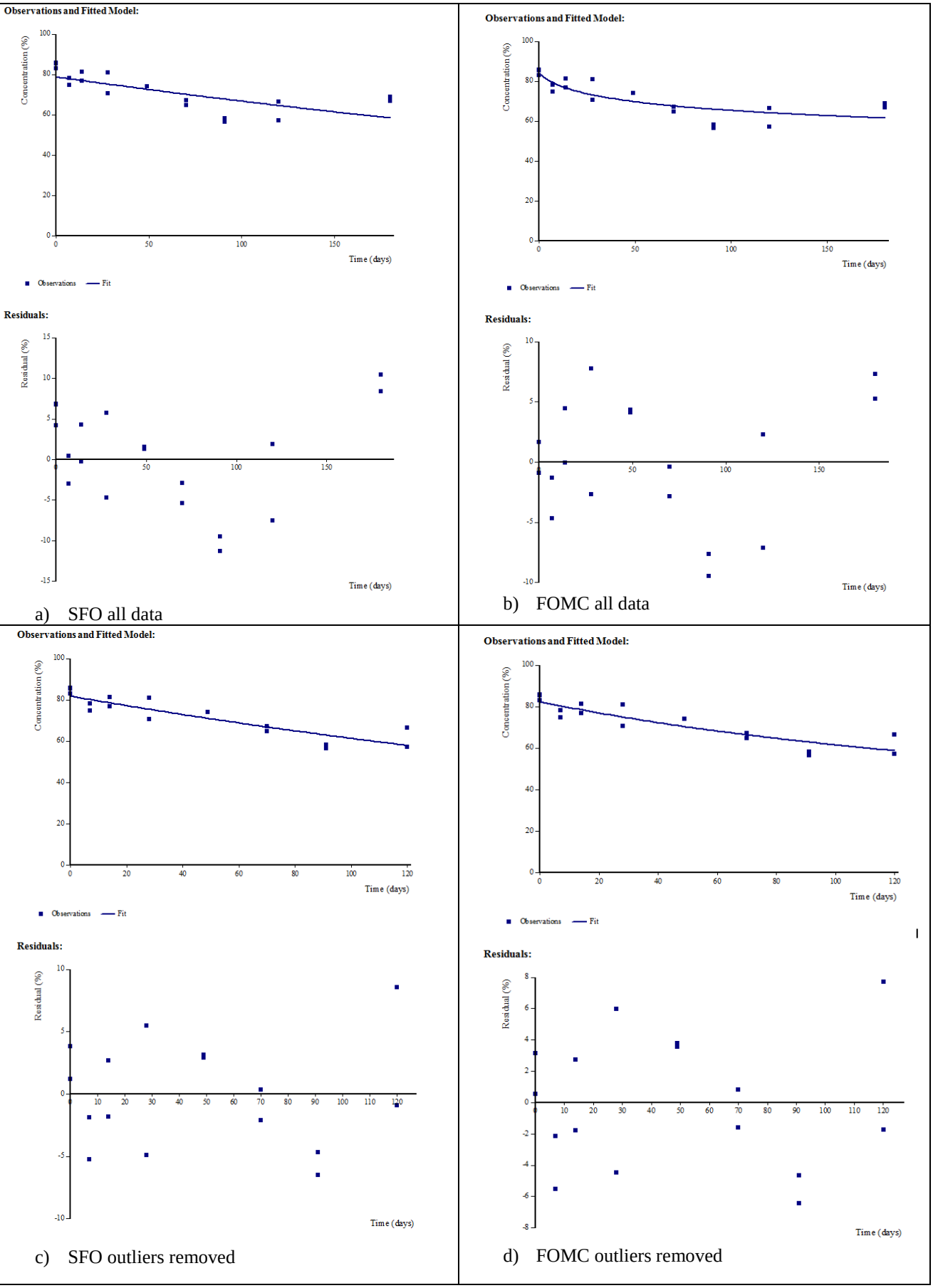


Table B.8.1.1.2-10 provides a summary of the results obtained from both CAKE and KINGUI regarding the anaerobic degradation of napropamide-M in clay. The DT_{50} of 241 days indicates persistence under laboratory conditions.

Table B.8.1.1.2-10 Summary of the kinetic assessment of the degradation of napropamide-M under anaerobic laboratory conditions.

Soil	Kinetic model	χ^2 err%	DT_{50}	DT_{90}
Clay	SFO	3.39 (3.33)	241	799

Applicant values in parenthesis

B.8.1.1.3 **Photodegradation in soil**

Study author	Bianca, C. (2015a)
Study title	[Naphthyl-1-^{14}C] Napropamide-M: Photodegradation on Soil
Study date	10/02/2015
Annex point	CA 7.1.1.3-01
Previous evaluation	New active substance, no previous studies submitted.

A soil photolysis experiment was conducted according to the OECD Guideline Draft Document: Phototransformation of Chemicals on Soil Surfaces (2002) and the US EPA fate, transport and transformation test guidelines OPPTS 835.2410: Photodegradation of chemicals on soil surfaces. The study was performed to GLP with the one deviation: some of the reference substances, with the exception of napropamide-M, were not GLP characterised. Since no major metabolites are formed in this study, accurate identification is not considered to be critical in this case.

A test solution of approx. 0.6 mg/mL [naphthyl-1-^{14}C] napropamide-M solution was prepared by dissolving radiolabelled napropamide-M (3.18 mg) and non-radiolabelled napropamide-M (12.0 mg) in methanol (up to volume of 25 mL). Test solution was applied at a rate of 0.0243 mg/cm^2 soil, equivalent to an application rate of 2.43 kg a.s./ha to each slide. The specific radioactivity of the prepared test material was 43.03 µCi /mg.

Photodegradation was assessed in a single loam soil from Spain (pH 7.4 and 1.28% OC). Full details of soil properties are presented in Table 8.1.1.3-1. The soil was received by the US test facility within two days of collection and stored at 4°C until use. No information on the history of pesticide use at the collection site was provided. Soil was sieved (2 mm) and air dried. Moisture content was measured at the beginning of the study.

B.8.1.1.3-1 Physicochemical properties of test soils used in the photodegradation study

Soil (JRFA ID no.[1])	pH (H_2O)	OM (%)	OC (%)	Sand[2] (%)	Silt[2] (%)	Clay[2] (%)	CEC (meq/ 100g)	Classification[2]	Moisture content at 1/3 bar (%)
Murcia, Spain (102171)	7.4	2.2	1.28	29	47	24	11.8	Loam	28.6

[1] JRFA ID= Test facility soil identification number
[2] USDA textural class

Layers of soil (12.5 cm^2, 2 mm thick) were prepared on glass slides; 21 treated slides prepared for irradiation and 21 treated slides as dark controls, providing samples for 7 sampling points and one contingency at each interval. Dark samples were wrapped in aluminium foil and placed in the chamber. An additional set of 12 soil slides were prepared but were not dosed to act as untreated irradiated controls. Preliminary checks for potential for adsorption of radiolabelled test substance to glass slides confirmed no absorption occurred.

All samples were placed in a test chamber, sealed with a quartz glass lid and placed approximately 10 cm directly under the centre of a xenon light source for continuous exposure (Atlas SunTest XLS +unit with quartz filters). The lamp intensity was set to 760 W/m^2 at a range of 290 to 800 nm. The chamber was immersed in chilled water and placed under simulated sunlight for 30 days. Samples were taken in duplicate at 0, 4, 8, 12, 18, 24 and 30 days. The flow through system was maintained at 16 to 19°C. Temperature was monitored continuously except for the 0 to 4 day sampling period when it was visually checked but not recorded. A stream of pure air, drawn by vacuum, passed through a series of traps containing 2M potassium hydroxide, ethylene glycol, 1M sulphuric acid, and Harvey cocktail respectively to trap volatile organics and CO_2. Traps were replenished with fresh solution at each sampling interval. No trapping media was associated with the zero day samples.

At each sampling interval, the soil samples were extracted sequentially three times with acetonitrile, once with acetonitrile: water (1:1 v/v) and once with methanol: 2N hydrochloric acid (1:1 v/v). Samples were concentrated with nitrogen and partition with hexane, followed by centrifugation and then re-dissolved in acetonitrile. Radioactivity was identified by LSC and napropamide-M and any metabolites were identified by HPLC-RAD-MS. The average LOD and LOQ for extracts were 4.14 and 24.8 dpm respectively. All extracts were stored at *ca* -20 °C prior to HPLC analysis.

Soil remaining after extractions was air dried, homogenised and analysed by combustion on an R.J Harvey Biological Oxidiser (OX 501) followed by LSC analysis of the CO^2 associated with the unextracted residues. Combustion efficiencies were approximately 95%. Radioactivity associated with unextracted residues was low (<8.5% mean for all sampling intervals for both irradiated and dark samples) and so it was not characterised by organic matter fractionation. The LOD and LOQ for combustions were 22.5 and 77.6 dpm respectively.

Radioactivity in the trapping solutions was quantified by LSC and the 30 day samples were characterised by the addition of barium chloride solution as the $^{14}CO_2$ exceeded 5% AR. The test confirmed that the trapped material was CO_2.

Chiral analysis was undertaken to determine the individual D and L isomers of napropamide so that any isomerisation could be observed. The 0, 12 and 30 day samples were analysed by chiral HPLC.

Results

Material balances ranged 88.3-104% AR for all samples. The mean mass balance ranged from 94 -100% AR for the irradiated samples (Table B.8.1.1.3-2), and 93 - 95% AR for the dark controls (Table B.8.1.1.3-3). All photodegradation products were observed in quantities <5% except for carbon dioxide which was detected at 8% at day 30.

Table B.8.1.1.3-2 Material Balance of Radioactivity from Loam Soil (102171) (Expressed as AR%) for Irradiated Samples

Description	Replicate	Sampling Interval (days)						
		0	4	8	12	18	24	30
$^{14}CO_2$ +	R1	N/A	0.8	2.4	3.7	3.5	3.4	7.7
	R2							
Volatiles +	R1	N/A	<0.1	0.1	0.1	0.1	1.2	1.4
	R2							
Acetonitrile	R1	97.9	71.7	58.4	54.5	54.3	55.6	51.2
	R2	91.2	75.3	58.9	57.9	52.0	55.2	52.4
	Mean	94.6	73.5	58.7	56.2	53.2	55.4	51.8
Acetonitrile/ Water	R1	1.2	14.7	25.2	25.2	21.5	23.0	24.5
	R2	1.2	14.2	20.1	21.8	22.8	26.2	27.5
	Mean	1.2	14.5	22.7	23.5	22.2	24.6	26.0
Acidified Methanol	R1	0.4	3.1	5.5	7.1	8.2	6.6	7.3
	R2	0.4	3.1	5.5	6.2	7.9	7.2	8.5
	Mean	0.4	3.1	5.5	6.7	8.1	6.9	7.9
Total extractable	Mean	96.2	91.0	86.8	86.4	83.4	86.9	85.7
Unextracted residues	R1	1.6	2.2	9.5	5.3	7.1	4.1	4.7
	R2	1.4	2.5	5.6	5.1	9.4	7.2	6.0
	Mean	1.5	2.4	7.5	5.2	8.2	5.6	5.4
Material Balance	R1	101.0	92.6	101.1	96.1	94.8	93.8	96.8
	R2	94.2	95.9	92.4	94.8	95.7	100.4	103.5
	Mean	97.6	94.2	96.7	95.4	95.3	97.1	100.2

N/A not analysed
+ individual replicate values not reported

Table B.8.1.1.3-3. Material Balance of Radioactivity from Loam Soil (102171) (Expressed as AR%) for Dark Control Samples

Description	Replicate	Sampling Intervals (days)						
		0	4	8	12	18	24	30
$^{14}CO_2$ +	R1	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	R2							
Volatiles +	R1	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	R2							
Acetonitrile	R1	90.4	89.1	91.1	84.1	87.3	86.3	76.8
	R2	91.3	88.0	82.3	85.7	84.2	79.7	83.7
	Mean	90.9	88.6	86.7	84.9	85.8	83.0	80.3
Acetonitrile/ Water	R1	1.2	3.4	4.0	5.2	5.2	6.3	8.8
	R2	1.3	3.3	4.1	5.1	4.9	8.2	8.3
	Mean	1.3	3.4	4.1	5.2	5.1	7.3	8.6
Acidified Methanol	R1	0.4	0.7	0.8	1.1	1.6	1.7	2.4
	R2	0.4	0.7	0.8	1.1	1.3	2.1	2.2
	Mean	0.4	0.7	0.8	1.1	1.5	1.9	2.3
Total extractable	Mean	92.5	92.5	91.6	91.2	92.3	92.1	91.1
Unextracted residues	R1	1.0	1.2	1.1	1.5	2.2	1.7	2.3
	R2	1.0	0.7	1.1	1.6	2.2	1.2	1.6
	Mean	1.0	0.9	1.1	1.6	2.2	1.4	1.9
Material Balance	R1	93.1	94.4	97.0	92.0	96.4	96.0	90.3
	R2	94.0	92.6	88.3	93.6	92.6	91.1	95.8
	Mean	93.6	93.5	92.7	92.8	94.5	93.5	93.1

N/A not analysed
+ individual replicate values not reported

In the irradiated samples mean concentrations of napropamide-M decreased from 95% AR at 0 day to 79% AR at 18 day (Table B.8.1.1.3-4), while in the dark controls mean concentrations of napropamide-M remained fairly constant with 93% AR at 0 day to 90% AR at 30 day (Table B.8.1.1.3-5). The results of the chiral chromatography analysis confirmed that napropamide-M remained in the D-form with no indication of isomerisation to the L-form. The metabolites identified in the irradiated samples were DE-napropamide (maximum mean 1.9% AR, 8 day), 1-naphthyl (maximum mean 2.2% AR, 18 day) and NOPA (maximum mean 2.8% AR, 12 day). All metabolites were found <1.0 %AR in the dark samples.

Table B.8.1.1.3-4. Photolysis of Napropamide-M on Soil Surface (%AR) in Irradiated Samples

Description		Sampling Intervals (days)						
		0	4	8	12	18	24	30
napropamide-M	R1	98.8	87.4	85.8	82.4	80.8	83.0	79.3
	R2	92.1	90.0	81.7	78.7	77.8	87.5	85.2
	Mean	95.4	88.7	83.8	80.6	79.3	85.3	82.3
DE-NAP	R1	0.7	1.2	2.0	0.0	1.2	1.4	1.1
	R2	0.8	0.0	1.7	1.9	1.5	0.0	1.0
	Mean	0.8	0.6	1.9	0.9	1.4	0.7	1.1
1-Naphthyl	R1	0.0	0.9	1.3	1.9	2.0	0.0	1.2
	R2	0.0	1.4	0.0	2.3	2.5	1.1	1.2
	Mean	0.0	1.2	0.7	2.1	2.2	0.5	1.2
NOPA	R1	0.0	0.0	0.0	2.7	0.0	0.8	1.3
	R2	0.0	1.2	1.0	3.0	0.9	0.0	1.1
	Mean	0.0	0.6	0.5	2.8	0.5	0.4	1.2

Maximum mean metabolite %AR shown in bold

Table B.8.1.1.3-5 Photolysis of Napropamide-M on Soil Surface (%AR) in Dark Samples

Description		Sampling Intervals (days)						
		0	4	8	12	18	24	30
napropamide-M	R1	92.0	93.2	95.1	89.7	93.4	93.6	87.0
	R2	93.0	91.9	86.8	91.5	89.7	89.7	93.8
	Mean	92.5	92.5	90.9	90.6	91.5	91.7	90.4
DE-NAP	R1	0.0	0.0	0.8	0.8	0.8	0.6	0.6
	R2	0.0	0.0	0.4	0.0	0.8	0.2	0.0
	Mean	0.0	0.0	0.6	0.4	0.8	0.4	0.3
1-Naphthyl	R1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	R2	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Mean	0.0	0.0	0.0	0.0	0.0	0.0	0.0
NOPA	R1	0.0	0.0	0.0	0.0	0.0	0.0	0.5
	R2	0.0	0.0	0.0	0.5	0.0	0.0	0.4
	Mean	0.0	0.0	0.0	0.2	0.0	0.0	0.4

Maximum mean metabolite %AR shown in bold

The photolysis half-life for napropamide-M was calculated by the Applicant using regression analysis of log transformed data. Under FOCUS degradation kinetics guidance it is no longer recommended to use linear regression analysis for this purpose. The RMS repeated the calculations using non-linear regression in the DegKin v.2 spreadsheet, (SFO, 2 reps) and reports DT_{50} of 174.4 experimental days (3.6% χ^2), extrapolated well beyond the study duration.

The Applicant used a conversion of 1 experimental day equated to 2.8 days of summer sunlight The value of 2.8 solar days comes from a study on the racemic mixture, napropamide (Lee, 1989) where lamp intensity was equated to summer sunlight integrated intensity at Richmond, California (latitude 37˚ 56' N) of 680 W.h/m2. The RMS then used the following equation from the OECD (2002) guidance:

$$d = \frac{h \cdot r}{0.75 \cdot 12}$$

where d = days of summer sunlight
h = hours of irradiation by the Xenon lamp
r = ratio of intensity (irradiance) of the Xenon radiation to that of summer sunlight
0.75 = correction for diurnal variation of natural sunlight
12 = conversion factor of hours to days.

24* (760/680) = 2.98 days
0.75* 12

Using this value the RMS calculated the conversion to natural summer sunlight as 2.98 days. The Applicant has said that they "*compensated for filter ray deviation which is calculated by taking the 0.78 irradiance conversation value minus the 0.6 which gives the 0.18 value. This was subtracted from the calculated 2.98 value to give 2.8*". Either way, the RMS accepts that difference is small and the impact is minimal. The 30 experimental days are equated to 84 or 89.4 summer sunlight days (37˚N) using 2.8 or 2.98 days, respectively. On that basis the DT_{50} calculated of 174.4 experimental days would be equivalent to *ca* 488-519 summer sunlight days (37˚N). The kinetic reassessment according to FOCUS guidance is reported below.

Kinetic assessment of photodegradation in soil

Study author	Croucher, A. & Ford, S. (2015a)
Study title	Napropamide-M: kinetic assessment for laboratory photodegradation on soil
Study date	August 2015
Annex point	CA 7.1.1.3-02
Previous evaluation	New active substance, no previous studies submitted.

The photodegradation of radiolabelled [napthyl-1-^{14}C] napropamide-M was determined in a single European loam soil under simulated sunlight for 30 experimental days (see 3CA B.8.1.1.3). The degradation kinetics were reassessed using CAKE modelling package (v 3.1) in accordance with FOCUS guidance (2006). The data were directly fitted, un-weighted, with the complete data set and unconstrained initial concentration (M0). Confidence in the resulting parameters was assessed visually and according to statistical measures (χ^2 error, the t-test functions or with the FOMC model, the confidence intervals for the α and β parameter estimates were assessed, and a fit was considered acceptable if the intervals did not include zero).

The RMS confirmed the results in the KINGUI modelling package (see Table B.8.1.1.3-6). For both irradiated and dark samples, degradation followed first order kinetics and so SFO models were accepted as "best fit". Figures B.8.1.1.3-1 and B.8.1.1.3-2 present graphically the kinetic assessment for napropamide-M in irradiated and dark samples respectively. These graphs are taken from the Applicant's kinetics report.

Table B.8.1.1.3- 6 RMS' kinetic assessment of the photodegradation of napropamide-M using KINGUI

Data	Model	χ^2	Visual assessment	Statistical parameters	DT_{50}
Irradiated samples	SFO	3.635	Intermediate	p<0.05	174 (175)
	FOMC	2.369	Intermediate	α 95th%ile C.I. includes zero, β 95th %ile C.I. includes zero	>10, 000
	The visual fit for the SFO was acceptable. In the residual plots time zero was under-predicted slightly, mid-points are over-predicted and end-points are under-predicted. However, the FOMC model did not offer any visual improvement and parameters were statistically unfavourable. Therefore SFO was chosen as the best model.				
Dark samples	SFO	0.542	Good	p>0.2	1261
	FOMC	0.535	Good	α 95% ile C.I. includes zero β 95% ile C.I. includes zero	>10, 000
	Both models showed a good visual fit and residual scattering. However FOMC parameters contained zero. Therefore SFO accepted as "best fit".				

Applicant's values in parenthesis

Figure B.1.1.3-1 Graphs and residual plots showing the degradation of napropamide-M in irradiated soil samples under laboratory conditions

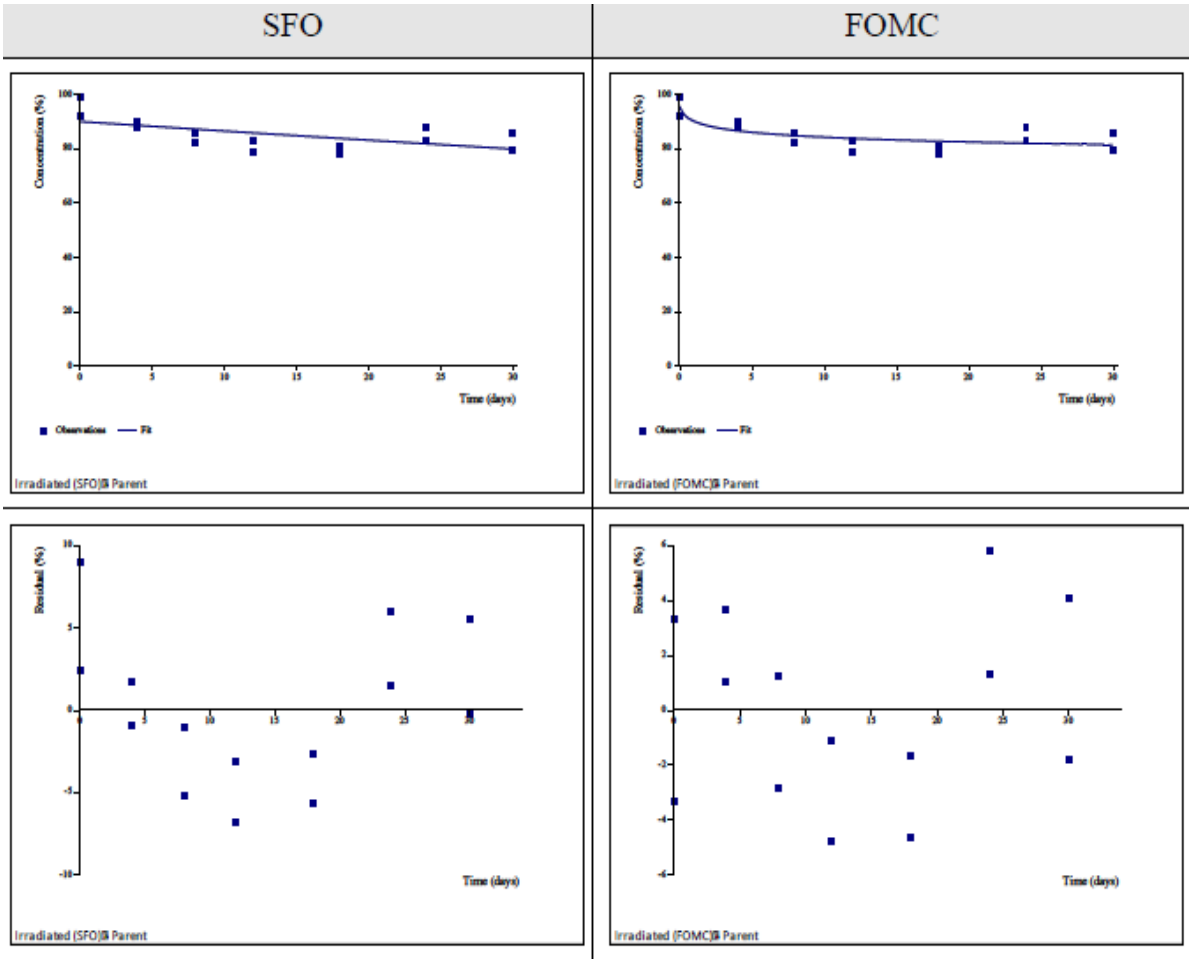
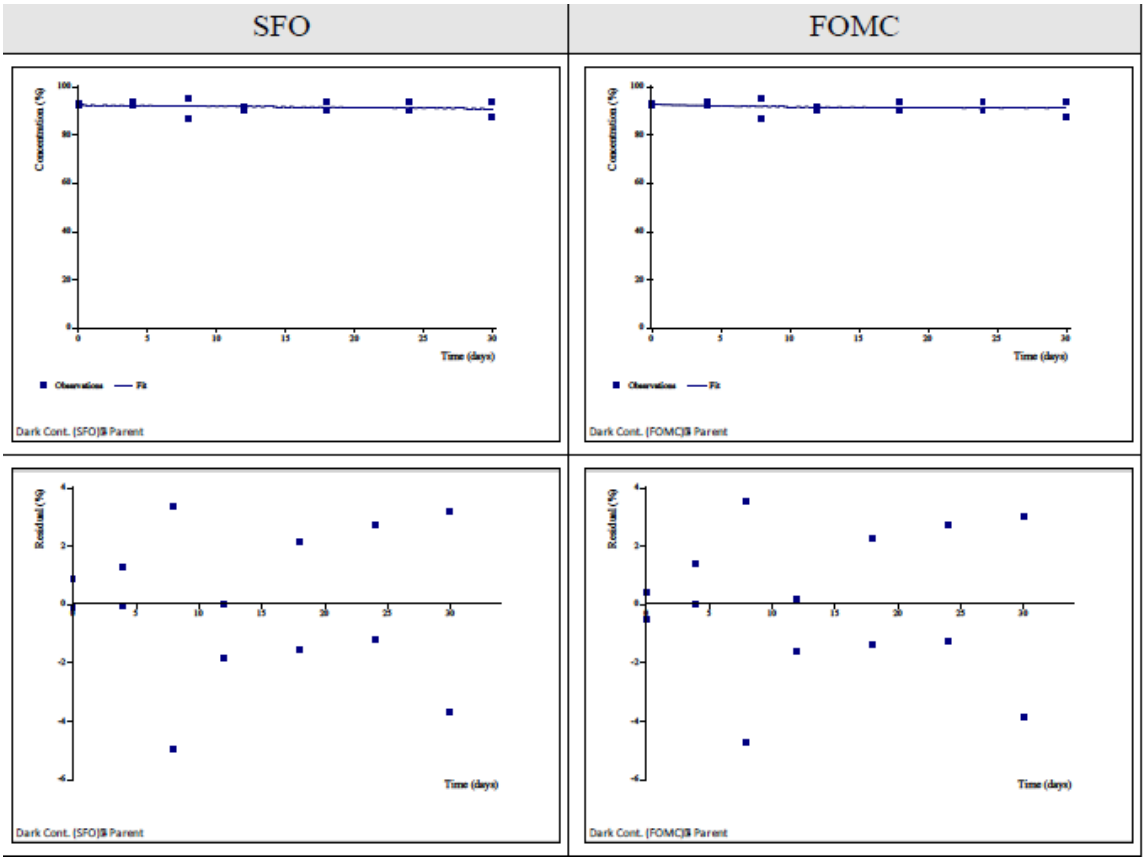


Figure B.8.1.1.3-2 Graphs and residual plots showing the degradation of napropamide-M in dark control soil samples under laboratory conditions.



A summary of the photodegradation of napropamide-M under laboratory conditions is presented below (Table B.8.1.1.3-7). The rate of photodegradation of napropamide-M was slow. The DT_{50} values obtained are extrapolated well beyond the study duration, so are considered uncertain and the DT_{90} values were all >500 days. The RMS considers napropamide-M to be photolytically stable in soil.

Table B.8.1.1.3-7 Summary of kinetic assessment of the photodegradation of napropamide-M

Soil	$\chi 2$ err %	Kinetics	DT_{50} (d)	DT_{90} (d)
Irradiated	3.63	SFO	174	580
Dark Control	N/A*	N/A*	1261	>10,000

* Insufficient degradation to allow calculation of endpoints

B.8.1.1.4 **Field Dissipation Studies**

Study author	Wilson, A. (2015)
Study title	Napropamide-M: Terrestrial Field Dissipation Study with a Suspension Concentrate Formulation Containing 450 g/L Napropamide-M Applied to Bare Soil in Italy, Spain, United Kingdom and Germany, 2013
Study date	27/05/2013
Annex point	CA 7.1.2.2-01
Previous evaluation	New active substance, no previous studies submitted.

Study Design

Napropamide-M exhibited low degradation rates in soil laboratory studies and so it was considered necessary to assess the fate and behaviour of the compound under field conditions. A field study was performed following the US EPA OPPTS 835.6100 guideline in conjunction with 1107/ 2009 guidance and SETAC procedures. It was performed to UK GLP standards with the exception that the meteorological data, details of maintenance pesticides and soil characterisation data were not GLP.

Soil dissipation of napropamide-M and one of its metabolites, 2-(1-naphthyloxy) propionic acid (NOPA) was investigated at four European locations under field conditions: Lombardo (Italy), Burjassot (Spain), Lawford (UK) and Nienberg (Germany). The sites were located in representative oilseed rape and brassica growing regions, on soil types typical for production of these crop types. Table B.8.1.1.4-1 below presents the soil characteristics of each study site. Maps provided indicate that the trial sites were in North Italy, Mid-East Spain, North Germany and South East UK. Pesticide history details were given and included metazachlor (a chloroacetamide) and flufenacet (an oxyacetamide) applied at the German site in 2010 and 2011 respectively. These pesticides display a similar mode of action (cell division inhibition) to napropamide-M (an acetamide). However, the RMS considers it unlikely that the study will have been materially affected by previous application of these pesticides.

Table B.8.1.1.4-1 Physicochemical soil properties of the trial sites used in field dissipation studies

Trial Site	pH (H_2O)	OC (%)	Sand[1] (%)	Silt[1] (%)	Clay[1] (%)	CEC (meq/ 100g)	Classification[1]	Water holding capacity at 0.33 bar (%)
Italy	5.5	1.0	58	27	15	10.3	Sandy loam	21.5
Spain	8.7	1.0	53	26	21	9.8	Sandy clay loam	18.9
Germany	7.3	1.3	96	2	2	6.8	Sand	3.3
UK	6.8	0.8	60	32	8	6.8	Sandy loam	9.4

[1] USDA textural class
OC = organic carbon, CEC = cation exchange capacity

A single application of the formulated napropamide-M (HBW03, batch no. JM230) was applied as suspension concentrate to bare soil at a nominal rate of 750 g as/ha. The certificate of analysis does not report the chemical purity or specify the D- and L-isomer ratio. The RMS cannot confirm that the test item was 100% of the desired D-isomer.

The test substance was applied using a research boom sprayer (flat fan nozzle type) using a nominal water volume of ~200 L/ ha (range 190- 207 L/ha) at all test sites. This is appropriate as the intended GAP application method is broadcast spray. Actual application volumes and rates were determined by measuring the start volume and the final volume of solution in the spray tank. Spray cards (filter papers) were also used to determine the field application rate. The soil surface at time of application was reported as dry for all trials with the exception of the Italian site where the soil surface was damp. Incorporation of the test substance into the soil was carried out within two hours of the application. The incorporation was conducted manually with a rake to a depth of 5 to 10 cm.

Each trial consisted of a single non-treated control plot (plot 1; range 52.5- 70 m^2), split into seven sampling zones and two treated plots (plot 2 treated in spring, and plot 3 treated in autumn). Treated plots were divided into two subplots (A and B; each between 50-60 m^2), each divided into ten sampling zones. The plots were separated by > 20 m to avoid contamination from spray drift. The trial sites were maintained using glyphosate and oxyfluorfen herbicides with no irrigation. Daily records of air temperature, relative humidity and precipitation were taken from the nearest weather stations (Italy ~8 km away; Spain ~7 km away; Germany ~ 15 km away; UK onsite weather station, except for a few dates when data was obtained at a weather station 8 km away). Soil temperature was measured directly at each site to a depth of 10 cm. For three of the sites, there were some periods when the soil

dataloggers failed. Consequently, soil temperatures were taken approximately 20 km away from the Italian site at a weather station between 31st May and 24th June 2014. They were taken approximately 40 km away from the German trial site between 15th March and 25th July 2014. When the data loggers failed at the UK site, between 23rd to 26th May and 14th to 24th September 2014, no alternative data could be obtained from any regional weather station. Table B.8.1.1.4-2 reports the weather conditions on the day of application at each trial site for each plot. Table B.8.1.1.4-3 provides a more detailed summary of any rainfall event on the day of application and precipitation over the first month after application. No heavy rainfall event was reported for the application date (day 0) for any of the trials. Precipitation was higher during the autumn trials than the spring trials for all sites with the exception of the Spanish trials. Detailed meteorological data was provided but not summarised or compared to climatic data typical of the representative region.

Table B.8.1.1.4-2 Meteorological conditions of the field dissipation trials at time of application

Trial	Plot	Application date (0 DAT)	Air temperature (°C)	Soil temperature mean (°C)	Soil surface	Relative humidity (%)	Wind speed (m/s) and direction
Italy	Spring	31/05/13	19	15.0	Damp	54	0.2 N
	Autumn	18/10/13	19	13.9	Damp	44	0.1 NW
Spain	Spring	28/03/13	19.2	19.0	Dry	36	<2 SW
	Autumn	15/10/13	23.3	23.2	Dry	50	1.5 SW
Germany	Spring	15/04/13	24	18.4	Dry	47	<1 W
	Autumn	14/10/13	13	10.5	Dry	81	<1 S
UK	Spring	09/04/13	9.4	4.7	Dry	56	<2 E
	Autumn	08/10/13	15.5	13.6	Dry	85	<1 W

Table B.8.1.1.4-3 Precipitation on the day of application and one month after application

Trial	Plot	Day 0 precipitation (mm)	Precipitation range over first month (mm)	Total precipitation over first month (mm)	Comments
Italy	Spring	0.0	0- 39.6	46.6	Very little rainfall over first month after application, with the exception of a single high rainfall event of 39.6 mm on day 9.
	Autumn	0.0	0- 41.4	106.2	High rainfall over first month. Three main rainfall events were 27.4 mm on day 5, 11.4 mm on day 12 and 41.4 mm on day 28.
Spain	Spring	0.0	0- 10.5	31.8	Little rainfall over first month. Highest values were 9.3 mm on day 8 and 10.5 mm on day 30. Data not available for days 3 and 20.
	Autumn	0.0	0- 1.2	1.2	Virtually no rainfall over the first month after application. Only 1.2 mm rainfall on day 14. No data for day 26.
Germany	Spring	3.7	0- 8.9	19.5	Very little rainfall in first month after application. Highest amount 8.9 mm on day 11.
	Autumn	2.9	0- 10.5	51	Moderate rainfall over first month. Highest amount 10.5 mm on day 19.
UK	Spring	0.0	0- 4.2	22	Little rainfall over first month after application. Highest value 4.2 mm on day 17.
	Autumn	0.0	0- 23.2	109.81	High rainfall over first month. Highest values were 23.2 mm on day 3, 14.2 mm on day 5, 13.6 mm on day 20 and 13.4 mm on day 27.

For the treated plots, at each sampling interval, one sample (10 cores) was collected from a sampling zone in each sub-plot (A and B) to give a single sample of 20 cores for each treated plot. For the treated plots (plots 2 and 3), soil cores were taken prior to

treatment (PTT) and then at 0, 3, 7, 15±1, 30±2, 90±4, 180±4 and 365±4 days after treatment. For the control plots, one sample (20 cores) was taken from a sampling zone at PTT and 0 day (corresponding to plot 2 sampling) and at PTT, 0, 180±4 and 365±4 days (corresponding to plot 3 sampling). Samples were collected using a zero contamination acetate tube (30 cm length x 2.5 cm diameter). All samples were stored frozen within six hours of collection, transported frozen and cut into 0 to 10 cm, 10 to 20, 20 to 30 cm horizons prior to analysis. The RMS notes that some soil samples were stored frozen for a maximum *ca* 21 months prior to analysis. The Applicant referred to a previous study on the storage stability of napropamide, the racemate of napropamide-M. The study demonstrated storage stability of napropamide over a 12 month period under frozen conditions, with no evidence of decline. The Applicant considers it unlikely that any significant degradation would have occurred over a further 9 months. The RMS accepts this as a comparable study and believes residues of napropamide-M in soil samples were not subject to significant decline during storage.

Soil samples were homogenised and 50 g soil was extracted overnight by shaking with acetonitrile: water (1:1, v:v, 100 mL). Subsamples were centrifuged and filtered prior to analysis by LC-MS/MS for napropamide-M and NOPA. The LOQ values for napropamide-M and NOPA were 0.001 and 0.005 mg/ kg respectively. The chemical purity of the reference substances napropamide-M and NOPA were reported as 99.91% and 99.15% respectively.

Results and Discussion

Mean procedural recoveries were within the acceptable range of 70-110% with the mean standard deviation at each fortification <20%. Fortifications were performed at 0.001, 0.001, 0.1, 0.2, 0.5 and 2.0 mg/kg levels for the parent compound and 0.005, 0.01, 0.1, 0.2, 0.5 and 2 mg/kg for the metabolite, NOPA. Results were not corrected for recoveries. Tables B.8.1.1.4-4 and -5 present the procedural recoveries for napropamide-M and the metabolite NOPA respectively. Table B.8.1.1.4-6 below reports the application rates measured via the spray tank and spray cards compared to the measured amount of napropamide-M in the zero day samples.

Table B.8.1.1.4-4 Procedural recoveries for the parent compound napropamide-M for field dissipation studies

Fortification level (mg/kg)	Napropamide-M (parent)	
	Mean recovery ± SD (%)	replicates (n)
0.001 (LOQ)	105 ± 8.0	49
0.01	101 ± 10.5	19
0.1	99 ± 5.8	5
0.2	105 ± 6.5	8
0.5	100 ± 4.8	14
2.0	92 ± 5.8	3
Overall	103 ±8.4	

Table B.8.1.1.4-5 Procedural recoveries for the metabolite NOPA for field dissipation studies

Fortification level (mg/kg)	NOPA (metabolite)	
	Mean recovery ± SD (%)	replicates (n)
0.005 (LOQ)	97 ±9.1	47
0.01	98 ±9.1	18
0.1	95 ±9.3	5
0.2	106 ±7.0	7
0.5	101 ±5.4	14
2.0	92 ±13.2	3
Overall	98± 8.8	

Table B.8.1.1.4-6 Applied rates and measured zero day residues of napropamide-M in the terrestrial field dissipation study, compared to the nominal concentration of 750 g a.s/ha

Trial	Season	Applied rate via spray volume (g/ha) [1]	Applied rate via spray cards(mg) [2]	Theoretical napropamide-M in day 0 samples (mg) [3]	Measured day 0 residues (g/ha)	Measured day 0 all horizons (mg)
Italy	Spring	765	1.926	0.594	617.8	0.6067
	Autumn	785	2.504	0.773	304.9	0.2994
Spain	Spring	812	No sample	No sample	658.4	0.6465
	Autumn	798	2.296	0.709	532.5	0.5229
Germany	Spring	833	2.519	0.777	350.8	0.3445
	Autumn	813	3.129	0.966	304.2	0.2987
UK	Spring	817	3.013	0.930	427.8	0.4201
	Autumn	800	2.501	0.772	457	0.4488

[1] Application rate determined by the start volume and final volume of the spray tank solution.
[2] Application rate measured from five spray cards per plot
[3] Based on 318.08 cm^2 for 5 spray cards (9 cm) and 98.17 cm^2 for 20 soil cores (2.5 cm).

The RMS notes that some of the measured zero day residues are much lower than the nominal applied rates, in some cases almost half. This occurs whether nominal applied rates are measured using spray tank volumes or the intercept cards. The Applicant was asked for any possible explanation on why initial measured residues were so low compared to nominal applied rates. Their response was as follows:

"*We agree that there is a large discrepancy in the measured soil values at day 0 and the nominal applied values, despite reasonable agreement between the spray targets and the nominal applied. The agreement between the nominal and the spray targets confirms that the correct rate of test substance was applied to the soil. With some of the day 0 soil concentration being quite close to half the expected value, we have investigated the possibility of a calculation error such as 10 core instead of 20, but we cannot find any errors in the calculation. We also considered if different size core samples could have been taken at some of the sites, but this looks very unlikely as the difference between samples using 5 cm core compared to 2.5 cm would be 4x. Any difference in soil core diameter would also be obvious from the weight of the soil samples at each horizon. We also feel that the difference is unlikely to be due to photolysis as incorporation took place immediately after application. You would also expect the effect of any photolysis to be greater in the Southern EU trial, but the discrepancy was if anything larger in the UK and German trials. Any variation in the incorporation technique leading to uneven distribution across the surface should have been even out from the random sampling of 20 cores. There is also the possibility that some irreversible binding occurs in some soils, but even this looks unlikely with good agreement between measured day 0 values and the nominal application for the spring application in Italy, but poor agreement at the same site for autumn application. Procedural recoveries were also good for all soils.*

Although we are unable to explain the discrepancy we feel that the way we have handled that data and the fact that we have used only measured soil values in the kinetic evaluation, maintains the validity of the study. If anything, the degradation may have been underestimated."

The analytical method was validated by a chemistry specialist so the RMS accepted the study for purpose of normalisation. The RMS considers that there does not appear to be a calculation error in converting the filter paper to a soil loading rate, as the Applicant also compared the amount in the spray tank before and after to determine the nominal application and this gave similarly low levels. The RMS believes the Applicant has tried to follow the guidance in EFSA $DegT_{50}$ for checking application rate, but the amount applied is clearly lower than intended in many cases. The Applicant has thought through a variety of possible reasons but is unable to explain the results. Although the nominal concentration was not reached after application, it is considered degradation should be independent of concentration. Whilst not ideal, the RMS has on balance accepted these data for the purpose of deriving endpoints for the exposure assessment.

No residues of napropamide-M were detected above the LOQ for any non-treated samples, except the 0 day samples corresponding to the spring application for all trials. Insufficient cleaning of the milling machine between the treated plot and control plot at the sample preparation stage was suspected. No residues of NOPA were detected above the LOQ for any non-treated samples.

Measured residues in the treated plots for all trial sites are reported in Tables B.8.1.1.4-7 to B.8.1.1.4-10. The mean concentration of napropamide-M in the 0-10 cm soil cores decreased from 0.266 – 0.560 mg/kg for spring trials and 0.217 – 0.432 mg/kg for autumn trials at 0 day to 0.018 – 0.075 mg/kg for spring trials and 0.001 – 0.097 mg/kg for autumn trials at the end of the study period (362 to 366 days).Very small amounts of napropamide-M were found in the lowest horizon sampled (20- 30 cm). The Applicant assumes this is due to contamination during sampling as opposed to leaching, citing the high residues of napropamide-M in the lowest layer of the zero day samples are proposed as evidence for this theory. However no supporting evidence was provided. Furthermore, it was reported that sampling was undertaken with "zero contamination" soil coring equipment, implying

that contamination should have been minimal. NOPA was detected at >LOQ in the 0-10 cm cores in the UK field trial only: three instances in the spring trial (maximum of 0.025 mg/kg at 30 DAT) and one instance in the autumn trial (0.013 mg/kg at 30 DAT).

The results indicate that napropamide-M dissipated more quickly from the soil under field conditions than under laboratory conditions. The kinetic assessment of the degradation rate was performed in a separate report. Chiral analysis of representative samples from each trial indicated that napropamide-M remained in the D-form with no indication of isomerisation to the L-form.

Table B.8.1.1.4-7 Measured residues of napropamide-M at the Italian site for the terrestrial field dissipation study

Horizon (cm)	Spring trial (plot 2)		Autumn trial (plot 3)	
	Sample day	napropamide-M (mg/kg dry weight)	Sample day	napropamide-M (mg/kg dry weight)
0-10	0	0.303	0	0.221
10-20		0.004		<0.001
20-30		0.141		NA
0-10	3	0.289	3*	0.352
10-20		0.026		0.003
20-30		0.020		0.007
0-10	7	0.150	7	0.296
10-20		0.009		0.008
20-30		0.022		<0.001
0-10	14	0.238	15	0.218
10-20		0.001		0.004
20-30		<0.001		0.001
0-10	32	0.083	32	0.149
10-20		0.004		0.004
20-30		<0.001		0.001
0-10	94	0.056	94	0.134
10-20		0.006		0.018
20-30		0.004		0.014
0-10	182	0.06	183	0.059
10-20		<0.001		0.003
20-30		NA		<0.001
0-10	365	0.038	363	0.004
10-20		0.004		<0.001
20-30		0.002		NA

* The Applicant regarded this time-point as an outlier during kinetic assessment.

N/A= not analysed

Table B.8.1.1.4-8 Measured residues of napropamide-M at the Spanish site for the terrestrial field dissipation study

Horizon (cm)	Spring trial (plot 2)		Autumn trial (plot 3)	
	Sample day	napropamide-M (mg/kg dry weight)	Sample day	napropamide-M (mg/kg dry weight)
0-10	0	0.560	0	0.432
10-20		0.001		0.002
20-30		<0.001		0.001
0-10	3	0.445	3	0.413
10-20		<0.001		<0.001
20-30		NA		NA
0-10	7	0.228	7	0.362
10-20		<0.001		0.001
20-30		NA		0.001
0-10	15	0.185	15	0.226
10-20		<0.001		<0.001
20-30		NA		NA
0-10	29*	0.016	30	0.253
10-20		<0.001		<0.001
20-30		NA		NA
0-10	90	0.142	91	0.307
10-20		<0.001		<0.001
20-30		NA		NA
0-10	182	0.161	180	0.215
10-20		<0.001		<0.001
20-30		NA		NA
0-10	365	0.075	365	0.097
10-20		<0.001		<0.001
20-30		NA		NA

* The Applicant regarded this time-point as an outlier during kinetic assessment

N/A= not analysed

Table B.8.1.1.4-9 Measured residues of napropamide-M at the German site for the terrestrial field dissipation study

Horizon (cm)	Spring trial (plot 2)		Autumn trial (plot 3)	
	Sample day	napropamide-M (mg/kg dry weight)	Sample day	napropamide-M (mg/kg dry weight)
0-10	0	0.266	0	0.217
10-20		<0.001		<0.001
20-30		NA		NA
0-10	3	0.237	3	0.293
10-20		0.002		<0.001
20-30		<0.001		NA
0-10	7	0.266	7	0.358
10-20		<0.001		<0.001
20-30		NA		NA
0-10	15 *	0.344	15	0.219
10-20		0.001		<0.001
20-30		0.029		NA
0-10	29	0.272	30	0.19
10-20		0.001		<0.001
20-30		<0.001		NA
0-10	89	0.059	91	0.055
10-20		<0.001		<0.001
20-30		NA		NA
0-10	182	0.013	180	0.011
10-20		<0.001		<0.001
20-30		NA		NA
0-10	362	0.019	365	0.001
10-20		<0.001		<0.001
20-30		NA		NA

* The Applicant regarded this time-point as an outlier during kinetic assessment

N/A= not analysed

Table B.8.1.1.4-10 Measured residues of napropamide-M at the UK site for the terrestrial field dissipation study

Horizon (cm)	Spring trial (plot 2)		Autumn trial (plot 3)	
	Sample day	napropamide-M (mg/kg dry weight)	Sample day	napropamide-M (mg/kg dry weight)
0-10	0	0.364	0	0.319
10-20		0.004		0.002
20-30		0.001		0.001
0-10	3	0.448	3	0.413
10-20		0.002		0.001
20-30		0.001		<0.001
0-10	7	0.386	7	0.282
10-20		0.002		0.001
20-30		<0.001		<0.001
0-10	15	0.33	15	0.303
10-20		0.002		0.001
20-30		0.001		<0.001
0-10	30	0.265	30	0.209
10-20		0.002		0.002
20-30		0.001		0.001
0-10	86	0.046	90	0.139
10-20		0.001		0.002
20-30		0.001		<0.001
0-10	178	0.029	178	0.063
10-20		0.002		0.005
20-30		<0.001		<0.001
0-10	365	0.018	366	0.008
10-20		0.002		0.001
20-30		<0.001		0.002

Kinetic assessment of the field dissipation study

Study author	Croucher, A. & Ford, S. (2015d)
Study title	Napropamide-M: Kinetic assessment of field dissipation studies
Study date	February 2015
Annex point	CA 7.1.2.2.1-02
Previous evaluation	New active substance, no previous studies submitted.

Kinetic assessment to derive persistence endpoints

The degradation and behaviour of napropamide-M (HBW03) was studied via terrestrial field dissipation trials at sites in Italy, Spain, Germany and the UK (Wilson, 2015, see 3CA B.8.1.1.4 above). The kinetic degradation rate of napropamide-M was assessed using the modelling software package CAKE.

Data handling

Tables B.8.1.1.4-11 to B.8.1.1.4-18 report the modelling input data generated by the Applicant for the spring and autumn trials in Italy, Spain, Germany and the UK respectively. Residues reported below the limit of detection (LOD) were corrected according to FOCUS (2006). Top soil layer values below LOD just after a detectable amount were set to half of the LOD on a temporal basis. The Applicant also corrected residue values below LOD on a spatial basis as well. Their procedure was as follows: where residues reported in the lower soil layers were below the LOD, these residues were set to half of the LOD only where a detectable residue was recorded in a neighbouring data point, either temporally (previous or next sampling occasion) or spatially (sampling horizon above or below). Although this approach differs from that proposed by FOCUS (2006), the RMS accepts the Applicant's values as the overall difference to total residues at each time-point is negligible.

The Applicant used the following calculation to determine napropamide-M residues in g/ha to input into kinetic modelling. The calculated mass napropamide-M in the top 30 cm of soil was divided by the surface area of the sampling core. The RMS has independently verified these values. Marked values (*) in tables B.8.1.1.4-9 to B.8.1.1.4-16 refer to values considered to be outliers by the Applicant.

$$\text{Napropamide-M residue (g/ha)} = \frac{100000}{\text{Sample core area (cm}^2\text{)} \times \text{No. cores in sample}} \times \text{Measured residue in sample (mg)}$$

Where: Sample core area is based on a diameter of 2.5 cm ($\pi r^2 = \pi(1.25)^2$)

Number of cores in sample is 20

Table B.8.1.1.4-11 Italy spring trial observed residues (mg/kg) and model input data (g/ha)

Sampling day	Horizon (cm)	Dry weight of soil (g)	Measured napropamide-M residue (mg/ Kg)	Adjusted napropamide-M residue (mg/Kg)	Total mass in each horizon (mg)	Total mass in all horizons (mg)	Equivalent in g/ha
0	0-10	1215.5	0.303	0.303	0.3683	0.6067	617.8
	10- 20	1461.6	0.004	0.004	0.0058		
	20- 30	1649	0.141	0.141	0.2325		
3	0- 10	1317.5	0.289	0.289	0.3808	0.4495	457.7
	10- 20	1377.8	0.026	0.026	0.0358		
	20- 30	1644.75	0.02	0.02	0.0329		
7	0- 10	1204	0.15	0.15	0.1806	0.2329	237.2
	10- 20	1411	0.009	0.009	0.0127		
	20- 30	1802	0.022	0.022	0.0396		
14	0- 10	1186.8	0.238	0.238	0.2825	0.2847	289.9
	10- 20	1462	0.001	0.001	0.0015		
	20- 30	1559.75	<0.001	0.0005	0.0007		
32	0- 10	1192.6	0.083	0.083	0.0990	0.1051	107.1
	10- 20	1357.2	0.004	0.004	0.0054		
	20- 30	1431.15	<0.001	0.0005	0.0007		
94	0- 10	1094.7	0.056	0.056	0.0613	0.0734	74.7
	10- 20	1200.6	0.006	0.006	0.0072		
	20- 30	1218	0.004	0.004	0.0049		
182	0- 10	1142.4	0.06	0.06	0.0685	0.0692	70.5
	10- 20	1379.5	<0.001	0.0005	0.0007		
	20- 30	0	0	0	0.000		
365	0- 10	999	0.038	0.038	0.0380	0.0452	46.1
	10- 20	1258.4	0.004	0.004	0.0050		
	20- 30	1126.4	0.002	0.002	0.0023		

Table B.8.1.1.4-12 Italy autumn trial observed residues (mg/kg) and model input data (g/ha)

Sampling day	Horizon (cm)	Dry weight of soil (g)	Measured napropamide-M residue (mg/ Kg)	Adjusted napropamide-M residue (mg/Kg)	Total mass in each horizon (mg)	Total mass in all horizons (mg)	Equivalent in g/ha
0	0- 10	1351.5	0.221	0.221	0.2987	0.2994	304.9
	10- 20	1496	<0.001	0.0005	0.0007		
	20- 30	0	0	0	0.000		
3	0- 10	1352.4	0.352	0.352	0.4760	0.4887	497.7 *
	10- 20	1520.4	0.003	0.003	0.0046		
	20- 30	1163.4	0.007	0.007	0.0081		
7	0- 10	1263.6	0.296	0.296	0.3740	0.3865	393.6
	10- 20	1495.2	0.008	0.008	0.0120		
	20- 30	1083.75	<0.001	0.0005	0.0005		
15	0- 10	992.2	0.218	0.218	0.2163	0.2212	225.3
	10- 20	1008	0.004	0.004	0.0040		
	20- 30	875.5	0.001	0.001	0.0009		
32	0- 10	1344.8	0.149	0.149	0.2004	0.2078	211.6
	10- 20	1513	0.004	0.004	0.0061		
	20- 30	1390.4	0.001	0.001	0.0014		
94	0- 10	1049.6	0.134	0.134	0.1406	0.1786	181.9
	10- 20	1157.1	0.018	0.018	0.0208		
	20- 30	1226.4	0.014	0.014	0.0172		
183	0- 10	1495.2	0.059	0.059	0.0882	0.0934	95.1
	10- 20	1486.8	0.003	0.003	0.0045		
	20- 30	1504.5	<0.001	0.0005	0.0008		
363	0- 10	1428	0.004	0.004	0.0057	0.0064	6.5
	10- 20	1402.5	<0.001	0.0005	0.0007		
	20- 30	0	0	0	0.000		

*This value was regarded as an outlier by the Applicant.

Table B.8.1.1.4-13 Spain spring trial observed residues (mg/kg) and model input data (g/ha)

Sampling day	Horizon (cm)	Dry weight of soil (g)	Measured napropamide-M residue (mg/ Kg)	Adjusted napropamide-M residue (mg/Kg)	Total mass in each horizon (mg)	Total mass in all horizons (mg)	Equivalent in g/ha
0	0- 10	1152	0.56	0.56	0.6451	0.6465	658.4
	10- 20	1400.7	0.001	0.001	0.0014		
	20- 30	1521.5	<0.001	0	0.0000		
3	0- 10	1107	0.445	0.445	0.4926	0.4933	502.4
	10- 20	1393.2	<0.001	0.0005	0.0007		
	20- 30	2040	0	0	0.0000		
7	0- 10	1026	0.228	0.228	0.2339	0.2339	238.2
	10- 20	1313.7	<0.001	0	0.0000		
	20- 30	2070	0	0	0.0000		
15	0- 10	1112.5	0.185	0.185	0.2058	0.2058	209.6
	10- 20	1418.1	<0.001	0	0.0000		
	20- 30	1810	0	0	0.0000		
29	0- 10	1419	0.016	0.016	0.0227	0.0227	23.1*
	10- 20	1339.8	<0.001	0	0.0000		
	20- 30	1840	0	0	0.0000		
90	0- 10	1131.6	0.142	0.142	0.1607	0.1607	163.6
	10- 20	1361.7	<0.001	0	0		
	20- 30	1950	0	0	0		
182	0- 10	1140	0.161	0.161	0.1835	0.1835	186.9
	10- 20	1377	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		
365	0- 10	1186.8	0.075	0.075	0.0890	0.0890	90.6
	10- 20	1422	<0.001	0	0.000		
	20- 30	1740	0	0	0.0000		

*This value was regarded as an outlier by the Applicant.

Table B.8.1.1.4-14 Spain autumn trial observed residues (mg/kg) and model input data (g/ha)

Sampling day	Horizon (cm)	Dry weight of soil (g)	Measured napropamide-M residue (mg/ Kg)	Adjusted napropamide-M residue (mg/Kg)	Total mass in each horizon (mg)	Total mass in all horizons (mg)	Equivalent in g/ha
0	0- 10	1201.2	0.432	0.432	0.5189	0.5229	532.5
	10- 20	1302.4	0.002	0.002	0.0026		
	20- 30	1361.7	0.001	0.001	0.0014		
3	0- 10	1165.6	0.413	0.413	0.4814	0.4821	490.9
	10- 20	1406.2	<0.001	0.0005	0.0007		
	20- 30	1630		0	0.0000		
7	0- 10	1106.7	0.362	0.362	0.4006	0.4035	410.9
	10- 20	1370.6	0.001	0.001	0.0014		
	20- 30	1504.8	0.001	0.001	0.0015		
15	0- 10	1165.6	0.226	0.226	0.2634	0.2641	268.9
	10- 20	1341	<0.001	0.0005	0.0007		
	20- 30	1850	0	0	0.0000		
30	0- 10	1149.5	0.253	0.253	0.2908	0.2908	296.2
	10- 20	1317.2	<0.001	0	0.0000		
	20- 30	1700	0	0	0.0000		
91	0- 10	1143.9	0.307	0.307	0.3512	0.3512	357.6
	10- 20	1379.5	<0.001	0	0.0000		
	20- 30	1930	0	0	0.0000		
180	0- 10	1128.4	0.215	0.215	0.2426	0.2426	247.1
	10- 20	1388.4	<0.001	0	0.0000		
	20- 30	1580	0	0	0.0000		
365	0- 10	1164.8	0.097	0.097	0.1130	0.1130	115.1
	10- 20	1397.3	<0.001	0	0.0000		
	20- 30	1410	0	0	0.0000		

Table B.8.1.1.4-15 Germany Spring trial observed residues (mg/kg) and model input data (g/ha)

Sampling day	Horizon (cm)	Dry weight of soil (g)	Measured napropamide-M residue (mg/ Kg)	Adjusted napropamide-M residue (mg/Kg)	Total mass in each horizon (mg)	Total mass in all horizons (mg)	Equivalent in g/ha
0	0- 10	1292.7	0.266	0.266	0.3445	0.3445	350.8
	10- 20	1302	<0.001	0.0005	0.0007		
	20- 30	1620	0	0	0.0000		
3	0- 10	1264.8	0.237	0.237	0.2998	0.3025	308.1
	10- 20	1376.4	0.002	0.002	0.0028		
	20- 30	1598	<0.001	0	0.0000		
7	0- 10	1339.2	0.266	0.266	0.3562	0.3569	363.5
	10- 20	1391.2	<0.001	0.0005	0.0007		
	20- 30	1950	0	0	0.0000		
15	0- 10	1485.2	0.344	0.344	0.5109	0.5614	571.7*
	10- 20	1532.2	0.001	0.001	0.0015		
	20- 30	1688.2	0.029	0.029	0.0490		
29	0- 10	1278.4	0.272	0.272	0.3477	0.3500	356.4
	10- 20	1438.2	0.001	0.001	0.0014		
	20- 30	1598	0.0005	0.0005	0.0008		
89	0- 10	1251.3	0.059	0.059	0.0738	0.0745	75.9
	10- 20	1381.8	<0.001	0.0005	0.0007		
	20- 30	2000	0	0	0.0000		
182	0- 10	1478.7	0.013	0.013	0.0192	0.0192	19.6
	10- 20	1497.3	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		
362	0- 10	1381.8	0.019	0.019	0.0263	0.0263	26.7
	10- 20	1565.1	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		

*This value was regarded as an outlier by the Applicant.

Table B.8.1.1.4-16 Germany autumn trial observed residues (mg/kg) and model input data (g/ha)

Sampling day	Horizon (cm)	Dry weight of soil (g)	Measured napropamide-M residue (mg/ Kg)	Adjusted napropamide-M residue (mg/Kg)	Total mass in each horizon (mg)	Total mass in all horizons (mg)	Equivalent in g/ha
0	0- 10	1376.4	0.217	0.217	0.2987	0.2987	304.2
	10- 20	1553.1	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		
3	0- 10	1334	0.293	0.293	0.3909	0.3909	398.0
	10- 20	1571.7	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		
7	0- 10	1297.2	0.358	0.358	0.4644	0.4644	472.9
	10- 20	1553.1	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		
15	0- 10	1416.8	0.219	0.219	0.3103	0.3103	316.0
	10- 20	1579.2	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		
30	0- 10	1453.6	0.19	0.19	0.2762	0.2762	281.2
	10- 20	1571.7	<0.001	0	0.0000		
	20- 30	1990	0	0	0.0000		
91	0- 10	1547	0.055	0.055	0.0851	0.0851	86.6
	10- 20	1627.5	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		
180	0- 10	1104.5	0.011	0.011	0.0121	0.0121	12.4
	10- 20	1269	<0.001	0	0.0000		
	20- 30	0	0	0	0.0000		
365	0- 10	1453.6	0.001	0.001	0.0015	0.0015	1.5
	10- 20	1441.5	<0.001	0	0.0000		
	20- 30	1420	0	0	0.0000		

Table B.8.1.1.4-17 UK spring trial observed residues (mg/kg) and model input data (g/ha)

Sampling day	Horizon (cm)	Dry weight of soil (g)	Measured napropamide-M residue (mg/ Kg)	Adjusted napropamide-M residue (mg/Kg)	Total mass in each horizon (mg)	Total mass in all horizons (mg)	Equivalent in g/ha
0	0- 10	1134	0.346	0.346	0.4128	0.4201	427.8
	10- 20	1397.3	0.004	0.004	0.0056		
	20- 30	1753.3	0.001	0.001	0.0018		
3	0- 10	1147.5	0.448	0.448	0.5141	0.518	527.5
	10- 20	1300.5	0.002	0.002	0.0026		
	20- 30	1293.6	0.001	0.001	0.0013		
7	0- 10	1246	0.386	0.386	0.4810	0.4845	493.4
	10- 20	1432.9	0.002	0.002	0.0029		
	20- 30	1404	<0.001	0.0005	0.0007		
15	0- 10	1219.4	0.33	0.33	0.4024	0.4066	414.0
	10- 20	1379.5	0.002	0.002	0.0028		
	20- 30	1430	0.001	0.001	0.0014		
30	0- 10	1219.4	0.265	0.265	0.3231	0.3275	333.5
	10- 20	1422	0.002	0.002	0.0028		
	20- 30	1468.5	0.001	0.001	0.0015		
86	0- 10	1237.6	0.046	0.046	0.0569	0.0597	60.8
	10- 20	1359	0.001	0.001	0.0014		
	20- 30	1386	0.001	0.001	0.0014		
178	0- 10	1264.9	0.029	0.029	0.0367	0.0401	40.9
	10- 20	1400.6	0.002	0.002	0.0028		
	20- 30	1302	<0.001	0.0005	0.0007		
365	0- 10	1263.8	0.018	0.018	0.0227	0.0257	26.1
	10- 20	1458	0.002	0.002	0.0029		
	20- 30	1530.8	<0.001	0	0.0000		

Table B.8.1.1.4-18 UK autumn trial observed residues (mg/kg) and model input data (g/ha)

Sampling day	Horizon (cm)	Dry weight of soil (g)	Measured napropamide-M residue (mg/ Kg)	Adjusted napropamide-M residue (mg/Kg)	Total mass in each horizon (mg)	Total mass in all horizons (mg)	Equivalent in g/ha
0	0- 10	1395	0.319	0.319	0.4450	0.4488	457.0
	10- 20	1325.4	0.002	0.002	0.0027		
	20- 30	1099.8	0.001	0.001	0.0011		
3	0- 10	1092	0.413	0.413	0.4510	0.4527	461.0
	10- 20	1231.4	0.001	0.001	0.0012		
	20- 30	916.5	<0.001	0.0005	0.0005		
7	0- 10	1426.8	0.282	0.282	0.4024	0.4044	411.8
	10- 20	1530.8	0.001	0.001	0.0015		
	20- 30	1080	<0.001	0.0005	0.0005		
15	0- 10	1470.6	0.303	0.303	0.4456	0.4477	455.9
	10- 20	1487.2	0.001	0.001	0.0015		
	20- 30	1188	<0.001	0.0005	0.0006		
30	0- 10	1393.2	0.209	0.209	0.2912	0.2952	300.6
	10- 20	1418.1	0.002	0.002	0.0028		
	20- 30	1204	0.001	0.001	0.0012		
90	0- 10	1505	0.139	0.139	0.2092	0.2130	216.9
	10- 20	1513.6	0.002	0.002	0.0030		
	20- 30	1548.6	<0.001	0.0005	0.0008		
178	0- 10	114.6	0.063	0.063	0.0722	0.0798	81.3
	10- 20	1372.8	0.005	0.005	0.0069		
	20- 30	1399.2	<0.001	0.0005	0.0007		
366	0- 10	1416.8	0.008	0.008	0.0113	0.0150	15.3
	10- 20	1435.2	0.001	0.001	0.0014		
	20- 30	1122	0.002	0.002	0.0022		

Kinetic evaluation

The kinetic degradation rate of napropamide-M was reassessed using the modelling software package CAKE (v 3.1) in accordance with guidance provided by FOCUS *Generic guidance for Estimating Persistence and Degradation Kinetics* (2014). Persistence endpoints were derived by best-fit kinetics using non-normalised day lengths. In the first instance, the data were directly fitted, un-weighted, with the complete data set and unconstrained initial concentration (M0). The acceptability of kinetic fits was judged both visually and statistically (according to the χ^2 error and t-test functions for SFO models; α and β parameter estimates for FOMC confidence intervals; K1 and K2 parameters for DFOP, with fits considered acceptable if the intervals did not include zero).

The RMS independently validated the persistence endpoints using CAKE (v.3.2) and has drawn conclusions broadly in agreement with the Applicant's assessment. The Applicant derived degradation kinetics for both Spanish trials using HS models. The RMS notes that according to FOCUS (2014) guidance, only DFOP is recommended in addition to FOMC if biphasic modelling is required. The HS model should only be used in exceptional circumstances, and the RMS believes that this criterion has not been met. However, the use of HS models for the Spanish trials has resulted in DT_{50} values that are either very similar to those obtained by DFOP kinetics or provide a worst case scenario. Therefore the RMS has accepted the Applicant's approach.

Furthermore, the Applicant identified and removed what they believed to be an outlier for three out of the eight trials but gave little justification or reasoning for doing so. According to FOCUS (2014) guidance identification of outliers should be based on expert judgement and any experimental errors should be identified where possible. The RMS notes that field data is subjected to high natural variability and it is not uncommon for second sampling data points to be higher than initial measured concentrations. In each case where an outlier was removed, it improved the fit and resulted in an equivalent or more conservative DT_{50}. On balance, the removal of outliers will not materially affect the study in this case and so the RMS has accepted the Applicant's persistence trigger endpoints (reported in table B.8.1.1.4-19). The arithmetic and geometric mean DT_{50}s were 53.62 days and 36.24 days respectively.

B.8.1.1.4-19 Summary of persistence endpoints for napropamide-M from field dissipation studies

Trial	Plot	Model	χ^2 error%	tb	Overall DT_{50} (days)	DT_{90} (days)
Italy	Spring	FOMC	14.4	-	6.91	138
	Autumn	SFO (modified)	17.9	-	94.4	313
Spain	Spring	HS (modified)	8.86	8.858	5.31	605
	Autumn	HS	10.5	14.14	101.0	900
Germany	Spring	SFO (modified)	17.7	-	57.9	192
	Autumn	SFO	18.2	-	49.0	163
UK	Spring	SFO	12.1	-	40.7	135
	Autumn	SFO	7.43	-	73.7	245
Arithmetic mean			-	-	53.62	336.38
Geometric mean			-	-	36.24	265.03

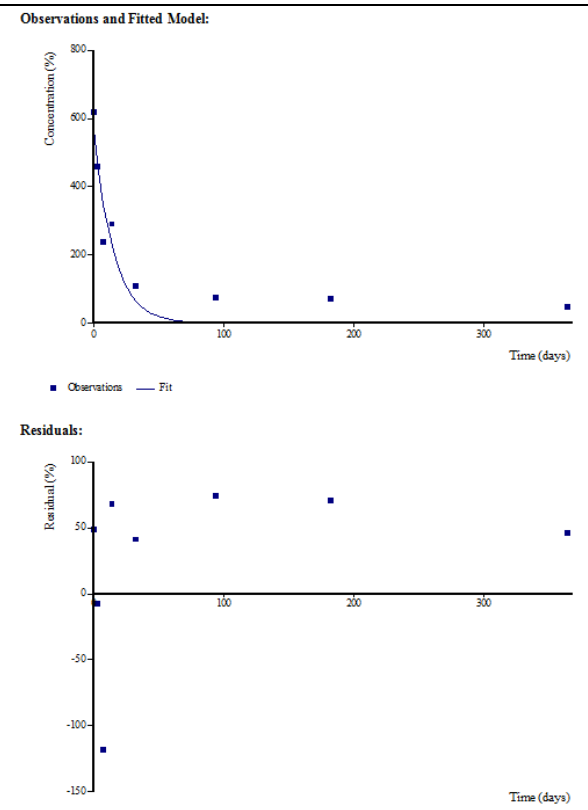
Modified models refer to instances where an outlier has been removed

The Applicant ran the modelling software using the automatic IRLS optimiser rather than OLS. However the RMS verified that the choice of optimiser does not materially affect the results for this study. The RMS notes that some details reported in the main body of the kinetics report do not correspond with the results in the appendices. The results in the appendices were all found to be correct. Tables B.8.1.1.4-20 to B.8.1.1.4-27 present the process for deriving persistence degradation kinetics with corresponding figures B.8.1.1.4-1 to B.8.1.1.4-8. The RMS also used an alternative modelling package (KINGUI) to verify that results were consistent between software packages.

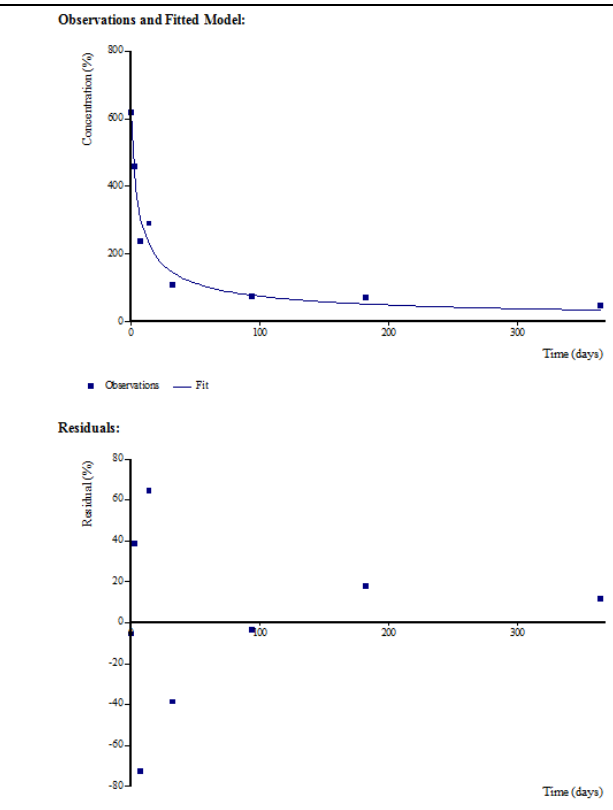
Table B.8.1.1.4-20 RMS' kinetic assessment of napropamide-M for deriving persistence endpoints (Italy spring field trial)

Model	χ^2 error%	Visual assessment	Statistical assessment	DT_{50}	DT_{90} (overall)
SFO	22.3	poor	$p<0.01$	10.3	34.2
FOMC	14.4	good	α C.I.s do not include zero; β 90th and 95th %ile C.I.s include zero.	6.91	138
SFO gave a reasonable prediction of the initial time-points but systematically under predicted the later points. The FOMC provided a better fit and residual scattering. The statistical parameters were better with FOMC i.e. lower χ^2 error%. Therefore other biphasic models were investigated.					
DFOP	16.9	good	K1 95th %ile C.I. includes zero; K2 90th and 95th %ile C.I.s include zero g=0.7524	7.1 (overall) K1= 4.64 K2= 153	200
DFOP gave a similar visual fit to FOMC and statistically offered no improvement. FOMC was selected as best-fit. The RMS agrees with Applicant decision.					

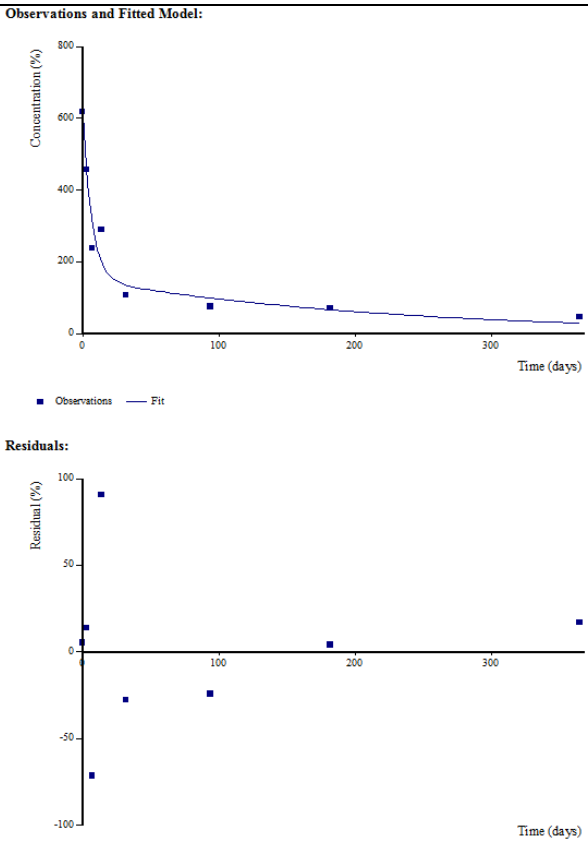
Figure B.8.1.1.4-1 RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (Italy spring field trial)



SFO



FOMC (best-fit)

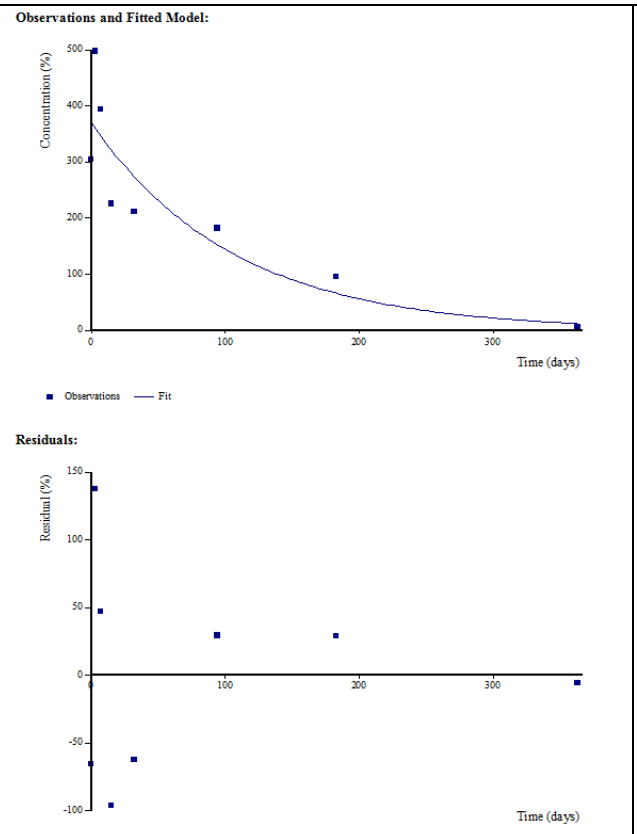


DFOP

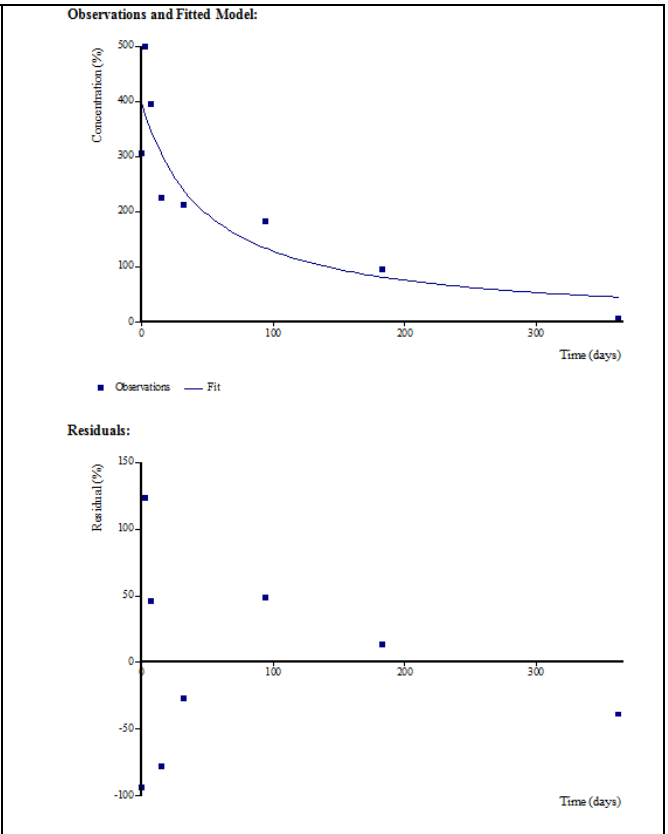
B.8.1.1.4-21 RMS' kinetic assessment of napropamide-M for deriving persistence endpoints (Italy autumn field trial)

Model	χ^2 error%	Visual assessment	Statistical assessment	DT_{50}	DT_{90} (overall)
SFO	23.6	poor	$p<0.05$	73.5	244
FOMC	24.1	poor	Both α and β 90th and 95th %ile C.I.s include zero	47.8	421
Both SFO and FOMC models over-predicted the initial concentration and residuals showed wide scattering. The χ^2 error% values were high (>15%). The Applicant proposed day 3 as a possible outlier and removed it.					
SFO modified	17.9	intermediate	$p<0.05$	94.4	313
FOMC modified	19.3	intermediate	Both α and β 90th and 95th %ile C.I.s include zero.	90.5	330
Removal of day 3 data improved the fit slightly, including a better prediction of the initial concentration. The χ^2 error% values were acceptable for both models. FOMC did not offer any major improvements over SFO. Therefore the modified SFO model was selected as best fit. Although no justification was given for the removal of the outlier by the Applicant, the RMS will use the modified SFO DT_{50} as it provides a more worse-case scenario.					

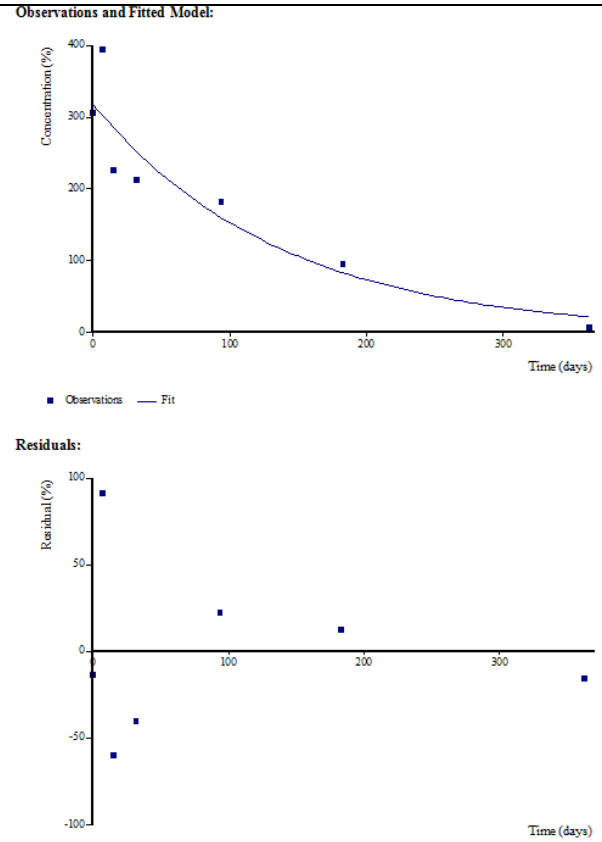
Figure B.8.1.1.4-2 RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (Italy autumn field trial)



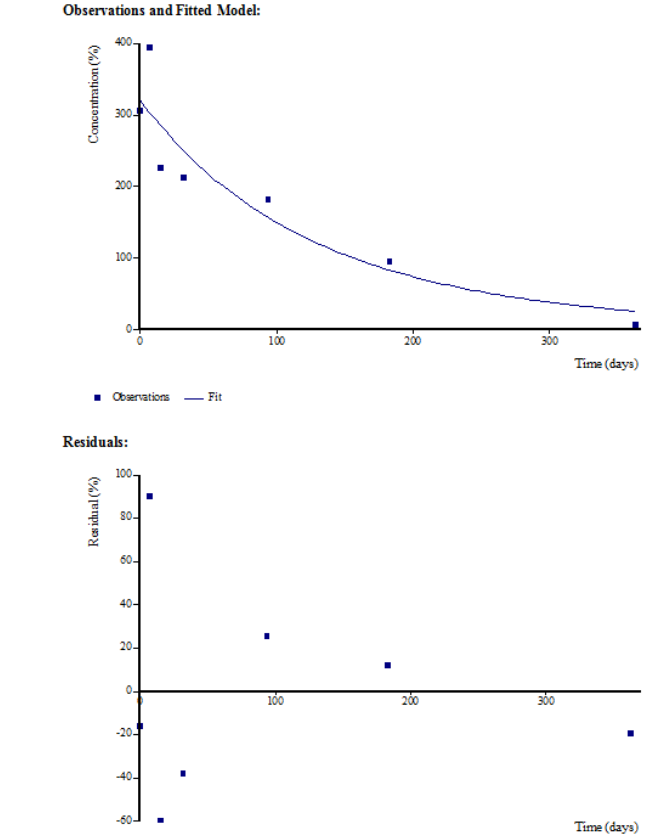
SFO



FOMC



SFO modified (best fit)



FOMC modified

B.8.1.1.4-22 RMS' kinetic assessment of napropamide-M for deriving persistence endpoints (Spain spring field trial)

Model	χ^2 error%	Visual assessment	Statistical assessment	DT_{50}	DT_{90} (overall)
SFO	31.1	poor	$p<0.05$	6.71	22.3
FOMC	26.7	intermediate	Both α and β 90th and 95th %ile C.I.s include zero.	5.23	272
SFO model predicted initial time points well but the residual plot showed systematic under-prediction of later time-points, indicating a biphasic degradation pattern. FOMC better predicted the later time-points but only gave an intermediate fit. The χ^2 error% values for both models were very high. The Applicant investigated day 29 as an outlier and removed it.					
SFO modified	29.3	poor	$p<0.05$	6.79	22.6
FOMC modified	17.1	good	α 95th %ile C.I. includes zero; β both 90th and 95th %ile C.I.s include zero	6.59	1250
The modified SFO model under predicted the later data points whereas the modified FOMC estimated data points well and gave a good fit. The statistical parameters were acceptable with the FOMC. Therefore other biphasic models were investigated.					
DFOP modified	11.7	good	K1 95th %ile C.I. includes zero; K2 both 90th and 95th %ile C.I.s include zero g= 0.7208	5.53 (overall) K1= 3.27 K2= 506	749
HS modified	8.86	good	K1 C.I.s do not include zero; K2 both 90th and 95th %ile C.I.s include zero tb= 8.858	5.31 (overall) K1= 5.31 K2= 361	605
DFOP and HS models both gave a similar visual and statistical fit. The Applicant chose the HS model based on a more favourable χ^2 error% value. However, according to FOCUS guidance (2014), the HS model should not be used for deriving persistence endpoints unless in exceptional circumstances. In this case, RMS has accepted the decision as it does not significantly alter the DT_{50} value. The RMS ran the DFOP and HS models with the full data set for transparency i.e. day 29 was included. The visual fits were acceptable but the χ^2 error% values were higher than those for the modified DFOP and HS models (>15%). On balance, the RMS will use the modified HS model for the Spanish spring trial trigger endpoint.					
DFOP	19.7	intermediate-good	K1 95th %ile C.I. includes zero; K2 both 90th and 95th %ile C.I.s include zero g= 0.8207	5.61 (overall) K1= 4.14 K2 >10, 000	>10, 000
HS	21.1	intermediate-good	K1 C.I.s do not include zero; K2 both 90th and 95th %ile C.I.s include zero tb= 16.88	6.78 (overall) K1= 6.78 K2 >10, 000	>10, 000

Figure B.8.1.1.4-3 RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (Spain spring field trial)

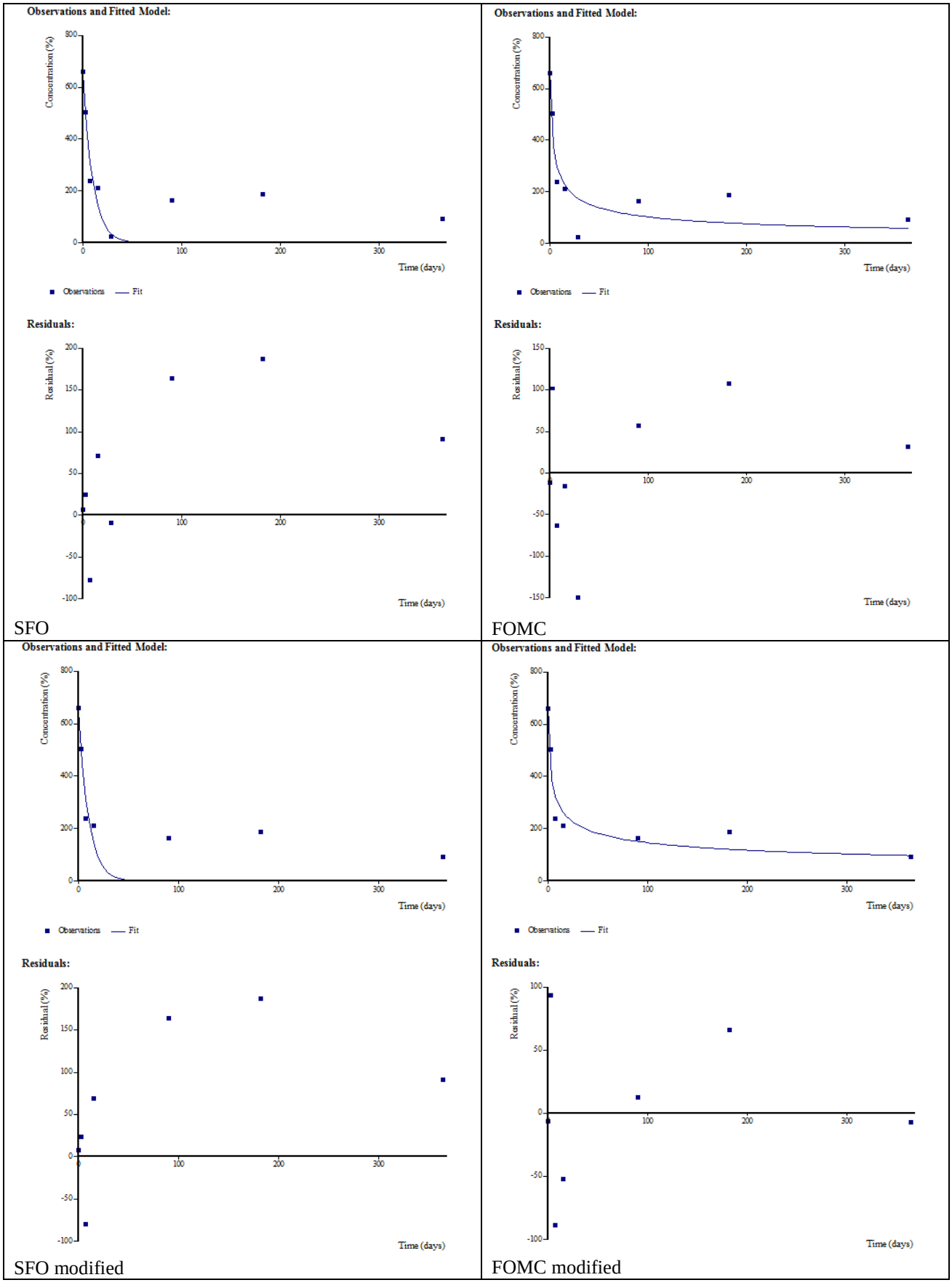
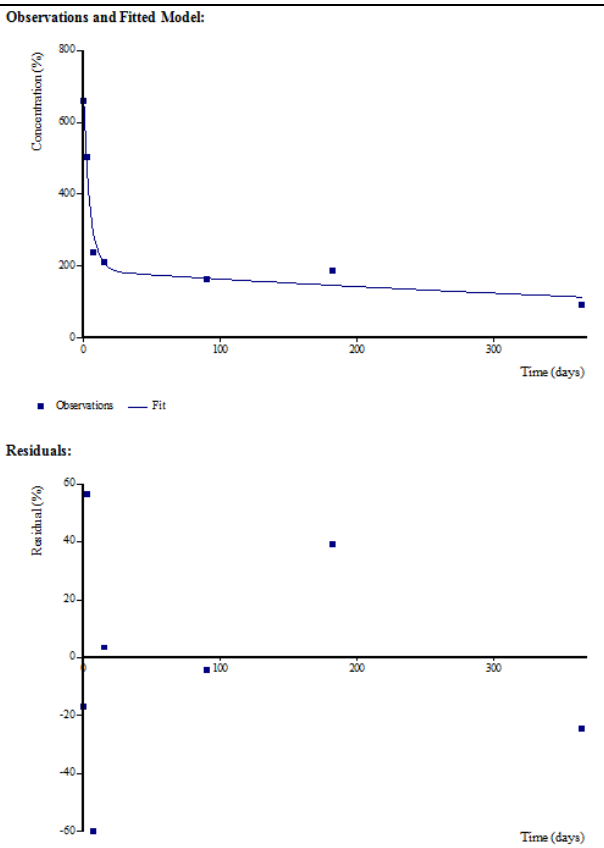
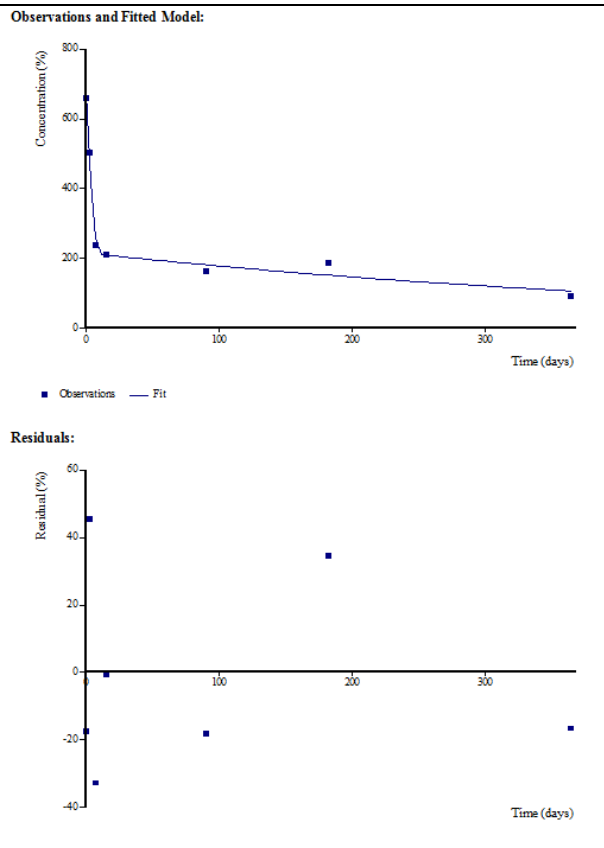


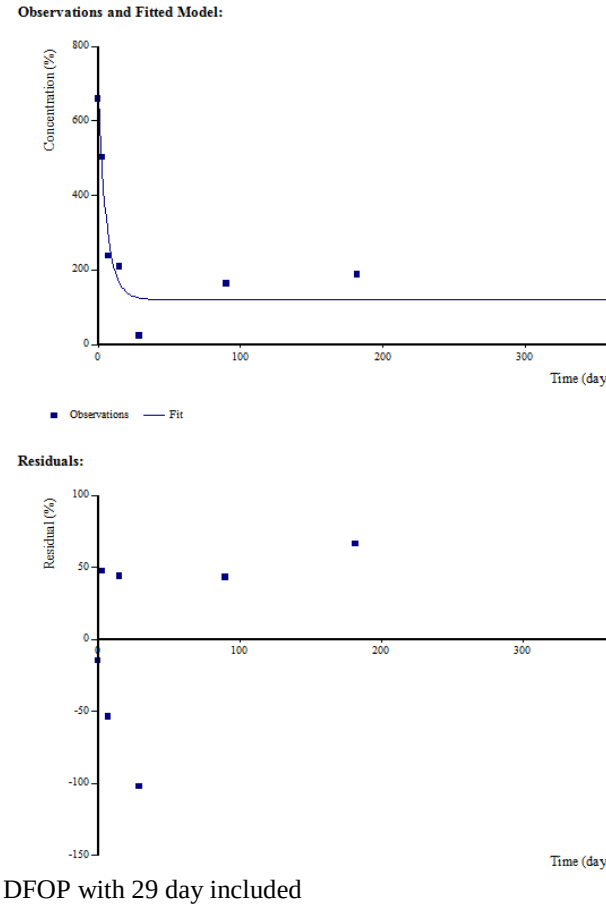
Figure B.8.1.1.4-3 (continued) RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (Spain spring field trial)



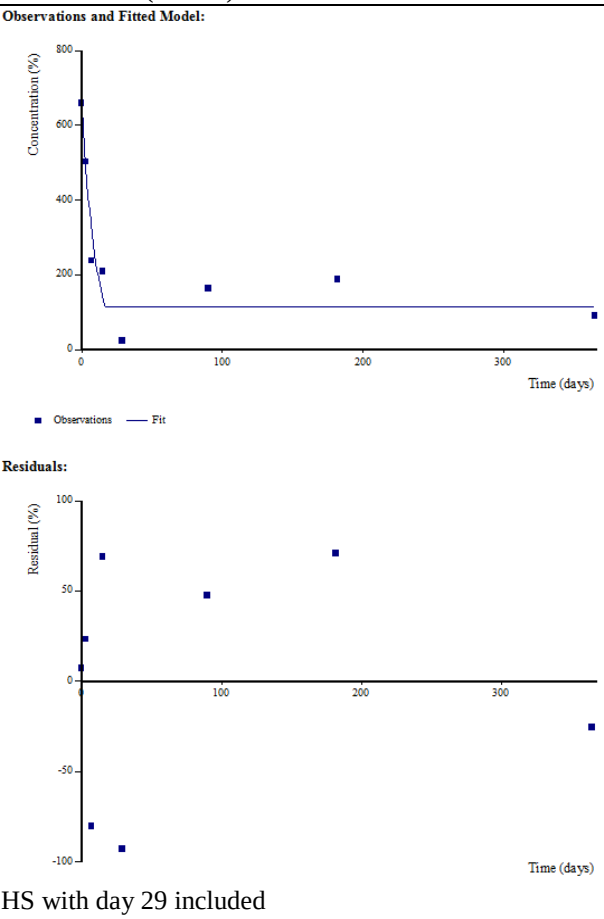
DFOP modified



HS modified (best fit)



DFOP with 29 day included

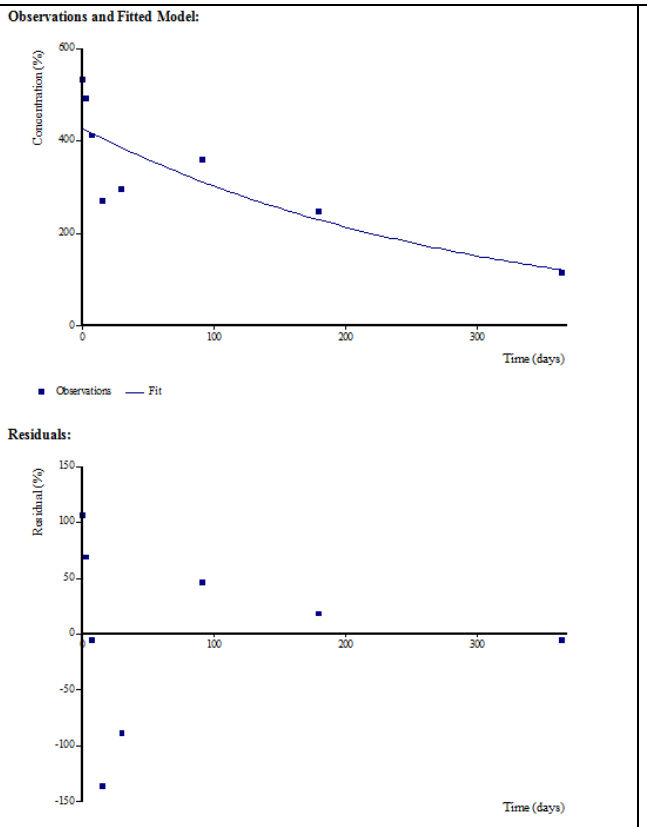


HS with day 29 included

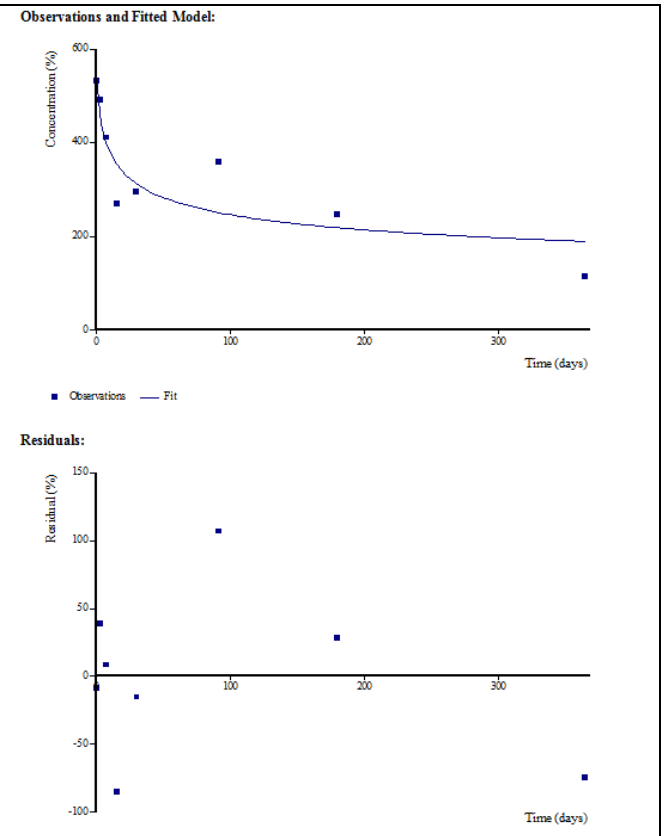
B.8.1.1.4-23 RMS' kinetic assessment of napropamide-M for deriving persistence endpoints (Spain autumn field trial)

Model	χ^2 error%	Visual assessment	Statistical assessment	DT_{50}	DT_{90} (overall)
SFO	17.6	poor	$p<0.05$	201	667
FOMC	14.5	intermediate	α 95th %ile C.I. includes zero; β both 90th and 95th %ile C.I.s include zero	62.3	>10,000
The field data for this trial were very variable and so neither model could give an excellent fit. SFO model under-predicted the initial concentration but statistical parameters were acceptable. FOMC predicted time zero values well, giving a better fit and so other biphasic models were investigated.					
DFOP	11.9	Intermediate-good	Both K1 and K2 C.I.s include zero g= 0.3902	94.4 (overall) K1= 4.06 K2= 330	860
HS	10.5	Good	K1 90th and 95th %ile C.I.s include zero K2 95th %ile C.I.s includes zero tb= 14.14	101 (overall) K1= 18.9 K2=344	900
DFOP and HS models both gave a similar visual and statistical fit. The Applicant chose the HS model based on a more favourable χ^2 error% value. DFOP fit could have been accepted without testing HS, (according to FOCUS guidance HS should only be used exceptionally for persistence endpoints, for example where DFOP is not acceptable). However, since both models gave essentially identical results, the RMS has not rejected the applicant's choice of HS as best fit. (The HS DT_{50} is also conservative).					

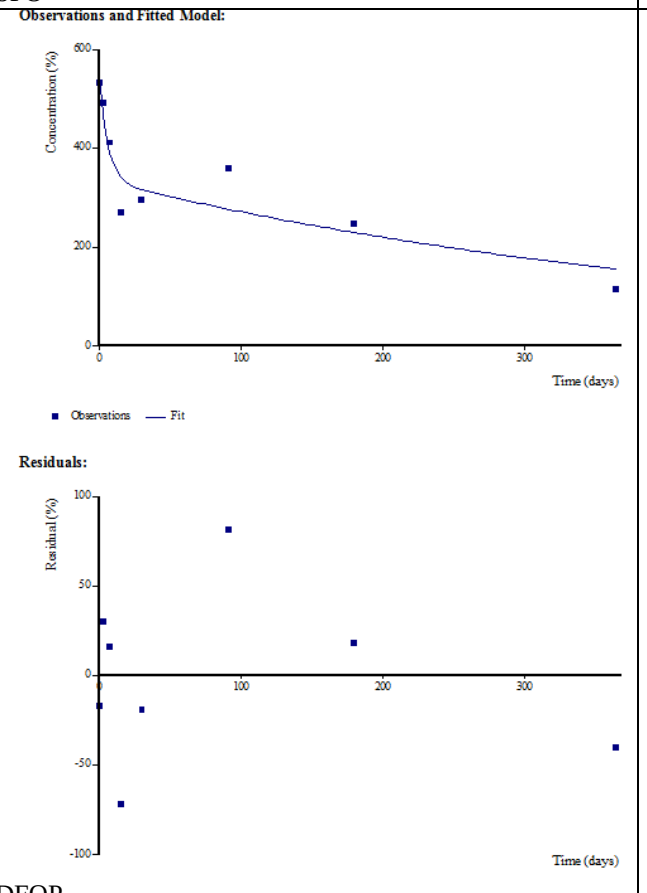
Figure B.8.1.1.4-4 RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (Spain autumn field trial)



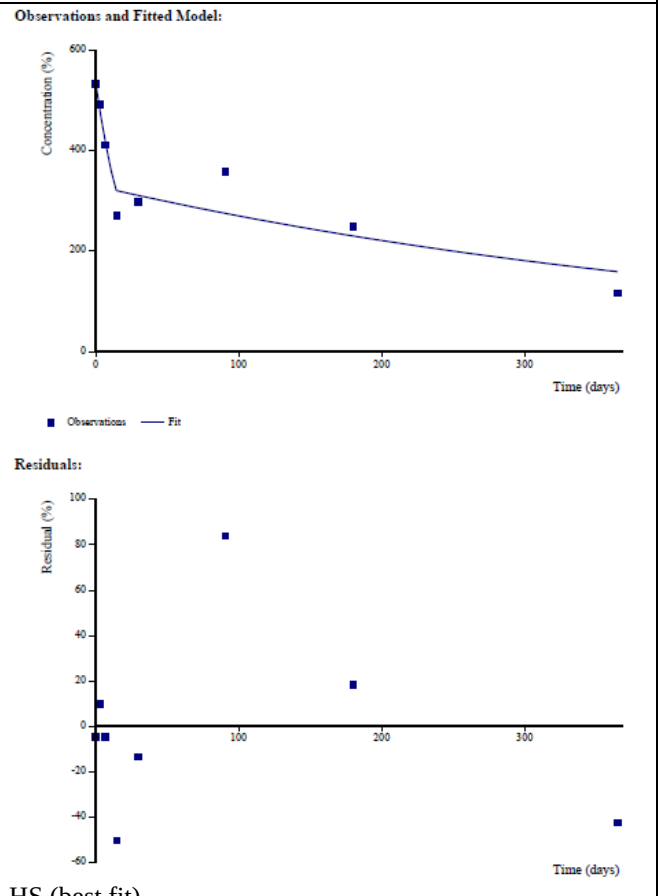
SFO



FOMC



DFOP

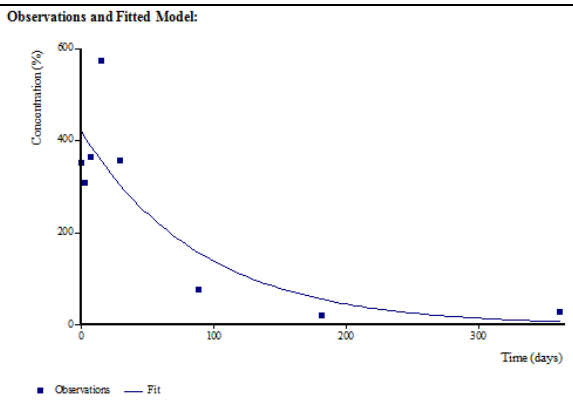


HS (best fit)

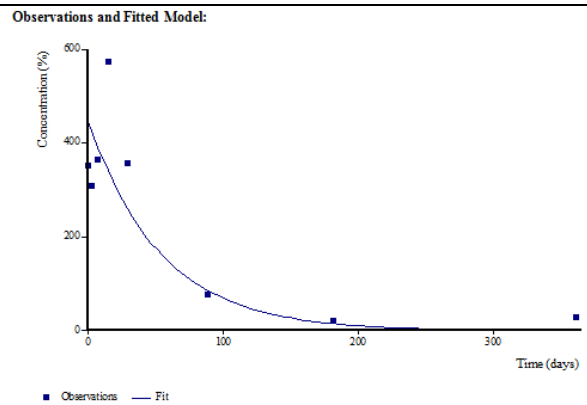
B.8.1.1.4-24 RMS' kinetic assessment of napropamide-M for deriving persistence endpoints (Germany spring field trial)

Model	χ^2 error%	Visual assessment	Statistical assessment	DT_{50}	DT_{90} (overall)
SFO	29.3	poor	p>0.05	62.4	207
FOMC	31.3	intermediate	Both α and β 95th %ile C.I.s do not include zero	37	123
SFO over-predicted initial data points and the residual plot showed large scale scattering. were wide and uneven. The FOMC gave a slightly better visual fit. The χ^2 error% values for both models were much higher than 15%. The day 15 data point was removed by the Applicant as a possible outlier.					
SFO modified	17.7	good	p<0.05	57.9	192
FOMC modified	19.2	good	Could not calculate α and β parameters	37.7	126
Both models gave a good visual assessment, yet FOMC fitted later time-points slightly better. FOMC did not improve the fit statistically and so SFO was selected as the best-fit model. Although no justification was given for the removal of the outlier by the Applicant, the RMS agrees that the modified SFO provides a more acceptable visual fit and χ^2 error% value and does not affect the degradation values significantly.					

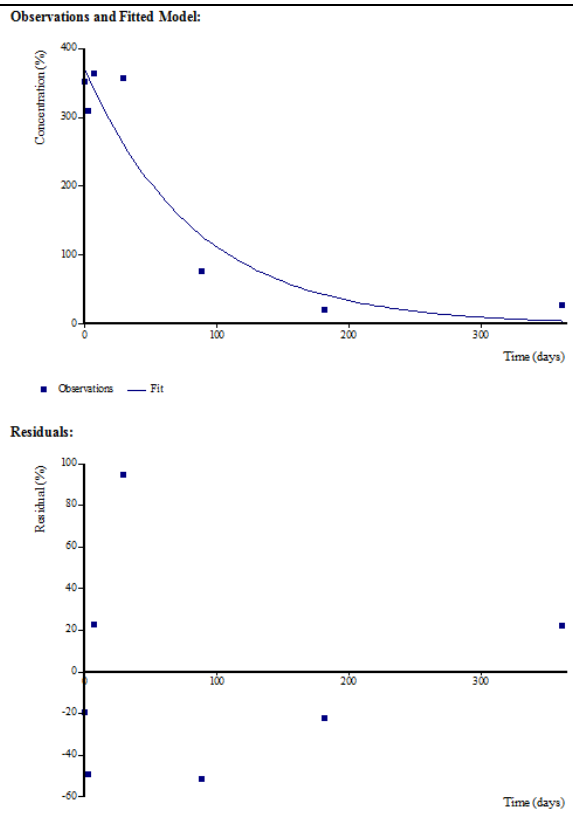
Figure B.8.1.1.4-5 RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (Germany spring field trial)



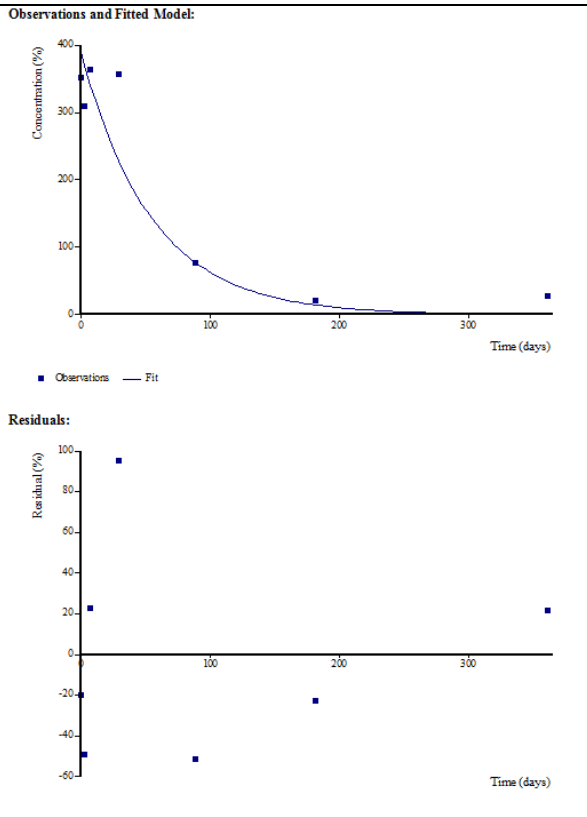
SFO



FOMC



SFO modified (best fit)

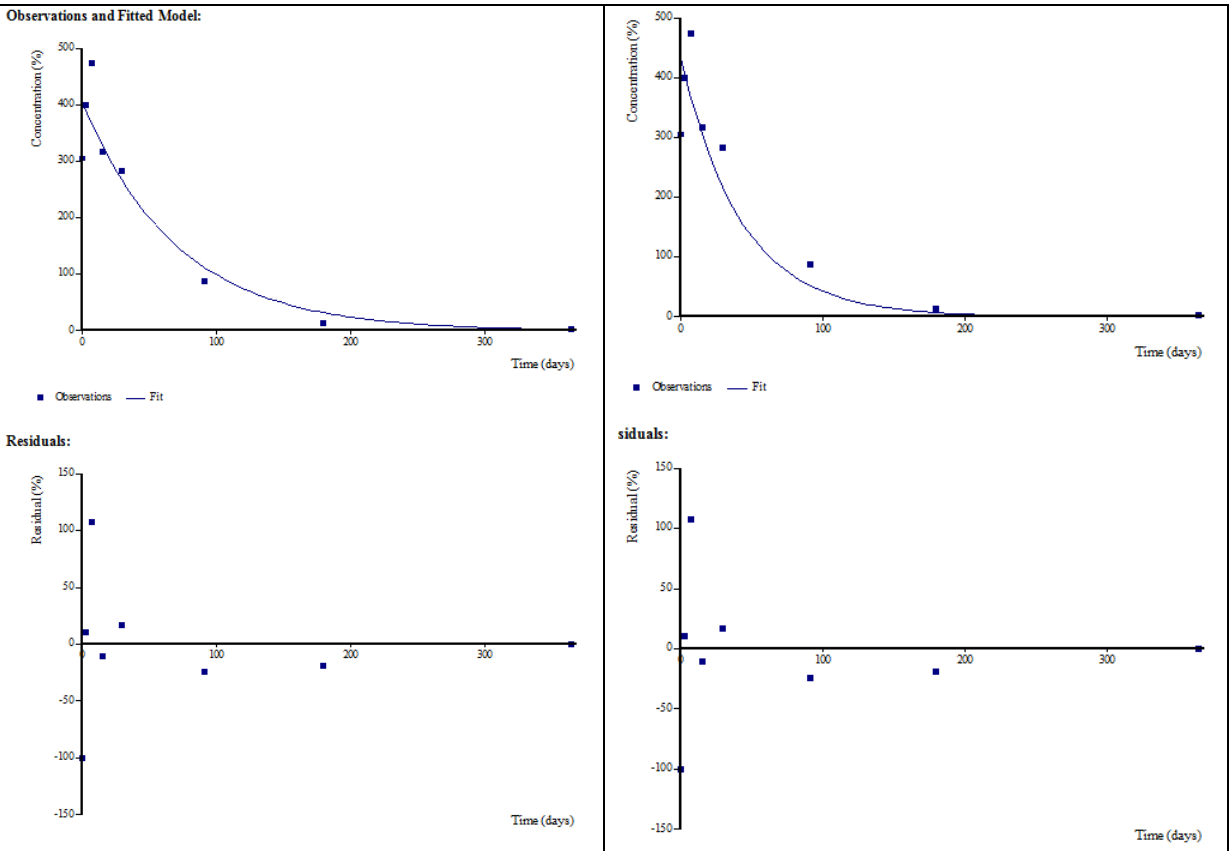


FOMC modified

B.8.1.1.4-25 RMS' kinetic assessment of napropamide-M for deriving persistence endpoints (Germany autumn field trial)

Model	χ^2 error%	Visual assessment	Statistical assessment	DT_{50}	DT_{90} (overall)
SFO	18.2	good	p<0.05	49	163
FOMC	19.4	intermediate	Both α and β 90th %ile C.I.s include zero	29.2	98.7
SFO model over-predicted the initial concentration but otherwise showed a good fit for field data. The χ^2 error% was acceptable for field data as 15% is not an absolute cut off criterion. FOMC model did not offer any visual or statistical improvement over the fit. Therefore, SFO was selected as best fit model. RMS agrees with Applicant decision.					

Figure B.8.1.1.4-6 RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (Germany autumn field trial)

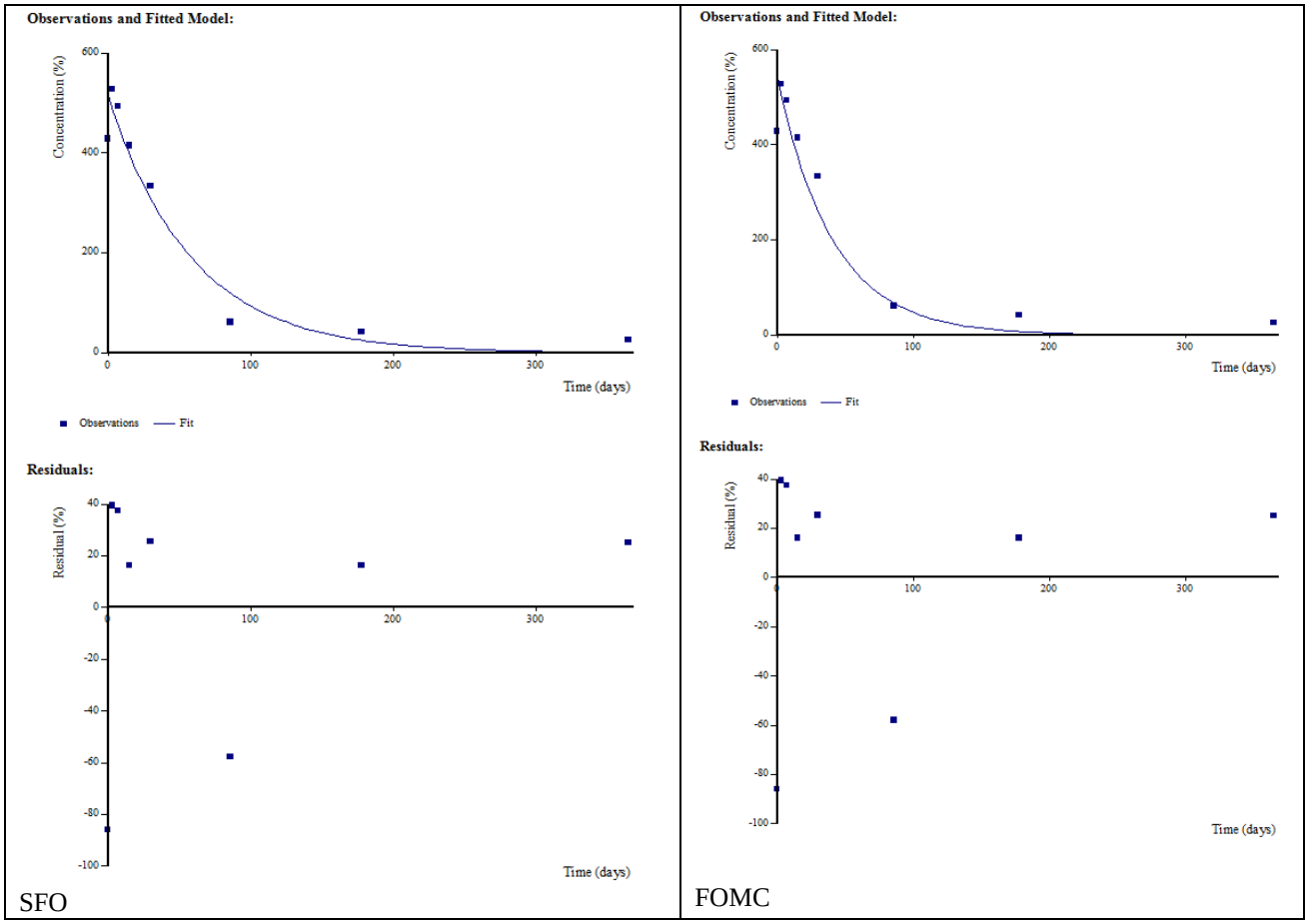


SFO (best fit) FOMC

B.8.1.1.4-26 RMS' kinetic assessment of napropamide-M for deriving persistence endpoints (UK spring field trial)

Model	χ^2 error%	Visual assessment	Statistical assessment	DT_{50}	DT_{90} (overall)
SFO	12.1	good	p<0.01	40.7	135
FOMC	12.9	good	α 95th %ile C.I. includes zero; β 95th %ile C.I does not include zero.	28.2	94.1
SFO over predicted the initial concentration slightly but gave an overall acceptable fit and statistical measures. FOMC gave a similar visual fit and did not offer any improvement over SFO statistically. Therefore SFO was selected as best-fit model. RMS agrees with Applicant decision.					

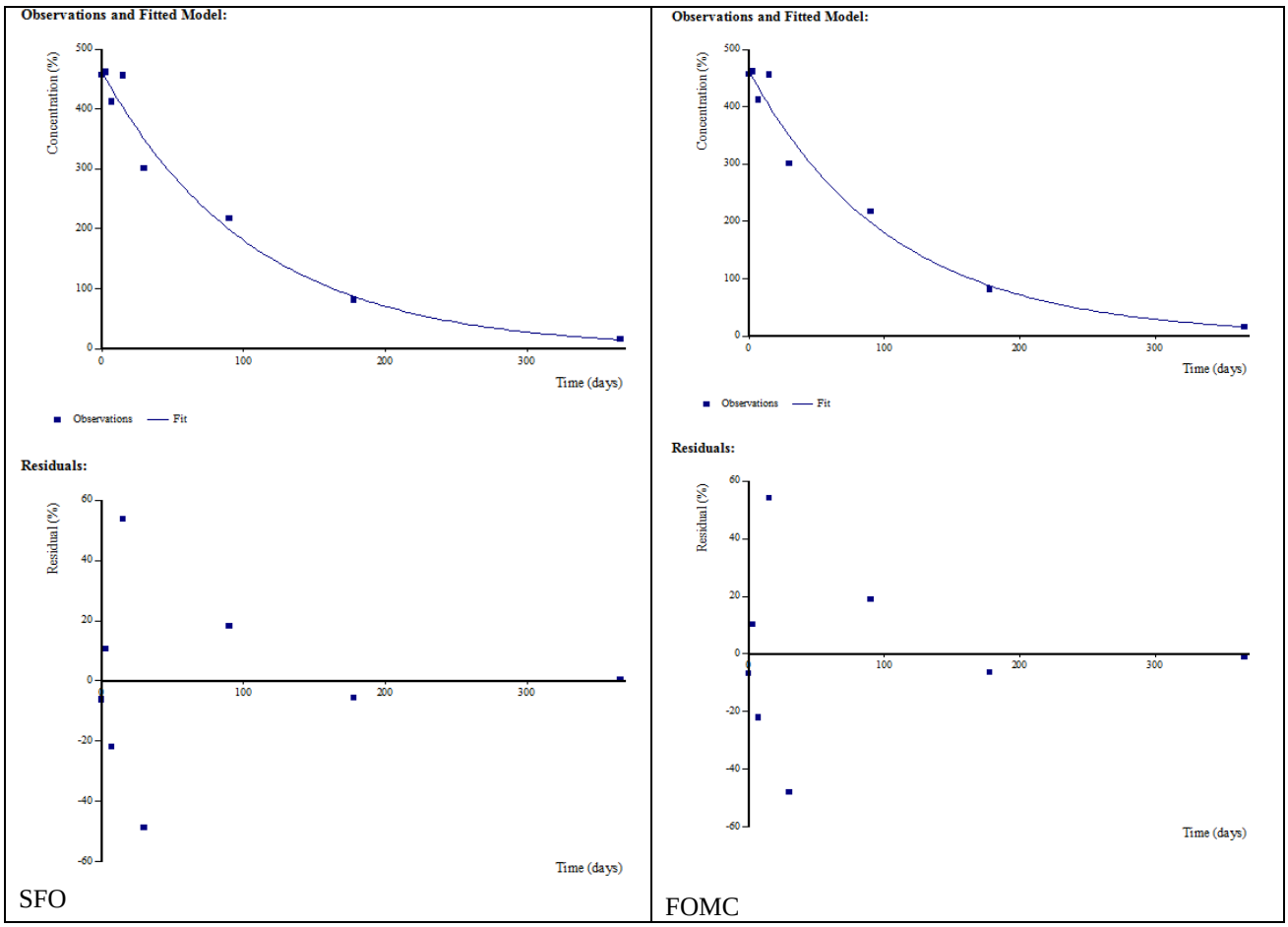
Figure B.8.1.1.4-7 RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (UK spring field trial)



B.8.1.1.4-27 RMS' kinetic assessment of napropamide-M for deriving persistence endpoints (UK autumn field trial)

Model	χ^2 error%	Visual assessment	Statistical assessment	DT_{50}	DT_{90} (overall)
SFO	7.43	good	p<0.01	73.7	245
FOMC	7.92	good	Both α and β 95th %ile C.I.s include zero.	73.2	248
SFO predicted the initial concentration well and showed good, even residual scattering. FOMC showed a similar fit, also very good for field data. FOMC did not offer any visual or statistical improvement. SFO was selected as best fit model. RMS agrees with Applicant decision.					

Figure B.8.1.1.4-8 RMS' kinetic plots and residuals of napropamide-M for deriving persistence endpoints (UK autumn field trial)



Kinetic assessment of field dissipation studies to derive modelling endpoints

Study author	Croucher, A. & Ford, S. (2015d)
Study title	Napropamide-M: Kinetic assessment of field dissipation studies
Study date	February 2015
Annex point	CA 7.1.2.2.1-02
Previous evaluation	New active substance, no previous studies submitted.

The degradation of formulated napropamide-M (HBW03) was studied at four terrestrial field dissipation trial sites: Italy, Spain, Germany and the UK (Wilson, 2015, section B.8.1.1.4). The kinetic degradation rate of napropamide-M was reassessed by the Applicant using the modelling software package CAKE (v 3.1) in accordance with guidance provided by FOCUS (2006) and EFSA (2014).

The suitability of the field dissipation study for use in kinetic evaluation was assessed against the criteria in FOCUS generic guidance checklist section 9.1. Each point from the FOCUS checklist is addressed below. The points below broadly cover those in Appendix A of the EFSA SANCO 12177/2014 guidance on the suitability of the data for normalisation. The criteria in the SANCO guidance specify the required information on the test substance, the experimental set up of the field plot, the site selection and the design of the field plot to derive a true DegT50.

- Critical assessment of the significance of photodegradation and specific transfer processes.

  The Applicant believes that napropamide-M is susceptible to photolysis and minimised this route of dissipation by incorporating the application into the top 5-10 cm soil manually using a rake within two hours of spraying. The RMS notes that the rate of degradation in soil via photolysis studied under laboratory conditions was 174.4 experimental days

(equated to well over a year under natural summer sunlight at 37°N). It can be concluded that photodegradation in the field is unlikely to be a major route of dissipation for napropamide-M. Furthermore, napropamide-M has low volatility (vapour pressure 3.80 $x10^{-6}$ Pa; HLC 2.644 $x10^{-5}$ Pa). Volatilisation is unlikely to be a significant route of dissipation in the field environment.

All field trials involved application of napropamide-M to bare soil, which is consistent with all proposed GAP uses. Therefore the potential for plant uptake of the active substance was negligible. Losses due to run-off were minimised by selecting level field plots without any significant slope. Napropamide-M has low to medium mobility in soil so rapid dissipation via leaching is considered unlikely. Residues at the lowest soil horizons were generally <LOD which supports this.

- Determination of a true degradation rate in soil

  The RMS considers transfer and dissipation processes to have been sufficiently addressed. The data from the field dissipation trials can be used to derive a DegT50 value for pesticide fate modelling.

- Proper measurement of the applied dose

  The applied dose was determined by two methods. Firstly by measuring the start volume and final volume in the spray tank and secondly by the use spray targets (5 per plot, positioned diagonally across the treated plots) which were analysed to determine the likely maximum soil residue. The spray cards for the Spanish spring trial were left outside of the freezer for several days and so were discarded.

- Soil well characterised at different depths

  Soil samples were taken at each trial site at a depth of 0- 20 cm and characterised on a range of parameters (pH, particle size distribution, cation exchange capacity, density, organic carbon and maximum water holding capacity). Although the soils were not characterised at different horizon depths (i.e. 0- 10, 10-20, 20-30 cm), the sampling depth used was considered acceptable for characterisation of the bulk of the parent material.

- Soil sampling depth and analytical method should allow to capture the bulk of the applied material

  The soil core depth was 30 cm. Measured residues showed that leaching to the lower layers was minimal (<LOD) so it can be assumed that sampling below 30 cm was not necessary. Analytical method has been validated by Applicant and independently by the RMS.

- Meteorological measurements should be available at least for the duration of the field study

  Daily records of air temperature, relative humidity, precipitation and soil temperature were taken. For certain trials and dates, the weather data had to be obtained from alternative weather stations. The RMS considers these deviations from the study plan acceptable. Soil moisture was not measured at the trial sites and so the Applicant has modelled theoretical values using PERSIST (see details below).

- Pesticide history in preceding years should be available. The active substance or a chemical analogue should not have been applied on the plot prior to experiment.

  Pesticide history details were given for the previous four years. Neither napropamide or napropamide-M were used at the trial locations. The pesticides metazachlor (a chloroacetamide) and flufenacet (an oxyacetamide) were applied at the German site in 2010 and 2011 respectively. These pesticides display a similar mode of action (cell division inhibition) to napropamide-M (an acetamide). However, the RMS considers it unlikely that the study will have been materially affected by previous application of these pesticides.

Data handling

In order to calculate suitable modelling endpoints, time-step normalisation was performed to correct day length for soil temperature (20 °C) and soil moisture (pF2). As soil moisture was not measured at the trial sites, the Applicant used daily weather data to model daily soil moisture using the PERSIST model (Walker and Barnes, 1981). The model requires inputs of daily minimum and maximum temperatures, precipitation, latitude and elevation. Soil temperature was measured at the trial sites, however for some dates the data-loggers failed and soil temperatures were obtained from the nearest weather stations. For the UK trial site between 23rd -26th May and 14th -24th September 2014 there was no alternative site to get data from. The Applicant

modelled soil temperature in PERSIST for these days. The PERSIST model requires the soil bulk density and moisture holding capacity of the soil at 5 kPa. The water holding properties of the soils were not reported for the trial sites and so the Applicant has used the FOCUS default value of pF2 as the moisture reference. Table B.8.1.1.4-28 below reports the input values used in the PERSIST model. Though the RMS has not independently reproduced the modelling in PERSIST, the RMS considered whether the model was appropriately parameterised to reflect the simulated soil conditions against the measured data. The RMS checked that measured soil temperature values corresponded to those reported in the original field dissipation study. Simulated soil moisture values were considered reasonably representative of EU conditions. The RMS has accepted the Applicant's simulated PERSIST values for use in the time-step normalisation process.

Table B.8.1.1.4-28 Applicant's input parameters used in the PERSIST model for simulations of soil temperature and moisture

Site	Soil type*	Soil bulk density (g/ cm^3)	Soil moisture holding capacity at pF2
Italy	Sandy loam	1.157	19
Spain	Sandy clay loam	1.200	22
Germany	Sand	1.405	12
UK	Sandy loam	1.235	19

*USDA classification system

The day length normalisation procedure was performed by reducing or increasing the length of each day in the study period depending on the measured soil temperature and the modelled soil moisture values, by means of correction factors calculated according to FOCUS guidance. The RMS independently checked the normalised day lengths in EXCEL.

The normalisation procedure uses a Q_{10} approach for temperature correction as follows:

$$D_{Norm} = D \cdot f_{Temp}$$

$$f_{Temp} = Q_{10}^{(T-T0)/10}$$

Where:

D_{Norm}	= Normalised day length
D	= 1 day
f_{temp}	= Correction factor for soil temperature
Q10	= 2.58 (FOCUS default, EFSA 2007)
T	= Actual soil temperature
T_0	= Reference soil temperature (e.g. 20°C)

A similar procedure is then done for soil moisture normalisation, employing the Walker equation for moisture correction.

$$D_{Norm} = D \cdot f_{Moisture}$$

$$f_{Moisture} = \left(\frac{theta_{actual}}{theta_{reference}} \right)^{0.7}$$

Where:

D_{Norm}	= Normalised day length
D	= 1 day
$f_{moisture}$	= Correction factor for soil moisture
$theta_{actual}$	= Actual soil moisture (v/v or w/w)
$theta_{reference}$	= Reference soil moisture (=v/v or w/w at field capacity)

The two corrections are then applied together to yield corrected day lengths for the field data set:

$$D_{Norm} = D \cdot f_{Temp} \cdot f_{Moisture}$$

Table B.8.1.1.4- 29 below presents the normalised day lengths for use in field dissipation kinetic modelling and compares these to the actual trial sampling days and the measured residues at each sampling interval.

Table B.8.1.1.4- 29 Comparison of field sampling time-points with normalised time-points (20 °C, pF2)

Trial	Sampling days	Normalised days	Measure residues (g/ha)
Italy Spring	0	0	617.8
	3	1.2	457.7
	7	3.5	237.2
	14	8.6	289.9
	32	19.3	107.1
	94	81.5	74.7
	182	126.2	70.5
	363	187.1	46.1
Italy Autumn	0	0	304.9
	3	1.1	497.7*
	7	2.9	393.6
	15	7.1	225.3
	32	14.1	211.6
	94	28.7	181.9
	183	54.4	95.1
	363	215.5	6.5
Spain Spring	0	0	658.4
	3	1.6	502.4
	7	3.4	238.2
	15	7.8	209.6
	29	15.7	23.1*
	90	61.2	163.6
	182	163.3	186.9
	365	240.4	90.6
Spain Autumn	0	0	532.5
	3	2	490.9
	7	4.8	410.9
	15	9.7	268.9
	30	17.2	296.2
	91	35.4	357.6
	180	68.3	247.1
	365	234.4	115.1
Germany Spring	0	0	350.8
	3	1.3	308.1
	7	2.3	363.5
	15	4.6	571.7*
	29	9.1	356.4
	89	40.4	75.9
	182	88.2	19.6
	362	135.1	26.7
Germany Autumn	0	0	304.2
	3	1.2	398
	7	2.8	472.9
	15	6.1	316
	30	11.5	281.2
	91	25.9	86.6
	180	46.9	12.4
	365	167.6	1.5
UK Spring	0	0	427.8
	3	0.5	527.5
	7	1.7	493.4
	15	4.0	414
	30	8.8	333.5
	86	29.1	60.8
	178	69.0	40.9
	365	124.7	26.1
UK Autumn	0	0	457

	3	1.2	461
	7	2.8	411.8
	15	6.4	455.9
	30	13.2	300.6
	90	29.5	216.9
	178	52.4	81.3
	366	142.4	15.3

*The Applicant considered these samples to be outliers.

Kinetic evaluation

The RMS independently verified the DT_{50} values using the normalised day lengths in the modelling software package CAKE (v 3.2) according to FOCUS (2014) guidance. Initially an SFO model was run with all data points, unweighted and using an unconstrained initial value (M0). The acceptability of kinetic fits was judged both visually and statistically (according to the χ^2 error and the t-test functions). A χ^2 error of 15% or less is recommended, although as field data are often highly variable this was not implemented as an absolute cut-off criterion. If the fit was not acceptable, then a step-wise modified fitting routine was applied by excluding outliers and constraining M0. If the fit was still considered unacceptable, then biphasic modelling was considered. If 10% of the initial concentration was reached by the end of the experimental study, a DT_{50} was calculated from the DT_{90} of an FOMC by dividing it by 3.32. If this concentration was not reached within the study period, then the longer K2 DT_{50} of HS or DFOP models was used. Statistical acceptability of the biphasic models was assessed according to the χ^2 error and if confidence intervals were significantly different from zero (α and β parameter estimates for FOMC models, and K1 and K2 parameters for DFOP and HS models). Tables B.8.1.1.4- 30 - B.8.1.1.4- 37 and figures B.8.1.1.4- 9 - B.8.1.1.4- 16 present the kinetic procedures using the normalised data to derive modelling endpoints for field data.

Table B.8.1.1.4- 30 RMS' kinetic assessment of napropamide-M for deriving modelling endpoints using normalised data (Italian spring field trial)

Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50} (days)	DT_{90} (days)
SFO	24.9	poor	$p<0.05$	6.49	21.6
SFO under-predicted the initial concentration and the later sampling points. Residual plot showed systematic under-prediction of later time-points, indicating a biphasic degradation pattern. The χ^2 err% was high (>15%). As 10% of the initial concentration was reached by the study end, the FOMC model could be assessed.					
FOMC	14.6	good	α 90^{th} and 95 %ile C.I.s do not include zero; β 90^{th} and 95 %ile C.I.s include zero	3.34 (modelling DT_{50} =35.5)	118
FOMC predicted the initial concentration well. Residual plot showed even scattering and predicted the later points well. The χ^2 err% was <15%. Despite the β parameter confidence interval including zero, the overall visual and statistical fit was considered acceptable for calculating modelling endpoints. The DT_{50} was calculated as the FOMC DT_{90} value divided by 3.32 days.					

Figure B.8.1.1.4- 9 RMS' kinetic plots and residuals for deriving modelling endpoints (Italian spring field trial)

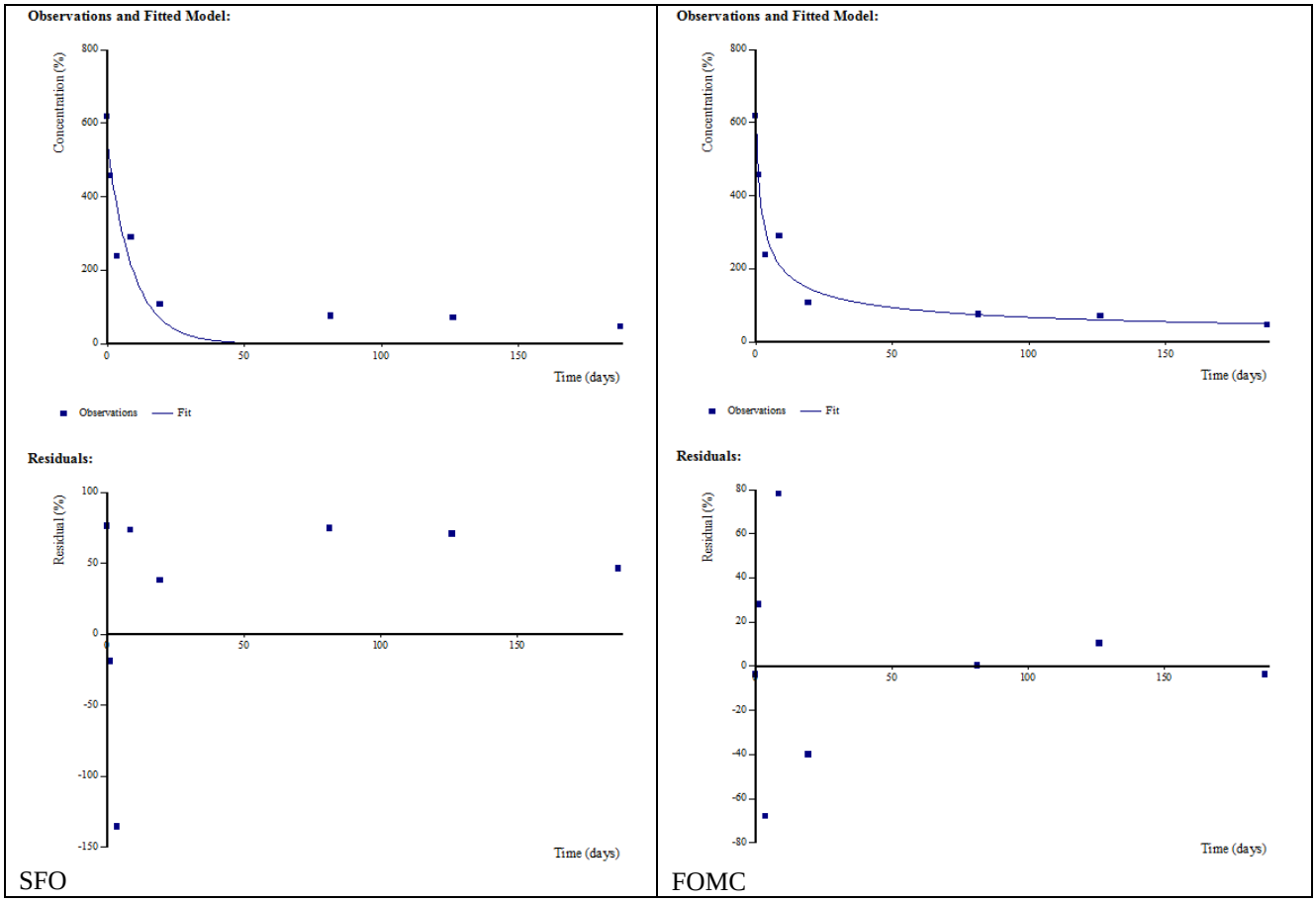


Table B.8.1.1.4- 31 RMS' kinetic assessment of napropamide-M for deriving modelling endpoints using normalised data (Italian autumn field trial)

Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50} (days)	DT_{90} (days)
SFO	21.5	Intermediate	p<0.05	21.8	72.6
SFO over-predicted the time-zero concentration but showed intermediate fitting for the other data points with the exception of the day 3 sampling interval (normalised day 1.1) which was higher than the 1st and 3rd sampling points. The χ^2 err% was high (>15%). The Applicant proposed day 3 (normalised day 1.1) to be investigated as an outlier.					
SFO modified	16	good	p<0.05	28.6	95.1
Removal of day 3 (1.1) outlier improved visual and statistical fit, reducing the χ^2 err% from 21.5 to 16. No justification was provided for the exclusion of the outlier and the RMS notes that it is not uncommon for second sampling points to have higher values than the initial concentration for field data. However, RMS has accepted the Applicant's decision as it improves the SFO fit and resulted in a more conservative DT_{50}. The modified SFO was considered acceptable for deriving modelling endpoints.					

Figure B.8.1.1.4- 10 RMS' kinetic plots and residuals for deriving modelling endpoints (Italian autumn field trial)

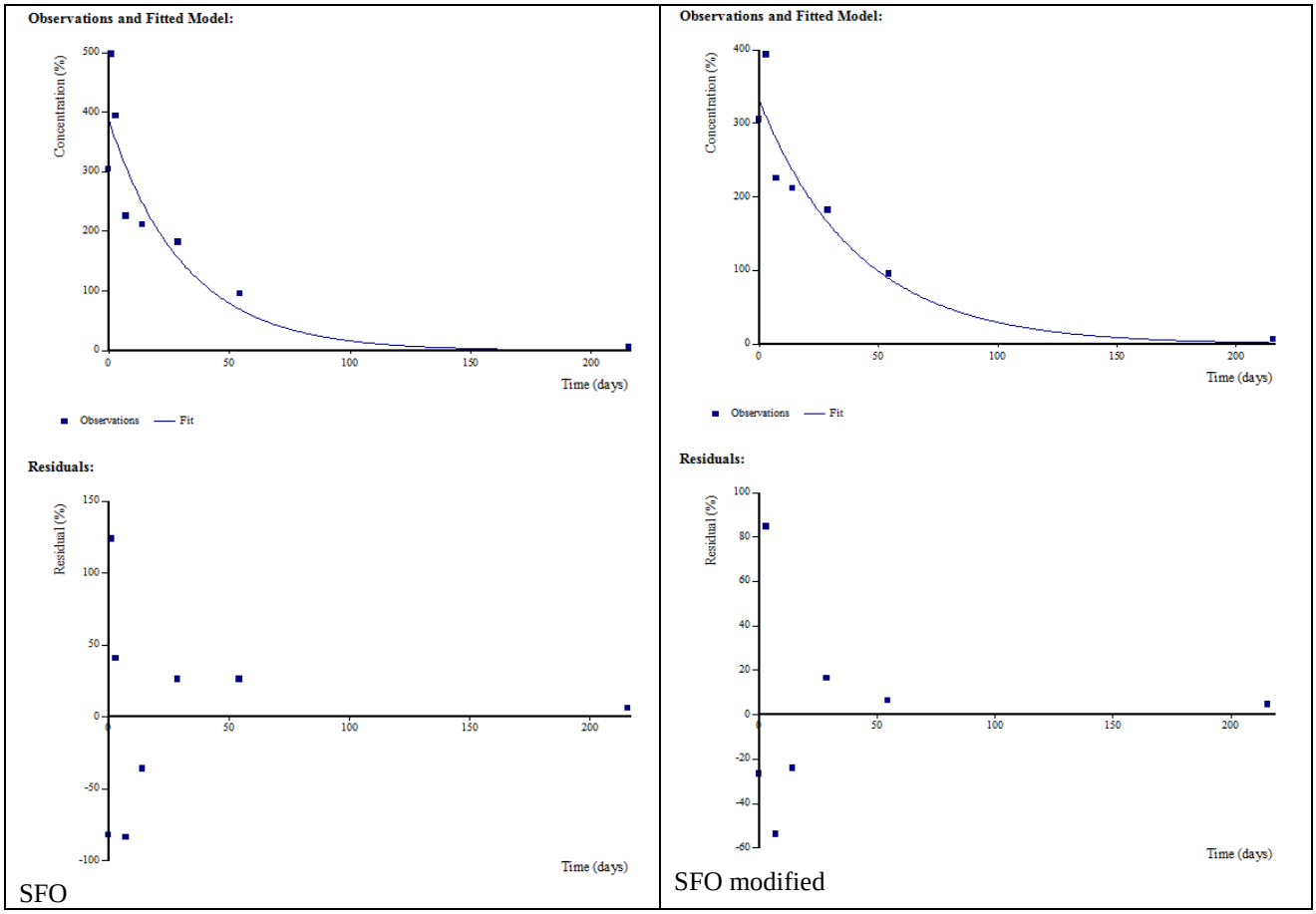
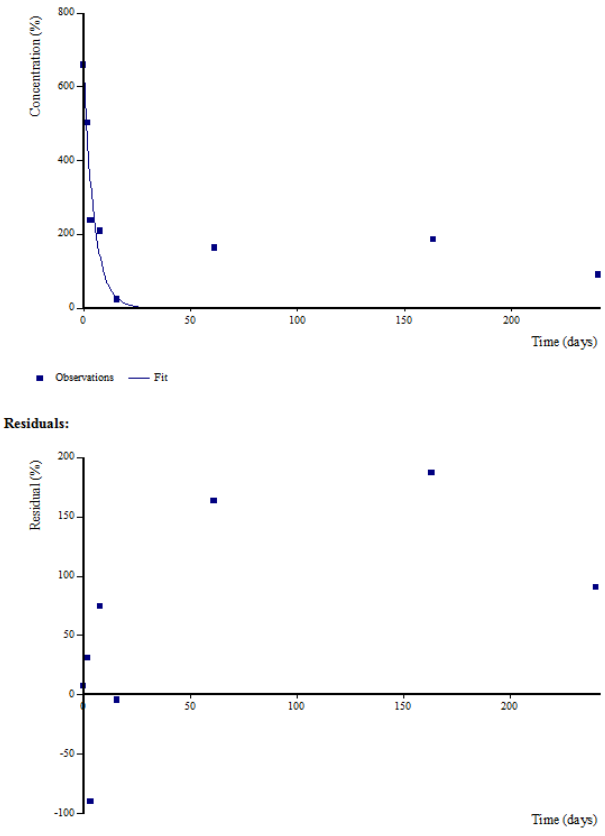


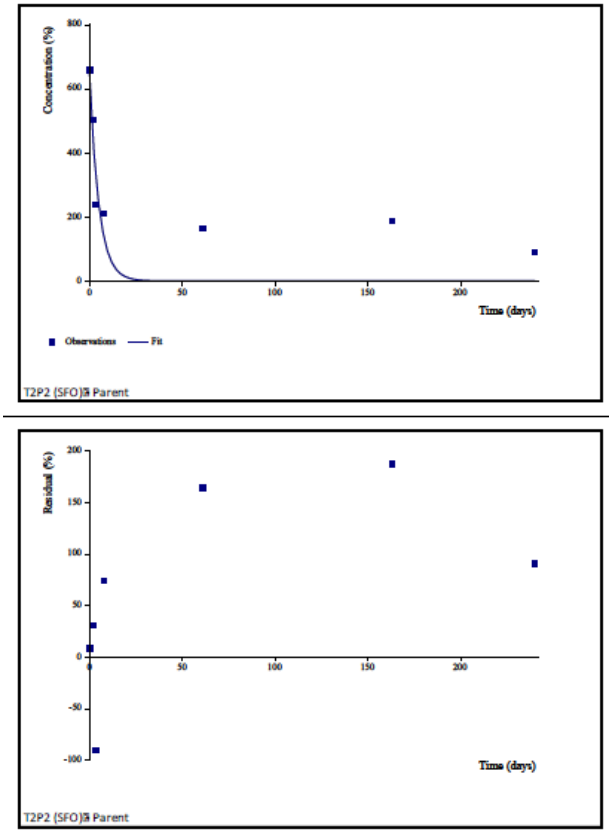
Table B.8.1.1.4- 32 RMS' kinetic assessment of napropamide-M for deriving modelling endpoints using normalised data (Spanish spring field trial)

Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50} (days)	DT_{90} (days)
SFO	31.6	poor	p<0.05	3.44	11.4
SFO predicted initial data points well but greatly under-predicted later sampling intervals. Residual plot showed systematic under-prediction of later time-points, indicating a biphasic degradation pattern. The χ^2 err% was very high (>15%). The Applicant proposed 29 day (normalised 15.7 day) time point as an outlier and removed it. The M0 was set to 1000 but not fixed.					
SFO modified	29.8	poor	p<0.05	3.46	11.5
The removal of day 29 (normalised 15.7 day) outlier did not improve the SFO fit visually or statistically. As 10% initial concentration was not reached before study termination, the DFOP and HS models were tested. Both models were run without the 29 day outlier.					
DFOP modified	13.5	good	K1 90th %ile C.I. does not include zero, 95th %ile C.I does; K2 both 90th and 95th %ile C.I.s include zero. g=0.73	2.82 (overall) K1 DT_{50}= 1.7 K2 DT_{50} = 440	630
HS modified	11.1	good	K1 both 90th and 95th %ile C.I.s do not include zero; K2 both 90th and 95th %ile C.I.s include zero. tb= 4.531	2.66 (overall) K1 DT_{50}= 2.66 K2 DT_{50}= 292	478
Both DFOP and HS models estimated time-zero values well and showed good residual scattering, giving good visual fits overall. The Applicant chose the HS model based on slightly more favourable statistical parameters (χ^2 error%). However, the two models gave very similar fits, so as DFOP gave an acceptable fit (aside from t-test for k2) and more conservative DT_{50} of the two models, on balance the RMS has accepted DFOP as a reasonable representation of the decline. Furthermore, the RMS notes that DFOP is preferred for deriving modelling endpoints. The slower phase (K2) DT_{50} value was selected for use in modelling.					

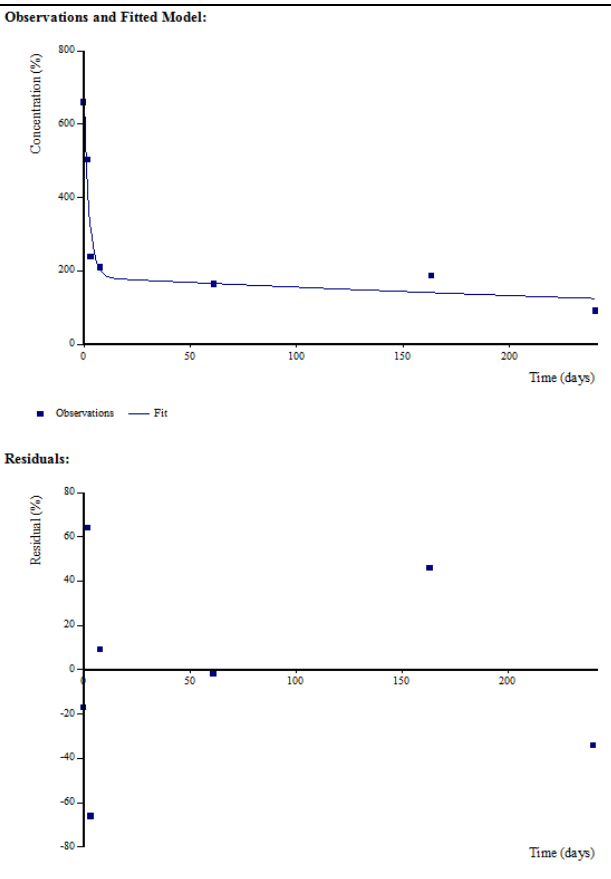
Figure B.8.1.1.4- 11 RMS' kinetic plots and residuals for deriving modelling endpoints (Spanish spring field trial)



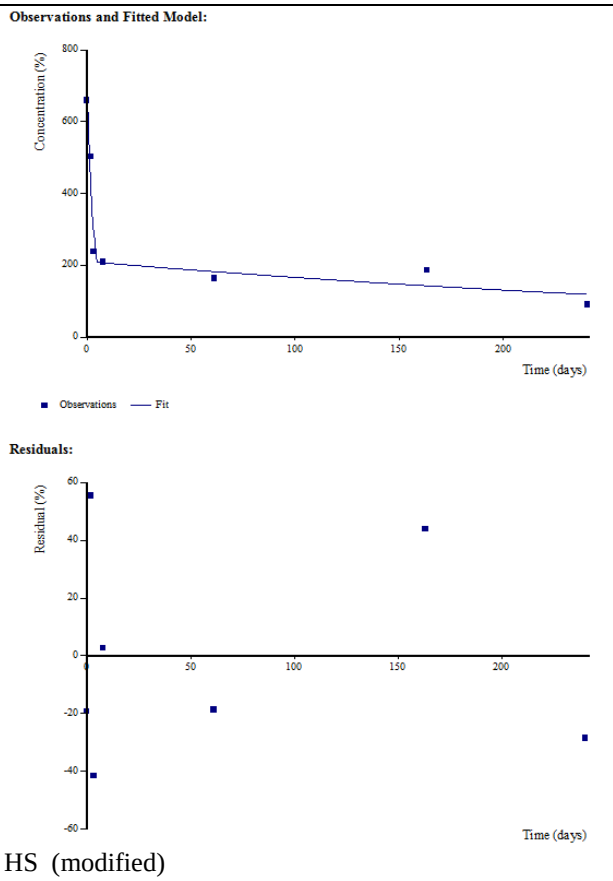
SFO



SFO modified



DFOP (modified)

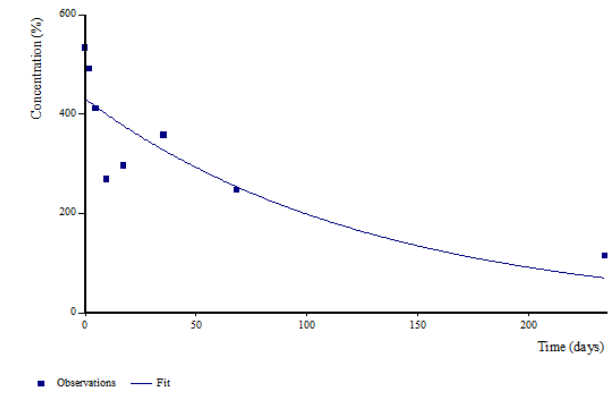


HS (modified)

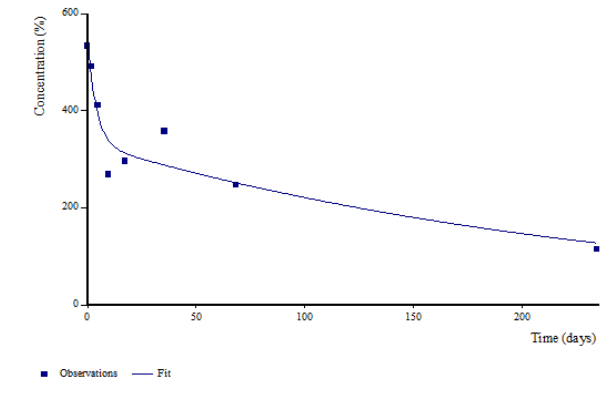
Table B.8.1.1.4- 33 RMS' kinetic assessment of napropamide-M for deriving modelling endpoints using normalised data (Spanish autumn field trials)

Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50} (days)	DT_{90} (days)
SFO	16.9	intermediate	$p<0.05$	89.6	298
The SFO underestimated the initial concentration but residuals showed even scattering, giving an overall intermediate visual assessment. Statistical parameters were acceptable. The Applicant described the fit as poor and so investigated biphasic modelling. The measured concentration did not reach 10% initial concentration by the end of the study so DFOP and HS models were tested.					
DFOP	10.4	intermediate	Both K1 and K2 90^{th} and 95^{th} %ile C.I.s include zero g=0.3947	46.7 (overall) K1 DT_{50}= 2.77 K2 DT_{50}= 170	441
HS	8.48 (8.49)	intermediate	K1 both 90^{th} and 95^{th} %ile C.I.s include zero; K2 90^{th} %ile C.I. does not include zero, 95^{th} %ile C.I. does include zero. tb=9.59 (9.424)	50.5 (overall) K1 DT_{50}= 12.5 K2 DT_{50}= 176	459 (458)
Both DFOP and HS provided good prediction of time zero values and an intermediate fit for later data points. The Applicant chose HS model as it had a more favourable χ^2err%. The slower phase (K2) DT_{50} value was selected. The RMS considers that the SFO fit provides a reasonable description of the long term decline, and does not lead to any significant underestimate of later time points. Although it doesn't match the initial rapid loss, for long term modelling, such as groundwater, this is less important. As both the German and UK trial fits were also SFO and ideally SFO is preferred for modelling purposes, the RMS considers SFO is sufficiently acceptable (visually and statistically) for use as the modelling endpoint in this case.					

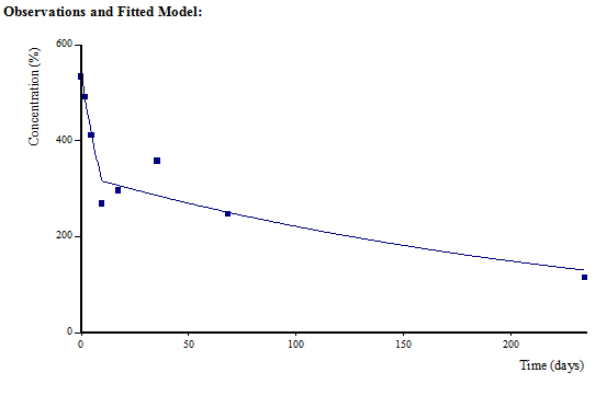
Figure B.8.1.1.4- 12 RMS' kinetic plots and residuals for deriving modelling endpoints (Spanish autumn field trials)



SFO



DFOP



HS

Table B.8.1.1.4- 34 RMS' kinetic assessment of napropamide-M for deriving modelling endpoints using normalised data (German spring field trials)

Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50} (days)	DT_{90} (days)
SFO	26.9	intermediate	p>0.05	25.1	83.2
The SFO gave a reasonable fit for most of the points except the day 15 (normalised 4.6 d) time point. The Applicant proposed this data point to be an outlier and removed it. The χ^2 err% was high (>15%).					
SFO modified	14.1	good	p<0.05	24	79.7
The visual fit was improved after the removal of the day 15 (4.6) time-point. The statistical parameters were more favourable (e.g. χ^2 err% was <15%). Although no justification was given as to why that particular time-point was considered an outlier, the RMS accepts that its removal has improved the fit and doesn't affect the DT_{50}. The RMS considers the modified SFO acceptable for deriving modelling endpoints.					

Figure B.8.1.1.4- 13 RMS' kinetic plots and residuals for deriving modelling endpoints (German spring field trials)

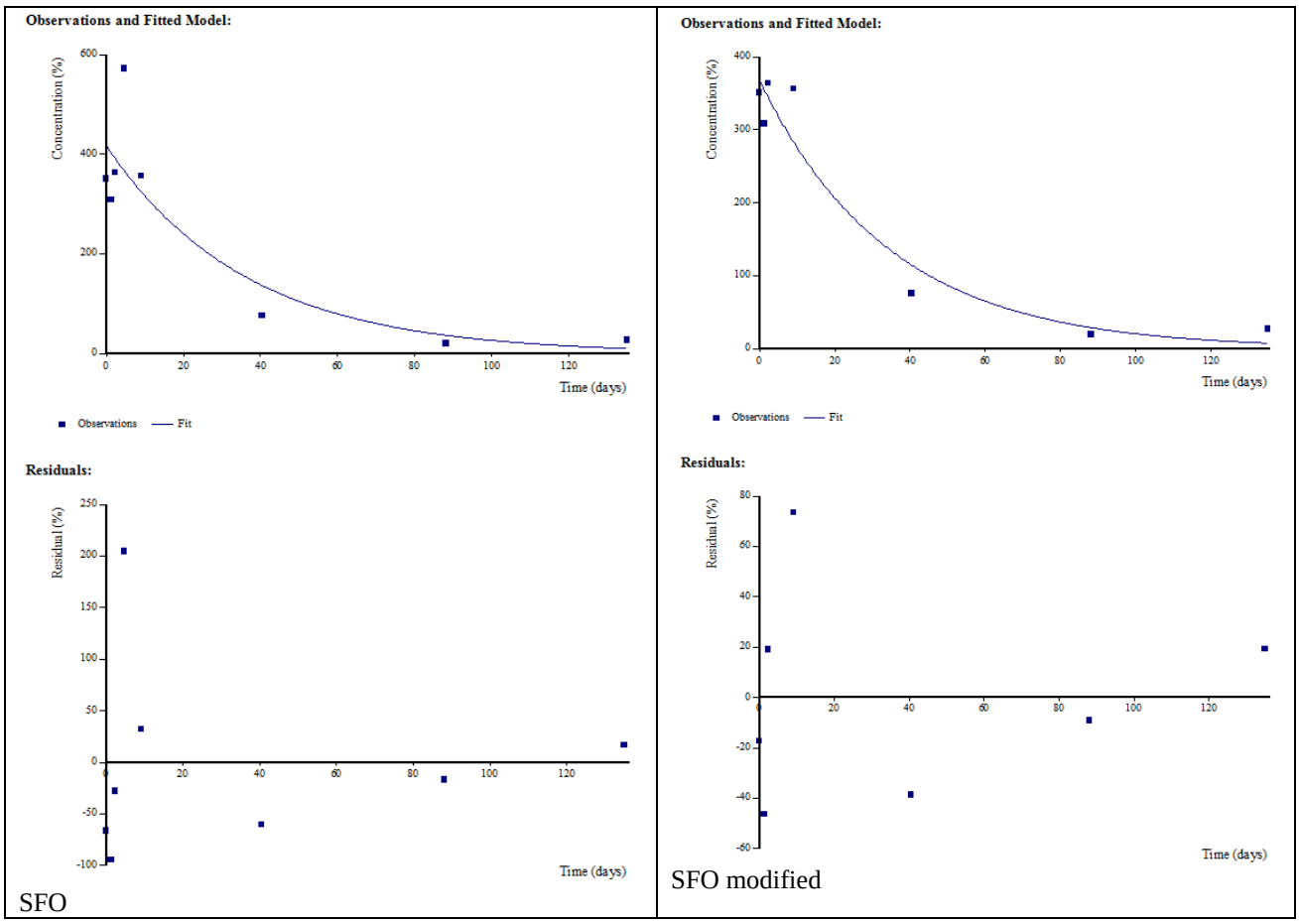
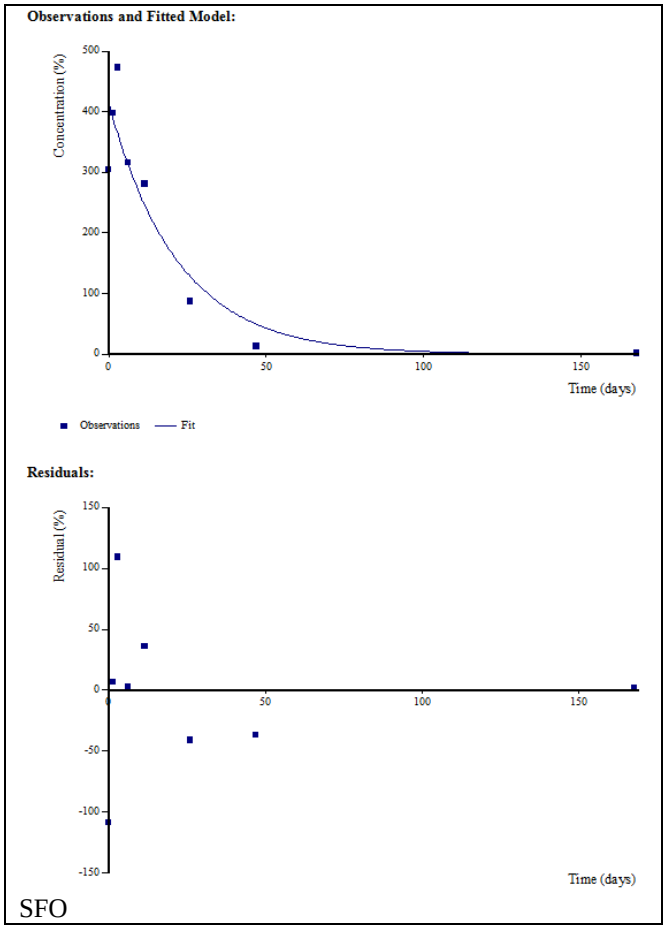


Table B.8.1.1.4- 35 RMS' kinetic assessment of napropamide-M for deriving modelling endpoints using normalised data (German autumn field trial)

Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50} (days)	DT_{90} (days)
SFO	20.2	intermediate	p<0.05	15.3	50.8
	SFO gave an intermediate visual fit, with time zero concentration over-predicted and some midpoints slightly over-predicted. The χ^2 err% was >15% but as this value should not be used as absolute cut-off criteria, it was considered acceptable for field data. The SFO was considered acceptable for deriving modelling endpoints.				

Figure B.8.1.1.4- 14 RMS' kinetic plot and residual for deriving modelling endpoint (German autumn field trial)

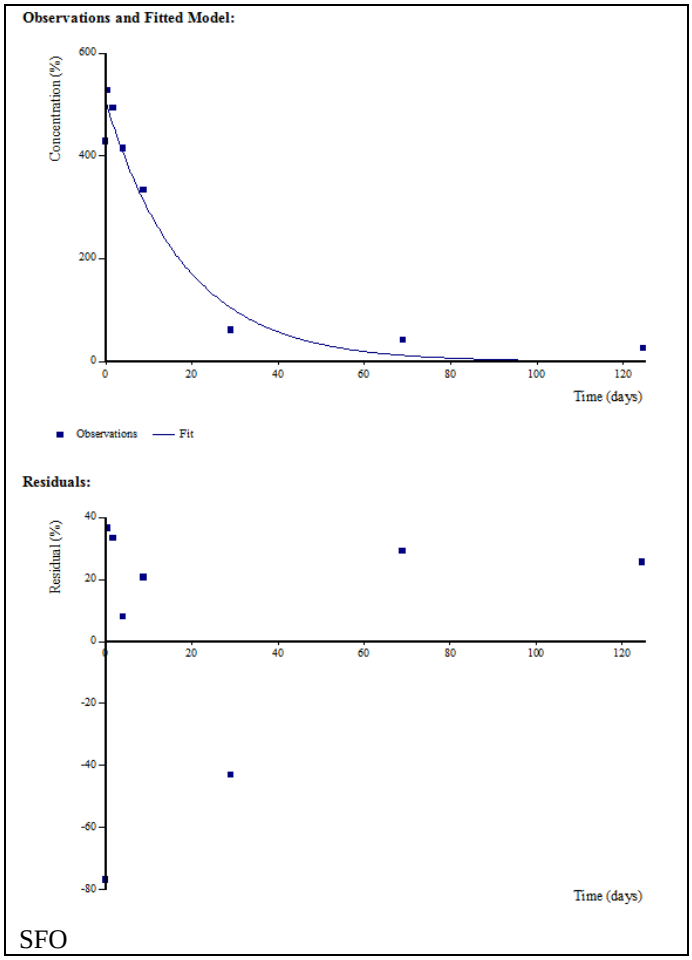


SFO

Table B.8.1.1.4- 36 RMS' kinetic assessment of napropamide-M for deriving modelling endpoints using normalised data (UK spring field trial)

Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50} (days)	DT_{90} (days)
SFO	10.7	good	p<0.01	12.8	42.4
	SFO showed a good visual fit, although it over predicted the initial time point. The χ^2 err% <15%. The model was considered acceptable for deriving modelling endpoints.				

Figure B.8.1.1.4- 15 RMS' kinetic plot and residual for deriving modelling endpoint (UK spring field trial)

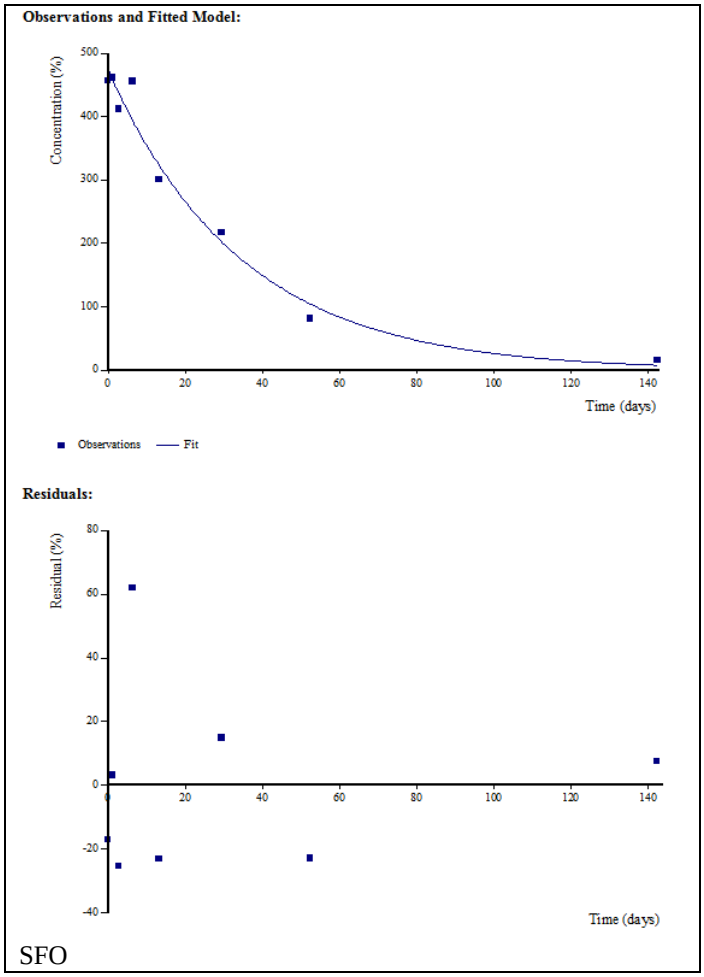


SFO

Table B.8.1.1.4- 37 RMS' kinetic assessment of napropamide-M for deriving modelling endpoints using normalised data (UK autumn field trial)

Model	χ^2 err%	Visual assessment	Statistical parameters	DT_{50} (days)	DT_{90} (days)
SFO	7.35	good	p<0.001	24.0	79.7
	SFO predicted the initial concentration well. The residual plot showed even scattering, distributed randomly above and below the line. Statistical parameters were good. The SFO was considered acceptable for deriving modelling endpoints.				

Figure B.8.1.1.4- 16 RMS' kinetic plot and residual for deriving modelling endpoint (UK autumn field trial)



SFO

Table B.8.1.1.4- 38 summarises the Applicant's chosen modelling endpoints for the degradation of napropamide-M under field conditions normalised to pF2 and 20 °C. The geometric mean DT_{50} of all four field trials for both seasons was calculated as 39.4 days. The Applicant excluded both spring and autumn Spanish trials from the overall modelling endpoint and recalculated the geometric mean as 22 days. They state that conditions at the Spanish trial site were extremely dry and this resulted in very pronounced biphasic degradation behaviour with very little or no degradation occurring during the second (slow) phase of the decline. The Applicant accepts this decline pattern to be a true reflection of the dissipation of napropamide-M in dry southern European climates and therefore found it acceptable to provide valid persistence endpoints. However, the Applicant believed the dry conditions reduced the rate of degradation to a degree that cannot be corrected to reflect other moisture conditions when implemented with moisture correction in regulatory models. On this basis they excluded both Spanish trials from the modelling geometric mean DT_{50}. No comparable average climatic data was provided to give evidence of how the Spanish weather was "extreme" for the study period.

The RMS considers that all the results from this study should be retained unless there is strong justification for exclusion. Although conditions in the Spanish trial were dry, no detailed case was provided as to why the climatic conditions in the Spanish trial might be considered extreme, or not representative of typical conditions in Southern Europe. The RMS is also not aware of a lower limit for validity of the moisture correction; PERSIST did not appear to include any constraint on moisture normalisation below a certain minimum moisture level.

To exclude this trial would result in fewer than 4 soils being available to provide field $DegT_{50}$ values. The EFSA $DegT_{50}$ guidance (2014) states that at least four $DegT_{50}$ values are required for parent. The flowchart on page 15 of the $DegT_{50}$ guidance indicates that if the field $DegT_{50}$ values are significantly shorter than the laboratory $DegT_{50}$ values, then it is acceptable to discard the laboratory values. However, if there are not four field values for parent in this case, then the laboratory and field datasets need to be combined to achieve at least four data points. (The field $DegT_{50}$ were shorter than the lab in EFSA 3662ax1 excel spreadsheet). Therefore, on balance the RMS has opted to retain the Spanish trial in the modelling dataset.

The Applicant pooled spring and autumn DT_{50} values to derive mean values and did not consider any seasonal difference in the results and the suitability of this approach. There is not a clear pattern of spring DT_{50} values being shorter than autumn DT_{50} values as the German trial showed the opposite. The RMS has evaluated the data as presented and used the geometric mean of all the trials, spring and autumn (n=8). However, the RMS proposes that the issue of whether the spring and autumn DT_{50} data can be considered together or should have been treated separately should be discussed further at EU expert peer review.

Table B.8.1.1.4- 39 presents RMS' chosen modelling endpoints for napropamide-M using normalised field degradation values. The overall modelling geometric mean DT_{50} including all four field trials was 15.11 days. However, the geometric means based on the K1 and K2 phases of 14.19 and 28.41 days respectively have been used in further modelling. Section 3CP B.8.3 describes how these values have been applied to groundwater modelling. The Applicant's results are shown in Table B.8.1.1.4- 38. Table B.8.1.1.4- 39 shows the RMS's selection of persistence trigger DT_{50}s derived from non-normalised day lengths and modelling endpoints derived from normalised data.

Table B.8.1.1.4- 38 Summary of Applicant's chosen modelling endpoints and persistence endpoints for napropamide-M derived from field dissipation data

Trial	Modelling Endpoints (normalised data)						Persistence Endpoints	
	Plot	Model	χ^2 err%	DT_{50} (days)	DT_{90} (days)	Modelling DT_{50} (days)	Model	DT_{50} (days)
Italy	Spring	FOMC	14.6	3.34	118	35.5	FOMC	6.91
	Autumn	SFO modified	16.0	28.6	95.1	28.6	SFO modified	94.4
Spain	Spring	HS modified	11.1	2.66	478	292	HS modified	5.31
	Autumn	HS	8.48	50.4	458	175	HS	101.0
Germany	Spring	SFO modified	14.1	24.0	79.7	24.0	SFO modified	57.9
	Autumn	SFO	20.2	15.3	50.8	15.3	SFO	49.0
UK	Spring	SFO	10.7	12.8	42.4	12.8	SFO	40.7
	Autumn	SFO	7.35	24.0	79.7	24.0	SFO	73.7
Averages (all data)			Arithmetic mean	20.1	175.2	75.9	-	53.62
			Geometric mean	14.0	116.4	39.4	-	36.24
Averages (excluding Spanish spring and autumn trials)			Arithmetic mean	18.0	77.6	23.4	-	-
			Geometric mean	14.9	73.2	22.0	-	-

Kinetic models described as "modified" indicate where an outlier has been removed.

Table B.8.1.1.4- 39 Summary of the RMS' chosen modelling endpoints and persistence endpoints for napropamide-M derived from field dissipation data

Trial	Plot	Modelling Endpoints (normalised data)											Persistence Endpoints	
		Model	χ^2 err%	K	K1	K2	g	p value	Overall DT_{50}	Overall DT_{90}	K1 DT_{50} (fast phase)	K2 DT_{50} (slow phase)	Model	DT_{50} (days)
Italy	Spring	FOMC	14.6	-	-	-	-		3.34	118	3.34	3.34	FOMC	6.91
	Autumn	SFO modified	16.0	0.02421	-	-	-	<0.05	28.6	95.1	28.6	28.6	SFO modified	94.4
Spain	Spring	DFOP modified	13.5	-	0.4084	0.001577	0.73	K1= 0.04893 K2= 0.3004	2.82	630	1.7	440	HS modified	5.31
	Autumn	SFO	16.9	0.007736	-	-	-	<0.05	89.6	298	89.6	89.6	HS	101.0
Germany	Spring	SFO modified	14.1	0.02889	-	-	-	<0.05	24.0	79.7	24.0	24.0	SFO modified	57.9
	Autumn	SFO	20.2	0.04534	-	-	-	<0.05	15.3	50.8	15.3	15.3	SFO	49.0
UK	Spring	SFO	10.7	0.05431	-	-	-	<0.01	12.8	42.4	12.8	12.8	SFO	40.7
	Autumn	SFO	7.35	0.0289	-	-	-	<0.001	24.0	79.7	24.0	24.0	SFO	73.7
Arithmetic mean									25.06	174.21	24.92	79.71	-	53.62
Geometric mean									15.11	114.15	14.19	28.41	-	36.24

Kinetic models described as "modified" indicate where an outlier has been removed.
See section 3CP B.8.3 for groundwater modelling PEC calculations

B.8.1.2. **Adsorption and desorption in soil**

Study author	Dubey, P. (2013)
Study title	Determination of the adsorption coefficient (K_{OC}) for [naphthyl-1-^{14}C]napropamide-M
Study date	23/12/2013
Annex point	CA 7.1.3.1.1-01
Previous evaluation	New active substance, no previous studies submitted.

Study Design

A study on the sorption behaviour of radiolabelled [naphthyl-1-^{14}C] napropamide-M was undertaken according to the guidelines OECD 106: Adsorption- Desorption using batch equilibrium method (2000) and the US EPA Fate, Transport and Transformation Test Guideline OCSPP 835.1230, Adsorption/ Desorption (Batch Equilibrium) (2008). The study was conducted to US GLP standards.

The five test soils used were one from Spain, two from the UK, and two from France (range 1-2 % OC; pH 6.6-7.8). Table B.8.1.2-1 presents the full details of the physicochemical properties of the soil. No details of transportation and storage conditions of the soils have been reported. The duration of soil storage is unknown, but assumed to be less than three years. Furthermore, the pesticide histories of the collection sites were not reported. The RMS does not believe this will materially affect the study. Soils were air dried and sieved (2 mm).

Table B.8.1.2-1 Physicochemical properties of test soils used for adsorption- desorption studies

Soil location (JRFA ID No.[1])	pH (H_2O)	OC (%)	OM (%)	Sand[2] (%)	Silt[2] (%)	Clay[2] (%)	CEC (meq/100g)	Classification[2]	Moisture content at 1/3 bar (%)
Spain, 20573	7.6	1.0	1.8	42	33	25	22.3	Loam	21.4
UK, 20798	7.5	1.1	1.9	84	11	5	7.7	Loamy sand	9.7
UK, 20800 *	7.5	2.0	3.5	36	17	47	27.7	Clay	35.8
France, 20804	7.8	1.3	2.2	34	29	37	21.0	Clay loam	27.2
France,20807 *	6.6	0.93	1.6	60	23	17	8.8	Sandy loam	15.0

1JRFA ID= Test facility soil identification number

2USDA textural class; OC = organic carbon; CEC = cation exchange capacity

*These soils were used in the preliminary studies. OECD 106 guidance recommends the use of a soil with a high organic carbon content and a low clay content alongside a contrasting soil with a low organic carbon content and a high clay content for such purposes. The RMS notes that the properties for soils 20800 and 20807 are high organic carbon with high clay and low organic carbon with low clay respectively.

Preliminary studies (tier 1) were conducted with a high clay content soil (clay soil (20800)) and a low clay content soil (sandy loam (20807)) to determine the appropriate soil: solution ratio, equilibrium time, stability of the test compound and potential for adsorption to test vessels. The potential for the test substance to adsorb to the test vessels was assessed by equilibrating five test vessels (polypropylene) with 0.01 M $CaCl_2$ overnight. A stock solution was prepared by dissolving 3.8 mg radiolabelled test item in 1.89 mL acetonitrile. Concentrations of 3.0 and 0.01 µg/ mL napropamide-M were added and samples were agitated on a platform shaker. Triplicate aliquots were drawn at 24 and 48 h for LSC analysis.

The tier 1 test was performed initially using a 1:1 soil: solution ratio. For each of the two soils, eight tubes containing ~5 g soil were prepared. Solution of 4.5 mL 0.01 M $CaCl_2$ was added and shaken overnight. Seven of the tubes were dosed with 0.5 mL of the 10.0 µg/ mL standard solution to achieve a nominal concentration of 1.0 µg/ mL, whilst the eighth served as a control. Samples were shaken continuously, covered with aluminium foil. An individual tube was drawn at 2, 4, 6, 18, 48, and 72 hours, following the parallel method described in the OECD guideline. The samples were centrifuged and the supernatant was analysed by LSC. Samples drawn at 48 and 72 hours were assessed for stability of the test substance over the study duration using HPLC analysis. The pH of the test system before and after agitation was not reported.

The 1:1 soil: solution ratio used in the preliminary study resulted in 92.8% and 84.4% adsorption at 48 h equilibrium time for the clay and sandy loam soils respectively. Therefore, it was deemed necessary to use a 1:2 soil-to-solution ratio for the definitive test (tier 3). The RMS notes that there was a slight increase in adsorption from 48 hours to 72 hours in the sandy loam soil (84.4% to 84.6%). However the chosen equilibrium time of 48 hours is considered acceptable. The preliminary study confirmed that there was no significant adsorption of test substance to the test vessels (average recovery 95 and 88% for the 0.01 µg/mL samples at 24 and 48 h respectively, re-analysis showed 95 and 91%, respectively; average recovery at 48 and 72 hour intervals for duplicate 3.0 µg/ mL samples was 95 and 93% respectively). HPLC analysis presented a single napropamide-M peak with no degradation products, indicating stability of the test compound throughout the study duration.

Definitive studies (tier 3) were performed using all five soils presented in Table B.8.1.2-1 above to determine Kd values and corresponding Kom and Koc values, along with Freundlich isotherms. Experiments were performed in duplicate at five concentrations (5.0, 1.0, 0.25, 0.05, and 0.01 µg/ mL) for each of the test soils at 20-25°C in the dark. For each soil type, two controls (soil and 0.01 M $CaCl_2$ only) were prepared. Approximately 4 g of test soil was weighed into a centrifuge tube and 7.2 mL 0.01 M $CaCl_2$ was added to each sample, before equilibration overnight on a mechanical shaker. The samples were then dosed with 0.8 mL of the dose solutions to make up the corresponding dose concentrations above. The controls received 0.8 mL 0.01 M $CaCl_2$. Samples were placed on a mechanical shaker for the predetermined equilibrium time of 48 h, before centrifugation and analysis of the supernatant by LSC. HPLC analysis using a Flow Scintillation Analyser was performed for one replicate of the 0.05 and 5.0 µg/ mL concentrations of each soil to further verify the stability of the test substance.

Desorption behaviour of napropamide-M was also assessed. Immediately after the removal of the supernatant following the adsorption phase, the same volume of 0.01 M $CaCl_2$ without test compound was added to one control and two samples containing the highest test concentration (5.0 µg /mL) for each test soil. The samples were equilibrated for 48 h, before centrifugation and analysis using LSC. A second desorption equilibration and analysis were performed by additions of fresh 0.01 m $CaCl_2$ solution. Soil samples were combusted and analysed by LSC (oxidiser efficiency >95%).

The mass balance was calculated by summing the total radioactivity recovered in the adsorption solution, the two desorption solutions and the combusted soil for the high concentration test soil samples. The LOQ and LOD were reported as 0.04% dose and ~ 2 ng respectively.

Results

The definitive study mass balances for the highest test concentration samples (5.0 µg/mL) ranged from 93.14 to 110.2 % for all five soils (table B.8.1.2-2). These were determined based on the sum of adsorption and desorption solutions and combusted soil. The arithmetic mean Kd and Koc values for all five soils over the range of concentrations were 11.25 mL/g and 831.72 mL/g respectively (geometric mean values 9.49 mL/g and 780.01 mL/g; see Table B.8.1.2-3). The K_{FOC} values ranged from 313.09 – 746.69 mL/g, (geometric mean 472.61 mL/g) indicating that napropamide-M exhibits low to medium mobility. The mean 1/n value was 0.865. All 1/n values were <1, indicating non-linear sorption.

Table B.8.1.2-2 Mass balance of napropamide-M in the highest test concentration samples (5.0 µg/mL) in the adsorption laboratory studies

Soil	Mass balance (%AR)*
Spain, 20573	110.2
UK, 20798	93.14
UK, 20800	102.6
France, 20804	99.2
France,20807	109.06

*It was not reported if these values are mean values or for individual replicates

Table B.8.1.2-3 RMS adsorption coefficients for napropamide-M across five test soils

Soil	OC	OM	Kd (mL/g)	K_{OM} (mL/g)	K_{OC} (mL/g)	K_F (mL/g)	Log K_F (mL/g)	K_{FOC} (mL/g)	K_{FOM} (mL/g)	1/n	r^2
Loam (Spain)	1.0	1.8	7.076	676.2 393.11	707.60	5.39	0.732	539.00	299.44	0.917	0.9992
Loamy Sand (UK)	1.1	1.9	5.461	493.36 287.42	496.45	3.44	0.537	313.09	181.30	0.857	0.9993
Clay (UK)	2.0	3.5	21.47	1055.09 613.43	1073.50	10.57	1.024	528.35	301.91	0.843	0.9988 (0.9989)
Clay Loam (France)	1.3	2.2	16.71	1306.4 759.55	1285.39	9.707	0.987	746.69	441.23	0.868	0.9987
Sandy Loam (France)	0.93	1.6	5.536	595.12 346.00	595.27	3.31	0.520	355.81	206.81	0.843	0.9994
Arithmetic mean			11.25		831.64	6.48	-	496.30	286.14	0.865	-
Geometric mean			9.49		779.91	5.75	-	472.61	272.25*	0.865	-

* K_{FOM} values in this table were calculated from Kf/OM *100. Values reported by the Applicant for OM and OC have been rounded up and do not exactly equal OM =OC*1.724. Therefore, the geometric mean K_{FOM} of 272.25 differs slightly from geometric K_{FOC} of 472.61 divided by 1.724, which gives 274.4.
Applicant's results are reported in parenthesis. The RMS had independently verified the results. The Applicant calculated Koc values by multiplying Kom values by 1.72. The RMS calculated the Koc values using the equation: (Kd/ OC%) *100

Table B.8.1.2- 4 shows that desorption values for napropamide-M were relatively low across all five soil types, ranging 19.02- 21.26 mL/ g (arithmetic mean) or 16.71- 17.90 mL/g (geometric mean).

Table B.8.1.2-4 Applicant results for mean desorption coefficients for napropamide-M across five test soils

Soil (JRFA ID no.)	OC (%)	pH	D_1 (%)	D_2 (%)	D_t (%)	K_{des1} mL/g	K_{des2} mL/g
Loam (20573), Spain	1.0	7.6	14.35	13.67	28.02	12.38	10.92
Loamy Sand (20798), UK	1.1	7.5	14.39	10.76	25.14	11.96	14.67
Clay (20800), UK	2.0	7.5	4.99	5.90	10.89	39.18	30.95
Clay Loam (20804), France	1.3	7.8	5.90	6.18	12.08	33.24	29.68
Sandy Loam (20807), France	0.93	6.6	17.60	15.40	32.99	9.53	8.86
Arithmetic Mean						21.26	19.02
Geometric Mean						17.90	16.71

D_1=percentage desorbed from the soil after the desorption interval
D_2 = percentage desorbed after second desorption interval
D_t = totalled desorption
K_{des1} = quantity of substance desorbed after first desorption interval
K_{des2} = quantity of substance desorbed after second desorption interval
RMS results variable slightly to those of Applicant's based on small rounding differences

The RMS investigated the possibility of correlation between soil properties and coefficient values. Although no clear relationship was observed between soil pH and Kf or K_{FOC} (r^2 0.3363 and 0.4126 respectively), figures B.8.1.2 -1 and -2 show possible correlation between soil OC% and Kd and soil clay content and kf (r^2 0.8334

and 0.8942 respectively). However, it is difficult to draw definitive conclusions about trends based on a dataset of five soils.

Figure B.8.1.2-1 The relationship between soil organic carbon content and the sorption coefficient Kd for the soils used in the adsorption study of napropamide-M

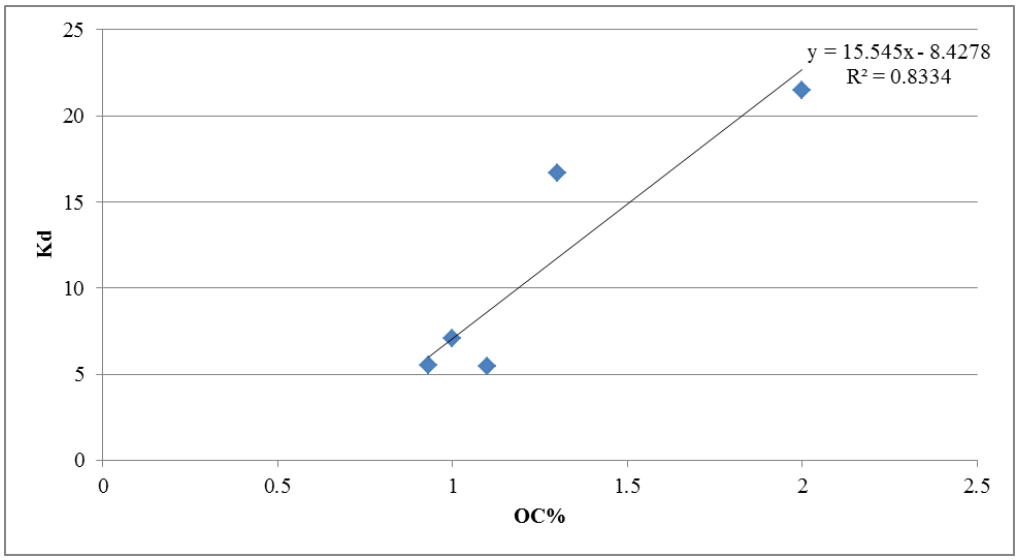
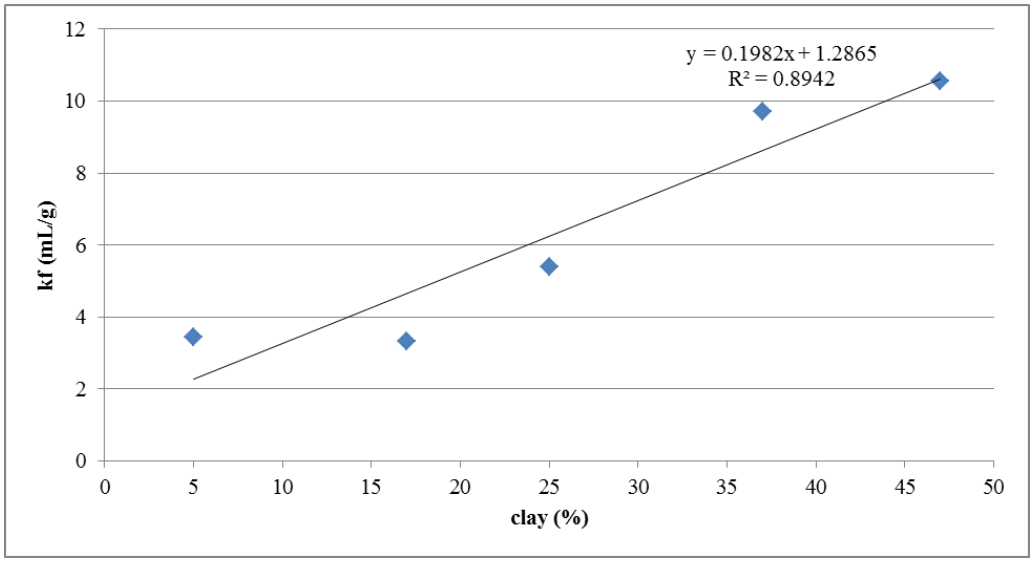


Figure B.8.1.2-2 The relationship between soil clay content and the sorption coefficient Kf for the soils used in the adsorption study of napropamide-M



B.8.1.3. **Mobility in soil**

B.8.1.3.1 **Column leaching**

Column leaching studies were not submitted for the active substance, napropamide-M. Adequate information on the adsorption and desorption properties and coefficients of napropamide-M can be found in section CA B.8.1.2. Therefore, column leaching studies are not required for the parent compound.

Data on the column leaching of metabolites, breakdown and reaction products are not available. Further data are not required as only minor components were observed and all were <10% of the applied radioactivity or <5% of applied radioactivity on two subsequent sampling occasions. Therefore, column leaching studies are not required for any metabolites of napropamide-M.

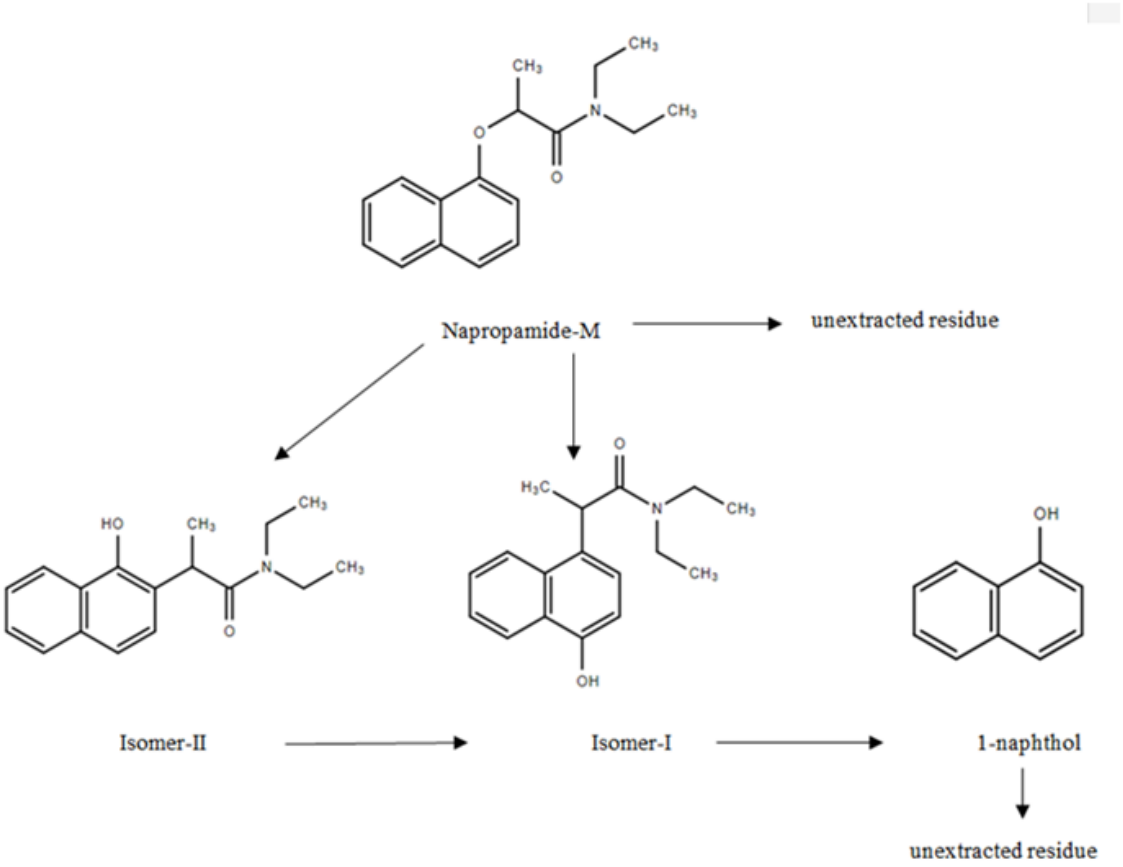
B.8.1.3.2 **Lysimeter studies**

No lysimeter or field leaching studies were submitted for napropamide-M. Sufficient information to evaluate the mobility and leaching potential of napropamide-M is available in the groundwater modelling assessment (CP B.8.3). All PEC_{GW} values were below the regulatory threshold for groundwater (i.e. <0.1 µg/L). The assessment indicated that use of napropamide-M within the proposed GAP would present minimal risk to groundwater via leaching.

Further data on metabolites are not required as only minor components were observed and all were <10% of the applied radioactivity or <5% of applied radioactivity on two subsequent sampling occasions. Furthermore, available laboratory and field data do not indicate a likelihood of any metabolites of napropamide-M leaching to groundwater in significant amounts. Therefore, lysimeter and field leaching studies are not required for napropamide-M or its metabolites.

B.8.2. FATE AND BEHAVIOUR IN WATER AND SEDIMENT

Figure B.8.2-1 Proposed degradation pathway of napropamide-M in water



Degradation pathway represents observed behaviour in the aqueous photolysis study, which resulted in the formation of three major metabolites. No major metabolites formed in the aerobic mineralisation, water sediment, hydrolysis or ready biodegradability studies.

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

B.8.2.1.1. Hydrolytic degradation

Study author	Li, F. (2013)
Study title	Hydrolytic stability of [naphthyl-1-^{14}C]napropamide-M in buffered aqueous solutions at pH 4, 7 and 9
Study date	19/06/2013
Annex point	CA 7.2.1.1-01
Previous evaluation	New active substance, no previous studies submitted.

Study Design

A study assessing the hydrolytic stability of napropamide-M was performed following OECD Guideline 111 and US EPA OCSPP 835.2120 to US EPA GLP standards, with no reported deviations. A stock solution of radiolabelled [naphthyl-1-^{14}C] napropamide-M was prepared by dissolving 3.8 mg test substance in 1.89 mL of

acetonitrile. An intermediate standard solution of approximately 400 µg/L was prepared. Test solutions were prepared by diluting 0.415 mL of intermediate standard solution with 83 mL buffer solution, to give a nominal test concentration of 2.0 µg/ mL. To verify that the test concentration did not exceed half of the maximum solubility, a standard solution was prepared and examined. The solution was clear, with no precipitate, indicating that dissolution of the test compound was sufficient.

Three buffer solutions of 1) 0.1 M potassium biphthalate and 0.1 N sodium hydroxide solution; 2) 0.1M monopotassium phosphate and 0.1N sodium hydroxide solution; and 3) 0.1M boric acid, 0.1N sodium hydroxide and 0.1 M potassium chloride were prepared at pH 4, 7 and 9 respectively. A pH meter confirmed that the pH values of all the buffer solutions varied by <0.1 of the required value. All solutions and buffers were prepared using sterilised equipment (autoclaved at 120 °C, ~30 minutes).

A tier 1 test was conducted at 50 ±0.5 °C in the dark, with samples incubated in a water bath. Duplicate samples (10 mL) and two contingency vessels were prepared for each pH solution. Samples were analysed at 0, 1, 3, 5, and 10 days using chiral HPLC. If samples were not analysed immediately, then they were stored frozen until analysis could be performed. The pH was measured at every sampling interval but only in one duplicate to ensure sterility in the other. Sterility was assessed for each pH solution at the end of the study using BBL ™ Sterile Pac Agar plates. After removal from the water bath, samples were immediately connected to a trap line for volatile trapping. Triplicate aliquots of the hydrolysate were analysed by LSC and separate aliquots by LC/UV/Ram analysis. Two samples were assessed for CO_2 at the study end. These samples were sparged for 30 minutes through a trap containing 25 mL of ethylene glycol and a trap in a series containing 25 mL of 1 N KOH and 25 mL of 1N H_2SO_4.

Results and Discussion

The LSC LOQ was reported as 0.04% dose and the LOD and LOQ values for HPLC analysis were 2.5% and 7.5% of AR respectively. The temperature of the study ranged from 49.8 to 50.0 °C, confirming no deviations from the correct test conditions. Chiral HPLC analysis confirmed that napropamide-M remained as the D-isomer throughout the study duration and no isomerisation to the L-form occurred. Actual test substance concentrations were 1.91 µg/ mL for pH buffer 4 and 1.95 µg/ mL for pH 7 and 9 buffers.

Mass balances for all buffer solutions and all individual replicates ranged from 96.4- 106.9 %AR. It was considered in light of these results that no significant amount of adsorption of the test compound to the test vessels had occurred. Table B.8.2.1.1-1 presents the mean applied radioactivity (%AR) for each of the buffer solutions at each of the sampling intervals. Mass balances for all traps for all buffer solutions were reported as 0.00% applied dose, indicating that formation of volatiles was insignificant. Furthermore, no hydrolysis products formed up to 10 d in any of the solutions. The RMS is satisfied from observing HPLC chromatograms that only the unchanged parent compound was present and no metabolites formed throughout the study. Hydrolytic degradation at 50±05 °C was <10% over the study duration in all three buffer solutions. The RMS concluded that napropamide-M is hydrolytically stable and its half-life at 25°C was predicted to be greater than 1 year. No DT_{50} values were calculated for this study. No further higher tier studies were required.

Table B.8.2.1.1-1 Mass balances of applied radioactivity in hydrolysis samples

Sample pH	Sampling interval (days)	Average recovery of AR (% AR)[1]
4	0	100.0
	1	104.9
	3	105.2
	5	106.3
	10	105.6
7	0	100.0
	1	99.3
	3	100.3
	5	100.3
	10	99.0
9	0	100.0
	1	101.0
	3	98.8
	5	98.3
	10	97.9

[1] = traps for volatiles were not included in the mass balance calculation due to low values.

B.8.2.1.2 **Aqueous photolysis**

Study author	Bianca, C. (2014)
Study title	Photodegradation of [napththyl-1-^{14}C]napropamide-M in sterile buffer
Study date	07/10/2014
Annex point	CA 7.2.1.2/01
Previous evaluation	New active substance, no previous studies submitted.

Study Design

The direct photodegradation of [naphthyl-1-^{14}C] napropamide-M in a sterile buffer was studied in accordance with guidelines OECD 316: Phototransformation of Chemicals in Water- Direct Photolysis (2008) and EPA OCSPP 835.2210 (1998). The study was performed to US GLP standards with no significant deviations.

A stock solution of final concentration 149.3 µg/mL was prepared by dissolving 1.5 mg radiolabelled [naphthyl-1-^{14}C] napropamide-M (99.5% purity) in 10 mL methanol. The test solution was prepared by adding approx. 6.7 mL of the stock solution to 500 mL pH 7 buffer to give a final concentration of 2.0 µg/mL. The sterile pH 7 ±0.2 buffer solution was prepared with 8.0373 g sodium hydroxide pellets, 27.2457 g monopotassium phosphate and MilliQ water in a 2000 mL volumetric flask. The pH was adjusted to 7 ± 0.2 with HCl.

Tier one- theoretical study

Firstly a tier one theoretical screen was undertaken. The UV-VIS spectrophotometer range was reported as 190 to 400 nm in the study report. The absorbance display spectrum was 190 to 400 nm and the actual used wavelengths ranged 290 to 350 nm. The quantum yield was assumed to be 1 as napropamide-M absorbs above the 290 nm cut-off of solar irradiation at the earth's surface. The use of a pH 7 buffer was acceptable as

napropamide-M is stable to abiotic hydrolysis and considered non-ionisable within a pH 4-9 range (see 3CA B.8.2.1.1 above). The molar absorption coefficient (ε), direct photolysis rate constant [$Kp^{c}_{(max)}$] and half-life (solar) were estimated using the spectral data. The estimated half-life was <30 days, showing potential for photolytic degradation and so a tier two experimental study was triggered.

Tier two- experimental study

The tier two study was conducted as follows. Quartz tubes containing 5 mL test solution (test substance and buffer) were exposed to a pressure quartz xenon arc lamp (Atlas XLS+ maximum 760 W/ m^2) for 120 minutes. Optical filters were set to the 200- 800 nm range. The Applicant claimed that the irradiance of the lamp was measured at the start and end of the study however the RMS could only find a single quoted value of 760 W/m^2. Irradiated samples were set up in duplicate. A single set of samples containing the test solution were kept in the dark to act as controls. Furthermore, a set of irradiated controls were prepared which contained the pH 7 buffer solution only. All samples were kept under a temperature of 25 ±2 °C. Samples were drawn at intervals of 0, 5, 10, 15, 20, 30, 60 and 120 minutes and analysed for parent compound and major phototransformation products using HPLC-RAM-MS and LSC. Three traps containing potassium hydroxide, ethylene glycol, and sulphuric acid respectively were set up to trap any volatile compounds. Sterility of the test solution was confirmed at the end of study using agar soy media. Chiral analysis was undertaken to investigate whether napropamide-M would isomerise to the L-form or remain as the D-isomer.

For the determination of the direct photolysis rate constant and quantum yield, quartz tubes containing 5 mL 0.0001M p-nitroanisole actinometer solution were prepared in the pH 7 buffer solution and also exposed to the pressure quartz xenon arc lamp at 25 ± 2°C for 120 minutes. Samples were taken at 0, 5, 10, 15, 20, 30, 60 and 120 minutes. Another set of samples were kept in the dark and analysed simultaneously. The photolytic rate and degradation of the test item and p-nitroanisole actinometer solution were calculated from the degradation pattern/kinetics and product formation. Direct photolysis rates were calculated based on pseudo first order kinetics and the quantum yield of the test item was calculated using the average photon flux of the light source and derived quantum yield of the p-nitroanisole actinometer solution. LOQ and LOD values for p-pitroanisole were 0.000018M and 0.00000625M respectively. LOQ and LOD values for the reference compound, diethylamine were 0.15 µg/mL and 0.05 µg/mL respectively. The LOQ for napropamide-M was 0.2 µg/mL (10% TRR). The LOD for parent and metabolites was not reported.

Results

The tier one theoretical screen half-life for direct photolysis in both summer and winter was 22.2 minutes assuming a quantum yield of 1. This is less than the 30 day trigger value for the tier two assessment.

In the tier two experimental study, mass balances ranged from 90- 107% AR (mean 93- 103.5 %AR) in irradiated samples, reported in table B.8.2.1.2-1. Napropamide-M degraded completely in the irradiated samples within the 30- 60 minute interval and so by the study end (120 minutes) it was undetectable. Three major photolytic metabolites >10% AR formed; isomer-I (max. mean 37.03% AR at 60 minutes), isomer-II (max. mean 57.1% AR at 30 minutes) and 1-naphthol (max. mean 23.31% AR at 120 minutes). A minor metabolite below LOQ was identified as diethylamine. At the study termination the proportion of applied radioactivity attributed to "other" transformation products was 30.59% AR (mean). The study report claims that the transformation products described collectively as "other" were individually <5% TRR. However the RMS notes that the limit of quantification was 10% and the LOD was not reported for parent or metabolites. Analysis of the trappings solution concluded that no volatile transformation products were formed.

The direct photolysis rate constant (Kp^{c}) and half-life values for napropamide-M were calculated as 0.1056 min^{-1} and 6.564 minutes respectively (elsewhere in the text these were reported as 0.1004 min^{-1} and 6.907 minutes, however this is assumed to be an error). The experimental half-life was not equated to a photolysis half-life under natural summer sunlight conditions. The Applicant equated the test duration of 120 minutes to 0.012 d midsummer sunlight 12h light/12h dark cycle but did not provide the underlying calculations nor equate the experimental half-life to natural sunlight days. The estimated Kp^{c} and half-life for the actinometer were 0.049 min^{-1} and 14.147 minutes respectively.

The quantum yield of ^{14}C napropamide-M was calculated using the average photon flux of the light source by Einstein molar concentration vs. photon flux, and by average daily solar photon flux and derived quantum yield

of the actinometer according to the study author. Quantum yield was stated to be calculated based on the definitive results of the study (using average photon flux of the light source and derived quantum yield of actinometer (p-niroanisole) and light absorbance). Quantum yields were given as 0.475 and 0.474 based on actinometer and absorbance respectively.

Table B.8.2.1.2-2 reports the mass balances for the dark controls (100-103% AR). No significant degradation of napropamide-M occurred in the dark samples.

Chiral analysis confirmed that napropamide-M remained in the D- form with no indication of isomerization to the L- form.

Table B.8.2.1.2-1 Mass balances and formation of metabolites as percentage applied radioactivity (%AR) in irradiated samples

Sampling interval time (**minutes**)	Rep	Mass Balance	parent	Isomer-I	Isomer-II	1-naphthol	Other *
0	1	100	99.24	0	0	0	0.76
	2	100	99.47	0	0	0	0.53
	Mean	100	99.36	0	0	0	0.64
5	1	93	47.61	12.85	30.89	0	1.65
	2	93	51	11.49	27.97	0	2.54
	Mean	93	49.3	12.17	29.43	0	2.1
10	1	100	29.34	21.41	46.09	0	3.16
	2	107	36.98	20.21	47.37	0	2.44
	Mean	103.5	33.16	20.81	46.73	0	2.8
15	1	92	17.86	21.53	48.28	0	4.33
	2	90	17.78	22.8	46.57	0	2.85
	Mean	91	17.82	22.16	47.42	0	3.6
20	1	98	13.11	27.47	53.92	0	3.5
	2	100	12.65	25.45	56.23	0	5.67
	Mean	99	12.88	26.46	55.07	0	4.59
30	1	100	4.24	31.38	57.15	4.79	2.44
	2	100	3.88	30.66	57.04	5.2	3.22
	Mean	100	4.06	31.02	57.1	5	2.82
60	1	100	0	34.34	37.86	11.57	16.23
	2	100	0	39.71	41.67	14.21	4.41
	Mean	100	0	37.03	39.77	12.89	10.31
120	1	100	0	30.69	12.94	23.54	32.83
	2	100	0	32.31	16.25	23.08	28.36
	Mean	100	0	31.5	14.6	23.31	30.59

* Other minor photolytic products were found summing up to 32.83% AR but individually they are less than 5%

Table B.8.2.1.2-2 Mass balances as percentage applied radioactivity (%AR) in dark control samples

Sampling interval time (**minutes**)	Mass Balance
0	100
5	101
10	101
15	102
20	103
30	102
60	103
120	102

Dark controls were not duplicated. Replicate values not available.

Kinetic assessment of aqueous photolysis of napropamide-M

Study author	Croucher, A. & Ford, S. (2015e)
Study title	Napropamide-M: kinetic assessment of degradation in a laboratory aqueous photolysis study
Study date	August 2015
Annex point	CA 7.2.1.2/02
Previous evaluation	New active substance, no previous studies submitted.

The aqueous photolysis of [naphthyl-1-^{14}C] napropamide-M was studied in a sterile buffer under laboratory conditions (see 3CA B.8.2.1.2). The degradation rate was recalculated according to FOCUS kinetic guidance (2006) to derive persistence trigger endpoints. The RMS independently performed the kinetic analysis using the software, CAKE v3.2 using the OLS optimiser throughout. Table B.8.2.1.2-3 presents the data used. Zero values before the first or after the last detectable level were set to half the LOD (1.25% AR) in accordance with FOCUS degradation kinetics guidance. Initial concentrations for metabolites at time zero were set to zero.

The kinetic procedure followed the FOCUS decision flow chart for deriving endpoints for use as triggers. The data were directly fitted, un-weighted, with the complete data set and unconstrained initial concentration (M0). Confidence in the resulting parameters was assessed visually and according to statistical measures. SFO fits were considered acceptable if the χ^2 error was less than 15% and the t-test function was significantly different to zero. The FOMC model was statistically acceptable if the confidence intervals for the α and β parameter estimates did not include zero.

The RMS' kinetic assessment for the parent compound is reported in table B.8.2.1.2-4 and corresponding figure B.8.2.1.2-1

Table B.8.2.1.2-3 RMS input data for the kinetic assessment of the aqueous photolysis of napropamide-M

Sampling interval (min)	replicate	RMS data (% applied radioactivity)			
		Parent	Isomer-II	Isomer-I	1-naphthol
0	1	99.24	0	0	0
0	2	99.47	0	0	0
5	1	47.61	30.89	12.85	
5	2	51	27.97	11.49	
10	1	29.34	46.09	21.41	
10	2	36.98	47.37	20.21	
15	1	17.86	48.28	21.53	
15	2	17.78	46.57	22.8	
20	1	13.11	53.92	27.47	0*
20	2	12.65	56.23	25.45	0*
30	1	4.24	57.15	31.38	4.79
30	2	3.88	57.04	30.66	5.2
60	1	0*	37.86	34.34	11.57
60	2	0*	41.67	39.71	14.21
120	1		12.94	30.69	23.54
120	2		16.25	32.31	23.08

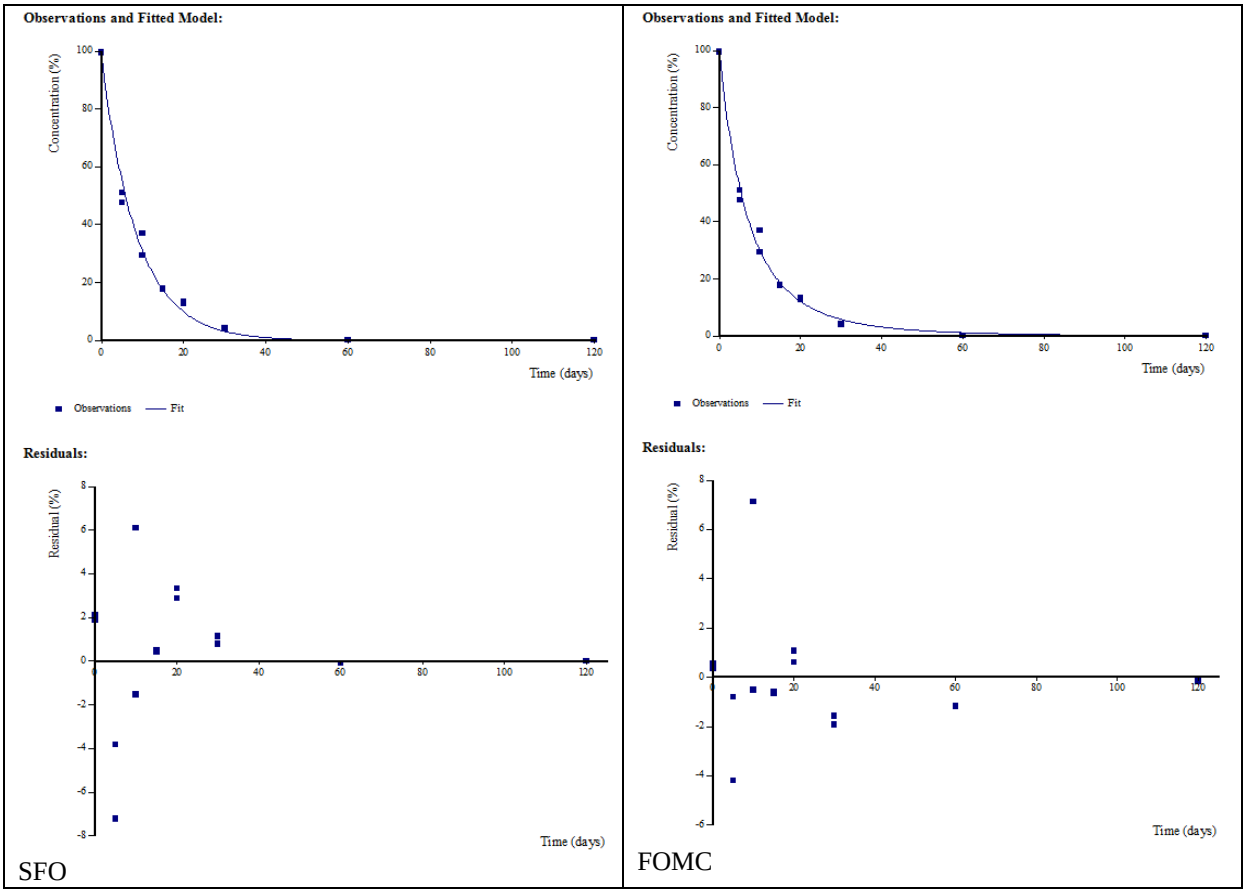
* Values to ½ LOD (1.25%)

Kinetic assessment of the aqueous photodegradation of the parent compound, napropamide-M

Table B.8.2.1.2-4 RMS kinetic assessment of the aqueous photolysis of parent compound, napropamide-M

Model	$\chi 2$ err%	Visual assessment	Statistical assessment	DT_{50} (mins)	DT_{90} (mins)
SFO	7.39	Good	t<0.001	6.03	20
FOMC	5.32	Good	Neither α or β 90th and 95th %ile C.I.s include zero	5.4	22.5
Both models gave a good visual assessment. FOMC predicted the initial values slightly better however, SFO predicted later points better. For both models the $\chi 2$ error was <15% and the statistical parameters were significantly different to zero. Although FOMC kinetics gave a slightly lower chi2 error% than SFO, and the applicant proposed DFOP kinetics as the best fit, there is minimal difference in the DT_{50} (which is *ca* 5-6 minutes for all fits). Therefore, the RMS has for simplicity accepted SFO, which also gave acceptable visual and statistical fit.					

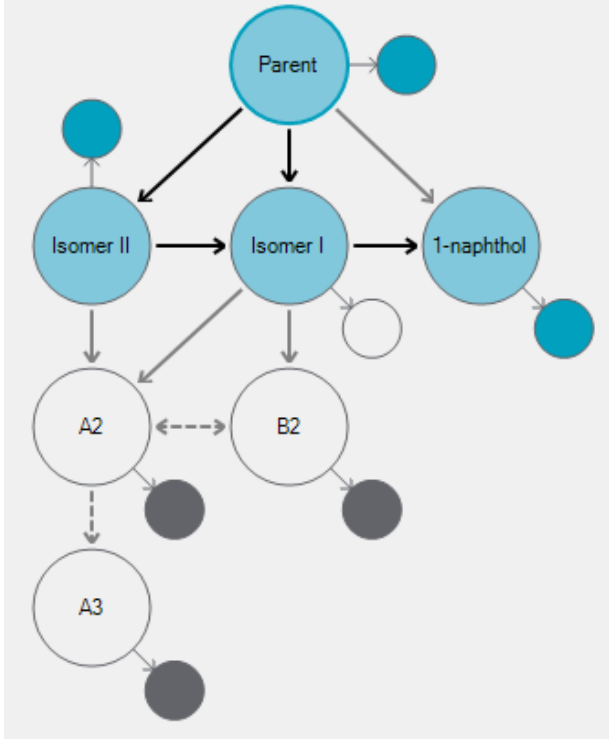
Figure B.8.2.1.2-1 RMS kinetic assessment of the aqueous photolysis of parent compound, napropamide-M



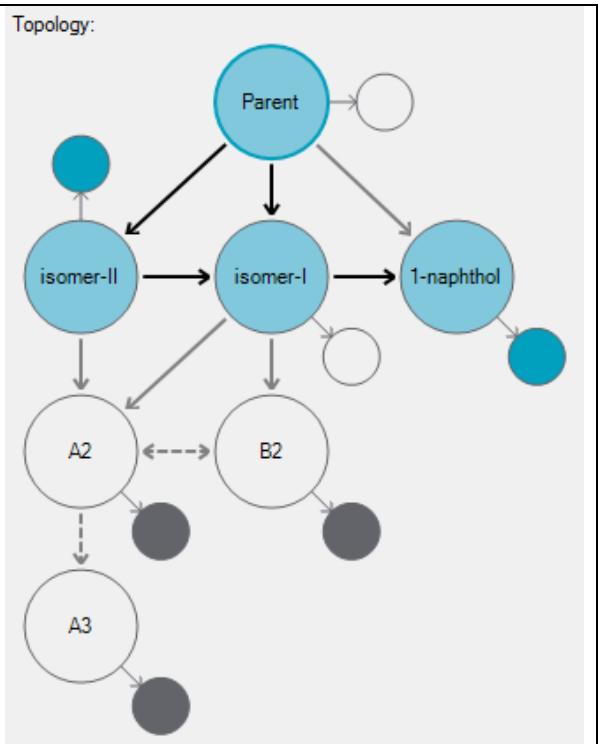
Kinetic assessment of the aqueous photodegradation of the parent compound and major metabolites, Isomer-I, Isomer-II and 1-naphthol

Over the duration of the laboratory study several aqueous photolysis transformation products formed. Three major metabolites were identified and so were included in the kinetic assessment. Figure B.8.2.1.2-2 below presents the degradation schemes used in the CAKE software to assess the formation and decline of the metabolites by the Applicant and by the RMS respectively. Both schemes assume the degradation pathway of napropamide-M degrading to Isomer-II and Isomer-I, with Isomer-II also degrading to Isomer-I and finally Isomer-I degrading to 1-naphthol. The RMS notes that the degradation scheme used in the kinetic assessment is different to that proposed in the original test facility report. The Applicant expresses that it was difficult to be certain over the exact pathway of degradation. The RMS has accepted the degradation pathway presented below for use in kinetic assessment. Table B.8.2.1.2-5 and corresponding figure B.8.2.1.2-3 reports the kinetic process for metabolites undertaken by the RMS. Parent and metabolites were fitted sequentially, with parent modelled with isomer-II and isomer-I initially, and then 1-naphthol added in the next step. RMS' assessment used SFO kinetics for parent and SFO kinetics for all metabolites.

Figure B.8.2.1.2-2 Degradation schemes used by the Applicant and by the RMS to represent the degradation of the parent compound, napropamide-M into three major aqueous photolysis metabolites



Applicant's degradation scheme

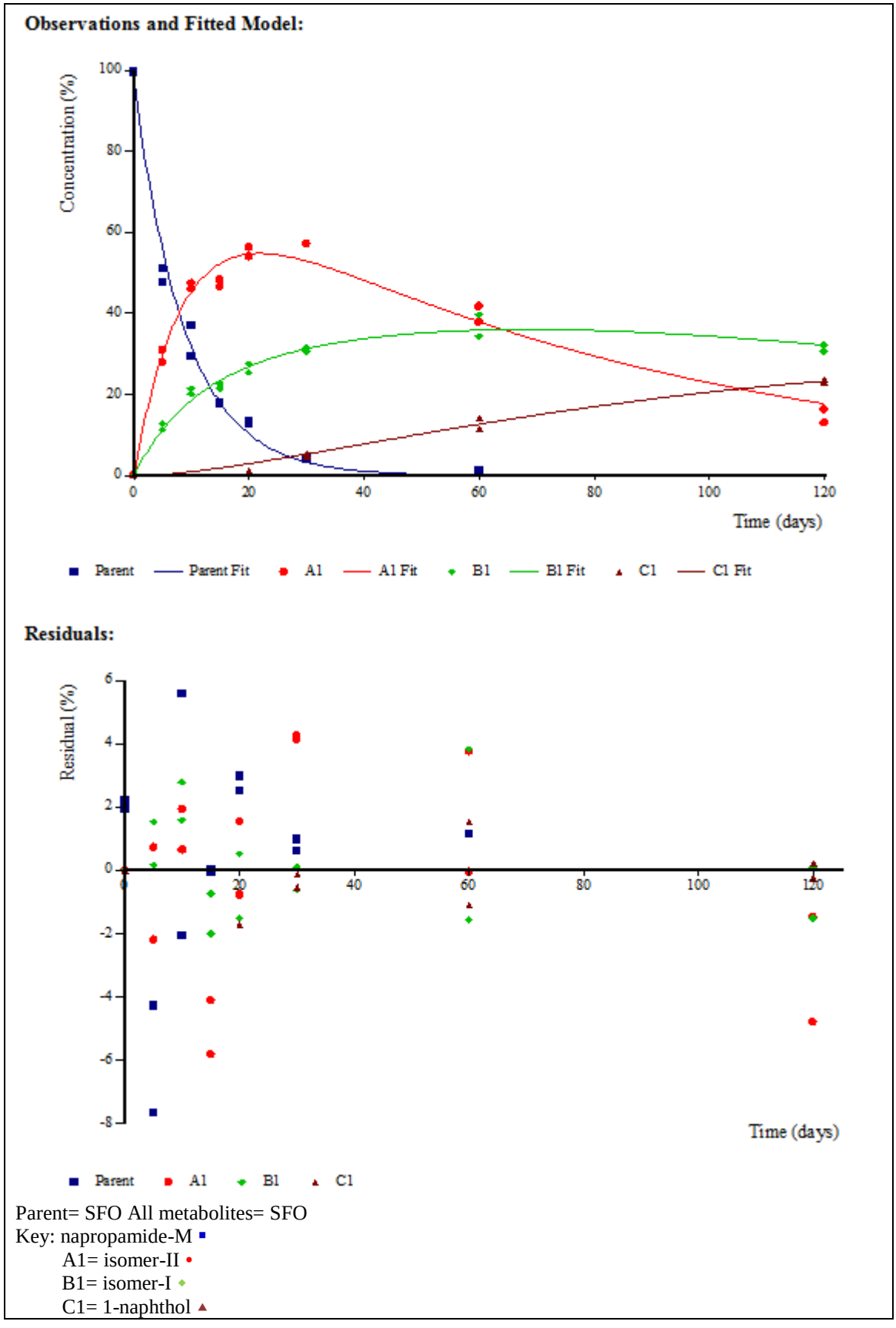


RMS' degradation scheme

Table B.8.2.1.2-5 RMS' kinetic assessment of the aqueous photolysis of parent compound, napropamide-M and major metabolites

compartment	Model	$\chi 2$ err%	Visual assessment	Statistical assessment	Fraction formed	DT_{50} (mins)	DT_{90} (mins)
All data	SFO	7.05	-	-	-	-	-
Parent	SFO	6.99	Good	t<0.001	Parent-A1: 0.7478	6.13	20.4
A1 (isomer-II)	SFO	5.51	Good	t<0.001	Parent-B1: 0.2522	54.5	181
B1 (isomer-I)	SFO	3.57	Good	t<0.001	A1-B1: 0.7137	75.5	251
C1 (1-naphthol)	SFO	5.86	Good	t<0.1	B1-C1: 1.0	90.5	301
All three metabolite fits were good visually. Residual scattering was small and random. The formation periods were well characterised. The t parameter was significantly different to zero for the Isomer-II and Isomer-I metabolites. However, it was not for 1-naphthol. The RMS notes that the decline phase for 1-naphthol was not reached during the study period. Therefore it is difficult to assess the overall degradation pattern for this metabolite. Overall, the SFO models were visually and statistically acceptable for both parent and metabolites. The RMS has accepted these as best fit models for use in deriving persistence endpoints.							

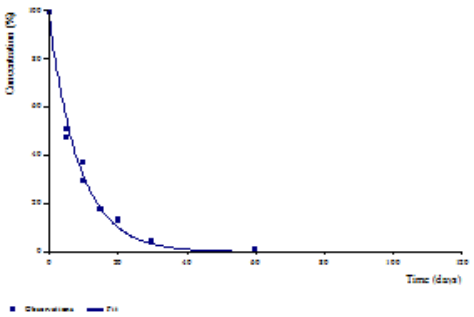
Figure B.8.2.1.2-3 RMS' kinetic assessment of the aqueous photolysis of parent compound, napropamide-M and major metabolites

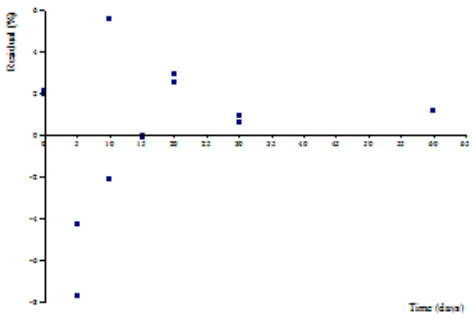


Parent= SFO All metabolites= SFO
Key: napropamide-M ▪
A1= isomer-II •
B1= isomer-I ◆
C1= 1-naphthol ▲

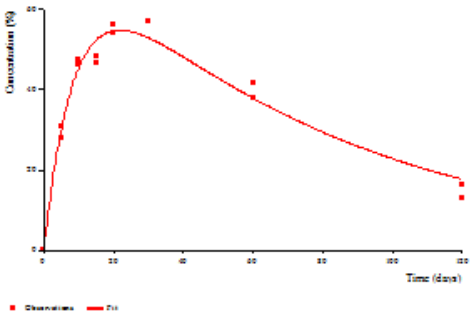
Figure B.8.2.1.2-3 RMS' kinetic assessment of the aqueous photolysis of parent compound, napropamide-M and major metabolites (continued)

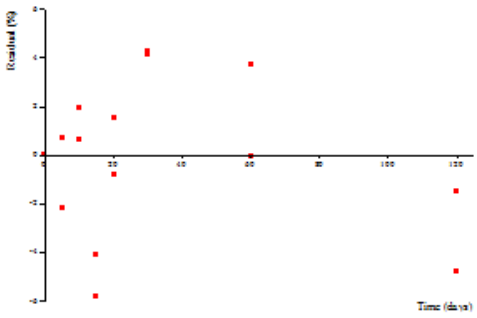
Compartment Parent:



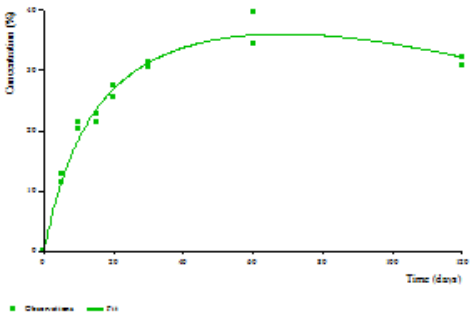


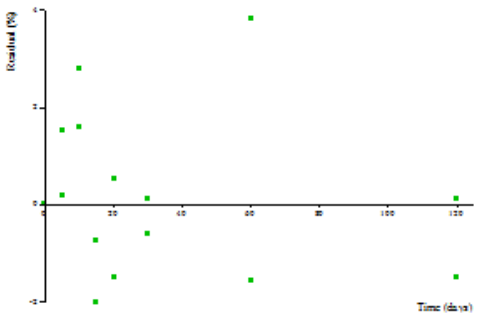
Compartment A1:



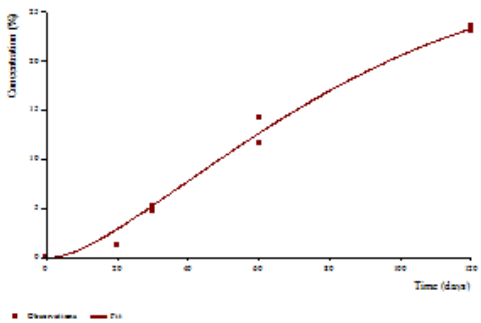


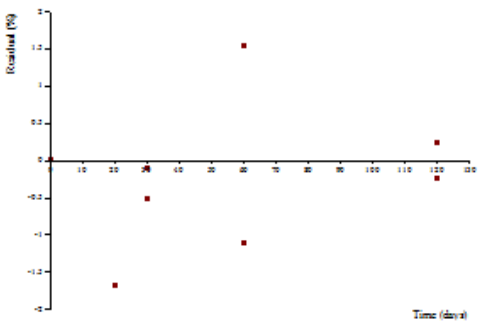
Compartment B1:





Compartment C1:





Key: A1= isomer-II ■
B1= isomer-I ■
C1= 1-naphthol ■

Table B.8.2.1.2-6 presents the best fit, persistence endpoints for the aqueous photolysis of napropamide-M and major metabolites chosen by the Applicant and the RMS respectively. The DT_{50} of the parent compound was 6.16 minutes. The metabolite with the greatest formation from parent, Isomer-II, had a half-life less than one hour. The DT_{50} of the second largest metabolite, Isomer-I was less than 90 minutes. The respective DT_{50} values for all three major metabolites were less than two hours. The endpoints chosen by the RMS will be used in the exposure assessment for surface water.

Table B.8.2.1.2-6 Summary of Applicant's and RMS' persistence endpoints for the aqueous photolysis of napropamide-M and major metabolites

Trigger endpoints	Substance	Model	χ2 err%	Fraction formed	DT_{50} (mins)	DT_{90} (mins)
Applicant's	Parent	DFOP	3.44	-	5.05	22.2
	Isomer-II	SFO*	5.90	0.75 (from parent)	54.7	182
	Isomer-I	SFO*	3.15	0.25 (from parent) 0.91 (from Isomer-II)	61.5	204
	1-naphthol	SFO*	6.40	0.77 (from Isomer-I)	116	385
RMS'	Parent	SFO	6.99	-	6.13	20.4
	Isomer-II	SFO	5.51	0.7433 (from parent)	54.5	181
	Isomer-I	SFO	3.57	0.2567 (from parent) 0.7629 (from Isomer-II)	75.5	251
	1-naphthol	SFO	5.86	1.0 (from Isomer-I)	90.5	301

*Applicant's chosen best fit model for parent was DFOP. However, the statistical parameters were unreliable when metabolites were added. Therefore the Applicant used a parent FOMC model for the fitting of metabolites. Given the similarity and shortness of the DT_{50} values from the various kinetic fits, the RMS has for simplicity accepted SFO.

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

B.8.2.2.1 **Ready biodegradability**

Study author	Raithatha, A. (2014)
Study title	Ready biodegradability of napropamide-M technical
Study date	18/06/2014
Annex point	CA 7.2.2.1/01
Previous evaluation	New active substance, no previous studies submitted.

Study Design

A study with napropamide-M followed the OECD Guideline 301: Ready Biodegradability (part D Closed Bottle Test) to GLP standards with no deviations reported. Secondary effluent from a treatment plant was filtered and pre-incubated at 20 ± 1°C for 6 days, without test substance application. Mineral medium was made from stock solutions and aerated for 20 minutes before standing for 20 hours. Test suspension was prepared by adding 20.55 mg napropamide-M (96.14% D- isomer and 3.86% L- isomer) and 4.0 mL of inoculum to 3996 mL of mineral medium. The analysed purity of the test material was stated as 97.26%. Final concentration of test substance was 5 mg/L.

The procedure control was prepared by adding 4.0 mL stock solution of the reference compound, potassium hydrogen phthalate and 4.0 mL of inoculum to 3992 mL of mineral medium. The final concentration of the reference substance in mineral medium was 5 mg/ L. A Toxicity control was prepared by adding 2.0 mL stock solution of potassium hydrogen phthalate, 10.32 mg of napropamide-M and 2.0 mL of inoculum to 1996 mL of mineral medium. The final concentrations of reference compound and test substance in the toxicity control were 5 mg/L respectively. The RMS notes that the OECD Guideline 301 states that "potassium hydrogen phthalate has been proposed but more evidence needs to be obtained with this chemical before it can be accepted as a reference compound." However, the use of this reference compound is considered unlikely to have materially affected the results for the biodegradability of napropamide-M.

Test vessels were prepared by dispensing the inoculum blank, test suspension and procedural control in BOD bottles in duplicate for the analysis of dissolved oxygen (DO) using a DO meter on 0, 7, 14, 21 and 28 days. Toxicity controls were prepared in single replication on 0, 7, 14, and 21 days and in duplicate on day 28. Each series of test suspension, procedure control and toxicity control were accompanied by a parallel series of inoculum blank. All of the air saturated mediums were transferred using siphons to ensure no bubbles were suspended in the solution. The test was performed in a horizontal laminar flow cabinet under aseptic conditions in the dark at 20 ± 1°C.

Investigations for nitrification were undertaken to correct for the uptake of any oxygen by this method and the theoretical oxygen demand corrected accordingly. Calibration standard solutions were made from potassium nitrate and sodium nitrite for comparison with test solutions. Absorbances were measured on 0, 7, 14, 21and 28 days using UV-Vis Spectrophotometer at 220 and 543 nm for nitrate and nitrite respectively.

For each sampling interval, the oxygen depletion values, oxygen consumption values and the nitrification corrected BOD (biological oxygen demand) were calculated (replicates averaged). The theoretical oxygen demands (ThOD) of napropamide-M (corrected for nitrification) and potassium hydrogen phthalate (without nitrification) were calculated to be 2.653 and 1.175 mg O_2/ mg respectively. The percentage degradation (BOD divided by ThOD) was calculated for the test suspension, procedure control and toxicity control along with the percentage inhibition of the test substance for the toxicity controls.

Results

Biodegradation of test substance reached 7.84% at day 21 and 7.01% at 28 days (see Table B.8.2.2.1-1) so napropamide-M cannot be classified as readily biodegradable. Maximum degradation was below 10 % but was not observed in a time-related manner (compared to the normal degradation pattern of the reference substance) over 28 days.

Table B.8.2.2.1 -1 The mean percentage biological degradation of napropamide-M based on the theoretical oxygen demand.

Treatment	Sampling interval (days)			
	7	14	21	28
Test Suspension	1.66	2.71	7.84	7.01
Procedure Control	51.57	72.17	74.55	70.47
Toxicity Control	54.81	77.28	78.98	72.85

Degradation of the reference substance reached 72.17% by day 14 meeting the study criteria of >60 % within 14 d. No nitrates or nitrites were formed over the course of the study. Napropamide-M did not inhibit degradation by >25 % after 14 days and thus napropamide-M was shown not to inhibit microbial degradation under the test conditions. Table B.8.2.2.1- 2 shows that all validity criteria were satisfied.

Table B.8.2.2.1- 2 Summary of the validity criteria for the ready biodegradability test for napropamide-M

Treatment	Criteria	Result	Conclusion
Inoculum Blank	Change in DO over 28 days must be ≤1.5 mg/L	0.52	Pass
Procedure Control	Degradation must be >60% of ThOD within 14 days	72.17	Pass
Test Suspension	Residual oxygen over 28 days must be >0.5 mg/L	7.60	Pass
	Degradable if oxygen consumption exceeds >60% ThOD over 28 days	7.01	Not readily biodegradable
Toxicity Control	Toxic if %inhibition >25% of procedure control within 14 days.	-7.08	Pass- not toxic

B.8.2.2.2 **Aerobic mineralisation in surface water**

Study author	Bianca, C. (2015b)
Study title	[naphthyl-1-^{14}C] Napropamide-M: aerobic mineralisation in surface water (pelagic test)
Study date	13/02/2015
Annex point	CA 7.2.2.2/01
Previous evaluation	New active substance, no previous studies submitted.

Study Design

The aerobic mineralisation of napropamide-M was studied in accordance to the OECD 309 Guideline: aerobic mineralisation in surface water- simulation biodegradation test (2004) (pelagic test). The study adhered to US EPA GLP standards. Minor deviations include the absence of an audit trail for LC/MS/MS chromatography and radiodetection analysis. As such the data print outs are considered to be the raw data documentation.

A stock solution of radiolabelled [naphthyl-1-^{14}C] napropamide-M was prepared (22.69 mg test substance and methanol in a 25 mL volumetric flask to give a concentration of 907.6 µg/mL). An intermediate solution was prepared by dissolving 1.10 mL of the 907.6 µg/mL stock solution in methanol for a concentration of 100 µg/mL. The final dosing solution was prepared by dissolving 0.5 mL of the intermediate solution with methanol into a 50 mL volumetric flask to obtain a final concentration of 1 µg/mL.

Natural surface water was collected from a location near Hoy Park, Audubon, Pennsylvania, USA at a depth of approximately 15 cm below the surface. The RMS assumes the samples were freshwater. The water samples were transported under aerobic conditions and stored at 4 °C until use. Physicochemical properties of the test water are presented below (table B.8.2.2.2-1). No information was provided regarding the duration of transportation or storage. The contamination history of the site is unknown.

Table B.8.2.2.2-1 Physicochemical properties of the test water

Parameter	Value
pH	8.1
Total OC (mg/L)	4.1
Dissolved OC (mg/L)	3.5
Total N (mg/L)	5.3
Total P (mg/L)	0.4
Potassium (ppm)	7.3
Calcium (ppm)	33
Magnesium (ppm)	10
Sodium (ppm)	102
Hardness (mg eq. $CaCO_3$/L)	124
Conductivity (mmhos/ cm)	0.72
Total dissolved solids (ppm)	366
Turbidity (NTU)	0.79

OC= organic carbon; N= nitrogen; P= phosphorous; NTU= nephelometric turbidity units

Test vessels were prepared by dispensing 100 mL water samples in 500 mL flasks. A volume of 100 µL or 500 µL test solution was applied onto the surface of the water test system and mixed thoroughly to give test concentrations of 1 and 5 µg/ L respectively. The test system was set up as follows: twelve incubation vessels were prepared in duplicate for each test concentration to provide ten sampling intervals and two contingencies. A set of sterile controls were prepared in duplicate for each test concentration for analysis at 90 days to account for any abiotic degradation. Ten additional control incubation vessels were prepared for each concentration with a volume of methanol equal to that used in treated samples but with no test substance to measure the effect of the methanol on the microbial biomass. Reference control vessels were prepared with ^{14}C sodium benzoate or ^{14}C sodium benzoate and methanol (overall concentration 10 µg/L) to assess both the microbial activity of the system and what effect the organic solvent had on the system. Two trapping vessels containing Harvey cocktail were set up for each sampling interval for collection of any volatiles produced. No trapping media was associated with zero-time samples.

The test system was maintained under aerobic, dark conditions at 20 ±2°C and continuous agitation. The pH, redox potential, conductivity and oxygen concentration were measured throughout the study. The microbial biomass was measured at the end of the incubation period. Whole flasks treated with test substance were drawn in duplicate at 0, 2, 5, 7, 14, 21, 28, 47, 60, and 90±2 days along with their associated traps. Reference controls and their associated traps were taken for analysis at 14, 16 and 28 days and sterile controls were drawn at 90 days.

The radioactivity in the water and trapping solutions was determined by LSC. At 0 - 5 days water samples were concentrated prior to analysis by HPLC-RAD-MS. For the 7 - 90 day water samples, the samples were concentrated and extracted twice with hexane, centrifuged and the supernatant further evaporated and reconstituted in acetonitrile prior to quantification by LSC and analysis by HPLC-RAD-MS. The additional extraction procedures for the later samples were deemed necessary due to increased microbial activity. Chiral HPLC analysis was undertaken for samples drawn at 0, 28 and 90 days for the identification of D- and L-isomers. The LOD and LOQ were not reported.

Results

The physicochemical properties of the test water measured throughout the study are reported in Table B.8.2.2.2-2. The dissolved oxygen ranged 78-89% indicating that aerobic conditions prevailed throughout the study duration.

Table B.8.2.2.2-2 Physicochemical properties of the test water throughout the aerobic mineralisation study

Day	Redox	pH	Oxygen concentration (% saturation)
7	233.4	6.87	88.2
14	259.7	7.09	89.4
21	195.0	7.16	81.9
28	232.5	7.38	88.1
47	395.1	4.89	83.7
60	281.3	6.47	82.5
90	170.1	6.06	78.0

Table B.8.2.2.2-3 presents the measurements of microbial activity at the start and end of the study. Microbial biomass was 159 CFU (colony forming units) at the approximate time of application which decreased to 64 CFU at the end of the study. A viable bacterial population was demonstrated throughout the study. The control vessels had 336,000 CFU after 90 days of incubation, indicating that the methanol did not adversely affect the bacteria. Analysis of the reference controls showed significant amounts of $^{14}CO_2$ with recoveries between 74 and 87% AR, demonstrating that the system was microbiologically active and the presence of methanol did not affect this.

Table B.8.2.2.2-3 Microbial activity of the test water throughout the aerobic mineralisation study

Microbial biomass before study (CFU)	Microbial biomass at study end (CFU)	Microbial biomass at study end in the methanol control (CFU)
142 16 1	58 6 0	336000 2 0

CFU= colony forming units

[1] Biomass results are for, bacteria, actinomycetes and fungi respectively

Table B.8.2.2.2-4 reports the mineralisation of the reference compound, ^{14}C sodium benzoate to CO_2 as identified in trappings solution at sampling intervals 14, 16 and 28 days. Table B.8.2.2.2-5 shows the mineralisation of the reference compound with methanol. At 14 days, 72.3 and 74.8 %AR sodium benzoate had degraded to CO_2, indicating sufficient biological activity of the test water and viability of the test.

Table B.8.2.2.2-4 Mineralisation of the reference compound ^{14}C sodium benzoate to CO_2

Sampling interval		Applied radioactivity (%AR)	Total applied radioactivity (%)
14	Source water	6.0	78.3
	Trap 1	72.3	
	Trap 2	0.0	
16	Source water	4.8	84.9
	Trap 1	80.1	
	Trap 2	0.5	
28	Source water	2.7	81.1
	Trap 1	78.4	
	Trap 2	0.0	

Table B.8.2.2.2-5 Mineralisation of the reference compound ^{14}C sodium benzoate plus methanol to CO_2

Sampling interval		Applied radioactivity (%AR)	Total applied radioactivity (%)
14	Source water	12.0	86.7
	Trap 1	74.8	
	Trap 2	0.0	
28	Source water	10.1	73.8
	Trap 1	63.7	
	Trap 2	0.0	

Mass balances ranged 88.0 to 104.9% for 1 µg/L test vessels and 85.0 to 103.9% AR for 5 µg/L test vessels, with the majority of the mass balances over 90%. Mass balances of applied radioactivity for each test concentration at each sampling interval can be found in tables B.8.2.2.2-6 and B.8.2.2.2-7 respectively. The formation of radioactive CO_2 accounted for mean values of $\leq$ 2.4% AR in all tests. Chiral analysis confirmed that napropamide-M remained in the D- form with no indication of isomerization to the L- form.

Table B.8.2.2.2-6 Percentage applied radioactivity (%AR) of 1 µg/L [naphthyl-1-^{14}C] napropamide-M in surface water

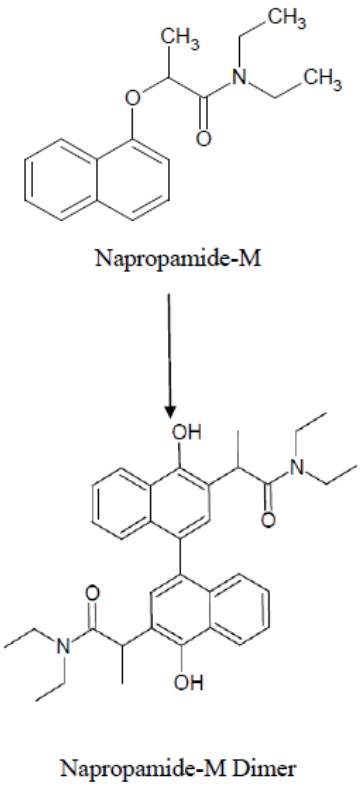
Sampling interval (days)		Applied radioactivity (%)	Napropamide-M		Napropamide dimer	
			(%AR)	Conc. (µg/L)	(%AR)	Conc. (µg/L)
0	Rep. 1	102	102	1.02	0.0	0.0
	Rep. 2	100.3	100.3	1.00	0.0	0.0
	Mean	101.2	101.2	1.01	0.0	0.0
2	Rep. 1	97.6	97.6	0.98	0.0	0.0
	Rep. 2	96.1	96.1	0.96	0.0	0.0
	Mean	96.9	96.9	0.97	0.0	0.0
5	Rep. 1	93.1	93.1	0.9	0.0	0.0
	Rep. 2	96.0	96.0	1.0	0.0	0.0
	Mean	94.6	94.6	0.95	0.0	0.0
7	Rep. 1	98.6	98.6	1.0	0.0	0.0
	Rep. 2	93.1	93.1	0.9	0.0	0.0
	Mean	95.9	95.9	1.0	0.0	0.0
14	Rep. 1	90.9	90.9	0.91	0.0	0.0
	Rep. 2	89.6	89.6	0.90	0.0	0.0
	Mean	90.3	90.3	0.90	0.0	0.0
21	Rep. 1	91.3	91.3	0.91	0.0	0.0
	Rep. 2	91.2	91.2	0.91	0.0	0.0
	Mean	91.3	91.3	0.91	0.0	0.0
28	Rep. 1	88.9	88.9	0.89	0.0	0.0
	Rep. 2	87.8	87.8	0.88	0.0	0.0
	Mean	88.4	88.4	0.88	0.0	0.0
47	Rep. 1	92.0	75.0	0.75	17.0	0.2
	Rep. 2	89.1	89.1	0.89	0.0	0.0
	Mean	90.6	82.0	0.82	8.5	0.1
60	Rep. 1	90.1	25.4	0.25	64.7	0.6
	Rep. 2	88.0	30.1	0.30	57.9	0.6
	Mean	89.1	27.8	0.28	61.3	0.6
90	Rep. 1	104.9	104.9	1.05	0.0	0.0
	Rep. 2	90	90	0.90	0.0	0.0
	Mean	97.5	97.5	0.97	0.0	0.0
90 (sterile)	Rep. 1	101.1	101.1	1.01	0.0	0.0
	Rep. 2	102.6	102.6	1.03	0.0	0.0
	Mean	101.9	101.9	1.02	0.0	0.0

Table B.8.2.2.2-7 Percentage applied radioactivity (%AR) of 5 µg/L [naphthyl-1-^{14}C] napropamide-M in surface water

Sampling interval (days)		Applied radioactivity (%)	Napropamide-M		Napropamide dimer	
			(%AR)	Conc. (µg/L)	(%AR)	Conc. (µg/L)
0	Rep. 1	102.5	102.5	5.1	0.0	0.0
	Rep. 2	103.9	103.9	5.2	0.0	0.0
	Mean	103.2	103.2	5.2	0.0	0.0
2	Rep. 1	98.1	98.1	4.9	0.0	0.0
	Rep. 2	98.9	98.9	4.9	0.0	0.0
	Mean	98.5	98.5	4.9	0.0	0.0
5	Rep. 1	97.9	97.9	4.9	0.0	0.0
	Rep. 2	100.0	100.0	5.0	0.0	0.0
	Mean	99.0	99.0	4.9	0.0	0.0
7	Rep. 1	93.2	93.2	4.7	0.0	0.0
	Rep. 2	95.1	95.1	4.8	0.0	0.0
	Mean	94.2	94.2	4.7	0.0	0.0
14	Rep. 1	94.9	94.9	4.7	0.0	0.0
	Rep. 2	98.0	98.0	4.9	0.0	0.0
	Mean	96.5	96.5	4.8	0.0	0.0
21	Rep. 1	89.9	89.9	4.5	0.0	0.0
	Rep. 2	88.1	88.1	4.4	0.0	0.0
	Mean	89.0	89.0	4.5	0.0	0.0
28	Rep. 1	92.0	88.2	4.4	3.8	0.2
	Rep. 2	91.3	85.6	4.3	5.7	0.3
	Mean	91.7	86.9	4.3	4.8	0.2
47	Rep. 1	94.7	14.1	0.7	80.6	4.0
	Rep. 2	94.3	44.2	2.2	50.1	2.5
	Mean	94.5	29.2	1.5	65.3	3.3
60	Rep. 1	90.5	48.7	2.4	41.8	2.1
	Rep. 2	85.0	19.8	1.0	65.2	3.3
	Mean	87.8	34.3	1.7	53.5	2.7
90	Rep. 1	102.3	82.2	4.1	20.1	1.0
	Rep. 2	100.4	76.0	3.8	24.4	1.2
	Mean	101.4	79.1	4.0	22.2	1.1
90 (sterile)	Rep. 1	92.5	92.5	4.6	0.0	0.0
	Rep. 2	90.5	90.5	4.5	0.0	0.0
	Mean	91.5	91.5	4.6	0.0	0.0

Napropamide-M remained fairly constant over the course of the incubation except for the appearance of a possible dimer moiety. No reference standard was available to identify the dimer but mass spectra work including TIC plus decoupling and neutral loss were performed. Figure B.8.2.2.2-1 presents the metabolic scheme proposed by the test facility showing the dimer, however the identity cannot be confirmed due to lack of reference standard and because of the low concentrations in the study. As the dimer was not detected in sterile samples, the test facility believes that its formation may be attributed to processes of bacterial dimerization.

Figure B.8.2.2.2-1 Test facility's proposed metabolic scheme for the aerobic mineralisation of napropamide-M



In the lower concentration samples (1 µg/L) the dimer did not appear until 47 days with a mean 8.5 %AR. It increased to a maximum 61.3 %AR in the 60 day sampling interval and was not detected in the 90 day samples. The dimer was detected in the day 28 samples for the 5 µg/L test samples at a mean of 4.8 %AR which peaked at 65.3 %AR in day 47samples and decreased to 22.2 %AR at the study end. The Applicant believes this product may be an artefact formed during sample processing. The test facility report states uncertainty as to whether the dimer decreased before the 90 day sampling or it was lost during the extraction process.

The RMS notes that the pH decreased and the redox potential increased (table B.8.2.2.2-2) at the day 47 sampling interval which broadly coincides with the formation of the dimer. By the study termination, the physicochemical properties revert back to values similar to those at the start of the study. The RMS proposes that the dimer formation may be a reversible reaction based on physicochemical properties. The RMS welcomes views from other member states on this issue and seeks expert judgement from EFSA on the matter.

The Applicant calculated first-order DT_{50} values using linear regression of log transformed data and obtained 1732.9 and 2310.5 days for 1 and 5 µg/L samples respectively. They believe there may have been sample processing issues with the 90 day samples and recalculated the DT_{50} values with those samples omitted to derive 433.2 and 385.1 days, for the two test concentrations respectively. As <20% degradation of napropamide-M occurred during the pelagic aerobic mineralisation test, a degradation rate constant cannot be properly derived and therefore any DT_{50} values are uncertain.

Conclusions

Mineralisation of napropamide-M in surface water under laboratory conditions was <20% during the 90 days of incubation, resulting in uncertain DT_{50} values. A transformation product that formed between days 28 and 90 was tentatively identified as a napropamide dimer, however the identity was not confirmed and the Applicant claims this product may have been an artefact of sample preparation.

Kinetic evaluation of the aerobic mineralisation of napropamide-M

Study author	Croucher, A. & Ford, S. (2015f)
Study title	Napropamide-M: kinetic assessment for aerobic mineralisation in surface water study
Study date	August 2015
Annex point	CA 7.2.2.2/02
Previous evaluation	New active substance, no previous studies submitted.

The aerobic mineralisation of napropamide-M was studied in surface water under laboratory conditions (see 3CA B.8.2.2.2, Bianca, 2015b). The rate of mineralisation was recalculated according to FOCUS kinetic guidance (2006) to derive persistence endpoints. Table B.8.2.2.2-8 shows the main differences in approach taken between the Applicant and the RMS in their kinetic assessment.

Table B.8.2.2.2-9 presents the full datasets used. The Applicant conducted the kinetic assessment on the total [naphthyl-1-^{14}C] napropamide-M content including the dimer. It is proposed that the dimer may represent two bacterially conjoined molecules of napropamide-M rather than a true degradation product or metabolite. Therefore the RMS has accepted this approach of combining the parent %AR and dimer %AR.

Values used by the Applicant and the RMS were identical except for the day 47 1st replicate and day 90 1st replicate values for the 5 µg/L dataset. The RMS assumes these to be typing or calculation errors. The Applicant believed that the levels of napropamide-M measured after 90 days in one replicate sample from each system was considerably higher than the other replicate and higher than previous samples. Therefore they removed the day 90 1st replicate from the 1 µg/L dataset and the day 90 2nd replicate from the 5 µg/L dataset. According to FOCUS guidance, all data must be included in the initial kinetic fit. Outliers may be removed on rare occasion based on expert judgement and fitting, but this needs to be clearly justified. The RMS considers the correct day 90 values fit with the rest of the dataset and has re-evaluated the kinetic assessment with the full dataset. Tables B.8.2.2.2-10 and B.8.2.2.2-11 (with corresponding figures B.8.2.2.2-1 and B.8.2.2.2-2) present the kinetic assessments for the 1 µg/L datasets by the RMS and those by the Applicant. Tables B.8.2.2.2-12 and B.8.2.2.2-13 (corresponding figures B.8.2.2.2-3 and B.8.2.2.2-4) report the kinetic assessment for the 5 µg/L dataset.

Table B.8.2.2.2-8 Differences in approach for the kinetic assessment of the aerobic mineralisation of napropamide-M

	Applicant	RMS
Software package	CAKE v3.1	CAKE v3.2
Optimiser	IRLS	OLS
Dataset	Constrained prior to any kinetic fitting. (1 µg/L dataset- day 90, rep 1 removed; 5 µg/L dataset- day 90, rep 2 removed. See tables B.8.2.2.2-6 and -7)	Full dataset used for both concentrations, no removal of outliers throughout kinetic process.
Approach	Included HS models in biphasic model investigations.	Followed FOCUS flowchart for deriving persistence endpoints, which does not recommend the use of HS kinetics.

Table B.8.2.2.2-9 Applicant's and RMS' datasets used in the kinetic assessment of the aerobic mineralisation of napropamide-M

Sampling interval	Replicate	Applicant values[1]		RMS values[1]	
		1 µg/L	5 µg/L	1 µg/L	5 µg/L
0	1	102	102.5	102	102.5
	2	100.3	103.9	100.3	103.9
2	1	97.6	98.1	97.6	98.1
	2	96.1	98.9	96.1	98.9
5	1	93.1	97.9	93.1	97.9
	2	96	100	96	100
7	1	98.6	93.2	98.6	93.2
	2	93.1	95.1	93.1	95.1
14	1	90.9	94.9	90.9	94.9
	2	89.6	98	89.6	98
21	1	91.3	89.9	91.3	89.9
	2	91.2	88.1	91.2	88.1
28	1	88.9	92	88.9	92
	2	87.8	91.3	87.8	91.3
47	1	92	**92.0** [2]	92	94.7
	2	89.1	94.3	89.1	94.3
60	1	90.1	90.5	90.1	90.5
	2	88	85	88	85
90	1	104.9 [3]	**87.8** [2]	104.9	102.3
	2	90	100.4 [3]	90	100.4

1. AR%= parent AR% + dimer AR%
2. Values in bold are incorrect values used by the Applicant
3. These values were considered outliers by the Applicant and were removed prior to kinetic fitting

Table B.8.2.2.2-10 RMS' kinetic assessment of the aerobic mineralisation of napropamide-M at 1 µg/L

Model	χ^2 err%	Visual assessment	Statistical assessment	DT_{50}	DT_{90}
SFO	3.36	Good	t>0.1	1840	6120
FOMC	2.56	Good	Both α and β C.I.s include zero	>10,000	>10,000

Figure B.8.2.2.2-1 RMS' kinetic assessment of the aerobic mineralisation of napropamide-M at 1 µg/L

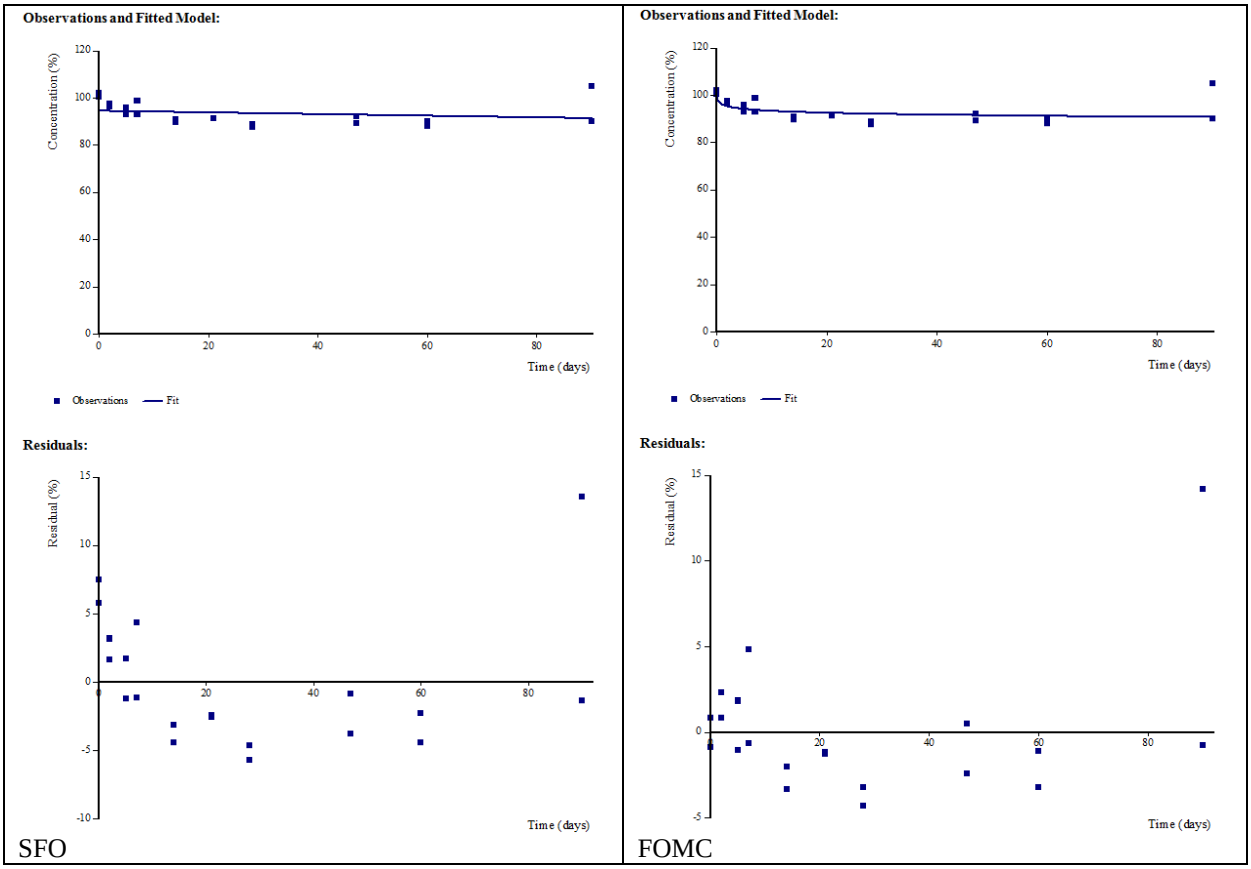


Table B.8.2.2.2-11 Applicant's kinetic assessment of the aerobic mineralisation of napropamide-M at 1 µg/L

Model	χ^2 err%	Visual assessment	Statistical assessment	DT_{50}	DT_{90}
SFO	2.56	Intermediate	t<0.01	562	1870
FOMC	1.24	Good	α: 95th %ile C.I. does not include zero β: 90th and 95th %ile C.I.s includes zero	>10,000	>10,000
DFOP	1.03	Intermediate	k1: p 0.01 k2: p 0.50 K1 90th and 95th %ile C.Is do not include zero K2 90th and 95th %ile C.Is do include zero	>10,000	>10,000
HS	1.1	Good	k1: p <0.01 k2: p 0.36 K1 90th and 95th %ile C.Is do not include zero K2 90th and 95th %ile C.Is do include zero (tb =12.9)	5850	>10,000

Figure B.8.2.2.2-2 Applicant's kinetic assessment of the aerobic mineralisation of napropamide-M at 1 µg/L

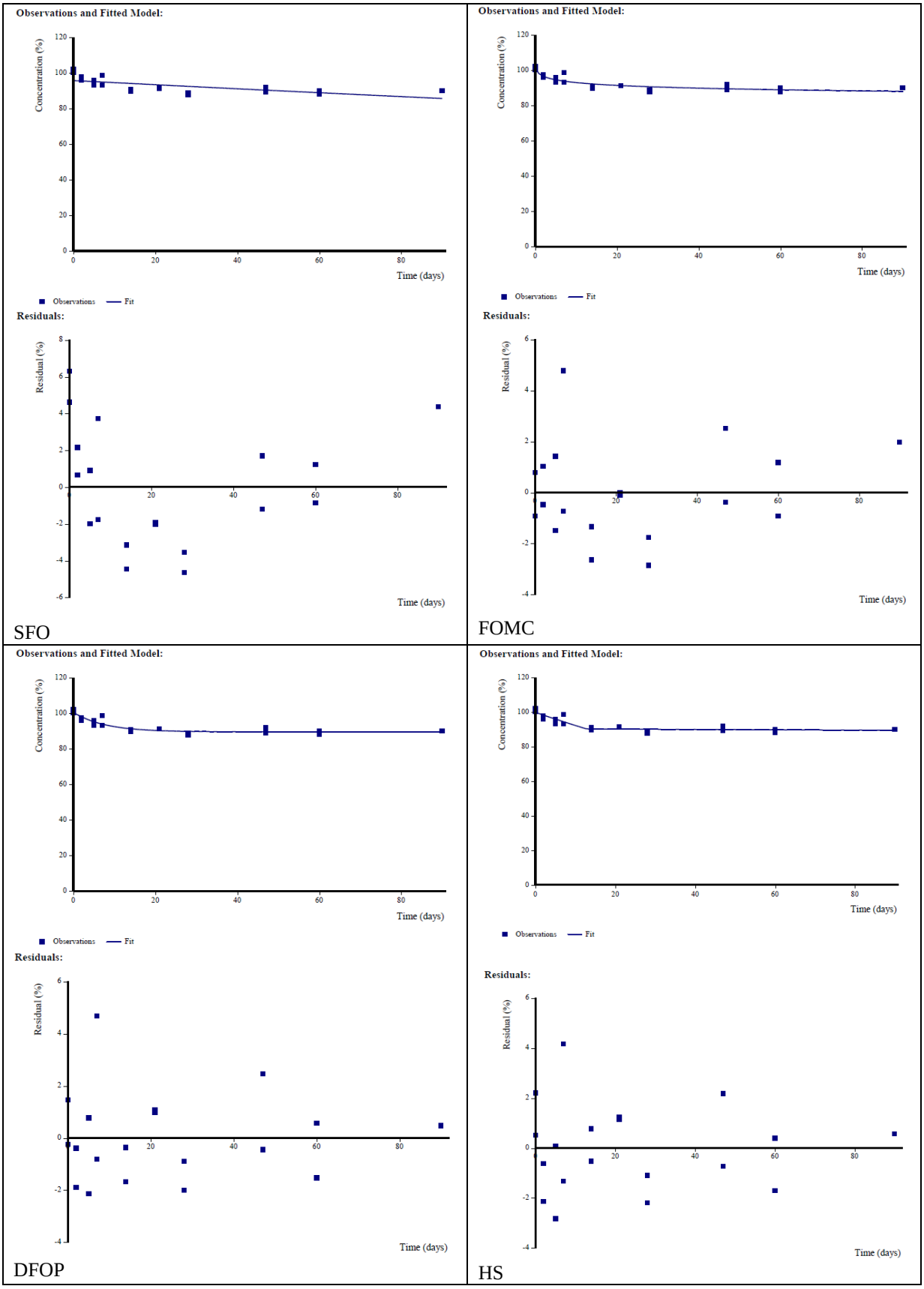


Table B.8.2.2.2-12 RMS' kinetic assessment of the aerobic mineralisation of napropamide-M at 5 µg/L

Model	χ^2 err%	Visual assessment	Statistical assessment	DT_{50}	DT_{90}
SFO	4.02	Good	t>0.2	2320	7690
FOMC	3.47	Good	Both α and β 90th and 95th %ile C.I. include zero	>10,000	>10,000

Figure B.8.2.2.2-3 RMS' kinetic assessment of the aerobic mineralisation of napropamide-M at 5 µg/L

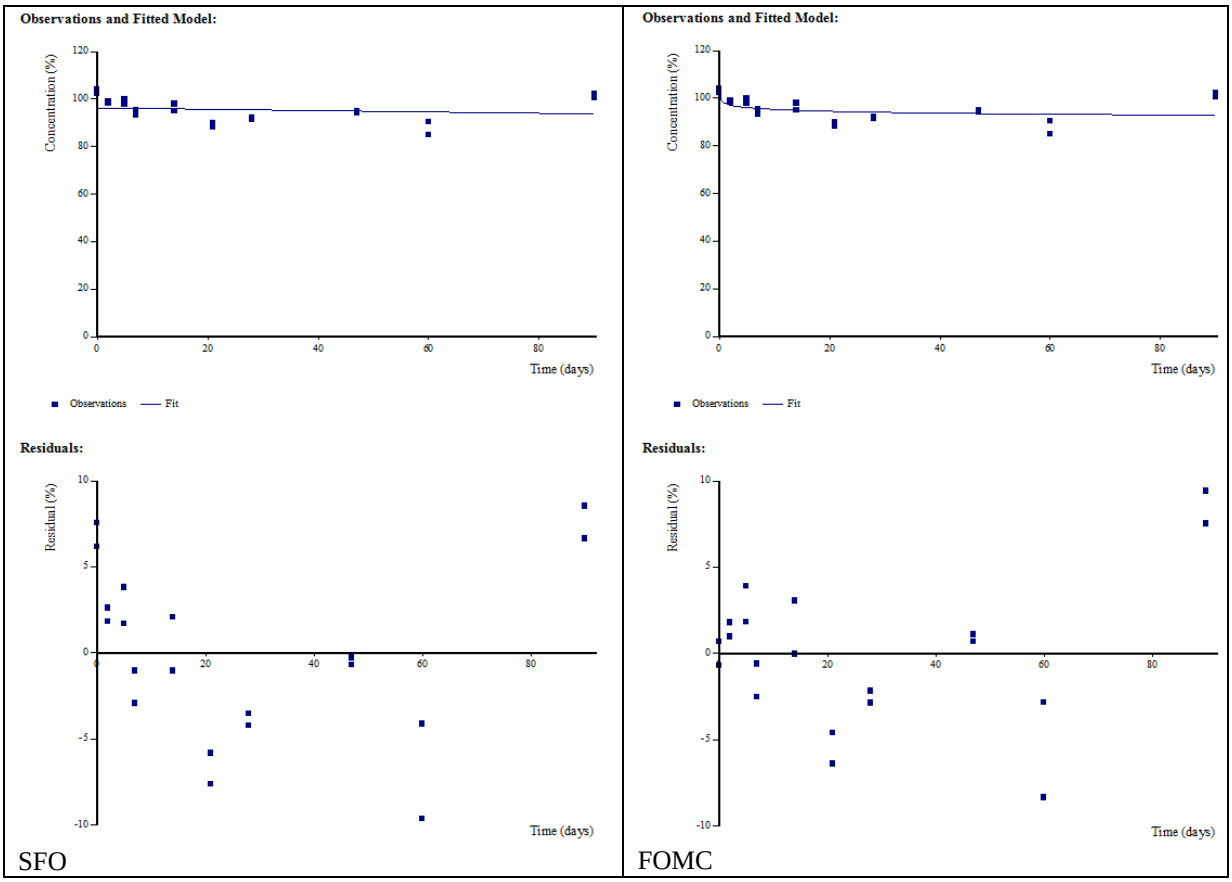
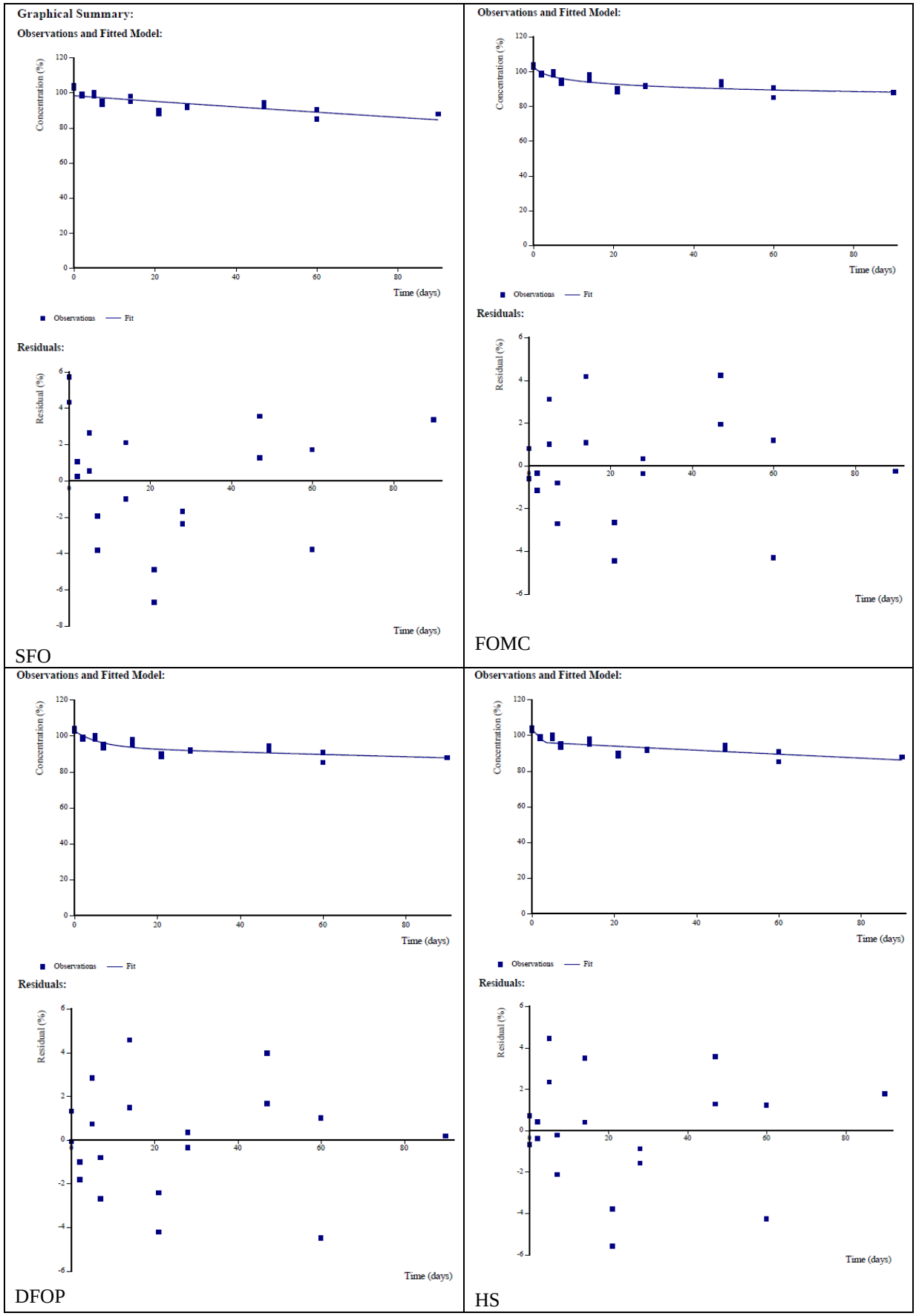


Table B.8.2.2.2-13 Applicant's kinetic assessment of the aerobic mineralisation of napropamide-M at 5 µg/L

Model	χ^2 err%	Visual assessment	Statistical assessment	DT_{50}	DT_{90}
SFO	2.6	Intermediate	t<0.01	414	1380
FOMC	1.78	Good	α: 90th and 95th %ile C.I. do not include zero β: 90th and 95th %ile C.I. include zero	>10,000	>10,000
DFOP	1.89	Intermediate	K1 90th and 95th %ile C.I. include zero K2 90th and 95th %ile C.I. include zero	848	3130
HS	2.15	Good	K1 90th and 95th %ile C.I. include zero K2 90th and 95th %ile C.I. do not include zero (tb=3.202)	503	1800

Figure B.8.2.2.2-4 Applicant's kinetic assessment of the aerobic mineralisation of napropamide-M at 5 µg/L



Conclusion

There were very low levels of degradation (<20%) throughout the aerobic mineralisation study duration in either concentration. Therefore, it was difficult to establish a true pattern of decline and appropriate kinetics. The half-life values calculated are extrapolated well beyond the 90 day study duration and so are uncertain. Table B.8.2.2.2-14 below summarises the persistence endpoints for the aerobic mineralisation of napropamide-M in surface water. The RMS calculated DT_{50} values were 1840 and 2320 days for the two datasets. Although the Applicant selected HS as best fit, due to the lack of degradation, clear decline pattern, and therefore poor statistical fit, the RMS has for simplicity reported the SFO values as the persistence endpoint.

Table B.8.2.2.2-14 Summary of RMS' and Applicant's persistence endpoints for the aerobic mineralisation of napropamide-M

	Dataset	Model	χ^2 err%	DT_{50}	DT_{90}
RMS' values	1 µg/L	SFO	3.36	1840	6120
	5 µg/L	SFO	4.02	2320	7690
Applicant's values	1 µg/L	HS	1.10	5850	>10,000
	5 µg/L	HS	2.15	503	1800

B.8.2.2.3 **Water sedimentation**

Study author	Ahmad, S. (2015c)
Study title	Aerobic transformation in sediment/water systems for [naphthyl-1-^{14}C] napropamide-M
Study date	04/05/2015
Annex point	CA 7.2.2.3/01
Previous evaluation	New active substance, no previous studies submitted.

Study Design

The distribution and degradation of napropamide-M was studied in natural water sediment systems in accordance with OECD guideline 308 *Aerobic and Anaerobic Transformation in Aquatic Sediment Systems (2002).* The study was performed to US EPA GLP standards with the exception of the one deviation: reference standards, with the exception of napropamide-M, were non-GLP characterised. Since no major metabolites are formed in this study, accurate identification is not considered to be critical in this case.

Two freshwater sediments were sampled from North Carolina, USA. Sandy loam and clay loam sediments were sampled with their associated waters from Cary and Lucana respectively. The sandy loam had a lower organic carbon content (3.9%) and a combined silt and clay fraction <50% (coarse texture), whereas the clay loam had a higher organic carbon content (5.4%) and a greater silt and clay fraction >50% (fine texture) in accordance to the OECD guideline. The RMS notes that the organic carbon content of the two sediments tested are fairly similar, being 3.9 % and 5.4 % and that no sediment with low organic carbon content (0.5%-2.5%) as recommended in the OECD guideline was included. Tables B.8.2.2.3-1 and B.8.2.2.3-2 below presents the physicochemical characteristics of the test sediments and associated test water respectively. The RMS notes the similarity of the two test systems regarding the pH values of both the sediments and the associated waters. The samples were stored at 4 °C until use. Although the duration of storage was not reported, table B.8.2.2.3-1 shows that the microbial biomass increased throughout the study duration in both test systems, indicating a viable population. The respective pesticide histories of the sampling sites were not reported.

Table B.8.2.2.3-1 Physicochemical properties of the test sediments

Parameter	Sandy Loam	Clay Loam
Geographic Location	500 yards west of the intersection of Swift Creek and Kildaire Farm Road, Cary, North Carolina 27518, U.S.A.	7209 Gourd Branch Road, Lucana, North Carolina 27851, U.S.A.
USDA Texture Class	Sandy Loam	Clay Loam
Sand (%)	65	23
Silt (%)	28	44
Clay (%)	7	33
A.D.A.S. Texture Class	Sandy Loam	Clay Loam
Sand (%)	61	21
Silt (%)	32	46
Clay (%)	7	33
pH (in 1:1 Sediment:WaterRatio)	5.7	5.8
Organic Carbon (%)	3.9	5.4
Initial Sediment Biomass (µg Organic Carbon/g Sediment)	323.0	286.1
Final Sediment Biomass (µg Organic Carbon/g Sediment)	841.8	475.8
Cation Exchange Capacity (mEq/100g)	5.2	8.2
Nitrogen, Total (% w/w)	0.13	0.27
Phosphorus, Total (ppm)	12	6.0
Moisture Content at 1/3 bar (%)	20	31.9

Table B.8.2.2.3-2 Physicochemical properties of the associated test waters

Parameter	Associated water of sandy loam	Associated water of clay loam
pH	7.4	7.3
Hardness (mg/L $CaCO_3$)	40	26
Electrical conductivity (µS/ cm)	0.15	0.19
Dissolved oxygen (mg/ L)	9.6	9.4
Sodium, total (mg/ L)	9.2	13
Sodium Adsorption Ratio (SAR)	0.63	1.07
Total dissolved solids (mg/ L)	116	106

Dosing solution was prepared by dissolving 37.3 mg test substance (9.785 mg [naphthyl-1-^{14}C] napropamide-M + 27.50 mg non-radiolabelled napropamide-M) in 60 mL methanol: water (1:3, v:v) to give a concentration of 0.746 mg/ mL. A volume of 1.2 mL dosing solution was applied drop wise to each test sample ensuring that the sediment was not disturbed. The application rate was based on a direct overspray of 2250 g a.s./ ha. An equal volume of blank application solution (methanol: water, 1:3, v:v) was applied to control vessels.

Sediment potions (50 g dry weight equivalent) were dispensed into incubation vessels and their associated waters were added to achieve sediment: water ratios of between 1:3 to 1:4. Water height in vessels was reported as between 3.5 to 4.5 cm. The RMS notes that the ratios may have been determined gravimetrically, with water

weighed out based on the weight of the sediment. Alternatively, water may have been added based on the height of the sediment. It was not specified in the study report which method was used. Overall, the RMS accepts that a ratio range has been reported rather than a specific single ratio.

Test vessels were acclimatised under test conditions (20 ± 2 °C, in the dark) for one week as part of a moist air flow-through system. The pH, redox and dissolved oxygen were monitored during this period. Seven test incubation vessels plus one contingency were prepared in duplicate. Seven additional control vessels were prepared for each sediment-water system to allow for measurement of oxygen, pH and redox potential. A series of traps included firstly a safety trap followed by those containing ethylene glycol, 0.1 M sulphuric acid and 1M potassium hydroxide to trap volatile organics and CO_2. No trapping media were associated with zero day samples. Water levels were marked and checked continuously throughout study. No significant water losses were reported. The test facility stated that there were several minor deviations from the intended test temperature, however no details were reported. They believe the integrity of the study to be unaffected. Considering that there was little degradation of napropamide-M in the water sediment systems, the RMS has accepted that these deviations in temperature are unlikely to have materially affected the study overall.

Samples were drawn in duplicate at 0, 7, 14, 30, 60, 90, and 100 days and allowed to equilibrate for one hour with the exception of the zero day samples which were analysed immediately. Sediment and surface water phases of each sample were separated by decanting the surface water into a measuring cylinder, before individual analysis of each phase. The volume of surface water was measured and triplicate aliquots were analysed via LSC. Concentrated water samples were analysed by HPLC-RAM-MS. The sediment phase was extracted three times with acetonitrile, once with acetonitrile: water (1:1; v/v) and once with methanol: 1N hydrochloric acid (1:1; v/v). Each extract was removed by centrifugation before analysis via LSC and HPLC-RAM-MS.

Water and sediment extracts from 0, 60 and 100 DAT were analysed for the identification of the D- and L-isomers of napropamide-M by chiral HPLC.

The radioactivity associated with unextracted residues was quantified by combustion with LSC. Soxhlet extraction was performed for 100 day samples. Samples of 30 g air dried sediment were extracted overnight with 0.01 M HCl, followed by overnight extraction with 0.5 N NaOH and triplicate aliquot analysis using LSC.

Results and Discussion

The mass balance was within the acceptable range for a radiolabelled study, being between 90 and 110 % AR for all samples, with the exception of one sample for the sandy loam system at 90 days with mass balance of 89.3 % AR and one sample for the same system at 100 days with mass balance of 89.5 % AR. Overall, the RMS considers the mass balance data to be within an acceptable range. The mass balances are reported for the sandy loam and clay loam water sediment test systems in tables B.8.2.2.3-3 and B.8.2.2.3-4 respectively.

The radioactivity in the surface water of the sandy loam water-sediment system declined from a mean value of 95.8% AR at zero-time to 10.7% AR after 100 days. Mean total extractable radioactivity in the sediment increased from 2.3% AR at day 0 to 77.1% AR after 100 days. Unextracted residues increased to a maximum mean of 6.0% AR at 60 days before declining slightly to 4.1% AR at study termination. Carbon dioxide accounted for a maximum mean of 0.1% AR at day 30.

The radioactivity in the surface water of the clay loam water-sediment system declined from 95.1% AR at zero-time to 8.2% AR at 100 days. Mean total extractable radioactivity in the sediment increased from 2.6% AR at day 0 to 76.9% AR at the study end. Unextracted residues increased to a maximum of 12.2% AR at 60 days before declining slightly to 5.3% AR at study termination. The RMS notes that given the rapid partitioning of applied radioactivity to the sediment phase, an additional sampling interval before 7 days may have been beneficial for this study.

Table B.8.2.2.3-3 Mass balance of radioactivity from sandy loam water- sediment system expressed as percentage of applied radioactivity (%AR)

Description		Sampling Interval (Days)						
		0	7	14	30	60	90	100
$^{14}CO_2$ volatiles	R1	N/A	<0.1	<0.1	0.22	<0.1	<0.1	<0.1
	R2		<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	mean		<0.1	<0.1	0.11	<0.1	<0.1	<0.1
Water	R1	95.91	33.63	21.01	10.14	7.15	10.22	11.68
	R2	95.70	27.63	29.63	17.50	11.60	11.89	9.63
	mean	95.81	30.63	25.32	13.82	9.38	11.06	10.66
Sediment extracts	R1	2.15	62.59	74.90	86.03	78.71	72.78	74.62
	R2	2.43	69.76	67.92	74.52	75.05	80.47	79.49
	mean	2.29	66.18	71.41	80.28	76.88	76.63	77.06
Unextracted residue	R1	0.06	0.75	1.51	2.35	6.47	6.29	3.24
	R2	0.04	1.19	1.46	2.62	5.50	2.97	4.95
	mean	0.05	0.97	1.49	2.49	5.99	4.63	4.10
Mass balance	R1	98.12	96.99	97.42	98.75	92.33	89.30	89.54
	R2	98.17	98.58	99.02	94.64	92.15	95.34	94.07
	mean	98.15	97.79	98.22	96.70	92.24	92.32	91.81

Table B.8.2.2.3-4 Mass balance of radioactivity from clay loam water- sediment system expressed as percentage of applied radioactivity (%AR)

Description		Sampling Interval (Days)						
		0	7	14	30	60	90	100
$^{14}CO_2$ volatiles	R1	N/A	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	R2		<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
	mean		<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Water	R1	95.41	39.25	21.74	15.81	10.38	8.53	5.93
	R2	94.78	43.75	38.94	19.80	13.49	13.08	10.52
	mean	95.10	41.50	30.34	17.81	11.94	10.84	8.23
Sediment extracts	R1	2.33	54.60	71.50	72.46	74.89	71.13	76.76
	R2	2.86	49.30	59.85	69.24	70.34	72.57	76.96
	mean	2.60	51.95	65.68	70.85	72.62	71.85	76.86
Unextracted residue	R1	0.14	1.06	2.26	6.53	9.67	10.69	7.60
	R2	0.21	5.94	1.97	5.16	14.76	8.09	2.97
	mean	0.18	3.50	2.12	5.85	12.22	9.39	5.29
Mass balance	R1	97.88	94.92	95.50	94.80	94.94	90.36	90.29
	R2	97.85	98.98	100.76	94.20	98.62	93.77	90.45
	mean	97.87	96.95	98.13	94.50	96.78	92.04	90.37

The distribution of radioactivity between the parent compound, napropamide-M, and its metabolites are presented in tables B.8.2.2.3-5 and B.8.2.2.3-6 for the two water-sediment systems. The highest amount of napropamide-M present in the water phase of the sandy loam system declined from 95.91% (mean 95.81%) AR at 0 day to 9.20% (mean 6.11%) AR at 100 day. The amount of parent associated with the sediment phase rose to 85.20% (mean 79.43%) AR at 30 day, before decreasing to 74.32% (mean 69.04%) AR at study termination. No major transformation products were detected in the surface water or the sediment extracts. Two minor metabolites were identified. DE-napropamide was present <1% AR in the water phase throughout the study, except in one replicate sample at 100 days, which was 7.91% AR. This made the overall system mean for DE-napropamide 5.09% AR at study end. The highest replicate value of DE-napropamide in sediment was 1.85% AR at study termination. The highest single replicate values of NOPA in the water and sediment phases were 2.19% AR (90 days) and 5.04% AR (100 days) respectively. This was the first detection in the sediment phase at the study end which may indicate a potential to increase. Several minor unknown degradation products were also detected, mostly associated with the sediment phase, however the highest %AR associated with a single replicate sample was 5.81% at the study end. The Applicant states that individually none of these unknowns exceeded 8%

AR. The RMS believes it is unlikely that a single unknown degradation product could be a major metabolite in the sandy loam test system.

Table B.8.2.2.3-5 Distribution of percentage applied radioactivity (%AR) between napropamide-M and its metabolites in the sandy loam water-sediment system

Sampling Interval	Rep	Water Phase				Sediment phase				System			
		Parent	DeNap	NOPA	Other*	Parent	DeNap	NOPA	Other *	Parent	DeNap	NOPA	Other *
0	1	95.91	0.00	0.00	0.00	2.15	0.00	0.00	0.00	98.06	0.00	0.00	0.00
	2	95.70	0.00	0.00	0.00	2.43	0.00	0.00	0.00	98.13	0.00	0.00	0.00
	Mean	**95.81**	0.00	0.00	0.00	2.29	0.00	0.00	0.00	98.10	0.00	0.00	0.00
7	1	33.33	0.00	0.30	0.00	62.47	0.12	0.00	0.00	95.81	0.12	0.30	0.00
	2	27.63	0.00	0.00	0.00	69.27	0.49	0.00	0.00	96.90	0.49	0.00	0.00
	Mean	30.48	0.00	0.15	0.00	65.87	0.30	0.00	0.00	96.35	0.30	0.15	0.00
14	1	20.52	0.15	0.34	0.00	74.63	0.27	0.00	0.00	95.15	0.42	0.34	0.00
	2	29.63	0.00	0.00	0.00	67.69	0.23	0.00	0.00	97.32	0.23	0.00	0.00
	Mean	25.07	0.08	0.17	0.00	71.16	0.25	0.00	0.00	96.23	0.33	0.17	0.00
30	1	9.43	0.20	0.30	0.21	85.20	0.83	0.00	0.00	94.62	1.04	0.30	0.21
	2	16.77	0.73	0.00	0.00	73.67	0.85	0.00	0.00	90.44	1.58	0.00	0.00
	Mean	13.10	0.47	0.15	0.11	**79.43**	0.84	0.00	0.00	92.53	1.31	0.15	0.11
60	1	6.00	0.57	0.58	0.00	77.69	1.02	0.00	0.00	83.69	1.58	0.58	0.00
	2	10.15	0.92	0.53	0.00	74.24	0.81	0.00	0.00	84.39	1.73	0.53	0.00
	Mean	8.07	0.75	0.56	0.00	75.97	0.91	0.00	0.00	84.04	1.66	0.56	0.00
90	1	7.62	0.41	2.19	0.00	71.88	0.90	0.00	0.00	79.51	1.31	2.19	0.00
	2	9.03	0.37	0.54	1.94	80.06	0.41	0.00	0.00	89.09	0.78	0.54	1.94
	Mean	8.33	0.39	**1.37**	**0.97**	75.97	0.65	0.00	0.00	84.30	1.04	1.37	0.97
100	1	3.02	7.91	0.76	0.00	63.77	0.00	5.04	5.81	66.79	7.91	5.80	5.81
	2	9.20	0.43	0.00	0.00	74.32	1.85	2.36	0.96	83.52	2.28	2.36	0.96
	Mean	6.11	**4.17**	0.38	0.00	69.04	**0.93**	**3.70**	**3.38**	75.15	**5.09**	**4.08**	**3.38**

*= sum of up to 5 unknowns.
Highest mean values are shown in bold

For the clay loam test system (table B.8.2.2.3-6), the highest amount of napropamide-M present in the water phase of the clay loam system declined from 95.41% (mean 95.10%) AR at the start of the study to 9.57% (mean 7.53%) AR at 100 days. The amount of parent in sediment rose to 74.56% (mean 60.65%) AR at day 60 before decreasing to 68.75% (mean 68.83%) AR at 100 days. No major transformation products were detected in the surface water or the sediment extracts. The minor metabolite DE-napropamide was detected <1% AR for all water samples and the highest replicate value in sediment was 2.83% AR at day 60. The highest replicate values of NOPA in water and sediment phases were 1.84% AR (60 day) and 6.33% AR (day 14) respectively, but this metabolite did not exceed 5 % mean AR at two consecutive time points. Several minor unknown degradation products were also detected. The highest amount applied radioactivity for a single replicate associated with the collective sum of unknowns was 28.18% AR total system at day 60 (7.43% AR in water and 20.76% AR in sediment). The Applicant stated that individually none of the unknown degradation products exceeded 10% AR, but no supporting evidence was provided. The Applicant believes that the second replicate from the day 60 samples may have been contaminated, considers the result an outlier and has consequently excluded this value from half-life calculations. However, no supporting evidence has been provided to explicitly show if the samples were contaminated.

Table B.8.2.2.3-6 Distribution of percentage applied radioactivity between napropamide-M and its metabolites in the clay loam water-sediment system

Sampling Interval	Rep	Water Phase				Sediment phase				System			
		Parent	DE-Nap	NOPA	Other *	Parent	DE-Nap	NOPA	Other*	Parent	DE-Nap	NOPA	Other*
0	1	95.41	0.00	0.00	0.00	2.33	0.00	0.00	0.00	97.74	0.00	0.00	0.00
	2	94.78	0.00	0.00	0.00	2.86	0.00	0.00	0.00	97.64	0.00	0.00	0.00
	Mean	**95.10**	0.00	0.00	0.00	2.60	0.00	0.00	0.00	97.69	0.00	0.00	0.00
7	1	39.25	0.00	0.00	0.00	54.60	0.00	0.00	0.00	93.85	0.00	0.00	0.00
	2	43.75	0.00	0.00	0.00	49.30	0.00	0.00	0.00	93.05	0.00	0.00	0.00
	Mean	41.50	0.00	0.00	0.00	51.95	0.00	0.00	0.00	93.45	0.00	0.00	0.00
14	1	21.74	0.00	0.00	0.00	61.21	1.22	6.33	2.74	82.95	1.22	6.33	2.74
	2	38.94	0.00	0.00	0.00	59.85	0.00	0.00	0.00	98.79	0.00	0.00	0.00
	Mean	30.34	0.00	0.00	0.00	60.53	0.61	**3.16**	1.37	90.87	0.61	**3.16**	1.37
30	1	15.81	0.00	0.00	0.00	72.01	0.45	0.00	0.00	87.82	0.45	0.00	0.00
	2	19.50	0.00	0.30	0.00	67.43	0.89	0.00	0.92	86.93	0.89	0.30	0.92
	Mean	17.65	0.00	0.15	0.00	69.72	0.67	0.00	0.46	87.37	0.67	0.15	0.46
60	1	9.94	0.44	0.00	0.00	74.56	0.19	0.14	0.00	84.50	0.63	0.14	0.00
	2 ***	3.62	0.60	1.84	7.43	46.74**	2.83	0.00	20.76	50.36**	3.44	1.84	28.18
	Mean	6.78	**0.52**	**0.92**	**3.71**	60.65	**1.51**	0.07	**10.38**	67.43	**2.03**	0.99	**14.09**
90	1	8.25	0.28	0.00	0.00	69.76	1.37	0.00	0.00	78.01	1.65	0.00	0.00
	2	11.95	0.67	0.46	0.00	71.32	0.00	1.25	0.00	83.28	0.67	1.71	0.00
	Mean	10.10	0.48	0.23	0.00	**70.54**	0.68	0.62	0.00	80.64	1.16	0.85	0.00
100	1	5.50	0.35	0.08	0.00	68.75	0.00	0.28	0.00	74.26	0.35	0.36	0.00
	2	9.57	0.57	0.12	0.26	68.90	1.69	0.22	0.00	78.47	2.25	0.34	0.26
	Mean	7.53	0.46	0.10	0.13	68.83	0.84	0.25	0.00	76.36	1.30	0.35	0.13

*= sum of up to 5 unknowns.
**= Applicant considers these values to be outliers and excluded them from degradation calculations.
*** = The Applicant believes that the sediment extract of Rep 2 is not consistent with the rest of the data and proposes possible contamination as a reason for inconsistency.
Highest mean values are shown in bold

Chiral analysis of water and sediment extracts from 0, 60 and 100 day samples indicated that napropamide-M remained in the D-form with no indication of isomerisation to the L-form. The measurements of test conditions in control samples throughout the study are reported in table B.8.2.2.3-7 and show that aerobic conditions were maintained throughout.

Table B.8.2.2.3-7 Measurements of pH, dissolved oxygen and redox potential the sediment-water test systems

Sampling interval (days)	Sandy loam control samples			Clay loam control samples		
	pH	Oxygen (%)	Redox potential (mV)	pH	Oxygen (%)	Redox potential (mV)
0	6.89	85	216	7.35	86	250
7	6.86	80	213	7.36	84	243
14	6.83	80	139	7.33	87	210
30	6.62	79	216	6.80	89	197
60	6.64	81	268	6.25	77.9	297
90	6.10	75	300.3	6.28	95.9	325.9
100	6.59	60.1	318.1	6.87	75.2	286

Following extraction, the organic matter in the 100 day samples for both test sediments was fractionated into fulvic and humic acid and quantified. The results are reported below in table B.8.2.2.3-8.

Table B.8.2.2.3-8 Organic matter fractionation of day 100 samples

Sediment	Percentage applied radioactivity characterised as :	
	Fulvic acid	Humic acid
Sandy loam	10.2	3.9
Clay loam	7.9	0.9

The whole system DT_{50} and DT_{90} values calculated by the Applicant by regression analysis of log transformed data were reported as 288.8 days and 959.4 days for the sandy loam system, and 330.1 and 1096.5 days for the clay loam system respectively. The kinetic evaluation according to FOCUS guidance was undertaken separately. The study showed that napropamide-M degraded slowly in aerobic water-sediment systems under laboratory conditions. Partitioning of the parent compound to the sediment phase was rapid, yet degradation overall was slow with little formation of minor metabolites and several minor unknowns.

Kinetic assessment of degradation in water sediment systems

Study author	Croucher, A. & Ford, S. (2015g)
Study title	Napropamide-M: kinetic evaluation of water sediment study
Study date	August 2015
Annex point	CA 7.2.2.3/02
Previous evaluation	New active substance, no previous studies submitted.

The fate and behaviour of radiolabelled [napthyl-1-^{14}C] napropamide-M was studied in two aerobic water sediment systems under laboratory conditions (Ahmad, 2015c). The original report calculated the degradation rate of napropamide-M in the whole system (water and sediment fractions combined) using linear regression of log transformed data. A separate evaluation was undertaken which recalculated the degradation kinetics in accordance with FOCUS (2006) and EFSA (2014) guidance. The assessment was conducted at levels P-I and P-II using the modelling software packages CAKE v3.1 and ModelMaker v4 respectively. Both persistence trigger endpoints and modelling endpoints were generated for napropamide-M in aquatic sediment systems.

Persistence endpoints

Level P-I evaluation

The RMS has independently performed the kinetic evaluation for napropamide-M in water sediment systems following the FOCUS (2014) decision flow chart for level P-I. Trigger endpoints were derived from best fit kinetics and were not constrained to any model type. In the first instance, the data were directly fitted, un-weighted, with the complete data set and unconstrained initial concentration (M0). SFO and FOMC models were compared. The acceptability of kinetic fits was judged both visually and statistically (according to the χ^2 error and additionally t-test functions for SFO models or α and β parameter estimates for FOMC confidence intervals). If SFO provided a more acceptable visual and statistical fit then it was selected as best fit kinetics. If FOMC was more favourable, then other biphasic models were tested (DFOP and HS). The models were assessed visually, according to the χ^2 error and whether K1 and K2 parameter confidence intervals were significantly different from zero. The best fit model was then determined from the three biphasic models.

All models were run firstly using the OLS optimiser and secondly using the IRLS optimiser. With the exception of the HS model, the choice of optimiser made no difference to the visual or statistical parameters observed. All models presented in this report are generated using OLS except where it is explicitly stated otherwise.

The Applicant identified what they believe to be an outlier in the clay loam sediment compartment (day 60, second replicate). They proposed that the sample may have been contaminated and excluded it from all degradation calculations. The Applicant excluded the day 60 second replicate value when calculating the clay loam whole system half-lives but included it for water only compartment evaluations. The respective data sets used in the kinetic evaluation for the sandy loam and clay loam systems are presented below (tables B.8.2.2.3-9 and B.8.2.2.3-10). The RMS has repeated clay loam whole system kinetic evaluations with the full data set and with the day 60 second replicate removed for comparison. The Applicant did not perform degradation kinetics for the sediment compartment at level P-I due to the low levels of degradation observed. The RMS can confirm that kinetic evaluation for the sediment compartments of either system does not produce meaningful DT_{50} values within acceptable statistical parameters. Table B.8.2.2.3-11summarises the trigger endpoints derived from best fit kinetics at P-I for napropamide-M. The RMS accepts all persistence endpoints generated by the Applicant.

Table B.8.2.2.3-9 Degradation of napropamide-M in sandy loam water sediment system (expressed as % applied radioactivity)

Sampling interval (days)	Replicate	Water phase	Sediment	System
0	1	95.91	2.15	98.06
	2	95.70	2.43	98.13
	Mean	95.81	2.29	98.10
7	1	33.33	62.47	95.81
	2	27.63	69.27	96.90
	Mean	30.48	65.87	96.35
14	1	20.52	74.63	95.15
	2	29.63	67.69	97.32
	Mean	25.07	71.16	96.23
30	1	9.43	85.20	94.62
	2	16.77	73.67	90.44
	Mean	13.10	79.43	92.53
60	1	6.00	77.69	83.69
	2	10.15	74.24	84.39
	Mean	8.07	75.97	84.04
90	1	7.62	71.88	79.51
	2	9.03	80.06	89.09
	Mean	8.33	75.97	84.30
100	1	3.02	63.77	66.79
	2	9.20	74.32	83.52
	Mean	6.11	69.04	75.15

Table B.8.2.2.3-10 Degradation of napropamide-M in clay loam water sediment system (expressed as % applied radioactivity)

Sampling Interval (days)	Rep	Water phase	Sediment	System
0	1	95.41	2.33	97.74
	2	94.78	2.86	97.64
	Mean	95.10	2.60	97.69
7	1	39.25	54.60	93.85
	2	43.75	49.30	93.05
	Mean	41.50	51.95	93.45
14	1	21.74	61.21	82.95
	2	38.94	59.85	98.79
	Mean	30.34	60.53	90.87
30	1	15.81	72.01	87.82
	2	19.50	67.43	86.93
	Mean	17.65	69.72	87.37
60	1	9.94	74.56	84.50
	2	3.62	46.74*	50.36*
	Mean	6.78	60.65	67.43
90	1	8.25	69.76	78.01
	2	11.95	71.32	83.28
	Mean	10.10	70.54	80.64
100	1	5.50	68.75	74.26
	2	9.57	68.90	78.47
	Mean	7.53	68.83	76.36

*= Applicant identified sediment phase day 60 rep 2 as an outlier due to possible contamination and excluded it from half-life calculation.

Table B.8.2.2.3-11 Persistence endpoints for napropamide-M in water sediment systems at level P-I

Compartment	Sediment type	Kinetics	χ2 error %	DT_{50}	DT_{90}
Whole system	Sandy loam	SFO	1.9	301	1000
	Clay loam	SFO	1.43	333	1110
			Arithmetic mean	317.00	1055.00
			Geometric mean	316.60	1053.57
Water phase	Sandy loam	FOMC	4.87	2.96	57.4
	Clay loam	FOMC	5.24	5.53	68.9
			Arithmetic mean	4.25	63.15
			Geometric mean	4.05	62.89

Level P-I kinetic evaluation for deriving persistence endpoints for whole system $DegT_{50}$s

Table B.8.2.2.3-12 Kinetic evaluation of napropamide-M in sandy loam whole system level P-I

Model	χ2 error %	Visual assessment	Statistical assessment	$DegT_{50}$	$DegT_{90}$
SFO	1.9	good	p<0.001	301	1000
FOMC	2.07	good	Errors and t-test values could not be calculated	319	1530
	SFO and FOMC both gave good visual fits. Residual plots showed narrow even scattering and good prediction of replicate values. χ2 error % values were <15%. However, statistical parameters could not be calculated for FOMC, therefore SFO kinetics were selected as best fit.				

Figure B.8.2.2.3-1 Graphs and residual plots representing the kinetic evaluation of sandy loam whole system

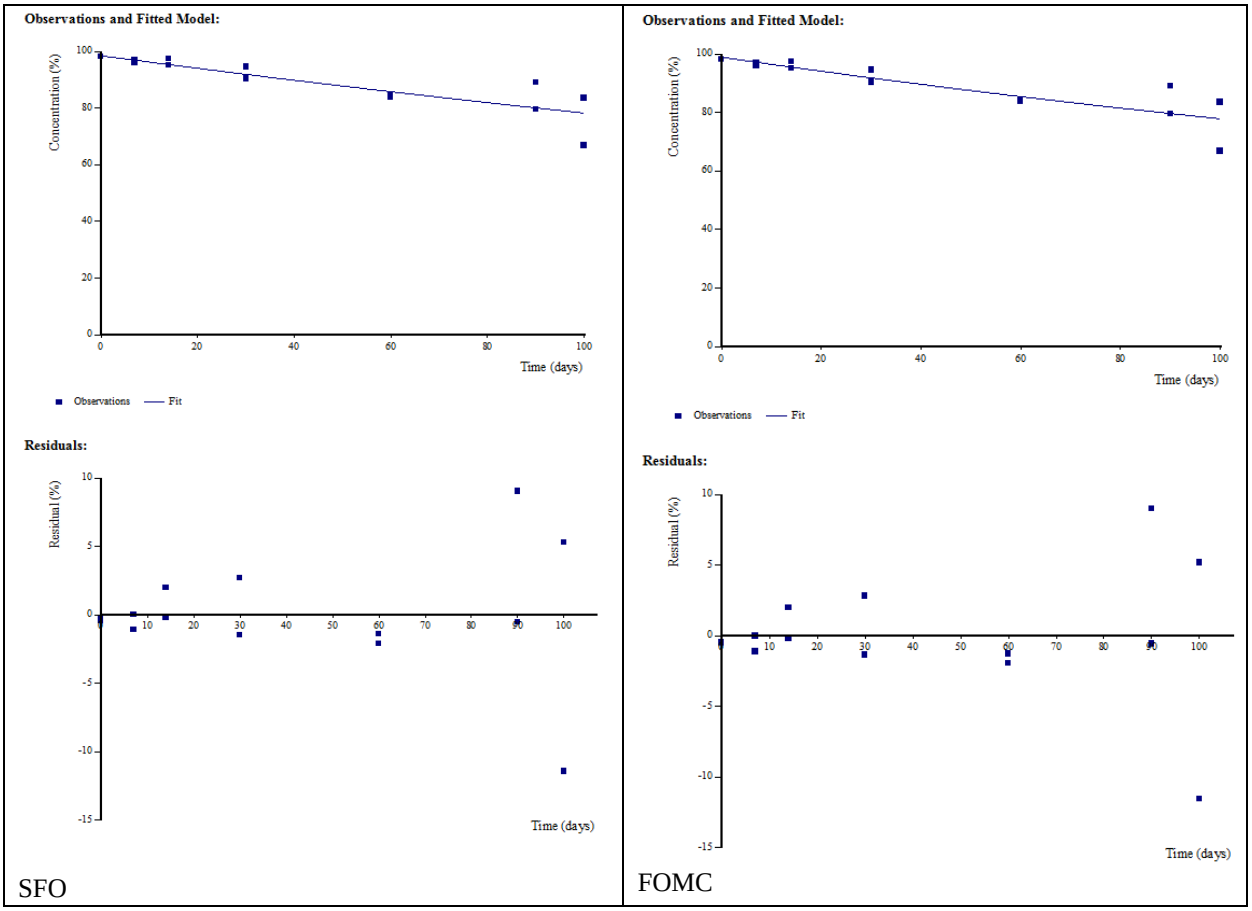


Table B.8.2.2.3-13 Kinetic evaluation of napropamide-M in clay loam whole system in CAKE- all data (including the day 60 rep II outlier) level P-I

Model	$\chi 2$ error %	Visual assessment	Statistical assessment	$DegT_{50}$	$DegT_{90}$
SFO	5.46	good	$p<0.01$	270	896
FOMC	5.02	good	α and β 90^{th} and 95^{th} %ile C.I.s include zero	3100	>10,000
	The RMS independently evaluated the clay loam whole system kinetics using the full dataset with the day 60 second replicate value included. Both models provide a good visual assessment, although this was noticeably not as good as the visual assessment with the constrained dataset (see table B.8.2.2.3-14 and corresponding figure B.8.2.2.3-3). The $\chi 2$ error % values are <15%. FOMC confidence intervals include zero but SFO is statistically acceptable. The RMS has accepted the Applicant's kinetic assessment (table B.8.2.2.2.3-14) with the outlier removed as it provides a longer, more worst-case $DegT_{50}$ (i.e. 333 days, SFO).				

Figure B.8.2.2.3-2 Graphs and residual plots representing the kinetic evaluation of clay loam whole system (including the day 60 rep II outlier) level P-I

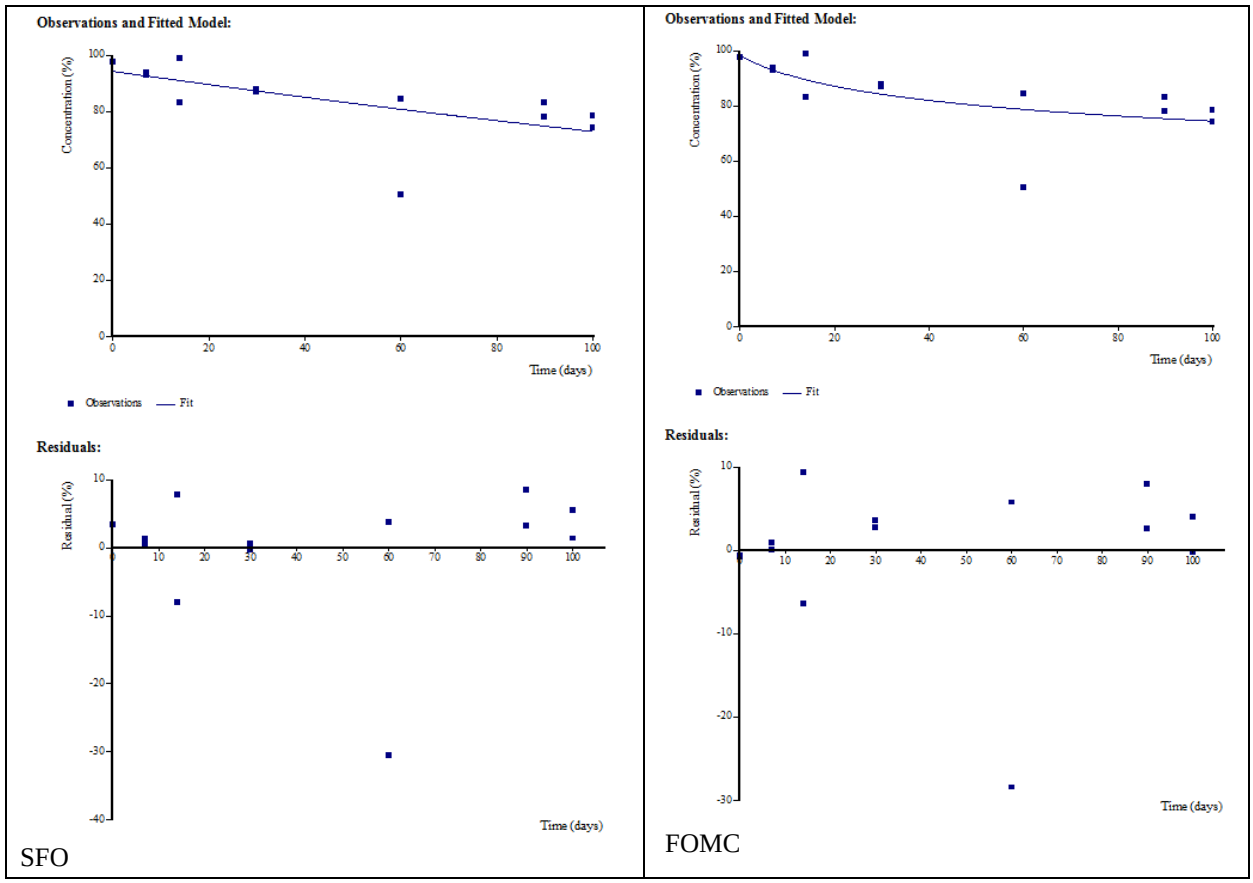
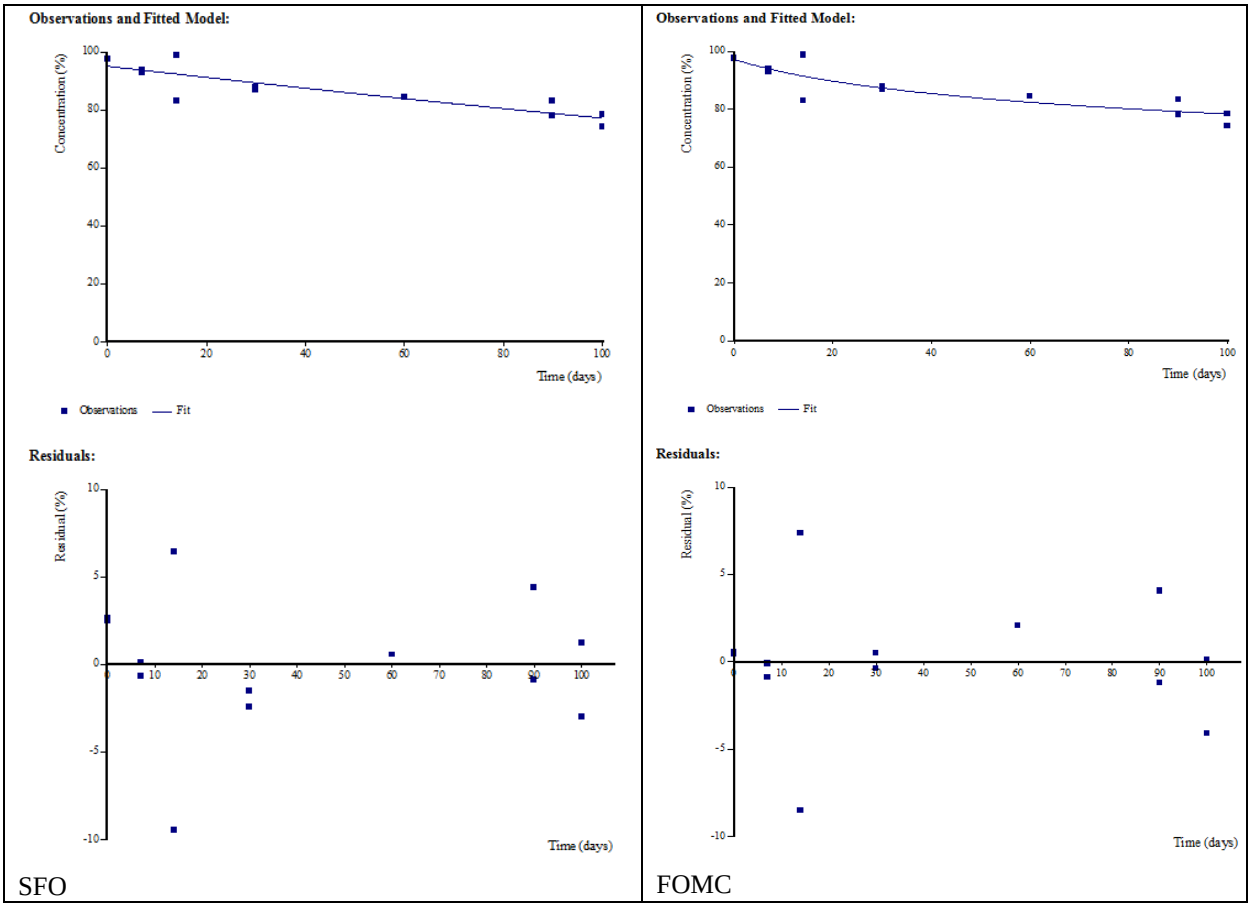


Table B.8.2.2.3-14 Kinetic evaluation of napropamide-M in clay loam whole system- constrained dataset (day 60 rep II outlier excluded) level P-I

Model	χ2 error %	Visual assessment	Statistical assessment	DegT50	DegT90
SFO	1.43	good	p<0.001	333	1110
FOMC	1.24	good	α and β 90th and 95th %ile C.I.s include zero	5040	>10,000
	Both models gave a good visual fit. Residual scattering was small and predicted replicate values well. Although the χ2 error % was slightly lower for FOMC, confidence intervals included zero. SFO kinetics selected as best fit. (The Applicant additionally tested other biphasic models due to the lower χ2 error % for FOMC but overall accepted SFO as the most appropriate fit. The RMS did not believe it necessary to independently replicate these other models, but has reported the Applicant's value below)				
DFOP	0.987	good	K1 and K2 90th and 95th %ile C.I.s include zero K2 90th and 95th %ile C.I.s do not include zero	371	1310
HS	0.977	good	K1 and K2 90th and 95th %ile C.I.s include zero K2 90th and 95th %ile C.I.s do not include zero	362	1270

Figure B.8.2.2.3-3 Graphs and residual plots representing the kinetic evaluation of clay loam whole system (excluding the day 60 rep II outlier) level P-I



Level P-I kinetic evaluation for deriving persistence endpoints for water compartment DT_{50}s

Table B.8.2.2.3-15 Kinetic evaluation of napropamide-M in sandy loam water compartment level P-I

Model	χ2 error %	Visual assessment	Statistical assessment	DT_{50}	DT_{90}
SFO	23.7	poor	p<001	5.75	19.1
FOMC	4.87	good	α C.I.s do not include zero β 90th %ile C.I. does not include zero, 95th %ile C.I does	2.96	57.4
	SFO gave a poor visual fit and χ2 error % >15%. The residual plot showed systematic under-prediction of the final five sampling intervals, indicating a biphasic degradation pattern. FOMC gave a good prediction of all time-points. It was more statistically favourable and so other biphasic models were tested.				
DFOP	7.3	good	K1 and K2 90th and 95th %ile C.I.s do not include zero	3.45	61.6
HS	16.8 (7.62)	good	K1 90th and 95th %ile C.I. s do not include zero K2 90th and 95th %ile C.I.s include zero	5.38 (4.24)	60.3 (60.8)
	Both DFOP and HS provided good visual fits. The HS model run using IRLS as the optimiser matches the Applicant's and provided a slightly better visual fit and χ2 error %. However, neither model offered any visual or statistical improvement over the FOMC which was selected as the best fit kinetics to represent the degradation in the sandy loam water compartment.				

Applicant results in parenthesis. Results vary for the HS model due to the Applicant's use of the IRLS optimiser. Their K1 and K2 90th and 95th %ile C.I.s did not include zero.

Figure B.8.2.2.3-4 Graphs and residual plots representing the kinetic evaluation of the sandy loam water compartment level P-I

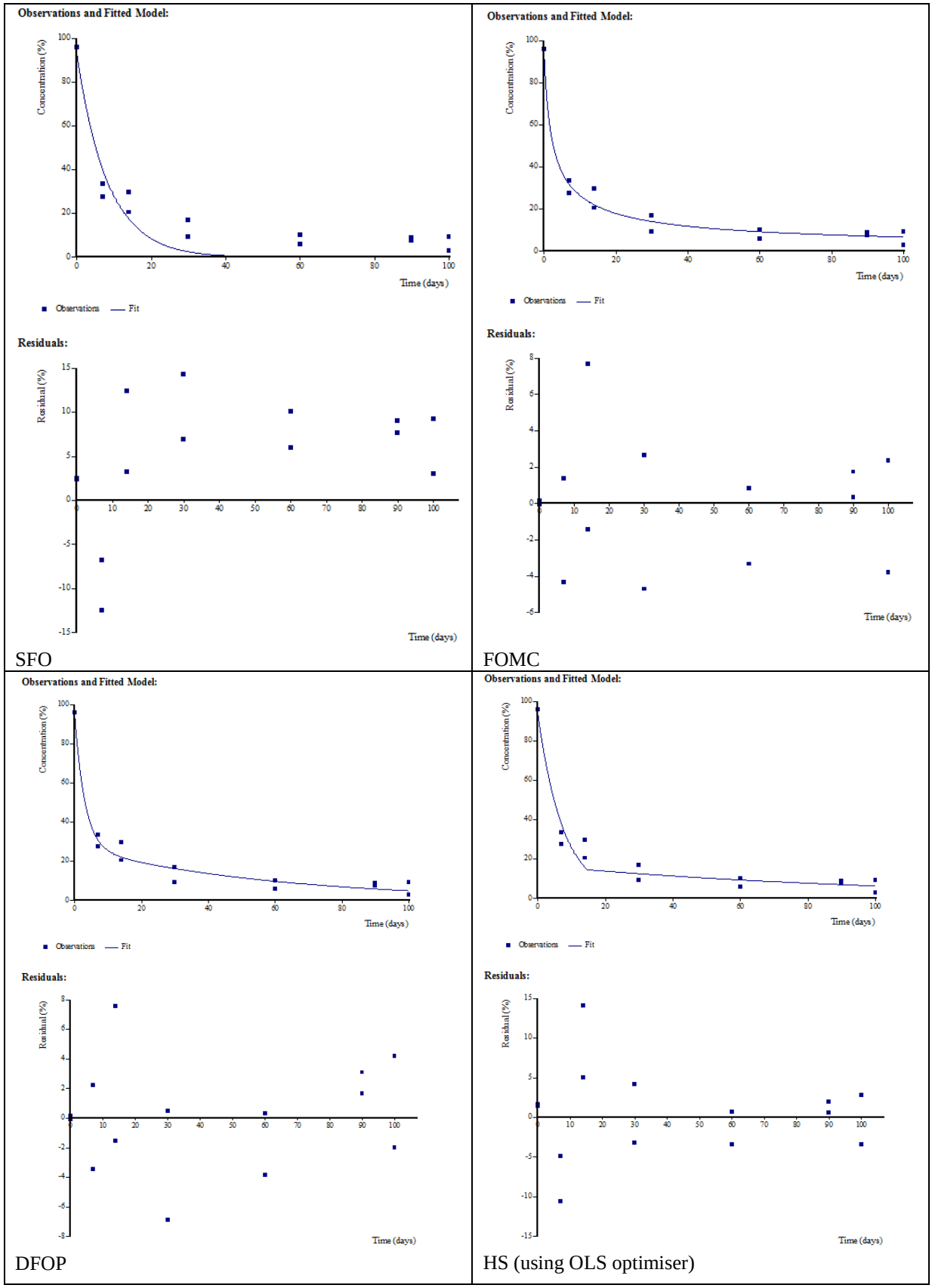
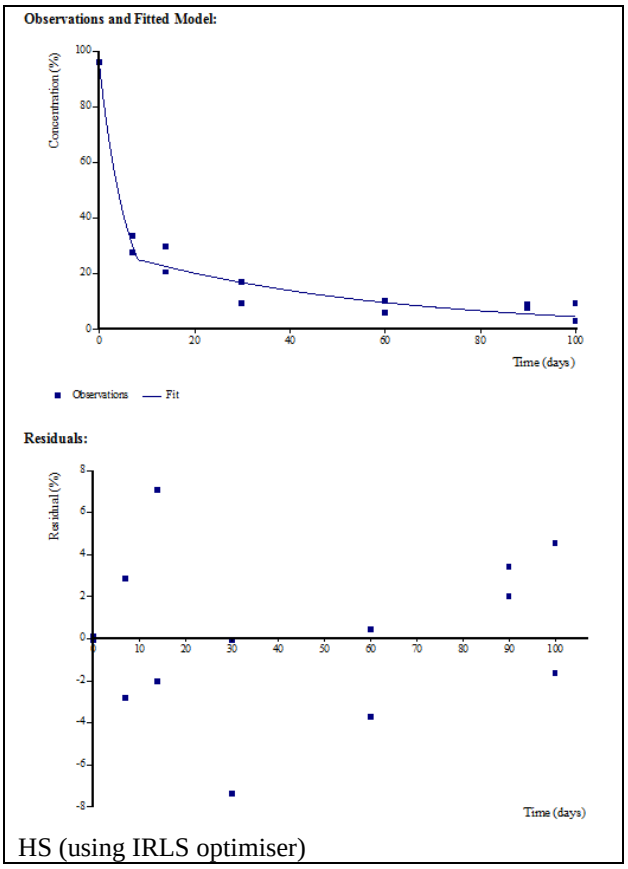


Figure B.8.2.2.3-4 (continued) Graphs and residual plots representing the kinetic evaluation of the sandy loam water compartment level P-I



HS (using IRLS optimiser)

Table B.8.2.2.3-16 Kinetic evaluation of napropamide-M in clay loam water compartment level P-I

Model	χ2 error %	Visual assessment	Statistical assessment	DT_{50}	DT_{90}
SFO	20.3	poor	p<0.01	8.3	27.6
FOMC	5.24	good	α and β C.I.s do not include zero	5.53	68.9
	SFO gave a poor visual fit and χ2 error % >15%. The residual plot showed systematic under-prediction of later sampling intervals, indicating a biphasic degradation pattern. FOMC gave a good prediction of all time-points. It was more statistically favourable and so other biphasic models were tested.				
DFOP	7.75	good	K1 and K2 C.I.s do not include zero	5.88	71.4
HS Using OLS	12.3	good	K1 C.I.s do not include zero K2 C.I.s include zero	7.2	74.2
HS using IRLS	8.8	good	K1 and K2 C.I.s do not include zero	5.85	67.1
	Both DFOP and HS provided good visual fits. The HS model run using IRLS as the optimiser matches the Applicant's and provided a slightly better visual fit and χ2 error %. However, neither model offered any visual or statistical improvement over the FOMC which was selected as the best fit kinetics to represent the degradation in the sandy loam water compartment.				

Figure B.8.2.2.3-5 Graphs and residual plots representing the kinetic evaluation of the clay loam water compartment level P-I

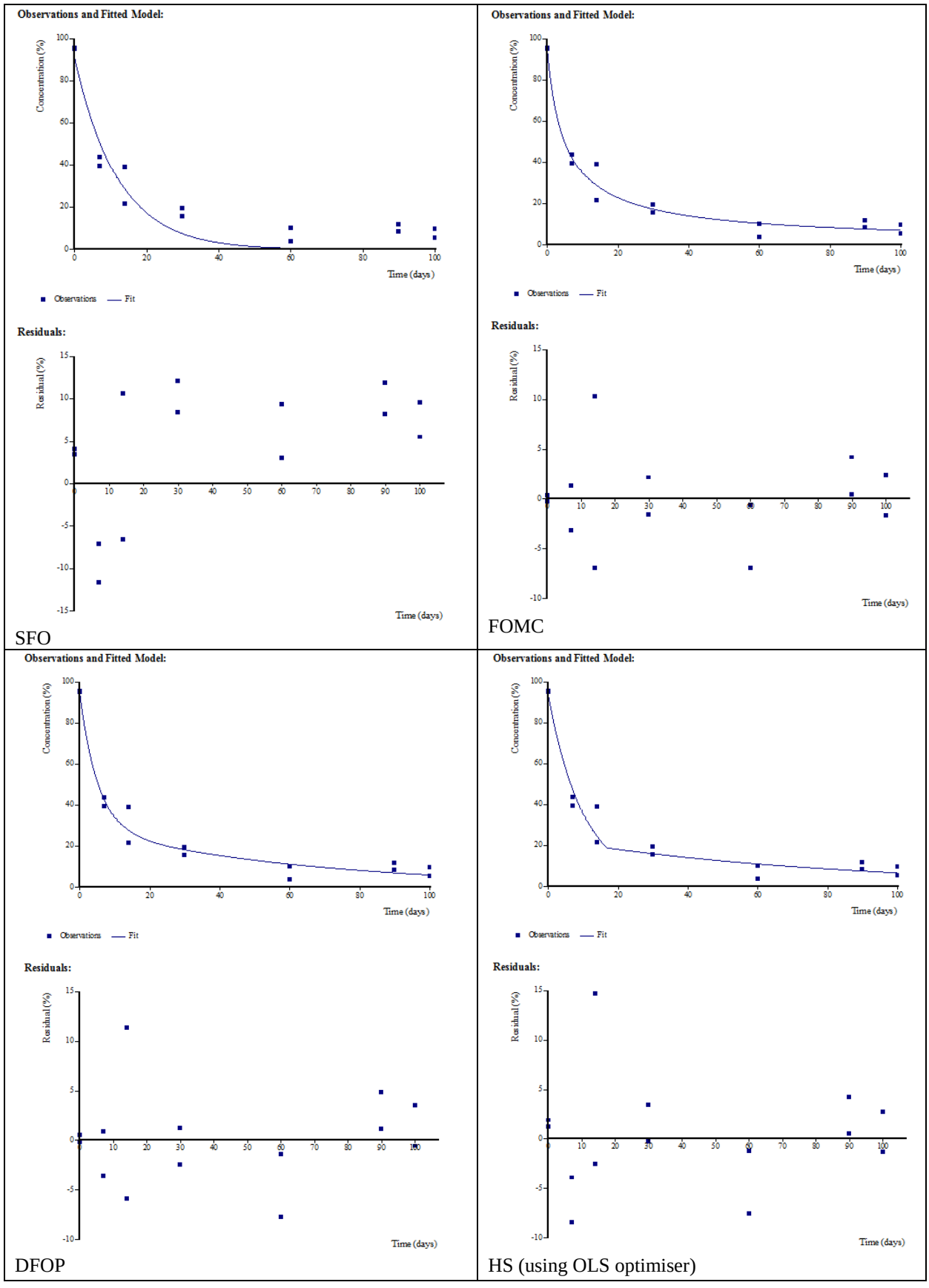
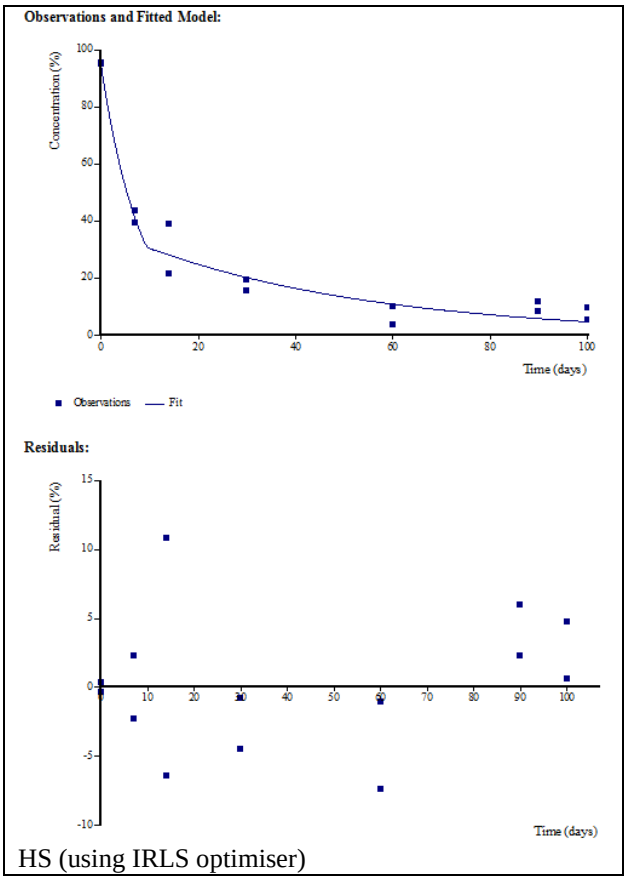


Figure B.8.2.2.3-5 (continued) Graphs and residual plots representing the kinetic evaluation of the clay loam water compartment level P-I



HS (using IRLS optimiser)

Level P-II evaluation

The Applicant performed a P-II level kinetic evaluation for the degradation of napropamide-M in water sediment systems using the modelling package ModelMaker v4.0. As is commonly the case, the P-II level evaluations failed the statistical fit tests. Therefore RMS has not independently repeated the P-II assessment as it is not relied upon in the risk exposure assessment. The Applicant's text and model generated using ModelMaker (figure B.8.2.2.3-6) are reproduced below:

The model was optimised in accordance with the FOCUS kinetic guidance to obtain the Level P-II evaluations. The predicted values for water and sediment from the simulations were compared to the measured values using the FOCUS DEGKIN v2 spreadsheet to obtain the χ2 error. The FOCUS DEGKIN v2 spreadsheet was also used to perform the T-test for the rates of degradation using the optimisation error calculated by ModelMaker. The Fsed check was performed to ensure that the results of the simulations were consistent with the physical parameters of the molecule. The simulation model for each system was also extrapolated beyond the experimental phase to estimate the DT_{50} of the simulated system for comparison with the DT_{50} calculated at Level P-I.

Figure B.8.2.2.3-6 Applicant model generated using ModelMaker V4.0 used for the kinetic assessment of degradation of napropamide-M in water sediment systems

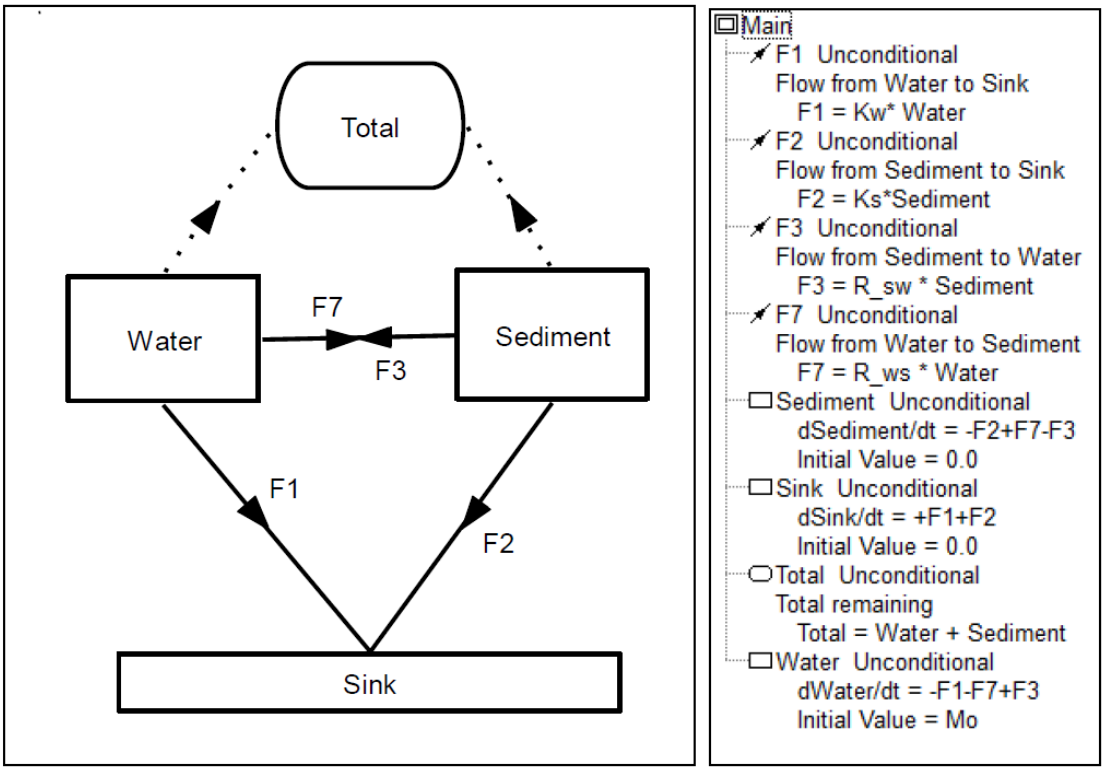


Table B.8.2.2.3-17 below summarises the P-II level evaluation for the degradation of napropamide-M in water sediment systems. The $\chi 2$ error values for both water and sediment compartments in both systems were all <15%. The Fsed test passed for both systems. The t-test performed for the sandy loam system showed that parameters were not significantly different from zero in both the water and sediment phases. The simulations predicted the rate of degradation in the water compartment to be ten times higher than that of the sediment compartment. The t-test also failed for the clay loam system. The simulation showed a much greater rate of degradation in the water compartment compared to the sediment phase, where very little degradation was predicted.

Table B.8.2.2.3-17 Applicant summary of the kinetic assessment of degradation of napropamide-M in water sediment systems at level P-II

Parameter	Sandy loam system	Clay loam system
Water degradation rate (Kw)	0.007595	0.010191
Water DT_{50} / DT_{90} (days)	91.26 / 303.2	68.01 / 225.9
Chi2 error (%)	12.2	10.3
t- test error	0.261	0.115
Sediment degradation rate (Ks)	0.000709	0
Sediment DT_{50} / DT_{90} (days)	977.36 / >1000	>1000 / >1000
Chi2 error (%)	3.5	4.5
t-test error	0.347	0.500
M0	97.9658	96.4767
Rate of dissipation from water to sediment (R_ws)	0.16763	0.106241
Rate of dissipation from sediment to water (R_sw)	0.024435	0.017629
Fsed check	Pass	Pass
Extrapolated system DT_{50} from simulation	327 days	435 days
Conclusion	Fsed check and $\chi 2$ errors show that simulation is consistent with compound properties and with the observed data. However degradation rates are low and t-test indicates that rates in both water and sediment are not significantly different from zero.	Fsed check and $\chi 2$ errors show that simulation is consistent with compound properties and with the observed data. However degradation rates are low and t-test indicates that rates in both water and sediment are not significantly different from zero.

Modelling Endpoints

The degradation of napropamide-M was assessed at level P-II (see above section on persistence endpoints). However the t-tests failed for both systems indicating that degradation rates for either water or sediment could not be determined with sufficient precision. The Fsed test passed for both systems and the model simulations are believed to represent the fate and behaviour of napropamide-M. The default approach in this situation is to accept degradation values generated at P-I, following the FOCUS generic guidance on surface water v1.4 (page 213). Experience of following this FOCUS kinetics guidance has shown that in the vast majority of cases first order whole system DT_{50} values are selected for calculating the geometric mean (in accordance with the procedures defined for P-I, as the statistical criteria for accepting a P-II approach are rarely satisfied). In this situation (only P-I assessment accepted) the usual evaluation practice has been to ascribe the whole system DT_{50} to the water phase for compounds with a Koc< ca. 100mL/g or to the sediment phase for compounds with a Koc> ca. 2000 mL/g and use a default of 1000 days for the other compartment. This is considered by Member State regulators to be a reasonable 'rule of thumb'. For compounds with Koc between 100 and 2000 mL/g , the FOCUS kinetics advice regarding running simulations with both combinations for ascribing the whole system DT_{50} and default and selecting the results that give the highest concentrations for the risk assessment should be followed.

Table B.8.2.2.3-18 below presents the chosen modelling endpoints for the surface water exposure assessment of napropamide-M based on values derived at level P-I. Sediment compartment DT_{50} values could not be calculated. The whole system $DegT_{50}$ has been assigned to the water compartment and a default value of 1000 days assigned to the sediment compartment.

Table B.8.2.2.3-18 Modelling endpoints for napropamide-M in water sediment systems at level P-I

Compartment	Sediment type	Kinetics	$\chi 2$ error %	DT_{50}	DT_{90}
Water	Sandy loam	SFO	1.9	301	1000
	Clay loam	SFO	1.43	333	1110
			Arithmetic mean	317.00	1055.00
			Geometric mean	316.60	1053.57
Sediment	Sandy loam	N/A	N/A	1000 (default)	N/A
	Clay loam	N/A	N/A	1000 (default)	N/A
			Arithmetic mean	1000	N/A
			Geometric mean	1000	N/A

B.8.2.3. **Degradation in the saturated zone**

B.8.2.3.1 **Water treatment processes**

This is a new requirement, under Article 4.3(b) of Regulation 1107/2009, which states that active substances shall not have harmful effects on human health, taking account of substances resulting from water treatment. There is no guidance available at present. The Applicant provided the following statement in the original submission:

"*Studies on the impact on water treatment procedures are not considered necessary as predicted environmental concentrations in groundwater indicate that napropamide-M will not contaminate groundwater. Additionally napropamide-M does not possess any obvious structural characteristics that may react with water treatment processes. Therefore the risk of producing substances or degradation products at levels harmful to human health as a result of water treatment processes is extremely low*."

The RMS considered this statement insufficient and requested the Applicant provide a more detailed reasoned case. In response to the request for further information, the Applicant has provided the following statement:

"*…there is very little guidance on this requirement and no specific data requirement or acceptable study design, therefore it is not possible for the notifier to provide a definitive response to this information request.*

However, in addition to the statements already provided the following could be considered.

Ozonolysis of napropamide-M and any metabolites would most likely breakdown the organic heterocyclic structure, via complex intermediates to glyoxal. Glyoxal is a very common chemical used in many industrial processes and is present in trace amounts in many food stuffs. It is readily biodegradable and is endogenous in the environment. The concentration produced from the water treatment process from napropamide-M would not significantly increase normal background levels of glyoxal. Numerous other components both natural and contaminants would also produce glyoxal as a result of ozonolysis treatment of drinking water.

Chemical reaction of napropamide-M with chlorine under the conditions used for the chlorination of water are extremely unlikely. High temperatures, high concentration of chlorine and a catalyst would be required to obtain any significant reactions. Even if the reaction with chlorines could be achieved the resulting concentration of potentially harmful by products such as trihalomethanes formed would be well below the 100 µ/L drinking water standard, based on the very conservative PEC calculation in the dossier. The chlorination process could also oxidise napropamide-M and metabolites which under aqueous conditions are likely to form as hydroxylated products. These hydroxylated forms are likely to be more polar and far less toxic the parent material and will be rapidly eliminated by most organism. Therefore, hydroxylation is very unlikely to produce substances more toxic than the parent molecule.

Concentration of napropamide-M and metabolites at groundwater abstraction points will be far lower than the levels than those predicted by the conservative FOCUS models at a depth of 1 m. As such any component formed from water treatment processes will be well below the toxicological threshold of concern (TCC).

Concentration in surface water are potentially higher, however treatment of water from surface water typically involves many processes including storage in reservoirs, clarification, filtration, aeration, treatment with activated carbon all of which are likely to help deplete any napropamide-M related residues from the water before any ozonolysis or chlorination takes place. The chances of any significant toxic products forming as a result of the water treatment processes reacting with napropamide-M or metabolites are therefore extremely remote."

The RMS considers that the Applicant has provided a reasoned case for the potential by-products that may be formed and their toxicological relevance. The RMS accepts that glyoxal is used in several industrial processes. However, no supporting evidence for evaluation has been provided in terms of quantifying theoretical levels of any of these by-products that might be expected or providing TTC levels to compare these against. Predicted environmental concentrations in groundwater were <0.001µg/L, significantly below the regulatory threshold of 0.1 µg/L, indicating the risk from drinking water processing using abstracted groundwater is low.

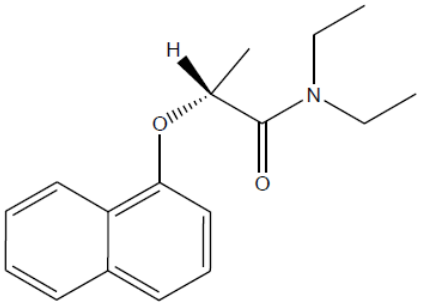
B.8.3. FATE AND BEHAVIOUR IN AIR

B.8.3.1. **Route and rate of degradation in air**

Study author	Croucher, A. (2015)
Study title	Estimation of the atmospheric oxidation rate for napropamide-M
Study date	08/05/2015
Annex point	CA 7.3.1-01
Previous evaluation	New active substance, no previous studies submitted

The potential for atmospheric transformation of napropamide-M and likelihood of significant long-range transport was investigated. The atmospheric oxidation rate for napropamide-M was estimated using the Atmospheric Oxidation Program (AOPWIN; Meylan and Howard, 1993). The model estimated the gas-phase rate of reaction between napropamide-M and the most prevalent atmospheric oxidant and hydroxyl radicals to generate an atmospheric half-life. The RMS independently verified the atmospheric half-life in the EPI Suite program. Table B.8.3.1-1 below reports the input values and SMILES notation (Simplified Molecular Input Line Entry System) used. The RMS notes that the SMILES reported in the main text of the Applicant report, CC(Oclcccc2cccccI2)C(=O)N(CC)CC, is incorrect and had used the correct SMILES notation from the appendix.

Table B.8.3.1-1 Input values for EPI Suite to assess the atmospheric degradation of napropamide-M

Structural formula	
Molecular formula	C17H21NO2
Molecular weight (g/mol)	271.35
Melting point (°C)	92.2
Boiling point (°C)	319.4
Water solubility (mg/L)	39
SMILES	CC(Oc2c1ccccc1ccc2)C(=O)(N(CC)CC)

AOPWIN estimated the atmospheric half-life of napropamide-M as 0.046 days (0.552 hours, at 1.5 $x10^6$ OH/ cm^3) under a diurnal cycle of 12 hours. Furthermore the active substance possesses low volatility (3.80 $x10^{-6}$ Pa at 25 °C vapour pressure) and a low Henry's Law constant (2.644 $x10^{-5}$ Pa m^3 mol). In light of these results, napropamide-M is not considered to persist in the atmosphere. The DT_{50} is less than two days and so napropamide-M is unlikely to be subjected to significant long-range transport.

B.8.3.2. **Transport via air**

Napropamide-M possesses relatively low vapour pressure and Henry's Law Constant values. These values suggest that volatility from soil or plant surfaces is likely to be negligible. Furthermore, in the event of aerosol formation after spraying, napropamide-M is unlikely to be subject to long-range transport with an atmospheric oxidation half-life below the two day trigger value (0.046 days) (see 3CA B.8.3.1) .

B.8.3.3. **Local and global effects**

The local and global atmospheric effects of napropamide-M were considered negligible (see 3CA B.8.3.1).

POP, PBT and vPvB classification

The RMS has assessed the potential for napropamide-M to be considered a persistent organic pollutant (POP), persistent bioaccumulative and toxic (PBT) substance or a very persistent, very bioaccumulative (vPvB) substance according to the criteria described below. Annex II, section 3.7 of Regulation 1107/2009 states that substances deemed to meet the POP, PBT or vPvB criteria cannot be approved. Furthermore, if an active substance meets two out of three PBT criteria, it will be a 'Candidate for Substitution'.

POP assessment

A POP is defined as a chemical which is extremely stable or persistent in the environment; will bioaccumulate in organisms or the food chain; is toxic to humans or animals and has potential to be transported in the environment over long distances far from the place of release. A substance that fulfils all three of the criteria shown in table B.8.3.3-1 is a POP.

Napropamide-M was shown to be persistent in fresh surface water as the aerobic mineralisation DT_{50} exceeded two months. The RMS notes that the half-life was extrapolated beyond the study duration of 90 days and is uncertain. Furthermore, the aerobic mineralisation test is more representative of behaviour in open waters or larger water bodies rather than small water bodies at the edge of field margins. The whole system $DegT_{50}$ in water sediment systems exceeded 6 months. The RMS notes that dissipation of napropamide-M from the water phase into the sediment was rapid. It is likely that entry of the parent compound to ditches or shallow water bodies with high sediment content would not result in persistence in the water phase. However, napropamide-M is likely to persist in aquatic sediment.

Napropamide-M persisted in soil under aerobic laboratory conditions. However, degradation was more rapid under field conditions.

The bioaccumulation criteria were not triggered for napropamide-M. The BCF in the Bluegill sunfish species <100 and there is no evidence of bioaccumulation in any other non-target species.

The atmospheric DT_{50} is <2 days so the potential for long-range transport is low. Napropamide-M possesses low volatility (3.80×10^{-6} Pa at 25 °C vapour pressure) and a low Henry's Law constant (2.644×10^{-5} Pa m^3 mol). Volatility from plant or soil surfaces is likely to be low. The RMS considers it acceptable that no monitoring data has been provided for napropamide-M as it is a new active substance.

Napropamide-M, although potentially persistent in the environment, is neither bioaccumulative nor susceptible to long range transport; therefore it is not a Persistent Organic Pollutant.

Table B.8.3.3-1 Comparison of napropamide-M endpoints against trigger criteria for a POP

Trigger criteria	Value	Study	Comments	Criteria met?
Persistence criteria				
DT_{50} water >2 months (marine and fresh)	>1000	[naphthyl-1-^{14}C] napropamide-M: aerobic mineralisation in surface water (pelagic test) (Bianca, C., 2015b) (Section 3CA B.8.2.2.2)	As <20% degradation occurred, any DT_{50} values calculated are uncertain and extrapolated beyond the study duration. DT_{50}= 1840 days (1 µg/L dosing solution; SFO kinetics) DT_{50}= 2320 days (5 µg/L dosing solution; SFO kinetics)	Yes
DT_{50} water >2 months (marine and fresh)	5.53	Aerobic transformation in sediment/water systems for [naphthyl-1-^{14}C] napropamide-M (Ahmad, S., 2015) (Section 3CA B.8.2.2.3)	Worst case freshwater dissipation DT_{50}= 5.53 days (clay loam system; FOMC kinetics) [Geometric mean DT_{50}=4.05 days (n=2)] Persistence endpoints calculated at level P-I. A true degradation $DegT_{50}$ could not be calculated for the separate compartments.	No
DT_{50} sediment >6 months	333	Aerobic transformation in sediment/water systems for [naphthyl-1-^{14}C] napropamide-M (Ahmad, S., 2015) (Section 3CA B.8.2.2.3)	Whole system $DegT_{50}$= 333 days (clay loam system; SFO kinetics) [Geometric mean DT_{50}= 316.60 days (n=2); SFO kinetics] Persistence endpoints calculated at level P-I.	Yes
DT_{50} soil >6 months	1150 (lab) 101.0 (field)	[Naphthyl-1-^{14}C] napropamide-M: aerobic soil metabolism and transformation. (Ahmad, S., 2015) (Section 3CA B.8.1.1.1) Terrestrial field dissipation study with a suspension concentrate formulation containing 450 g/L napropamide-M applied to bare soil in Italy, Spain, UK and Germany (Wilson, A., 2013) (Section 3CA B.8.1.1.4)	<u>Soil aerobic lab (normalised):</u> Longest worst case DT_{50}= 1150 days, clay loam, HS kinetics, DT_{90}= 5250] [Geometric mean DT_{50}=608; range 382-1150 days] <u>Field dissipation (non-normalised):</u> Longest worst case DT_{50}= 101.0 days, Spain autumn trial, HS kinetics, DT_{90}= 900] [Geometric mean DT_{50}= 36.24 days; range 5.31-101 days]	Yes
Bioaccumulation criteria				
BCF in aquatic species >5000 (or Log Kow >5)	98	Bluegill sunfish *Lepomis macrochirus* (Sankey *et al.,* 1995) (See 3CA B.9 Ecotoxicology)	Bioconcentration assessment undertaken for the structurally comparable racemate, napropamide. The BCF in the fish species was shown to be <100. The log Kow (3.27) was <5.	No
Evidence of bioaccumulation in	none	(See 3CA B.9 Ecotoxicology)	No evidence of high bioaccumulation in other non-	No

Trigger criteria	Value	Study	Comments	Criteria met?
other non-target species			target species of concern as all TER values >5 (annex VI trigger) For example: earthworm-eating birds TER=35.2; earthworm-eating mammals TER=6.1; fish-eating birds TER=760 and fish-eating mammals TER=128.	
Potential for long-range transport				
DT_{50}air > 2 days	0.046	Estimation of the atmospheric oxidation rate for napropamide-M (Croucher, A., 2015) (Section 3CA B.8.3.1)	Estimated using the AOPWIN programme in EPI Suite. The atmospheric half-life was 0.046 days (1.5 x10^6 OH/ cm^3; cycle of 12 hours) <2 days.	No
Relevant monitoring data that demonstrates the potential for long range transport via air, water or migratory species.	No data	-	-	-
Measured levels in locations distant from the source of release that are of potential concern.	No data	-	-	-

PBT assessment

A substance which fulfils all three criteria in table B.8.3.3-2 is considered PBT.

Napropamide-M was shown to be persistent in fresh surface water as the aerobic mineralisation DT_{50} exceeded 40 days. The RMS notes that the half-life was extrapolated beyond the study duration of 90 days and is uncertain. Furthermore, the aerobic mineralisation test is more representative of behaviour in open waters rather than small water bodies at the edge of field margins. The whole system $DegT_{50}$ in water sediment systems exceeded 120 days. The RMS notes that dissipation of napropamide-M from the water phase into the sediment was rapid. It is likely that entry of the parent compound to ditches or shallow water bodies with high sediment content would not result in persistence in the water phase. However, napropamide-M is likely to persist in aquatic sediment.

Napropamide-M persisted in soil under aerobic laboratory conditions. However, degradation was more rapid under field conditions. Field degradation half-lives varied considerably, but DT_{50} values for all trial sites were <120 days.

The RMS also considered the outcomes of the hydrolysis and ready biodegradability studies. Napropamide-M was shown to be hydrolytically stable at a range of pH values and not readily biodegradable. On balance, in light of these conclusions, Napropamide-M is persistent in the environment.

The bioaccumulation criterion was not met as the BCF (Bluegill sunfish spp.) was less than the trigger value of 2000. The NOEC for *Daphnia magna* was 0.3 mg/L, >0.01 mg/L trigger value. This was representative for the most sensitive group, the aquatic invertebrates.

The mammalian toxicology assessment was still ongoing at the time of writing. Please refer to the relevant Toxicology and Metabolism section 3CA B.6.

Napropamide-M is persistent in the environment. The bioaccumulation criteria are not met and therefore it cannot be classified as a PBT substance. The toxicity classification is yet to be determined.

Table B.8.3.3-2 Comparison of napropamide-M endpoints against trigger criteria for a PBT substance

Trigger criteria	Value	Study	Comments	Criteria met?
Persistence criteria				
DT_{50} marine water >60 days	No data	-	-	-
DT_{50} fresh or estuarine water >40 days	>1000	[naphthyl-1-^{14}C] napropamide-M: aerobic mineralisation in surface water (pelagic test) (Bianca, C., 2015b) (Section 3CA B.8.2.2.2)	As <20% degradation occurred, any DT_{50} values calculated are uncertain and extrapolated beyond the study duration. DT_{50}= 1840 days (1 µg/L dosing solution; SFO kinetics) DT_{50}= 2320 days (5 µg/L dosing solution; SFO kinetics)	Yes
DT_{50} fresh or estuarine water >40 days	5.53	Aerobic transformation in sediment/water systems for [naphthyl-1-^{14}C] napropamide-M (Ahmad, S., 2015) (Section 3CA B.8.2.2.3)	Worst case freshwater dissipation DT_{50}= 5.53 days (clay loam system; FOMC kinetics) [Geometric mean DT_{50}=4.05 days (n=2)] Persistence endpoints calculated at level P-I. A true degradation $DegT_{50}$ could not be calculated for the separate compartments.	No
DT_{50} marine sediment >180 days	No data	-	-	-
DT_{50} fresh or estuarine sediment >120 days	333	Aerobic transformation in sediment/water systems for [naphthyl-1-^{14}C] napropamide-M (Ahmad, S., 2015) (Section 3CA B.8.2.2.3)	Whole system DegT50= 333 days (clay loam system; SFO kinetics) [Geometric mean DT_{50}= 316.60 days (n=2); SFO kinetics] Persistence endpoints calculated at level P-I.	Yes
DT_{50} soil >120 days	1150 (lab) 101.0 (field)	[Naphthyl-1-^{14}C] napropamide-M: aerobic soil metabolism and transformation. (Ahmad, S., 2015) (Section 3CA B.8.1.1.1) Terrestrial field dissipation study with a suspension concentrate formulation containing 450 g/L napropamide-M applied to bare soil in Italy, Spain, UK and Germany (Wilson, A., 2013) (Section 3CA B.8.1.1.4)	<u>Soil aerobic lab (normalised):</u> Longest worst case DT_{50}= 1150 days, clay loam, HS kinetics, DT_{90}= 5250] [Geometric mean DT_{50}=608; range 382-1150 days] <u>Field dissipation (non-normalised):</u> Longest worst case DT_{50}= 101.0 days, Spain autumn trial, HS kinetics, DT_{90}= 900] [Geometric mean DT_{50}= 36.24 days; range 5.31-101 days (HS kinetics)]	Yes
Other considerations: Evidence of hydrolytic degradation Evidence of ready	-	Hydrolytic stability of [naphthyl-1-^{14}C] napropamide-M in buffered aqueous solutions at ph4, 7, and 9 (Fenn Li, 2013).	Hydrolytic degradation was <10%. Napropamide-M can be considered hydrolytically stable at pH 4, 7, and 9.	Yes

Trigger criteria	Value	Study	Comments	Criteria met?
biodegradability		(Section 3CA B.8.2.1.1) Ready biodegradability of napropamide-M technical (Raithatha, A., 2014) (Section 3CA B.8.2.2.1)	Biodegradation <10% over study duration. Napropamide-M is not considered readily biodegradable.	
Bioaccumulation criteria				
BCF for aquatic species >2000 (fresh or marine)	98	Bluegill sunfish *Lepomis macrochirus* (Sankey *et al.,* 1995) (See 3CA B.9 Ecotoxicology)	Bioconcentration assessment undertaken for the structurally comparable racemate, napropamide. The BCF in the fish species was shown to be <100.	No
Toxicity criteria				
Long term NOEC for marine or freshwater organisms <0.01 mg/L	0.3	*Daphnia magna* (Kamile, M.K., 2014) (See 3CA B.9 Ecotoxicology)	The most sensitive group was aquatic invertebrates. The long term NOEC for *Daphnia magna* was 0.3 mg/L.	No
Substance is categorised as carcinogenic (category 1A or 1B), mutagenic (category 1 A or 1 B) or toxic for reproduction (category 1A or 1B)	-	-	Mammalian toxicology assessment still ongoing at time of writing. Classification of napropamide-M may be subject to change. Please refer to the relevant Toxicology and Metabolism section 3CA B.6.	-
Evidence of chronic toxicity (classifications STOT RE 1 or STOT RE 2)	none	See 3CA B.6 Toxicology and Metabolism	There is no evidence of chronic toxicity according to the 1272/2008 classifications STOT RE 1 or STOT RE 2.	No

vPvB assessment

A substance needs to fulfil both "very persistent" and "very bioaccumulative" criteria shown in table B.8.3.3-3 below to be considered vPvB.

Napropamide-M was shown to be persistent in fresh surface water as the aerobic mineralisation DT_{50} exceeded 60 days. The RMS notes that the half-life was extrapolated beyond the study duration of 90 days and is uncertain. Furthermore, the aerobic mineralisation test is more representative of behaviour in open waters rather than small water bodies at the edge of field margins. Water sediment studies showed that napropamide-M persisted in the sediment compartment as $DegT_{50}$ exceeded 180 days. The RMS notes that dissipation from the water phase to the sediment phase was rapid and does not believe napropamide-M would persist in the water phase in shallow water bodies. However, napropamide-M is potentially very persistent in aquatic sediment.

Napropamide-M persisted in soil under aerobic laboratory conditions. However, degradation was more rapid under field conditions.

Napropamide-M is not considered to be very bioaccumulative as the BCF <5000 trigger value.

Therefore, although Napropamide-M is potentially very persistent in the environment, it is not very bioaccumulative and cannot be considered a vPvB substance.

Table B.8.3.3-3 Comparison of napropamide-M endpoints against trigger criteria for a vPvB substance

Trigger criteria	Value	Study	Comments	Criteria met?
Very persistent criteria				
DT_{50} water >60 days (marine, fresh or estuarine)	>1000	[naphthyl-1-^{14}C] napropamide-M: aerobic mineralisation in surface water (pelagic test) (Bianca, C., 2015b) (Section 3CA B.8.2.2.2)	As <20% degradation occurred, any DT_{50} values calculated are uncertain and extrapolated beyond the study duration. DT_{50}= 1840 days (1 µg/L dosing solution; SFO kinetics) DT_{50}= 2320 days (5 µg/L dosing solution; SFO kinetics)	Yes
DT_{50} sediment >180 days (marine, fresh or estuarine)	333	Aerobic transformation in sediment/water systems for [naphthyl-1-^{14}C] napropamide-M (Ahmad, S., 2015) (Section 3CA B.8.2.2.3)	Whole system $DegT_{50}$= 333 days (clay loam system; SFO kinetics) [Geometric mean DT_{50}= 316.60 days (n=2); SFO kinetics] Persistence endpoints calculated at level P-I.	Yes
DT_{50} soil >180 days	1150 (lab) 101 (field)	[Naphthyl-1-^{14}C] napropamide-M: aerobic soil metabolism and transformation. (Ahmad, S., 2015) (Section 3CA B.8.1.1.1) Terrestrial field dissipation study with a suspension concentrate formulation containing 450 g/L napropamide-M applied to bare soil in Italy, Spain, UK and Germany (Wilson, A., 2013) (Section 3CA B.8.1.1.4)	<u>Soil aerobic lab (normalised):</u> Longest worst case DT_{50}= 1150 days, clay loam, HS kinetics, DT_{90}= 5250] [Geometric mean DT_{50}=608; range 382-1150 days] <u>Field dissipation (non-normalised):</u> Longest worst case DT_{50}= 101.0 days, Spain autumn trial, HS kinetics, DT_{90}= 900] [Geometric mean DT_{50}= 36.24 days; range 5.31-101 days (HS kinetics)]	Yes
Very bioaccumulative criteria				
BCF >5000	98	Bluegill sunfish *Lepomis macrochirus* (Sankey *et al.*, 1995)	Bioconcentration assessment undertaken for the structurally comparable racemate, napropamide. The BCF in the fish species was shown to be <100. (See 3CA B.9 Ecotoxicology)	No

B.8.4. MONITORING DATA CONCERNING FATE AND BEHAVIOUR OF THE ACTIVE SUBSTANCE, METABOLITES, DEGRADATION AND REACTION PRODUCTS

Napropamide-M is a new active substance not authorised yet in the EU. Monitoring data are not available or identified as required by this assessment.

B.8.5. REFERENCES RELIED ON

Literature review process

Study author	Wilkinson, D. & Tucker, K.
Study title	Napropamide-M Literature Review Report
Study date	11/08/2016
Annex point	CA 9-01
Previous evaluation	New active substance, no previous studies submitted

A literature search for napropamide-M and its metabolites was undertaken by the Applicant (Literature Review Report, KCA Section 9/ KCP Section 11, dated August 2016) which combined all specialist evaluation areas. The RMS will only describe the literature review process and results relevant to the environmental fate evaluation here.

Search databases, terms and strategy

The Applicant carried out the search process using databases from the STN platform alongside PubMed, Science Direct and Wiley Online Library. Table B.8.5-1 presents the databases used for the entire literature review for all specialist areas. The RMS considers there to be a sufficient number of databases suitable for retrieving environmental fate related literature. The RMS has not independently conducted a literature search but has considered the appropriateness of the search terms, databases and criteria for exclusion used by the Applicant in their literature review.

Table B.8.5-1 Databases from the STN platform provided used in the Applicant's literature search

Provider	Database	Description/ justification
STN international	*ANABSTR - Analytical abstracts	Analytical chemistry, also covers agriculture, environment and food.
STN international	*BIOSIS	Life sciences: agriculture, biochemistry, biophysics, botany, environmental biology, physiology, toxicology.
STN international	CAPLUS - chemical abstracts plus	Biochemistry, chemistry and chemical engineering, and related sciences.
STN international	CHEMLIST	No justification provided
STN international	*EMBASE - The Excerpta Medica database	Biomedical and pharmaceutical fields, including biological science, biochemistry, human medicine, forensic science, pediatrics, pharmacy, pharmacology and drug therapy, pharmacoeconomics, psychiatry, public health, biomedical engineering and instrumentation, and environmental science.
STN international	MEDLINE	Medicine
STN international	RTECS- Registry of Toxic Effects of Chemical Substances	Toxicity data for commercially important substances from research and government reports.
STN international	*SCISEARCH- Science Citation Index	Multidisciplinary database covering science, technology, and biomedicine.
STN international	TOXCENTER	Pharmacological, biochemical, physiological, and toxicological effects of drugs and other chemicals.
US National Library of Medicine National Institutes of Health	PUBMED	Biomedical literature.
Elsevier BV	*Science Direct	Scientific literature.
John Wiley &Sons Inc.	*Wiley Online Library	Broad range of topics including sciences.

*Databases which the RMS believes are most relevant for environmental fate and behaviour

The search terms for napropamide-M and its synonyms and any metabolites and their synonyms used by the Applicant are provided in table B.8.5-2. An initial search in all databases was performed just with these terms.

Table B.8.5-2 Parent and metabolite search terms used by the Applicant

Code number / name	Search terms (name and CAS number)
Napropamide-M	"napropamide-M", "D-Devrinol", "D-napropamide", "HBW07", "napropamide", "Devrinol", "R-7465", "R65728", "R-007465", "N,N-diethyl-2-(1-naphthalenyloxy)propanamide", CAS numbers "41643-35-0" and "15299-99-7". "(R)-(-)-N,N-diethyl-2-(1-naphthyloxy)propionamide", "(-)-N,N-diethyl-2-(1-naphthalenyloxy)propanamide" and "(RS)-N,N-diethyl-2-(1-naphthyloxy)propionamide" were expanded and found to not be contained in the databases being searched.
NOPA * R7465/15 Compound 15 Compound VIII U12	"2-naphthoxypropionic acid", "naphthoxypropionic acid", "1- naphthoxypropionic acid", "2- (naphthalen-1-yloxy) propanoic acid", "2-(1-napthyloxy) propionic acid", "2- (α-naphthoxy)-propionic acid), "13949-67-2"
Isomer I	"N,N-diethyl-2-(4-hydroxy-1- naphthyl)propanamide", "N,N-diethyl- 2-(4-hydroxy naphthalen-1-yl) propanamide", the fragment "1- Naphthaleneacetamide", 131933-40-9"
Isomer II	"N,N-diethyl-2-(1-hydroxy-2- naphthyl)propanamide", "N,N-diethyl- 2-(1-hydroxy naphthalen-2-yl) propanamide", the fragment "2- Naphthaleneacetamide", "131933-41-0"
1-Naphthol Compound XI	"1-Naphthol", "naphthalene-1-ol", "1- Naphthalenol", "90-15-3"
PA+ R7465/11 Compound 11 Compound XII	"o-Phthalic acid"," phthalic acid", "88- 99-3"
2-OH-NQ * Compound XIII	"2-hydroxy-1,4-Napthoquinone", "2- hydroxynaphthalene-1,4-dione", "83- 72-7"

*The Applicant believed these metabolites are not found within environmental fate studies. Literature on these compounds was considered not relevant to the environmental risk assessment

+ The Applicant believes this compound is not a significant metabolite within environmental fate studies.

The Applicant states that the STN databases produced a large number of articles and refined the search further. Napropamide-M and its synonyms or relevant metabolites and their synonyms (reported in table B.8.5-2) were searched in combination, using the Boolean operator "AND", with sets of search terms presented below in table B.8.5-3.

Table B.8.5-3 Environmental fate and behaviour specific search terms used in the Applicant's literature search

Environmental fate search terms
(FATE# OR DEGRAD? OR PERSIST? OR DECOMP? OR DECAY? OR MINERALI?)
(TRANSFORM? OR DETERIORAT? OR METAB? OR DEGENERAT?)
(BIODEGRAD? OR BIOTRANSFORM? OR BIODETERIORAT?)
(BIODEGENERAT? OR BREAKDOWN? OR BREAKSDOWN?)
(((BROKEN? OR BREAK?)(W)(UP OR DOWN)) OR HALFLIFE#)
(HALFLIVES OR HALF(W)(LIFE OR LIVES) OR DEGRDN# OR DECOMPN#)
(BIODEGRDN# OR DEGN# OR BIODEGN# OR DISSIP? OR RESIDUE?)
(LEACH? OR TRANSPORT? OR MOBIL? OR MOVEMENT? OR HYDROLY?)
(ADSORP? OR ADSORB? OR SORP? OR SORB? OR DESORP?)
(DESORB? OR RUNOFF OR (RUN#(W)OFF) OR DRAIN? OR PERCOLAT?)
(PHOTOLY? OR PHOTODEGRAD? OR PHOTODECOMP?)
(PHOTOTRANSFORM? OR PHOTOSTAB? OR PHOTODEGRDN# OR PHOTODEGN#)
((PHOTO(W)(DECOMP? OR DEGRAD? OR TRANSFORM? OR STAB? OR CHEM?)))
(PHOTOCHEM? OR VOLATIL? OR VAPOUR? OR VAPOR? OR DT50 OR DT90)
((DT(W)50) OR (DT(W)90) OR KDOC OR (K(W)DOC) OR KD OR KOC OR KF OR KFOC)
((K(W)OC) OR (PARTITION?(3W)COEFF?) OR FREUNDLICH)
(SEDIMENT? OR SOIL OR SOILS OR PODZOL? OR CLAY? OR SAND?)
(SILT? OR LOAM? OR PEAT?)
((ORGANIC(2W)MATTER?) OR HUMIC?)
(HUMUS? OR SUBSOIL? OR AIR OR WATER? OR ATMOSPHER?)
(RAIN### OR RAINWATER? OR RAINFALL? OR LEACH?)
(GROUNDWATER? OR ENVIRONMENT? OR PRECIPITAT? OR POND#)
(STREAM# OR RIVER# OR DELTA# OR ESTUAR? OR SEDIMENT?)
(AQUATIC? OR LAKE# OR OPEN(W)WATER)
(FRESHWATER? OR SEAWATER?)
(SALTWATER? OR ((GROUND? OR FRESH OR SEA OR SALT)(W)WATER? OR SURFACE(W)WATER?))
(CATCHMENT? OR DITCH? OR DRAIN# OR DRAINAG?)
(((FOLIAGE OR FOLIAR OR LEAF OR LEAVES)(5A)EVAPORAT?))
((SPRAY? OR DUST?)(3A)DRIFT)
Key
represents one or zero characters at the designated position ? represents any number of characters to the right of the term ! represents only one character at the designated position W represents terms must be adjacent and in the order specified (nw) represents terms must be adjacent and in the order specified with n or fewer intervening terms (nA) represents terms must be adjacent but in any order with n or fewer intervening terms L represents terms must occur in the same information unit

The Applicant states that the Science Direct, Wiley online library and Pubmed search of the potential relative metabolite, 1-Naphthol, produced a large number of articles. They believed that the large number of articles retrieved would be impractical to review and therefore required further refinement. The initial number of articles retrieved was not reported but implied to be >3000 after refinement for Wiley online. The same additional search parameters for the STN search (table B.8.5-3) could not be used due to the limitations of the search platforms and therefore a search was performed as before with the following additional search terms:

Tox OR hazard OR adverse OR health OR NOAEL OR NOEL OR LOAEL OR LOEL OR BMD OR"vivo" OR "vitro" or 'storage stability' OR storage OR stability OR metabolic OR metabolism OR degradation OR breakdown OR 'residues' OR residue OR 'processing' OR hydrolysis OR rotation OR plant OR crop OR feed OR animal OR livestock OR hen OR cattle OR ruminant OR goat OR cow OR pig OR 'risk assessment' OR

consume OR exposure or 'soil' OR 'water' OR 'air' OR environment OR fate OR endocrine disrupt OR bioaccumulation OR biomagnification OR bioconcentration OR poison OR effect.

The Wiley Online Library database retrieved >3000 records for the metabolite 1-Naphthol even after further refinement. It was considered by the Applicant to be impractical to review these and so this single database was excluded from the literature search for 1-Naphthol. The RMS considers the use of the STN database, Pubmed and Science Direct acceptable literature sources for this metabolite.

The literature search was limited to non-patent, peer reviewed literature published within ten years prior to the dossier submission date. This is in accordance with EFSA recommended guidance for limiting search results. Duplicate documents were also removed.

The Applicant excluded the metabolites, 2-hydroxy-1,4-Napthoquinone and 2-naphthoxypropionic acid stating that they are not found in environmental fate studies and o-Phthalic acid is not considered a significant metabolite in this area. Therefore, the Applicant believed publicly available literature documents on these substances were not considered relevant for the environmental fate risk assessment. The RMS notes that the metabolite 2-naphthoxypropionic acid (NOPA) was a major soil metabolite in the field dissipation trials for the Annex 1 assessment of the racemate, napropamide. Furthermore, the RMS notes that NOPA appeared as a minor metabolite in the soil photolysis and water sedimentation laboratory studies of the new active substance napropamide-M. It was also considered in the field dissipation trial.

Relevance and reliability criteria

Studies were first assessed on their relevance to the active substance evaluation. The Applicant's relevance criteria for environmental fate studies are reported as:

1. Appropriate and clearly defined test material
2. Well characterised and relevant test system
3. Relevant to the data requirements or the EU regulatory risk assessment e.g. study design, European conditions
4. Relevant to supported uses (or agricultural exposure in general)
5. Use of a comparable formulation for field studies which would not impact the release/dissipation of the active substance
6. Use of validated or acceptable analytical methods

RMS considers the relevance criteria provided by the Applicant to be acceptable and in accordance to EFSA guidance, *submission of scientific peer-reviewed open literature for the approval of pesticide active substances under regulation (EC) No 1107/2009*. The studies considered relevant were then assessed for reliability using the Klimisch score definitions from Klimisch *et al* (1997) '*A systematic approach for evaluating the quality of experimental toxicological and ecotoxciological data'*. Regulatory Toxicology and Pharmacology 25, 1-5 (1997). Table B.8.5-4 presents the Applicant's table defining the Klimisch scores for reliability of studies.

Table B.8.5-4 Applicant's table defining the Klimisch[1] score definitions for reliability of studies

Score	Description	Definition
1	Reliable without restriction	This includes studies or data from the literature or reports which were carried out or generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline (preferably performed according to GLP) or in which all parameters described are closely related/comparable to a guideline method.
2	Reliable with restriction	This includes studies or data from the literature, reports (mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable.
3	Not reliable	This includes studies or data from the literature/reports in which there are interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g., unphysiologic pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for an assessment and which is not convincing for an expert judgment.
4	Not assignable	This includes studies or data from the literature, which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.).

[1] Klimisch, H-J., Andreae, M. & Tillmann, U. (1997) A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. Regulatorty Toxicology and Pharmacology **25** pp 1-5

The Applicant's selection process resulted in three categories of publication:

- Publications that did not meet the relevance criteria.
- Publications which met the relevance criteria but were assessed to be non-reliable were referenced and a justification for not meeting the reliability criteria provided.
- Publications which met the relevance criteria and were assessed to be reliable and where the endpoints would have an impact on the risk assessment.

The initial number of environmental fate studies retrieved using the STN databases for the parent compound, napropamide-M was 2331. This fell to 401 after the date span of the search was limited to the past 10 years (2005- 2015), and patent documents and duplicate documents were removed. These approaches are in accordance with EFSA recommendations for limiting search results. A rapid assessment for relevance was undertaken which resulted in 400 studies excluded from any further analysis. Table B.8.5-5 reports the single study for environmental fate which was assessed for relevance in detail. The RMS accepts the justification given for not considering the study relevant and its exclusion from the dossier. There were no studies on the parent compound, napropamide-M which were considered relevant to the environmental fate section of the dossier.

The total number of records retrieved for napropamide-M for all specialist areas using the Pubmed, Science Direct and Wiley Online Library databases was 183. The Applicant did not specify how many of these studies were related to environmental fate. None of these studies were considered relevant.

Table B.8.5-5 Applicant's detailed assessment of environmental fate studies for relevance in the literature review process

Author(s)	Year	Title	Source	Reason(s) for not including this study in the dossier
Biswas, P. K.; Pramanik, S. K.; Mitra, S. R.; Bhattacharyya, Anjan	2009	Effect of pH on the persistence of napropamide in water under laboratory simulated condition	Pesticide Research Journal (2009), 21(1), 116-118	The study does not follow OECD study guidelines, therefore does not fulfil environmental fate relevance criteria During the study sterile conditions are not maintained in test system, therefore does not fulfil environmental fate relevance criteria The study does not use a validated analytical method, as prescribed in point 6 of the environmental fate relevance criteria.

The Applicant also included potentially relevant metabolites in the literature search process. The total number of records retrieved from the STN databases for the metabolite, 1-naphthol was 21023. This decreased to 2154 after search restrictions were implemented. After a rapid assessment for relevance, all studies found were excluded. There were no studies on the metabolite, 1-naphthol which were considered relevant to the environmental fate section of the dossier. Furthermore, none of the initial 642 records retrieved from the Pubmed and Science Direct databases were considered relevant.

The total number of records retrieved from the STN databases for the metabolite, N,N-diethyl-2-(4-hydroxy-1-naphthyl)propanamide was 207. This decreased to 10 after search restrictions were implemented. After a rapid assessment for relevance, all studies found were excluded. There were no studies on the metabolite, N,N-diethyl-2-(4-hydroxy-1-naphthyl)propanamide which were considered relevant to the environmental fate section of the dossier. The Pubmed, Science Direct and Wiley Online Library databases collectively retrieved 35 records, none of which were considered relevant.

The total number of records retrieved for the metabolite, N,N-diethyl-2-(1-hydroxy-2-naphthyl)propanamide was 47. This decreased to zero after search restrictions were implemented. There were no studies on the metabolite, N,N-diethyl-2-(1-hydroxy-2-naphthyl)propanamide which were considered relevant to the environmental fate section of the dossier. The Pubmed, Science Direct and Wiley Online Library databases collectively retrieved 1 record, which was not considered relevant.

Conclusion

The RMS considers that the literature search undertaken by the Applicant is acceptable in terms of the search strategy used and the search criteria applied. The literature search presented here did not generate any references of relevance to the environmental fate and behaviour assessment.

Table B.8.5-6 References relied upon in the environmental fate and behavior assessment of napropamide-M

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
CA 7.1.1. 1/01	Ahmad, S.	2015a	[naphthyl-1-^{14}C] Napropamide-M: aerobic soil metabolism and transformation Company Report No. AU-2014-01 Jai Research Foundation, USA GLP, Unpublished Study submitted to meet data requirements	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CA 7.1.1. 2/01	Ahmad, S.	2015b	[naphthyl-1-^{14}C] Napropamide-M: anaerobic soil metabolism and transformation Company Report No. AU-2014-02 Jai Research Foundation, USA GLP, Unpublished Study submitted to meet data requirements	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CA 7.1.1. 3/01	Bianca, C.M.	2015a	[naphthyl-1-^{14}C] Napropamide-M: photodegradation on soil Company Report No. AU-2012-52 Jai Research Foundation, USA GLP, Unpublished Study submitted to meet data requirements	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CA 7.1.1. 3/02	Croucher, A., Ford, S.	2015a	Napropamide-M: kinetic assessment for laboratory	N	N	NA	UPL	None

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
			photodegradation on soil Company Report No. UPL/16/01-KIN4 JSC International Ltd, UK Not GLP, Unpublished Study submitted to meet data requirements					
CA 7.1.2. 1.1/01	Ahmad, S.	2015a	[naphthyl-1-^{14}C] Napropamide-M: aerobic soil metabolism and transformation Company Report No. AU-2014-01 Jai Research Foundation, USA GLP, Unpublished ⇒ CA 7.1.1.1/01 Study submitted to meet data requirements	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CA 7.1.2. 1.1/02	Croucher, A., Ford, S.	2015b	Napropamide-M: kinetic assessment for laboratory aerobic soil degradation study Company Report No. UPL/16/01-KIN2 JSC International Ltd, UK Not GLP, Unpublished Study submitted to meet data requirements	N	N	NA	UPL	None
CA 7.1.2. 1.3/01	Ahmad, S.	2015b	[naphthyl-1-^{14}C] Napropamide-M: anaerobic soil metabolism and	N	Y	Data protection is claimed in accordance with Article 59 of	UPL	None

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
			transformation Company Report No. AU-2014-02 Jai Research Foundation, USA GLP, Unpublished ⇒ CA 7.1.1.2/01 Study submitted to meet data requirements			Regulation (EC) No 1107/2009		
CA 7.1.2. 1.3/02	Croucher, A., Ford, S.	2015c	Napropamide-M: kinetic assessment for laboratory anaerobic soil degradation study Company Report No. UPL/16/01-KIN3 JSC International Ltd, UK Not GLP, Unpublished Study submitted to meet data requirements	N	N	NA	UPL	None
CA 7.1.2. 2.1/01	Wilson, A.	2015	Terrestrial field dissipation study with a suspension concentrate formulation containing 450 g/L napropamide-M applied to bare soil in Italy, Spain, United Kingdom and Germany, 2013 Company Report No. ACI3-033 Agrochemex International Ltd., UK GLP, Unpublished Study submitted	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None

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
			to meet data requirements					
CA 7.1.2. 2.1/02	Croucher, A., Ford, S.	2015d	Napropamide-M: Kinetic assessment of field dissipation studies Company Report No. UPL/16/01-KIN1 JSC International Limited, UK Not GLP, Unpublished Study submitted to meet data requirements	N	N	NA	UPL	None
CA 7.1.3. 1.1/01	Dubey, P.	2013	Determination of the adsorption coefficient (K_{OC}) for [naphthyl-1-^{14}C]napropamide-M Company Report No. AU-2012-54 Jai Research Foundation, USA GLP, Unpublished Study submitted to meet data requirements	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CA 7.2.1. 1/01	Li, F.	2013	Hydrolytic stability of [naphthyl-1-^{14}C]napropamide-M in buffered aqueous solutions at pH 4, 7 and 9 Company Report No. AU-2012-55 Jai Research Foundation, USA GLP, Unpublished Study submitted to meet data	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None

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
			requirements					
CA 7.2.1.2/01	Bianca, C.M.	2014	Photodegradation of [napththyl-1-^{14}C]napropamide-M in sterile buffer Company Report No. AU-2012-56 Jai Research Foundation, USA GLP, Unpublished Study submitted to meet data requirements	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CA 7.2.1.2/02	Croucher, A., Ford, S.	2015e	Napropamide-M: kinetic assessment of degradation in a laboratory aqueous photolysis study Company Report No. UPL/16/01-KIN6 JSC International Ltd, UK Not GLP, Unpublished Study submitted to meet data requirements	N	N	NA	UPL	None
CA 7.2.2.1/01	Raithatha, A.	2014	Ready biodegradability of napropamide-M technical Company Report No. 604-3-15-8445 Jai Research Foundation, India GLP, Unpublished Study submitted to meet data requirements	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CA	Bianca,	2015b	[naphthyl-1-^{14}C]	N	Y	Data protection	UPL	None

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
7.2.2.2/01	C.M.		Napropamide-M: aerobic mineralisation in surface water (pelagic test) Company Report No. AU-2012-58 Jai Research Foundation, USA GLP, Unpublished Study submitted to meet data requirements			is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009		
CA 7.2.2.2/02	Croucher, A., Ford, S.	2015f	Napropamide-M: kinetic assessment for aerobic mineralisation in surface water study Company Report No. UPL/16/01-KIN5 JSC International Ltd, UK Not GLP, Unpublished Study submitted to meet data requirements	N	N	NA	UPL	None
CA 7.2.2.3/01	Ahmad, S.	2015c	Aerobic transformation in sediment/water systems for [naphthyl-1-^{14}C] napropamide-M Company Report No. AU-2012-59 Jai Research Foundation, USA GLP, Unpublished Study submitted to meet data requirements	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CA 7.2.2.	Croucher,	2015g	Napropamide-M: kinetic evaluation	N	N	NA	UPL	None

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
3/02	A., Ford, S.		of water sediment study Company Report No. UPL/16/01-KIN7 JSC International Ltd, UK Not GLP, Unpublished Study submitted to meet data requirements					
CA 7.3.1/ 01	Croucher, A.	2015	Estimation of the atmospheric oxidation rate for napropamide-M Company Report No. UPL/16/01-AIR1 JSC International Limited, UK Not GLP, Unpublished Study submitted to meet data requirements	N	N	NA	UPL	None

Additional information

Study author	Date	Title	Relevance to evaluation	Used in previous DAR of napropamide (racemate)
Lee, K.S.	1989	Aqueous Photolysis of Napropamide: Lab Project Number: WRC 88-80: ENV-002. Unpublished study prepared by ICI Americas Inc. 82 p.	The factor for conversion of experimental days to equivalent natural sunlight days was derived from this study on napropamide. This was used to verify the Applicant's calculations in the soil photolysis study of napropamide-M (section 3CA B.8.1.1.3)	Yes Evaluated in the DAR for napropamide (racemate). RMS = Demark, September 2005)