

European Commission



**Draft Renewal Assessment Report prepared according to the Commission
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INDOXACARB

Volume 3 – B.8 (AS)

Rapporteur Member State : France
Co-Rapporteur Member State : Spain

Version History

When	What
2016-12	Initial RAR

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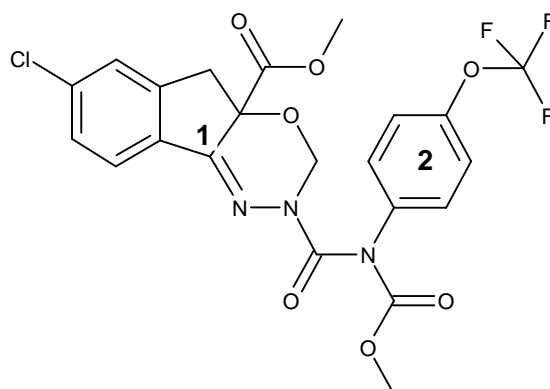
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B.8. ENVIRONMENTAL FATE AND BEHAVIOUR

Fate and behaviour in soil, water, and air

In this document, information is provided with respect to the fate and behaviour of indoxacarb (DPX-KN128) in soil, water, and air. Indoxacarb is an insecticide used against a wide variety of plant pests of agricultural and horticultural significance.

The studies concerning the fate and behaviour of indoxacarb in the environment were conducted using two labeled forms of indoxacarb, [indanone-1-¹⁴C]indoxacarb and [trifluoromethoxyphenyl-¹⁴C(U)]indoxacarb. These ¹⁴C-radiolabels were placed in the most stable ring positions of DPX-KN128 as indicated in Figure 1.



Label 1: [Indanone-1-¹⁴C]indoxacarb (abbreviated as [I-¹⁴C]indoxacarb)

Label 2: [Trifluoromethoxyphenyl-¹⁴C(U)]indoxacarb (abbreviated as [TFMP-¹⁴C]indoxacarb)

Figure 1: Positions of radiolabeling in indoxacarb

Indoxacarb (DPX-KN128) is the insecticidally active, S-enantiomer, compound belonging to the novel oxadiazine class of insecticides. The R-enantiomer, IN-KN127, is not insecticidally active. DPX-MP062 and DPX-JW062 are enantiomer blends of DPX-KN128 and IN-KN127.

DPX-MP062 contains the respective isomers in a ratio of approximately 75:25, while DPX-JW062 is a racemic (50:50) mixture. Development of the oxadiazine class of insecticides began with DPX-JW062. Processes were subsequently developed that allowed for commercial production of DPX-MP062, whose enhanced ratio of the insecticidally active enantiomer allowed for lower use rates of the end-use product and thus lower environmental and dietary exposures. Process breakthroughs in the mid 2000's allowed for the commercial production of >99% indoxacarb (DPX-KN128) technical containing ≤1% IN-KN127. Today, DPX-KN128 is the primary technical material used as basis for formulation of end-user products. A summary of the enantiomeric ratios is found in Table 8-1.

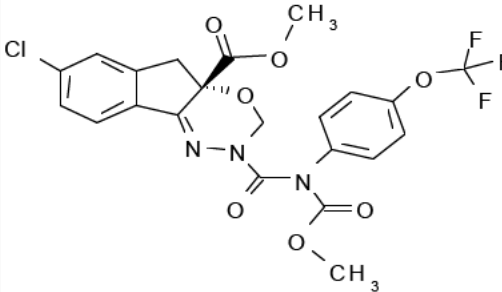
Table 8-1: Test materials used in environmental fate studies

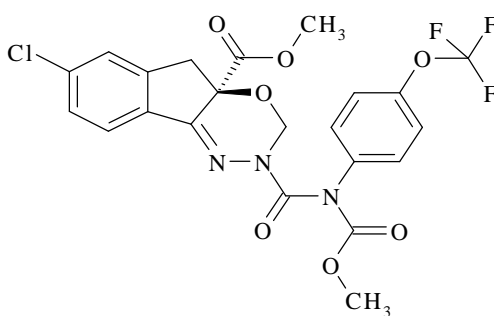
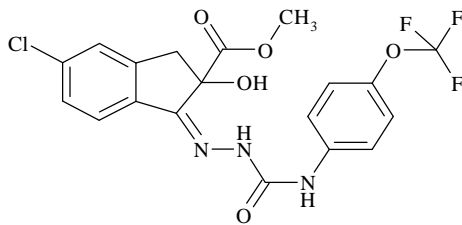
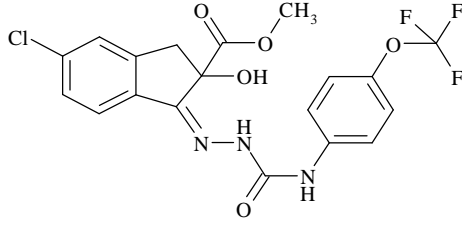
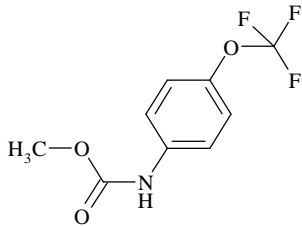
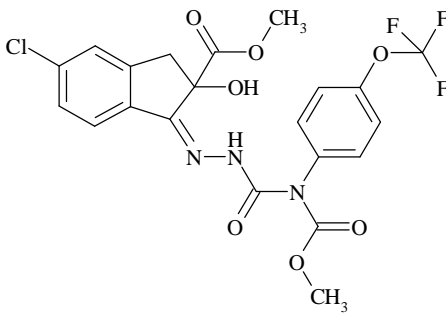
Test material code	DPX-KN128 (active isomer)	IN-KN127 (inactive isomer)	Description
DPX-JW062	50%	50%	Racemic technical material
DPX-MP062	75%	25%	Enriched technical material
DPX-KN128	>99%	<1%	Pure technical material

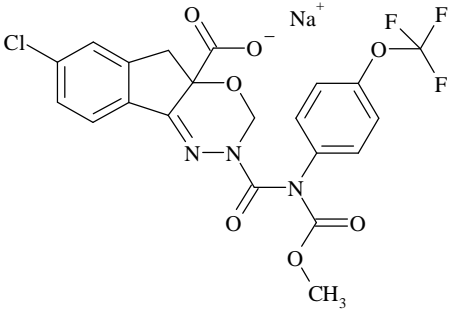
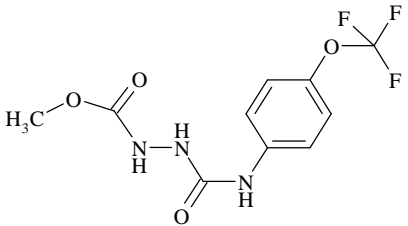
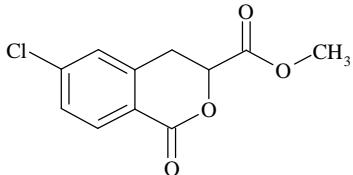
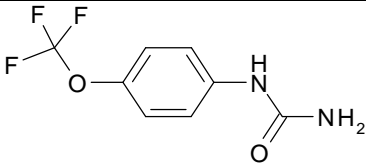
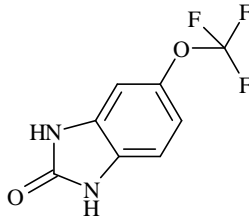
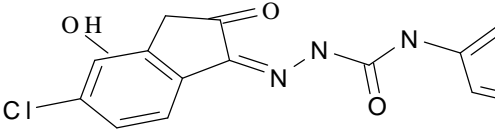
The code used throughout the Draft Renewal Assessment Report, CAS, IUPAC name and synonyms, and chemical structure of indoxacarb and its metabolites, which have been identified in environmental

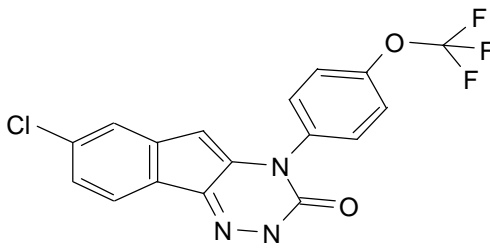
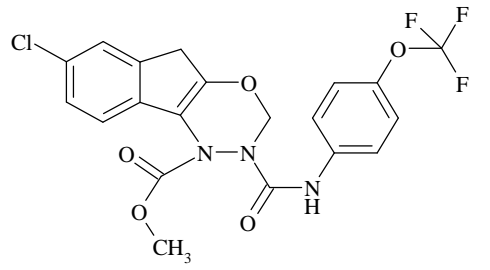
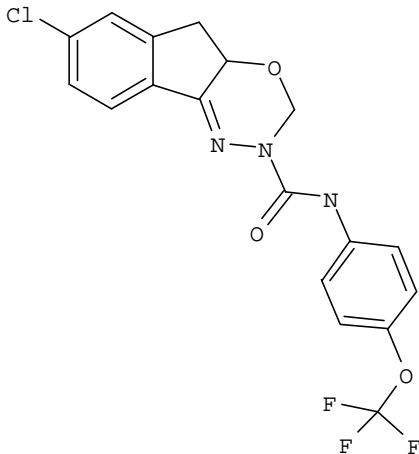
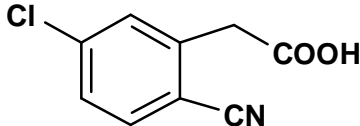
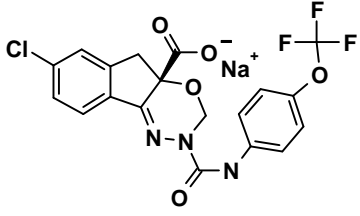
compartments are summarised in Table 8-2: Code, name and description of each metabolite identified in the different environmental compartments. Table 8-2.

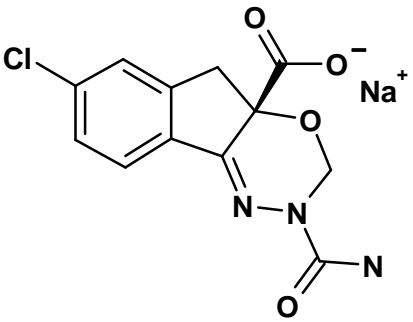
Table 8-2: Code, name and description of each metabolite identified in the different environmental compartments.

Code Number (Synonyms)	Description	Compound found in:	Structure
DPX-KN128	<p>CAS name: (S)-methyl 7-chloro-2,5-dihydro-2-[[[(methoxycarbonyl) [4-(trifluoromethoxy)phenyl]amino] carbonyl]indeno[1,2-e][1,3,4] oxadiazine-4a(3H)-carboxylate</p> <p>IUPAC: (S)-7-chloro-3-[methoxycarbonyl-(4-trifluoromethoxy-phenyl)-carbamoyl]-2,5-dihydro-indeno [1,2-e][1,3,4]oxadiazine-4a(3H)-carboxylic acid methyl ester</p> <p>Common name: Indoxacarb</p> <p>CAS number: 173584-44-6</p> <p>Molecular Weight: 527.84 g/mole</p>	Parent substance, active substance	
DPX-MP062	<p>CAS name: (R,S)-methyl 7-chloro-2,5-dihydro-2-[[[(methoxycarbonyl) [4-(trifluoromethoxy)phenyl]amino] carbonyl]indeno[1,2-e][1,3,4] oxadiazine-4a(3H)-carboxylate</p> <p>IUPAC: Not available</p> <p>CAS number: Not available</p> <p>Common name: None</p> <p>Molecular Weight: 527.84 g/mole</p>	<p>Parent active substance, enriched material</p> <p>Reference technical material for first inclusion (75:25 DPX-KN128: IN-KN127)</p>	See structure for DPX-KN128
DPX-JW062	<p>CAS name: (R,S)-methyl 7-chloro-2,5-dihydro-2-[[[(methoxycarbonyl) [4-(trifluoromethoxy)phenyl]amino] carbonyl]indeno[1,2-e][1,3,4] oxadiazine-4a(3H)-carboxylate</p> <p>IUPAC: Not available</p> <p>CAS number: 144171-61-9</p> <p>Common name: None</p> <p>Molecular Weight: 527.84 g/mole</p>	Racemic mixture (50:50 DPX-KN128: IN-KN127)	See structure for DPX-KN128

IN-KN127	<p>CAS name: (R)-methyl 7-chloro-2,5-dihydro-2-[[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-<i>e</i>][1,3,4]oxadiazine-4a(3<i>H</i>)-carboxylate</p> <p>IUPAC: (R)-7-chloro-3-[methoxycarbonyl-(4-trifluoromethoxy-phenyl)-carbamoyl]-2,5-dihydro-indeno[1,2-<i>e</i>][1,3,4]oxadiazine-4a(3<i>H</i>)-carboxylic acid methyl ester</p> <p>CAS number: Not available</p> <p>Molecular Weight: 527.84 g/mole</p>	In-active isomer	
IN-JT333	<p>CAS name: methyl 7-chloro-2,5-dihydro-2-[[[4-(trifluoromethoxy)phenyl]amino]=carbonyl]indeno[1,2-<i>e</i>][1,3,4]oxadiazine-4a(3<i>H</i>)-carboxylate</p> <p>IUPAC: Not available</p> <p>CAS number: 144171-39-1</p> <p>Molecular Weight: 469.81 g/mole</p>	Soil, sediment	
IN-JU873	<p>CAS name: methyl 5-chloro-2,3-dihydro-2-hydroxy-1-[[[4-(trifluoromethoxy)phenyl]=amino]carbonyl]hydrazono]-1<i>H</i>-indene-2-carboxylate</p> <p>IUPAC: Not available</p> <p>CAS number: 144172-25-8</p> <p>Molecular Weight: 457.8 g/mole</p>	Soil	
IN-KB687	<p>CAS name: methyl [4-(trifluoromethoxy)phenyl]carbamate</p> <p>IUPAC: Not available</p> <p>CAS number: 177905-10-1</p> <p>Molecular Weight: 235.16 g/mole</p>	Soil, water	
IN-KG433	<p>CAS name: methyl 5-chloro-2,3-dihydro-2-hydroxy-1-[[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]hydrazono]-1<i>H</i>-indene-2-carboxylate</p> <p>IUPAC: Not available</p> <p>CAS number: Not available</p> <p>Molecular Weight: 515.83 g/mole</p>	Soil, sediment	

IN-KT413	CAS name: sodium 7-chloro-2,5,-dihydro-2-[[[(methoxycarbonyl)[4-(trifluoromethoxy)=phenyl]amino]carbonyl]indeno[1,2-e][1,3,4]oxadiazine-4a(3H)-carboxylic acid IUPAC: Not available CAS number: Not available Molecular Weight: 535.8 g/mole (Na salt); 513.8 g/mole (free acid)	Water, soil, sediment	
IN-MF014	CAS name: methyl 2-[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]hydrazine carboxylate IUPAC: Not available CAS number: Not available Molecular Weight: 293.2041 g/mole	Water	
IN-MH304	CAS name: methyl 6-chloro-3,4-dihydro-1-oxo-1H-2-benzopyran-3-carboxylate IUPAC: Not available CAS number: Not available Molecular Weight: 240.6 g/mole	Water	
IN-MK638	CAS name: [4-(trifluoromethoxy)phenyl]urea IUPAC: Not available CAS number: 82971-90-2 Molecular Weight: 220 g/mole	Soil	
IN-MK643	CAS name: 1,2-dihydro-5-(trifluoromethoxy)-2H-benzimidazol-2-one IUPAC: Not available CAS number: Not available Molecular Weight: 218.1365 g/mole	Soil	
IN-ML437 Hydroxide	CAS name: (5-chloro-2,3-dihydro-x-hydroxy-2-oxo-1H-inden-1-ylidene)-N-[4-(trifluoromethoxy)phenyl]hydrazinecarboxamide IUPAC: Not available CAS Number: Not available Molecular Weight: 413.75 g/mole	Soil (artifact)	 <p>Note: The structure shown is the best representation of IN-ML437 Hydroxide since the position of the hydroxyl group is not definitively known.</p>

IN-ML438	CAS name: 7-chloro-2,4-dihydro-4-[4-(trifluoromethoxy)phenyl]-3H-indeno[2,1-e]-1,2,4-triazin-3-one IUPAC: Not available CAS number: Not available Molecular Weight: 379 g/mole	Soil, sediment	
IN-MP819	CAS name: indeno[1,2- <i>e</i>][1,3,4]oxadiazine-1(2 <i>H</i>)-carboxylic acid, 7-chloro-3,5-dihydro-2-[[[4-(trifluoromethoxy)-phenyl]amino]carbonyl]-, methyl ester IUPAC: Not available CAS Number: Not available Molecular weight: 469.8079 g/mole	Soil, water, sediment	
IN-MS775	CAS name: 7-Chloro-4a,5-dihydro- <i>N</i> -[4-(trifluoromethoxy)phenyl]indeno[1,2- <i>e</i>][1,3,4]oxadiazine-2(3 <i>H</i>)-carboxamide IUPAC: Not available CAS Number: Not available Molecular Weight: 411.766 g/mole	Sediment	
IN-U8F52	CAS name: Not available IUPAC: Not available CAS number: Not available Molecular Weight: 195.61 g/mole	Soil, sediment	
IN-U8E24	CAS name: Not available IUPAC: Not available CAS number: Not available Molecular Weight: 454.77 g/mole	Water, sediment	

IN-UYG24	CAS name: Not available IUPAC: Not available CAS number: Not available Molecular Weight: 294.68 g/mole	Water	
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B.8.1. FATE AND BEHAVIOUR IN SOIL**B.8.1.1. ROUTE AND RATE OF DEGRADATION IN SOIL****B.8.1.1.1. ROUTE OF DEGRADATION****B.8.1.1.1.1. Aerobic degradation**

Three specific studies to describe soil metabolism of indoxacarb were provided in the original Annex II dossier. One study submitted to describe rate of degradation of indoxacarb in soil was also considered providing information on soil metabolism. These four studies are summarised below.

No additional studies on soil metabolism were submitted by applicant for the purpose of renewal.

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Author(s)	Spare, W.C. (1997)
Title:	Aerobic soil metabolism of DPX-MP062, an ~3:1 mixture of DPX-KN128 and IN-KN127
Organisation:	Agrisearch Incorporated – Frederick, MD 21704
Document No:	AMR 3633-95
Dates of experimental work	November 6, 1995 – August 8, 1997
Guidelines:	U.S. EPA 162-1, SETAC (1995)
Deviations :	No major deviation
GLP:	
Previous evaluation:	Yes, Indoxacarb DAR (2001) and addendum 3 (2005)
Acceptability:	The study is still considered valid.

Author(s)	Singles, S.K. (2003);
Title:	Measurement of the enantiomeric ratio of IN-JT333 in soil
Organisation:	DuPont Stine-Haskell Research Center, Newark, Delaware, USA
Document No:	DuPont-12971
Guidelines:	Not applicable
Deviations :	Not applicable
GLP:	Not applicable
Previous evaluation:	Yes, Indoxacarb addendum 3 (2005)
Acceptability:	See RMS comments

MATERIAL AND METHOD**Test material**

Radiolabeled test material:	¹⁴ C-DPX-JW062 (enriched to DPX-MP062 for study)
Lot/Batch #:	[Indanone-1- ¹⁴ C]-DPX-JW062EL HOTC 461
Radiochemical purity:	99.6%
Specific activity:	33.536 µCi/mg
Description:	White powder
Stability of test compound:	Shown to be stable under the conditions of the test.

Experimental conditions

The metabolism of DPX-MP062 in fresh soil was investigated using [indanone-1-¹⁴C]DPX-MP062. Soil characteristics are shown in Table 8-3. Test substance was prepared in acetonitrile and applied to the soil at a rate of 1 mg/kg soil (dry weight).

Soil samples were incubated in darkness under aerobic conditions at 20 ± 2°C and maintained at 75% of 0.33 bar moisture for up to 12 months.

Volatilised radioactivity was trapped in caustic solution and polyurethane foam. Microbial viability was verified by standard plate counts at study initiation, at 4 months, and at the last sampling point.

Soil samples were exhaustively extracted (acetonitrile/water (90/10) shaking, tetrahydrofuran reflux, overnight shaking with 0.5 N HCl and 5% Triton X-100 followed by overnight shaking with 0.5 N NaOH and 5% Triton X-100), and analysed using HPLC and TLC with radiodetection to determine the distribution of extractable radiolabeled degradates.

Unextracted radioactivity was characterised by fractionating into fulvic and humic acids and by combusting the exhaustively extracted soil pellet (humin).

Chiral HPLC chromatography was performed on selected samples to monitor the enantiomeric ratio of DPX-MP062 and IN-JT333 over time.

Table 8-3: Characteristics of test soil

Characteristic	Soil
Soil Name or Designation	Tama
Origin Location	Illinois, USA
pH	6.2
% Sand (2000–50 µm)	<Detection Limit*
% Silt (<50–2 µm)	78.0
% Clay (<2 µm)	20.8
Texture ^a	Silt loam
Organic matter (%)	2.5
Organic carbon (%) ^a	1.45
Cation exchange capacity (meq/100 g)	16.8
Moisture holding capacity at 0.33 bar (%)	22.6
Bulk density (g/cm ³)	1.17
Soil viability (Fungi - bacteria), cfu/g ^c	
Initial	5.2×10^4 - 3.0×10^7
4 months	4.4×10^5 - 4.6×10^7
12 months	5.7×10^5 - 6.7×10^7

* detection limit 2%

^a USDA soil classification system

^b organic carbon = organic matter/1.72

^c cfu = colony forming units

RESULTS AND DISCUSSION

Material balance

Average recovery of applied radioactivity at all sampling intervals ranged from 99–105% (Table 8-5).

Principal degradation products

IN-JT333, an insecticidally active metabolite, reached a maximum concentration of 15% of total radioactivity at Day 7 after test substance application. IN-KG433 reached a maximum concentration of 21% at Days 7 and 14, while IN-JU873 reached its maximum of 8% at Day 21. After 12 months, CO₂ comprised 33% of total radioactivity (Table 8-5).

The enantiomeric ratio of DPX-MP062 and IN-JT333 were monitored using chiral HPLC chromatography at selected time points. The enantiomeric ratios of the R- and S-enantiomers of both compounds remained stable over time. This showed that the enantiomers of both molecules degrade at the same rate in soil.

Table 8-4: Chiral chromatography of DPX-MP062 and IN-JT333

	DPX-MP062 IN-KN127 (R) / DPX-KN128 (S)	IN-JT333 IN-KN124 (R) / IN-KN125 (S)
Purity check of test substance	21.2% / 78.8%	-
Day 14	19.6 % / 80.4 %	7.4 % / 92.6 %
Day 21	21.2 % / 78.4 %	8.3 % / 91.7 %

Non-extractable residue (NER)

Unextractable residues accumulated quickly, and exceeded 10% of applied radioactivity at 14 days post-treatment. Non-extractable radioactivity was distributed throughout the soil fractions (Table 8-5).

Degradation pathway

Degradation of DPX-MP062 in aerobic soil proceeds through a combination of biotic and abiotic processes. IN-JT333 and IN-KG433, CO₂, and bound residues were major degradation products, while IN-JU873 was a minor degradation product.

Table 8-5: Percent distribution of radiolabeled components in aerobic soil after application of ¹⁴C-DPX-MP062*

Time	Average % applied radiolabel											
	DPX-MP062	IN-JT333	IN-KG433	IN-JU873	Polar	Un-known	Fulvic acid	Humic acid	Humin	Organic volatiles ^a	CO ₂	Total
0 Time	103.0	<0.1	0.4	0.7	0.2	<0.1	NP ^b	NP	0.9	NP	NP	105
1 Day	90.0	5.0	2.0	2.0	3.0	0.6	NP	NP	2.0	<0.1	0.2	105
3 Days	70.0	11.0	6.0	2.0	12.0	<0.1	NP	NP	4.0	<0.1	0.4	105
7 Days	43.0	15.0	21.0	5.0	11.0	<0.1	1.7	0.9	4.0	<0.1	1.3	105
14 Days	20.0	14.0	21.0	7.0	14.0	<0.1	6.0	4.0	12.0	0.1	7.0	105
21 Days	13.0	12.0	15.0	8.0	15.0	<0.1	9.0	5.0	15.0	<0.1	12.0	103
30 Days	7.0	9.0	14.0	5.0	16.0	2.0	8.0	8.0	19.0	0.2	15.0	104
2 Months	5.0	5.0	12.0	3.0	15.0	1.7	14.0	6.0	19.0	0.1	23.0	104
3 Months	3.0	3.0	7.0	4.0	17.0	3.0	15.0	7.0	19.0	0.4	25.0	103
4 Months	3.0	3.0	10.0	4.0	16.0	0.7	15.0	8.0	16.0	<0.1	29.0	103
6 Months	2.0	2.0	9.0	5.0	16.0	1.1	12.0	6.0	19.0	0.1	31.0	103
9 Months	2.0	0.3	13.0	5.0	11.0	<0.1	15.0	7.0	17.0	0.1	32.0	102

12 Months	<0.1	<0.1	9.0	2.0	17.0	<0.1	17.0	7.0	15.0	0.2	33.0	99
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^a Cumulative volatile organics trapped in polyurethane foam.

^b NP = Not performed.

* the values reported are mean of two replicates. Individual values used for kinetics are reported in appendix 1

Stability of the isomeric ratio (position paper of Singles (2003))

This position paper provides additional clarification of results from the original soil metabolism study performed with DPX-MP062 in Tama soil (Spare, 1997, AMR 3633-95). The study included chiral chromatography of the enantiomers of DPX-MP062 and IN-JT333. The chiral chromatography shows that the enantiomeric ratio of DPX-MP062 (DPX-KN128 and IN-KN127) remained constant over time, showing that the enantiomers degrade at the same rate in soil. This shows that data generated with either DPX-JW062 or DPX-MP062 (or DPX-KN128) are equivalent. This result is expected since the degradation of DPX-MP062 in soil does not involve the chiral center. It was assumed that the elution order for the IN-JT333 enantiomers (IN-KN125 and IN-KN124) would be the same as for the DPX-MP062 enantiomers, in that the R-isomer would elute before the S-isomer. No standards (IN-KN125 and IN-KN124) were analyzed to support this assumption. Chromatographic evidence from other studies shows that the R- and S-enantiomers of IN-JT333 elute in a reversed order relative to the enantiomers of DPX-MP062 (Singles, 2003). Therefore, the peak assignments made in this report were incorrect. The chromatographic analysis did show that the enantiomeric ratio of IN-JT333 was stable, by chiral analysis of extracts. Using the corrected peak assignments, the enantiomeric ratio of IN-JT333 is consistent with the enantiomeric ratio of DPX-MP062. These data showed no differential degradation of the enantiomers of DPX-MP062 or IN-JT333 in soil, which supports the conclusion that the rate and route of degradation of DPX-MP062 and DPX-JW062 would be equivalent.

RMS Comments (2016)

The study is in compliance with the OECD 307 guideline without major deviations. However, some issues may be noted:

- the polar fraction was not identified, although it represents a great part of unidentified radioactivity (>10 % from day 3, and up to 16 or 17% on several sampling points, till the end of study). No further attempts to identify the polar fraction was made at the time of 1st inclusion as in the soil metabolism study of Singles 2002 performed on the same soil (summarized hereafter in the document), the polar fraction contained multiple peaks, none of which reaching 10% of AR (update 2016: none of individual peaks are reaching 5% of AR at two consecutive points). It is however noted that in the study of spare 97 the whole polar fraction is reaching a higher level than in Single 2002, and it cannot be excluded that an individual peak would reach 5% at two consecutive points. On the more the two soils are not exactly the same, as not having the same characteristics. However, only three metabolites were investigated in the present study of Spare and it could be assumed that the polar fraction contains metabolites that have been further identified in other metabolism studies available and summarized hereafter.
- the chromatograms provided in the study reports showed that the peaks baseline separation was not good, especially for the polar region, and for the metabolites IN-KG433 and IN-JU873. RMS had some doubt on the reliability of the residue level determined for these 3 régions from the chromatographic method used. Applicant indeed confirmed that the chromatographic method used fraction collection to quantify the individual component and did not allow identifying the polar fraction and getting clear separation of some of the peaks.

Then, RMS considers that the study can be still considered valid, but is not sufficient on its own to describe the whole soil metabolism, as a significative part of polar fraction remains unidentified.

RMS also considers that chromatographic method did not provide sufficient resolution to get robust data for metabolites IN-KG433 and IN-JU873. In contrast, DPX-MP062 and metabolite IN-JT333 were well retained and did have a good baseline separation: the data for these compounds are considered reliable for kinetic evaluation (provided under point B.8.1.1.2.1.3.)

Concerning the enantiomeric ratio, the data collected from the chiral chromatography at day 14 and 21 tend to show that the R/S ratios of DPX-MP062 and IN-JT333 are stable throughout time, indicating no preferential degradation of one isomer. It can however be seen that active substance and metabolite do not have the same

ratio (20/80 and 10/90 respectively), which is quite unexpected given that the degradation of indoxacarb to IN-JT333 does not involve the chiral center. Applicant further indicated that this could be due to small failure in fraction collection of IN-KN125 (S enantiomer of IN-JT333) which could not be easily isolated from DPX-KN128 (S enantiomer of DPX-MP062) as the peaks were very close. Peak of IN-KN125 (S) could be abnormally higher as containing small amount of DPX-KN128 (S). This global concern about stability of isomeric ratio is discussed further under point B.8.1.1.3.

* * * *

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Author(s)	Mellor, S.J. (2003)
Title:	¹⁴C-DPX-MP062 (a 3:1 mixture of DPX-KN128 and IN-KN127): Aerobic soil metabolism
Organisation :	Huntingdon Life Science Ltd – Cambridgeshire, England
Document No:	DuPont-8516
Dates of experimental work	November 12, 2001 – January 28, 2003
Guidelines:	U.S. EPA 162-1, SETAC (1995)
Deviations :	No major deviation
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR (2001) and addendum 3 (2005)
Acceptability:	The study is still considered valid.

MATERIALS AND METHODS

Test material

Test material:	DPX-MP062 technical
Lot/Batch #:	MP062-160
Purity:	99.4%
Description:	Off-white solid
CAS#:	144171-61-9
Stability of test compound:	Shown to be stable under the conditions of the test
Radiolabeled test material:	¹⁴ C-DPX-MP062 technical
Lot/Batch #:	[Indanone-1- ¹⁴ C]DPX-MP062: 481 [Trifluoromethoxyphenyl(U)- ¹⁴ C]DPX-MP062: 462
Radiochemical purity:	[Indanone-1- ¹⁴ C]DPX-MP062: >95% [Trifluoromethoxyphenyl(U)- ¹⁴ C]DPX-MP062: >95%
Specific activity:	[Indanone-1- ¹⁴ C]DPX-MP062: 31.4 µCi/mg [Trifluoromethoxyphenyl(U)- ¹⁴ C]DPX-MP062: 48.4 µCi/mg
Description:	Off-white solid
Stability of test compound:	Shown to be stable under the conditions of the test

Soil

A Speyer 2.2 standard soil, a loamy sand, was used. Standard soils are collected from specific locations with restricted access managed to ensure that no pesticides or organic fertilizer treatments take place for at least five years prior to collection.

Experimental conditions

The metabolism of radiolabeled DPX-MP062 (1) labelled with ^{14}C at the indanone-1 carbon and (2) uniformly labelled with ^{14}C in the trifluoromethoxyphenyl ring was investigated in field-fresh Speyer 2.2 loamy sand soil, from Speyer, Germany (Table 8-6).

DPX-MP062 was dissolved in acetonitrile to give two solutions for each radiolabeled form of DPX-MP062 at 100 and 800 $\mu\text{g/mL}$. An aliquot of the 100 and 800 $\mu\text{g/mL}$ solutions was applied to the surface of soil samples (equivalent to 50 g on a dry weight basis) to give nominal concentrations of 0.5 and 4 mg/kg (ppm), respectively; the latter soil sample was prepared for isolation and identification of soil metabolites.

Soil samples were incubated under aerobic conditions in the dark at $20 \pm 2^\circ\text{C}$ at a water content of approximately 50% of its maximum water holding capacity (mwhc) for up to 365 days.

Provisions were made to trap radiolabeled $^{14}\text{CO}_2$ and volatiles.

The microbial biomass of the soils was measured before application of the test substance, approximately four months after treatment and one year after treatment.

The soil was extracted three times with a mixture of acetonitrile and water (4:1 by volume) followed by one more extraction with a mixture of acetone and water (1:1 by volume), where necessary.

Extractable soil radioactivity was quantified by LSC. Radioactive components in soil extracts were quantified by reversed phase HPLC radio detection. Identification of DPX-MP062 and other components was performed variously by reversed phase HPLC, normal phase HPLC, normal phase TLC, UV spectroscopy, and mass spectrometry. Non-extractable ^{14}C -residues were quantified by combustion analysis.

Chiral chromatography was processed to determine the relative proportion of the enantiomers of DPX-MP062 and IN-JT333 in soil extract treated with ^{14}C -Ind label at each sampling time.

Table 8-6 - Soil characteristics

Characteristic	Soil
Soil name or designation	Speyer 2.2
Origin location	Hanhofen, Rheinland-Pfalz, Germany
pH	6.2
% Sand (2000–50 μm)	79.57
% Silt (<50–2 μm)	13.39
% Clay (<2 μm)	7.03
Texture ^a	Loamy sand
Organic carbon (%) ^b	2.8
Cation exchange capacity (meq/100g)	11.8
Maximum water-holding capacity (%)	59.35
Microbial biomass (mg microbial C/kg soil):	
Study start	705.17
120 days after treatment	118.77
Study end	323.57

^a USDA soil classification system

^b organic carbon = organic matter/1.72

RESULTS AND DISCUSSION

Material balance

Material balance for soils treated with [TFMP(U)- ^{14}C]DPX-MP062 ranged from 73.5 to 108% applied radioactivity (AR; two samples <90% AR) (

Table 8-9). Material balance for soils treated with [indanone-1- ^{14}C]DPX-MP062 ranged from 78.0 to 110.4% AR (one sample <90% AR and one sample >110% AR)

Principal degradation products

The distribution of the radiolabeled components in the soil extracts are shown in

Table 8-9 and Table 8-10. The two major degradation products found in soil were IN-JT333 (maximum of 18.6% applied radioactivity) and IN-KT413 (maximum of 18.4% applied radioactivity). Minor metabolites were IN-KG433 (maximum of 8.6% of applied radiolabel), IN-ML438 (maximum of 9.1% of applied radiolabel), and IN-JU873 (maximum of 7.3% of applied radiolabel). IN-MK638 and IN-MP819 accounted for less than 2% of the applied radiolabel at any sampling point.

Carbon dioxide was a significant degradation product with generally higher proportions measured in soil treated with [indanone-1-¹⁴C]DPX-MP062, reaching a maximum of 22.6% AR compared to a maximum of 15.0% AR for soil treated with [TFMP(U)-¹⁴C]DPX-MP062.

Non-extractable residues

Non-extractable residues reached a maximum after 365 days at 61.8% AR for soil treated with [TFMP(U)-¹⁴C]DPX-MP062 and 66.1% AR for soil treated with [indanone-1-¹⁴C]DPX-MP062, respectively.

The non-extractable residues from Days 7, 59, and 120 were extracted under basic and acidic conditions to determine the distribution of radiolabeled material in the fulvic acid, humic acid, and humin fractions, and these are tabulated in Table 8-11. Non-extractable residues for both radiolabels were mostly associated with the humic acid fraction.

Degradation pathway

Degradation of DPX-MP062 proceeded by 3 major pathways: demethylation followed by N-decarboxylation to form IN-JT333, ester hydrolysis to form IN-KT413, and opening of the oxadiazine ring to form IN-KG433. These primary metabolites also degraded further. IN-JT333 undergoes additional transformation *via* opening of the oxadiazine ring to form IN-JU873. IN-JU873 proceeds through de-esterification and decarboxylation reactions and a ring closure to form IN-ML438. Both IN-JU873 and IN-ML438 are further transformed by bridge cleavage to form IN-MK638. IN-MK638 contained only the trifluoromethoxyphenyl radiolabel. IN-KG433 degraded *via* N-decarboxylation to form IN-JU873 and also cleavage of the urea bridge to form IN-KB687 (containing only the trifluoromethoxyphenyl radiolabel). IN-KT413 rearranged to form IN-MP819, which also rearranged to form IN-ML438. Mineralisation to ¹⁴CO₂ and formation of non-extractable (bound) residues were significant degradation processes.

Chiral chromatography

The ratio of the enantiomers of DPX-MP062 (DPX-KN128 and IN-KN127) varied with each sampling point, but generally remained constant around 3:1 to 4:1 (Table 8). Variability may be due to analysis of only a single replicate and the decreasing amount of radioactivity over time in each sample.

The ratios of the enantiomers of IN-JT333 were much more variable, probably due to the very low amounts of radioactivity present at each time point (4 to 14.3% of applied radioactivity, Table 9). Data generated from another study with a higher application rate of DPX-MP062 (1 ppm, with 12 to 14% applied radioactivity as radioactivity IN-JT333), indicated that the enantiomer ratio of IN-JT333 is stable over time in aerobic soil (Reference 6).

Table 8-7: Proportions of enantiomers of DPX-MP062 expressed as percentage of applied radioactivity, in soil extracts from samples treated with [indanone-1-¹⁴C]DPX-MP062

	SAMPLING TIMES (DAYS)							
	0	3	7	14	30	59	90	120
R-enantiomer (IN-KN127 % AR)	24	8.7	7.3	10	4.8	3.5	7.2	3.9
S-enantiomer (DPX-KN128, % AR)	72.5	35.2	29.4	20	12.4	12.6	9.7	11.9
Enantiomeric ratio R:S	1:3.0	1:4.0	1:4.0	1:2.0	1:2.6	1:3.6	1:1.3	1:3.1
Total radioactivity (% AR)	96.5	43.9	36.7	30	17.2	16.1	16.9	15.8

Table 8-8: Proportions of enantiomers of IN-JT333 expressed as percentage of applied radioactivity, in soil extracts from samples treated with [indanone-1-¹⁴C]DPX-MP062

	SAMPLING TIMES (DAYS)			
	3	7	14	30
R-enantiomer (% AR)	0.4	0.9	3.0	1.9
S-enantiomer (% AR)	10.0	13.4	8.8	2.1
Enantiomeric ratio R:S	1 :25	1 :15	1 :2.9	1 :1.1
Total radioactivity (% AR)	10.4	14.3	11.8	4.0

Table 8-9: Percent distribution of radiolabeled components in aerobic soils after application of [trifluoromethoxyphenyl (U)-¹⁴C]DPX-MP062

Sampling point (Days)	DPX-MP062	IN-KT413 ^a	IN-MK638	IN-KG433 ^b	IN-JU873 ^b	IN-ML438	IN-MP819	IN-JT333	Oth. ^c	CO ₂	Org. volatil	NER ^d	Total Recover
0	95.4	nd ^e	nd	nd	nd	nd	nd	nd	nd	ns ^f	ns	1.7	97.1
3	42.9	10.7	1.0	2.8	7.3	nd	1.6	10.4	4.7	nd	nd	9.1	90.5
7	38.2	13.3	2.9	nd	nd	nd	0.8	18.6	6.1	nd	nd	13.8	93.7
14	23.9	11.9	nd	2.2	1.3	nd	1.0	11.2	9.8	0.5	nd	33.5	95.3
30	18.6	4.3	nd	nd	nd	6.2	nd	7.5	6.7	3.9	0.2	44.5	91.9
59	15.1	2.4	0.4	0.8	0.8	4.7	0.8	2.9	7.5	7.0	nd	50.0	92.4
90	10.0	1.4	1.8	1.7	nd	7.6	nd	1.9	5.0	9.0	0.2	57.9	96.5
120	7.5	4.0	1.7	2.8	nd	3.7	nd	3.1	5.3	8.4	0.2	52.9	89.6
162	7.6	1.2	0.7	nd	nd	8.7	nd	0.8	4.7	9.6	nd	74.7	108.0
220	12.8	0.8	0.7	nd	nd	3.7	0.9	1.6	4.9	13.7	nd	34.4	73.5
269	6.0	2.2	0.6	nd	0.3	3.9	nd	1.4	6.0	15.0	nd	58.9	94.3
365	7.8	nd	nd	nd	nd	7.6	nd	2.1	2.2	8.8	nd	61.8	90.3

^a IN-KT413 was comprised of two peaks, due to ionisation of the molecule.^b Tentatively identified on the basis of HPLC retention time.^c Others: Combination of unidentified radioactivity in the chromatogram, no single peak exceeded 4.3% of the applied radioactivity.^d Non-extractable residues^e Not detected^f Not sampled**Table 8-10: Percent distribution of radiolabeled components in aerobic soils after application of [indanone-1-¹⁴C]DPX-MP062**

Sampling point (Days)	DPX-MP062	IN-KT413 ^a	IN-KG433 ^b	IN-JU873 ^b	IN-ML438	IN-MP819	IN-JT333	Oth. ^c	CO ₂	Org volatil	NER ^d	Total Recover
0	96.5	nde	nd	nd	nd	nd	nd	nd	nsf	ns	0.8	97.3
3	43.9	18.4	4.1	nd	nd	1.3	10.4	7.1	1.4	nd	7.7	94.3
7	36.7	17.1	8.6	nd	nd	nd	14.3	2.4	3.2	nd	10.8	93.1
14	30.0	11.1	2.0	4.0	nd	nd	11.8	3.1	6.9	nd	22.7	91.6
30	17.2	7.9	4.7	nd	3.2	nd	4.0	6.8	11.9	nd	35.2	90.9
59	16.1	12.5	0.8	1.0	8.9	nd	2.5	10.8	5.4	nd	34.2	92.2
90	16.9	0.7	nd	nd	3.9	nd	4.8	12.9	14.5	nd	38.8	92.5
120	15.8	1.9	2.7	nd	4.1	nd	3.2	6.8	16.1	nd	42.4	93.0
162	16.2	0.8	nd	nd	9.1	nd	4.0	3.3	15.4	nd	46.3	95.1
220	8.3	nd	nd	nd	9.0	nd	2.1	6.7	22.6	nd	61.7	110.4
269	6.4	2.6	nd	nd	6.9	nd	2.1	5.4	20.1	nd	34.5	78.0
365	9.7	nd	nd	nd	7.8	nd	2.4	2.3	19.1	nd	66.1	107.4

^a IN-KT413 was comprised of two peaks, due to ionisation of the molecule.^b Tentatively identified on the basis of HPLC retention time.^c Others: Combination of unidentified radioactivity in the chromatogram, no single peak exceeded 5.8% of applied radioactivity, and no single peak was >5% two consecutive points.^d Non-extractable residues^e Not detected^f Not sampled

Table 8-11: Characterisation of non-extractable soil radioactivity

Sampling time (Days)	Soil fraction	% of applied radioactivity	
		[TFMP(U)- ¹⁴ C] DPX-MP062 residues	[Indanone-1- ¹⁴ C] DPX-MP062 residues
7	Fulvic acid	1.6	1.8
	Humic acid	7.0	4.8
	Humin	5.2	4.2
59	Fulvic acid	5.8	4.9
	Humic acid	25.2	15.2
	Humin	19.0	14.2
120	Fulvic acid	6.7	8.2
	Humic acid	27.5	20.8
	Humin	18.7	13.4

CONCLUSION

DPX-MP062 degraded rapidly in aerobic soils to yield IN-JT333, IN-KT413, and IN-KG433. Subsequently, IN-JT333 and IN-KG433 degrade rapidly to multiple minor products including IN-JU873, IN-ML438, IN-KB687, and IN-MK638. IN-KT413 rearranges to form the minor metabolite IN-MP819 that further rearranged to IN-ML438. Mineralisation to form CO₂ and the formation of non-extractable residues are major degradation pathways.

RMS (2016)

DT₅₀ calculations have been removed from this summary, as updated kinetic evaluation according to FOCUS recommendations (FOCUS kinetic, 2014) is available for indoxacarb and its major metabolites. See Point B.8.1.1.2.1.2.

The study is in compliance with the OECD 307 guideline without major deviations. However, some issues may be discussed:

Microbial biomass

It is noticeable that the microbial biomass undergoes significant variation along the study duration. Although the microbial biomass was at least 1 % of the total organic carbon at the end of the study, the biomass level decreased with more than factor 5 and represents less than 0.5 % at 120 days, and then increased again to reached 1.1 % at the end of study duration. However this is not considered to have impact on the level of residue of the active substance and its major metabolites.

Chiral chromatography

Chiral chromatography was performed for sample treated with [¹⁴C-Ind]label at several sampling times. It appears that the ratios were not stable with variation from 1/3 or 1/4 to 1/2 of 1/1 for indoxacarb and from 1/25 to 1/1 for metabolite IN-JT333. This is explained in the study being due to decreasing of radioactivity over time in each sample (for indoxacarb) and to the very low radioactivity present at each sampling time (for metabolite). However, RMS notes that this explanation is quite not reliable, as each item is detected at levels that are much higher than the theoretical LOQ (up to 15% AR as indoxacarb at the end of the study, and between 4 and 14% of AR for metabolite over time in each sample). The variations are likely a result of the procedures used to isolate the peaks in preparation for chiral analyses.

The results from this chiral chromatography do not provide conclusive evidence of the stability of the ratio. However, it does not either show a trend in the ratio evolution through time, which would reveal faster degradation of one isomer. This global concern about stability of isomeric ratio is discussed further under point B.8.1.1.3.

* * * *

The following study was already assessed in the original indoxacarb DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Author(s)	Singles, S.K. (2002)
Title:	Aerobic soil metabolism of ¹⁴C-DPX-JW062
Organisation:	DuPont Experimental Station, Wilmington, Delaware, USA
Document No:	AMR 2803-93, Revision No. 1
Dates of experimental work	November 12, 2001 – January 28, 2003
Guidelines:	U.S. EPA 162-1, SETAC (1995)
Deviations :	No major deviation
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR Addendum 3 (2005)
Acceptability:	The study is still considered valid.

MATERIALS AND METHODS

Test materials

Test material:	DPX-JW062 technical
Lot/Batch #:	JW062-33
Purity:	98.6%
Description:	white powder
CAS#:	144171-61-9
Stability of test compound:	Shown to be stable under the conditions of the test
Radiolabeled test material:	¹⁴ C-DPX-JW062 technical
Lot/Batch #:	[Indanone-1- ¹⁴ C]DPX-JW062: 421 or 428 [Trifluoromethoxyphenyl(ring)- ¹⁴ C]DPX-JW062: 423 or 433
Radiochemical purity:	[Indanone-1- ¹⁴ C]DPX-JW062: ≥98% (both lots) [Trifluoromethoxyphenyl(ring)- ¹⁴ C]DPX-JW062: ≥98% (both lots)
Specific activity:	[Indanone-1- ¹⁴ C]DPX-JW062 File no. 421: 55.5 µCi/mg [Indanone-1- ¹⁴ C]DPX-JW062 File no. 428: 45.1 µCi/mg [Trifluoromethoxyphenyl(ring)- ¹⁴ C]DPX-JW062 File no. 423: 54.0 µCi/mg [Trifluoromethoxyphenyl(ring)- ¹⁴ C]DPX-JW062 File no. 433: 46.4 µCi/mg
Description:	White powder
Stability of test compound:	Shown to be stable under the conditions of the test.

Experimental conditions

The metabolism of DPX-JW062 in fresh soil was investigated in two separate experiments using [indanone-1-¹⁴C]DPX-JW062 (HOTC File no. 421 and HOTC File no. 428) and [trifluoromethoxyphenyl(ring)-¹⁴C]DPX-JW062 (HOTC File no. 423; and HOTC File no. 433). Soil characteristics are shown in Table 8-12. Radiolabeled DPX-JW062 was applied to soil in acetone at a rate of 7 mg/kg soil (dry weight). Soils were incubated in the dark at 25°C and soil moisture of 75% of 0.33 bar for up to 1 year. Provisions were made to trap radiolabeled CO₂. Microbial viability was measured at study initiation. Soil samples were exhaustively extracted using a 4-step process: 1) wrist-action shaking in acetonitrile/water, 9/1 (v/v) (2 × 1 hour); 2) shaking in methylene chloride/methanol, 7/3 (v/v) (1 × 1 hour) for the original study OR refluxing in tetrahydrofuran (1 × 2 hours) for the supplemental study; 3) shaking overnight in 0.5 N HCl/5% Triton X-100, 75/25 (v/v); and 4) shaking overnight in 0.5 N NaOH/5% Triton X-100, 75/25 (v/v). Soil extracts were concentrated and analysed by LSC and HPLC. Extracted soil samples were combusted to determine levels of non-extractable

residues (NER). Non-extractable (bound) residues were further fractionated and analysed by LSC and combustion analysis. The volatiles traps were assayed directly by LSC.

Table 8-12: Characteristics of test soil

Characteristic	Soil	
Soil Name or Designation	Tama	
Origin Location	USA	
	Batch 1	Batch 2
pH	6.3	6.2
% Sand (2000–50 µm)	15.2	9.6
% Silt (<50–2 µm)	63.6	66.0
% Clay (<2 µm)	21.2	24.4
Texture ^a	silt loam	silt loam
Organic matter (%)	2.7	2.4
Organic carbon (%) ^b	1.6	1.4
Cation exchange capacity (meq/100 g)	16.6	16.7
Moisture holding capacity at 0.33 bar (%)	30.0	23.0
Initial microbial biomass (cfu/g soil) ^c	9.0 e ⁶	2.2 e ⁷

^a USDA classification system

^b % organic carbon = % organic matter/1.72

^c cfu = colony forming units

RESULTS AND DISCUSSION

Material balance

The material balance ranged from 84 to 116% for the [indanone-1-¹⁴C]DPX-JW062 samples. For the [trifluoromethoxyphenyl(ring)-¹⁴C]DPX-JW062 samples, the material balance ranged from 68 to 106%. Mean recovery of theoretically applied radiolabel across all samples was 95 ± 7% for [indanone-1-¹⁴C]DPX-JW062 and 91 ± 9% for [trifluoromethoxyphenyl(ring)-¹⁴C]DPX-JW062.

Principal degradation products

DPX-JW062 degraded quickly under aerobic conditions. The major degradation products (>10% AR) were IN-JT333 (maximum of 16.68% applied radiolabel), IN-KG433 (maximum of 16.88% applied radiolabel), non-extractable residues (maximum of 65.55% applied radiolabel), and ¹⁴CO₂ (maximum of 35.73% applied radiolabel). IN-KG433 and IN-JT333, an insecticidally active metabolite, formed rapidly in soil and declined during the course of the study. Low levels of IN-ML438 (maximum 7.55% AR) and IN-JU873 (maximum 7.52% AR) were found in soils treated with both radiolabels. IN-KB687 (maximum 6.89% AR), IN-MK643 (maximum 8.22% AR), and IN-MK638 (maximum 6.95% AR) were minor cleavage products generated from the trifluoromethoxyphenyl label. The proposed degradation product IN-ML437-OH appears to be an artefact of the analytical procedure. The structure was proposed solely on the basis of LC/MS and no standard has been successfully synthesised to confirm the proposed structure. Further, this compound has never been confirmed in any other soil metabolism study, including an additional study performed in Tama soil.

Non-extractable residues (NER)

Non-extractable (bound) residues reached a maximum of 52 (indanone label) to 66% (trifluoromethoxyphenyl label) of the applied radioactivity. Radioactivity remaining in the soil was fractionated into humic acid, fulvic acid, and humus fractions. The proportions of applied radiolabel associated with each fraction can be found in Table 8-17.

Degradation pathway

Two major degradative pathways occur in soil: demethylation followed by N-decarboxylation to form IN-JT333 and opening of the oxadiazine ring to form IN-KG433. IN-JT333 undergoes additional transformation *via* opening of the oxadiazine ring to form IN-JU873, a minor soil degradation product. IN-JU873 is further transformed by bridge cleavage to form the minor degradation products IN-MK643 and IN-MK638. Alternately,

IN-JU873 proceeds through de-esterification and decarboxylation reactions and a ring closure to form IN-ML438, also a minor soil degradation product. IN-KG433 is further transformed through cleavage of the urea bridge to form IN-KB687 (minor degradation product).

Mineralisation to $^{14}\text{CO}_2$ and formation of non-extractable (bound) residues were significant degradation processes.

Table 8-13: Original study, Percent distribution of radiolabeled components in aerobic soil treated with [indanone-1-¹⁴C]DPX-JW062

Time	Percentage of applied radioactivity									
	DPX-JW062	IN-JT333	IN-ML438	IN-JU873	IN-KG433	IN-ML437-OH	¹⁴ CO ₂	Polar ^a	NER ^b	Total
Day 2	53.26	10.57	nd	0.12	9.89	nd	0.38	6.6	2.09	100
Day 3	39.76	16.68	7.55	6.81	6.06	nd	1.62	3.07	26.96	116
Day 7	17.39	6.95	6.27	1.31	1.65	nd	4.71	15.33	30.77	97
Day 15	8.2	6.16	3.8	0.92	2.12	1.6	8.42	12.18	37.47	90
Day 21	6.02	8.09	3.91	1.09	1.8	1.19	11.64	8.16	40.4	89
Month 1	3.86	4.48	2.91	0.84	3.53	1.32	10.64	8.51	42.99	84
Month 2	4.2	3.37	2.46	1	2.21	2.42	18.57	nd	45.45	95
Month 3	2.37	1.82	1.72	0.32	1.43	3.09	12.46	2.65	52.09	88
Month 4	nd	nd	nd	nd	nd	6.53	18.52	4.5	45.47	84
Month 6	nd	nd	nd	nd	nd	4.66	19.96	1.85	47.24	85
Month 9	0.26	nd	0.45	0.89	1.06	0.87	27.13	nd	47.69	91
Month 12	0.55	nd	nd	nd	1.17	nd	35.73	nd	45.19	96

^a Polar peak was resolved into at least 5 components with each less than 10% AR.

^b Unextracted radioactivity remaining in soil pellet after Extraction 3.

^c O = Original and R = Supplement

^d nd = not detected

Table 8-14: : Original study, Percent distribution of radiolabeled components in aerobic soil treated with [TFMP-¹⁴C]DPX-JW062

Time	Percentage of applied radioactivity												
	DPX-JW062	IN-JT333	IN-ML438	IN-JU873	IN-KG433	IN-KB687	IN-ML437-OH	IN-MK638	IN-MK643	¹⁴ CO ₂	Polar	Bound residues _a	Total Recovery
Day 2	66.57	12.9	nd	7.52	7.43	5.04	0.03	0.07	nd	0	nd	1.82	101

Day 3	24.61	11.26	3.78	5.88	16.88	5.63	6.84	3.78	5.63	0.09	nd	21	106
Day 7	14.64	9.64	2.5	1.89	1.65	6.89	2.75	6.71	4.39	0.28	nd	30.08	93
Day 15	8.11	10.46	4.08	1.15	0.72	0.72	2.3	4.08	5.57	0.7	nd	37.69	89
Day 21	7.74	6.34	4.84	1.1	0.84	nd	2.68	6.95	3.74	0.74	0.88	45.58	92
Month 1	6.16	7.53	5.77	1.44	1.87	1.23	2.34	3.63	3.59	1.51	0.74	46.51	89
Month 2	4.21	2.54	3.45	0.11	2.12	nd	1.56	nd	nd	1.75	nd	38.4	68
Month 3	4.74	2.14	4.21	nd	2.42	2.08	3.15	2.91	3.7	0.75	nd	65.55	94
Month 4	nd	nd	nd	nd	nd	1.5	6.58	2.05	4.84	1.91	nd	56.24	83
Month 6	nd	nd	nd	nd	nd	nd	8.3	nd	8.22	4.05	nd	55.08	82
Month 9	2.5	nd	1.33	nd	0.93	3.26	0.1	5.01	0.24	3.53	nd	54.66	79
Month 12	2.19	2.91	nd	1.06	1.38	3.53	0.62	5.14	nd	7.46	nd	51.34	79

Table 8-15: Supplemental study, Percent distribution of radiolabeled components in aerobic soil treated with [indanone-1-¹⁴C]DPX-JW062

Time	Percentage of applied radioactivity									
	DPX-JW062	IN-JT333	IN-ML438	IN-JU873	IN-KG433	IN-ML437-OH	¹⁴ CO ₂	Polar ^a	NER ^b	Total
Day 0	99.87	nd ^d	nd	nd	nd	nd	0	nd	0.4	102
Day 5	20.58	12.35	5.73	4.15	3.11	0.3	5.45	nd	20.54	96
Day 7	26.03	8.04	6.59	nd	nd	3.97	8.45	nd	21.9	99
Day 14	11.07	5.83	4.56	nd	1.7	3.01	16.33	nd	29.23	87
Day 21	10.16	6.52	6.99	nd	nd	3.18	19.88	nd	41.69	98
Month 1	5.21	3.84	4.4	nd	1.04	1.65	21.99	0.95	39.03	99
Month 2	8.78	4.42	4.22	0.33	0.29	2.71	25.31	nd	38.77	96
Month 3	7.76	3.51	5.89	2.63	0.47	3.14	26.11	nd	40.63	96

Month 4	9.93	2.06	3.52	nd	0.3	1.52	25.65	nd	41.2	95
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Table 8-16: Supplemental study, Percent distribution of radiolabeled components in aerobic soil treated with [TFMP-¹⁴C]DPX-JW062

Time	Percentage of applied radioactivity												
	DPX-JW062	IN-JT333	IN-ML438	IN-JU873	IN-KG433	IN-KB687	IN-ML437-OH	IN-MK638	IN-MK643	¹⁴ CO ₂	Polar	Bound residues _a	Total Recovery
Day 0	98.13	nd ^c	nd	nd	nd	nd	nd	nd	nd	0	nd	0.52	104
Day 5	17.31	17.01	5.01	nd	6.24	3.77	4.08	3.32	3.77	0.29	4.04	20.05	96
Day 7	22.62	12.07	4.76	3.89	1.14	5.9	6.07	5.56	4.49	0.39	0.32	18.2	94
Day 14	10.74	4.66	3.44	nd	2.32	6.84	3.87	4.6	5.12	0.86	0.76	47.65	99
Day 21	8.06	7.07	5.96	nd	nd	nd	4.03	4.33	4.92	1.41	0.96	45.76	92
Month 1	6.4	3.32	2.93	nd	2.32	2.32	7.06	3.85	6.57	1.88	1.06	47.21	94
Month 2	8.48	5.71	4.59	nd	nd	0.38	3.19	1.57	6.62	3.42	0.95	51.34	93
Month 3	10.62	3.93	5.23	nd	nd	0.34	1.78	1.8	1.75	4.51	1.6	57.43	97
Month 4	7.19	2.08	7.19	nd	nd	nd	1.41	nd	3.43	5.35	3.61	51.45	89

Table 8-17 - Distribution of non-extractable components in soil organic matter

Sample	% applied radiolabel			
	Total bound	Fulvic acid	Humic acid	Humus
[Indanone-1- ¹⁴ C]DPX-JW062				
Month 4 - O ^a	45.47	11.95	14.48	19.04
Month 4 - R ^a	41.20	17.96	4.08	19.16
Month 6 - O	47.24	13.01	16.24	17.99
Month 9 - O	47.69	13.66	10.78	23.25
Month 12 - O	45.19	13.95	10.42	20.82
[Trifluoromethoxyphenyl(ring)- ¹⁴ C]DPX-JW062				
Day 2 - O	1.82	0.45	0.20	1.17
Day 3 - O	21.00	8.48	4.01	8.51
Day 5 - R	20.05	10.30	2.35	7.40
Day 7 - O	30.08	14.91	3.36	11.81
Day 7 - R	18.20	7.27	2.47	8.46
Day 14 - R	47.65	15.72	4.91	27.02
Day 15 - O	37.70	15.86	7.48	14.35
Day 21 - O	45.58	19.89	6.76	18.93
Day 21 - R	45.75	14.87	5.12	25.77
Month 1 - O	46.50	17.45	6.25	22.81
Month 1 - R	47.22	13.21	5.17	28.83
Month 2 - O	38.41	21.95	3.88	12.57
Month 2 - R	51.34	19.11	5.53	26.70
Month 3 - O	65.55	37.25	10.22	18.08
Month 3 - R	57.42	21.18	5.01	31.24
Month 4 - O	56.24	14.62	12.30	29.32
Month 4 - R	51.45	18.41	6.99	26.05
Month 6 - O	55.08	10.54	14.45	30.09
Month 9 - O	54.66	9.13	10.55	34.98
Month 12 - O	51.33	8.82	13.22	29.30

^a O = Original and R = Supplement

CONCLUSIONS

DPX-JW062 degrades rapidly in aerobic soils to yield IN-JT333 and IN-KG433. Subsequently, IN-JT333 and IN-KG433 degrade rapidly to multiple minor products including IN-JU873, IN-ML438, IN-KB687, IN-MK638, and IN-MK643. Mineralisation to form CO₂ and formation of non-extractable residues are major degradation pathways.

RMS (2016)

The study is in compliance with the OECD 307 guideline without major deviations. However, some issues may be noted:

This study is a revision of the original aerobic soil metabolism study of Rhodes (1997). The results of two (a 12 months' and a 4 months' study) aerobic soil degradation studies were revised because the automatic integration of the on-line radiographic detector failed to include all relevant peaks in samples at 4 and 6 months after treatment. Chromatograms were re-interpreted using manual integration. Peak areas have been calculated by multiplying the peak width at half peak height with the peak height. The manual integration method has been performed according a common method and proven valid by the Wilcoxon paired sample test (comparing manual integration and the original automatic integration for samples where integration did not fail).

Regardless of this, as already stated during first EU inclusion review, the reliability of the analyses at month 4 and 6 of the original study can be questioned for active substance and metabolites IN-JT333, IN-ML438 and IN-KG433 as no residues of these compounds were detected at these sampling time although significant level are detected at previous and following sampling point. Applicant indicated that a different analytical method was used to accommodate the analytical challenges for the months 9 and 12 samples. The samples from day 0

through month 6 were analyzed by HPLC with online flow radiochemical detector, while the sample from months 9 and 12 were expected to have very low radioactivities. Therefore the method of HPLC with fraction collector for off line LSC counting was used to increase the sensitivities. Though the samples from Months 4 and 6 had enough radioactive counts for the radiochemical detector, the metabolites of low concentration could be below the detection limit. That could have been the case for the metabolites IN-JT333 and IN-KG433. However, this is not considered having potential impact on the degradation rate, since kinetic evaluation is not performed beyond 120 days.

Metabolite IN-ML437OH and unidentified polar fraction

One metabolite IN-ML437OH is detected at level > 5% at two consecutive sampling points in soil treated with ^{14}C -TFMP in the original study (6.58 and 8.3 % at month 4 and month 6 respectively). Applicant considered this item was an artefact of the analytical procedure, and no standard has been successfully synthesised to confirm the proposed structure. It is indicated in the study that “this compound has never been confirmed in any other soil metabolism study, including an additional study performed in Tama soil”. RMS however indicates that in the additional study performed with Tama soil (Spare 1997, summarized above) a significant part of radioactivity remained unidentified.

In addition, it cannot also be excluded that the polar fraction in the soil treated with Ind^{14}C could contain individual peaks exceeding 5% at two consecutive points. The polar peak can represent up to 15% and 12% of AR in this soil at day 7 and 15, but was not further investigated at these particular sampling points. It was further investigated in sampling of month 1 (8.51 % AR) of the same soil, and the highest peak contained 40% of the peak area in the sample. This resolution was used to demonstrate during first review that it was unlikely that individual peak in the polar fraction would be > 10% AR, at any sampling points. RMS is of the opinion that this demonstration is however too weak to demonstrate that no individual peak would exceed 5% at two consecutive sampling points.

As a consequence, considering these two latter issues, RMS is of the opinion that further investigation should be done on the identity of metabolite IN-ML437-OH and on the identification and characterisation of the polar fraction. A data gap is thus proposed.

Reliability of data for kinetic evaluation:

In the “original study” the concentration of the parent at day 0 has not been determined. For the kinetic evaluation, the %AR at T0 for the original study was thus set equal to the %AR at T0 of from the supplemental study (i.e. 104 and 102% respectively for Indanon and TFMP label). This is not considered acceptable since the extraction procedure were not exactly the same for the original and the supplemental study. The %AR at T0 should be set to 100% for the original study.

Concerning the “supplemental study”: Time intervals of sampling at the beginning of the study seem to be not adapted to the degradation rate of the active substance (T0, T5, T7). It does not allow having a good description of the decline of active substance and formation and decline of metabolite. Indeed, in the first sampling interval (5 days) the level of indoxacarb residue has decreased of more than 80%, and the level of IN-JT33 residue reaches its maximum at 12.4 and 17% for both labels respectively. RMS considers that, although this experiment is reliable to describe the route of degradation, the data are not robust enough to be used for kinetic fitting.

* * * *

The following study was already assessed in the original DAR (2000) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

It is submitted to support rate of degradation of active substance in soil but is also considered to provide information on soil metabolism, as several metabolite appear in this study at occurrence level higher than in previous study. It is then summarized hereafter.

Author(s)	Rhodes, B.C. (1997)
Title:	Degradation rates of DPX-MP062 in soil
Organisation:	DuPont Experimental Station, Wilmington, Delaware, USA
Document No:	AMR 4251-96
Dates of experimental work	November 12, 2001 – January 28, 2003
Guidelines:	SETAC (1995)
Deviations :	No major deviation
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR (2000)
Acceptability:	The study is still considered valid.

MATERIALS AND METHODS

Test material

1. Radiolabeled test material: [¹⁴C]DPX-MP062EL
 Lot/Batch #: [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062EL
 DuPont HOTC #462
 Radiochemical purity: [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062EL: >99%
 Specific activity: [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062EL: 48.4 µCi/mg
 Description: White powder
 Stability of test compound: Shown to be stable under the conditions of the test.

Test soils

Three soils were chosen to represent conditions of use; Speyer sandy loam, Nambsheim silt loam, and Chino loam. The test soils were received fresh and stored for 1–9 months at 5°C prior to use. Soils were collected from specific locations with restricted access to ensure that no pesticides or organic fertiliser treatments had taken place for at least five years prior to collection. Soils were equilibrated in flasks at 25°C for two weeks prior to use, were sieved (2-mm) and their microbial viability was verified by induced respirometry and standard plate counts.

Table 8-18: Characteristics of test soils

Characteristic	Soil		
Soil Name or Designation	Speyer	Nambsheim	Chino
Origin Location	Germany	France	California, USA
pH	5.9	7.7	8.2
% Sand (2000-50 µm)	76.0	32.0	43.2
% Silt (<50-2 µm)	17.6	55.6	46.0
% Clay (<2 µm)	6.4	12.4	10.8
Texture ^a	Sandy loam	Silt loam	Loam
Organic matter (%)	3.3	1.6	1.4
Organic carbon (%) ^b	1.92	0.93	0.81
Cation exchange capacity (meq/100 g)	11.5	9.8	20.5
Maximum water-holding capacity (%)	49.0	39.8	43.0
Initial Soil Respirometry (mg C/100 g soil)	48	19	29
Initial Plate Counts (cfu/g soil)	5.5 x 10 ⁶	9.7 x 10 ⁶	1.8 x 10 ⁷
Final Plate Counts (cfu/g soil)	3.0 x 10 ⁶	5.3 x 10 ⁶	2.0 x 10 ⁷

^a USDA soil classification system

^b organic carbon = organic matter/1.72

Experimental conditions

The rate of degradation of [trifluoromethoxyphenyl (ring(U))-¹⁴C]DPX-MP062 was performed in three soils at 20°C and 50-60% of maximum water-holding capacity of soil. One soil was also tested at 10°C (Table 8-18). Test substance was prepared in acetone and applied to the soil at a rate of 1 mg/kg soil. Treated soils were incubated in the dark for up to 120 days. Provisions were made to trap radiolabeled volatiles, but no data on volatiles was presented in the report. Microbial viability was verified by induced respirometry and standard plate counts at study initiation and at the last sampling point. Samples were extracted with acetonitrile/water, 4/1 (v/v), followed by acetone/0.1 N hydrogen chloride, 1/1 (v/v). Soil extracts were analysed by LSC and reversed-phase HPLC with radiochemical detection. Extracted soil samples were combusted to determine levels of non-extractable residues (NER).

RESULTS AND DISCUSSION

Material balance

Recovery of applied radioactivity ranged from 86.8–113.2% at all sampling intervals across all test soils (Table 8-19).

Principal degradation products

IN-JT333 reached a significant concentration (maximum 10-11% of applied radioactivity in Speyer, Nambsheim-20, and Nambsheim-10 soils), but declined to <1% by Day 120. IN-KG433 reached maxima of 30 and 40% of applied radioactivity in Nambsheim-20 and Nambsheim-10 soils, respectively, and remained at 21 and 36% after 120 days. IN-ML438, IN-JU873, IN-MK643, and IN-MK638 were all seen in at least one of the test soils, but levels >10% of applied radioactivity were sporadic (Table 8-19).

Non-extractable residue (NER)

The maximum amount of NER at the last sampling point ranged from 4.9 to 46.9% of applied radioactivity (Table 8-19).

Degradation pathway

Two major degradation pathways occur in these soils: demethylation followed by N-decarboxylation to form IN-JT333 and opening of the oxadiazine ring to form IN-KG433. IN-JT333 undergoes additional transformation *via* opening of the oxadiazine ring to form IN-JU873, a minor soil degradation product. IN-JU873 is further transformed by bridge cleavage to form the minor degradation products IN-MK643 and IN-MK638. Alternately, IN-JU873 proceeds through de-esterification and decarboxylation reactions and a ring closure to form IN-ML438, also a minor soil degradation product. IN-KG433 is further transformed through cleavage of the urea bridge to form IN-KB687 (minor degradation product). Mineralisation to ¹⁴CO₂ and formation of non-extractable (bound) residues were significant degradation processes.

Table 8-19: Percent distribution of radiolabeled components in aerobic soils after application of [trifluoromethoxyphenyl(U)-¹⁴C]-DPX-MP062

Soil	Day	% Applied radiolabel											Total recover
		DPX-MP062	IN-JT333	IN-ML438	IN-JU873	IN-KG433	IN-KB687	IN-MK638	IN-MK643	Pol ar	Ot h ^a	Soil NER	
Speyer	0	109.0	nd ^b	nd	nd	nd	nd	nd	nd	nd	nd	2.0	111.2
	1	100.0	nd	nd	nd	nd	nd	nd	nd	nd	nd	3.7	104.1
	3	88.5	7.6	nd	nd	nd	nd	nd	nd	nd	nd	6.2	102.5
	7	72.4	nd	1.4	5.1	nd	nd	nd	nd	nd	nd	11.7	96.3
	10	46.6	10.2	8.9	2.2	1.2	nd	1.1	1.0	nd	nd	29.2	105.9
	14	49.6	11.2	8.0	nd	nd	nd	nd	1.0	nd	1.1	25.6	102.0

	24	41.0	6.5	9.7	nd	0.8	nd	nd	1.2	nd	0.7	32.1	97.1
	30	34.6	4.0	9.6	1.0	0.6	0.6	0.7	2.5	2.4	nd	37.9	94.4
	62	32.5	1.1	7.0	nd	nd	0.5	1.9	1.9	1.3	nd	43.9	93.3
	90	28.4	1.5	7.9	nd	nd	2.4	nd	nd	nd	0.5	44.3	91.9
	120	26.3	0.7	6.7	nd	nd	3.0	nd	nd	nd	nd	42.8	86.8
Nambs heim (20°C)	0	106.0	nd	nd	nd	nd	nd	nd	nd	nd	nd	2.5	108.1
	1	108.3	0.8	nd	nd	nd	nd	nd	1.0	nd	nd	3.2	113.2
	3	97.5	1.0	nd	nd	1.5	nd	nd	nd	nd	nd	2.2	101.7
	7	70.2	4.9	nd	2.7	15.2	nd	nd	nd	nd	nd	9.4	102.7
	10	38.3	8.7	1.5	3.8	24.7	nd	2.4	9.7	nd	nd	12.7	104.5
	14	39.3	9.8	nd	1.3	27.8	nd	2.8	5.1	nd	nd	14.0	103.2
	24	27.0	8.9	1.4	6.5	29.6	nd	5.4	5.1	nd	nd	15.3	103.2
	30	21.8	6.3	2.0	12.9	14.1	nd	nd	9.5	nd	nd	22.5	97.6
	62	19.1	2.0	2.6	nd	22.0	nd	3.8	3.3	2.6	nd	33.0	90.1
	90	13.7	2.2	5.6	nd	29.4	nd	0.6	0.5	nd	nd	49.6	104.0
	120	13.4	0.6	4.8	nd	20.8	nd	1.4	nd	nd	nd	46.9	91.2
Nambs heim(1 0°C)	0	106.0	nd ^b	nd	nd	nd	nd	nd	nd	nd	nd	2.5	108.1
	1	103.0	nd	nd	nd	nd	nd	nd	nd	nd	nd	2.1	104.8
	3	85.2	2.1	nd	nd	3.5	nd	nd	9.2	nd	nd	5.3	105.4
	7	81.7	4.8	2.0	0.7	6.3	nd	nd	4.6	nd	nd	3.8	103.6
	10	74.1	7.0	0.7	1.1	9.4	nd	1.3	6.5	nd	nd	4.5	104.4
	17	61.1	7.1	nd	nd	16.9	nd	0.9	10.0	nd	nd	5.9	102.1
	21	60.8	8.8	nd	5.5	16.8	nd	nd	3.3	nd	nd	7.4	102.5
	30	37.4	9.1	nd	3.2	21.9	0.6	4.4	2.0	nd	6.6	8.9	93.8
	62	30.1	9.9	1.5	4.0	39.7	nd	2.0	4.8	nd	nd	10.5	102.4
	90	19.7	7.1	nd	nd	8.5	nd	28.1	6.5	nd	2.5	17.7	101.9
	120	15.5	nd	nd	nd	35.6	nd	6.6	8.3	3.7	nd	28.6	101.2
Chino	0	106.1	nd	nd	nd	nd	nd	nd	nd	nd	0.8	2.6	109.2
	1	104.9	nd	nd	nd	nd	nd	nd	nd	nd	1.1	3.4	109.2
	3	103.0	nd	nd	nd	nd	nd	nd	nd	nd	nd	1.1	104.0
	7	101.0	nd	nd	nd	nd	nd	nd	nd	nd	nd	4.9	105.4
	10	86.0	nd	0.8	nd	nd	nd	nd	12.0	nd	5.2	2.2	105.8
	14	97.3	nd	nd	nd	nd	nd	nd	nd	nd	4.7	2.6	104.6
	24	102.1	nd	nd	nd	nd	nd	nd	nd	nd	0.9	2.8	106.1
	30	98.0	nd	nd	nd	nd	nd	nd	nd	nd	nd	4.4	101.9
	62	94.8	nd	nd	nd	nd	nd	nd	2.3	nd	nd	7.7	104.3
	90	100.0	nd	nd	nd	nd	nd	nd	nd	nd	nd	1.9	103.4
	120	84.4	1.9	nd	nd	nd	0.8	1.0	0.9	4.1	3.5	4.9	104.0

^a Others = Unidentified extracted radioactivity.

^b Not detected

In all soils except the Chino soil, DPX-MP062 degraded extensively in aerobic soils to yield IN-JT333 and IN-KG433. Subsequently, IN-JT333 and IN-KG433 degrade rapidly to multiple minor products including IN-JU873, IN-ML438, IN-KB687, IN-MK638, and IN-MK643. Mineralisation to form CO₂ and the formation of non-extractable residues are major degradation pathways. The rate of degradation of DPX-MP062 did not correlate with soil pH. The Chino soil was left fallow for several years and flooded several times. Therefore, this soil does not provide representative data for DPX-MP062. Therefore, this data is excluded from further use for exposure modelling.

Comments RMS 2015

The study is in compliance with the OECD 307 guideline without major deviations. However, some issues may be noted:

Global recovery

Reliability of the global recovery could be questioned because $^{14}\text{CO}_2$ has not been measured. However, other experiments in Speyer 2.2 and Tama soil with same radio label ^{14}C -TFMP (Mellor, 2003 and Single 2002) showed very low level of CO_2 release (no release until day 30 and increase to 9.6% at 162 days in Speyer 2.2 soil; no more than 4% during 9 month in Tama soil). Considering similar level of release in the present experiment, mass balance would still be in an acceptable range (< 110%).

Extract analyses

It is noted that samples from 2nd extraction were not analysed when their total contain of AR was <7%. This implies that the residue level of DPX-MP062 and its major metabolite could be underestimated at some of the sampling points. This is the case for the soil Speyer 2.2 for which samples of soil extract 2 containing each more than 5% AR were not characterized at day 7, 10, 14 and 24. However, this is not considered as a major deviation from OECD 307 to adequately describe the route of degradation study.

Chino soil

No degradation is observed in the chino soil, although the biomass viability was checked and did not seem to be abnormal or significantly lower than the other soils. It is noted that this phenomenon is also observed in the field study at Madera, CA, which was the source for chino loam soil used in the current study. It was further justified by applicant by the fact that the soil was left fallow during several years and flooded several times prior to study and that the identity of microbial colonies was not determined and could be different than in a normal agricultural soil.

It is considered by RMS that the soil history (flooding) might explain the very slow degradation in the chino soil. Although this soil does not differ from other tested soils on biomass viability and typical characteristics predictive of degradation potential, it is clear that the results are outliers compared to all other tested soils (all DT_{50} < 10.3 days). This soil will not be considered further for kinetic evaluation.

B.8.1.1.2. Anaerobic degradation

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb.

Author(s)	Smyser, B.P. (2002)
Title:	Anaerobic aquatic metabolism of [indanone-1-^{14}C] DPX-JW062 and [trifluoromethoxyphenyl(U)-^{14}C] DPX-JW062, a racemic (50:50) mixture of DPX-KN128 and DPX-KN127
Document No:	AMR 3236-94, Revision No. 2
Guidelines:	U.S. EPA 162-3
Deviations :	See summary
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR Addendum 3 (2005)
Acceptability:	Study superseded by new one.

- Test material: ^{14}C -DPX-JW062
 Lot/Batch #: [I- ^{14}C]DPX-JW062, HOTC 428 [Trifluoromethoxyphenyl-ring- ^{14}C]DPX-JW062, HOTC 423
 Radiochemical purity: 98.2% (HOTC 428), 99.8% (HOTC 423)

The anaerobic degradation study AMR 3236-94, Revision No. 2, originally submitted under EU Rev8 Point IIA 7.1.1.1.2 and conducted with test material ^{14}C -DPX-JW062, was conducted under guideline U.S. EPA 162-3. A review of this study indicates that it does not meet the current guidelines (OECD 307); deviations include 1) no aerobic phase was established in the study before flooding; 2) study duration was too long (365 days) without microbial activity confirmation at the end of the study; 3) transitional unknown metabolites were present above the 5% threshold.

A new study (DuPont-35049) was conducted following the current guideline (OECD 307). Within this new study: 1) an aerobic phase was established until approximately 50% of the parent degraded; 2) The duration of the study was 122 days with microbial activity determined before and the end of the test; 3) All major metabolites ($\geq 5\%$ AR) were identified.

AMR 3236-94, Revision No. 2 is superseded with the anaerobic soil metabolism study DuPont-35049 following OECD 307 guideline.

Study submitted to the EU for the first time for the purpose of renewal.

Data point:	CA 7.1.1.2/01
Author(s)	Allan, J. (2015)
Title:	^{14}C-Indoxacarb (DPX-KN128): Anaerobic degradation in soil
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-35049
Dates of experimental work	
Guidelines:	OECD 307, OPPTS 835.4200, SETAC (1995)
Deviations :	None
GLP:	Yes
Previous evaluation:	No, study submitted for the purpose of renewal.
Acceptability:	The study is considered valid.

MATERIALS AND METHODS

Test Material

Radiolabelled test material:	^{14}C indoxacarb (DPX-KN128) technical	
Lot/Batch #:	Indanone-1- ^{14}C indoxacarb:	1643850
	(abbreviated as [I- ^{14}C]indoxacarb	
	[Trifluoromethoxyphenyl- ^{14}C (U)]indoxacarb:	1643851A
	abbreviated as [TFMP- ^{14}C]indoxacarb	
Radiochemical purity:	[I- ^{14}C]indoxacarb:	98.8%
	[TFMP- ^{14}C]indoxacarb:	99.5%
Specific activity:	[I- ^{14}C]indoxacarb:	49.50 $\mu\text{Ci}/\text{mg}$
	[TFMP- ^{14}C]indoxacarb:	46.3 $\mu\text{Ci}/\text{mg}$
Stability of test compounds:	Stable during study	

Test soil

A Nambenheim sandy loam was used. Standard soils are collected from specific locations with restricted access managed to ensure that no pesticides or organic fertiliser treatments take place for at least five years prior to collection.

Table 8-20 : Soil characteristics

Parameter	Results/units
Geographic location	Nambenheim, Alsace, France
Texture class	Sandy Loam
Sand	58%
Silt	31%
Clay	11%

pH	7.6
Organic matter	2.5%
Organic carbon ^a	1.5%
Initial & final soil biomass or microbial activity	810.5 and 501.7 (µg C/ g dry soil)
Cation exchange capacity (CEC)	9.6 meq/100 g
Field moisture capacity at 0.33 bar	12.6%
Field moisture capacity at 15 bar	5.6%
Bulk density (disturbed)	1.05 g/cc

^a Per study protocol, % organic carbon = % organic matter/1.724.

Experimental conditions

The test soil was treated with [I-¹⁴C]indoxacarb or [TFMP-¹⁴C]indoxacarb at a concentration of 0.4 µg a.s./g dry weight soil and incubated in darkness at approximately 20 ± 2°C. Aerobic conditions were maintained for 2.5 days by passing a steady stream of humidified air through the test apparatus. After the addition of the water phase, anaerobic conditions were promoted by passing a steady stream of humidified nitrogen through the test apparatus. The flow-through systems were designed to trap evolved carbon dioxide (CO₂) and volatile organic compounds.

Microbial biomass was determined at zero time and Day 122. Two samples (one per radiolabel) were withdrawn immediately after treatment (Day 0) and at 2, 2.5, 4, 6, 9, 16, 23, 31, 52, 77, 111, and 122 days after application. The soil systems were extracted and combined with the overlying water (Days 2 through 122).

Soil samples were extracted three times with acetonitrile/water (100 mL of 4:1; v/v). Extracts were combined and triplicate aliquots were analysed by liquid scintillation counting (LSC) to determine total extractable radioactivity. Sub-samples (100 mL) were concentrated using a rotary evaporator to dryness. The residue was re-dissolved using a combination of acetonitrile and 0.01 M ammonium acetate for a final volume of 10 mL and analysed by reverse phase HPLC (Thermo Scientific, Polar Acclaim II C18 (250 mm × 4.6 mm × 5 µm id), eluted with a gradient of 0.01 M ammonium acetate (aq) and acetonitrile. Extracted soil samples were combusted to determine levels of non-extractable residues. Degradation products were identified by mass spectrometry and by co-chromatography by HPLC using authentic standards.

RESULTS AND DISCUSSION

Mass balance

Material balance for the [I-¹⁴C]indoxacarb label ranged from 97.1 to 105.4%. Material balance for the [TFMP-¹⁴C]indoxacarb label ranged from 99.0 to 103.9% (Table 8-22).

Bound and extractable residues

Non-extractable residues reached maximum levels at study termination of 37.3% and 33.4% for the [I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb labels, respectively (Table 8-22). The non-extractable residue from Day 52 and Day 122 samples was extracted under basic and acidic conditions to determine the distribution of radiolabel in the fulvic acid, humic acid, and humin fractions (Table 8-21).

Table 8-21: Distribution of unextractable components in soil organic matter

Soil fraction (52-day)	% of Radiolabel	
	[I- ¹⁴ C]indoxacarb	[TFMP- ¹⁴ C]indoxacarb
Fulvic acid	4.0	3.4
Humic acid	2.6	2.2
Humin	19.6	17.6
Total Unextracted:	26.8	23.8
Soil fraction (122-day)	% of Radiolabel	
	[I- ¹⁴ C]indoxacarb	[TFMP- ¹⁴ C]indoxacarb
Fulvic acid	2.7	2.4
Humic acid	2.4	2.2
Humin	21.1	20.5
Total Unextracted:	32.1	29.6

Volatilisation

Volatile radioactivity, identified as $^{14}\text{CO}_2$ represented up to 1.2% of applied radioactivity at Day 122 (Table 8-23).

Transformation of parent compound

Under anaerobic conditions, levels of indoxacarb at the point of flooding (Day 2.5) in the soil decreased from 53.7 and 52.0% of applied radioactivity for [I- ^{14}C]indoxacarb and [TFMP- ^{14}C]indoxacarb labels, respectively, to 2.5 and 2.9% after 122 days (Table 8-23).

The DT_{50} and DT_{90} values for indoxacarb were 2.08 and 33.2 days, respectively (Table 8-24). The kinetic calculation was performed using CAKE (ver 2.0) via first-order multi-compartment regression analysis.

Seven major degradation products were formed in anaerobic soil, which were IN-KT413, IN-U8E24, IN-MP819, IN-KN125, IN-MS775, IN-U8F52, and IN-MK638. IN-KT413 accounted for 25.2 and 23.2% of applied radioactivity for [I- ^{14}C]indoxacarb and [TFMP- ^{14}C]indoxacarb labelled treated soil at Day 4, respectively, declining to 2.5 and 2.9% after 122 days. IN-U8E24 accounted for 39.4/40.0% of applied radioactivity for the [I- ^{14}C]indoxacarb and [TFMP- ^{14}C]indoxacarb treated soil at Day 23, respectively, declining to 17.6 and 19.5% after 122 days. IN-MP819 accounted for 5.9 and 4.8% of applied radioactivity for the [I- ^{14}C]indoxacarb and [TFMP- ^{14}C]indoxacarb treated soil, respectively at Day 52, declining to 3.8 and 3.5% after 122 days. IN-KN125 accounted for 10.1 and 10.6% of applied radioactivity for [I- ^{14}C]indoxacarb and [TFMP- ^{14}C]indoxacarb treated soil, respectively at Day 4, declining to 0.4 and 0.5% after 122 days. IN-MS775 increased during the study and accounted for 28.2 and 34.4% of applied radioactivity for the [I- ^{14}C]indoxacarb and [TFMP- ^{14}C]indoxacarb treated soil, respectively, at Day 122. In the [I- ^{14}C]indoxacarb treated soil, IN-U8F52 reached a maximum of 14.7% of applied radioactivity at Day 31 and then declined to 5.8% after 122 days. In the [TFMP- ^{14}C]indoxacarb treated soil, IN-MK638 reached a maximum of 9.4% of applied radioactivity at Day 31 and then declined to 2.6% after 122 days.

The unassigned radioactivity observed was consisted of multiple minor components, all of which were below 5% AR. The proposed degradation pathway for indoxacarb in anaerobic soil is shown and explained in the section CA 7.1.1.4 (Overall assessment: Route of degradation).

Table 8-22: Percent distribution of applied radioactivity and mass balance in water/sediment systems treated with indoxacarb

Day	% AR [I- ^{14}C]indoxacarb			
	Labelled CO_2 /volatiles	Sediment extractable	Sediment NER	Total recovered
Aerobic conditions				
0	N/A	98.9	1.5	100.4
2	0.9	97.9	4	102.7
2.5	1.0	92.1	3.9	97.1
After establishment of anaerobic conditions				
4	1.0	94.5	5.2	100.8
6	1.0	90.8	6.8	98.7
9	1.0	86.7	10.1	97.8
16	1.1	88.7	15.5	105.4
23	1.1	84.4	18.8	103.5
31	1.1	79.8	21.0	102.0
52	1.2	70.7	26.8	98.7
77	1.2	72.3	27.4	100.8
111	1.2	68.6	31.3	101.1
122	1.2	65.2	37.3	103.7
Day	% AR [TFMP- ^{14}C]indoxacarb			
	Labelled CO_2 /volatiles	Sediment extractable	Sediment NER	Total recovered

Aerobic conditions				
0	N/A	99.5	1.3	100.9
2	0.0	98.6	3.3	101.9
2.5	0.0	96.3	3.4	99.7
After establishment of anaerobic conditions				
4	0.0	94.1	4.9	99.0
6	0.0	95.4	6.3	101.7
9	0.0	89.9	9.4	99.3
16	0.1	87.8	15	102.8
23	0.1	83.4	16.5	100
31	0.1	79.2	19.8	99.0
52	0.1	80.1	23.8	103.9
77	0.1	74.7	27.5	102.3
111	0.1	68.8	31.3	100.2
122	0.1	69.5	33.4	103.0

ND = No detection

Table 8-23: Percent distribution of applied radioactivity in anaerobic systems treated with ^{14}C -indoxacarb

% AR [I- ^{14}C]indoxacarb											
Day	DPX-KN128	IN-U8F52	IN-KT413	IN-U8E24	IN-MP819	IN-KN125	IN-MS775	Others*	CO ₂ (volatiles)	NER	Total recovered
Aerobic conditions (pre-flooding)											
0	96.1	0.0	2.7	0.0	0.0	0.0	0.0	0.0	N/A	1.5	100.4
2	54.9	0.5	20.5	12.8	1.3	7.8	0.0	0.0	0.9	4.0	102.7
2.5	53.7	2.0	18.4	10.4	1.1	6.5	0.0	0.0	1	3.9	97.1
After establishment of anaerobic conditions (post-flooding)											
4	30.9	3.6	25.2	23.6	1.2	10.1	0.0	0.0	1	5.2	100.8
6	22.2	6.7	23.7	25.8	2.5	9.9	0.0	0.0	1	6.8	98.7
9	14.6	4.9	16.4	39.8	3.2	7.7	0.0	0.0	1	10.1	97.8
16	7.8	12.7	10.8	39.3	5.1	6.7	2.7	3.5	1.1	15.5	105.4
23	6.4	12.5	7.2	39.4	5.0	4.4	2.6	6.8	1.1	18.0	103.5
31	5.0	14.7	3.3	29.7	4.7	4.2	6.8	11.5	1.1	21.0	102.0
52	3.9	14.4	2.6	19.8	5.9	1.8	13.1	9.3	1.2	26.8	98.7
77	3.7	11.5	1.1	28.5	4.2	1.3	18.8	3.3	1.2	27.4	100.8
111	3.4	7.8	1.5	23.5	3.5	1.3	23.9	3.6	1.2	31.3	101.1
122	2.5	5.8	0.7	17.6	3.8	0.4	28.2	6.3	1.2	37.3	103.7
% AR [TFMP- ^{14}C]indoxacarb											
Day	DPX-KN128	IN-KT413	IN-U8E24	IN-MK638	IN-MP819	IN-KN125	IN-MS775	Others*	CO ₂ (volatiles)	NER	Total recovered
Aerobic conditions (pre-flooding)											
0	95.2	4.3	0.0	0.0	0.0	0.0	0.0	0.0	N/A	1.3	100.9
2	55.4	21.1	13.8	0.0	1.7	6.7	0.0	0.0	0.0	3.3	101.9
2.5	52.0	23.0	13.5	0.0	1.3	6.5	0.0	0.0	0.0	3.4	99.7
After establishment of anaerobic conditions (post-flooding)											
4	32.0	23.2	22.7	3.8	1.9	10.6	0.0	0.0	0.0	4.9	99.0
6	25.3	22.3	28.4	5.4	3.1	10.0	0.9	0.0	0.0	6.3	101.7
9	15.9	18.4	35.0	3.4	5.2	10.4	0.5	1.1	0.0	9.4	99.3
16	12.1	11.2	33.0	9.4	4.9	7.6	2.9	6.7	0.1	15.0	102.8
23	8.3	6.9	40.0	6.4	5.3	5.8	3.2	7.6	0.1	16.5	100.0
31	6.2	4.7	38.0	7.2	5.0	3.7	6.4	7.9	0.1	19.8	99.0
52	4.2	1.6	36.7	8.6	4.8	2.9	12.9	8.4	0.1	23.8	103.9
77	3.7	1.1	32.6	5.0	3.7	1.6	19.6	7.3	0.1	27.5	102.3
111	3.0	0.0	28.4	3.1	3.6	0.9	27.5	2.3	0.1	31.3	100.2

122	2.9	0.0	19.5	2.6	3.5	0.5	34.4	6.2	0.1	33.4	103.0
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NER = Non-extractable residue

N/A = Not applicable

others*: consisted of multiple components, no single component was $\geq 5\%$ AR

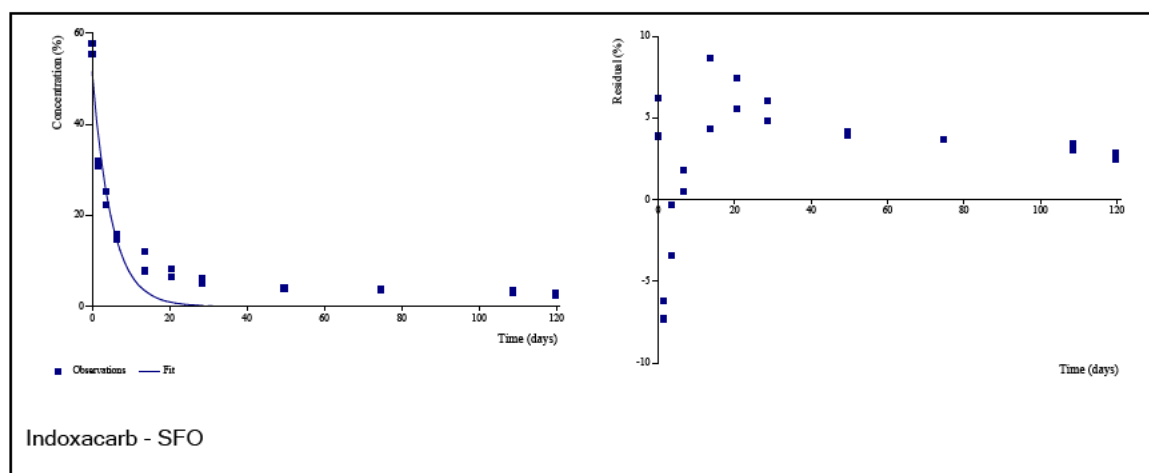
Rate of degradation

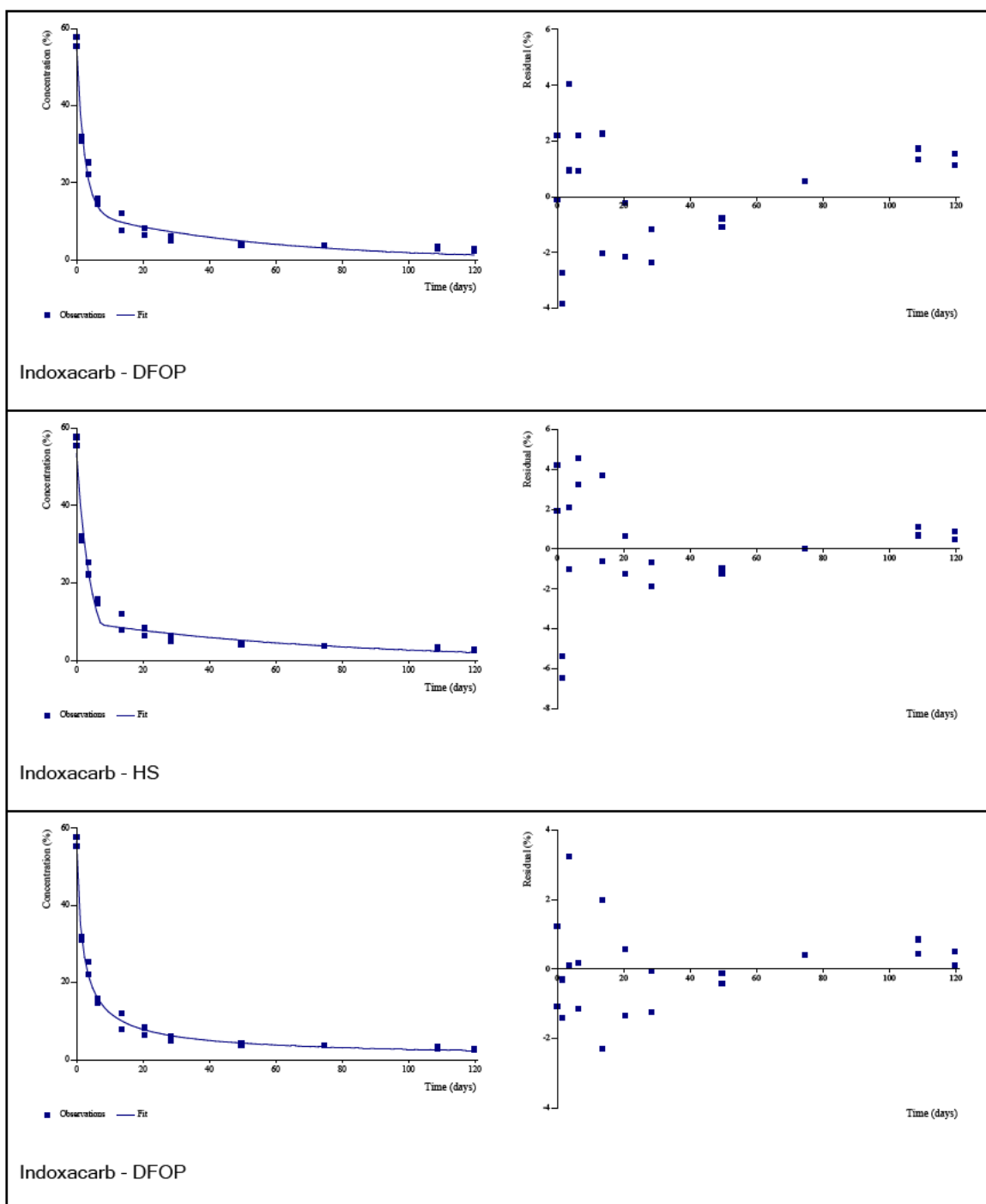
The DT_{50} was determined based on FOCUS (2014) recommendations. Applicant had run all models, but only SFO and FOMC were presented in Table 13 on page 55 in the study report DuPont-35049. Other two models HS and DFOP were not reported since they did not provide an improved statistical fit compared FOMC model but the full summary of kinetics fitting is provided tables below (applicant provided full summary and visual fits upon request of RMS)

Table 8-24 : DT_{50} and DT_{90} value for indoxacarb in anaerobic system

Components Modeled	Model	Optimized parameters \pm standard error	χ^2	r^2	DT_{50} (days)	DT_{90} (days)
Sandy Loam Parent only	SFO	M_0 (%AR) = 51.51 ± 3.111 k (d^{-1}) = 0.1996 ± 0.02858	25.2	0.9541	3.47	11.5
Sandy Loam Parent only	FOMC	M_0 (% AR) = 56.47 ± 0.901 α = 0.6843 ± 0.04205 β = 1.189 ± 0.169	3.86	0.9944	2.08	33.2
Sandy Loam Parent only	HS	M_0 (% AR) = 53.47 ± 1.902 $K1$ = 0.2386 ± 0.02026 $K2$ = 0.01358 ± 0.005833 Tb = 7.409 ± 1.045	14.7	0.9726	2.91	46.8
Sandy Loam Parent only	DFOP	M_0 (% AR) = 55.49 ± 1.469 $K1$ = 0.4294 ± 0.04837 $K2$ = 0.01855 ± 0.00479 g = 7754 ± 0.0325	9.86	0.9856	2.33	43.6

Visual fit for degradation of indoxacarb in anaerobic system





CONCLUSION

The study provides evidence that indoxacarb degrades rapidly ($DT_{50}=2.08$ days) in anaerobic soil through degradation to multiple metabolites and through binding to sediment. At recommended use rates, indoxacarb is unlikely to result in any significant environmental loading of the soil environment.

RMS (2016)

The study is acceptable.

A new metabolite IN-U8E24 reaches a maximum level of 40.0% at 23 days (anaerobic phase) and is accordingly considered as a major anaerobic metabolite. However, it is noticeable that this metabolite is also seen at more

than 10 % AR (13.2% after 2 days) during the preliminary aerobic phase, with samples treated with either [^{14}C -Ind] or [^{14}C -TFMP] labels. Thus, as the study conditions and soil characteristics are very close to aerobic study conditions (soil Nambshiem, 20°C, 50% of 0-bar moisture), it should also be considered as a major aerobic metabolite although not seen in any of the soil metabolism studies. RMS proposal was to include this metabolite in the residue definition for risk assessment for all compartments.

In response to RMS request, applicant acknowledged that risk assessment should be performed for this metabolite, although not seen in the soil aerobic metabolism studies. Risk assessment was conducted by applicant using DT_{50} developed from anaerobic condition and Koc parameter from EPA EPI Suite 4.11 modeling (see point B.8.1.2. for details of Koc determination), but this proposition was found not reliable by RMS since DT_{50} derived from anaerobic conditions data cannot obviously represent degradation behavior under aerobic condition. In addition, no details of the kinetic evaluation of the anaerobic degradation rate for IN-U8E24 were provided by applicant.

Thus, as no reliable DT_{50} was available for this metabolite, a data gap is identified by RMS for DT_{50} (see also B.8.1.2. for details of RMS comments on Koc from EPISuite for metabolite IN-U8E24).

B.8.1.1.1.3. Photodegradation in soil

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Author(s)	Berg, D.S. (1997);
Title:	Photodegradation of radiolabeled DPX-JW062, a racemic mixture of DPX-KN128 and IN-KN127, on soil under simulated sunlight
Document No:	AMR 2818-93
Guidelines:	
Deviations :	No major deviation
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR (2000)
Acceptability:	

MATERIALS AND METHODS

Test material

1. Radiolabeled test material:	^{14}C DPX-JW062 technical
Lot/Batch #:	[Indanone-1- ^{14}C]DPX-JW062: HOTC: 428 [Trifluoromethoxyphenyl(U)- ^{14}C]DPX-JW062: HOTC: 423
Radiochemical purity:	[Indanone-1- ^{14}C]DPX-JW062: >98.2% [Trifluoromethoxyphenyl(U)- ^{14}C]DPX-JW062: >99.8%
Specific activity:	[Indanone-1- ^{14}C]DPX-JW062: 45.1 $\mu\text{Ci}/\text{mg}$ [Trifluoromethoxyphenyl(U)- ^{14}C]DPX-JW062: 54.0 $\mu\text{Ci}/\text{mg}$
Description:	White powder
Stability of test compound:	Shown to be stable under the conditions of the test.

Experimental conditions

The photodegradation of DPX-JW062 (1) uniformly labeled with carbon-14 in the trifluoromethoxyphenyl(U) and (2) indanone-1- ^{14}C labeled was studied on non-sterile silt loam soil (Table 8-25).

Soil thin layers (~2 mm thickness) were treated with 450 µL of radiolabeled DPX-JW062 dissolved in methylene chloride (0.308 mg/L for trifluoromethoxyphenyl(U)-¹⁴C ring, 0.298 mg/mL for indanone-1-¹⁴C) to give an application rate of approximately 1 kg a.s./ha.

One set of the treated thin layers were placed into ventilated Lucite[®] boxes with a quartz glass window in the upper side.

The temperature of the soil thin layers was maintained at 25 ± 1°C with a continuous flow of circulated, temperature-controlled water. These samples were continuously irradiated for up to 15 days with simulated sunlight from a xenon arc light source (equivalent to 41.7 days of natural sunlight at a latitude of 39.4°N).

Since this study is performed under continuous irradiation, the study conditions are expected to exaggerate soil photolysis.

The other set of samples (non-irradiated) were incubated at 25 ± 1°C in the dark simultaneously.

Provisions were made for trapping radiolabeled CO₂ and organic volatiles.

For each radiolabeled form of DPX-JW062, a single irradiated and non-irradiated plate was taken for analysis at each time point.

The soil was extracted a total of three times with 15–20 mL of acetonitrile: water, 90:10, v:v, followed by one extraction of 15–20 mL with acetonitrile:0.01% sodium dodecyl sulphate 90:10, v:v. The first set of soil extracts were radioassayed and analysed by HPLC separately from the second set.

The composition of the second set did not differ greatly from the first set.

The non-extractable residues (NER) were combusted and analysed by LSC.

The volatile organic traps were assayed directly by LSC.

Table 8-25: Soil characteristics

Characteristic	Soil
Soil name or designation	Tama silt loam
Origin location	Illinois, U.S.A.
pH	6.2
% Sand (2000–50 µm)	<2.0
% Silt (<50–2 µm)	78.0
% Clay (<2 µm)	20.8
Texture ^a	Silt loam
Organic carbon (%) ^b	4.3
Cation exchange capacity (meq/100g)	16.8
Maximum water-holding capacity (%)	22.6

^a USDA soil classification system

^b Organic carbon = organic matter/1.72

RESULTS AND DISCUSSION

Material balance

Recovery of radiolabel from non-irradiated and irradiated samples ranged from 93.5 to 101.2% for the [trifluoromethoxyphenyl(U)-¹⁴C] label, and from 92.2 to 101.8% for the [indanone-1-¹⁴C] label. Radioactivity was detected in ethylene glycol volatile traps in both radiolabeled irradiated samples at 0.1% on only Days 13 and 15. Radioactivity was not detected in volatile traps from the non-irradiated systems.

After 15 days of irradiation, the amount of the [trifluoromethoxyphenyl(U)-¹⁴C]DPX-JW062 mineralised to ¹⁴CO₂ was 2.9% of the applied radioactivity. In the same time frame, [indanone-1-¹⁴C]DPX-JW062 mineralised to ¹⁴CO₂ was 4.5% of the applied radioactivity.

Principal degradation products

The major soil photolysis degradation products (maximum % of applied in parenthesis) extracted from soil treated with [trifluoromethoxyphenyl(U)-¹⁴C]-DPX-JW062 were IN-KB687 (22.0% at Day 13 and declining to 16.2% at Day 15) and IN-JT333 (2.5% at Day 8 and declining to 1.6% at Day 15). The major degradation products from the non-irradiated soil of the same radiolabel were IN-KB687 (12.6% at Day 15), and IN-JT333 (5.7% at Day 15). Composition of radioactivity for [trifluoromethoxyphenyl(U)-¹⁴C]DPX-JW062 is in Table 8-26.

The major soil photolysis degradation products extractable from soil treated with indanone-1-¹⁴C-DPX-JW062 were IN-JT333 (2.4% at Day 6, declining to 1.4% at Day 15). In the non-irradiated indanone-1-¹⁴C samples, IN-JT333 was the degradate (5.8% at Day 13, declining to 3.5% by Day 15). Composition of radioactivity for [indanone-1-¹⁴C]DPX-JW062 is in Table 8-27.

After 15 days of irradiation, 2.9% of the applied [trifluoromethoxyphenyl(U)-¹⁴C]DPX-JW062 and 4.5% of the [indanone-1-¹⁴C] DPX-JW062 radioactivity mineralised to ¹⁴CO₂. Radiolabeled carbon dioxide was not a significant photolysis degradation product of either radiolabeled non-irradiated samples (<0.1% by Day 15).

Non-extractable residues

For all samples tested, unextracted radioactivity never exceeded 10% of the applied radioactivity.

Degradation pathway

The primary degradation pathway involves the loss of a carboxymethyl group to form IN-JT333, followed by hydrolysis of an amide bond to form IN-KB687 and degradation of the ring system to form CO₂. Based on the rate of degradation, photolysis is a minor process in the environment.

Table 8-26: Composition of radioactivity from irradiated and control soils treated with trifluoromethoxyphenyl(U)-¹⁴C-DPX-JW062 (results are expressed as % of applied)

Sample	Days	DPX-JW062	IN-JT333	IN-KB687	Others ^a	¹⁴ CO ₂	Volatiles	NER ^b	Total
Irradiated	0	98.8	1.0	0.0	0.0	0.0	0.0	0.2	100.0
	1	84.5	1.8	5.6	4.0	0.2	0.0	1.4	97.5
	4	73.2	1.4	11.0	7.4	0.8	0.0	2.9	96.7
	6	77.2	1.3	9.5	2.7	1.2	0.0	3.2	95.1
	8	67.8	2.5	14.9	5.2	1.6	0.0	4.6	96.6
	11	66.2	2.2	16.4	3.9	2.0	0.0	4.6	95.3
	13	59.8	2.2	22.0	2.7	2.4	0.1	4.3	93.5
	15	62.4	1.6	16.2	5.8	2.9	0.1	5.8	94.8
Non-irradiated	1	96.6	1.0	0.8	1.4	0.0	0.0	0.2	100.0
	4	92.9	2.3	3.3	0.6	0.0	0.0	0.4	99.5
	6	93.4	3.5	3.9	0.1	0.0	0.0	0.5	101.2
	8	93.4	2.7	4.0	0.1	0.0	0.0	0.4	100.6
	11	88.8	3.7	6.0	0.3	0.0	0.0	0.5	99.3
	13	86.8	3.6	8.6	0.1	0.0	0.0	0.5	99.6
	15	76.4	5.7	12.6	0.0	0.0	0.0	0.5	95.2

^a One or more unidentifiable peaks

^b Non-extractable residues

Table 8-27: Composition of radioactivity from irradiated and control soils treated with indanone-1-¹⁴C-DPX-JW062 (results are expressed as % of applied)

Sample	Days	DPX-JW062	IN-JT333	Others ^a	¹⁴ CO ₂	Volatiles	NER ^b	Total
Irradiated	0	99.7	0.0	0.0	0.0	0.0	0.3	100.0

	1	93.6	0.1	3.0	0.3	0.0	3.6	100.6
	4	80.0	1.4	2.6	1.3	0.0	9.3	94.6
	6	79.3	2.3	4.2	2.1	0.0	9.8	97.7
	8	78.1	0.3	2.9	2.9	0.0	9.4	93.6
	11	73.4	2.4	4.4	3.6	0.0	8.8	92.6
	13	77.8	0.7	4.2	4.2	0.1	6.9	93.9
	15	69.4	1.4	7.0	4.5	0.1	9.8	92.2
Non-irradiated	1	98.3	0.7	0.5	0.0	0.0	0.8	100.3
	4	96.4	0.2	0.8	0.0	0.0	2.6	100.0
	6	89.4	2.6	2.2	0.0	0.0	3.8	98.0
	8	96.7	2.7	1.5	0.0	0.0	3.9	101.8
	11	89.0	4.6	1.7	0.0	0.0	5.4	100.7
	13	85.2	5.8	1.2	0.0	0.0	4.9	97.1
	15	93.5	3.5	0.4	0.0	0.0	4.8	102.2

^a One or more unidentifiable peaks

^b Non-extractable residues

Chiral HPLC chromatography was performed on dark control samples at Day 11 and showed a ratio of R/S enantiomers of 52/48% in the soil treated with ¹⁴C-Ind and 49/51 in soil treated with ¹⁴C-TFMP.

CONCLUSION

Degradation of DPX-JW062 was faster on irradiated soil than identical samples under non-irradiated conditions. After continuous exposure at 25°C for 15 days, DPX-JW062 degraded with a calculated average half-life of 28.9 days. Under non-irradiated conditions, the half-life averaged 68.4 days. After correcting for processes occurring in the dark, the half-life due to photolysis averaged 50 days of constant irradiation. The major degradates of irradiated samples were IN-KB687 and ¹⁴CO₂. The major degradate for non-irradiated samples was IN-JT333. Other detectable peaks were each <2% of the applied radioactivity.

RMS (2016)

The study is acceptable. Degradation of DPX-JW062 was faster under irradiated condition than in the dark control. The major degradates under irradiated conditions was IN-KB687 (max 22%), which is also a minor non transient metabolite seen in soil metabolism studies. This metabolite will be including in risk assesement in soil compartment considering the maximum level of formation of 22%.

Very few degradation of active substance is observed in the non irradiated control samples but this is likely a result of the very specific conditions of incubation in the study (dry soil).

Chiral chromatography results available showed that the enantiomeric ratio was stable around 50/50% at day 11, but this was controlled only in the dark samples. In these conditions at day 11, level of active substance has decreased of only 8 or 9%, and it is not sufficient to assure that the two isomers would degrade at an equal rate. Testing the stability of the ratio in the irradiated samples would have been more conclusive.

B.8.1.1.2. RATE OF DEGRADATION**B.8.1.1.2.1. Laboratory studies****B.8.1.1.2.1.1. Laboratory studies for indoxacarb**

The following studies are considered to provide data on rate of degradation of Indoxacarb.

Author(s)	Spare, W.C. (1997)
Title:	Aerobic soil metabolism of DPX-MP062, an ~3:1 mixture of DPX-KN128 and IN-KN127
Organisation:	Agrisearch Incorporated – Frederick, MD 21704
Document No:	AMR 3633-95
Dates of experimental work	November 6, 1995 – August 8, 1997
Guidelines:	U.S. EPA 162-1, SETAC (1995)
Deviations :	No major deviation
GLP:	
Previous evaluation:	Yes, Indoxacarb DAR (2001) and addendum 3 (2005)
Acceptability:	The study is still considered valid.

See summary under point B 8.1.1.1.1.

RMS (2016)

The study is in compliance with the OECD 307 guideline without major deviations. The study is considered acceptable.

However, only data for DPX-MP062 and metabolite IN-JT333 are considered reliable for kinetic evaluation.

Author(s)	Mellor, S.J. (2003)
Title:	¹⁴C-DPX-MP062 (a 3:1 mixture of DPX-KN128 and IN-KN127): Aerobic soil metabolism
Organisation :	Huntingdon Life Science Ltd – Cambridgeshire, England
Document No:	DuPont-8516
Dates of experimental work	November 12, 2001 – January 28, 2003
Guidelines:	U.S. EPA 162-1, SETAC (1995)
Deviations :	No major deviation
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR (2001) and addendum 3 (2005)
Acceptability:	The study is still considered valid.

See summary under point B 8.1.1.1.1.

RMS (2016)

The study is in compliance with the OECD 307 guideline without major deviations. The study is considered as acceptable.

Author(s)	Singles, S.K. (2002)
Title:	Aerobic soil metabolism of ¹⁴C-DPX-JW062
Organisation:	DuPont Experimental Station, Wilmington, Delaware, USA
Document No:	AMR 2803-93, Revision No. 1
Dates of experimental work	November 12, 2001 – January 28, 2003
Guidelines:	U.S. EPA 162-1, SETAC (1995)
Deviations :	No major deviation
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb Addendum 3 (2005)
Acceptability:	The study is still considered valid.

See summary under point B 8.1.1.1.1.

RMS (2016)

The study is acceptable. However, only data from the “original” experiment are considered reliable for further kinetic fitting.

Data from the “supplemental” experiment cannot be used for kinetic fitting since the long interval of sampling at the beginning of the study does not allow having a good description of the decline of active substance and formation and decline of metabolite (decrease of more than 80% of indoxacarb during first sampling interval of 5 days).

Author(s)	Rhodes, B.C. (1997)
Title:	Degradation rates of DPX-MP062 in soil
Organisation:	DuPont Experimental Station, Wilmington, Delaware, USA
Document No:	AMR 4251-96
Dates of experimental work	November 12, 2001 – January 28, 2003
Guidelines:	SETAC (1995)
Deviations :	No major deviation
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb Addendum 3 (2005)
Acceptability:	The study is still considered valid.

See summary under point B 8.1.1.1.1.

RMS (2016)

This study describes the rate of degradation of indoxacarb in four conditions (Speyer 2.2 soil at 20°C, Nambsheim soil at 10 and 20°C and Chino soil at 20°C)

The study is acceptable although it is noted that samples from 2nd extraction were not analysed when their total contain of AR was <7%. It has been questioned whether this could have impact on the kinetic fitting of data from speyer 2.2 soil experiment, for which extrat 2 contains about 5% of non-attributed AR at sampling times 7, 10, 14 and 24. The data were however retained for kinetic fitting and it has been checked that this did not have extensive impact on the final kinetic fitting retained for modelling for the Speyer 2.2 soil (see kinetic evaluation under point B.8.1.1.2.1.3 for details).

Data from Nambsheim soil at 10°C are not retained for kinetic fitting as data are available for the same soil at 20°C, and data from Chino soil were discarded as considered as clear outliers.

B.8.1.1.2.1.2. Laboratory studies for relevant metabolites, breakdown and reaction products**Metabolite IN-JT333**

Study submitted to the EU for the first time for the purpose of renewal.

Data point:	CA 7.1.2.1.2/03
Author(s)	Clark, B. (2014)
Title:	¹⁴ C-IN-JT333: Rate of degradation in five aerobic soils
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-35168
Dates of experimental work	
Guidelines:	OECD 307, OPPTS 835.4100, SETAC (March 1995), USEPA 162-1
Deviations :	None
GLP:	Yes
Previous evaluation:	No, study submitted for the purpose of renewal
Acceptability:	Yes

MATERIALS AND METHODS**Test Materials**

Radiolabelled test material:	¹⁴ C IN-JT333 technical metabolite
Lot/Batch #:	[Heterocycle methylene ¹⁴ C]-IN-JT333 Lot # 69027-1-4-1
Radiochemical purity:	97.11%
Specific activity:	33.57 µCi/mg (1.24 Mbq/mg)
Stability of test compound:	Stable during study

Soils

Five soils were chosen to represent conditions of use: a sandy loam from Nambshheim, Alsace, France (Nambshheim); a sandy loam from Hanhofen, Germany (Speyer 2.2); a light clay from Stark County, Illinois, USA (Tama); a sandy loam from Hessen, Germany (Gross-Umstadt); and a light clay from Lleida, Spain (Lleida). Prior to use, each test soil was homogenised and passed through a 2-mm mesh sieve. Soils were then stored at approximately 20°C in the dark, in closed bags when not in use. Pre-incubation was performed to acclimatize soil samples to the test temperature and achieve aerobic conditions prior to study initiation. Samples were pre-incubated for 4 to 6 days for the definitive test sample series before the test substance was applied.

Table 8-28: Characteristics of test soils

Characteristic	Soil		
Soil name or designation	Nambshheim	Speyer 2.2	Tama
Origin location	Nambshheim, Alsace, France	Hanhofen, Rein-Pfalz-Kreis, Germany	Stark County, Illinois, USA
pH (in water 1:1 ratio)	7.7	5.6	6.0
% Sand (2000-50 µm)	67	73	11
% Silt (<50-2 µm)	21	22	57
% Clay (<2 µm)	12	5	32
Texture ^a	Sandy Loam	Sandy Loam	Light Clay

% Organic matter	2.4	3.0	4.3
Cation exchange capacity	9.3	9.3	17.3
% Moisture at 0 bar (%)	51.8	49.6	70.9
Microbial biomass ($\mu\text{g C g}^{-1}$ soil)			
Initial	540.8	427.6	559.0
Final	557.8	469.9	703.6
Characteristic	Soil		
Soil name or designation	Gross-Umstadt	Lleida	
Origin location	Darmstadt, Hessen, Germany	Lleida, Spain	
pH (in water 1:1 ratio)	7.1	8.0	
% Sand (2000-50 μm)	43	11	
% Silt (<50-2 μm)	43	45	
% Clay (<2 μm)	14	44	
Texture ^a	Sandy Loam	Light Clay	
% Organic matter	2.0	1.9	
Cation exchange capacity	10.3	16.9	
% Moisture at 0 bar (%)	54.8	59.3	
Microbial biomass ($\mu\text{g C g}^{-1}$ soil)			
Initial	356.1	211.7	
Final	489.8	468.5	

^a USDA soil classification system

Experimental conditions

Portions of sieved soils (50 g dry-soil equivalent) were adjusted to 50% of their respective maximum water holding capacities. A solution of the radiolabelled form of the test substance was prepared in water and applied to soil samples (0.4 $\mu\text{g/g}$ dry soil) in separate 200-mL glass tubes. The soils were mixed after dosing to ensure homogeneity. Water lost to evaporation was replaced, and soils were incubated in the dark at $20 \pm 2^\circ\text{C}$ under aerobic conditions for up to 122 days in closed systems to trap evolved carbon dioxide and volatile organic compounds.

Soil samples were taken and analysed for IN-JT333 and other degradation products. Additional samples were prepared and incubated for determination of biomass.

Sampling

Microbial biomass was determined at zero time and at the approximately same time as the definitive test samples. Soil samples were taken for analysis immediately after treatment (Day 0) and 3, 7, 15, 21, 31, 51, 91, and 122 days.

Description of analytical procedures

The KOH traps for collecting $^{14}\text{CO}_2$ produced by the systems were collected at each sampling day after Day 0 and replaced with fresh material at each sampling event.

Soil samples were typically extracted four times with 80:20 acetonitrile:water (the fourth extraction used 80:20 acetone:water), shaken, centrifuged, and decanted. The extracts were analysed in triplicate for total radioactivity by LSC analysis. Soil extracts were combined, concentrated with rotary evaporator, taken to dryness and reconstituted, then analysed using reverse phase HPLC (Phenomenex Luna C18(2), 250 mm \times 4.6 mm \times 5 μm id), and eluted with a gradient of 0.1% formic acid in water and 0.1% formic acid in acetonitrile. The effluent was passed through a UV detector (254 nm) to detect reference standards and a radioactivity detector to determine the quantities of radiolabelled degradation products present. The limit of detection (LOD) for IN-JT333 in KOH traps, organic extracts, soil combustions, and HPLC analyses (organic) were 0.0299, 0.3139, 0.1089, and 0.5231% of applied ^{14}C for the Nambesheim, Speyer 2.2, Tama, and Gross-Umstadt test soils, respectively. The LOD for IN-JT333 in KOH traps, organic extracts, soil combustions, and HPLC analyses (organic) were 0.0314, 0.3296, 0.1143, and 0.5494% of applied ^{14}C , respectively, for the Lleida test soil.

Soil samples were combusted, and unextracted ^{14}C levels were measured using LSC.

RESULTS AND DISCUSSION

Mass balance

Material balance for the [^{14}C] label IN-JT333 ranged from 91.7 to 96.5%

Bound and extractable residues

The percentage of radioactivity in the extractable fraction decreased from Day 0 to Day 122. The level of bound residue increased steadily throughout the course of the study with all five soils. Mean extractability values ranged from 96.8% AR (Day 0) to 13.5% AR (Day 122) for Nambsheim soil, 96.1% AR (Day 0) to 16.2% AR (Day 122) for Speyer 2.2 soil, 95.9% AR (Day 0) to 4.9% AR (Day 122) for Tama soil, 96.3% AR (Day 0) to 6.3% AR (Day 122) for Gross-Umstadt soil, and 97.0% AR (Day 0) to 19.9% AR (Day 122) for Lleida soil.

Mean bound residue values increased and reached a maximum of 8.7% AR (Day 91) for Nambsheim soil, 6.1% AR (Day 21) for Speyer 2.2 soil, 12.0% AR (Day 21) for Tama soil, 9.3% AR (Day 31) for Gross-Umstadt soil, and 10.8% AR (Day 122) for Lleida soil.

Volatilisation

Confirmation of $^{14}\text{CO}_2$ in the KOH was performed for all soils. A barium chloride test performed on this system confirmed that the activity trapped was due to the presence of $^{14}\text{CO}_2$. At study termination, evolved $^{14}\text{CO}_2$ values were 70.1%, 70.4%, 76.1%, 76.3%, and 63.9% of the applied amount in the Nambsheim, Speyer 2.2, Tama, Gross-Umstadt, and Lleida soils, respectively.

Transformation of metabolite

Levels of IN-JT333 in the soil declined continuously over a period of 122 days. IN-JT333 is transformed in soils over time and would extensively degrade to other metabolites and non-extractable residues and be mineralised to CO_2 . The degradation rate was re-evaluated in DuPont-34821 EU according to FOCUS (2006, 2011) guidelines.

Chiral column analysis from three representative sampling intervals indicated that enantiomer ratio of IN-JT333 was stable during the course of the study. These data showed no differential degradation of enantiomers of IN-JT333 in soil, which further confirmed the conclusion from the position paper DuPont-12971.

Table 8-29 : Distribution of radiolabelled components in aerobic soils after application of [^{14}C]IN-JT333 (% applied radioactivity, mean of duplicate replicates)

Soil (20°C)	Sampling interval (days)	IN-JT333	Total as others ^a	Total extractable residues	Bound residue ^b	Organic volatiles	$^{14}\text{CO}_2$	Total
Nambsheim	0	96.8	0.0	96.8	0.0	NA	NA	96.8
	3	66.9	24.8	91.7	2.5	NA	0.4	94.6
	7	46.5	42.6	89.0	3.1	NA	3.8	95.9
	15	15.8	57.5	73.3	4.4	NA	17.4	95.1
	21	19.7	44.0	63.7	5.2	NA	26.4	95.2
	31	12.9	38.8	51.7	6.2	NA	35.7	93.6
	52	7.1	27.0	34.0	6.7	NA	50.6	91.3
	91	5.7	13.6	19.3	8.7	NA	64.2	92.2
	122	6.9	6.6	13.5	7.8	NA	70.1	91.4
Speyer 2.2	0	96.1	0.0	96.1	0.0	NA	NA	96.1
	3	69.8	16.3	86.1	2.2	NA	5.7	93.9
	7	54.0	21.0	75.0	3.8	NA	12.5	91.3
	15	28.6	20.5	49.1	5.2	NA	34.8	89.1
	21	31.0	5.9	36.9	6.1	NA	47.3	90.4
	31	24.8	4.0	28.8	5.8	NA	54.2	88.8
	52	22.5	2.1	24.6	5.3	NA	61.7	91.6
	91	19.3	0.0	19.3	5.0	NA	67.7	92.0
	122	14.9	1.4	16.2	5.6	NA	70.4	92.2
Tama	0	95.9	0.0	95.9	0.0	NA	NA	95.9
	3	67.8	16.2	93.9	4.0	NA	9.6	97.5
	7	36.7	24.2	60.9	8.7	NA	20.1	89.7
	15	29.8	13.9	43.7	7.1	NA	43.7	94.5

	21	24.0	6.8	30.7	12.0	NA	55.6	98.3
	31	14.0	5.8	19.7	9.3	NA	64.5	93.5
	52	5.6	4.8	10.4	6.2	NA	71.0	87.6
	91	4.9	1.7	6.6	5.2	NA	74.8	86.5
	122	4.1	0.8	4.9	5.5	NA	76.1	86.4
Gross- Umstadt	0	96.3	0.0	96.3	0.0	NA	NA	96.3
	3	58.5	37.4	96.0	1.8	NA	0.9	98.7
	7	34.8	53.5	88.3	3.2	NA	4.5	96.0
	15	11.3	30.3	41.6	8.4	NA	40.6	90.6
	21	15.3	14.8	30.1	8.2	NA	54.2	92.6
	31	12.4	9.2	21.6	9.3	NA	62.6	93.5
	52	6.8	5.2	12.0	9.1	NA	69.8	90.9
	91	5.9	1.8	7.8	8.6	NA	74.5	90.9
Lleida	122	4.4	1.8	6.3	8.6	NA	76.3	91.1
	0	96.7	0.2	97.0	1.0	NA	NA	97.9
	3	77.0	18.0	95.1	2.7	NA	0.6	98.3
	7	60.3	33.3	93.6	3.1	NA	1.8	98.5
	15	33.8	43.9	77.7	7.0	NA	8.9	93.6
	21	28.7	43.5	71.9	8.8	NA	14.9	95.6
	31	20.6	42.4	63.0	9.6	NA	23.5	96.1
	52	14.6	34.2	48.8	9.8	NA	39.2	97.8
	91	8.5	21.5	30.0	10.7	NA	55.4	96.1
	122	5.3	14.6	19.9	10.8	NA	63.9	94.6

^a Sum of all other unidentified products

^b Unextractable Residue in soil

NA = Not Applicable/Not analysed

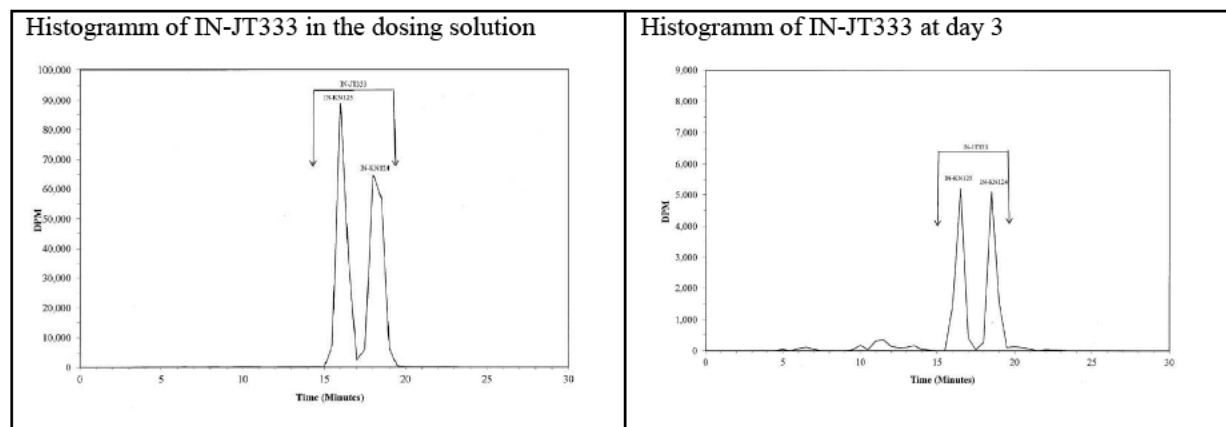
CONCLUSION

The results demonstrate that IN-JT333 is transformed in soils over time and would extensively degrade to other metabolites and non-extractable residues and be mineralised to CO₂, with the degradation values (DT₅₀) ranging from 4.3 days to 9.6 days.

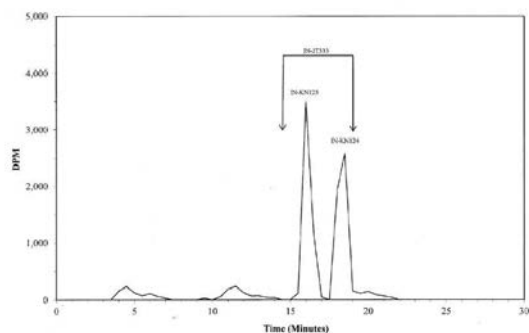
RMS (2016)

New study submitted for the purpose of AIR III. This study is acceptable.

Chiral chromatography was performed to evaluate the stability of the isomeric ratio of IN-JT333 in the Nambenheim soil samples at day 3 and day 7. However, it was not clear from visual assessment of the chromatograms whether the ratios of areas of the peaks of isomers were not significantly different at each sampling time (see chromatograms below).



Histogramm of IN-JT333 at day 7



Applicant then provided the radioactivity counts of the peaks (table below).

Isomeric ratio calculation based on peak area integration for IN-KN125 and IN-KN124

Sampling ID	Peak area counted in dpm		Area ratio of IN-KN125:IN-KN-124
	IN-KN125	IN-KN124	
Dosing solution	134674	135181	1:1
Day 3	7115	7010	1:1
Day 7	4798	4669	1:1

Applicant agrees the two peaks were nearly identical from three representative sample analyses, indicating that there was no preferential degradation for the two enantiomers of IN-KN125 and IN-KN124 until day 7. Still, no foresight can be done for later sampling points.

* * * *

Metabolite IN-JU873

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Author(s)	Mellor, S.J. (2002)
Title:	Degradation rates of [¹⁴C]IN-JU873 in five soils
Organisation:	
Document No:	DuPont-8137
Dates of experimental work	8 november 2001 – 19 June 2002
Guidelines:	SETAC 1995, OECD Draft (October 1999)
Deviations :	
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR (2000) and Addendum 3 (2005)
Acceptability:	Yes

MATERIALS AND METHODS**Test material**

1. Radiolabeled test material: [¹⁴C]IN-JU873 technical metabolite
 Lot/Batch #: [Urea carbonyl-¹⁴C]IN-JU873: HOTC: 0572
 Radiochemical purity: [Urea carbonyl-¹⁴C]IN-JU873: >95%
 Specific activity: [Urea carbonyl-¹⁴C]IN-JU873: 39.3 µCi/mg
 Description: White solid
 Stability of test compound: Shown to be stable under the conditions of the test.

Soils

Five soils were chosen to represent conditions of use; Speyer 2.2 loamy sand, Mattapex silt loam, Pesaro silty clay loam, Lleida clay loam, and Hidalgo sandy clay loam. The soils were freshly collected from the field and stored at approximately 4°C for 39–48 days prior to use. Soils were collected from specific locations with restricted access to ensure that no pesticides or organic fertilizer treatments had taken place for at least five years prior to collection. Soils were equilibrated in flasks at 25°C for two weeks prior to use and their microbial viability was checked by microbial biomass determination.

Table 8-30: Characteristics of test soils

Characteristic	Soil				
Soil name or designation	Speyer 2.2	Mattapex	Pesaro	Lleida	Hidalgo
Origin	Germany	USA	Italy	Spain	USA
pH (in water)	6.2	6.2	8.5	8.2	8.4
% Sand (2000–50 µm)	79.57	27.47	14.45	28.44	60.83
% Silt (<50–2 µm)	13.39	58.97	48.92	42.80	17.65
% Clay (<2 µm)	7.03	13.56	36.63	28.76	21.51
Texture ^a	Loamy sand	Silt loam	Silty clay loam	Clay loam	Sandy clay loam
Organic carbon (%) ^b	2.8	1.0	1.0	1.2	0.5
Cation exchange capacity (mEq/100 g)	11.8	9.3	24.6	20.5	14.2
Maximum water-holding capacity (%)	59.35	47.78	65.34	56.28	53.82
Field capacity at pF2.0 (%)	21.1	29.7	33.1	29.1	26.7
Microbial biomass (mg microbial C/kg soil)					
Initial	785.57	411.17	354.37	359.17	229.17
Final	511.97	240.37	519.57	551.37	241.57

^a USDA soil classification system

^b organic carbon = organic matter/1.724

Experimental conditions

The rate of degradation of [urea carbonyl-¹⁴C]IN-JU873 was determined under laboratory conditions in five field-fresh soils at 20 ± 2°C. IN-JU873 was dissolved in acetonitrile: water (1:1 by volume) at a nominal concentration of 50 µg/mL and 0.5 mL was applied to 50 g dry weight of soil to give a nominal soil concentration of 0.5 mg/kg. Soil samples were incubated under aerobic conditions in darkness at a soil moisture content of 50% of maximum water holding capacity for up to 120 days. The testing system included an ethyl digol trap followed by two 1.0 N KOH traps to test for the production of organic volatiles and carbon dioxide, respectively. Soil microbial biomass analyses were conducted on Day 0 and upon completion of the incubation period for each soil.

The soil was extracted three times with a mixture of acetonitrile: water (4:1 by volume) generally followed by a single extract with acetone: water solution (1:1 by volume). Soil extracts were concentrated and analysed by LSC followed by HPLC with fraction collection of the eluate and LSC analysis. The post extraction soil solids (PES) were combusted and analysed by LSC. The volatile organic traps were assayed directly by LSC.

RESULTS AND DISCUSSION

Material balance

Material balances were generally satisfactory (Table 8-31). The average recovered radioactivity ranged from 102.8 to 85.7% applied radiolabel in all soils. Volatile radioactivity reached a maximum of 20.2, 26.8, 35.6, 39.9, and 49.3% AR in Speyer 2.2, Lleida, Hidalgo, Mattapex, and Pesaro soils after 120 days.

Principal degradation products

Only the concentration of IN-JU873 was monitored during the course of this study (rate of degradation study, metabolite identification is not required).

Non-extractable residue (NER)

Non-extracted radioactivity reached a maximum of 38.9% applied radiolabel in Speyer 2.2 soil (after 120 days), 24.1% applied radiolabel in Mattapex soil (after 120 days), 39.2% applied radiolabel in Pesaro soil (after 30 days), 37.4% applied radiolabel in Lleida soil (after 120 days), and 29.6% applied radiolabel in Hidalgo soil (after 120 days). The data are summarised in Table 8-31.

Table 8-31: Percent distribution of radiolabeled components in aerobic soils after application of ^{14}C -IN-JU873

Soil	Sampling point (days)	Average % applied radioactivity				
		IN-JU873	CO ₂	Volatile organics	NER	Total % recovery
Speyer 2.2	0	91.4	ns ^a	ns	6.3	101.1
	3	83.8	0.2	nd ^b	5.2	100.8
	7	74.5	0.6	nd	8.3	100.9
	14	60.5	1.7	nd	16.8	100.6
	30	54.7	5.4	nd	23.2	99.7
	45	40.6	8.9	nd	31.8	101.0
	60	40.2	12.6	nd	30.2	102.8
	91	28.9	16.3	nd	28.9	93.7
	120	18.1	20.2	nd	38.9	95.4
Mattapex	0	91.3	ns	ns	5.8	99.7
	3	79.8	1.6	nd	7.1	97.4
	7	68.7	4.4	nd	9.3	100.0
	14	58.5	9.6	nd	19.6	100.4
	30	38.9	19.5	nd	22.5	95.8
	45	34.5 4	26.8	nd	24.5	95.6
	60	36.4	31	nd	20.8	98.2
	91	30	36.5	nd	22.8	97.0
	120	19.1	39.9	nd	24.1	94.4
Pesaro	0	89.7	ns	ns	8.2	100.3
	3	73.3	0.3	nd	10.4	102.5
	7	55.9	2	nd	32.1	99.5
	14	46.3	8.2	nd	29.1	99.4
	30	24.4	22.5	nd	39.2	96.2
	45	18.8	28.2	nd	34.3	94.8
	60	11.9	35.6	nd	36.7	90.6
	91	5.5	44.2	nd	34	91.8
	120	5.4	49.3	nd	34.2	96.7
Lleida	0	92.9	ns	ns	4.0	99.8
	3	75.4	0.3	nd	12.6	97.0
	7	64.2	1.6	nd	18.2	98.2
	14	51.3	5.5	nd	24.1	94.3
	30	32.9	8.6	nd	33.9	91.2
	45	31.4	11.9	0.1	36.9	91.0
	60	32.5	15.1	0.1	28.5	90.4
	91	19.3	20.7	0.1	32.0	85.7
	120	12.5	26.8	0.1	37.4	87.5
Hidalgo	0	95.5	ns	ns	2.4	102.8
	3	82.4	0.1	nd	3.8	94.9
	7	72.0	0.5	nd	2.7	98.8
	14	56.4	2.5	nd	9.2	98.2
	30	40.0	8.5	nd	13.6	95.8
	45	31.8	14.8	nd	23.6	98.4

	60	43.9	20	nd	20.2	100.4
	91	26.3	28.7	nd	22.4	92.6
	120	17.0	35.6	nd	29.6	96.8

^a Not sampled

^b Not detected

CONCLUSION

IN-JU873 degraded in the five soils. There was no apparent correlation between soil pH and the rate of degradation.

RMS (2016)

This study is in compliance with OECD 307 without major deviation.

As mentioned during first review, soil history revealed intense use of pesticide in the two years before soil collection for Pesaro soil (chloridazon, desmedipham + ethofumesate + phenmedipham, haloxyfop-ethoxyethyl, clopyralid, metatriton, flusilazole, fluazifop-p-butyl). SETAC (1995) recommendation states that “the sites should not have been treated, during the previous 5 years, in any way which could severely affect the microbial populations (e.g. with a soil sterilant)”. From the residue data it can be seen that there is no really significant difference in degradation rate in the various soils, therefore it is expected that the pesticides used in this soil did not impact significantly the validity of the study. The study is still considered valid.

Metabolite IN-KB687

Study submitted to the EU for the first time for the purpose of renewal

Data point:	CA 7.1.2.1.2/01
Author(s)	Allan, J. (2012)
Title:	¹⁴C-IN-KB687: Rate of degradation in five aerobic soils
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-31717
Dates of experimental work	06 december 2011- 03 may 2012
Guidelines:	OECD 307 (2002), USEPA 162-1, SETAC Europe (1995), OPPTS 835.4100
Deviations :	See RMS comments
GLP:	Yes
Previous evaluation:	No, study submitted for the purpose of renewal
Acceptability:	Yes

MATERIALS AND METHODS**Test material**

Radiolabelled test material:	¹⁴ C IN-KB687 technical metabolite
Lot/Batch #:	[Methoxy- ¹⁴ C]IN-KB687, Lot #: 3638094
Radiochemical purity:	98.6%
Specific activity:	41.06 µCi/mg
Stability of test compound:	Stable during study

Soils

Five soils were chosen to represent conditions of use: a heavy clay from the Lleida region of Spain (Lleida); a loam from Kent County, Maryland, U.S.A. (Sassafras); a sandy loam from Nambsheim, France (Nambsheim); a sandy loam from Hanhofen, Germany (Speyer 2.2); and a light clay from Stark County, Illinois, U.S.A. (Tama). Prior to use, each test soil was homogenised and passed through a 2-mm mesh sieve. Soils were then stored at approximately 4°C in the dark, in closed bags when not in use. Pre-incubation was performed to acclimatise soil samples to the test temperature and achieve aerobic conditions prior to study initiation.

Table 8-32: Characteristics of test soils

Characteristic	Soil				
Soil name or designation	Lleida	Sassafras	Nambsheim	Speyer 2.2	Tama
Origin location	Lleida Region of Spain	Kent County, Maryland, USA	Nambsheim, France	Hanhofen, Germany	Stark County, Illinois, U.S.A.
pH (in water 1:1 ratio)	7.7	5.5	7.7	5.5	6.3
pH (in 0.01M CaCl ₂ 1:2 ratio)	7.6	5.1	7.4	5.5	6.0
% Sand (2000-50 µm)	13	50	64	80	16
% Silt (<50-2 µm)	40	40	30	16	54
% Clay (<2 µm)	47	10	6	4	30
Texture ^a	Clay	Loam	Sandy Loam	Loamy Sand	Silty Clay Loam
% Organic matter	4.1	2.6	2.9	5.9	3.3
% Organic carbon ^b	2.4	1.5	1.7	3.4	1.9

Cation exchange capacity (meq/100 g)	19.0	8.3	10.6	8.2	18.3
Maximum water-holding capacity (%)	64.7	49.6	56.2	45.1	73.6
Field capacity at pF 2.0	37.3	24.5	19.1	10.9	41.8
Microbial biomass ($\mu\text{g C g}^{-1}$ soil)					
Initial	386.4	96.2	241.2	184.3	184.2
Final	331.2	67.0	241.6	201.1	216.8

^a USDA soil classification system

^b Organic carbon = Organic matter/ 1.72

Experimental conditions

Portions of sieved soils (50 g dry-soil equivalent) were adjusted to 50% of their respective maximum water holding capacities. A solution of the radiolabelled form of the test substance was prepared in water and applied to soil samples (0.522 $\mu\text{g/g}$ dry soil) in separate 250-mL Nalgene bottles. No evaporation procedures were necessary since water was used as the dose solution solvent. The soils were mixed after dosing to ensure homogeneity. Water lost to evaporation was replaced, and soils were incubated in the dark at $20 \pm 2^\circ\text{C}$ under aerobic conditions for up to 48 hours (72 hours for Sassafras and Tama only) in closed systems to trap evolved carbon dioxide and volatile organic compounds.

Soil samples were taken and analysed for IN-KB687. Additional samples were prepared and incubated for determination of biomass.

Sampling

Microbial biomass was determined at zero time and after 12 days from dosing the definitive test samples. Soil samples were taken for analysis immediately after treatment (Hour 0) and 24 and 48 hours (and 72 hours for Sassafras and Tama only).

Description of analytical procedures

The KOH traps for collecting $^{14}\text{CO}_2$ produced by the systems were collected at each sampling hour after Hour 0 and replaced with fresh material at each sampling event.

Soil samples were typically extracted two times with 4:1 acetonitrile: water, shaken, centrifuged, and decanted. The extracts were analysed in triplicate for total radioactivity by LSC analysis. Soil extracts were combined, diluted, then analysed using HPLC with fraction collection (Agilent, Zorbax, 5 μm , SB-C8, 250×4.6 mm) and eluted with a gradient of water (pH adjusted to 2.3 with H_3PO_4) and acetonitrile. The effluent was passed through a UV detector (254 nm) to detect reference standards and a radioactivity detector to determine the quantities of radiolabelled degradation products present. The limit of detection (LOD) for IN-KB687 in the ethanolamine trap, KOH traps, organic extracts, organic Orbo extracts, soil combustions, and HPLC analyses (organic) were 0.013, 0.13, 0.17, 0.013, 0.070, and 0.22% of applied ^{14}C , respectively.

Soil samples were combusted, and unextracted ^{14}C levels were measured using LSC.

RESULTS AND DISCUSSION

Mass balance

Material balance for the [^{14}C]labelled IN-KB687 ranged from 84.0 to 102.7%.

Bound and extractable residues

The percentage of radioactivity in the extractable fraction decreased from Hour 0 to Hour 48 (or to 72 hours for Sassafras and Tama only). The level of bound residue increased steadily throughout the course of the study with all five soils. Mean extractability values ranged from 98.9% AR (Hour 0) to 3.4% AR (Hour 48) for Lleida soil, 95.5% AR (Hour 0) to 3.8% AR (Hour 72) for Sassafras soil, 101.4% AR (Hour 0) to 2.2% AR (Hour 48) for Nambshheim soil, 100.6% AR (Hour 0) to 3.6% AR (Hour 48) for Speyer 2.2 soil, and 94.8% AR (Hour 0) to 3.5% AR (Hour 72) for Tama soil.

Mean bound residue values ranged from 1.2% AR (Hour 0) to 9.2% AR (Hour 24) for Lleida soil, 0.5% AR (Hour 0) to 7.1% AR (Hour 72) for Sassafras soil, 0.9% AR (Hour 0) to 12.9% AR (Hour 48) for Nambenheim soil, 0.5% AR (Hour 0) to 4.1% AR (Hour 48) for Speyer 2.2 soil, and 1.2% AR (Hour 0) to 7.6% AR (Hour 48) for Tama soil.

Volatilisation

Confirmation of $^{14}\text{CO}_2$ in the KOH was performed for all soils. A barium chloride test performed on this system confirmed that the activity trapped was due to the presence of $^{14}\text{CO}_2$. At study termination, mean evolved $^{14}\text{CO}_2$ were 81.9%, 78.4%, 73.9%, 77.9%, and 55.9% of the applied amount in the Lleida, Sassafras, Nambenheim, Speyer 2.2, and Tama soils, respectively.

Transformation of metabolite

Levels of IN-KB687 in the soil declined continuously over a period of 48 hours (or 72 hours for Sassafras and Tama only). The degradation rate was re-evaluated in DuPont-34821 EU according to FOCUS (2006, 2011) guidelines.

IN-KB687 is transformed in soils in very short time and would extensively be mineralised to CO_2 .

Table 8-33 : Distribution of radiolabelled components in aerobic soils after application of ^{14}C -IN-KB687 (% applied radioactivity, mean of duplicate replicates)

Soil (20°C)	Sampling interval (hours)	IN-KB687	$^{14}\text{CO}_2$	Organic volatiles	Total as others ^a	Bound residue ^b	Total
Lleida	0	96.7	NA	NA	2.3	1.2	100.1
	24	18.9	59.0	0.9	0.2	9.2	88.2
	48	3.2	81.9	1.0	0.2	8.4	94.8
Sassafras	0	95.3	NA	NA	0.2	0.5	96.0
	24	32.7	51.2	0.7	0.0	5.4	89.9
	48	13.7	71.6	0.9	0.0	6.7	92.9
	72	3.8	78.4	0.9	0.0	7.1	90.2
Nambenheim	0	101.0	NA	NA	0.4	0.9	102.4
	24	15.2	34.2	0.6	0.0	8.8	92.6
	48	2.2	73.9	0.7	0.0	12.9	89.7
Speyer 2.2	0	99.5	NA	NA	0.7	0.5	101.1
	24	43.6	58.1	0.6	0.0	2.0	104.4
	48	3.6	77.9	0.7	0.0	4.1	86.2
Tama	0	93.6	NA	NA	1.2	1.2	96.0
	24	27.0	33.7	0.8	0.0	4.8	84.0
	48	8.3	52.6	1.0	0.0	7.6	92.0
	72	3.5	55.9	1.0	0.0	6.8	89.5

^a Sum of all other unidentified products

^b Unextractable residue in soil

NA = Not Applicable/Not analysed

CONCLUSION

IN-KB687 degraded rapidly at 20°C in all test soils with DT_{50} values ranging from 0.36 days to 0.68 days.

RMS (2016)

RMS notes that the storage duration of the soil samples was > 3 months, and the incubation period > 28 days which is longer than recommended in OECD 307. However, it does not seem to have significant impact on the degradation potential of the soils, given the level of microbial activity and given the very fast degradation of test substance observed.

Mass balance is not always >90% at DAT24 or DAT48, which is explained by author being probably due to CO₂ loss during sampling, given that the analytical method recovery at T0 is good. It is however not considered to impact significantly the final DT₅₀.

Overall, it is noted that sampling frequency should have been adapted to this very transient metabolite as only three measures are available for three of the soils, degradation being very fast (sampling times at 0, 24 and 48h). This is not sufficient to derive a reliable DT₅₀. RMS then considered that only data from the two remaining soils could be retained to derive endpoint (Sassafras and Tama) and RMS proposal is to retain worst-case DT₅₀ from these two soils for risk assessment.

Metabolite IN-KG333

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Author(s)	Aikens, P.J. (2002)
Title:	Degradation rates of [¹⁴C]IN-KG433 in five soils
Document No:	DuPont-8117
Dates of experimental work	27 november 2001 – 15 April 2002
Guidelines:	SETAC 1995, OECD Draft (October 1999)
Deviations :	
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR Adendum 3 (2005)
Acceptability:	Yes

MATERIALS AND METHODS

Test material

Radiolabeled test material:	¹⁴ C-IN-KG433 technical
Lot/Batch #:	[¹⁴ C]IN-KG433: HOTC: 573
Radiochemical purity:	[¹⁴ C]IN-KG433: >95%
Specific activity:	[¹⁴ C]IN-KG433: 54.65 µCi/mg
Description:	White solid
Stability of test compound:	Shown to be stable under the conditions of the test.

Experimental conditions

The rate of degradation of IN-KG433 radiolabeled with carbon-14 as [indanone-¹⁴C], was determined under laboratory conditions in five field-fresh soils (Table 8-34) at 20 ± 2°C. These soils were typical of agricultural soil types. IN-KG433 was dissolved in acetonitrile/water (1:1 by volume) at a nominal concentration of 50 µg/mL and 0.5 mL was applied to 50 g dry weight of soil to give a nominal soil concentration of 0.5 mg/kg. Soil samples were incubated under aerobic conditions in darkness at a soil moisture content of 50% of maximum water holding capacity for up to 59 days (Hidalgo, Lleida, Pesaro, and Mattapex soils) or 120 days (Speyer 2.2 soil). Soil samples were extracted with acetonitrile: water (4:1 by volume). Soil extracts were analysed by TLC for IN-KG433.

Table 8-34: Characteristics of test soils

Characteristic	Soil				
Soil name or designation	Speyer 2.2	Mattapex	Pesaro	Lleida	Hidalgo
Origin	Germany	USA	Italy	Spain	USA
pH (in water)	6.2	6.2	8.5	8.2	8.4
% Sand (2000–50 µm)	79.57	27.47	14.45	28.44	60.83

% Silt (<50–2 µm)	13.39	58.97	48.92	42.80	17.65
% Clay (<2 µm)	7.03	13.56	36.63	28.76	21.51
Texture ^a	Loamy sand	Silt loam	Silty clay loam	Clay loam	Sandy clay loam
Organic carbon (%) ^b	2.8	1.0	1.0	1.2	0.5
Cation exchange capacity (mEq/100 g)	11.8	9.3	24.6	20.5	14.2
Maximum water-holding capacity (%)	59.35	47.78	65.34	56.28	53.28
Field capacity at pF 2.0 (%)	21.1	29.7	33.1	29.1	26.7
Microbial biomass (mg microbial C/kg soil)					
Initial	681.17	451.17	481.97	393.97	344.77
Final	503.17	255.17	597.17	407.57	278.37

^a USDA soil classification system

^b organic carbon = organic matter/1.724

RESULTS AND DISCUSSION

Material balance

The average material balance was $98.6 \pm 4.2\%$ (range 108.2 to 90.4%, three values from a total of 114 excluded) at all sampling intervals in all soil groups (Table 8-35). Non-extracted radioactivity increased from 0.5–5.4% applied radioactivity at zero-time to up to 43.4% applied radioactivity in Speyer 2.2 soil (after 59 days), 35.2% applied radioactivity in Mattapex soil (after 30 days), 34.6% applied radioactivity in Pesaro soil (after 59 days), 38.7% applied radioactivity in Lleida soil (after 59 days), and 32.9% applied radioactivity in Hidalgo soil (after 59 days). Similarly, volatile radioactivity (labeled carbon dioxide) increased to 43.0% applied radioactivity, 59.3% applied radioactivity, 41.3% applied radioactivity, and 40.6% applied radioactivity in Mattapex, Pesaro, Lleida, and Hidalgo soils, respectively, after 59 days and to 38.6% applied radioactivity in Speyer 2.2 soil after 120 days.

Principal degradation products

Only the concentration of IN-KG433 was monitored during the course of this study (rate of degradation study, metabolite identification is not required).

Non-extractable residue (NER)

Non-extracted radioactivity increased from 0.5–5.4% applied radioactivity at zero-time to up to 43.4% applied radioactivity in Speyer 2.2 soil (after 59 days), 35.2% applied radioactivity in Mattapex soil (after 30 days), 34.6% applied radioactivity in Pesaro soil (after 59 days), 38.7% applied radioactivity in Lleida soil (after 59 days), and 32.9% applied radioactivity in Hidalgo soil (after 59 days).

Table 8-35 : Percent distribution of radiolabeled components in aerobic soils after application of ¹⁴C-IN-KG433

Soil	Sampling point (days)	Average % applied radiolabel					
		IN-KG433	Others ^a	CO ₂	Volatile organics	NER	Total % recovery
Speyer 2.2	0	98.8	2.6	ns ^b	ns	0.5	101.8
	0.5	77.7	17.1	0.1	nd ^c	2.8	97.6
	1	65.7	27.6	0.3	nd	6.4	99.9
	2	53.4	31.9	1.0	nd	13.3	99.6
	3	38.1	41.3	1.8	nd	15.5	96.6
	5	30.2	33	4.1	nd	34.7	101.9
	7	29.1	35.7	5.7	nd	25.5	95.9
	14	19.9	26.7	12.1	nd	36.4	95.1
	30	15.3	22.2	19.4	nd	39.7	96.6

Table 8-35 : Percent distribution of radiolabeled components in aerobic soils after application of ^{14}C -IN-KG433

Soil	Sampling point (days)	Average % applied radiolabel					
		IN-KG433	Others ^a	CO ₂	Volatile organics	NER	Total % recovery
	45	11.9	19.8	24.3	nd	39.9	95.9
	59	11.7	16.7	29.5	nd	43.4	101.3
	90	10.7	14.1	34.7	nd	38.2	97.6
	120	8.0	12.1	38.6	nd	42.5	101.1
Mattapex	0	99.1	1.2	ns	ns	0.7	100.7
	0.5	80	16.9	0.6	nd	6.3	103.8
	1	64.5	22.2	2.4	nd	10.3	99.4
	2	47.9	26.2	5.2	nd	15.3	94.5
	3	25.4	37	8.7	nd	24.8	95.9
	5	20.6	33.2	14.4	nd	31.9	100.1
	7	15.9	30.2	18	nd	32.6	96.7
	14	9.5	22.9	27.5	nd	33.9	93.7 9
	30	4.9	15.8	37.9	nd	35.2	93.8
	45	4.2	13.2	42.6	nd	33	92.9
Pesaro	59	4.1	12.6	43	nd	32.7	92.3
	0	92.5	4.5	ns	ns	5.4	102.4
	0.5	79.5	22.1	nd	nd	1.8	103.3
	1	73.7	25.5	0.1	nd	2.9	102.2
	2	55.6	38.5	0.3	nd	4.6	98.9
	3	49.1	44.6	0.8	nd	7.1	101.6
	5	26.5	56.3	1.7	nd	16.3	100.7
	7	18.8	54.1	3.9	nd	18.8	95.6
	14	9.1	37.0	16.1	nd	31.8	94.0
	30	3.4	19.8	35.4	nd	34.2	92.8
Hidalgo	45	3.8	13.3	44.6	nd	33.1	94.7
	59	2.8	11.5	59.3	nd	34.6	108.2
	0	90.9	12.6	ns	ns	0.4	103.9
	0.5	74.9	30.2	nd	nd	0.9	106.0
	1	59.7	40.9	0.1	nd	1.2	101.8
	2	59.8	39.9	0.2	nd	1.8	101.7
	3	38.0	58.1	0.4	nd	2.6	99.1
	5	26.2	67.8	1.1	nd	5.4	100.5
	7	18.3	73.9	1.5	nd	9.0	102.6
	14	7.2	67.7	6.2	nd	15.4	96.4
Lleida	30	3.4	41.4	2.2	nd	29.3	96.1
	45	2.3	28.2	33.4	nd	28.7	92.5
	59	1.9	20.1	40.6	nd	32.9	95.5
	0	100.3	1.1	ns	ns	0.7	102.0
	0.5	78.2	25.2	nd	nd	2.1	105.4
	1	65.0	34.0	0.1	nd	3.1	102.3
	2	47.5	45.7	0.2	nd	6.3	99.6
	3	35.5	52.8	0.5	nd	8.5	97.2
	5	22.9	58.0	1.4	nd	17.0	99.3
	7	18.0	59.0	2.6	nd	18.5	98.0
	14	9.5	44.5	10.1	nd	30.2	94.3
	30	4.4	26.2	26.8	nd	34.2	91.6
	45	3.7	17.5	47.7	nd	34.5	103.3

Table 8-35 : Percent distribution of radiolabeled components in aerobic soils after application of ^{14}C -IN-KG433

Soil	Sampling point (days)	Average % applied radiolabel					
		IN-KG433	Others ^a	CO ₂	Volatile organics	NER	Total % recovery
	59	3.4	14.3	41.3	nd	38.7	97.7

^a Sum of other radioactivity distributed through the chromatogram. Identification is not required

^b Not sampled

^c Not detected

CONCLUSION

IN-KG433 rapidly degraded in the five soils. There was no apparent correlation between soil pH and the rate of degradation.

RMS (2016)

This study is in compliance with OECD 307 without major deviation and is still acceptable.

As mentioned during first review, soil history revealed intense use of pesticide in the three years before soil collection (chloridazon, desmedipham + ethofumesate + phenmedipham, haloxyfop-ethoxyethyl, clopyralid, metamitron, flusilazole, fluazifop-p-butyl). SETAC (1995) recommendation states that “the sites should not have been treated, during the previous 5 years, in any way which could severely affect the microbial populations (e.g. with a soil sterilant)”. From the residue data it can be seen that there is no significant difference in degradation rate in the various soils, therefore it is expected that the pesticides used in this soil did not impact the validity of the study. Data can be used for kinetic fitting.

Metabolite IN-KT413

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Author(s)	Lentz, N.R. (2003)
Title:	Rates of degradation of [^{14}C]IN-KT413 in three soils
Organisation:	Ricerca Biosciences, LLC
Document No:	DuPont-10499
Dates of experimental work	November 4, 2002 - January 20, 2003
Guidelines:	SETAC Europe (1995), OECD 307
Deviations :	
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR Adendum 3 (2005)
Acceptability:	Yes

MATERIALS AND METHODS

Test material

Radiolabeled test material:	[^{14}C]IN-KT413 technical
Lot/Batch #:	3434-164
Radiochemical purity:	[Trifluoromethoxyphenyl- ^{14}C]IN-KT413: 99.3%
Specific activity:	[Trifluoromethoxyphenyl- ^{14}C]IN-KT413: 47.2 $\mu\text{Ci/mg}$
Description:	Solid

Stability of test compound:

Shown to be stable under the conditions of the test.

Soils

Three soils were chosen to represent conditions of use; Hidalgo County, Texas, USA sandy clay loam; Lleida, Spain, clay loam; and Chestertown, Maryland, USA (Mattapex) silt loam. The soils were freshly collected prior to use. Soils were collected from specific locations with restricted access to ensure that no pesticides or organic fertilizer treatments had taken place for at least five years prior to collection. Soils were air dried slightly under ambient conditions for less than 6 hours then sieved through a No. 10 (2 mm) mesh sieve prior to use and their microbial viability was checked by microbial biomass determination.

Table 8-36 : Characteristics of test soils

Characteristic	Soil		
Soil Name or Designation	Hidalgo	Lleida	Mattapex
Origin	USA	Spain	USA
pH (in water)	8.6	8.1	6.7
% Sand (2000-50 µm)	58.0	34.0	24.0
% Silt (<50-2 µm)	20	38.0	68.0
% Clay (<2 µm)	22.0	28.0	8.0
Texture ^a	Sandy clay loam	Clay loam	Silt loam
Organic carbon (%) ^b	0.5	1.2	2.2
Cation exchange capacity (mEq/100 g)	15.78	20.69	13.78
Maximum water-holding capacity (% at 0 bar)	38.1	45.2	60.9
Field capacity at pF 2.0	30.9	29.3	41.8
Water-holding capacity at pF 2 (% at 0.1 bar)	30.9	29.3	41.8
Microbial biomass (mg microbial C/kg soil)			
Initial	61.9	282	388
Final	56.1	244	364

^a USDA soil classification system

^b organic carbon = organic matter/1.72

Experimental conditions

The rate of degradation of [trifluoromethoxyphenyl-¹⁴C]IN-KT413 was examined in three soils (Table 8-36) under laboratory aerobic conditions. IN-KT413 was dissolved in borate buffer (pH 9) to ensure stability of the test substance. The test soils were treated at a concentration of 0.5 mg/kg soil and incubated in darkness at 20 ± 2°C with a soil moisture of 40–60% of maximum water holding capacity (0 bar moisture). The samples were incubated for a maximum of 35 days. The samples were incubated under aerobic conditions in flow through systems designed to trap evolved carbon dioxide and volatile organic compounds.

All soil samples were extracted 4 times with methanol: 0.01 M borate buffer, pH 9 (4:1, v:v). Soil extracts were combined and analysed by LSC followed by HPLC with radiochemical detection. The post extraction soil solids (PES) were combusted and analysed by LSC. The volatile organic traps were assayed directly by LSC.

RESULTS AND DISCUSSION

Material balance

The average recovery of applied radioactivity exceeded 98% for all soils (99.1% for Hidalgo soil, 99.7% for Lleida soil, and 98.9% for Mattapex soil, Table 8-37). The amount of ¹⁴CO₂ collected was minimal but steadily increased in each soil. At Days 35, 21, and 7, the ¹⁴CO₂ accounted for 2.1, 1.2, and 2.1% applied radioactivity in the Hidalgo, Lleida, and Mattapex soils, respectively. A small amount of radioactivity was detected in the volatile organic traps for each of the soils. By Days 35, 21, and 7, the volatile organics accounted for <1% applied radioactivity in the Hidalgo, Lleida, and Mattapex soils, respectively.

Principal degradation products

Only the concentration of IN-KT413 was monitored during the course of this study (rate of degradation study, metabolite identification is not required).

Non-extractable residue (NER)

As the level of extractable radioactivity decreased, the level non-extractable residues (NER) slowly increased for all three soils during the course of the study (Table 8-37). A maximum NER of 22.3% applied radioactivity was reached at Day 35 for the Hidalgo soil. The maximum NER of 28.5% applied radioactivity was reached at Day 21 for the Lleida soil. The maximum NER of 54.3% applied radioactivity was reached at Day 7 for the Mattapex soil.

Table 8-37 : Percent distribution of radiolabeled components in aerobic soils after application of ¹⁴C-IN-KT413

Soil	Sampling point (days)	Average % applied radioactivity				
		IN-KT413	CO ₂	Volatile organics	NER	Total % recovery
Hidalgo	0	96.1	ns ^a	ns	1.2	99.3
	1	81.9	nd ^b	nd	2.0	100.1
	2	69.3	0.1	nd	3.1	103.2
	3	59.2	0.1	nd	3.7	98.0
	4	48.2	0.2	nd	4.5	99.4
	7	32.9	0.3	nd	6.4	98.9
	14	16.4	0.6	0.2	11.6	101.4
	21	10.1	1.1	0.3	15.3	100.0
	28	5.0	1.6	0.4	19.4	95.5
	35	3.8	2.1	0.6	22.3	95.3
Lleida	0	94.7	ns	ns	3.6	99.9
	1	65.7	nd	nd	4.4	98.9
	2	48.6	0.1	nd	7.1	97.0
	3	38.9	0.1	nd	8.8	98.8
	4	28.7	0.2	nd	9.45	101.6
	7	14.1	0.3	nd	14.7	98.8
	10	10.2	0.4	0.1	18.6	102.7
	14	7.5	0.7	0.1	22.4	100.6
	21	4.3	1.2	0.2	28.5	99.1
Mattapex	0	93.0	ns	ns	4.1	98.3
	1	31.1	0.2	nd	16	100.8
	2	16.0	0.5	nd	27.5	99.5
	3	6.7	0.7	nd	34.5	98.0
	4	4.6	1.1	nd	43.7	98.3
	7	2	2.1	0.1	54.3	98.7

^a not samples

^b not detected

CONCLUSION

IN-KT413 degraded rapidly in the three soils tested. The rate of degradation was faster at more acidic pH.

Comments (RMS 2016)

This study is in compliance with OECD 307 without major deviation and is still acceptable. History of soil treatment is unknown. However, no significant impact on the data from this study is observed. DT₅₀ calculations have been removed from this summary, as updated kinetic evaluation according to FOCUS recommendation (2006) is available for this metabolite. See point B.8.1.1.2.1.3.

Metabolite IN-MK638

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Data point:	CA 7.1.2.1.2
Author(s)	Hatzenbeler, C.J. (2002)
Title:	Rates of degradation of [¹⁴C]IN-MK638 in five soils
Organisation:	Ricerca Biosciences, LLC, Concord, Ohio, USA
Document No:	DuPont-10278
Dates of experimental work	June 10, 2002 – September 23, 2002
Guidelines:	SETAC (1995), OECD Draft (August 2000)
Deviations :	None
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR Adendum 3 (2005)
Acceptability:	Yes

MATERIALS AND METHODS**Test material**

Radiolabeled test material:	[¹⁴ C]IN-MK638 technical
Lot/Batch #:	3489-035
Radiochemical purity:	[Carbonyl- ¹⁴ C]IN-MK638: 99%
Specific activity:	[Carbonyl- ¹⁴ C]IN-MK638: 45.01 µCi/mg
Description:	Solid
Stability of test compound:	Shown to be stable under the conditions of the test.

Soil

Five test soils were used. They were obtained from Hidalgo County, Texas, USA; Lleida, Spain; Chestertown, Maryland, USA (Mattapex); Pesaro, Italy; and Speyer, Germany (Speyer 2.2). Standard soils are collected from specific locations with restricted access managed to ensure that no pesticides or organic fertilizer treatments take place for at least five years prior to collection.

Table 8-38 : Characteristics of test soils

Characteristic	Soil				
Soil Name or Designation	Speyer 2.2	Mattapex	Pesaro	Lleida	Hidalgo
Origin	Germany	USA	Italy	Spain	USA
pH (in water)	6.3	6.2	8.1	8.2	8.4
% Sand (2000-50 µm)	87.6	32	19.6	25.6	58
% Silt (<50-2 µm)	7.2	46	43.2	37.2	16
% Clay (<2 µm)	5.2	22.0	37.2	37.2	26
Texture ^a	Loamy sand	Loam	Silty clay loam	Clay loam	Sandy clay loam
Organic carbon (%) ^b	2.0	1.0	1.0	1.1	0.4
Cation exchange capacity (mEq/100 g)	9.61	8.10	24.99	19.68	13.70
Maximum water-holding capacity (%)	40.4	51.6	54.0	46.0	38.3
Field capacity at pF 2.0	20.8	34.5	41.5	30.1	30.4

Microbial biomass (mg microbial C/kg soil)					
Initial	5.76	26.9	13.2	24.6	49.5
Final	5.24	21.8	12.1	19.6	44.3

^a USDA soil classification system

^b organic carbon = organic matter/1.72

Experimental conditions

The rate of degradation of [carbonyl-¹⁴C]IN-MK638, was examined in five soils (Table 8-38) under laboratory aerobic conditions. IN-MK638 was dissolved in acetonitrile, concentrated, and dissolved in water. Test soils were treated at a concentration of 0.5 mg/kg soil and incubated in darkness at 20 ± 2°C with a soil moisture of 40–60% of maximum water holding capacity (0 bar moisture). Soil samples were for up to 91 days. The samples were incubated under aerobic conditions in flow through systems designed to trap evolved carbon dioxide and volatile organic compounds. Soil microbial biomass analyses were conducted on Day 0 and upon completion of the incubation period for each soil.

Analytical methods

The soil was extracted a total of three times with acetonitrile: water (4:1 by volume). The extracts were combined, concentrated, and analysed by LSC and HPLC with radiochemical detection. The post extraction soil solids (PES) were combusted and analysed by LSC. The volatile organic traps were assayed directly by LSC.

RESULTS AND DISCUSSION

Material balance

The average recovery of total radioactivity exceeded 95% for all soils (100.7% for Hidalgo soil, 98.1% for Lleida soil, 99.2% for Mattapex soil, 95.7% for Pesaro, and 101.5% for Speyer 2.2 soil). The distribution of the applied radioactivity in all soils can be found in Table 8-39. The major degradation product was ¹⁴CO₂. The amount of ¹⁴CO₂ collected steadily increased in each soil. By Day 91 (or Day 60), ¹⁴CO₂ accounted for 94.7, 92.2, 72.5, 90.5, and 90.6% applied radioactivity in the Hidalgo, Lleida, Mattapex, Pesaro, and Speyer 2.2 soils, respectively. No radioactivity above the limit of detection was seen in the volatile organic traps for each of the soils.

Principal degradation products

Only the concentration of IN-MK638 was monitored during the course of this study (rate of degradation study, metabolite identification is not required).

Non-extractable residue (NER)

The level of non-extractable residues (NER) slowly increased for all five soils, reaching a maximum during the course of the study, and then slowly decreased (Table 8-39). The Hidalgo soil NER reached a maximum of 8.8% at Day 14 then slowly decreased to 5.1% applied radioactivity at Day 91. The Lleida soil NER reached a maximum of 7.8% at Day 3 then slowly decreased to 5.5% applied radioactivity at Day 60. The Mattapex soil NER reached a maximum of 9.3% at Day 28 then decreased to 6.5% applied radioactivity at Day 91. The Pesaro soil NER increased to 7.7% at Day 7 then steadily decreased to 3.1% applied radioactivity at Day 60. The Speyer 2.2 soil NER slowly increased to 6.6% at Day 28 and decreased to 5.6% applied radioactivity at Day 91.

Table 8-39 : Distribution of radiolabeled components in aerobic soils treated with ¹⁴C-IN-MK638

Soil	Average % applied radioactivity				
	Sampling point (days)	IN-MK638	¹⁴ CO ₂	NER	Total % recovery
Hidalgo	0	100.9	ns ^a	1.5	102.4
	1	102.6	1.6	4.3	108.45
	3	85.5	8.3	7.2	101.2
	7	68.8	24.2	7.7	100.75
	14	43.35	45.3	8.75	97.4
	28	14.55	72.1	8.0	94.55

	60	2.7	90.6	6.45	99.75
	91	1.05	94.7	5.1	100.9
Lleida	0	100.2	ns ^a	2.65	102.9
	1	92.1	4.3	4.3	100.8
	3	70	18.5	7.7	96.2
	7	43.85	44.8	7.25	95.9
	14	21.8	67.2	6.5	95.55
	28	5.45	84.3	6.5	96.35
	60	1.5	92.2	5.5	99.15
Mattapex	0	105.85	ns ^a	3.6	109.5
	1	102.75	1.9	3.35	107.9
	3	94.05	6.2	5.3	105.55
	7	82.15	16.1	7.1	105.4
	14	68.25	32.7	7.7	108.65
	28	32.35	50.9	9.3	92.55
	60	6.5	67.9	8	82.45
	91	2.55	72.5	6.45	81.45
Pesaro	0	100.95	ns ^a	7.05	108
	1	93.4	5.1	4	102.5
	3	73.85	15.9	6.5	96.2
	7	37.9	44.3	7.65	89.8
	14	13.9	67.5	5.65	87.05
	28	2.85	84.1	4.75	91.7
	60	0.95	90.5	3.1	94.5
Speyer 2.2	0	107.3	ns ^a	1.3	108.6
	1	102.8	2.2	2	107
	3	102.35	6.6	3.05	111.95
	7	78.7	17	5.3	101.05
	14	60.7	31.9	5.4	98.05
	28	30	55.3	6.45	91.75
	60	4.1	84.6	5.45	94.2
	91	3.4	90.6	5.6	99.6

^a not sampled

CONCLUSION

IN-MK638 degraded in the five soils. There was no apparent correlation between soil pH and the rate of degradation.

Comment RMS (2016)

This study is in compliance with OECD 307 without major deviation and is still acceptable.

History of soil treatment is unknown. However, no significant impact on the data from this study is observed.

DT₅₀ calculations have been removed from this summary, as updated kinetic fitting according to FOCUS recommendation (2006) is available for this metabolite. See point B.8.1.1.2.1.3.

Metabolite IN-MK643

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb and is still relied upon. Acceptability was updated in the framework of this renewal.

Data point:	CA 7.1.2.1.2
Author(s)	Caldwell, E. (2002)
Title:	Degradation rates of [¹⁴C]IN-MK643 in five soils
Organisation:	Huntingdon Life Sciences Ltd., Huntingdon, Cambridgeshire, England, UK
Document No:	DuPont-9783
Dates of experimental work	April 16, 2002 – September 19, 2002
Guidelines:	SETAC 1995, OECD Draft October 1999
Deviations :	None
GLP:	Yes
Previous evaluation:	Yes, Indoxacarb DAR Addendum 3 (005)
Acceptability:	Yes

MATERIALS AND METHODS**Test material**

Radiolabeled test material:	¹⁴ C-IN MK643 technical
Lot/Batch #:	[Carbonyl- ¹⁴ C]IN-MK643: BB8998
Radiochemical purity:	[Carbonyl- ¹⁴ C]IN-MK643: >95%
Specific activity:	[Carbonyl- ¹⁴ C]IN-MK643: 54.9 µCi/mg
Description:	White solid
Stability of test compound:	Shown to be stable under the conditions of the test.

Experimental conditions

The rate of degradation of [carbonyl-¹⁴C]IN-MK643 was determined under laboratory conditions in five field-fresh soils (Table 8-40) at 20 ± 2°C. IN-MK643 was dissolved in acetonitrile/water (1/1 by volume) at a nominal concentration of 50 µg/mL and 0.5 mL was applied to 50 g dry weight of soil to give a nominal soil concentration of 0.5 mg/kg. Soil samples were incubated under aerobic conditions in darkness at a soil moisture content of 50% of maximum water holding capacity for up to 120 days. The testing system included an ethyl digol trap followed by two 1.0 N KOH traps to test for the production of organic volatiles and carbon dioxide, respectively. Soil microbial biomass analyses were conducted on Day 0 and upon completion of the incubation period for each soil.

The soil was extracted three times with a mixture of acetonitrile: water (4:1 by volume), generally followed by a single extract with acetone:water solution (1:1 by volume). Soil extracts were concentrated and analysed by LSC followed by HPLC with fraction collection of the eluate and LSC analysis. The post extraction soil solids (PES) were combusted and analysed by LSC. The volatile organic traps were assayed directly by LSC.

Table 8-40: Characteristics of test soils

Characteristic	Soil				
Soil name or designation	Speyer 2.2	Mattapex #25	Pesaro	Lleida	Hidalgo
Origin	Germany	USA	Italy	Spain	USA
pH (in water)	6.3	6.1	8.2	8.0	8.1
% Sand (2000–50 µm)	96.0	40.0	26.4	24.4	52.0
% Silt (<50–2 µm)	2.0	42.0	37.6	39.6	24.0
% Clay (<2 µm)	2.0	18.0	36.0	36.0	24.0
Texture ^a	Sand	Loam	Clay loam	Clay loam	Sandy clay loam
Organic carbon (%) ^b	2.1	0.9	1.2	1.1	0.4
Cation exchange capacity (mEq/100 g)	5.9	8.22	23.06	18.08	14.38

Maximum water-holding capacity (%)	43.1	39.3	59.2	45.6	40.7
Field capacity at pF 2.0	18.8	30.8	38.1	29.2	32.6
Microbial biomass (mg microbial C/kg soil)					
Initial	1010	498	559	787	258
Final	545	92	304	584	98

^a USDA soil classification system

^b organic carbon = organic matter/1.724

RESULTS AND DISCUSSION

Material balance

The average material balance was $99.1 \pm 4.7\%$ (range 88.2 to 110.3%) at all sampling intervals in all soil groups (Table 8-41). Volatile radioactivity increased to 1.9, 3.4, 4.0, 1.9, and 5.5% applied radioactivity in Speyer 2.2, Mattapex #25, Pesaro, Lleida, and Hidalgo soils, respectively, after 120 days.

Principal degradation products

Only the concentration of IN-MK643 was monitored during the course of this study (rate of degradation study, metabolite identification is not required).

Non-extractable residue (NER)

Non-extracted radioactivity increased from 3.0–9.6% applied radioactivity at zero-time to up to 18.5% applied radioactivity in Speyer 2.2 soil (after 120 days), 16.1% applied radioactivity in Mattapex #25 soil (after 120 days), 30.1% applied radioactivity in Pesaro soil (after 120 days), 28.4% applied radioactivity in Lleida soil (after 120 days), and 26.0% applied radioactivity in Hidalgo soil (after 120 days).

Table 8-41: Percent distribution of radiolabeled components in aerobic soils after application of ¹⁴C-IN-MK643

Soil	Sampling point (days)	Average % applied radioactivity				
		IN-MK643	CO ₂	Volatile organics	NER	Total % recovery
Speyer 2.2	0	103.6	ns ^a	ns	3.0	106.6
	1	91.9	0.1	nd ^b	6.6	98.6
	3	98.3	0.2	nd	3.4	101.9
	7	94.5	0.2	nd	4.6	99.3
	14	90.9	0.3	nd	7.4	98.7
	30	84.8	1.1	nd	12.0	97.9
	59	82.9	1.1	nd	14.2	98.2
	90	76.0	1.6	nd	10.6	88.2
	120	79.7	1.9	nd	18.5	100.1
Mattapex #25	0	97.1	ns	ns	7.6	104.7
	1	97.0	0.1	nd	3.9	101.0
	3	92.2	0.3	nd	5.5	98.0
	7	92.3	0.4	nd	6.5	99.2
	14	91.3	0.5	nd	7.8	99.5
	30	82.3	0.9	nd	16.2	99.3
	59	76.8	2.9	nd	13.5	93.1
	90	73.4	3.2	nd	20.0	96.6
	120	77.8	3.4	nd	16.1	97.3
Pesaro	0	95.5	ns	ns	9.6	105.1
	1	84.3	0.1	nd	13.3	97.7
	3	89.2	0.1	nd	12.2	101.4
	7	88.7	0.3	nd	12.3	101.3
	14	86.9	0.6	nd	9.9	97.4

Table 8-41: Percent distribution of radiolabeled components in aerobic soils after application of ¹⁴C-IN-MK643

Soil	Sampling point (days)	Average % applied radioactivity				
		IN-MK643	CO ₂	Volatile organics	NER	Total % recovery
	30	71.7	1.3	nd	26.9	99.9
	59	67.5	2.6	nd	29.6	99.7
	90	63.1	3.4	nd	30.5	97.0
	120	63.8	4.0	nd	30.1	97.9
Lleida	0	96.7	ns	ns	8.9	105.6
	1	88.8	0.1	nd	11.5	100.4
	3	91.0	0.2	nd	7.7	98.9
	7	86.9	0.3	nd	12.6	99.8
	14	89.0	0.6	nd	9.9	99.5
	30	68.8	1.2	nd	28.7	98.7
	59	66.9	1.6	nd	28.5	97.0
	90	67.1	1.9	nd	28.6	97.6
	120	69.0	1.9	nd	28.4	99.2
Hidalgo	0	99.9	ns	ns	5.3	105.2
	1	100.6	nd	nd	9.8	110.3
	3	93.7	nd	nd	7.5	101.2
	7	86.6	0.1	nd	10.7	97.3
	14	89.6	0.2	nd	10.3	100.1
	30	69.4	0.8	nd	29.6	99.8
	59	62.8	3.2	nd	26.4	92.4
	90	58.8	5.4	nd	28.1	92.2
	120	57.4	5.5	nd	26.0	88.8

^a ns = not sampled^b nd = not detected

IN-MK643 degraded in the five soils. There was no apparent correlation between soil pH and the rate of degradation.

Comment RMS (2016)

The study is still acceptable. DT₅₀ calculations have been removed from this summary, as updated kinetic fitting according to FOCUS recommendation (2006) is available for this metabolite. See point B.8.1.1.2.1.3.

Metabolite IN-ML438

The following study was already assessed in the original DAR Addendum 3 (2005) of Indoxacarb but is not relied upon.

Author(s)	Singles, S.K. (2002)
Title:	Rate of degradation and estimated K_{oc} of IN-ML438 in soil
Organisation:	
Document No:	DuPont-11433
Dates of experimental work	n.a.
Guidelines:	US EPA 162-1 (1982), SETAC (1995), OECD 121 (2001)
Deviations :	-
GLP:	-
Previous evaluation:	Yes, Indoxacarb Addendum 3 (2005)
Acceptability:	Kinetic evaluation superseded

This study is a degradation rate evaluation for metabolite IN-ML438 based on the data of Rhodes 1997 and Singles 2002. It is superseded by the kinetic evaluation according to FOCUS recommendation (2006, 2011) provided for the purpose of renewal and summarized under point B.8.1.1.2.1.3.

The following study was submitted to the EU for the first time for the purpose of renewal.

Data point:	CA 7.1.2.1.2/02
Author(s)	Allan, J. (2014)
Title:	Rate of degradation of ^{14}C-IN-ML438 in five aerobic soils
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-36691
Dates of experimental work	
Guidelines:	OECD 307 (2002), USEPA 162-1, OPPTS 835.4100
Deviations :	None
GLP:	Yes
Previous evaluation:	No, study submitted for the purpose of renewal
Acceptability:	Yes

MATERIALS AND METHODS**Test material**

Radiolabelled test material:	^{14}C IN-ML438 technical metabolites		
Lot/Batch #:	[Indanone-1- ^{14}C] IN-ML438, Abbreviated as [I- ^{14}C]IN-ML438	Lot #:	1723247
Radiochemical purity:	99.3%		
Specific activity:	31.3 $\mu\text{Ci/mg}$		
Stability of test compound:	Stable during study		

Soils

Five soils were chosen to represent conditions of use: (international textures) a sandy loam from Hessen, Germany (Gross-Umstadt); a light clay from the Lleida Region of Spain (Lleida); a sandy loam from Alsace, France (Nambshheim); a loam from Kent County, Maryland (Sassafras), and a light clay from Stark County, Illinois (Tama). Soils were freshly collected from the field and stored under refrigeration for less than 30 days. Prior to use, each test soil was homogenised and passed through a 2-mm mesh sieve. Samples were

pre-incubated for 7 days for the definitive test sample series before the test substance was applied. See Table 8-42.

Table 8-42 : Characteristics of test soils

Characteristic	Soil				
Soil name or designation	Gross-Umstadt	Lleida	Nambsheim	Sassafras	Tama
Origin location	Hessen, Germany	Lleida Region of Spain	Alsace, France	Kent County, Maryland, USA	Stark County, Illinois, USA
pH (in water 1:2 ratio)	6.5	7.6	7.3	5.4	5.5
% Sand (2000–50 µm)	41	16	62	52	10
% Silt (<50–2 µm)	44	40	25	35	56
% Clay (<2 µm)	15	44	13	13	34
Texture (USDA) ^a	Loam	Clay	Sandy loam	Sandy loam	Silty clay loam
% Organic matter	2.0	3.2	3.0	1.3	3.1
% Organic carbon	1.2	1.9	1.7	0.76	1.8
CEC ^a (meq/ 100 g)	10.4	17.9	10.6	6.2	18.3
% Moisture at 0 bar (%)	54.2	61.0	51.7	43.2	68.3
Microbial biomass (µg C g ⁻¹ soil)					
Initial	427.0	615.0	679.2	315.7	462.7
Final	493.5	674.6	668.7	364.7	517.0

^a Cation exchange capacity

Experimental conditions

Portions of sieved soils (50 g dry-soil equivalent) were adjusted to 50% of their respective maximum water holding capacities. A solution of the radiolabelled form of the test substance was prepared in water and applied to soil samples (0.2 µg/g dry soil) in separate 250-mL glass bottle. No evaporation procedures were necessary since the amount of solvent was insignificant when compared to the total amount of soil. The soils were mixed after dosing to ensure homogeneity. Water lost to evaporation was replaced, and soils were incubated in the dark at 20 ± 2°C under aerobic conditions for up to 120 days in closed systems to trap evolved carbon dioxide and volatile organic compounds.

Soil samples were taken and analysed for IN-ML438 and other degradation products. Additional samples were prepared and incubated for determination of biomass.

Sampling

Microbial biomass was determined at zero time and at the approximately same time as the definitive test samples. Two samples for each soil system were withdrawn immediately after treatment (Day 0), and then at 3, 7, 14, 30, 44, 62, 93, and 120 days.

Description of analytical procedures

The KOH traps for collecting ¹⁴CO₂ produced by the systems were collected at each sampling day after Day 0 and replaced with fresh material at each sampling event.

Soil samples were typically extracted four times with 100 mL of acetonitrile (the fourth extraction used 100 mL of 80:20 acetonitrile: water), shaken, centrifuged, and decanted. The extracts were analysed in triplicate for total radioactivity by LSC analysis.

Soil extracts were combined, concentrated with rotary evaporator, taken to dryness and reconstituted, then analysed using reverse phase HPLC (Thermo Scientific, Polar Acclaim II C18 (250 mm × 4.6 mm × 5 µm id) eluted with a gradient of 0.01M Ammonium Carbonate (aq) and acetonitrile.

The effluent was passed through a UV detector (254 nm) to detect reference standards and a radioactivity detector to determine the quantities of radiolabelled degradation products present.

Soil samples were combusted, and unextracted ^{14}C levels were measured using LSC.

RESULTS AND DISCUSSION

Mass balance

Material balance for the [^{14}C]IN-ML438 ranged from 96.8 to 99.3%.

Extractable and bound residues

The percentage of radioactivity in the extractable fraction decreased from Day 0 to Day 120. The level of bound residue increased steadily throughout the course of the study with all five soils. Mean extractability values ranged from 95.5% AR (Day 0) to 65.5% AR (Day 120) for Gross-Umstadt soil, 97.6% AR (Day 0) to 66.7% AR (Day 120) for Lleida soil, 97.3% AR (Day 0) to 62.6% AR (Day 120) for Nambsheim soil, 98.4% AR (Day 0) to 71.7% AR (Day 120) for Sassafras soil, and 94.7% AR (Day 0) to 68.0% AR (Day 120) for Tama soil.

Mean bound residues increased with time in all soils. The mean bound residues at termination (Day 120) were 30.7% AR (Gross-Umstadt soil), 29.7% AR (Lleida soil), 33.5% AR (Nambsheim soil), 25.3% AR (Sassafras soil), and 30.1% AR (Tama soil).

Volatilisation

Confirmation of $^{14}\text{CO}_2$ in the KOH trap was performed for all soils. A barium chloride test performed on this system confirmed that the activity trapped was due to the presence of $^{14}\text{CO}_2$. At study termination, evolved $^{14}\text{CO}_2$ values were 2.9, 3.5, 3.0, 2.8, and 2.6% of the applied amount in the Gross-Umstadt, Lleida, Nambsheim, Sassafras, and Tama soils, respectively.

Transformation of metabolite

Levels of IN-ML438 in the soil declined continuously over a period of 120 days. IN-ML438 is transformed in soils over time and would extensively degrade to other metabolites and non-extractable residues. The degradation rate was re-evaluated in DuPont-34821 EU (Point CA 7.1.2) according to FOCUS (2006, 2011) guidelines. The degradation rate (DT_{50}) ranged from 40.6 days to 107.1 days.

The distribution of radiolabelled components at different sampling intervals in five soils are shown in Table 8-43.

Table 8-43 : Distribution of radiolabelled components in aerobic soils after application of [^{14}C]IN-ML438 (% applied radioactivity, mean of duplicate replicates)

Soil (20°C)	Sampling interval (days)	IN-ML438	Total extractable residues ^a	Bound residue ^b	Organic volatiles	$^{14}\text{CO}_2$	Total
Gross-Umstadt	0	88.6	95.5	1.3	NA	NA	96.8
	3	84.8	92.9	2.6	NA	0.7	96.3
	7	79.6	90.8	8.1	NA	1.1	99.9
	14	70.2	86.2	11.5	NA	1.5	99.1
	30	54.5	78.7	17.8	NA	1.7	98.2
	44	42.7	74.4	14.8	NA	1.9	91.0
	62	40.9	71.3	17.0	NA	2.1	90.4
	93	31.9	69.3	28.4	NA	2.6	100.3
	120	24.7	65.5	30.7	NA	2.9	99.0
Lleida	0	92.4	97.6	1.2	NA	NA	98.8
	3	84.5	90.0	4.4	NA	0.7	95.2
	7	83.3	89.1	8.8	NA	1.0	98.9
	14	76.3	85.9	11.9	NA	1.4	99.3
	30	66.1	80.1	16.0	NA	1.8	97.9
	44	62.8	77.2	18.0	NA	2.1	97.3
	62	55.8	71.7	22.2	NA	2.4	96.4
	93	50.9	69.7	26.7	NA	3.1	99.5
	120	47.1	66.7	29.7	NA	3.5	100.0

Nambasheim	0	90.9	97.3	0.0	NA	NA	97.3
	3	87.6	94.2	5.4	NA	0.6	100.3
	7	78.7	89.8	8.6	NA	0.9	99.3
	14	72.8	86.6	11.7	NA	1.3	99.6
	30	60.1	77.3	17.1	NA	1.7	96.1
	44	52.3	75.9	18.4	NA	1.9	96.2
	62	43.1	71.0	22.0	NA	2.2	95.2
	93	36.3	68.0	33.0	NA	2.7	103.7
	120	27.7	62.6	33.5	NA	3.0	99.1
Sassafras	0	92.6	98.4	0.0	NA	NA	98.4
	3	82.1	96.3	3.4	NA	0.5	100.3
	7	79.5	93.7	5.1	NA	0.9	99.7
	14	73.0	92.2	7.3	NA	1.3	100.8
	30	59.7	85.2	10.5	NA	1.6	97.3
	44	46.2	83.1	14.0	NA	1.8	98.8
	62	45.6	75.4	18.3	NA	2.0	95.7
	93	44.0	73.4	26.7	NA	2.6	102.6
	120	37.7	71.7	25.3	NA	2.8	99.8
Tama	0	88.9	94.7	1.3	NA	NA	96.0
	3	84.9	94.2	3.7	NA	0.7	98.6
	7	80.1	90.8	7.9	NA	1.0	99.7
	14	74.7	87.1	11.9	NA	1.3	100.3
	30	59.3	80.9	15.5	NA	1.7	98.0
	44	53.0	75.4	17.7	NA	1.8	94.9
	62	49.7	72.3	21.6	NA	2.0	95.9
	93	43.5	70.1	26.1	NA	2.4	98.7
	120	36.0	68.0	30.1	NA	2.6	100.7

^a Sum of IN-ML438 and all unidentified products

^b Unextractable Residue in soil

NA = Not Applicable/Not analysed

CONCLUSION

IN-ML438 degraded at 20°C in all test soils with DT₅₀ values ranging from 40.6 days to 107.1 days. The results demonstrate that IN-ML438 is transformed in soils over time and would degrade to other metabolites and bound residues.

Comment RMS (2016)

The study is acceptable. Data can be used for kinetic fitting.

B.8.1.1.2.1.3. Rate of degradation for indoxacarb and its relevant metabolites: kinetic evaluation of laboratory data

The following study was summarised in Indoxacarb DAR, Volume 3, B8, AD3, 2005 but is not relied upon.

Data point:	
Author(s)	Russell, M.H. (2004)
Title:	Revised kinetic calculations of DPX-MP062 and metabolites in laboratory soil and water studies following FOCUS guidance
Organisation:	
Document No:	DuPont-14984, Revision No. 1
Guidelines:	Focus, 2006, 2011
Deviations :	None
GLP:	N.a.
Previous evaluation:	Yes, Indoxacarb DAR addendum 3, 2005
Acceptability:	Yes

The kinetic calculation paper DuPont-14984, Revision No. 1, originally submitted under EU Rev8 Point IIA 7.1.1.1.1, has been superseded with DuPont-34821 EU since the modelling was updated with new data and guidance documents have changed since last review. This paper is not relied upon and superseded by the following.

The following study is submitted to the EU for the first time, for the purpose of renewal.

Data point:	CA 7.1.2/01
Author(s)	Partsch, S., Khanijo, I., Price, K., Ball, M. (2015)
Title:	Degradation of indoxacarb and its metabolites IN JT333 (IN-KN125), IN-JU873, IN-KB687, IN-KG433, IN-KT413, IN-MK638, IN-MK643, IN-ML438, IN MP819, IN-MS775, IN-UYG24, IN-U8E24, and IN-U8F52 in soil and water/sediment systems - kinetic calculations following Focus kinetics
Organisation:	Dr. Knoell Consult GmbH, Mannheim, Germany
Document No:	DuPont-34821 EU
Guidelines:	Focus, 2006, 2011
Deviations :	None
GLP:	N.a.
Previous evaluation:	No, study submitted for AIR 3 renewal
Acceptability:	Yes

The study evaluates persistence triggers and modelling endpoints (both DT_{50} and formation fractions) under aerobic conditions for indoxacarb and its metabolites IN-KT413, IN-KG433, IN-JT333, IN-JU873, IN-KB687, IN-ML438, IN-MK643 and IN-MK638.

MATERIAL AND METHOD

Data

Twelve aerobic soil degradation studies have been conducted to investigate the rate of degradation of indoxacarb (DPX-KN128) and its metabolites.

As indicated by RMS in the assessment of soil degradation rate studies, the data from the following soils were not considered for kinetic assessment, and removed from the following summary:

- Data from Chino soil in the study of Rhodes 1997 as slow decline was observed that might have been an indication of microbial inactivity.

- Data from Namsheim soil at 10°C in the study of Rhodes 1997, as data from the same soil at 20 °C are available in the same study.
- Data from Tama (supplemental) in the study of Singles 2002, as considered unreliable due to too long sampling interval at the beginning of the study.

In the end, the following data are retained for kinetic evaluation:

Table 8-44: Summary of reference and origin of the study data retained for kinetic fitting

Study reference	Substance applied	Soils	Substances observed	Origin
Mellor, 2003 (DuPont-8516)	Indoxacarb	Speyer 2.2 at 20°C (Both Labels)	Indoxacarb, IN-JT333, IN-JU873, IN-KG433, IN-KT413, IN-MK638, IN-ML438	DAR AD3 2005
Spare 1997 (AMR 3633-95)	Indoxacarb	Tama at 20°C (Both Labels)	Indoxacarb, IN-JT333	DAR, 2000
Singles 2002 (AMR 2803-93)	Indoxacarb	Tama (Original) at 25°C (Both Labels)	Indoxacarb, IN-JT333, IN-JU873, IN-KB687, IN-KG433, IN-ML438, IN-MK638, IN-MK643	DAR Addendum 3 2005
Rhodes 1997 (AMR 4251-96)	Indoxacarb	Speyer 2.2 at 20°C (TFMP)	Indoxacarb, IN-JT333, IN-JU873, IN-KB687, IN-KG433, IN-ML438, IN-MK638, IN-MK643	DAR, 2000
		Namsheim at 20°C (TFMP)		
Clark (2014) DuPont-35168	IN-JT333	Gross Umstadt at 20°C	IN-JT333	New study For AIR III renewal
		Lleida at 20°C		
		Namsheim at 20°C		
		Speyer 2.2 at 20°C		
		Tama at 20°C		
Mellor (2002) DuPont-8137	IN-JU873	Speyer 2.2 at 20°C	IN-JU873	DAR Addendum 3 2005
		Mattapex at 20°C		
		Pesaro at 20°C		
		Lleida at 20°C		
		Hidalgo at 20°C		
Allan (2012) DuPont 31717	IN-KB687	Lleida at 20°C	IN-KB687	New study For AIR III renewal
		Namsheim at 20°C		
		Sassafras at 20°C		
		Speyer 2.2 at 20°C		
		Tama at 20°C		
Aikens (2002) DuPont-8117	IN-KG433	Speyer 2.2 at 20°C	IN-KG433	DAR Addendum 3 2005
		Mattapex at 20°C		
		Pesaro at 20°C		
		Lleida at 20°C		
		Hidalgo at 20°C		
Lentz (2003) DuPont-10499	IN-KT413	Hidalgo at 20°C	IN-KT413	DAR Addendum 3 2005
		Lleida at 20°C		
		Mattapex at 20°C		
Hatzenbeler (2002) DuPont-10278	IN-MK638	Speyer 2.2 at 20°C	IN-MK638	DAR Addendum 3 2005
		Mattapex at 20°C		
		Pesaro at 20°C		
		Lleida at 20°C		

		Hidalgo at 20°C		
Caldwell (2002) DuPont-9783	IN-MK643	Speyer 2.2 at 20°C	IN-MK643	DAR Addendum 3 2005
		Mattapex at 20°C		
		Pesaro at 20°C		
		Lleida at 20°C		
		Hidalgo at 20°C		
Allan (2014) DuPont-36691	IN-ML438	Gross Umstadt at 20°C	IN-ML438	New study For AIR III renewal
		Lleida at 20°C		
		Nambsheim at 20°C		
		Sassafras at 20°C		
		Tama at 20°C		

Data handling

Input data were generated according to the data handling recommendations made in the FOCUS guidance for degradation kinetics (FOCUS 2006, 2011). In all of the studies where the degradation in each soil was studied using two separate radio-labelling positions ($[^{14}\text{C}\text{-IND}]$ and $[^{14}\text{C}\text{-TFMP}]$), the results for the individual labels were treated as true replicates in the kinetic analysis and not averaged in the parent only optimisations. For parent-metabolites optimizations, results for the individual label were fitted separately as not all same metabolites were observed with both labels.

In accordance with FOCUS guidance, all extractable radioactivity at the time zero samples was entered in the model as the parent substance, and metabolite concentrations at time zero were set to zero. Samples below the limit of detection (LOD), just before or after a detectable amount, were set to half of the LOD and preceding/subsequent samples below the LOD were omitted.

All detailed tables of data are reported in appendix I.

Kinetic model used

Kinetic calculations and optimizations were performed using the fitting program Model Maker version 4.0 and KINGUI software tool version 2.2012.209.845. KinGUI v2.1 was used to optimize complete pathway models (with 3 or more metabolites). Iteratively Least Square (IRLS) method was used instead of linear least square method to optimize complete pathway models for cases where it resulted in better t-test results. Model Maker was used to optimize parent only models and simpler pathway models.

Degradation model

Dissipation of DPX-JW062 proceeded largely via degradation, incorporation into the soil organic fraction (bound residues) and mineralisation to CO_2 . Two major degradative pathways occur in soil: demethylation followed by N-decarboxylation to form IN-JT333 and opening of the oxadiazine ring to form IN-KG433. IN-JT333 undergoes additional transformation via opening of the oxadiazine ring to form IN-JU873, a minor soil degradation product. IN-JU873 is further transformed by bridge cleavage to form the minor degradation products, IN-MK643 and IN-MK638. Alternately, IN-JU873 proceeds through de-esterification and decarboxylation reaction and a ring closure to form IN-ML438, also a minor soil degradation product. IN-KG433 is further transformed through cleavage of the urea bridge to form IN-KB687 (minor degradation product).

The degradation pathway of DPX-MP062 and DPX-JW062 in soil is described in Figure 2.

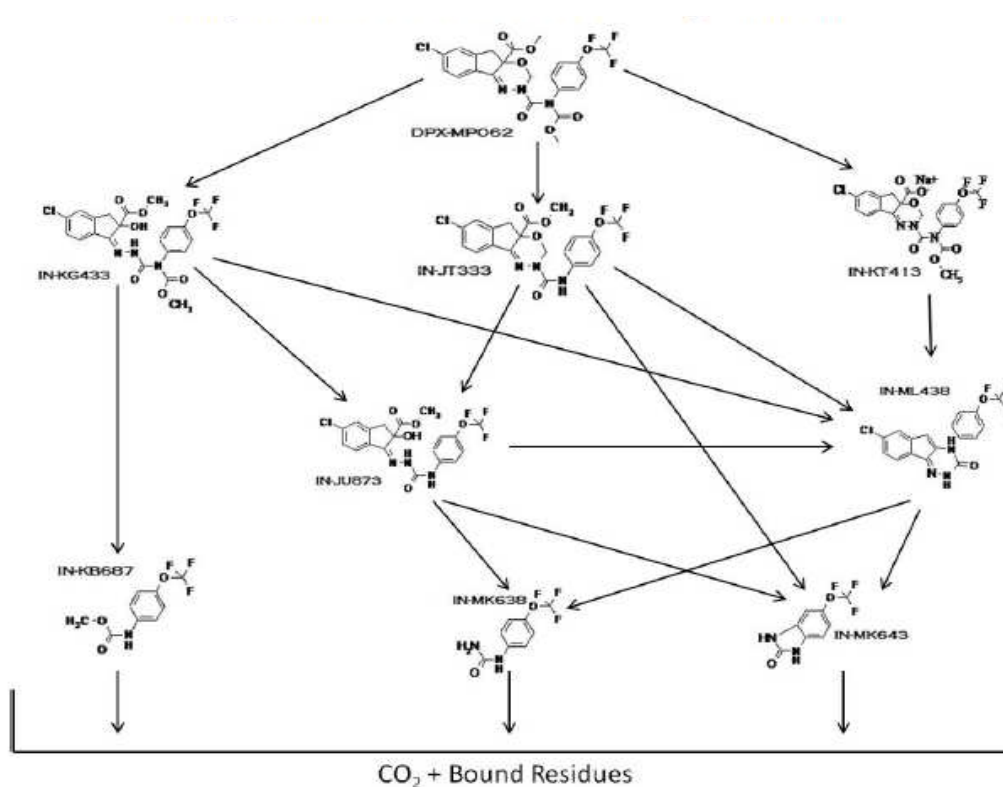


Figure 2: Conceptual model of DPX-MP062 and DPX-JW062 degradation in soil

Determination of persistence trigger and modelling endpoints in soil for parent (indoxacarb or applied metabolites)

Data were fitted at first step in a parent alone run, considering the results for both label (when available) as true replicates.

Persistence triggers

Degradation parameters (DegT_{50} and DegT_{90}) as persistence triggers were derived from degradation studies following the applicable decision tree. In all cases, the performance of SFO and FOMC models are compared. If the degradation curve was better described by the FOMC model, an additional bi-phasic model (DFOP) was attempted.

Modelling endpoints

Environmental fate models, which simulate the degradation of compounds in environmental compartments, usually rely on SFO kinetic models. As a result, the assessment of suitability of a particular kinetic model focuses on the acceptability of SFO kinetics using visual and statistical criteria. For cases where SFO kinetics were not acceptable, and where 10% of the initial value was reached, FOMC kinetics were considered and the modelling DT_{50} calculated as the $\text{DT}_{90}/3.32$. If not DFOP kinetics were considered and modelling DT_{50} calculated from the k_2 parameters.

RMS however notes that given the complexity of the degradation scheme of indoxacarb, and to derive reliable endpoints for modelling, the SFO model was selected as often as possible for metabolites (as recommended by FOCUS 2006), even if the statistical and/or visual assessment did not show that 90% of the degradation was adequately described. This was to ensure that the proposed degradation scheme for modelling is sufficiently conservative for each compound and its subsequent metabolite, as it could not be the case with conservative pseudo-SFO DT_{50} calculated from bi-phasic kinetics.

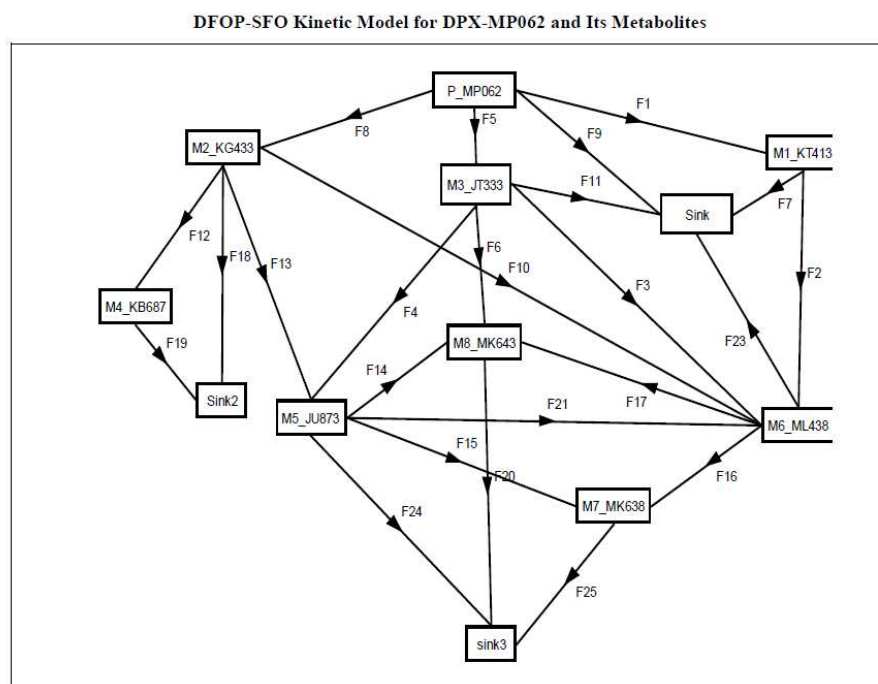
Goodness-of-fit assessment

An assessment of the goodness-of-fit of optimized degradation curves took into account statistical criteria (significance tests and χ^2 errors), and visual assessments were used to evaluate the reliability of all parameter estimates following the guidance of the FOCUS kinetics document (FOCUS, 2006, 2011).

T-test was performed using MS Excel using TDIST function, using standard errors generated by ModelMaker; Chi-square test was performed in Excel following FOCUS 2014 guidance.

Determination of persistence trigger and modelling endpoints in soil for metabolites (from indoxacarb applied studies)

Metabolites were fitted in a “parent-all metabolites” run using best-fit kinetic for parent and SFO for all metabolites, and following the degradation scheme as described in figure below.



Where reliable SFO kinetics could not be fitted to metabolite formation and decline in a given soil, metabolite decline (peak down) kinetics were fitted if clear decline was observed. If not, no reliable DT_{50} or ffm were considered for the given metabolite from the indoxacarb applied studies.

Normalisation

$DegT_{50}$ and $DegT_{90}$ for each soil were normalised when needed to a temperature of 20°C and to a soil moisture content equal to pF2 as recommended by FOCUS.

The reference soil moisture at 100% field capacity was taken from FOCUS (2000) if it was not reported in the study report.

RESULTS AND DISCUSSION

As seen in Table 8-44, for each metabolite data are available from studies with metabolite directly applied and for some of them data are available from one or more of the parent dosed studies. Attempts to fit metabolite formation and decline were made from this data, but did not often resulted in acceptable visual or statistic fits. Then attempts to fit data from decline were made when a clear decline could be observed in the data. When it was not the case, or when the fit from peak was of poor quality, the endpoints derived from parent dosed degradation studies were not considered reliable and only endpoints from metabolite dosed studies were retained. Details are given hereafter.

I. Fits from INDOXACARB dosed studies

Four laboratory degradation studies (Mellor, 2003, Spare, 1997, Rhodes, 1997, and Singles, 2002) were conducted with indoxacarb at different temperatures, including a total of five soils that were finally considered reliable for kinetic purpose by RMS, and resulted in the determination of indoxacarb degradation rate as well as degradation rates of IN-JT333, IN-JU873, IN-KB687, IN-KG433, IN-KT413, IN-MK638, IN-MK643 and IN-ML438.

Findings are reported below - Part A). indoxacarb only for all soils, then Part B). for each metabolite, fits in a parent-metabolite approach and fits from peak for all soils

A. INDOXACARB FITTING

Speyer 2.2 soil

Kinetic parameters and visual fits obtained for parent alone with different kinetics are reported below.

Table 8-45: Summary of kinetics and goodness of fit statistics for Indoxacarb in Speyer 2.2 soil from Mellor (2003)

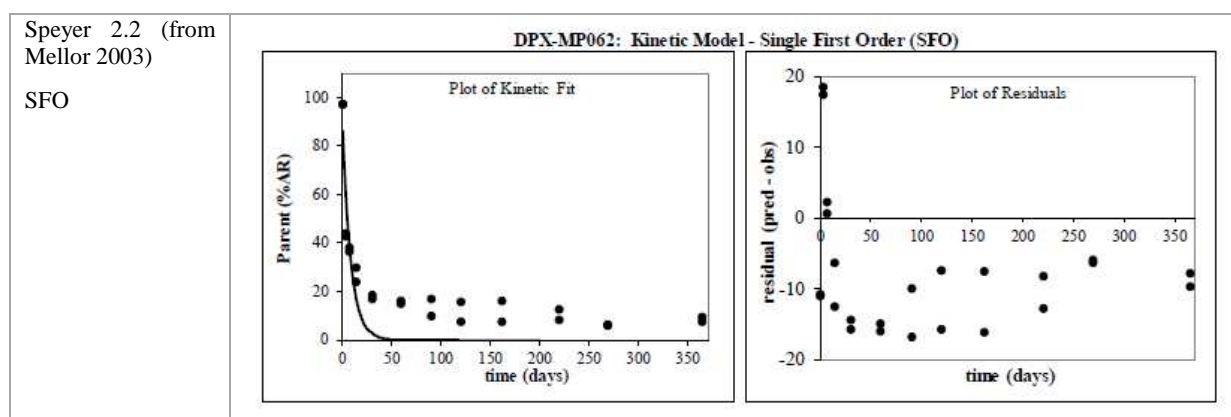
Soil	SFO				FOMC*				DFOP				HS			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)
Speyer 2.2 (Mellor 2003)	6.1	20.2	38	<0.05	2.4	216.9	65.3	5	3.0	193.4	--	p1<0.05; p2<0.05	2.6	171.5	--	p1<0.05; p2<0.05

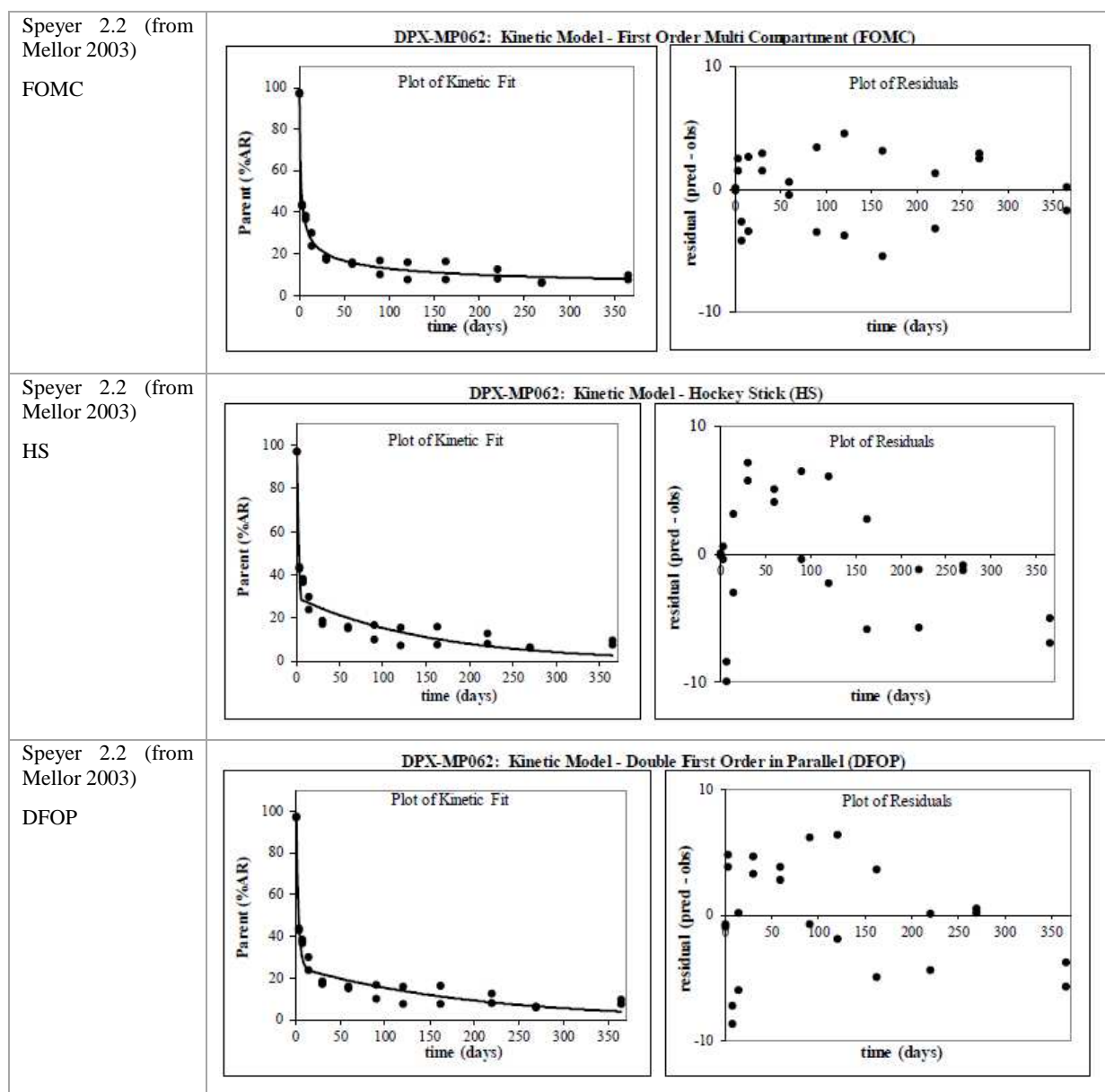
* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence: FOMC was considered best-fit.

Modelling: SFO model resulted in statistically and visually unacceptable fit. Since 10% of the initial value was reached at the end of the study, modelling DT₅₀ calculated as the FOMC DT₉₀/3.32 is proposed to be retained by applicant. This is discussed further in the overall conclusions/RMS comments

Visual fits and residuals for indoxacarb in Speyer 2.2 soil from Mellor 2003.





Tama soil

Kinetic parameters and visual fits obtained for parent alone with different kinetics are reported below.

Table 8-46: Summary of kinetics and goodness of fit statistics for Indoxacarb in Tama soil from Spare (1997)

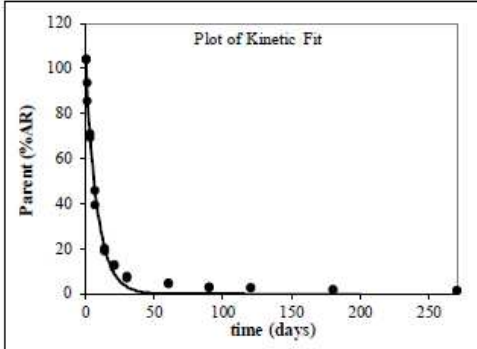
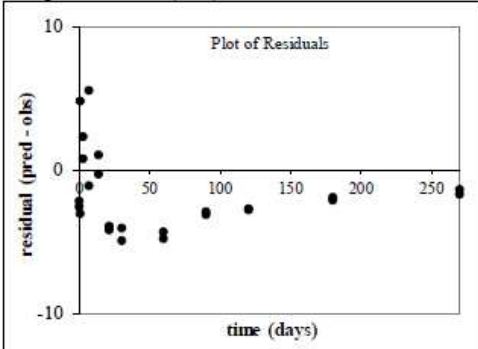
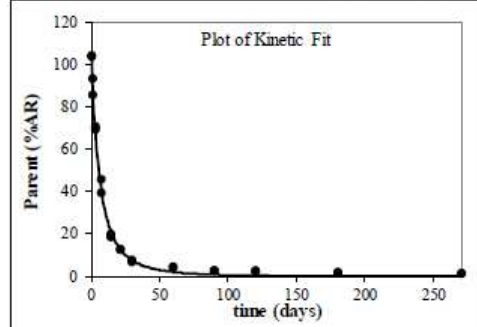
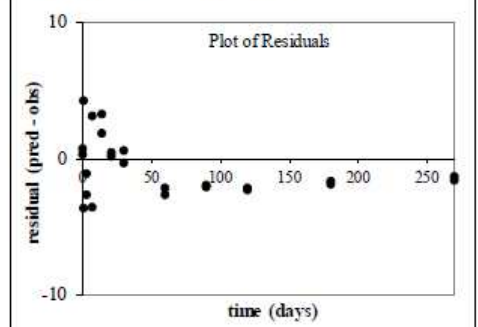
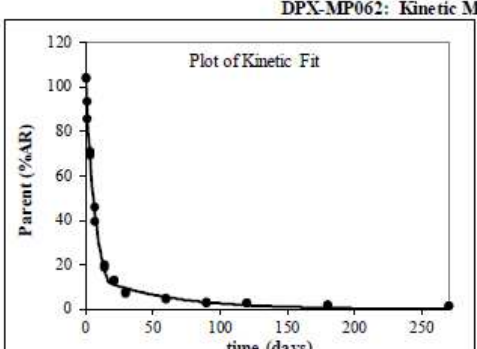
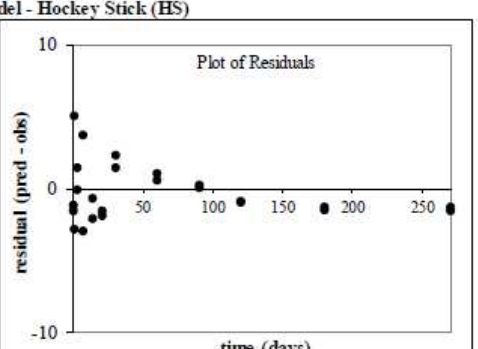
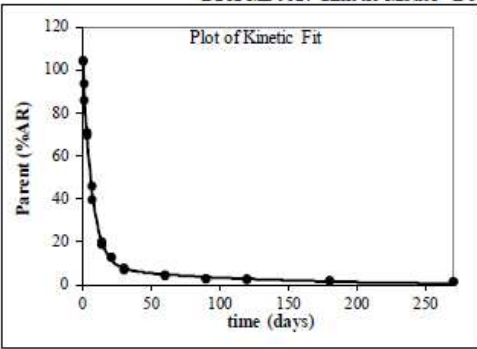
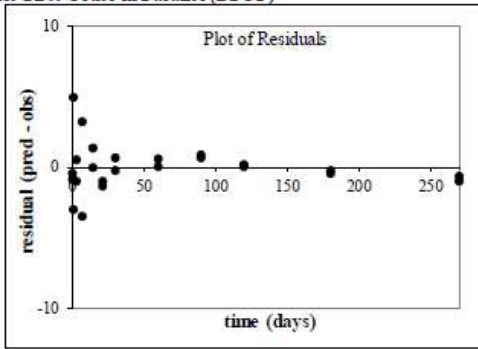
Soil	SFO				FOMC*				DFOP				HS			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)
Tama	6.0	19.8	8	<0.05	5.2	24.7	7.4	4	5.4	23.2	--	p1<0.05; p2<0.05	5.6	25.6	--	p1<0.05; p2<0.05

* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence: DFOP is considered best-fit.

Modelling: SFO model resulted in statistically and visually unacceptable fit. Since 10% of the initial value was reached at the end of the study, modelling DT_{50} calculated as the FOMC $DT_{90}/3.32$ is proposed to be retained by applicant. This is discussed further in the overall conclusions/RMS comments

Visual fits and residuals for indoxacarb in Tama soil from Spare 1997.

Tama (From Spare 1997) SFO	<p style="text-align: center;">DPX-MP062: Kinetic Model - Single First Order (SFO)</p> <div style="display: flex; justify-content: space-around;">   </div>
Tama (From Spare 1997) FOMC	<p style="text-align: center;">DPX-MP062: Kinetic Model - First Order Multi Compartment (FOMC)</p> <div style="display: flex; justify-content: space-around;">   </div>
Tama (From Spare 1997) HS	<p style="text-align: center;">DPX-MP062: Kinetic Model - Hockey Stick (HS)</p> <div style="display: flex; justify-content: space-around;">   </div>
Tama (From Spare 1997) DFOP	<p style="text-align: center;">DPX-MP062: Kinetic Model - Double First Order in Parallel (DFOP)</p> <div style="display: flex; justify-content: space-around;">   </div>

Speyer 2.2 soil (from Rhodes 1997)

Kinetic parameters and visual fits obtained for parent alone with different kinetics are reported below.

Table 8-47: Summary of kinetics and goodness of fit statistics for Indoxacarb in Speyer 2.2 soil from Rhodes 1997

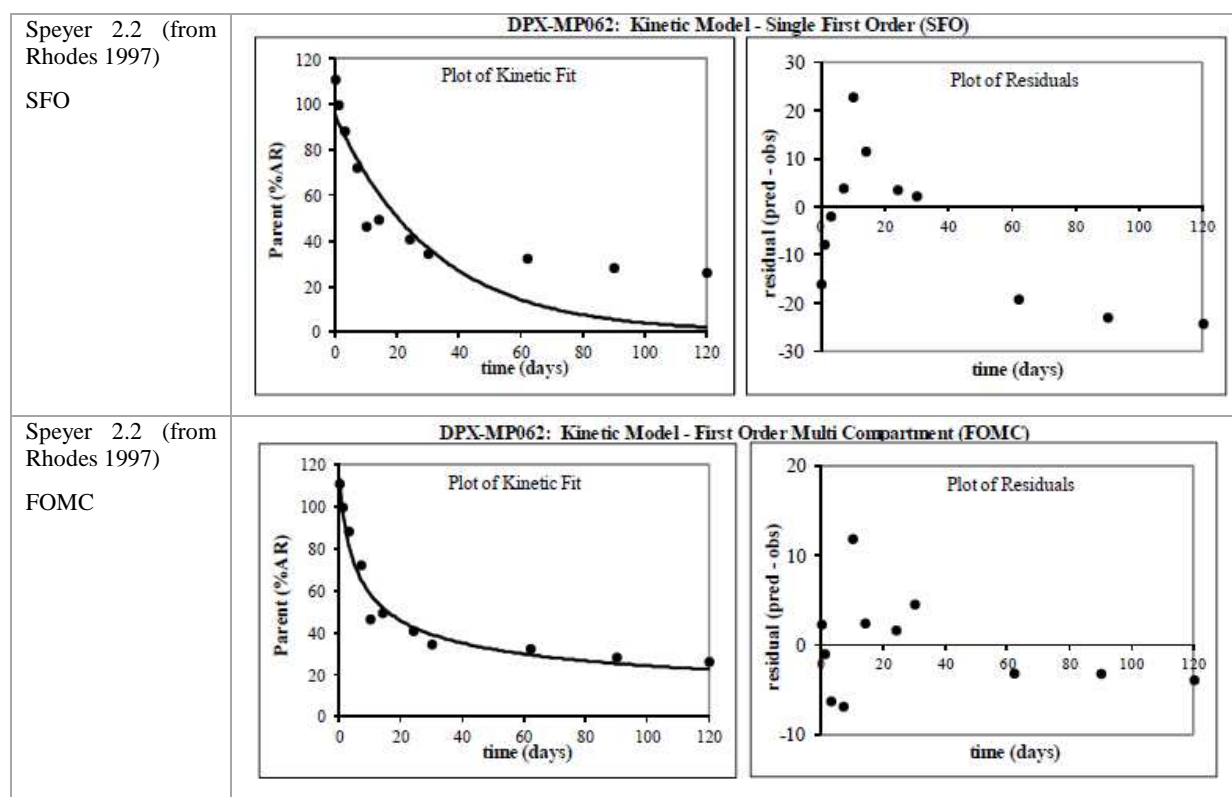
Soil	SFO				FOMC*				DFOP				HS			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)
Speyer 2.2	21.9	72.9	21	<0.05	11.0	618.4	--	8	10.3	404.7	--	p1<0.05; p2=0.108	10.5	322.9	164.5	p1<0.05; p2<0.05

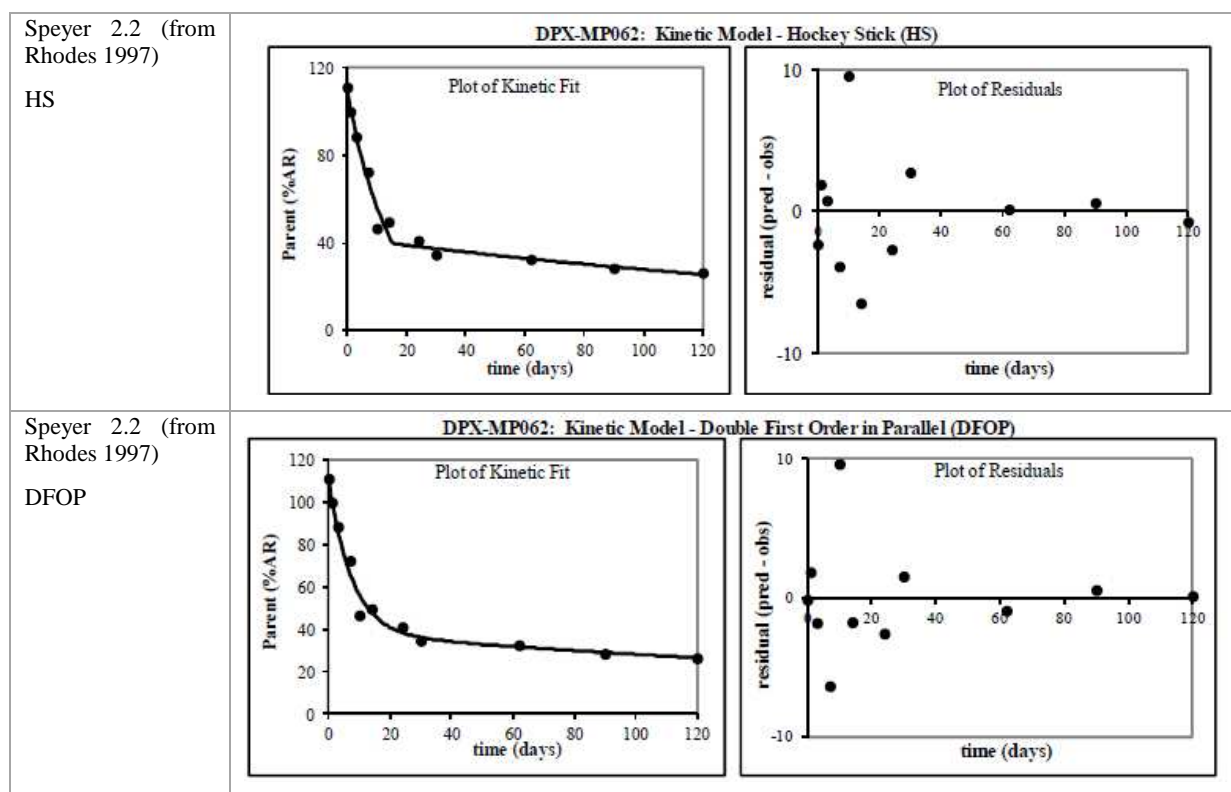
* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence: SFO and FOMC models resulted in non-random residual errors. DFOP model resulted in best visual fit but DFOP k_2 rate failed significance at $P=0.11$. Since DFOP had best visual fit and it was close to passing P value, and $g=0.7$, it was however selected as best fit model.

Modelling: SFO model resulted in statistically and visually unacceptable fit. Since 10% of the initial value was not reached at the end of the study, and that the slow phase of DFOP model failed significance test at $P=0.05$, HS kinetics is proposed to be retained by applicant for modelling. This is discussed further in the overall conclusions/RMS comments

Visual fits and residuals for indoxacarb in Speyer 2.2 soil from Rhodes 1997.





Nambsheim soil (from Rhodes 1997)

Kinetic parameters and visual fits obtained for parent alone with different kinetics are reported below.

Table 8-48: Summary of kinetics and goodness of fit statistics for Indoxacarb in Nambsheim soil from Rhodes 1997

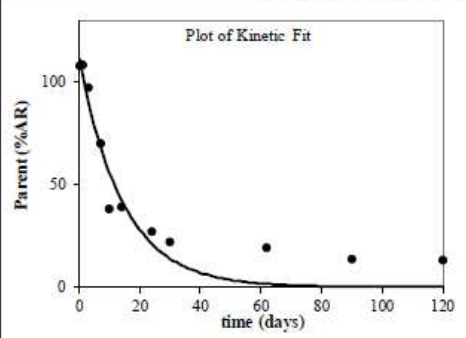
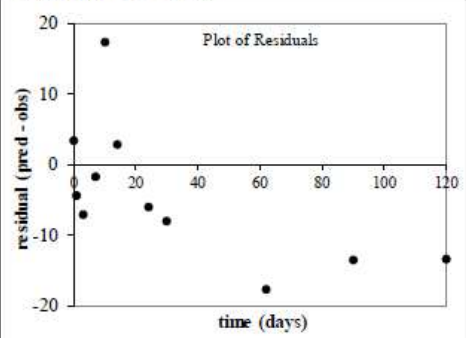
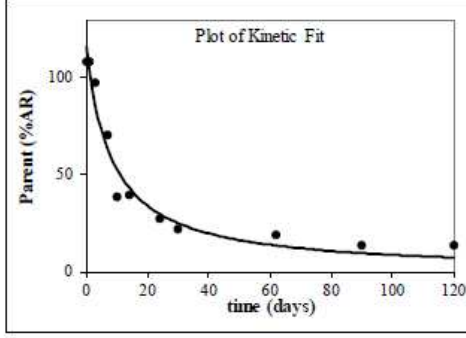
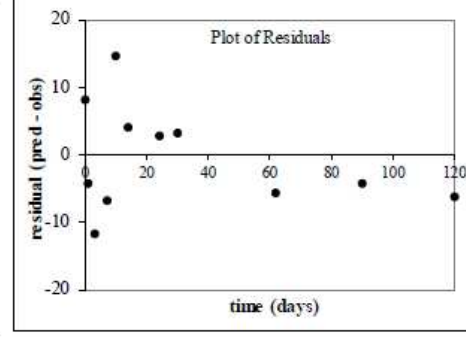
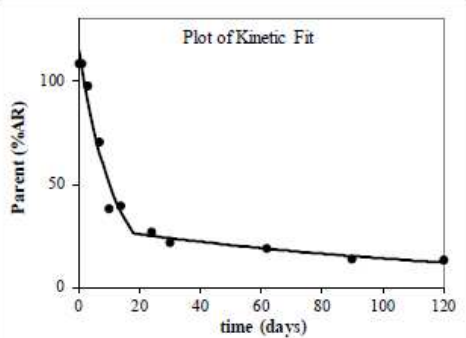
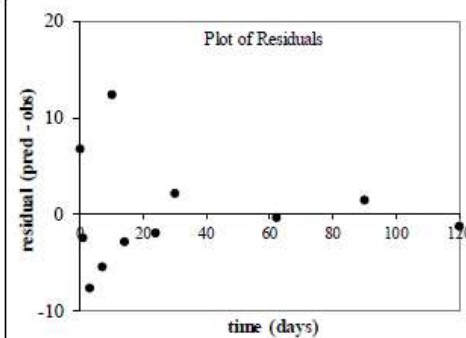
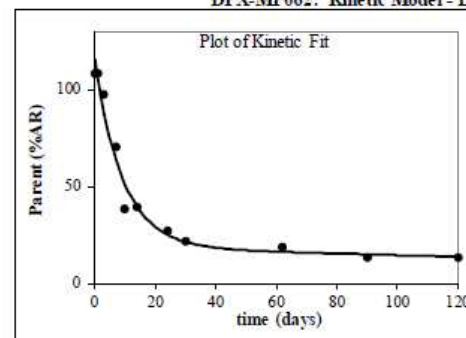
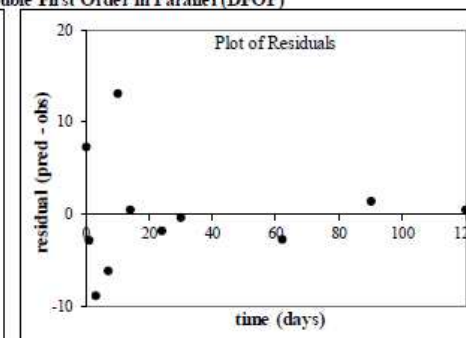
Soil	SFO				FOMC*				DFOP				HS			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)
Nambsheim-20°C	10.0	33.2	16	<0.05	8.4	72.4	--	12	7.0	134.1	120.1	p1<0.05; p2 ns ^g	8.5	127.4	91.1	p1<0.05; p2<0.1

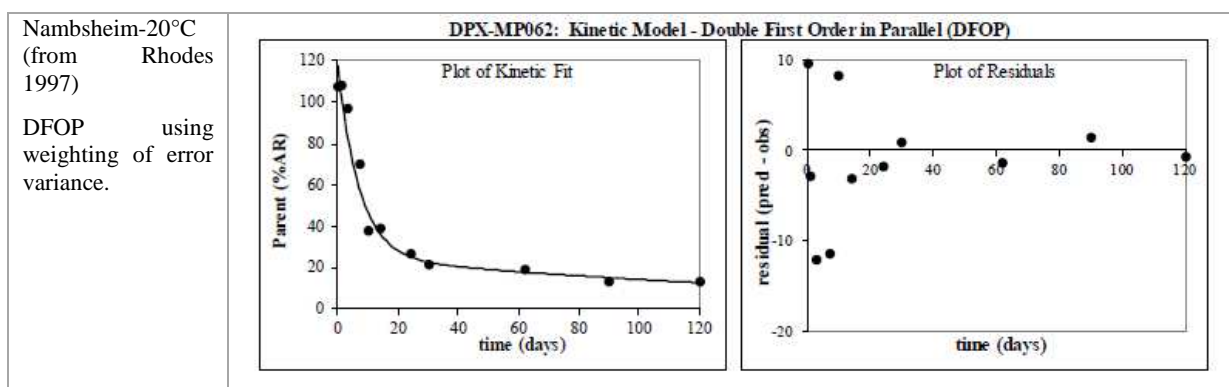
* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence: DFOP is considered best-fit. DFOP model was optimized by weighing of fits (inversely proportional to error variance) to estimate a statically and visually best fit model.

Modelling: Since 10% of the initial value was not reached at the end of the study, DFOP kinetics (best fit) is retained for modelling.

Visual fits and residuals for indoxacarb in Nambsheim soil from Rhodes 1997.

<p>Nambsheim-20°C (from Rhodes 1997)</p> <p>SFO</p>	<p>DPX-MP062: Kinetic Model - Single First Order (SFO)</p>  
<p>Nambsheim-20°C (from Rhodes 1997)</p> <p>FOMC</p>	<p>DPX-MP062: Kinetic Model - First Order Multi Compartment (FOMC)</p>  
<p>Nambsheim-20°C (from Rhodes 1997)</p> <p>HS</p>	<p>DPX-MP062: Kinetic Model - Hockey Stick (HS)</p>  
<p>Nambsheim-20°C (from Rhodes 1997)</p> <p>DFOP</p>	<p>DPX-MP062: Kinetic Model - Double First Order in Parallel (DFOP)</p>  



Tama soil, original (from Singles 2002)

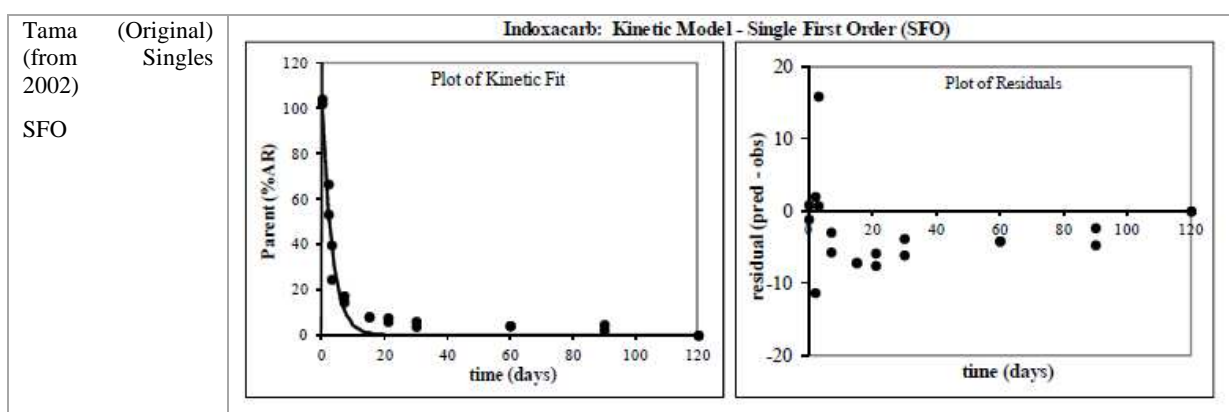
Kinetic parameters and visual fits obtained for parent alone with different kinetics are reported below. RMS notes that the fits provided by applicant were done considering the M0 residue level equal to those from the supplemental study, as no analyses were done at T0 for the original studies (i.e. 102.0 % and 104.0% respectively for Indanon and TFMP label). This was not validated by RMS as the extraction methods were not exactly the same in the two experiments. RMS provided additional fits considering default M0 value of 100%.

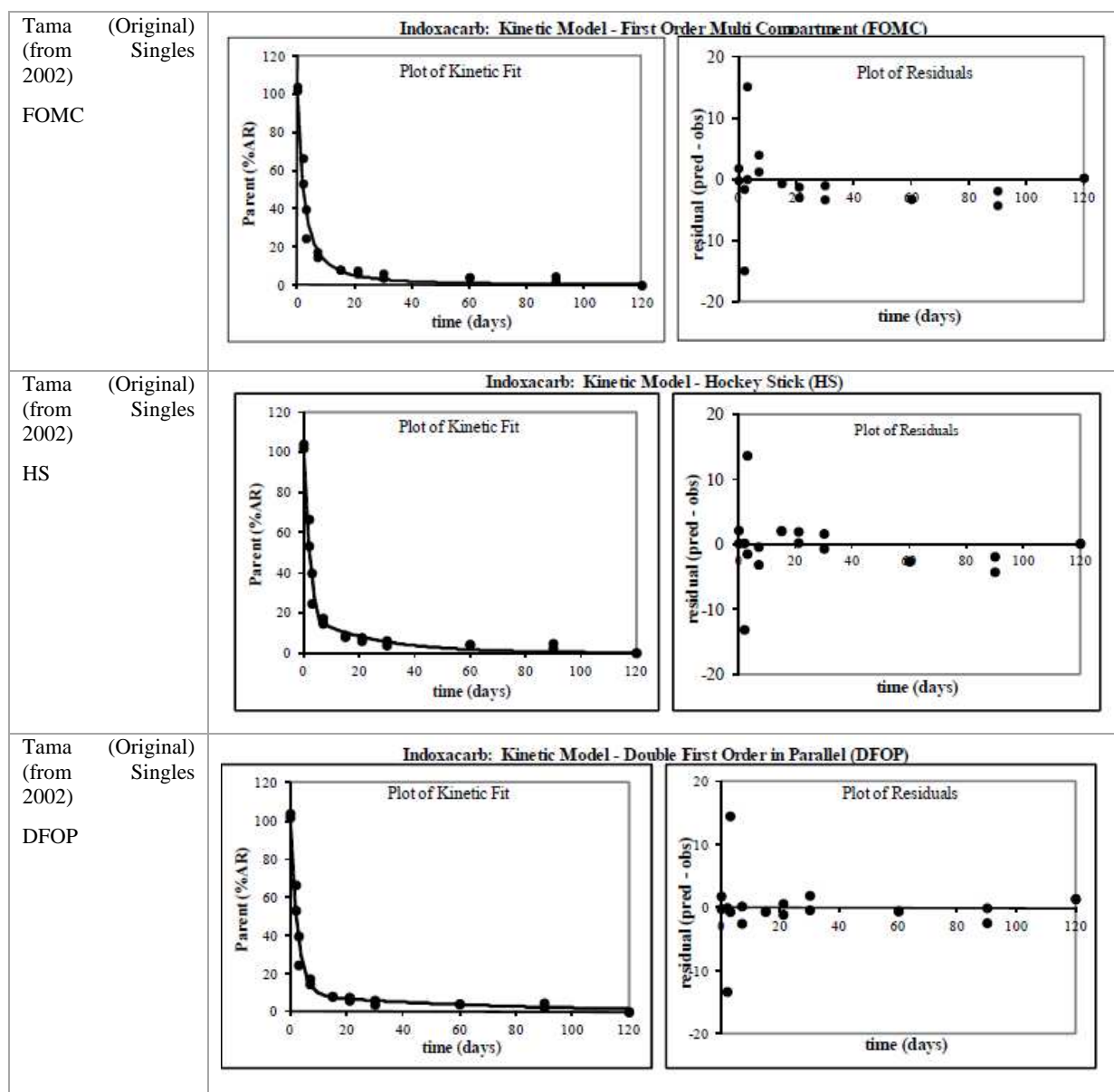
Table 8-49: Summary of kinetics and goodness of fit statistics for Indoxacarb in Tama soil from Singles 2002 (applicant, M0 residue from supplemental study)

Soil	SFO				FOMC*				DFOP				HS			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)
Tama (Original)	2.2	7.4	17	<0.05	2.0	11.8	3.6	14	2.1	9.7	--	p1<0.05; p2=0.15	2.1	14.6	--	p1<0.05; p2<0.05

* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Visual fits and residuals for indoxacarb in Tama soil (original), from Singles 2002.





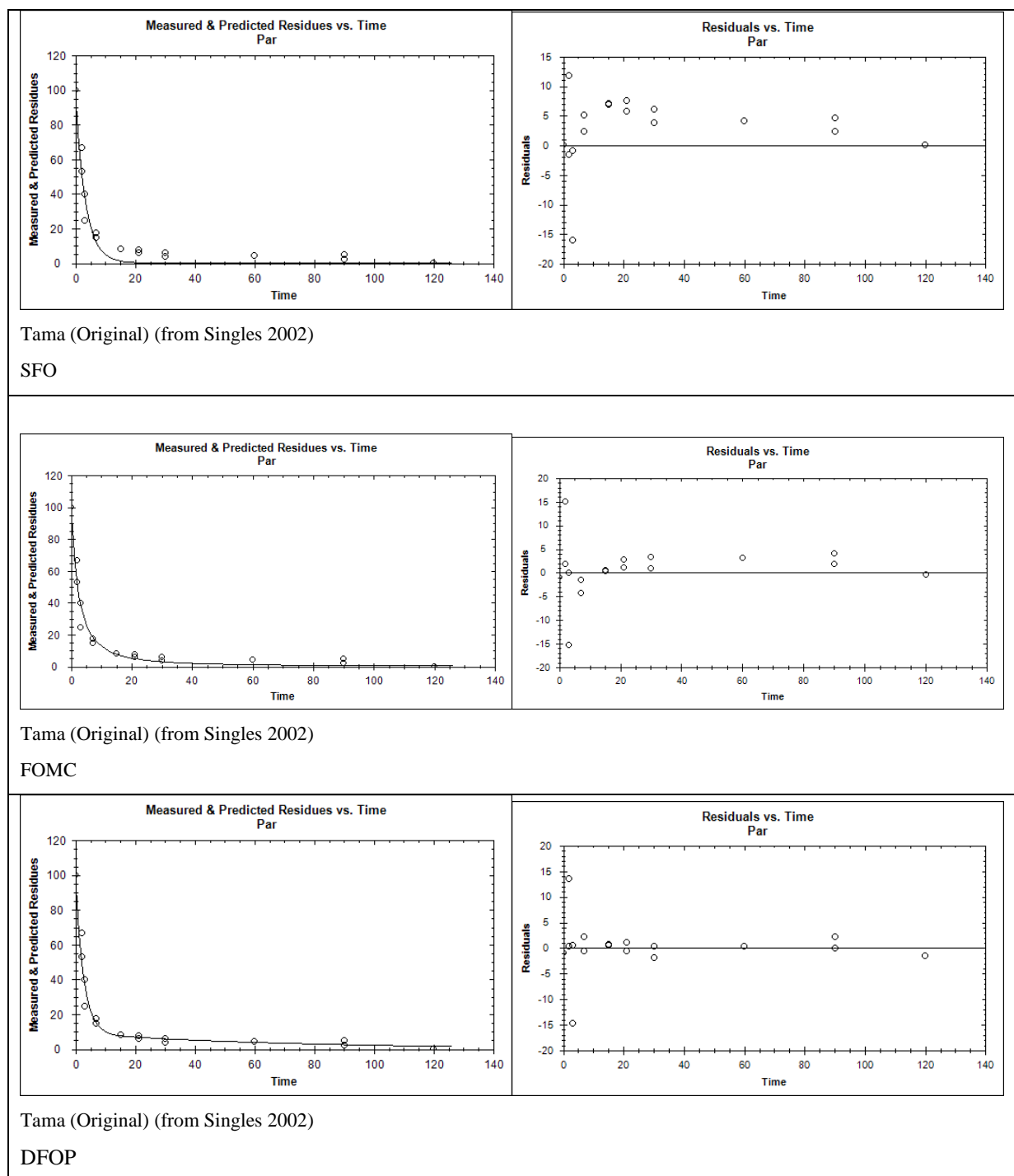
Additional fit from RMS, considering M0 at 100%

Soil	SFO				FOMC				DFOP			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	Slow Phase DegT ₅₀	p (t-test)
Tama (Original)	2.3	7.7	17.4	0.03	2	12	3.6	14.6 CI includes 0 for β	2.15	10	48.2	k1 >0.05 k2 = 0.123

Persistence: SFO and FOMC models resulted in non-random residual errors. DFOP model resulted in best visual fit but DFOP k2 failed significance rate failed at P=0.15. However, since DFOP had best visual fit and it was close to passing P value, it was selected as best fit model.

Modelling: SFO model resulted in statistically and visually unacceptable fit. Since 10% of the initial value was not reached at the end of the study, and that the slow phase of DFOP model failed significance test at $P=0.05$, FOMC is proposed to be retained by applicant for modelling. This is discussed further in the overall conclusions/RMS comments

Visual fits and residual for indoxacarb in Tama soil (original), from Singles 2002.



B. METABOLITES FITTING (from parent applied studies)

The formation and degradation of metabolites was considered in the five soils retained from the degradation studies undertaken with indoxacarb. All metabolites were firstly fitted in a parent best-fit (FOMC) – metabolites (SFO) model. When no reliable fit could be obtain, and if residue data showed a clear decline, fit from peak for separate metabolite were done.

Details of kinetic parameters and visual fits obtained for those fits for each soil are reported below.

Speyer 2.2 soil (from Mellor, 2003)**Formation and decline fit**

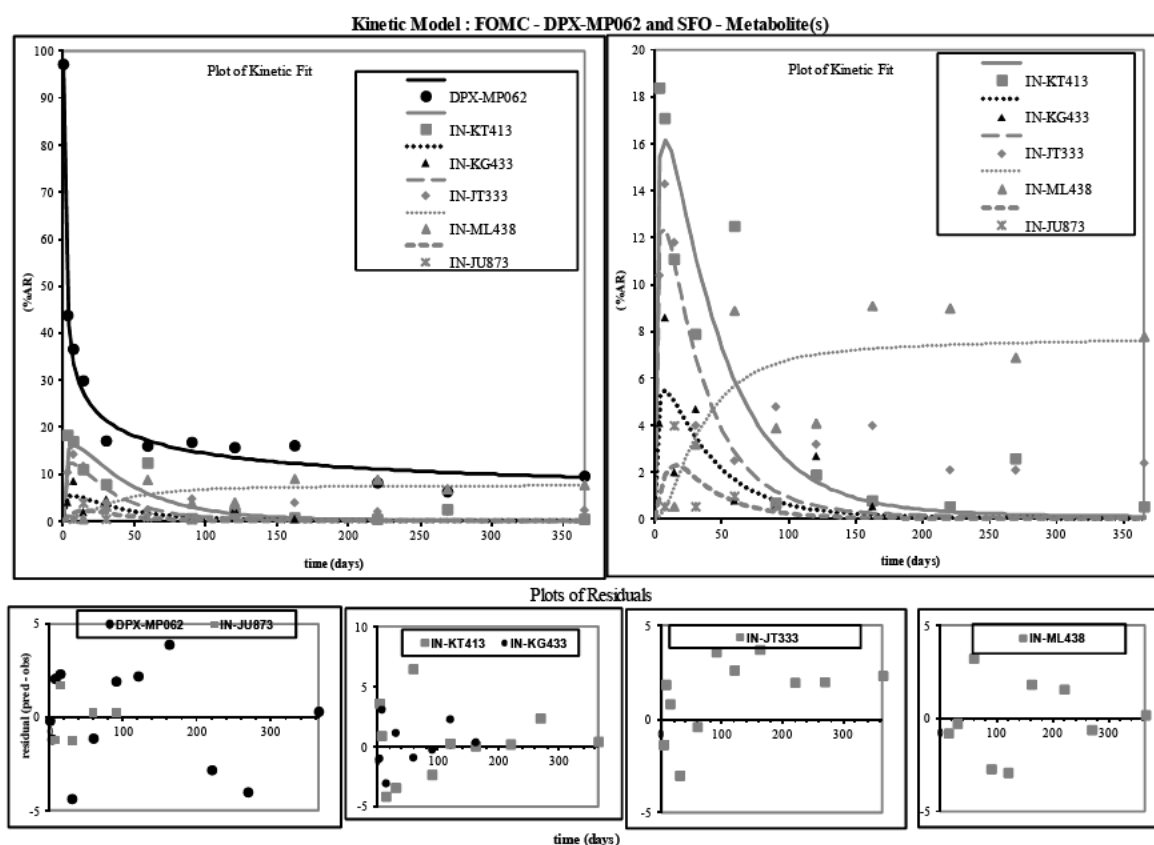
Table 8-50: Summary of kinetics and goodness of fit statistics for metabolites (derived from indoxacarb-degradation studies)

Metabolite	Soil/Label	IN-JT333 via Indoxacarb Kinetics					Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	Formation Fraction from Indoxacarb	
Indoxacarb	Speyer 2.2 (Indanone)	2.3	325.4	8		-	FOMC
IN-JT333	Speyer 2.2 (Indanone)	18.1	60.3	34	<0.1	0.24	FOMC-SFO
IN-JU873	Speyer 2.2 (Indanone)	3.9 ^a	13.0 ^a	75	0.140	0.0, 1.0	FOMC-SFO
IN-KG433	Speyer 2.2 (Indanone)	22.1 ^b	73.5 ^b	49	<0.1	0.10	FOMC-SFO
IN-KT413	Speyer 2.2 (Indanone)	25.5 ^a	84.7 ^a	35	<0.05	0.30	FOMC-SFO
	Speyer 2.2 – Fixed(Indanone)	18.6	61.7	38	<0.05	0.37 ^b	FOMC-SFO
IN-ML438 via IN-JU873 and IN-MP819 Kinetics	Speyer 2.2 (Indanone)	1000 ^{a,b}	3322 ^a	32	0.500	0, 0, 0.35, 0	FOMC-SFO

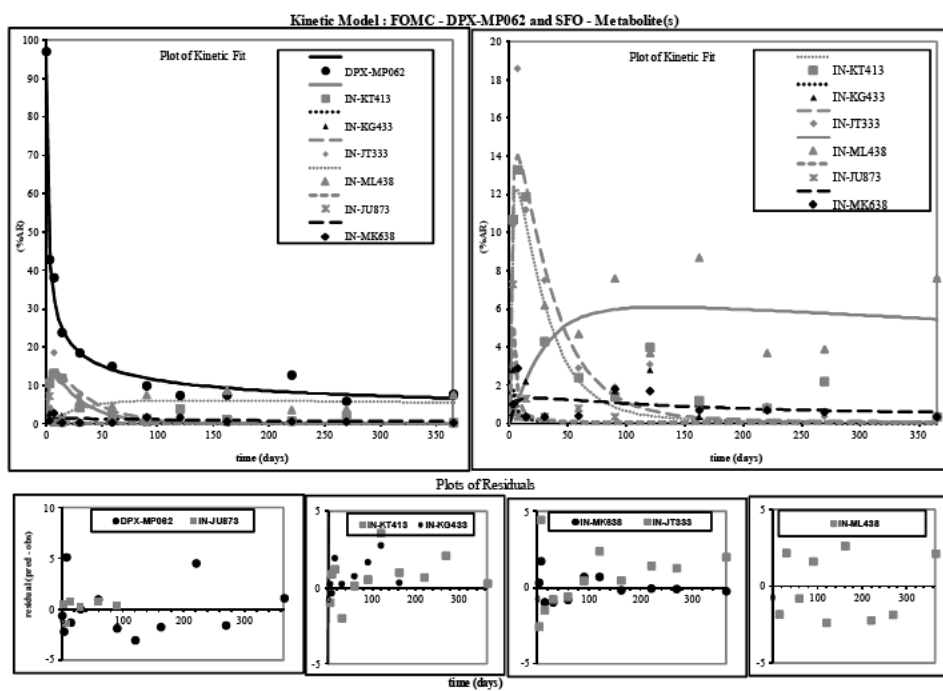
Table 8-51: Summary of kinetics and goodness of fit statistics for metabolites (derived from indoxacarb-degradation studies)

Metabolite	Soil/Label	IN-JT333 via Indoxacarb Kinetics					Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	Formation Fraction from Indoxacarb	
Indoxacarb	Speyer 2.2 (Indanone)	2.4	144.5	9		-	FOMC
IN-JT333	Speyer 2.2 (Indanone)	18.6 ^a	61.9 ^a	29	<0.05	0.27	FOMC-SFO
IN-JU873	Speyer 2.2 (TFMP)	0.8 ^a	2.7 ^a	39	<0.05	1.0, 0.0	FOMC-SFO
IN-KG433	Speyer 2.2 (TFMP)	0.5 ^b	1.5 ^b	78	<0.05	0.49	FOMC-SFO
IN-KT413	Speyer 2.2 (TFMP)	15.5 ^a	51.4 ^a	26	<0.05	0.24	FOMC-SFO
	Speyer 2.2 –Fixed (TFMP)	12.5	41.5	16	<0.05	0.28 ^b	FOMC-SFO
IN-MK638 via IN-ML438 and IN-JU873 Kinetics	Speyer 2.2 (TFMP)	82.5 ^a	270.8 ^a	67	Not calculated	1.0, 0.04	FOMC-SFO
IN-ML438 via IN-JU873 and IN-MP819 Kinetics	Speyer 2.2 (TFMP)	965.1	3206	38	0.258	0, 0, 0, 0.31	FOMC-SFO

Optimized FOMC-SFO kinetic model of indoxacarb and metabolites degradation in the Speyer 2.2 Soil at 20°C – Indanone Label –IRLS Method



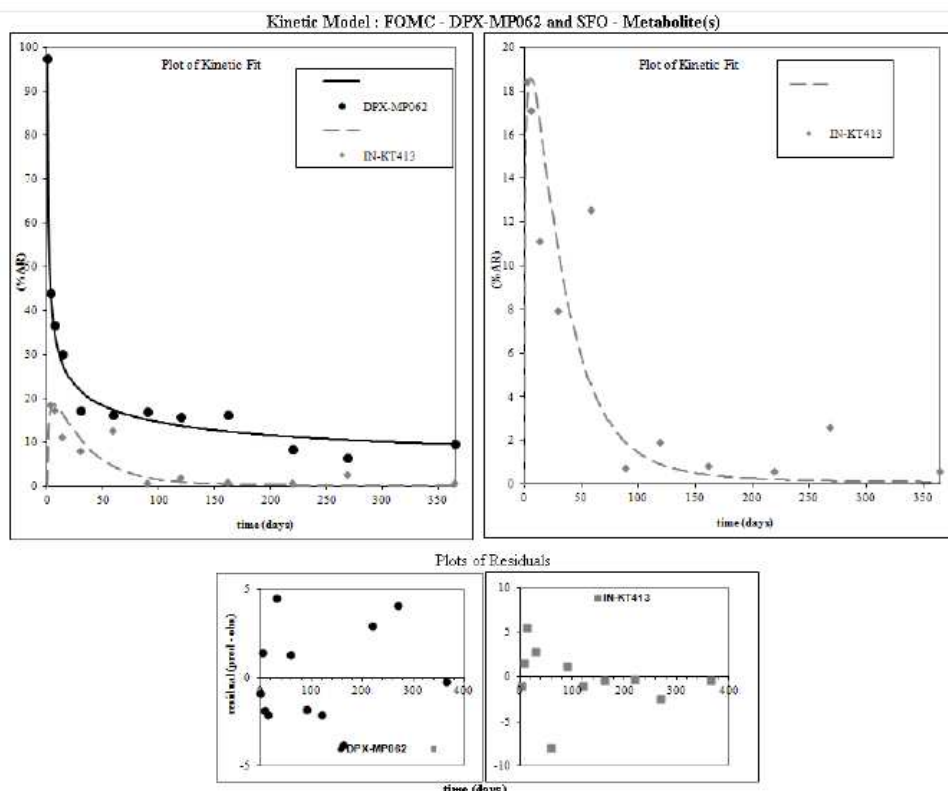
Optimized FOMC-SFO kinetic model of indoxacarb and metabolites degradation in the Speyer 2.2 Soil at 20°C – TFMP Label-IRLS Method



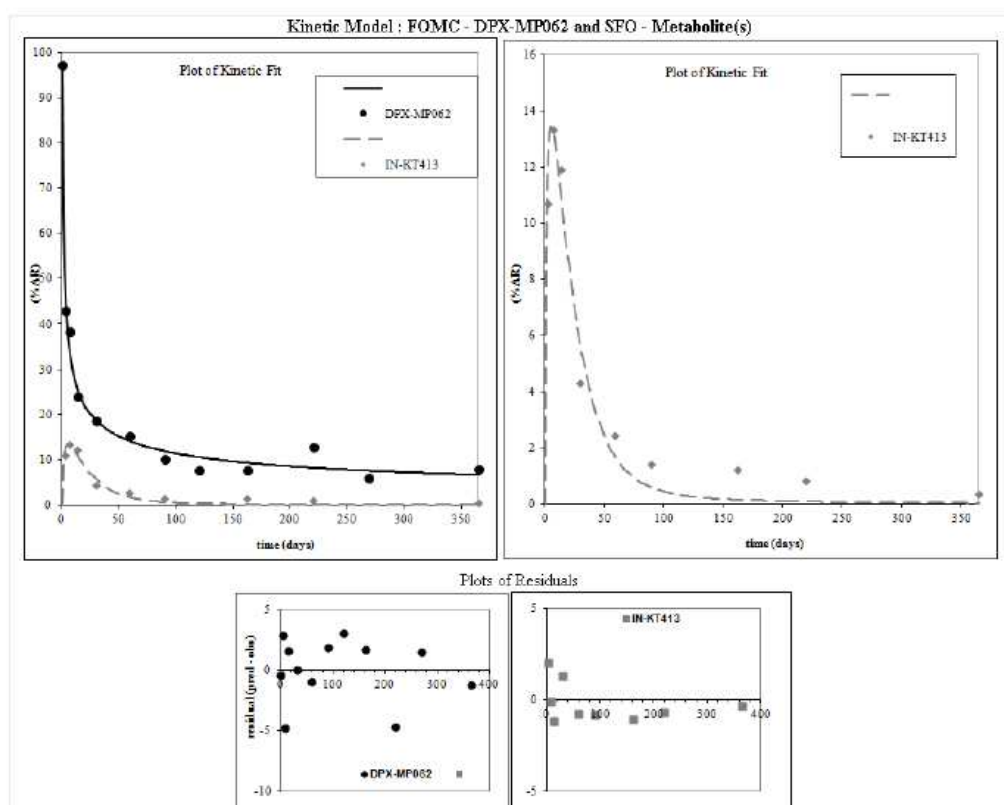
None of the fits resulted in acceptable statistical and visual fits, thus no reliable DT_{50} and formation fractions could be derived for any of the metabolites.

For metabolite IN-KT413 an additional parent FOMC – metabolite SFO run was attempted, to estimate reliable formation fraction. Since the peaks were underestimated, the formation fractions for both fits were fixed slightly higher than optimised value to estimate conservative formation fractions from reliable fits. The formation fractions estimated for modelling purposes from this method were 0.28 and 0.37. However, in these conditions, both fits resulted in unacceptable visual fit as well for degradation rate (see visual fit hereunder). As ffm and DT_{50} can only be retained as couple, none of these endpoints (DT_{50} and ffm) were retained by RMS.

Optimized FOMC-SFO kinetic model of indoxacarb and metabolite IN-KT413 degradation in the Speyer 2.2 Soil at 20°C – Indanone Label –FIXED ffm of 0.28



Optimized FOMC-SFO kinetic model of indoxacarb and metabolite IN-KT413 degradation in the Speyer 2.2 Soil at 20°C –TFMP Label –FIXED ffm of 0.37



Fit from peak

For metabolite IN-JT333, as clear decline phase was observed fits from peak were attempted for this metabolite to estimate degradation rates from the decline curve.

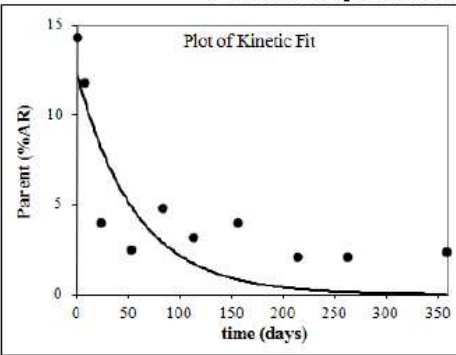
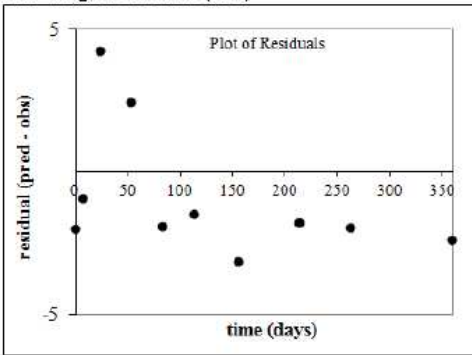
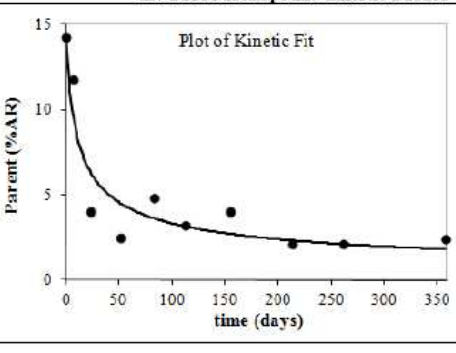
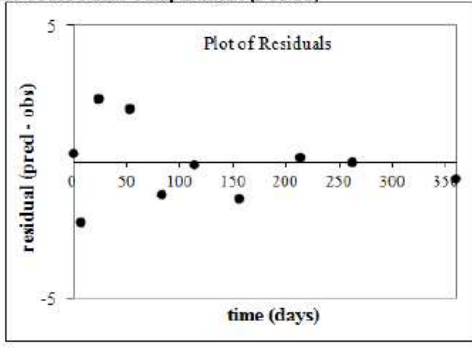
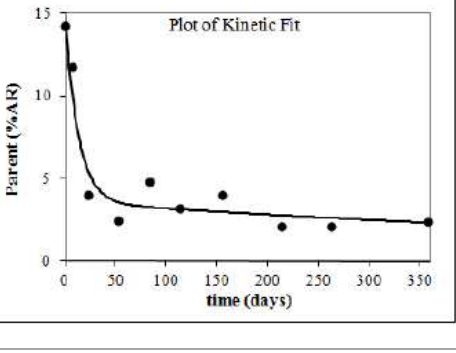
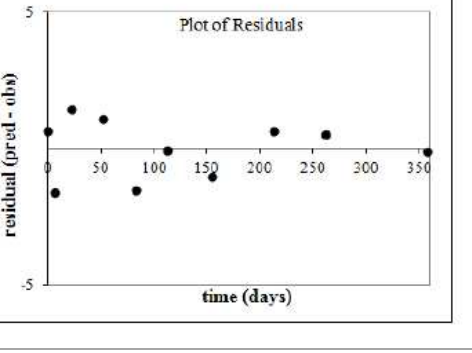
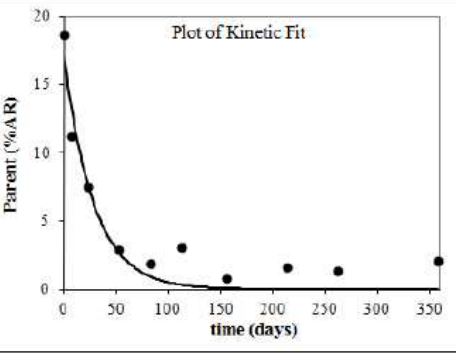
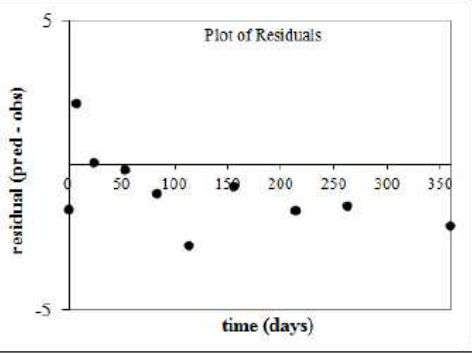
For all other metabolites, no clear decline of the residue are observed in none of these studies with parent applied, no fits from peak were proposed.

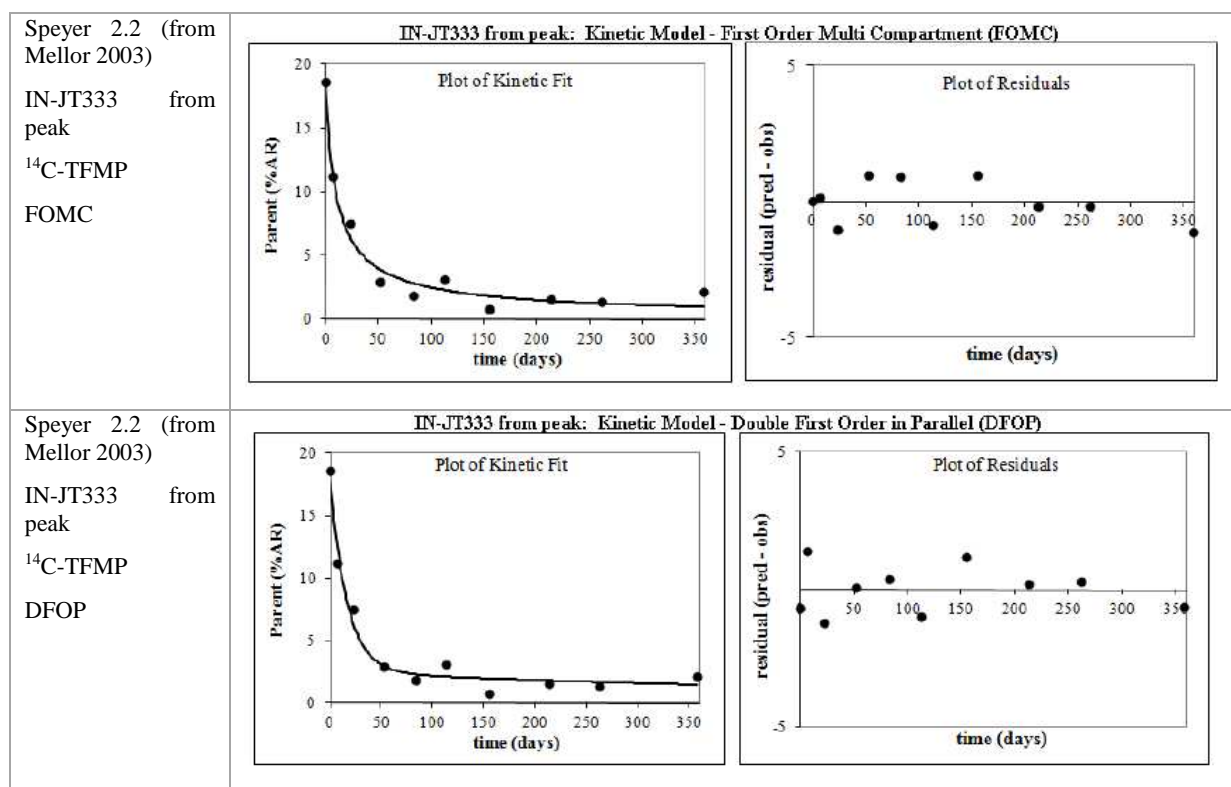
Table 8-52: Summary of kinetics and goodness of fit statistics for IN-JT333-fit from peak (derived from IN-JT333 decline curve from indoxacarb- degradation studies)

Study	Soil	SFO			p (t-test)	FOMC			DFOP			p (t-test)
		DegT ₅₀	DegT ₉₀	χ^2		DegT ₅₀	DegT ₉₀	χ^2	DegT ₅₀	DegT ₉₀	χ^2	
DuPont-8516	Speyer 2.2 (Indanone)	39.7	131.8	38	<0.05	16.2	557.4	22	13.9	725.1	18	p1<0.05; p2 ns
	Speyer 2.2 (TFMP)	19.8	65.6	25	<0.05	11.5	149.2	13	14.4	224.6	15	p1<0.05; p2 ns

ns: not significant

Visual fits and residuals for IN-JT333 in Speyer 2.2 soil from Mellor 2003.

Speyer 2.2 (from Mellor 2003) IN-JT333 from peak ¹⁴ C-Indanon SFO	<p>IN-JT333 from peak: Kinetic Model - Single First Order (SFO)</p>  
Speyer 2.2 (from Mellor 2003) IN-JT333 from peak ¹⁴ C-Indanon FOMC	<p>IN-JT333 from peak: Kinetic Model - First Order Multi Compartment (FOMC)</p>  
Speyer 2.2 (from Mellor 2003) IN-JT333 from peak ¹⁴ C-Indanon DFOP	<p>IN-JT333 from peak: Kinetic Model - Double First Order in Parallel (DFOP)</p>  
Speyer 2.2 (from Mellor 2003) IN-JT333 from peak ¹⁴ C-TFMP SFO	<p>IN-JT333 from peak: Kinetic Model - Single First Order (SFO)</p>  



For IN-JT333 (indanon) no fits were considered acceptable. For IN-JT333 (TFMP), FOMC was considered best-fit and DT₅₀ calculated from FOMC DT₉₀/3.32 was retained for modelling.

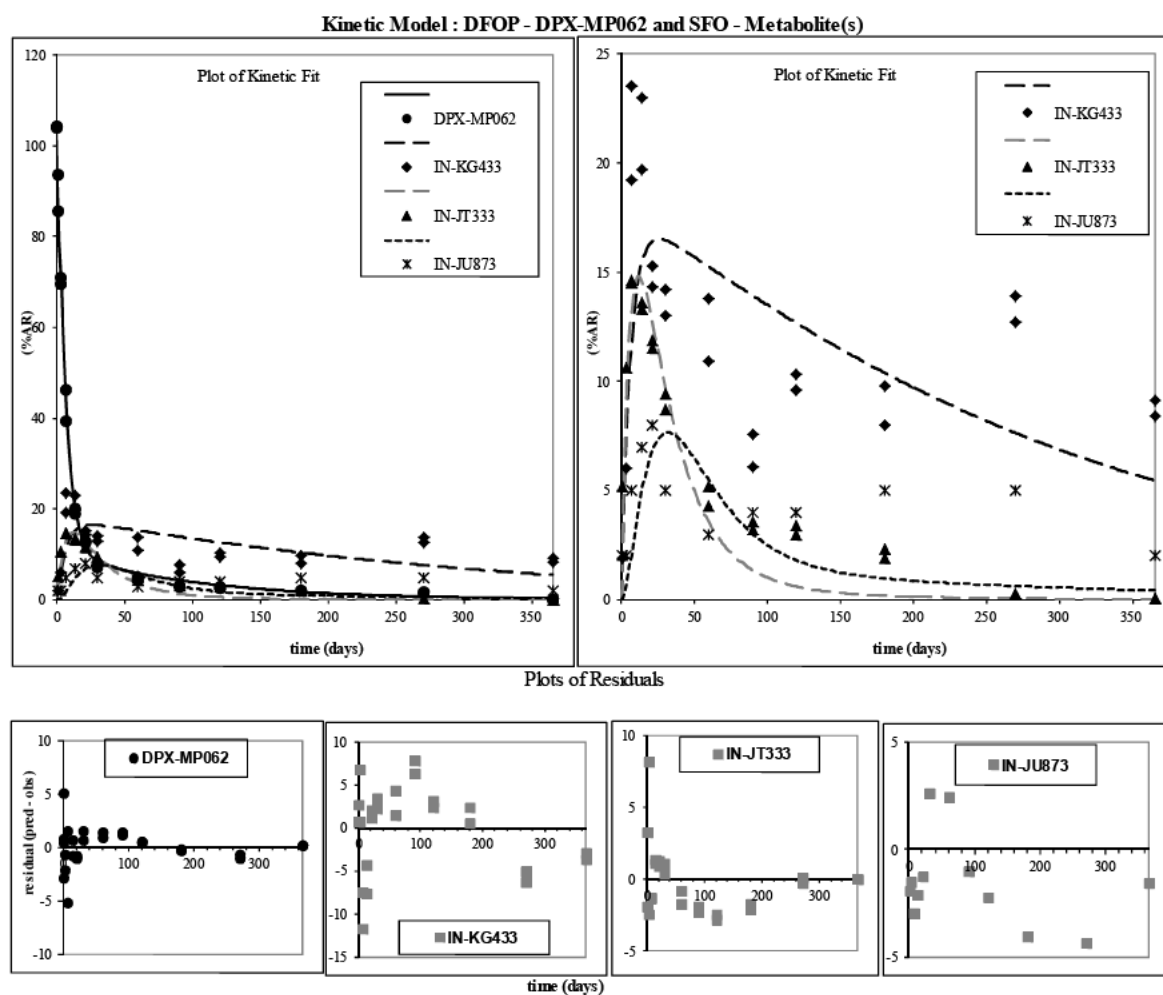
Tama soil (from Spare 1997)

Formation and decline fit

Table 8-53: Summary of kinetics and goodness of fit statistics for metabolites in the Tama soil (from Spare 1997)

Study	Soil/Label	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	Formation Fraction from Indoxacarb	Kinetic Representation
Indoxacarb	Tama (Indanon)	5.1	24.0	3	k1 <0.05 k2 <0.05	-	DFOP
IN-JT333 from indoxacarb	Tama (Indanon)	18.4 ^b	61.1 ^b	20	<0.05	0.24 ^b	DFOP-SFO
IN-JU873	Tama (Indanon)	Chromatographic analyses from the original study considered non reliable for kinetics for these metabolites (no good separation from the baseline)					
IN-KG433	Tama (Indanon)						

Optimized DFOP-SFO kinetic model of indoxacarb and metabolites degradation in the Tama Soil at 20°C Indanon

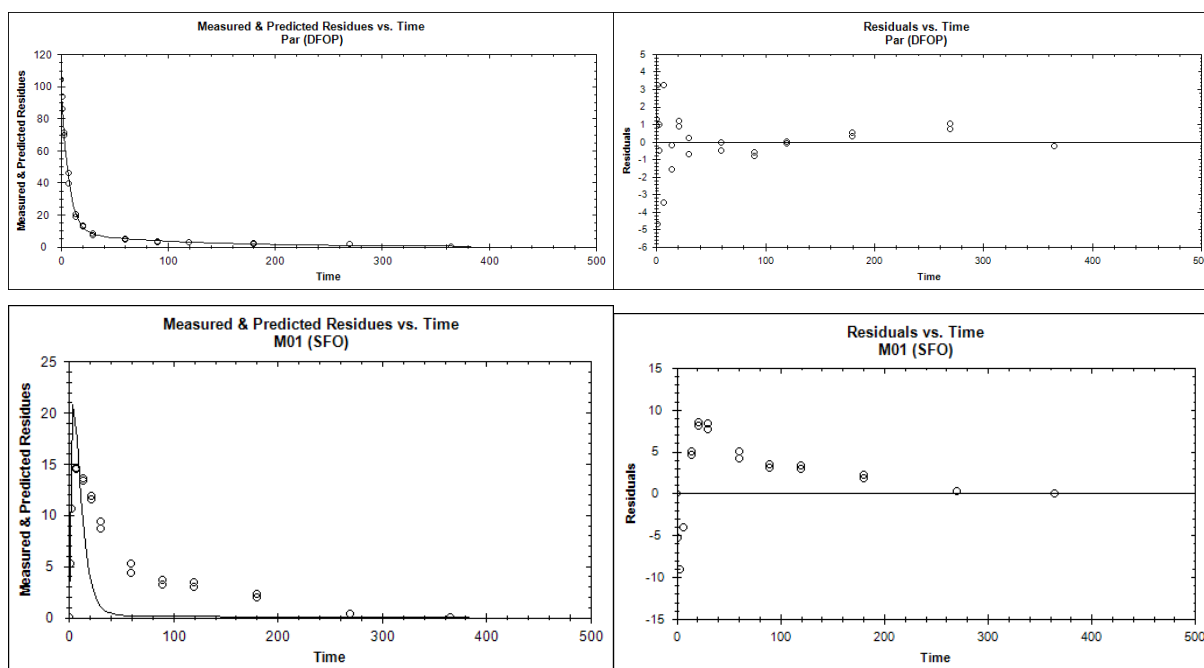


None of the fits resulted in acceptable statistical and visual fits, thus no reliable DT_{50} and formation fractions could be derived for any of the metabolites. Applicant proposed to keep the ffm of 0.24 for IN-JT333, as maximum peak was well represented in the fit.

This was not retained by RMS as the fit showed that the SFO DT_{50} for IN-JT333 derived together with the Ffm of 0.24 did not pass the χ^2 test and the fit was not visually acceptable due to non-random residual in the decline phase. Visual plots provided by applicant were not quite readable and RMS reproduced the fit (with fixed ffm of 0.24). It is however noticeable that different visual fit was obtained by applicant:

Table 8-54: RMS fit for IN-JT333 from parent, Tama soil (Indanon) ffm fixed to 0.24

Study	Soil/Label	DegT ₅₀	DegT ₉₀	χ^2	P (t-test)	Formation Fraction from Indoxacarb	Kinetic Representation
Indoxacarb	Tama (Indanon)	5.46	23.34	2	k1 <0.05 k2 <0.05	-	DFOP
IN-JT333 from indoxacarb	Tama (Indanon)	18.4 ^b	61.1 ^b	62.58	<0.05	0.24 (fixed)	DFOP-SFO



Fit from peak

As clear decline phase was observed for IN-JT333, fit from peak were attempted for this metabolite to estimate degradation rates from the decline curve, and DT_{50} from peak was finally retained for risk assessment (see below).

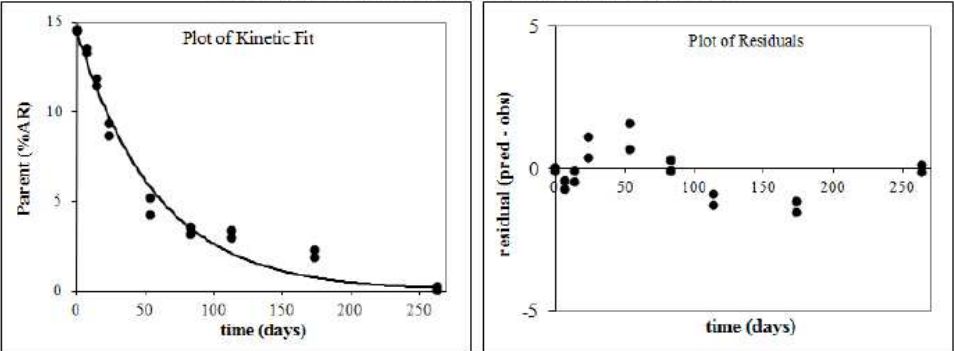
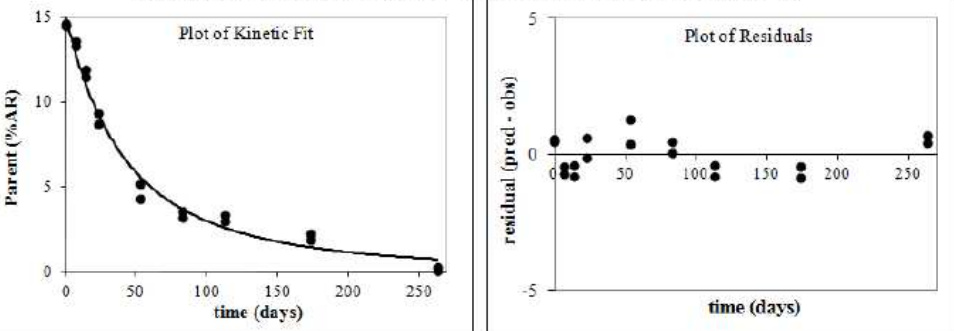
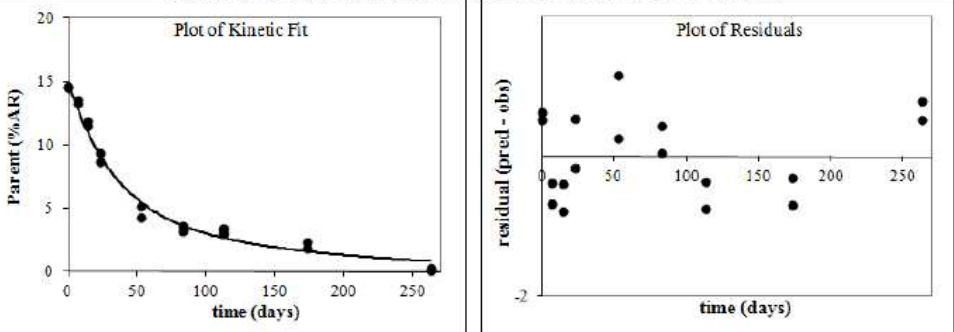
For all other metabolites, no clear decline of the residue are observed in none of these studies with parent applied, no fits from peak were proposed.

Table 8-55: Summary of kinetics and goodness of fit statistics for IN-JT333-fit from peak (derived from IN-JT333 decline curve from indoxacarb- degradation studies)

Soil	SFO				FOMC*			DFOP		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	DegT ₅₀	DegT ₉₀	p (t-test)
Tama (Both Labels)	40.6	134.7	9	<0.05	34.6	168.9	7	33.6	180.9	p1<0.05; p2<0.1

* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Visual fits and residuals for IN-JT333 in Tama soil from Spare 1997

Tama (from Spare 1997) IN-JT333 from peak Indanon SFO	<p>IN-JT333 from peak: Kinetic Model - Single First Order (SFO)</p> 
Tama (from Spare 1997) IN-JT333 from peak Indanon FOMC	<p>IN-JT333 from peak: Kinetic Model - First Order Multi Compartment (FOMC)</p> 
Tama (from Spare 1997) IN-JT333 from peak Indanon DFOP	<p>IN-JT333 from peak: Kinetic Model - Double First Order in Parallel (DFOP)</p> 

Persistence: FOMC was considered best-fit.

Modelling: SFO model resulted in statistically and visually acceptable fit, and was retained for modelling.

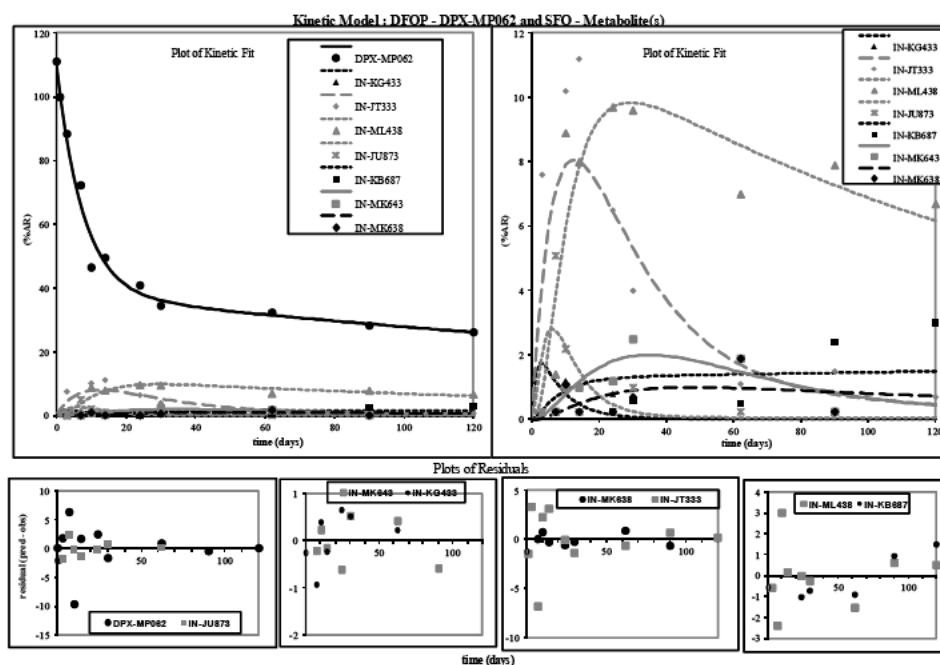
Speyer 2.2 soil (from Rhodes 1997)

Formation and decline fit

Table 8-56: Summary of kinetics and goodness of fit statistics for metabolites (derived from indoxacarb-degradation studies)

Study	Soil/Label	DegT ₅₀	DegT ₉₀	χ^2	P (t-test)	Formation Fraction from Indoxacarb/or metabolite	Kinetic Representation
IN-JT333	Speyer 2.2 (TFMP)	15.6 ^a	51.7 ^a	52	<0.1	0.19	DFOP-SFO
IN-JU873	Speyer 2.2 (TFMP)	2.0 ^a	6.5 ^a	81	<0.1	0.91, 0.0	DFOP-SFO
IN-KB687	Speyer 2.2 (TFMP)	1000 ^b	3322 ^b	46	---	0.89	DFOP-SFO
IN-KG433	Speyer 2.2 (TFMP)	0.8 ^c	2.8 ^c	79	<0.05	0.21	DFOP-SFO
IN-ML438 via IN-JT333, IN-KG433 and IN-JU873	Speyer 2.2 (TFMP)	91.7 ^c	304.4 ^c	19	0.322	0, 0.01, 0.81	DFOP-SFO
IN-MK638 via IN-ML438 Kinetics and IN-JU873	Speyer 2.2 (TFMP)	9.8 ^a	32.7 ^a	72	0.350	1.0, 0.03	DFOP-SFO
IN-MK643 via IN-KG433 and IN-JU873 Kinetics	Speyer 2.2 (TFMP)	18.7 ^a	62.0 ^a	35	<0.1	0.37, 0, 0	DFOP-SFO

Optimized DFOP-SFO kinetic model of indoxacarb and metabolites degradation in the Speyer 2.2 Soil at 20°C – TFMP Label-IRLS Method



None of the fits resulted in acceptable statistical and visual fits, thus no reliable DT₅₀ and formation fractions could be derived for any of the metabolites.

Fit from peak

A clear decline phase was observed for metabolite IN-JT333, therefore, fits from peak were attempted for this metabolite to estimate degradation rates from the decline curve.

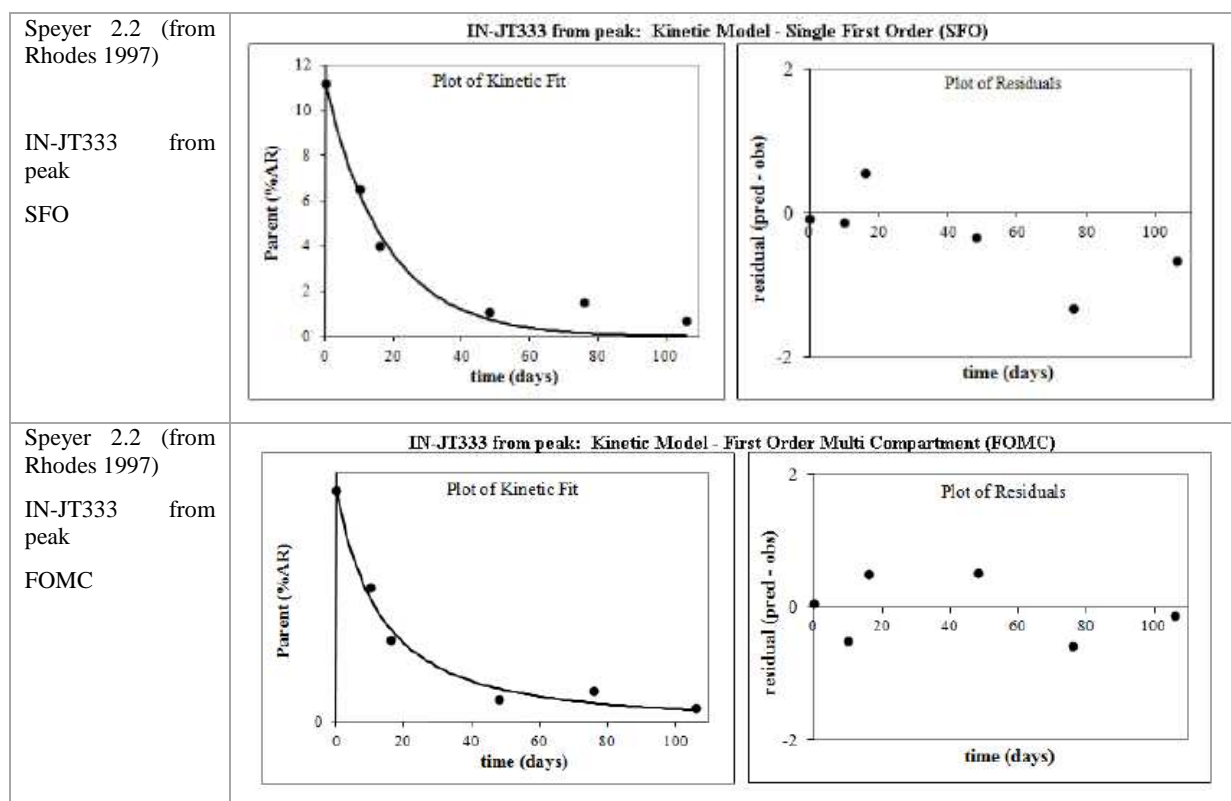
For all other metabolites, no clear decline of the residue are observed in none of these studies with parent applied, no fits from peak were proposed.

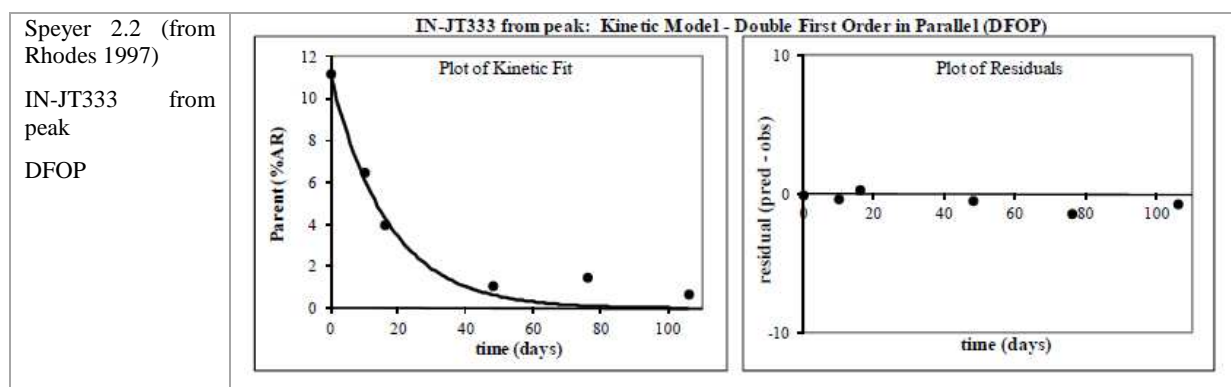
Table 8-57: Summary of kinetics and goodness of fit statistics for IN-JT333-fit from peak (derived from IN-JT333 decline curve from indoxacarb- degradation studies)

Study	Soil	SFO			p (t-test)	FOMC*			DFOP		
		DegT ₅₀	DegT ₉₀	χ ²		DegT ₅₀	DegT ₉₀	χ ²	DegT ₅₀	DegT ₉₀	p (t-test)
AMR 4251-96)	Speyer 2.2 (TFMP)	12.4	41.3	13	<0.05	11.3	65.2	9	11.8	39.1	p1 ns ^a , p2 ns ^a

* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Visual fits and residuals for IN-JT333 in Speyer 2.2 soil from Rhodes 1997.





Persistence: FOMC was considered best-fit.

Modelling: SFO model resulted in statistically and visually acceptable fit, and was retained for modelling

Nambsheim soil (from Rhodes 1997)

Formation and decline fit

Table 8-58: Summary of kinetics and goodness of fit statistics for metabolites (derived from indoxacarb-degradation studies)

Study	Soil/Label	IN-JT333 via Indoxacarb Kinetics					Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	P (t-test)	Formation Fraction from Indoxacarb	
IN-JT333	Nambsheim (TFMP)	6.2 ^a	20.7 ^a	49	<0.05	0.29	DFOP-SFO
IN-JU873	Nambsheim 20°C (TFMP)	18.0 ^b	59.6 ^b	64	0.150	0.0, 0.5	DFOP-SFO
IN-KG433	Nambsheim 20°C (TFMP)	205.4 ^b	682.2 ^b	25	0.202	0.31	DFOP-SFO
	Nambsheim 20°C (TFMP) - Fixed	90.1 ^c	299.1 ^c	29	---	0.37	DFOP-SFO
IN-ML438 via IN-JU873 and IN-MP819 Kinetics	Nambsheim 20°C (TFMP)	60.4 ^d	200.6 ^d	27	0.312	0, 1, 0	DFOP-SFO
IN-MK638	Nambsheim 20°C (TFMP)	12.9 ^d	42.8 ^d	73	0.231	0.0, 1.0	DFOP-SFO
IN-MK643 via IN-KG433 and IN-JU873 Kinetics	Nambsheim 20°C (TFMP)	20.8 ^d	69.1 ^d	57	<0.1	0.5, 0, 0	DFOP-SFO

^a Endpoint considered unreliable even though significance test passes at P=0.05, because visual fit considered unacceptable due to underestimation of the peak.

^b Endpoint considered unreliable because even though significance test passes at P=0.05, visual fit is unacceptable due to non-random residual errors and $\chi^2 > 15\%$.

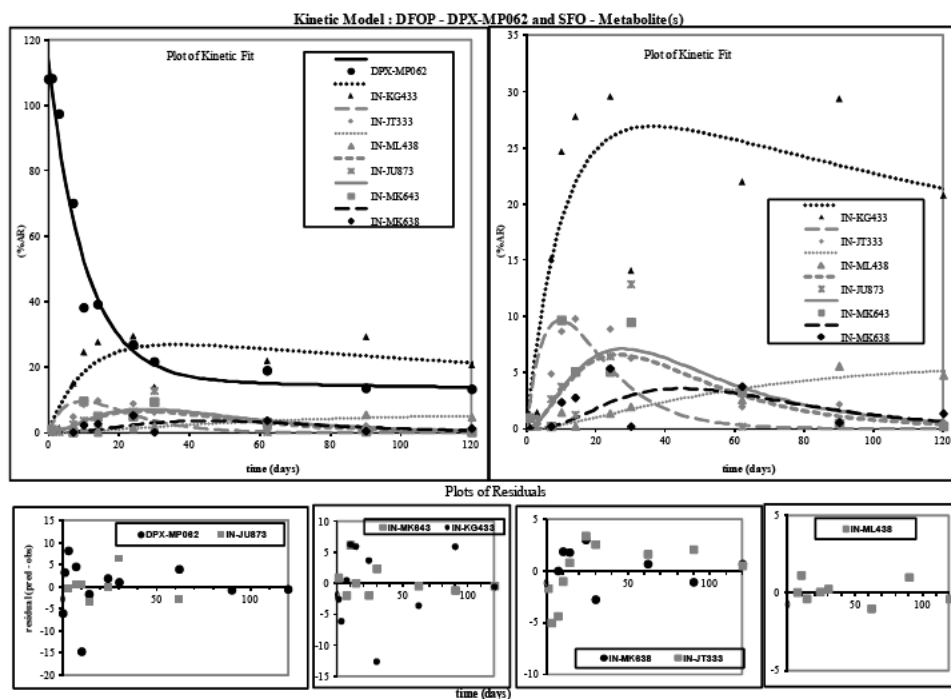
^c Fit attempted with parent and only IN-KG333 to estimate reliable formation fraction. Since the peak was underestimated, the formation fraction was fixed slightly higher than optimised value to estimate a reliable fit and conservative formation fraction

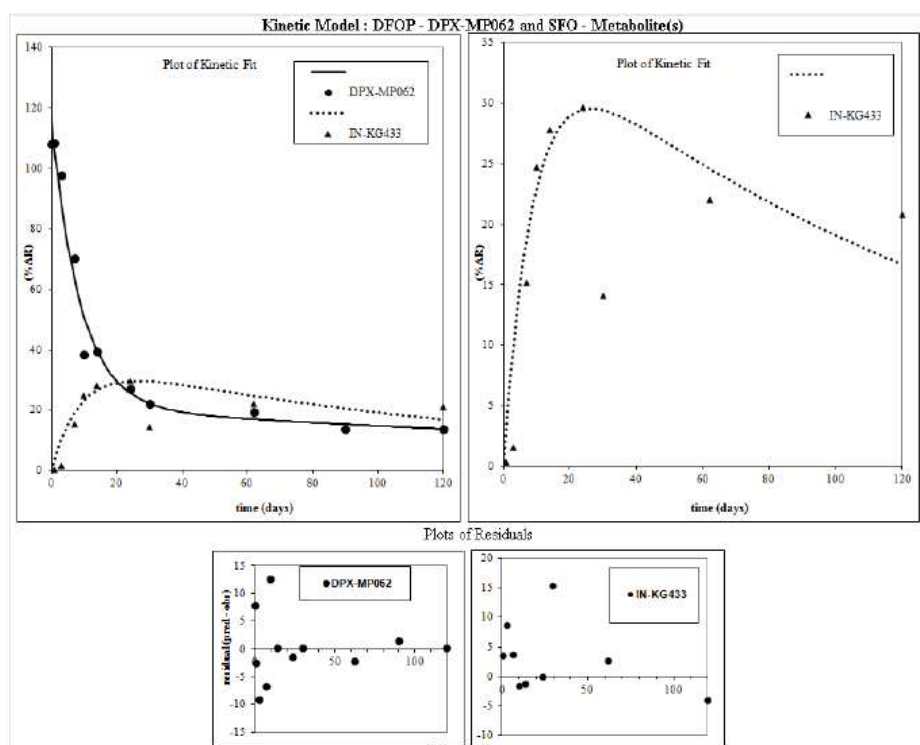
^d Endpoint considered unreliable because significance test fails at $P=0.05$, and visual fit unacceptable demonstrated by $\chi^2 > 15\%$.

None of the fits resulted in acceptable statistical and visual fits, thus no reliable DT_{50} and formation fractions could be derived for any of the metabolites.

For metabolite IN-KT433 an additional parent FOMC – metabolite SFO run was attempted, to estimate reliable formation fraction, as it was closest to being an acceptable in terms of both visual and statistical assessment. Since the peak was underestimated, the formation fraction was fixed slightly higher than optimised value to estimate a reliable fit and conservative formation fraction (0.37). However, if the metabolite formation was well described, the fit resulted was not acceptable the for degradation rate (see visual fit hereunder). As ffm and DT_{50} can only be retained as couple, none of these endpoints (DT_{50} and ffm) were retained by RMS.

Optimized DFOP-SFO kinetic model of indoxacarb and metabolites degradation in the Nambshiem Soil at 20°C – TFMP Label –IRLS Method





Fit from peak

A clear decline phase was observed for metabolite IN-JT333, therefore, fits from peak were attempted for this metabolite to estimate degradation rates from the decline curve.

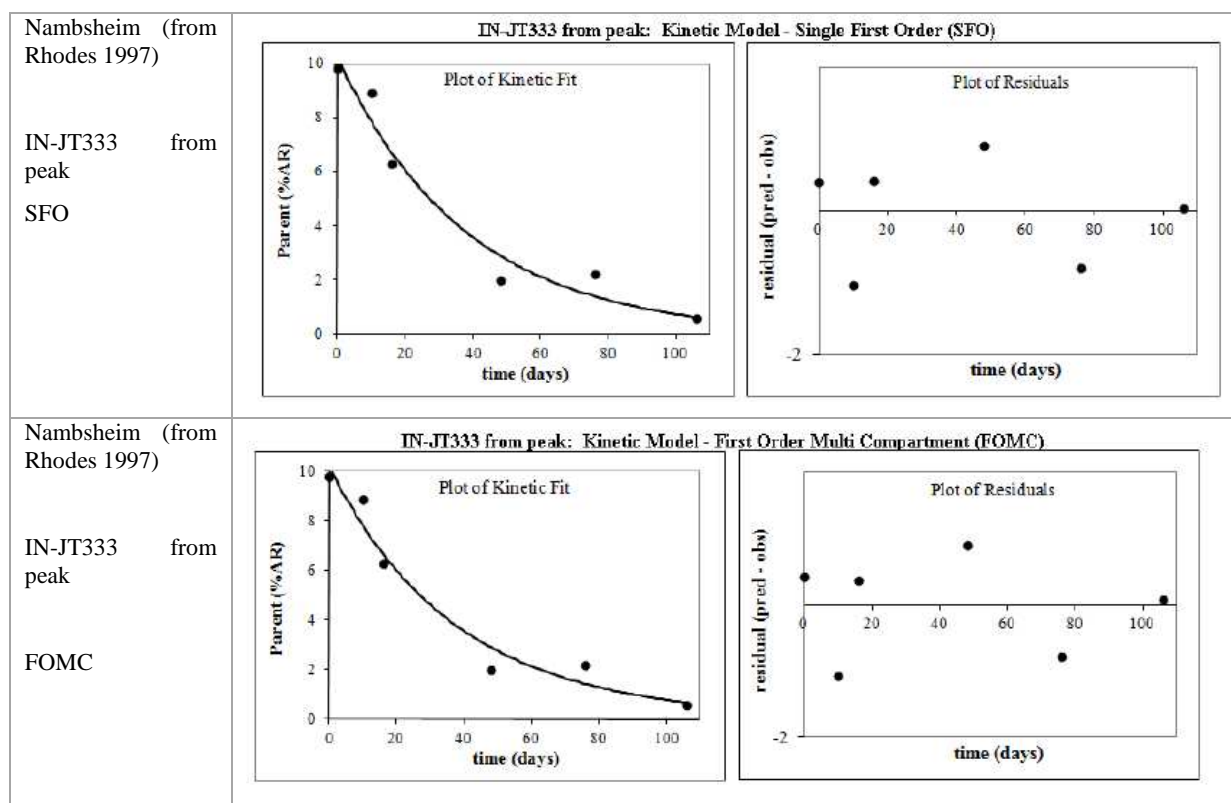
For all other metabolites, no clear decline of the residue are observed in none of these studies with parent applied, no fits from peak were proposed.

Table 8-59: Summary of kinetics and goodness of fit statistics for IN-JT333-fit from peak (derived from IN-JT333 decline curve from indoxacarb- degradation studies)

Study	Soil	SFO			p (t-test)	FOMC*			DFOP			
		DegT ₅₀	DegT ₉₀	χ^2		DegT ₅₀	DegT ₉₀	χ^2	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
AMR 4251-96)	Nambsheim 20°C (TFMP)	26.5	88.1	11	<0.05	26.2	89.6	12	Not Required			

* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Visual fits and residuals for IN-JT333 in Nambheim soil from Rhodes 1997.



Persistence and modelling: SFO model resulted in statistically and visually acceptable fit.

Tama soil, original (from Singles 2002)

Table 8-60: Summary of kinetics and goodness of fit statistics for metabolites (derived from indoxacarb-degradation studies)

	Soil/Label	IN-JT333 via Indoxacarb Kinetics					Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	Formation Fraction from Indoxacarb	
IN-JT333	Tama—Original (Indanone)	9.7 ^a	32.4 ^a	38	<0.05	0.21	DFOP-SFO
IN-JU873	Tama—Original (Indanone)	1.4 ^b	4.8 ^b	95	<0.1	0.14, 0.51	DFOP-SFO
IN-ML438 via IN-JU873 and IN-MP819 Kinetics	Tama—Original (Indanone)	20.3 ^b	67.5 ^b	47	Not calculated	0, 0.1, 0	DFOP-SFO

^a Endpoint considered unreliable even though significance test passes at P=0.05, because visual fit considered unacceptable due to underestimation of the peak.

^b Endpoint considered unreliable because significance test fails at P=0.05 and visual fit unacceptable demonstrated by $\chi^2 > 15\%$.

Table 8-61 : Summary of kinetics and goodness of fit statistics for metabolites (derived from indoxacarb-degradation studies)

	Soil/Label						Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	Formation Fraction from Indoxacarb	
IN-JT333	Tama—Original (TFMP)	17.7 ^a	58.8 ^a	22	<0.05	0.17 ^a	DFOP-SFO
IN-JU873	Tama—Original (TFMP)	0.5 ^b	1.5 ^b	27	<0.05	0.75, 0.0	DFOP-SFO
IN-KB687 via IN-KG433 Kinetics	Tama—Original (TFMP)	3.4 ^b	11.3 ^b	33	<0.05	0.22	DFOP-SFO
IN-KG433	Tama—Original (TFMP)	0.6 ^b	2.1 ^b	69	<0.05	0.70	DFOP-SFO
IN-ML438 via IN-JU873 and IN-MP819 Kinetics	Tama—Original (TFMP)	33.3 ^a	110.6 ^a	32	<0.05	0.44, 0.04, 0	DFOP-SFO
IN-MK638	Tama—Original (TFMP)	14.0 ^c	46.6 ^c	37	<0.05	1.0, 0.16	DFOP-SFO
IN-MK643 via IN-KG433 and IN-JU873 Kinetics	Tama—Original (TFMP)	101.4 ^a	336.9 ^a	47	0.108	0, 0, 0.1	DFOP-SFO

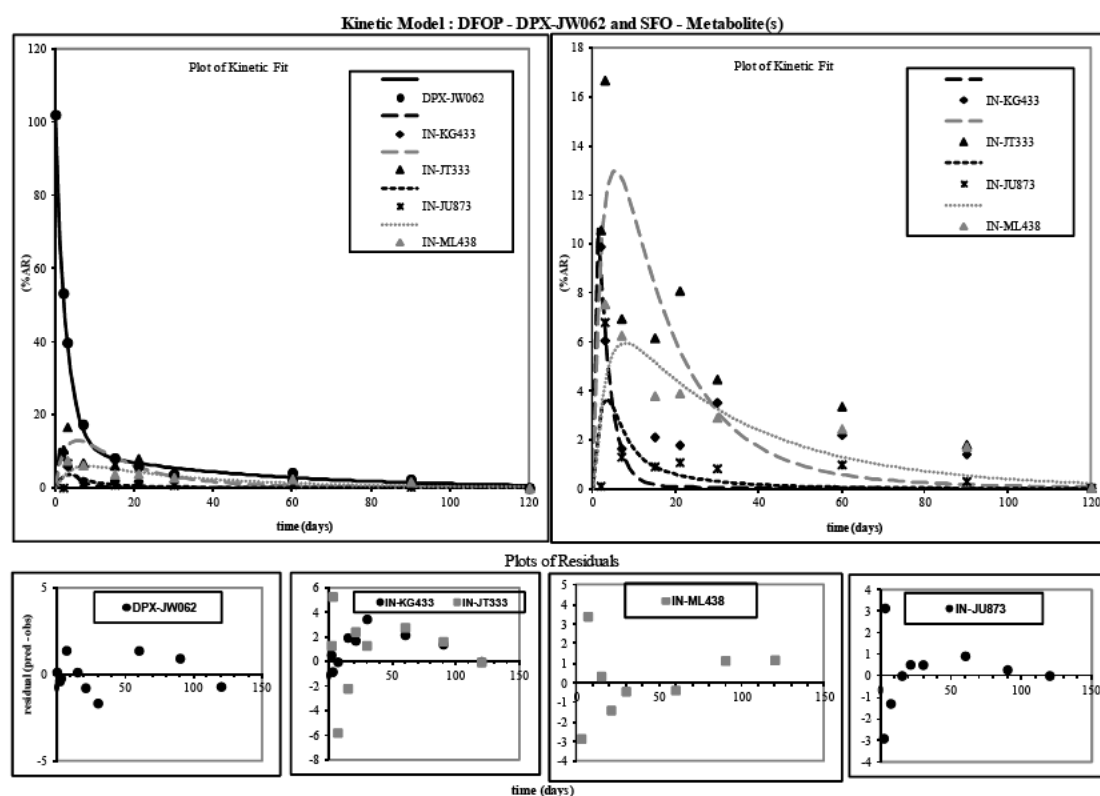
^a Endpoint considered unreliable even though significance test passes at P=0.05, because visual fit considered unacceptable due to underestimation of the peak and $\chi^2 > 15\%$.

^b Endpoint considered unreliable because even though significance test passes at P=0.05, visual fit is unacceptable due to non-random residual errors and $\chi^2 > 15\%$.

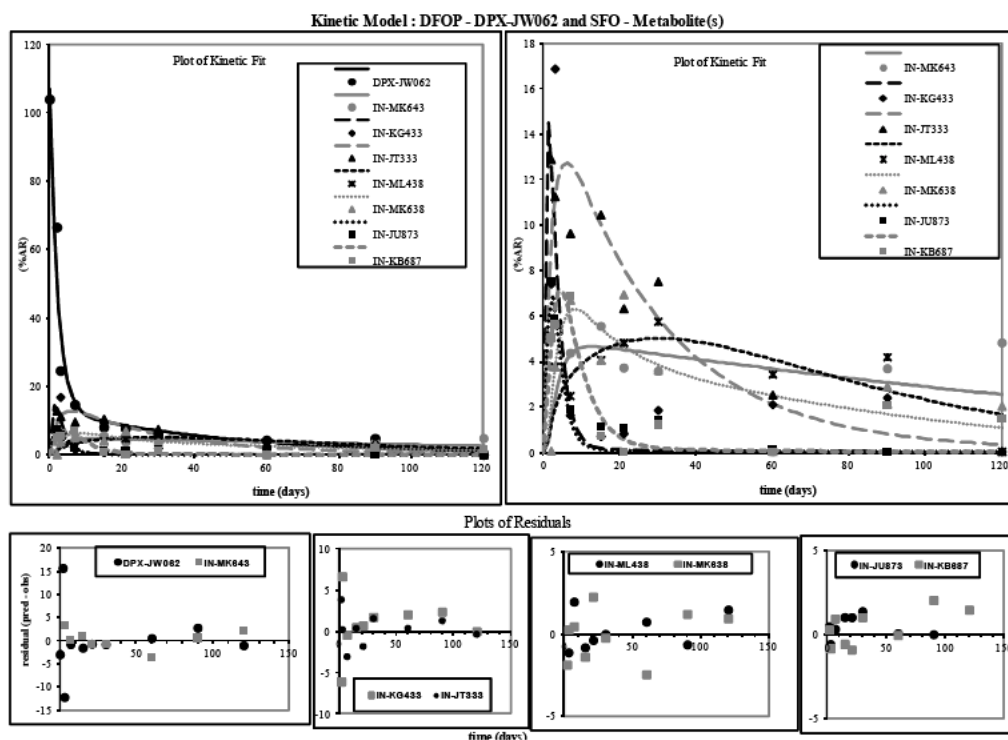
^c Endpoint considered unreliable because even though it passes significance test at P=0.05 and precursor fits are unreliable.

^d Endpoint considered unreliable because significance test fails at P=0.05 and visual fit unacceptable demonstrated by $\chi^2 > 15\%$.

Optimized DFOP-SFO kinetic model of indoxacarb and metabolites degradation in the Tama Soil at 20°C – Indanone Label—Original – IRLS method



Optimized DFOP-SFO kinetic model of indoxacarb and metabolites degradation in the Tama Soil at 20°C – TFMP Label—Original – IRLS method



None of the fits resulted in acceptable statistical and visual fits, thus no reliable DT_{50} and formation fractions could be derived for any of the metabolites.

Fit from peak

A clear decline phase was observed for metabolites IN-JT333 (Both labels) and IN-ML438 (indanon label), therefore, fits from peak were attempted for these metabolites to estimate degradation rates from the decline curve.

For all other metabolites, no clear decline of the residue are observed in none of these studies with parent applied, no fits from peak were proposed.

- **IN-JT333**

Indanon label

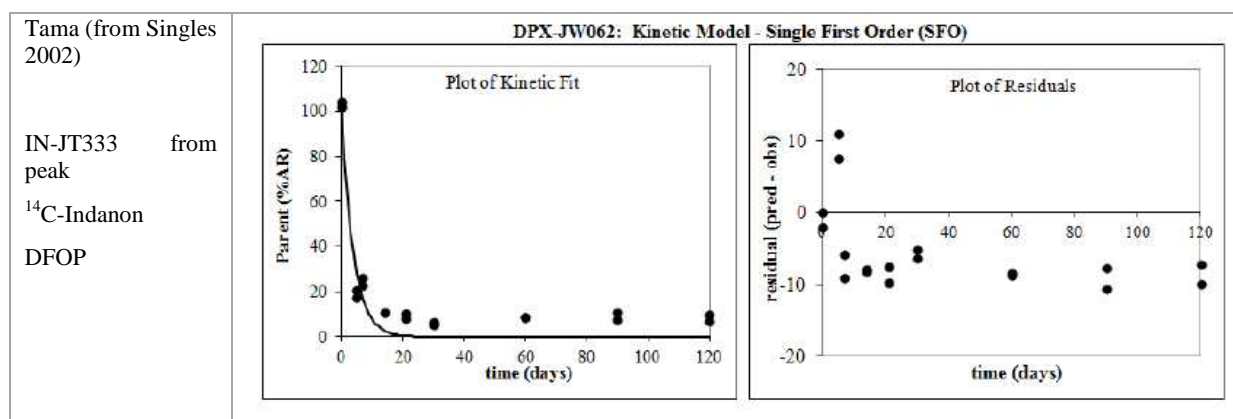
Table 8-62: Summary of kinetics and goodness of fit statistics for IN-JT333-fit from peak (derived from IN-JT333 decline curve from indoxacarb- degradation studies)

Study	Soil	SFO				FOMC			DFOP			
		DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
AMR 2803-93, Revision No. 1	Tama—Original (Indanone)	18.3	60.7	31	<0.05	4.4	297.8	22	1.0	92.9	14	

None of the models resulted in visually and statistically acceptable fits.

Visual fits and residuals for IN-JT333 in Tama soil soil (original) from Singles (2002), ¹⁴C-Indanon

Tama (from Singles 2002) IN-JT333 from peak ¹⁴ C-Indanon SFO		



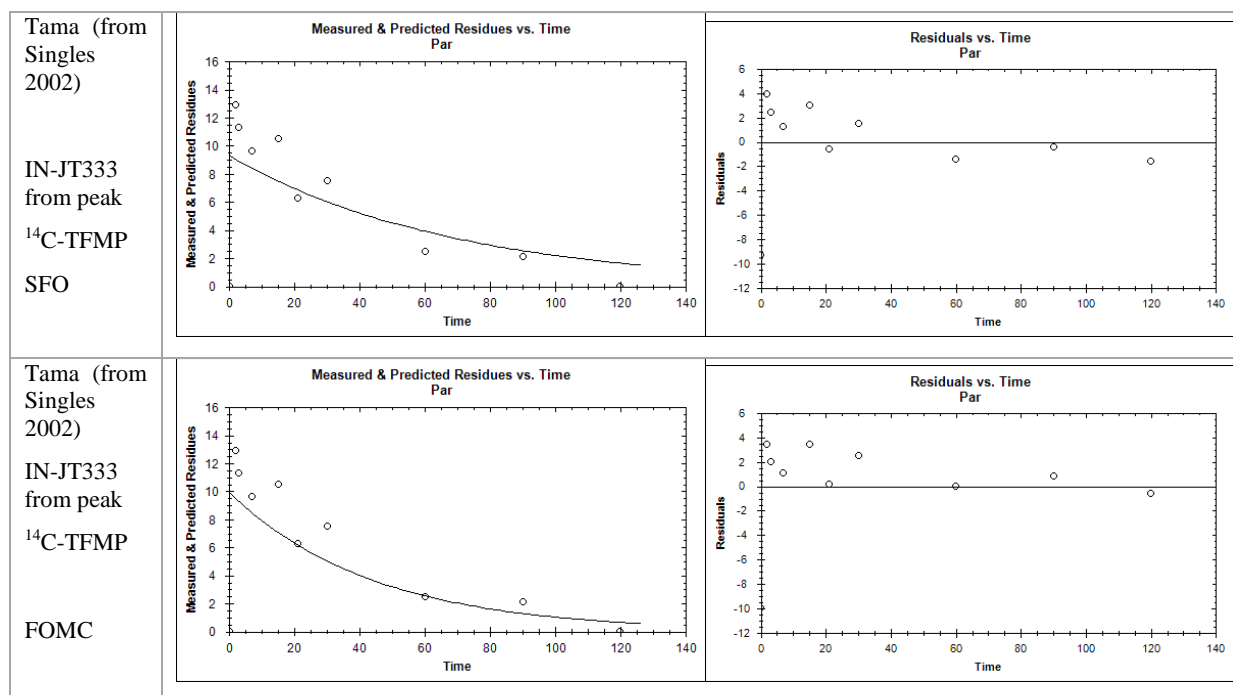
TFMP label

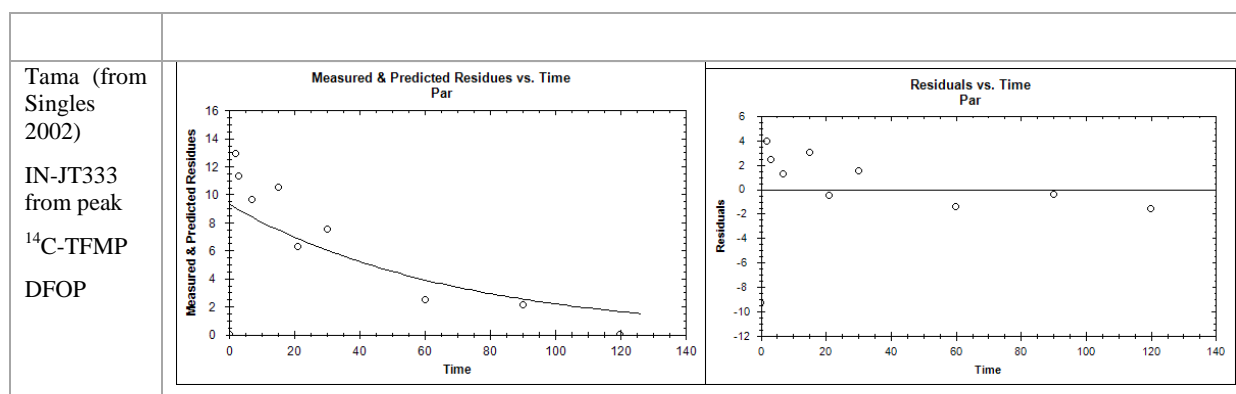
No fits from peak for IN-JT333 with data from the TFMP label was performed since applicant considered that the fit from parent was acceptable. RMS did not retain the fit from parent since the visual fit was not satisfactory (underestimation of the peak and $\chi^2 > 15\%$). RMS thus performed fits from peak for IN-JT333, TFMP label:

Study	Soil	SFO				FOMC			DFOP			
		DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	CI	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
AMR 2803-93, Revision No. 1	Tama—Original (TFMP)	48	159.50	23.93	0.072	30.35	100.8	CI includes 0	47.9	159	27	k1 = 0.49 k2 = 0.49

None of the models resulted in visually and statistically acceptable fits. No degradation data is retained from this soil.

Visual fits and residuals for IN-JT333 in Tama soil soil (original) from Singles (2002), ¹⁴C-TFMP





• IN-ML438

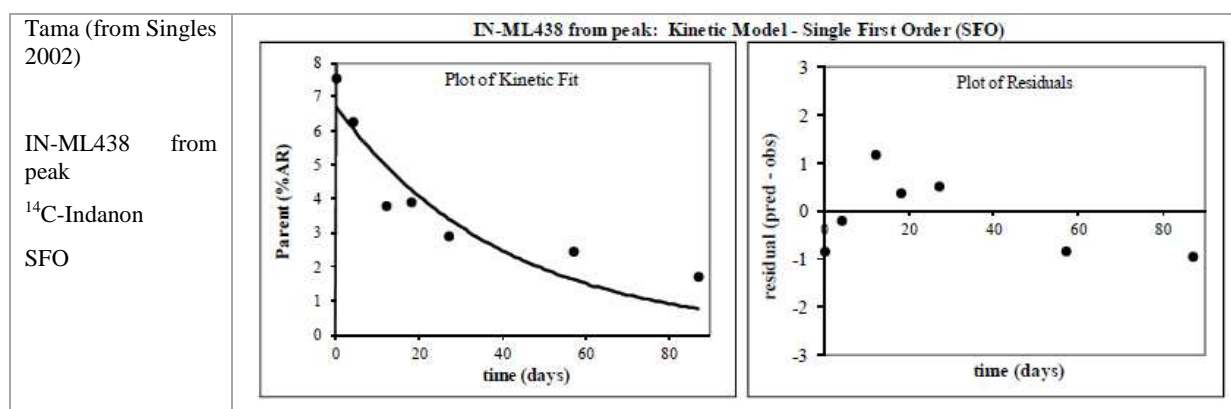
Indanon label

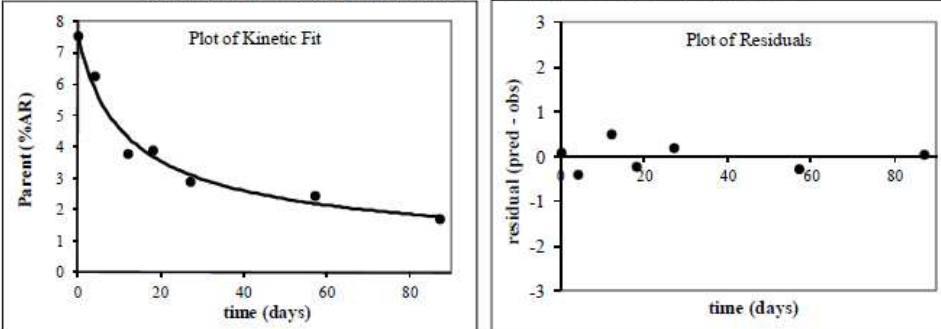
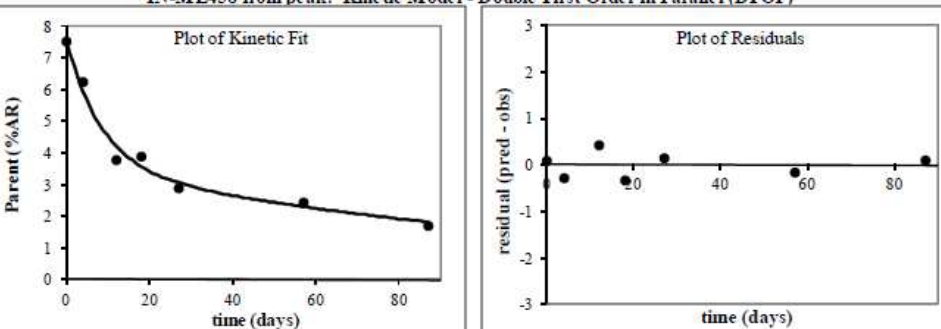
Table 8-63: Summary of kinetics and goodness of fit statistics for IN-ML438-fit from peak (derived from IN-ML438 decline curve from indoxacarb- degradation studies)

Study	Soil	SFO				FOMC*			DFOP			p (t-test)
		DegT ₅₀	DegT ₉₀	χ ²	p (t-test)	DegT ₅₀	DegT ₉₀	χ ²	DegT ₅₀	DegT ₉₀	χ ²	
AMR 2803-93, Revision No. 1	Tama—Original (Indanone)	27.8	92.5	15	<0.05	16.7	435.4	6	15.5	201.1	6	p1<0.1; p2=0.11
	Tama—Supplemental (Indanone)-outlier removed	110.5	367	14		Not required						

* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Visual fits and residuals for IN-ML438 in Tama soil (original) from Singles (2002), ¹⁴C-Indanon



<p>Tama (from Singles 2002)</p> <p>IN-ML438 from peak</p> <p>^{14}C-Indanon</p> <p>FOMC</p>	<p>IN-ML438 from peak: Kinetic Model - First Order Multi Compartment (FOMC)</p> 
<p>Tama (from Singles 2002)</p> <p>IN-ML438 from peak</p> <p>^{14}C-Indanon</p> <p>DFOP</p>	<p>IN-ML438 from peak: Kinetic Model - Double First Order in Parallel (DFOP)</p> 

Persistence and modelling: Although DFOP k_2 rate passed at $P=0.11$, It was considered close to the passing value, therefore, DFOP was selected as best fit for persistence and modelling

TFMP label

No clear decline in data, so no fits from peak was possible.

II. FITS from metabolites applied studies

A. Metabolite IN-JT333 (from Clark, 2014)

Gros Umstadt soil

Table 8-64: Summary of kinetics and goodness of fit statistics for IN-JT333 (applied as parent) in Gros Umstadt soil

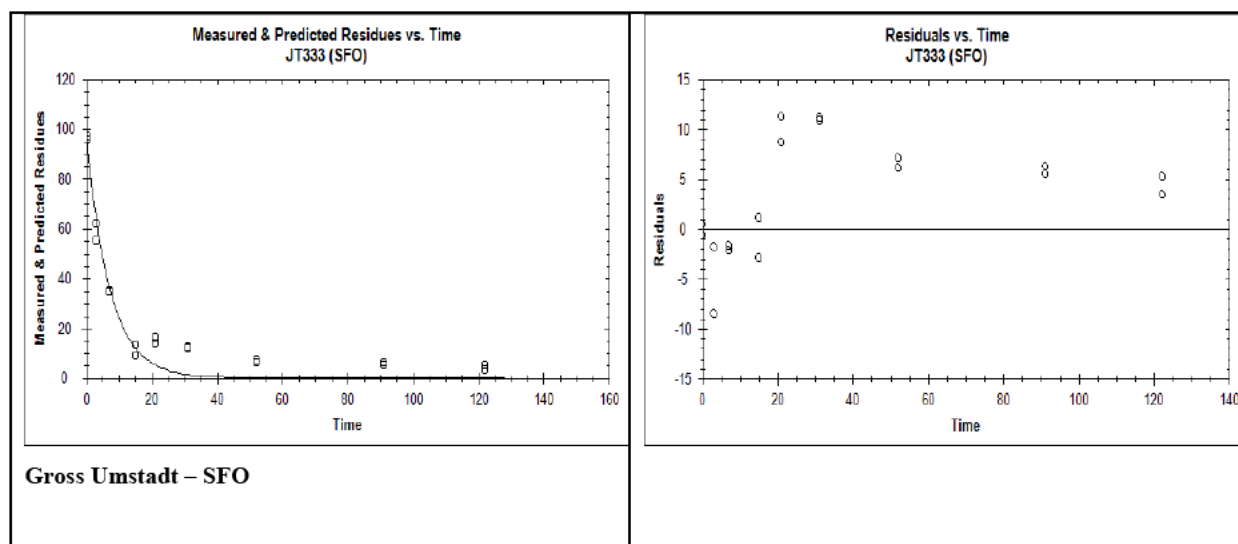
Soil	SFO				FOMC			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	95% CI contains 0	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Gross Umstadt ^a	5.0	16.7	17.4	<0.05	4.0	30.9	β no	4.3	37.8	p1<0.05; p2<0.05	4.6	45.4	p1<0.05; p2<0.05

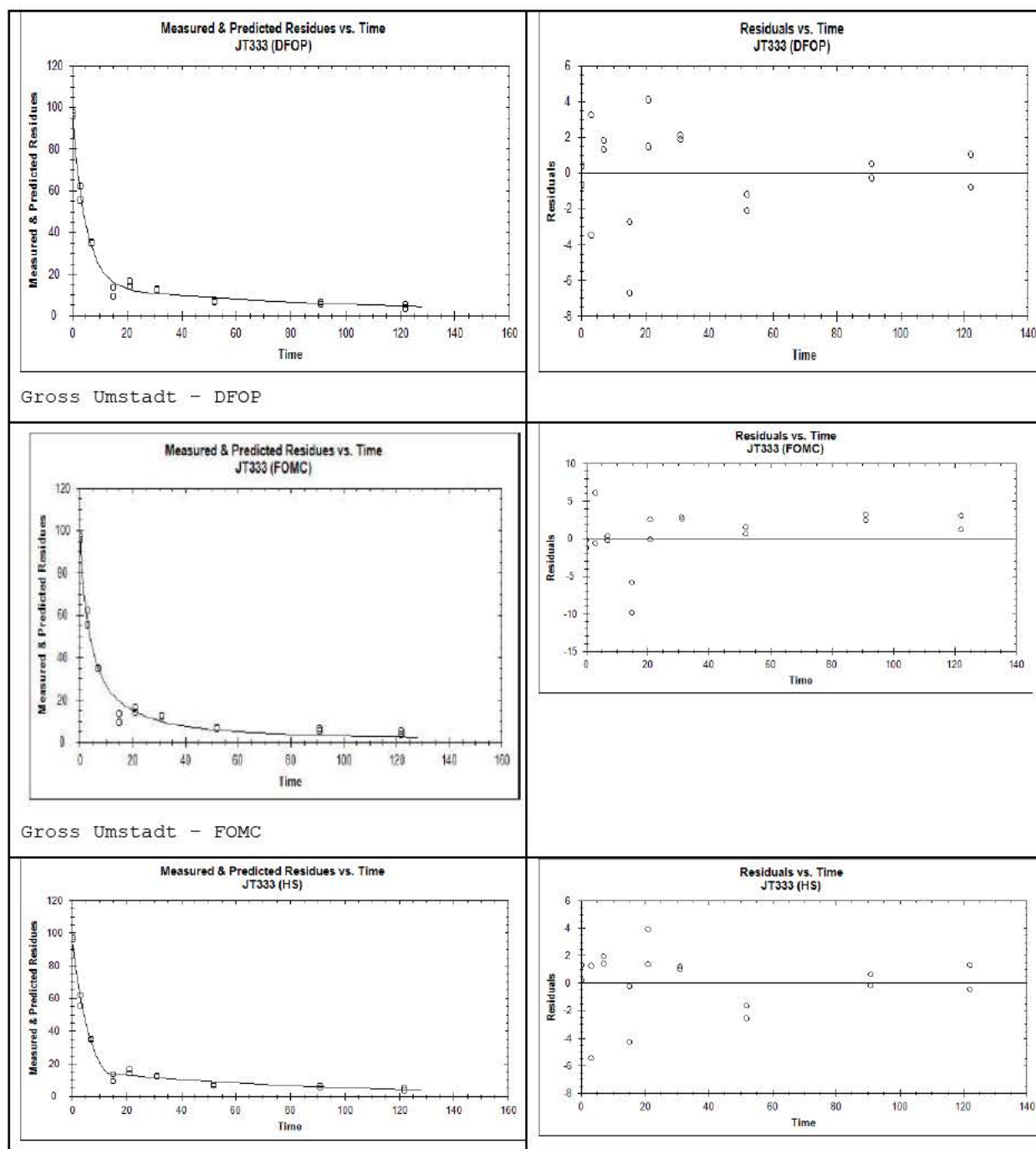
^a SFO M0 was fixed to achieve this fit.

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: As pragmatic approach and to ensure that the modelling endpoint choice for IN-JT333 will not prejudicial for risk assessment of its subsequent metabolites, the SFO DT₅₀ was retained by RMS for modelling, even if the visual assessment shows that it does not adequately describe 90% of the decline. Is is considered that this bias will be offset by default ffm of 1 for IN-JT333 in the PECgw modelling, and would be not more adapted for modelling of subsequent metabolites.

Visual fits and residuals for IN-JT333 in Gross Umstadt soil





Leida soil

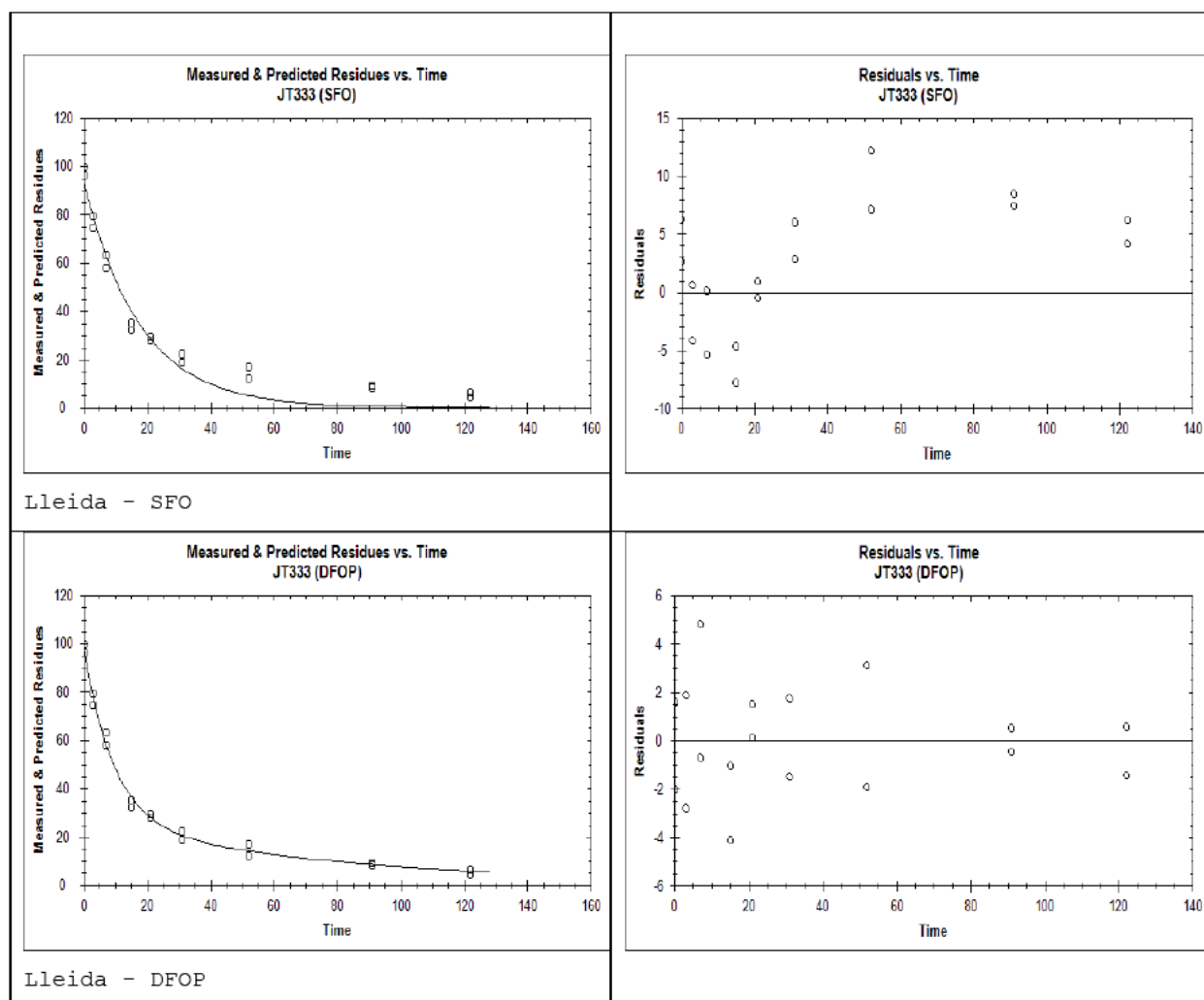
Table 8-65: Summary of kinetics and goodness of fit statistics for IN-JT333 (applied as parent) in Lleida soil

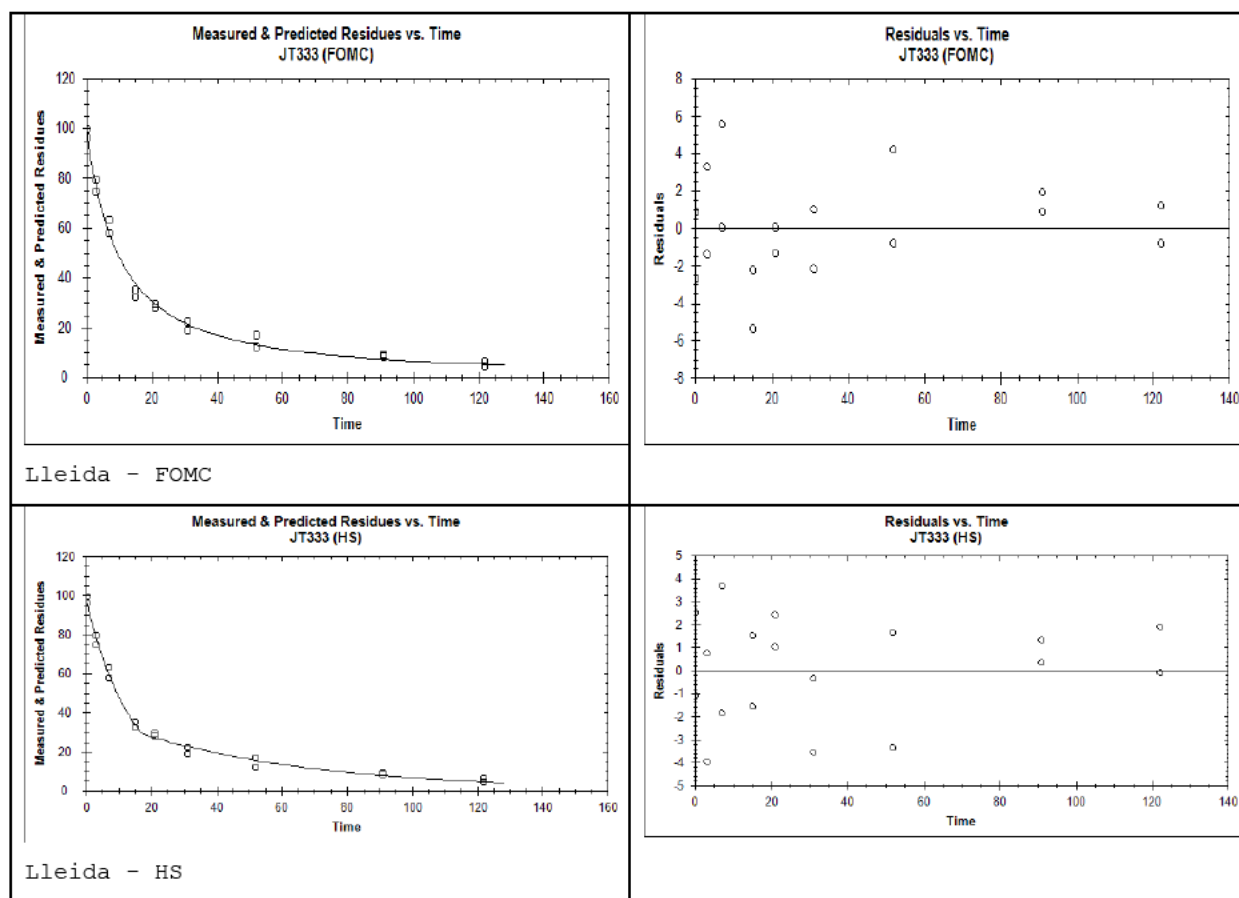
Soil	SFO				FOMC			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	95% CI contains 0	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Lleida	12.3	40.7	11.4	<0.05	9.5	67.2	β no	9.6	79.2	p1<0.05; p2<0.05	9.8	77.8	p1<0.05; p2<0.05

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: As pragmatic approach and to ensure that the modelling endpoint choice for IN-JT333 will not prejudicial for risk assessment of its subsequent metabolites, the SFO DT₅₀ was retained by RMS for modelling, even if the visual assessment shows that it does not adequately describe 90% of the decline. Is is considered that this bias will be offset by default ffm of 1 for IN-JT333 in the PECgw modelling, and would be not more adapted for modelling of subsequent metabolites.

Visual fits and residuals for IN-JT333 in Lleida soil





Nambsheim soil

Table 8-66: Summary of kinetics and goodness of fit statistics for IN-JT333 (applied as parent) in Nambsheim soil

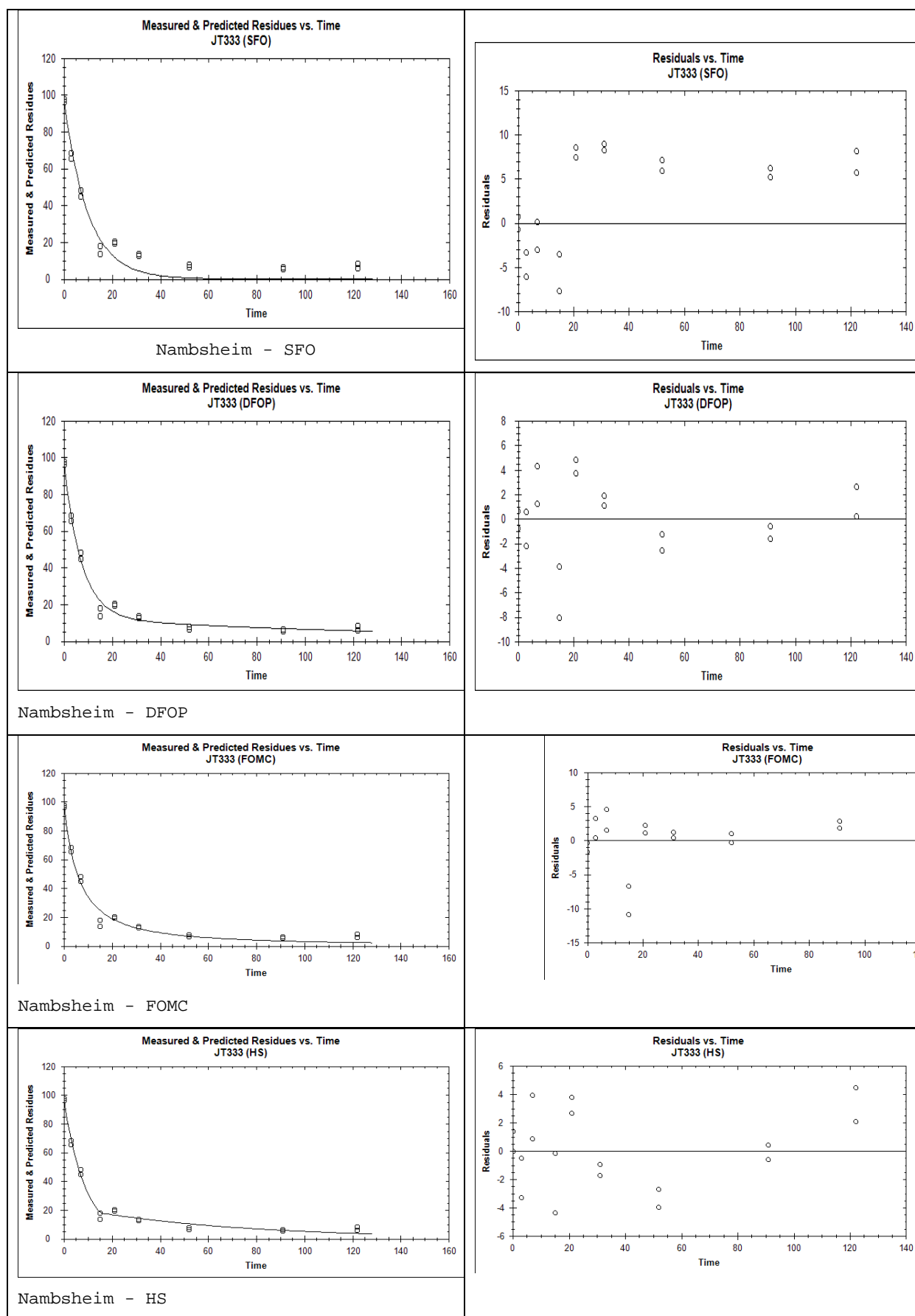
Soil	SFO				FOMC			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	95% CI contains 0	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Nambsheim ^a	6.9	22.9	14.6	<0.05	5.7	37.6	β no	6.0	43.2	p1<0.05; p2=0.078	6.2	57.2	p1<0.05; p2<0.05

^a SFO M0 was fixed to achieve this fit.

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: As pragmatic approach, the SFO DT₅₀ was retained by RMS for modelling, even if the visual assessment shows that it does not adequately describe 90% of the decline. It is considered that this bias will be offset by default ffm of 1 for IN-JT333 in the PECgw modelling, and would be not more adapted for modelling of subsequent metabolites.

Visual fits and residuals for IN-JT333 in Nambsheim soil

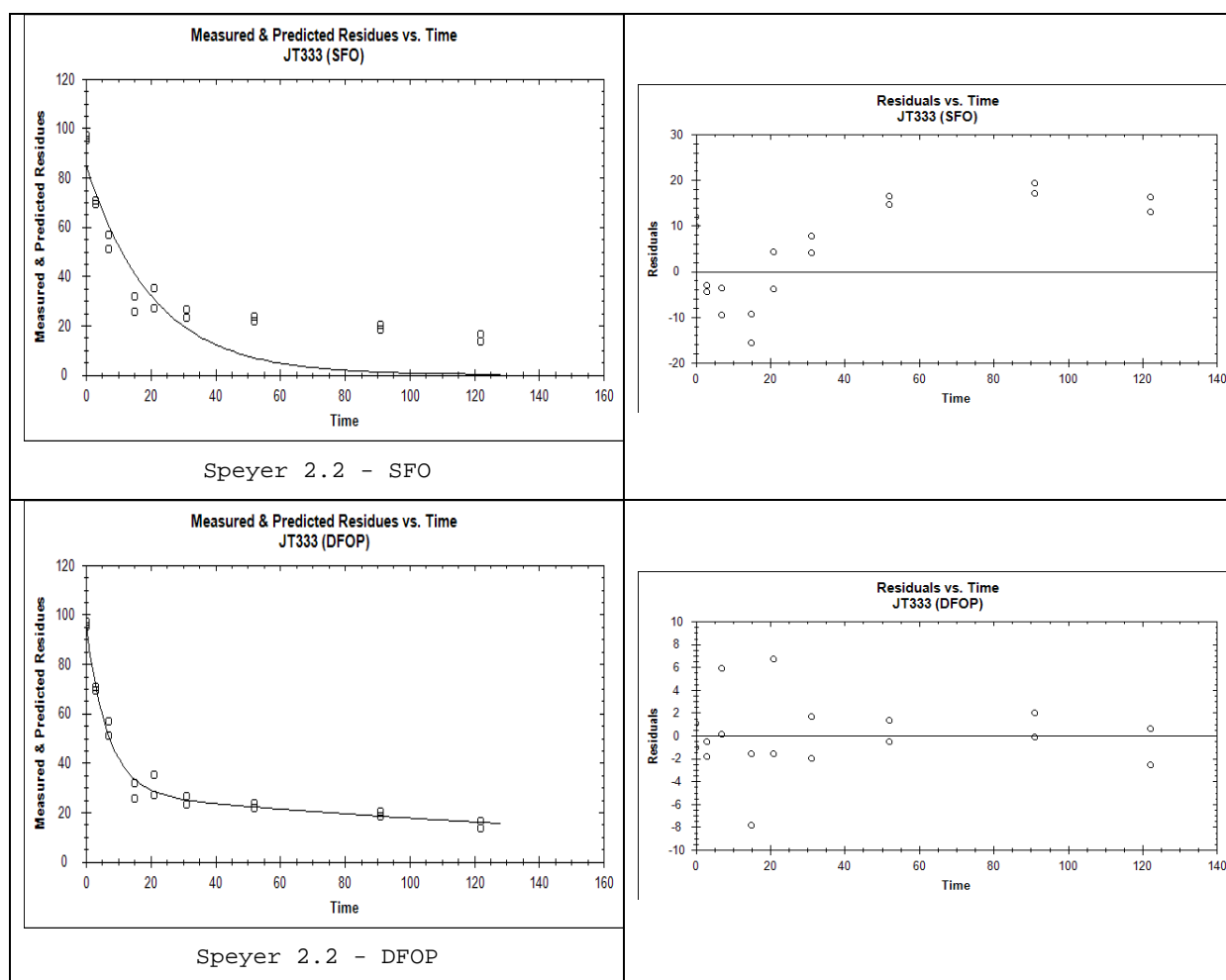


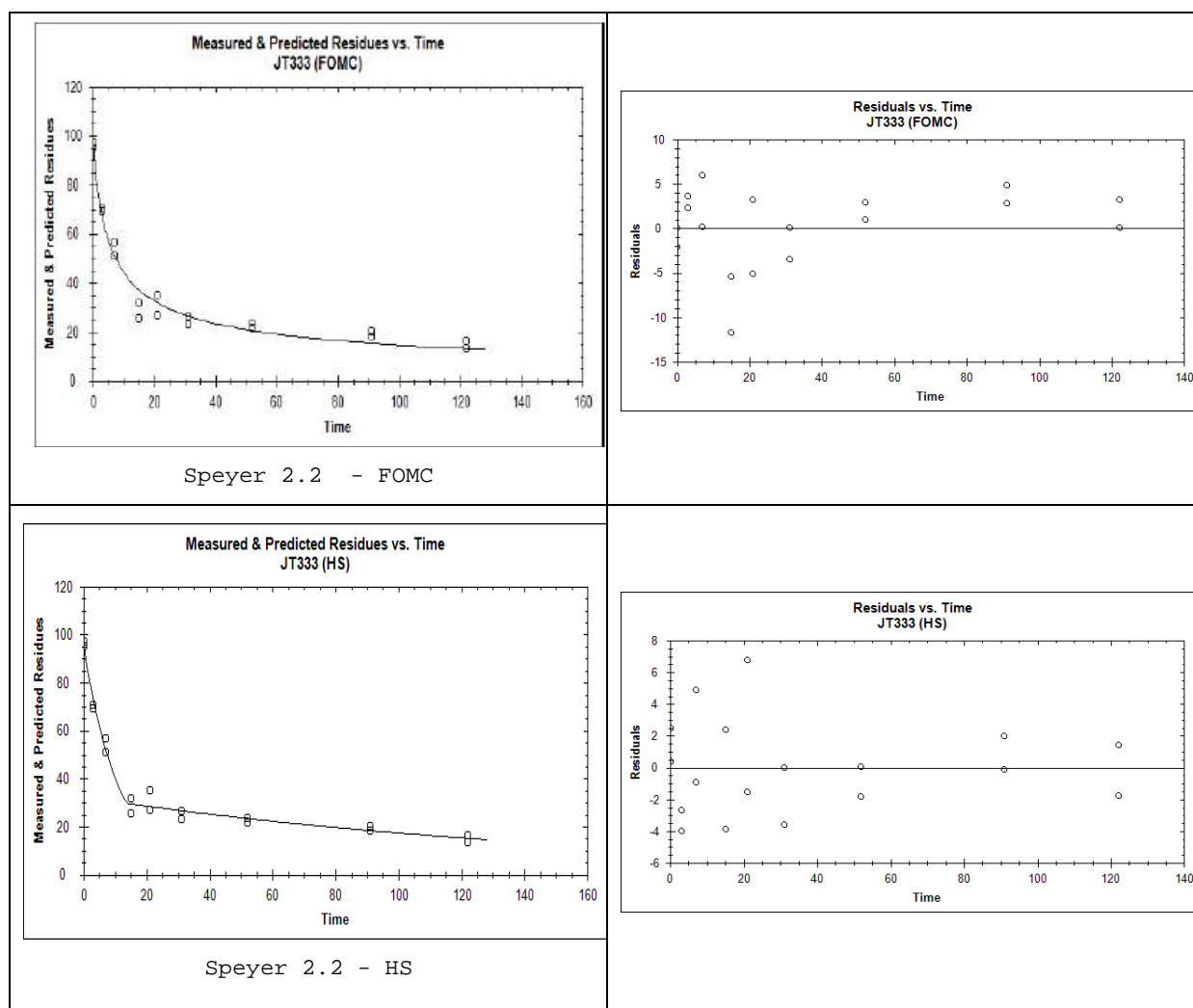
Speyer 2.2 soil**Table 8-67: Summary of kinetics and goodness of fit statistics for IN-JT333 (applied as parent) in Speyer 2.2 soil**

Soil	SFO				FOMC			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	95% CI contains 0	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Speyer 2.2	14.3	47.5	22.6	<0.05	7.9	220.8	β no	7.9	228.8	p1<0.05; p2<0.05	8.1	196.6	p1<0.05; p2<0.05

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: SFO model resulted in statistically and visually unacceptable fit. HS is retained

Visual fits and residuals for IN-JT333 in Speyer 2.2 soil



Tama soil

Table 8-68: Summary of kinetics and goodness of fit statistics for IN-JT333 (applied as parent) in Tama soil

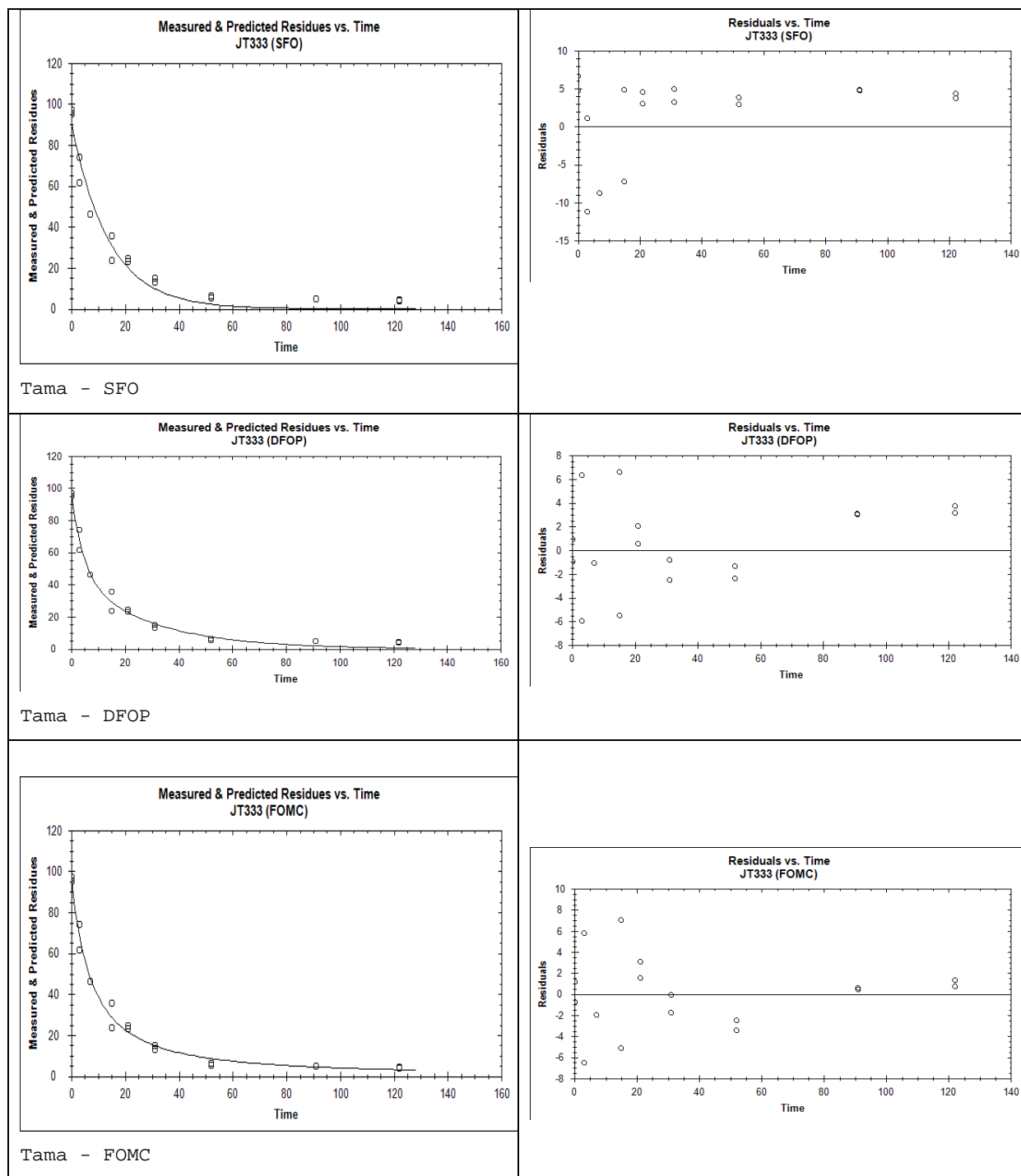
Soil	SFO				FOMC			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	95% CI contains 0	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Tama ^c	9.7	32.3	12.2	<0.05	7.0	47.0	β no	6.8	44.8	p1<0.05; p2<0.05	6.4	43.0	p1<0.05; p2<0.05

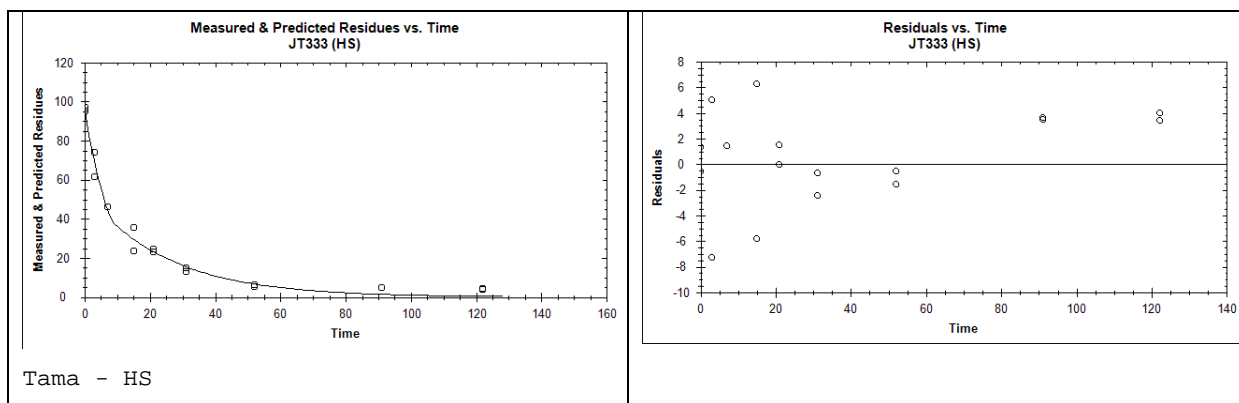
^c Replicate 2 at DAT 7 was excluded as outlier to achieve this fit.

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: SFO is considered visually acceptable although later data points are slightly underestimated. It is retained for modelling.

Visual fits and residuals for IN-JT333 in Tama soil





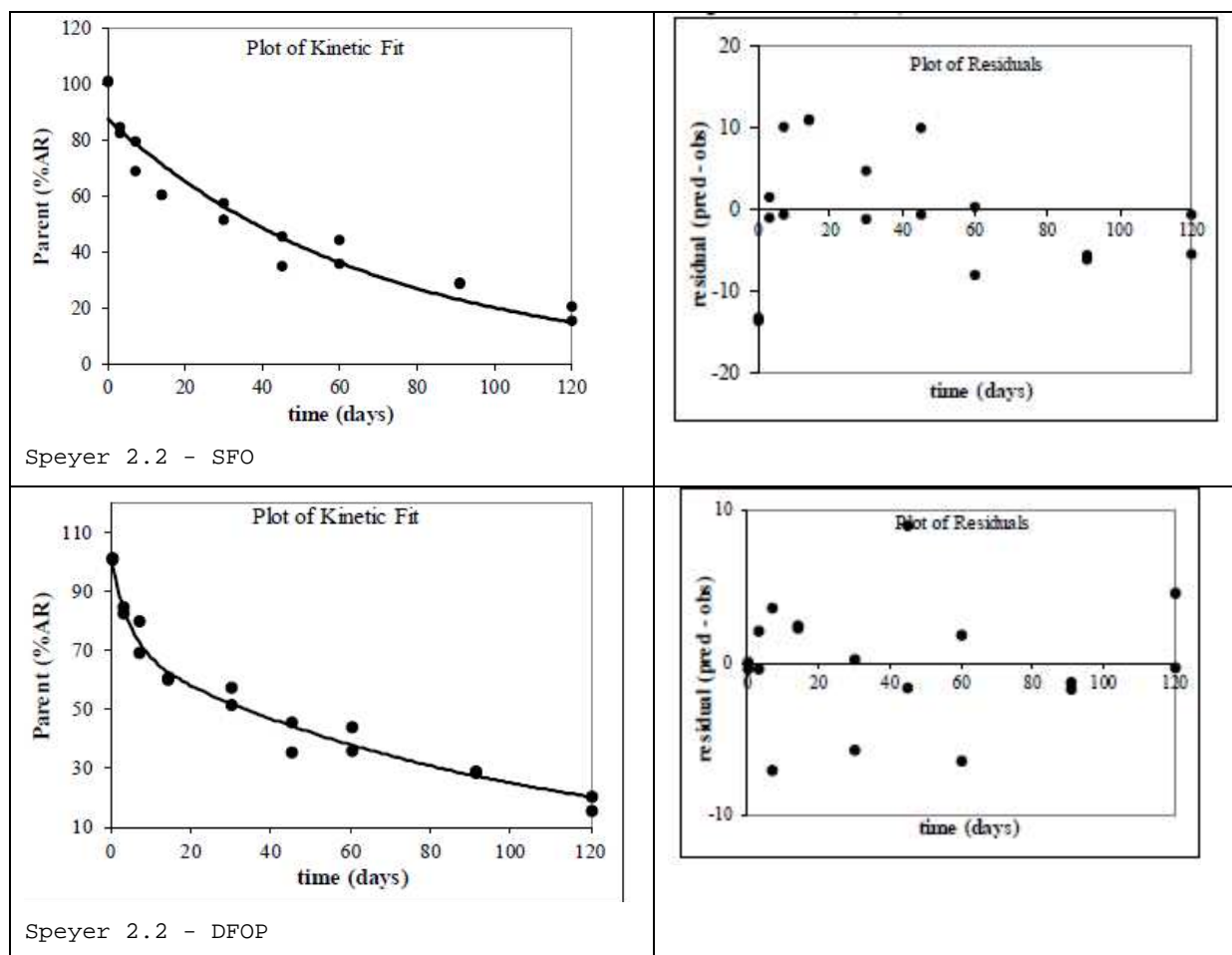
B. Metabolite IN-JU873 (from Mellor, 2002)**Speyer 2.2 soil****Table 8-69: Summary of kinetics and goodness of fit statistics for IN-JU873 (applied as parent) in Speyer 2.2 soil**

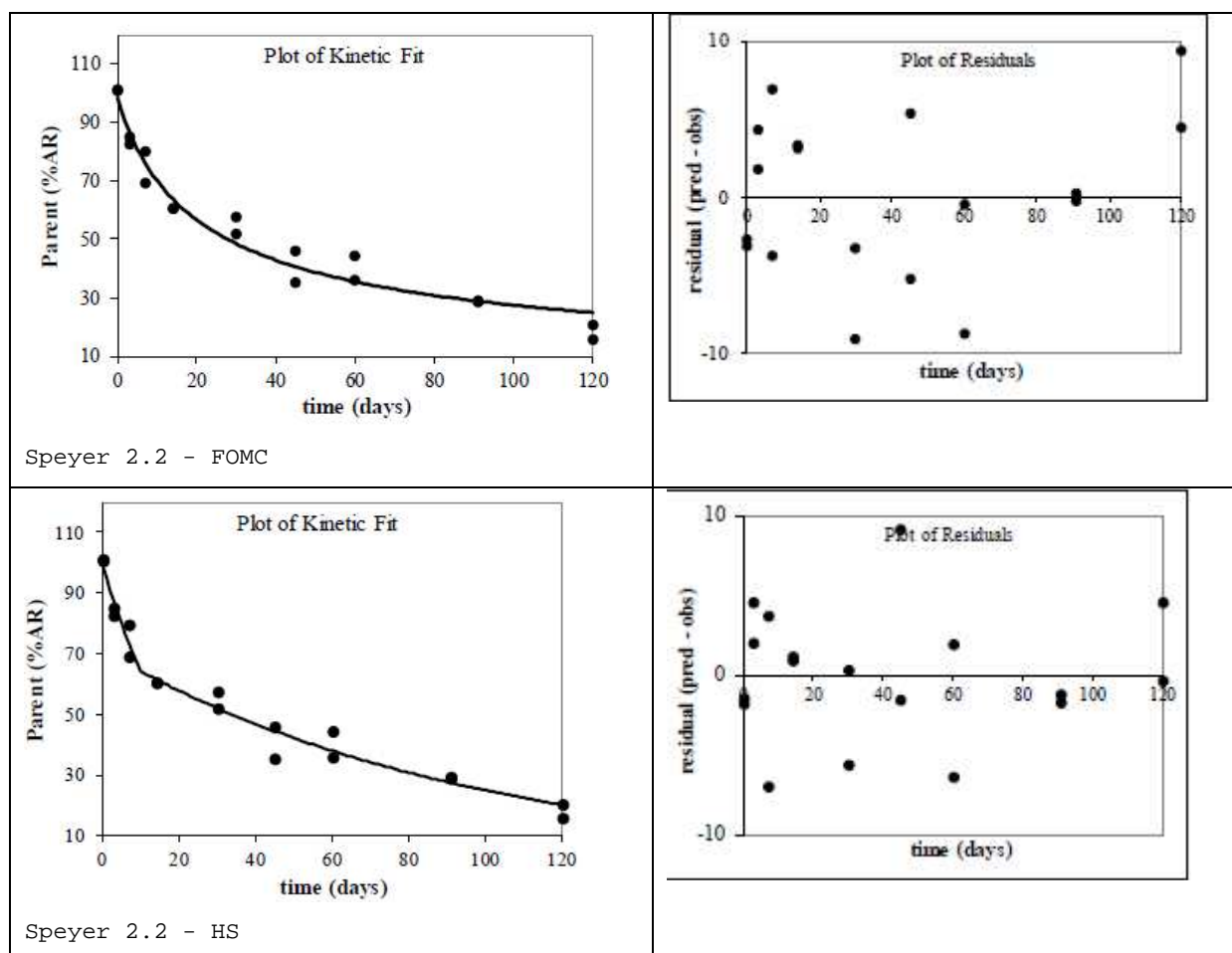
Soil	SFO				FOMC*			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	CI	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Speyer 2.2	47.2	156.8	10	<0.05	29.1	646.6	*	32.8	186.1	p1<0.05; p2<0.05	34.3	187.2	p1<0.05; p2<0.05

* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling.

Visual fits and residuals for IN-JU873 in Speyer 2.2 soil



Mattapex soil

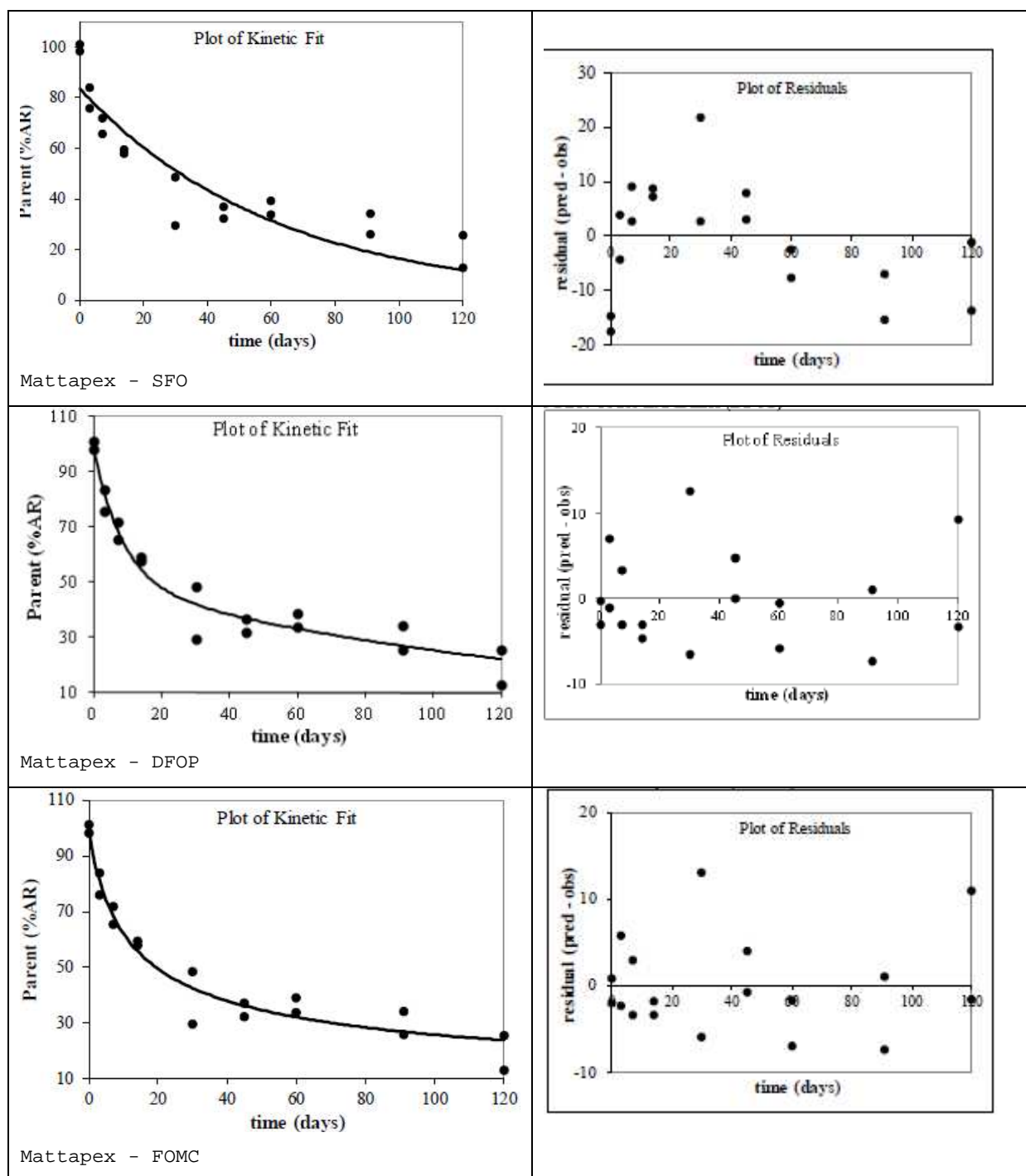
Soil	SFO				FOMC*			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	CI	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Mattapex	42.4	140.9	14	<0.05	19.9	831.7	*	19.0	242.5	p1<0.05; p2<0.05	21.7	195.7	p1<0.05; p2<0.05

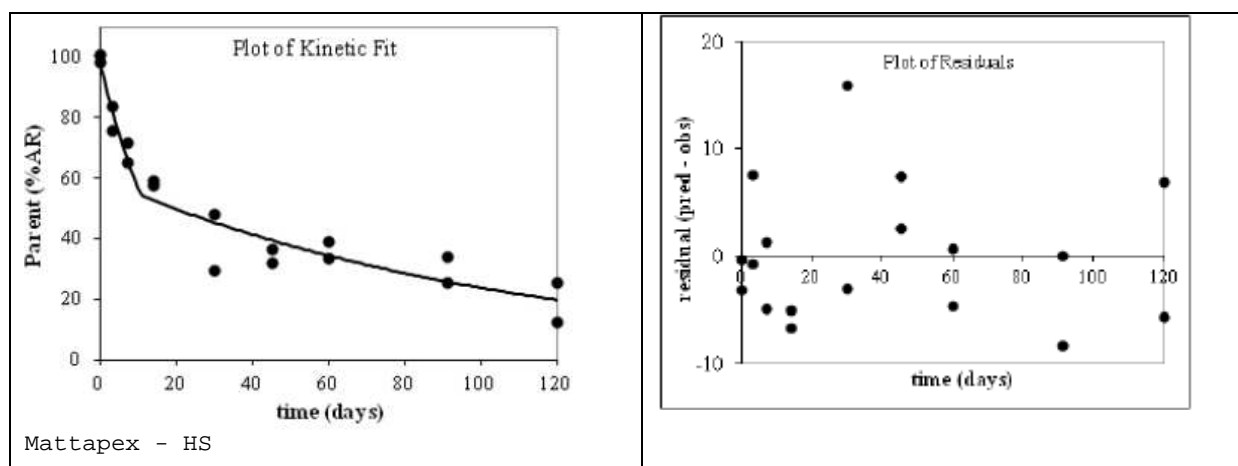
* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: SFO DT₅₀ was retained by RMS for modelling, even if the visual assessment shows that it does not adequately describe 90% of the decline. It is considered that this bias will be offset by default ffm of 1 for IN-JU873 in the PECgw modelling, and would be not more adapted for modelling of subsequent metabolites.

Visual fits and residuals for IN-JU873 in Mattapex soil





Pesaro soil

Table 8-70: Summary of kinetics and goodness of fit statistics for IN-JU873 (applied as parent) in Pesaro soil

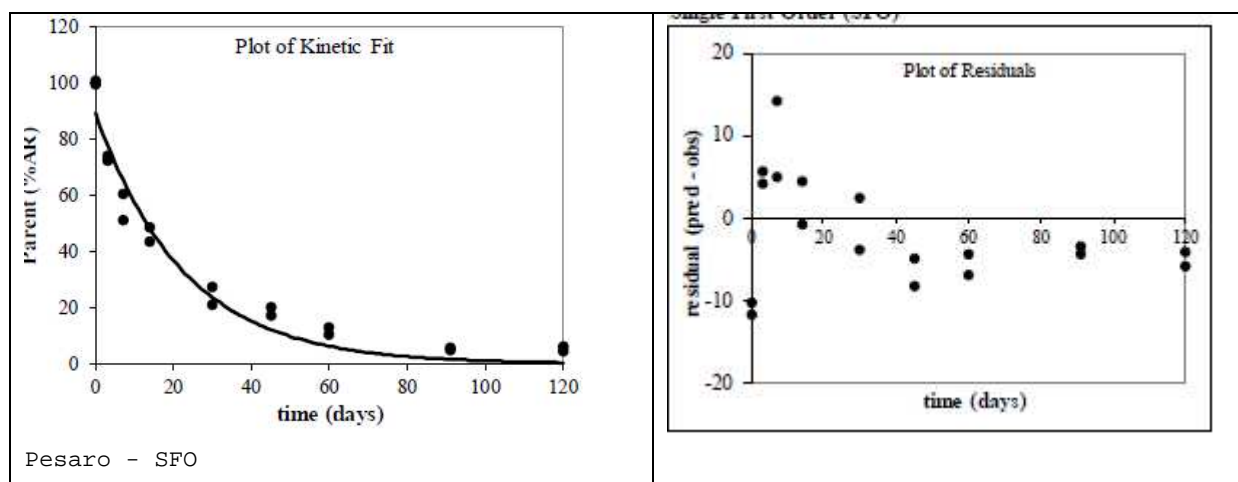
Soil	SFO				FOMC*			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	CI	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Pesaro	15.7	52.2	13	<0.05	10.2	80.8	*	10.0	66.4	p1<0.05; p2<0.05	11.1	74.4	p1<0.05; p2<0.05

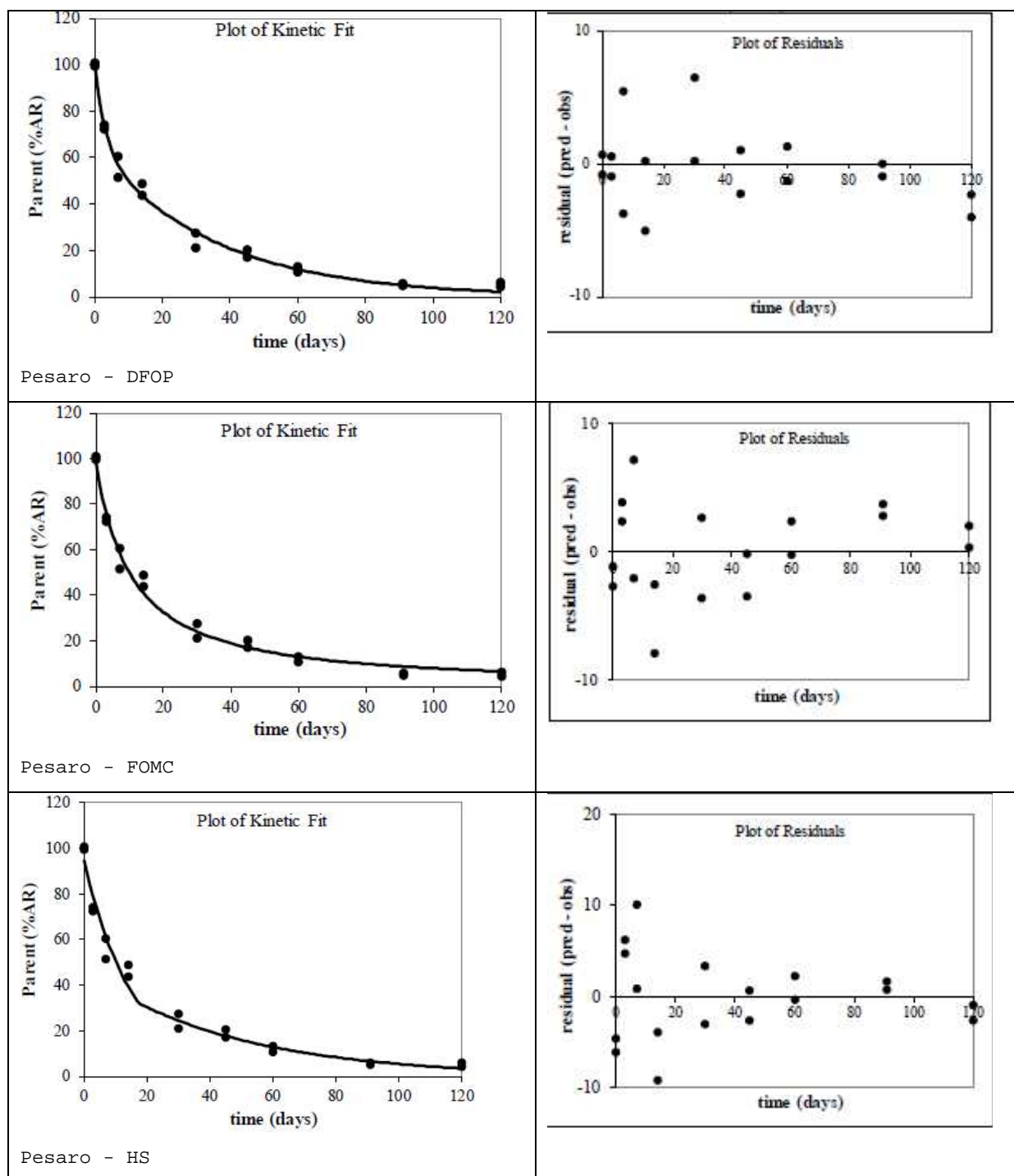
* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: SFO is considered visually acceptable although later data points are slightly underestimated. It is retained for modelling.

Visual fits and residuals for IN-JU873 in Pesaro soil





Lleida soil

Table 8-71: Summary of kinetics and goodness of fit statistics for IN-JU873 (applied as parent) in Lleida soil

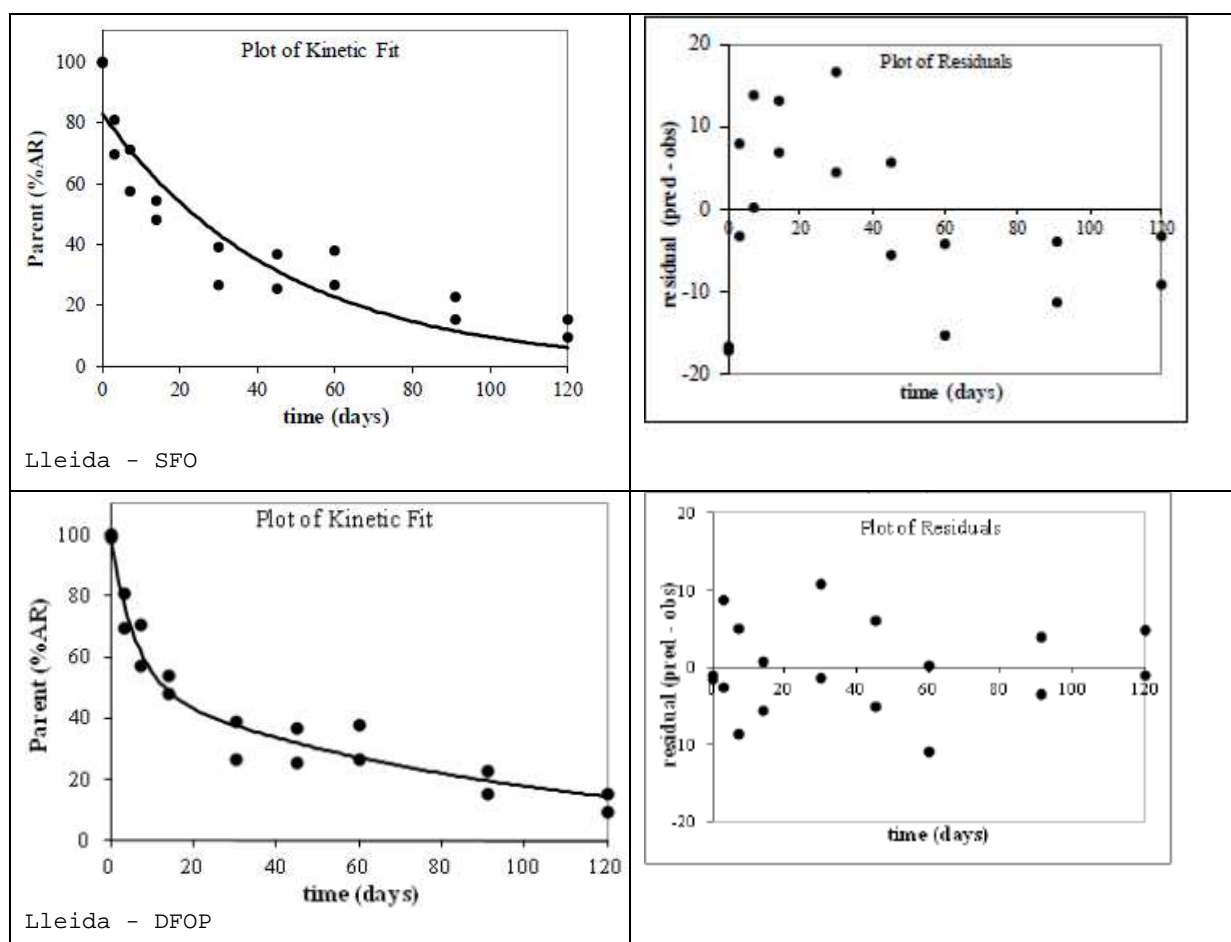
Soil	SFO				FOMC			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	CI	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Lleida	32.2	107.0	16	<0.05	14.4	367.1	*	13.8	156.6	p1<0.05; p2<0.05	12.2	146.8	p1<0.05; p2<0.05

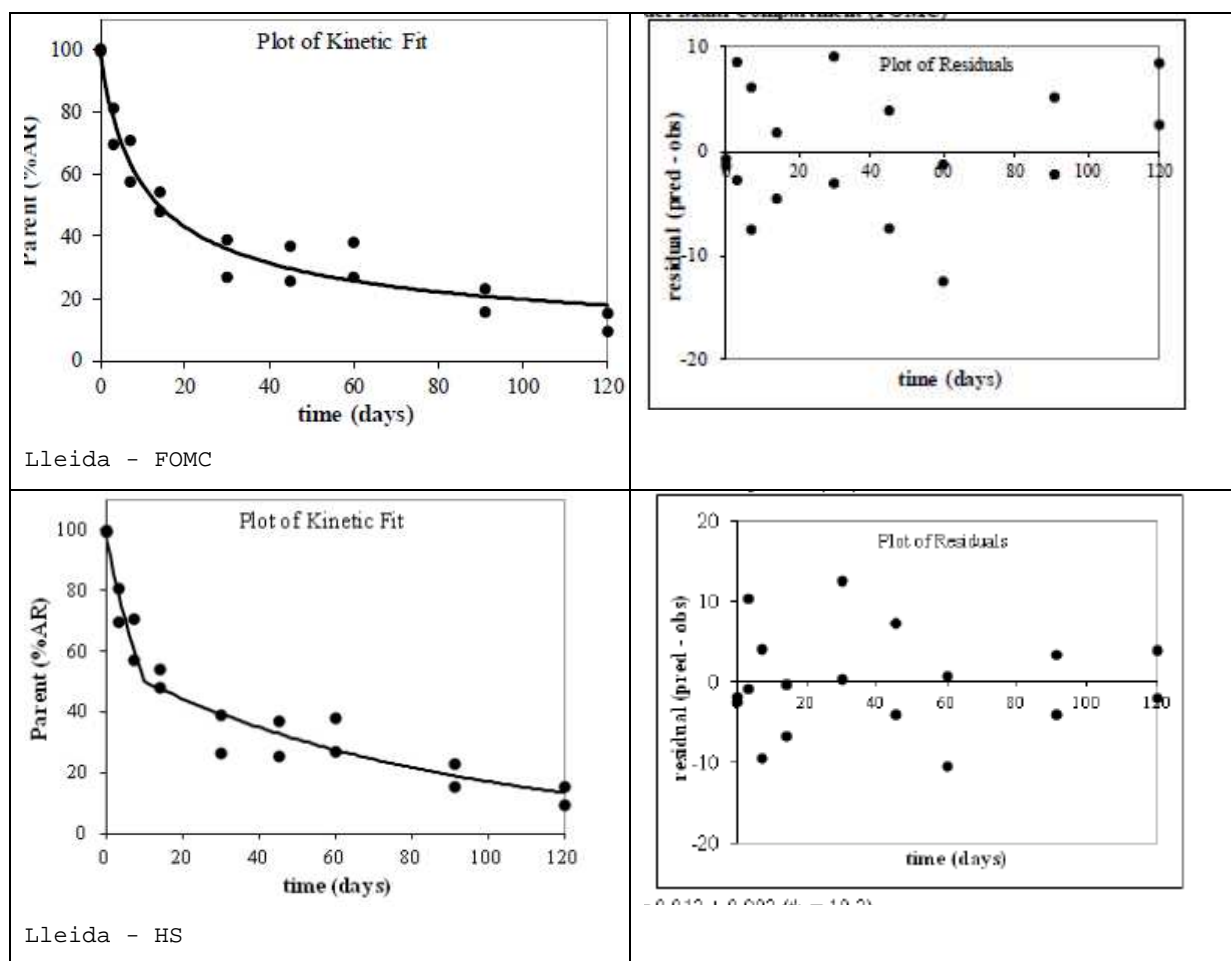
* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as more appropriate for modelling than any other models.

Visual fits and residuals for IN-JU873 in Lleida soil





Hidalgo soil

Table 8-72: Summary of kinetics and goodness of fit statistics for IN-JU873 (applied as parent) in Hidalgo soil

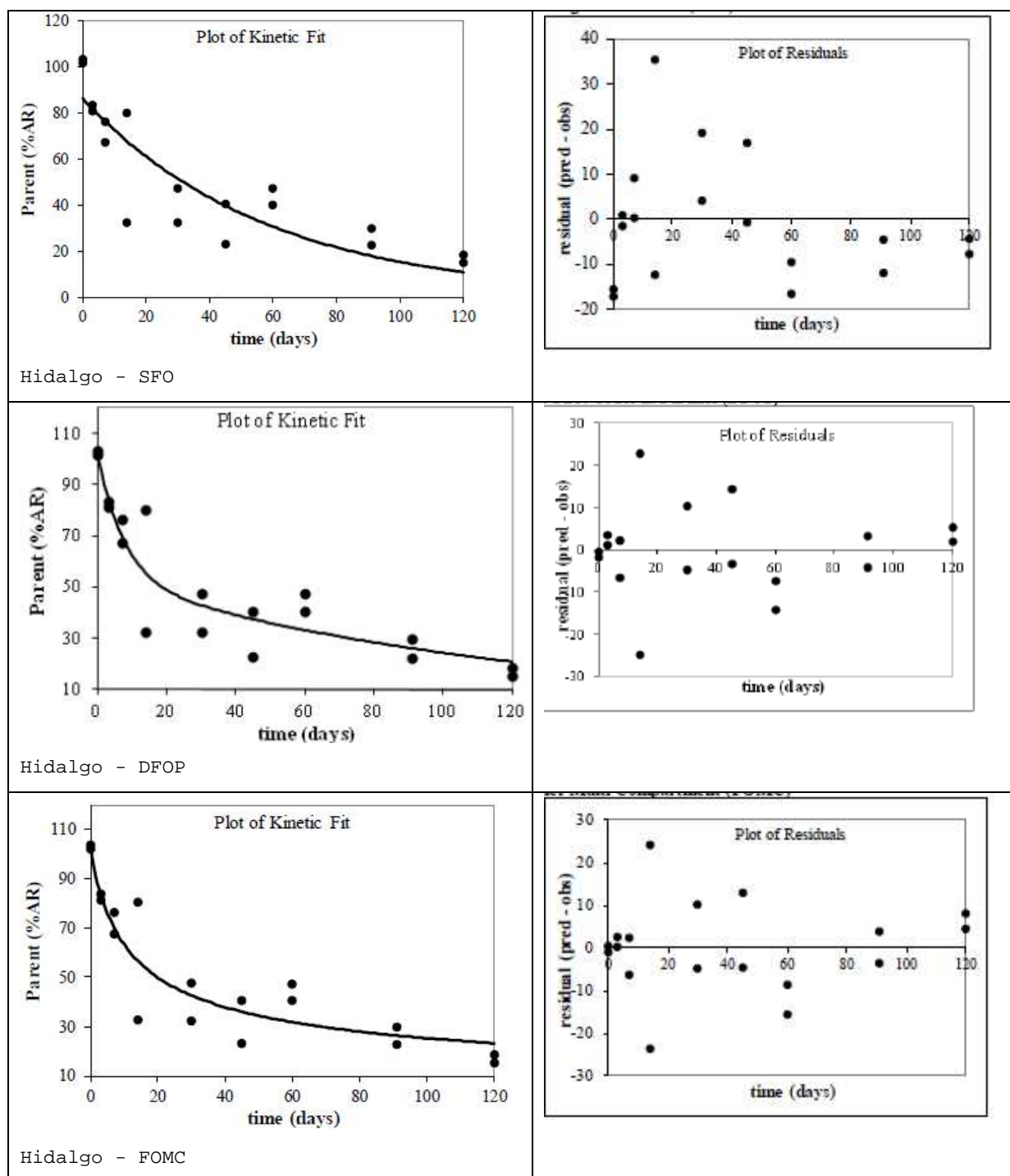
Soil	SFO				FOMC			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	CI	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Hidalgo	40.3	134.0	15	<0.05	18.7	692.4	*	18.1	212.5	p1<0.1; p2<0.1	18.4	189.1	p1<0.05; p2<0.05

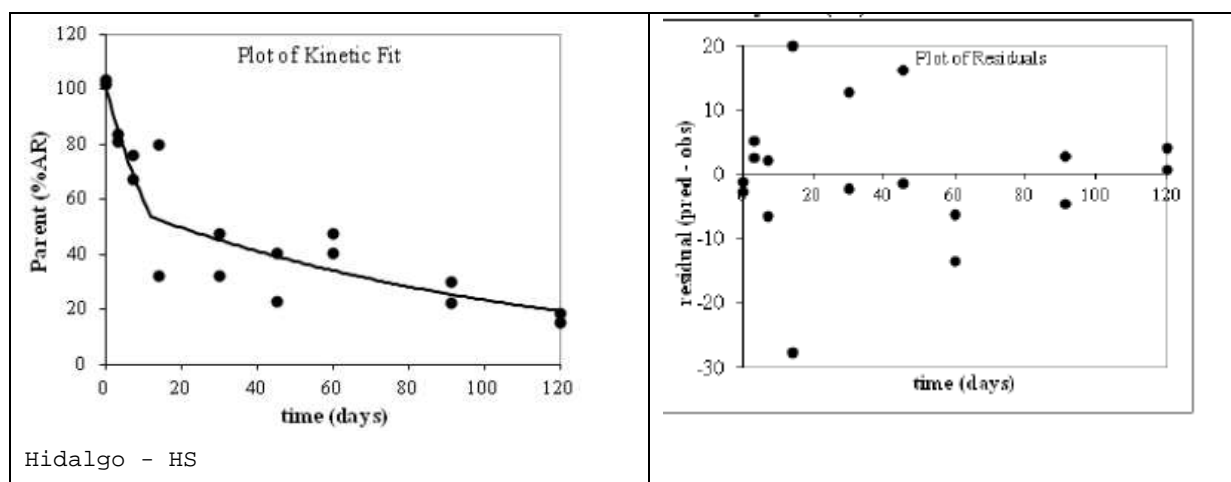
* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as more appropriate for modelling than any other models.

Visual fits and residuals for IN-JU873 in Hidalgo soil





C. Metabolite IN-KB687 (from Allan, 2012)

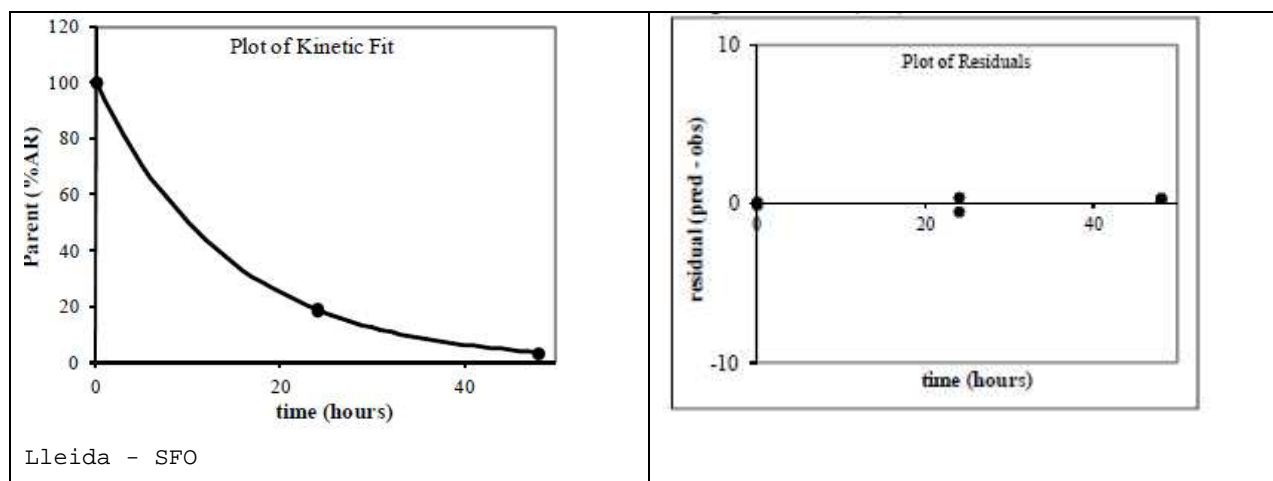
Table 8-73: Summary of kinetics for IN-KB687

Soil	SFO				FOMC*			Summary/ Comments Persistence Triggers	Modelling Inputs
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2		
Lleida	0.36	1.38	0.4	<0.05	Not Optimized ^a			SFO Best Fit	SFO Adequate $\chi^2 < 15\%$
Nambsheim	0.42	1.21	0.1	<0.05	Not Optimized ^a			SFO Best Fit	SFO Adequate $\chi^2 < 15\%$
Sassafras	0.67	2.21	2	<0.05	0.65	2.28	3	SFO Best Fit	SFO Adequate $\chi^2 < 15\%$
Speyer 2.2	0.68	2.25	12	<0.05	Not Optimized ^a			SFO Best Fit	SFO Adequate $\chi^2 < 15\%$
Tama	0.56	1.85	9	<0.05	0.53	1.91	1	FOMC Best Fit	SFO Adequate $\chi^2 < 15\%$

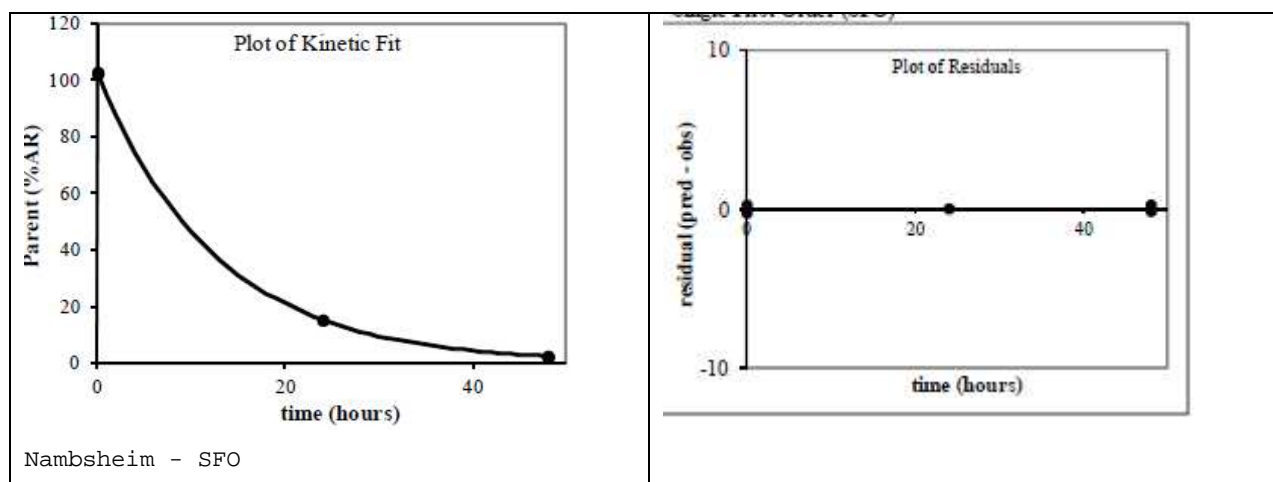
* Information on whether the confidence interval for α and β parameters of FOMC model includes 0 was not made available by applicant.

Persistence trigger and modelling endpoints: SFO is selected for all soils, as being best-fit.

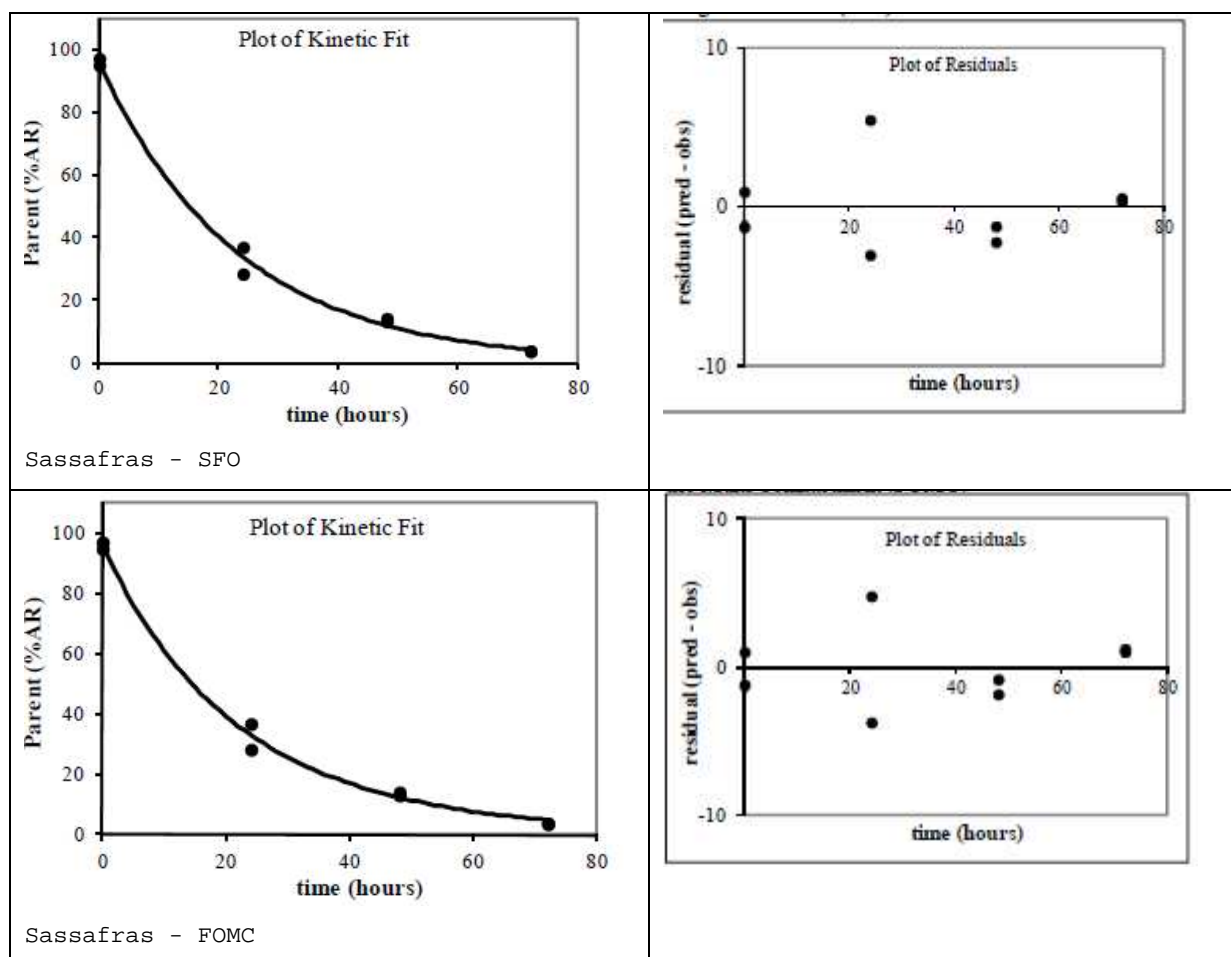
Visual fits and residuals for IN-KB687 in Lleida soil



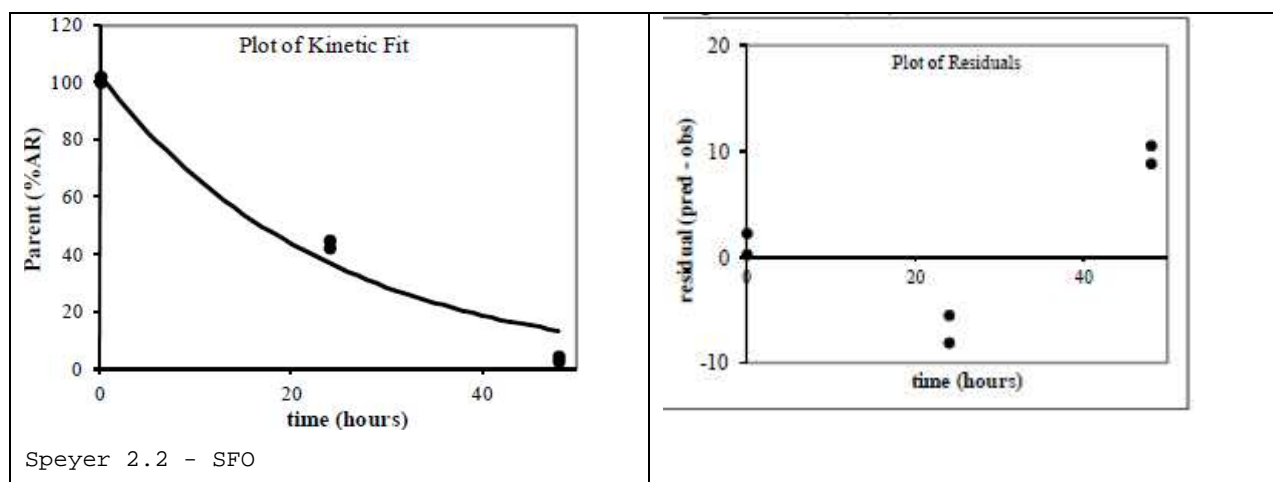
Visual fits and residuals for IN-KB687 in Nambsheim soil



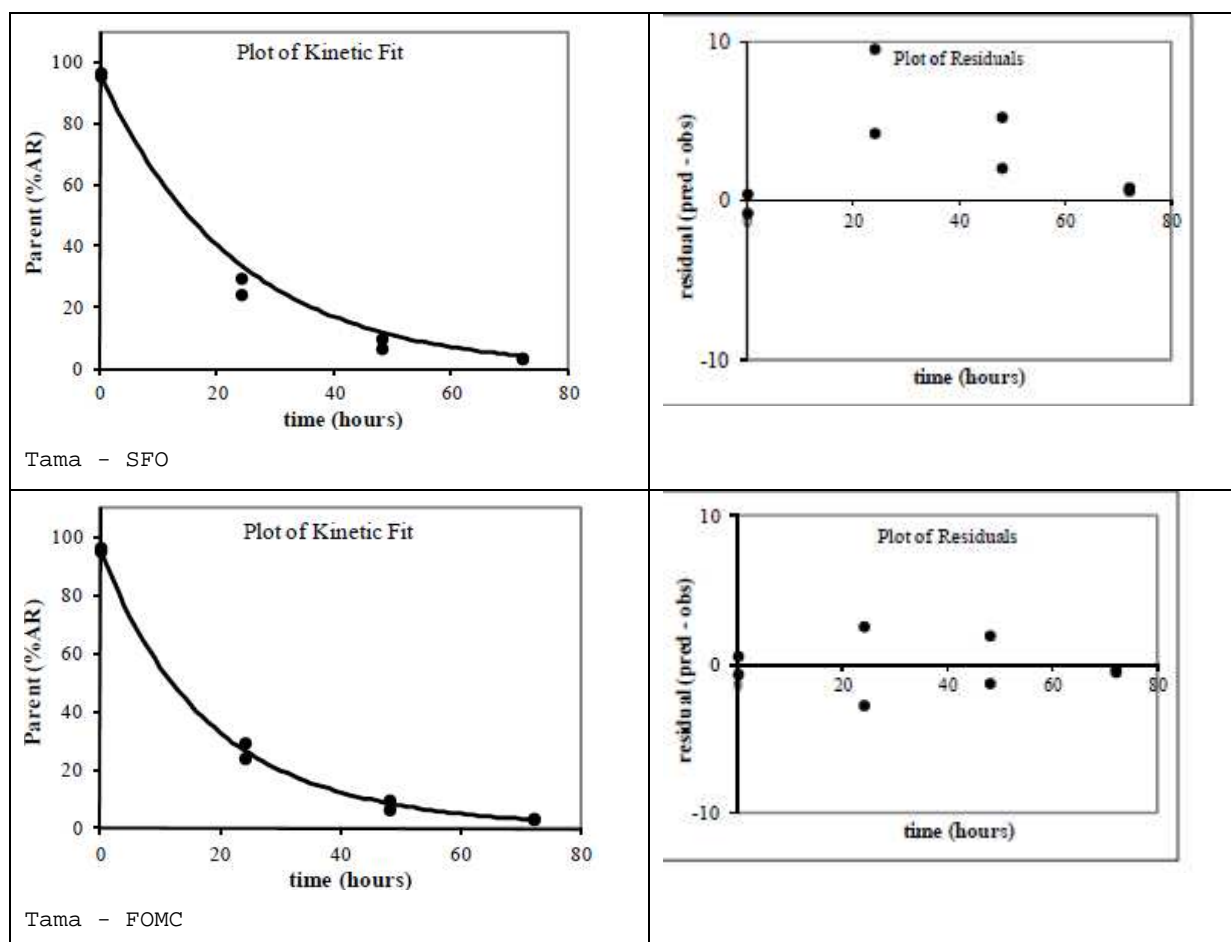
Visual fits and residuals for IN-KB687 in Sassafras soil



Visual fits and residuals for IN-KB687 in Speyer 2.2 soil



Visual fits and residuals for IN-KB687 in Tama soil

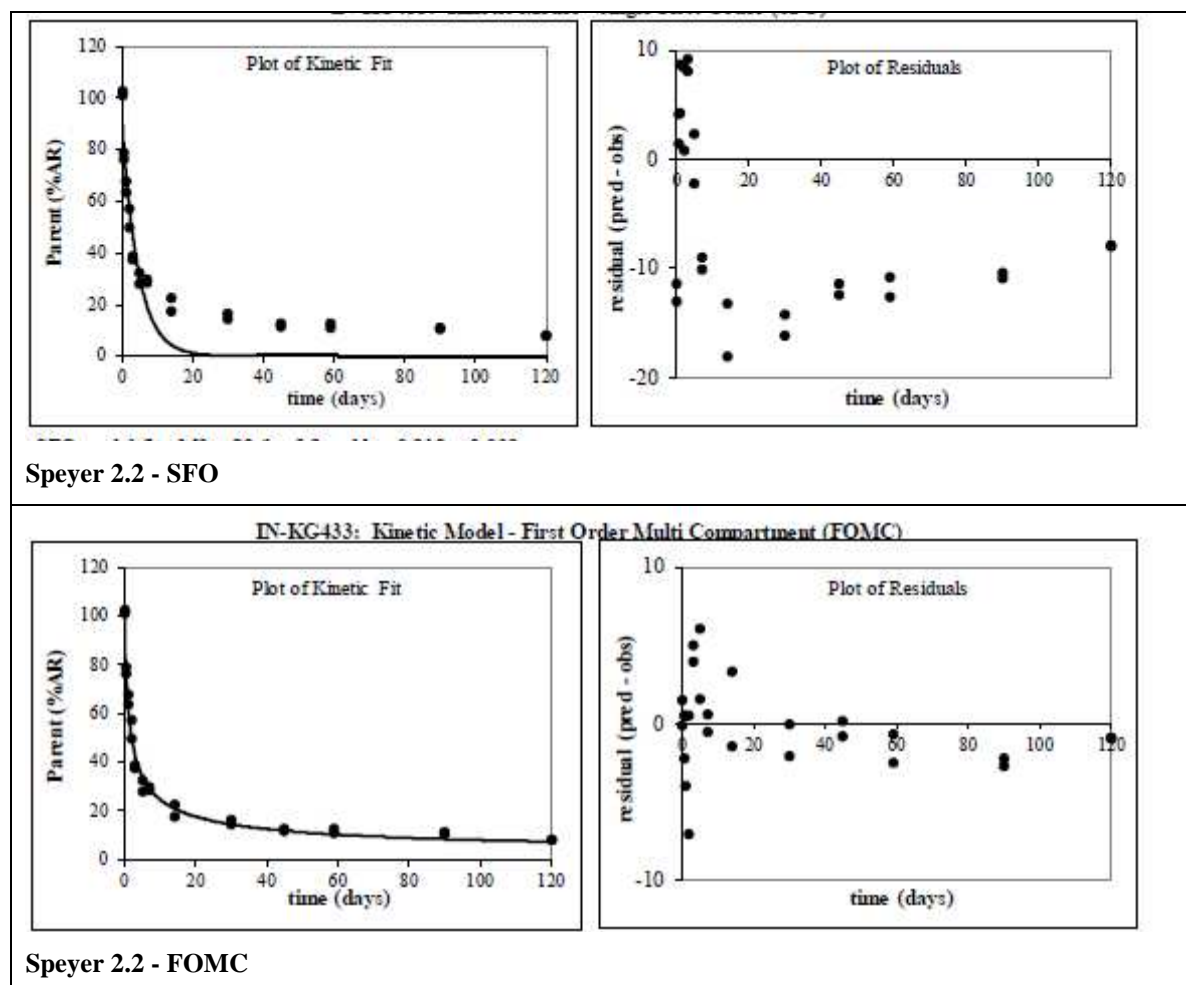


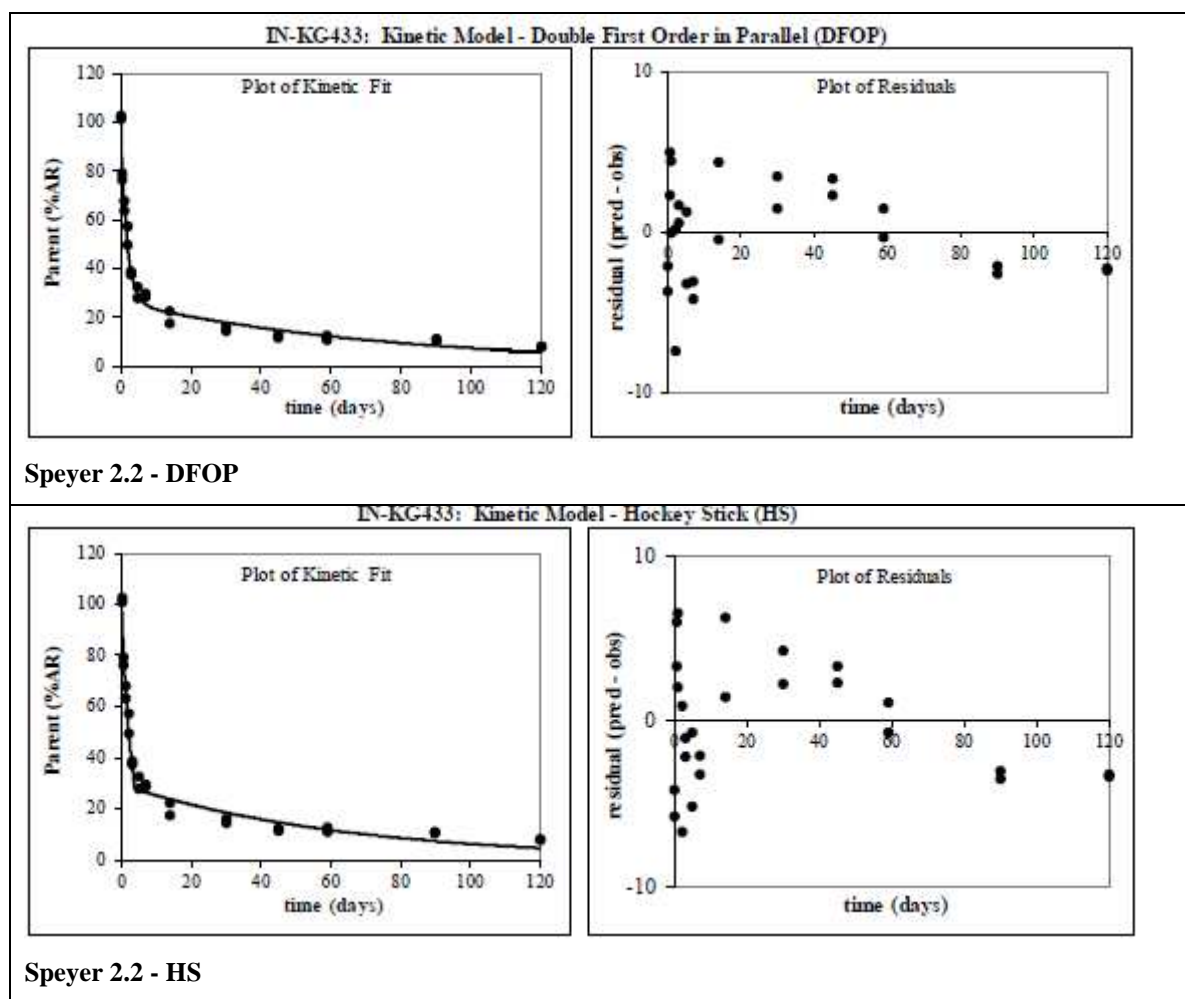
D. Metabolite IN-KG433 (from Aikens, 2002)**Speyer 2.2 soil****Table 8-74: Summary of kinetics and goodness of fit statistics for IN-KG433 (applied as parent) in Speyer 2.2 soil**

Soil	SFO				FOMC				DFOP				HS			
	DegT ₅ 0	DegT ₉ 0	χ^2	p (t-test)	DegT ₅ 0	DegT ₉ 0	DegT ₉₀ / 3.32	χ^2	DegT ₅ 0	DegT ₉ 0	χ^2	p (t-test)	DegT ₅ 0	DegT ₉ 0	χ^2	p (t-test)
Speyer 2.2	3.2	10.6	2.2	<0.05	1.9	57.8	17.4	5	2.0	76.4	6	p1<0.05 ; p2<0.05	2.1	72.4	8	p1<0.05 ; p2<0.05

Persistence trigger: SFO model resulted in visually unacceptable fit due to occurrence of non-random residual error. 10% of the initial concentration was reached; FOMC was selected as best-fit model.

Modelling endpoint: SFO model resulted in visually unacceptable fit due to occurrence of non-random residual error. 10% of the initial concentration was reached; therefore modeling endpoint of FOMC DegT₉₀/3.32 was selected.

Visual fits and residuals for IN-KG433 in Speyer 2.2 soil



Mattapex soil

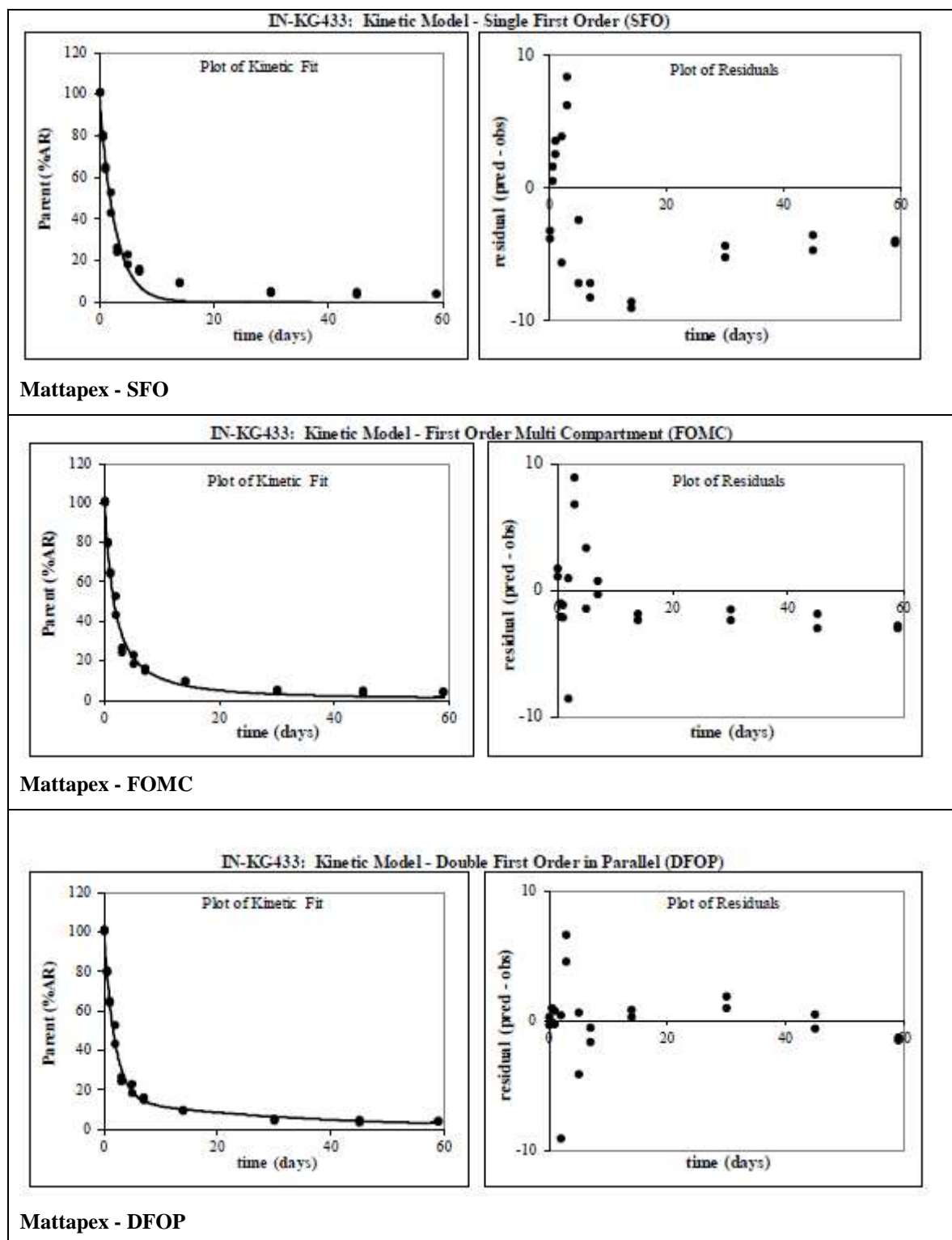
Table 8-75: Summary of kinetics and goodness of fit statistics for IN-KG433 (applied as parent) in Mattapex soil

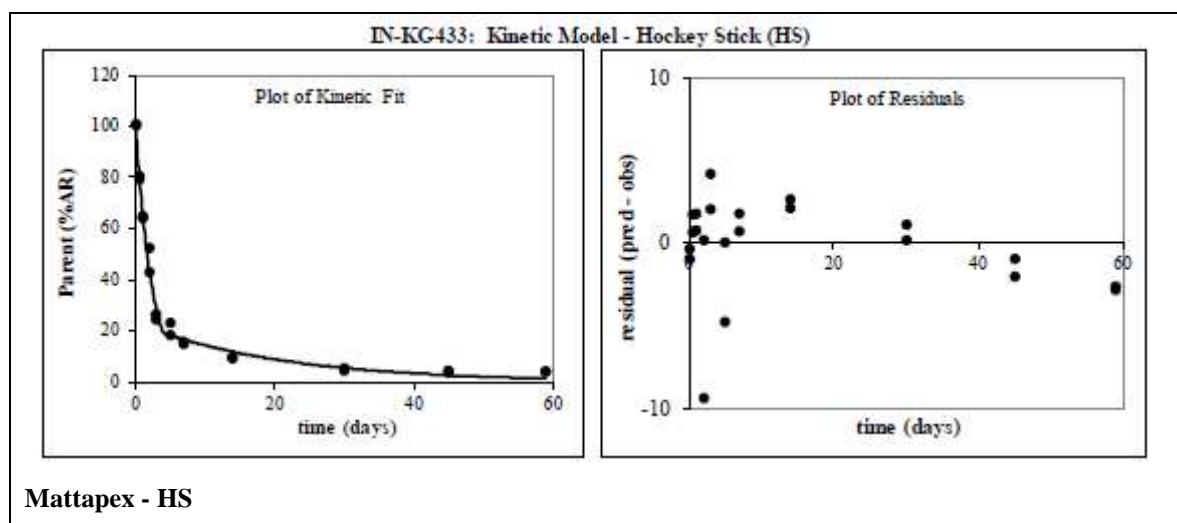
Soil	SFO				FOMC				DFOP				HS			
	DegT ₅ 0	DegT ₉ 0	χ^2	p (t-test)	DegT ₅ 0	DegT ₉ 0	DegT ₉₀ / 3.32	χ^2	DegT ₅ 0	DegT ₉ 0	χ^2	p (t-test)	DegT ₅ 0	DegT ₉ 0	χ^2	p (t-test)
Mattapex	1.9	6.3	12	<0.05	1.6	10.4	3.1	8	1.6	14.0	6	p1<0.05; p2<0.05	1.7	17.6	6	p1<0.05; p2<0.05

Persistence trigger: SFO model resulted in visually unacceptable fit due to occurrence of non-random residual error; DFOP was selected as best-fit model

Modelling endpoint: SFO model resulted in visually unacceptable fit due to occurrence of non-random residual error. 10% of the initial concentration was reached; therefore modeling endpoint of FOMC DegT₉₀/3.32 was selected.

Visual fits and residuals for IN-KG433 in Mattapex soil





Pesaro soil

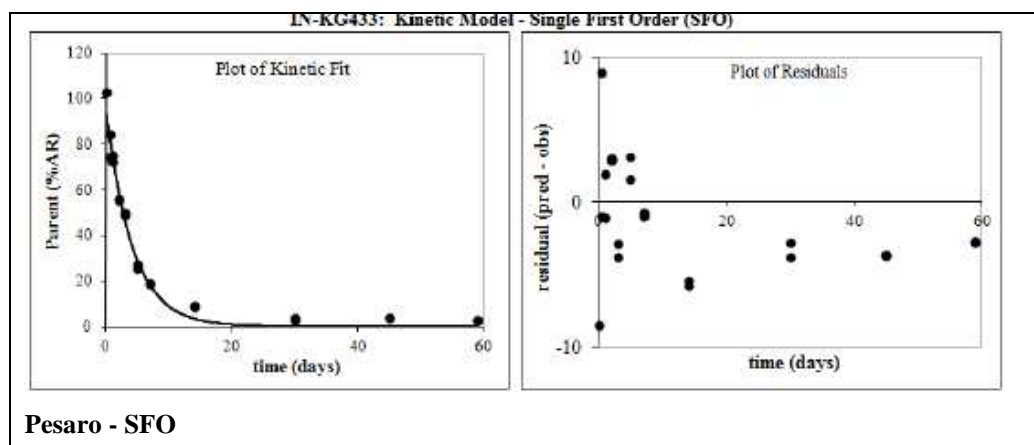
Table 8-76: Summary of kinetics and goodness of fit statistics for IN-KG433 (applied as parent) in Pesaro soil

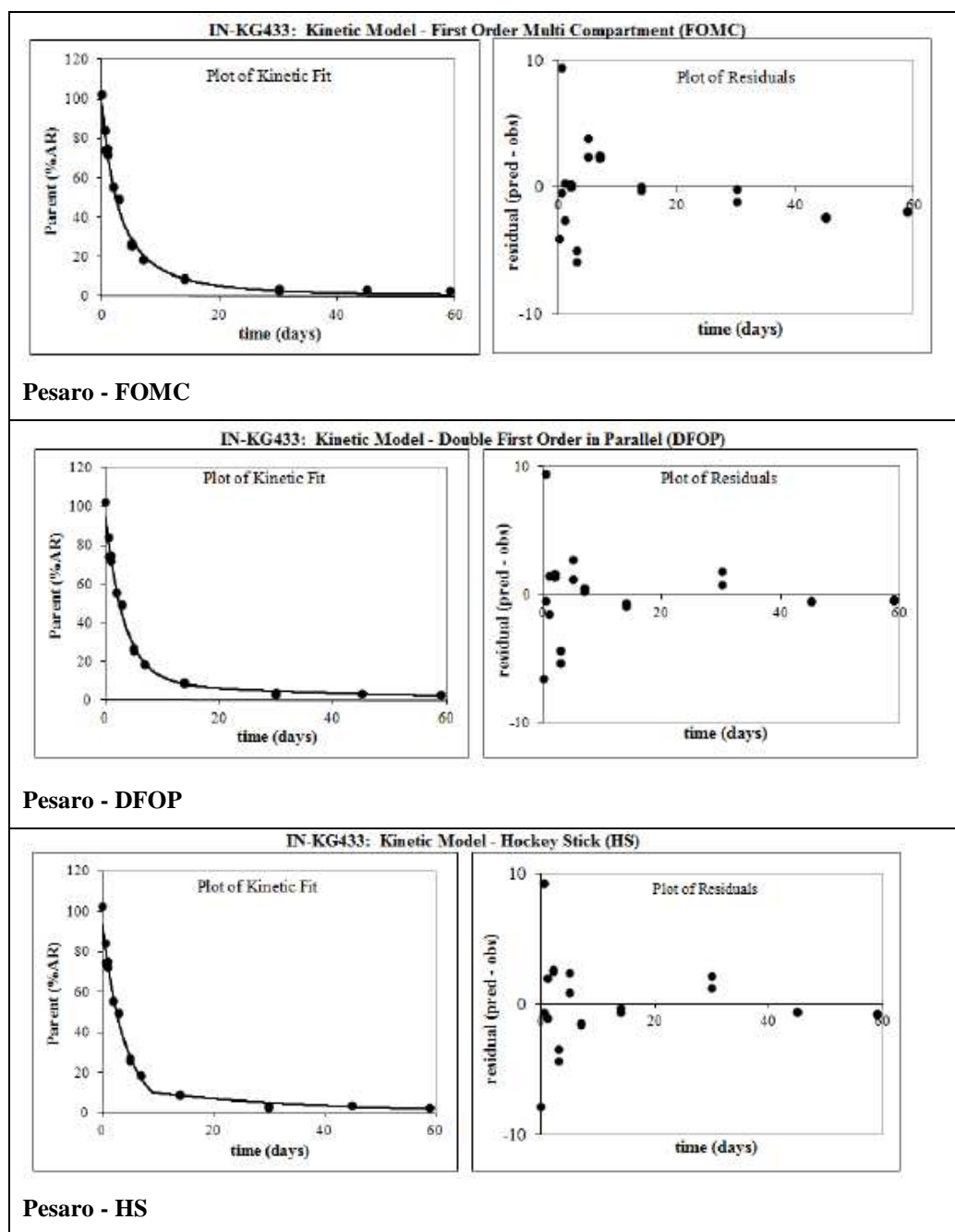
Soil	SFO				FOMC				DFOP				HS			
	DegT ₅ 0	DegT ₉ 0	χ^2 2	p (t-test)	DegT ₅ 0	DegT ₉ 0	DegT ₉₀ / 3.32	χ^2 2	DegT ₅ 0	DegT ₉ 0	χ^2 2	p (t-test)	DegT ₅ 0	DegT ₉ 0	χ^2 2	p (t-test)
Pesaro	2.9	9.7	9	<0.05	2.5	13.1	3.9	8	2.7	12.2	8	p1<0.05 ; p2 ns ^b	2.9	11.0	8	p1<0.05 ; p2<0.1

Persistence trigger: SFO model resulted in visually unacceptable fit due to occurrence of non-random residual error. 10% of the initial concentration was reached; FOMC was selected as best-fit model.

Modelling endpoint: SFO is considered visually acceptable although later data points are slightly underestimated. It is retained for modelling.

Visual fits and residuals for IN-KG433 in Pesaro soil





Lleida soil

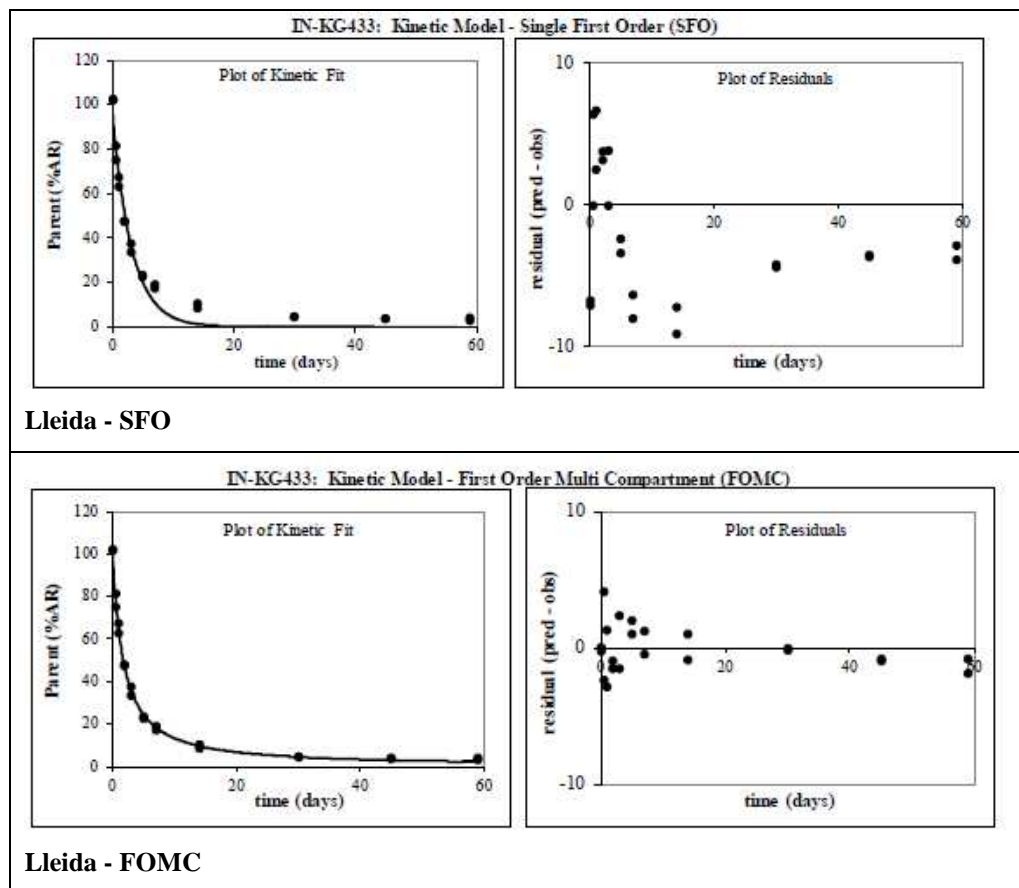
Table 8-77: Summary of kinetics and goodness of fit statistics for IN-KG433 (applied as parent) in Lleida soil

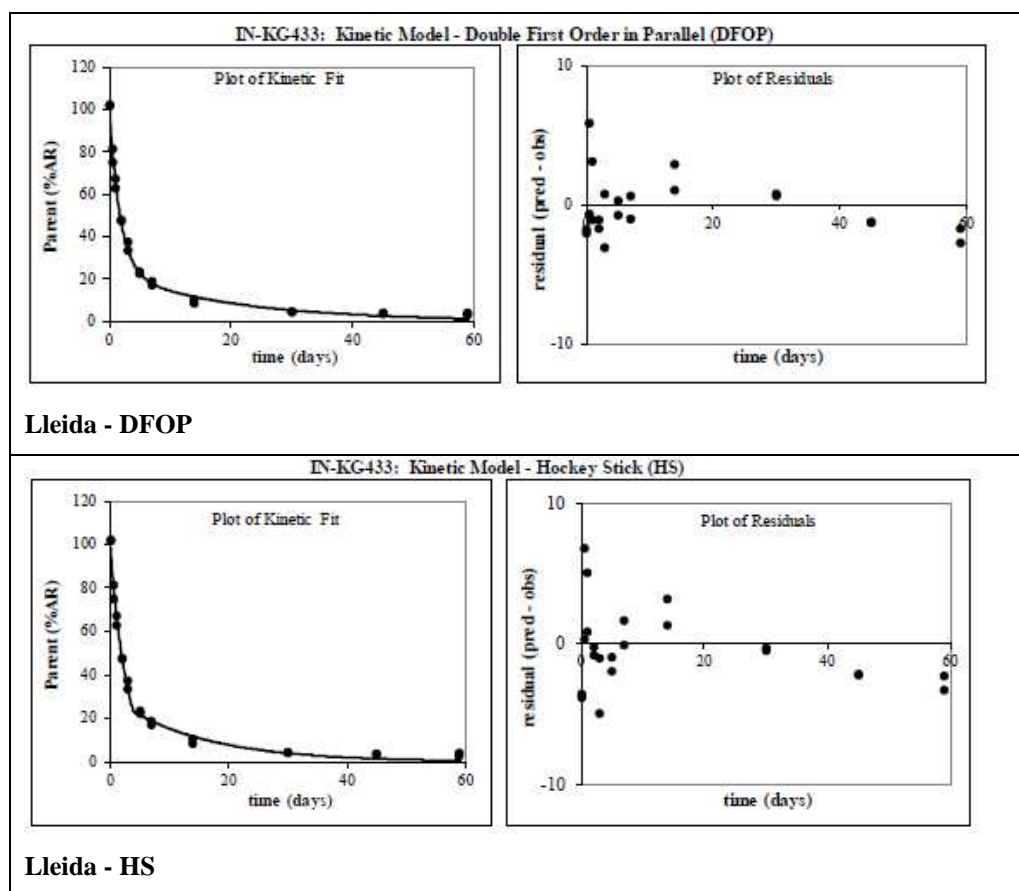
Soil	SFO				FOMC				DFOP				HS			
	DegT ₅ ₀	DegT ₉ ₀	χ^2	p (t-test)	DegT ₅ ₀	DegT ₉ ₀	DegT ₉₀ / 3.32	χ^2	DegT ₅ ₀	DegT ₉ ₀	χ^2	p (t-test)	DegT ₅ ₀	DegT ₉ ₀	χ^2	p (t-test)
Lleida	2.2	7.4	11	<0.05	1.7	13.1	3.9	2	1.8	16.7	4	p1<0.05 ; p2<0.05	1.9	16.6	6	p1<0.05 ; p2<0.05

Persistence trigger: SFO model resulted in visually unacceptable fit due to occurrence of non-random residual error. 10% of the initial concentration was reached; FOMC was selected as best-fit model.

Modelling endpoint: SFO model resulted in visually unacceptable fit due to occurrence of non-random residual error. 10% of the initial concentration was reached; therefore modeling endpoint of FOMC DegT₉₀/3.32 was selected.

Visual fits and residuals for IN-KG433 in Lleida soil





Hidalgo soil

Table 8-78: Summary of kinetics and goodness of fit statistics for IN-KG433 (applied as parent) in Hidalgo soil

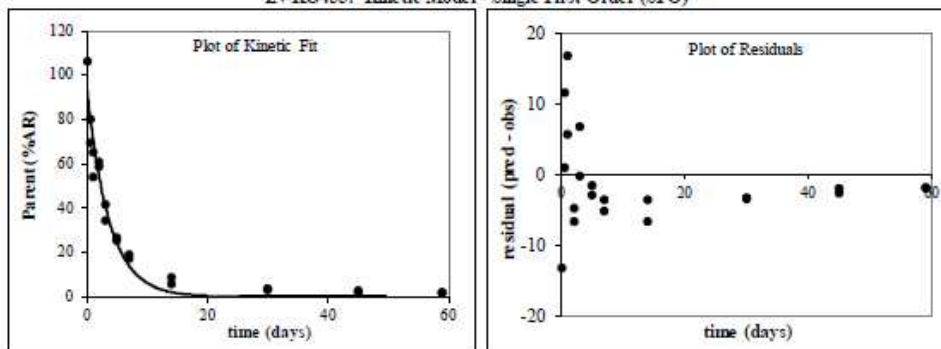
Soil	SFO				FOMC				DFOP				HS			
	Deg T ₅₀	Deg T ₉₀	χ^2	p (t-test)	Deg T ₅₀	Deg T ₉₀	DegT ₉₀ ^{3.32}	χ^2	Deg T ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
Hidalgo	2.6	8.5	17	<0.05	1.9	13.8	4.2	14	2.6	8.5	17	p1 ns ^b ; p2 ns ^b	2.5	8.4	16	p1<0.05; p2 ns ^b

Persistence trigger: SFO model resulted in visually unacceptable fit due to occurrence of non-random residual error. 10% of the initial concentration was reached; FOMC was selected as best-fit model.

Modelling endpoint: SFO is considered acceptable for modelling although later data points are slightly underestimated. It is retained for modelling.

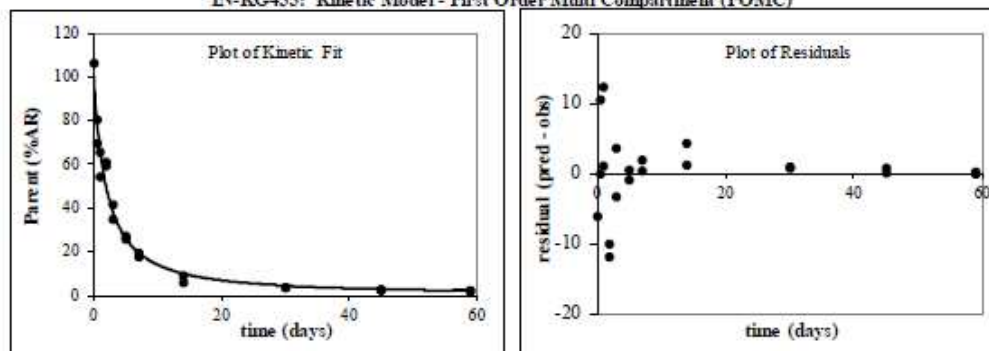
Visual fits and residuals for IN-KG433 in Hidalgo soil

IN-KG433: Kinetic Model - Single First Order (SFO)



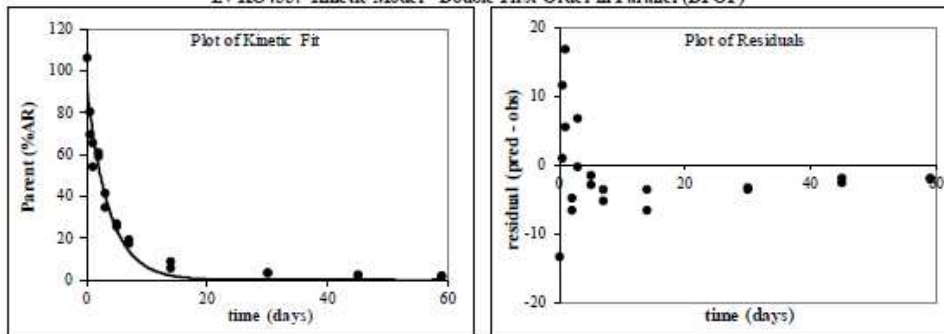
Hidalgo - SFO

IN-KG433: Kinetic Model - First Order Multi Compartment (FOMC)



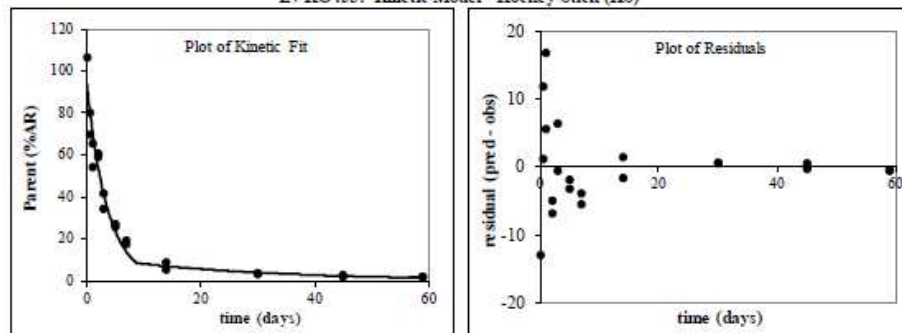
Hidalgo - FOMC

IN-KG433: Kinetic Model - Double First Order in Parallel (DFOP)



Hidalgo - DFOP

IN-KG433: Kinetic Model - Hockey Stick (HS)



Hidalgo - HS

E. Metabolite IN-KT413 (from Lentz, 2003)

Hidalgo soil

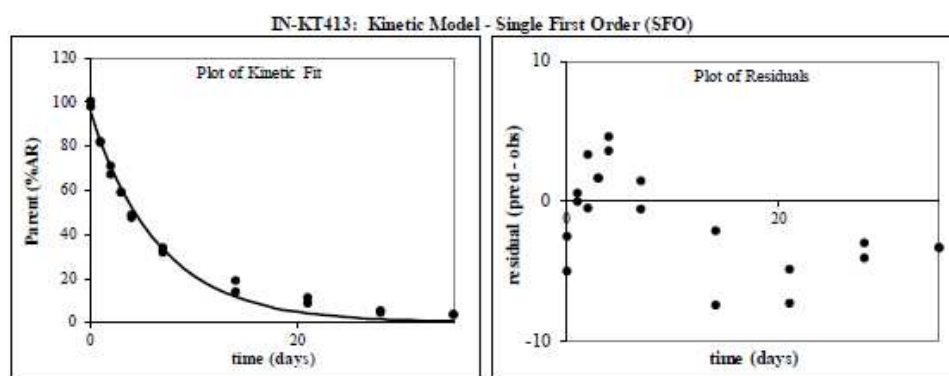
Table 8-79: Summary of kinetics and goodness of fit statistics for IN-KT413 (applied as parent) in Hidalgo soil

Soil	SFO				FOMC				DFOP				HS			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
Hidalgo	4.6	15.3	6	<0.05	4.0	19.9	6.0	2	4.0	20.5	1	p1<0.05; p2<0.05	3.9	20.6	2	p1<0.05; p2<0.05

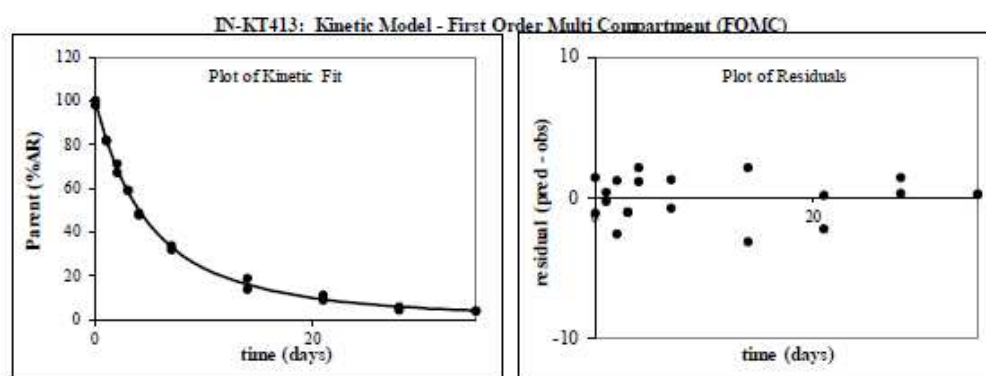
Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as visual and statistic assessment not too bad, and SFO more appropriate for modelling than any other models.

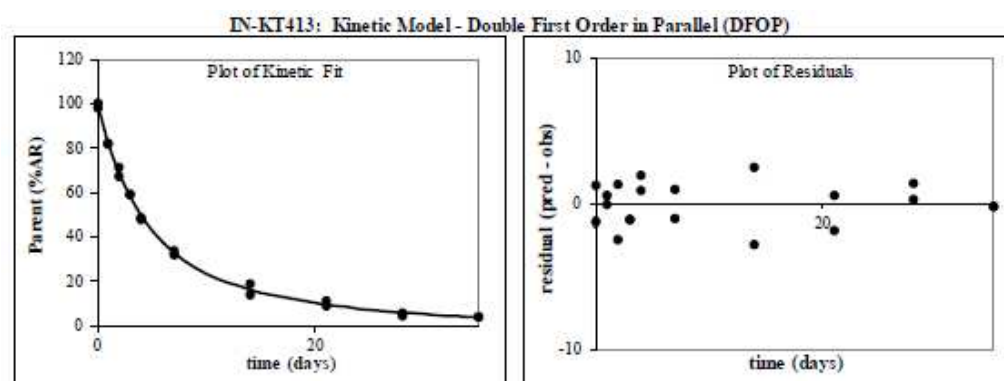
Visual fits and residuals for IN-KT413 in Hidalgo soil



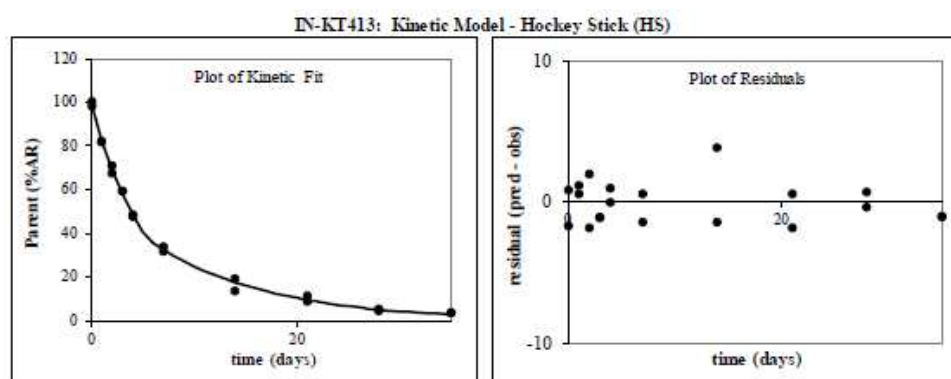
Hidalgo - SFO



Hidalgo - FOMC



Hidalgo - DFOP



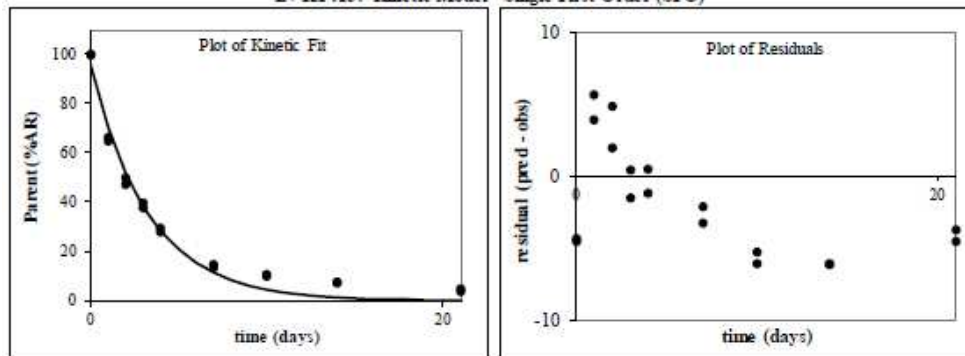
Hidalgo - HS

Lleida soil**Table 8-80: Summary of kinetics and goodness of fit statistics for IN-KT413 (applied as parent) in Lleida soil**

Soil	SFO				FOMC				DFOP				HS			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
Lleida	2.3	7.6	9	<0.05	1.9	10.4	3.1	3	2.0	10.8	4	p1<0.05; p2<0.05	2.1	11.1	6	p1<0.05; p2<0.05

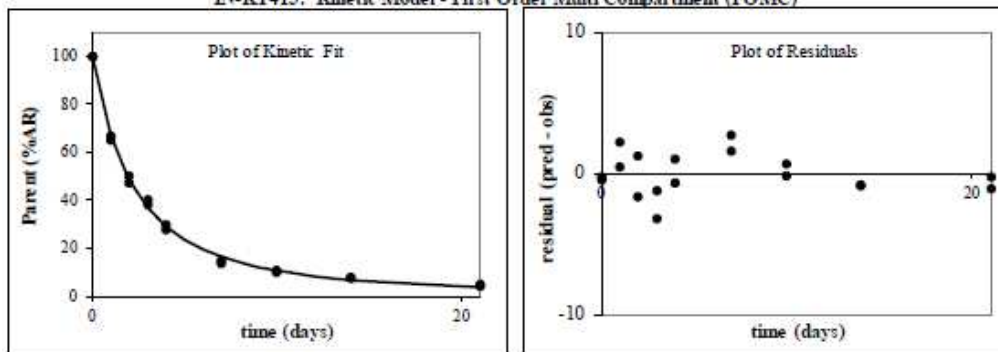
Persistence trigger: The FOMC model is the best-fit for this soil.Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as visual and statistic assessment not too bad, and SFO more appropriate for modelling than any other models.**Visual fits and residuals for IN-KT413 in Lleida soil**

IN-KT413: Kinetic Model - Single First Order (SFO)



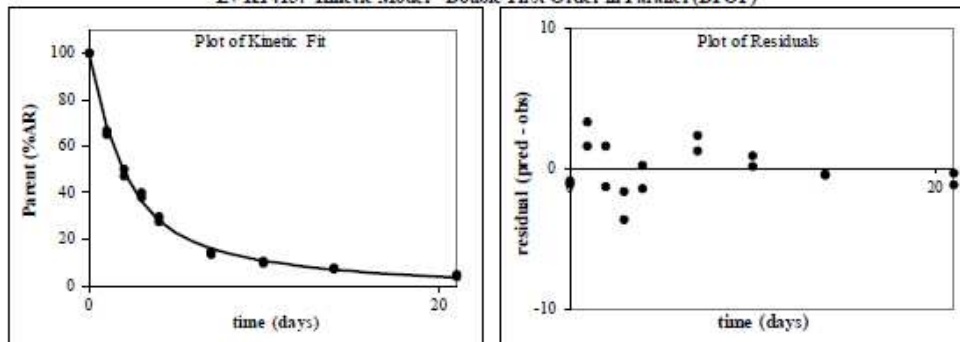
Lleida - SFO

IN-KT413: Kinetic Model - First Order Multi Compartment (FOMC)



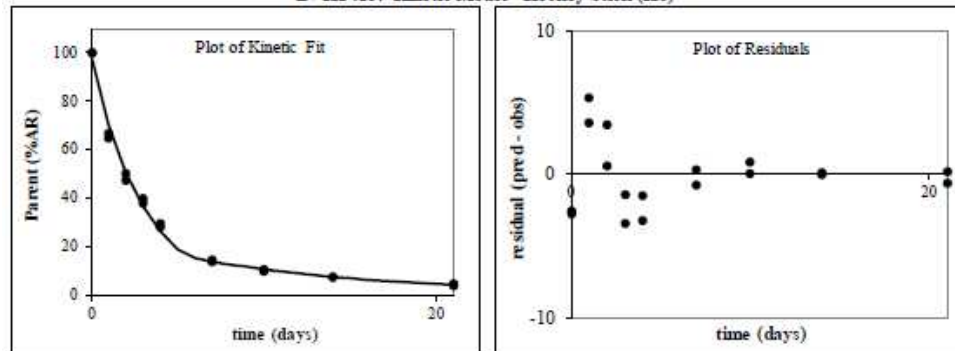
Lleida - FOMC

IN-KT413: Kinetic Model - Double First Order in Parallel (DFOP)



Lleida - DFOP

IN-KT413: Kinetic Model - Hockey Stick (HS)



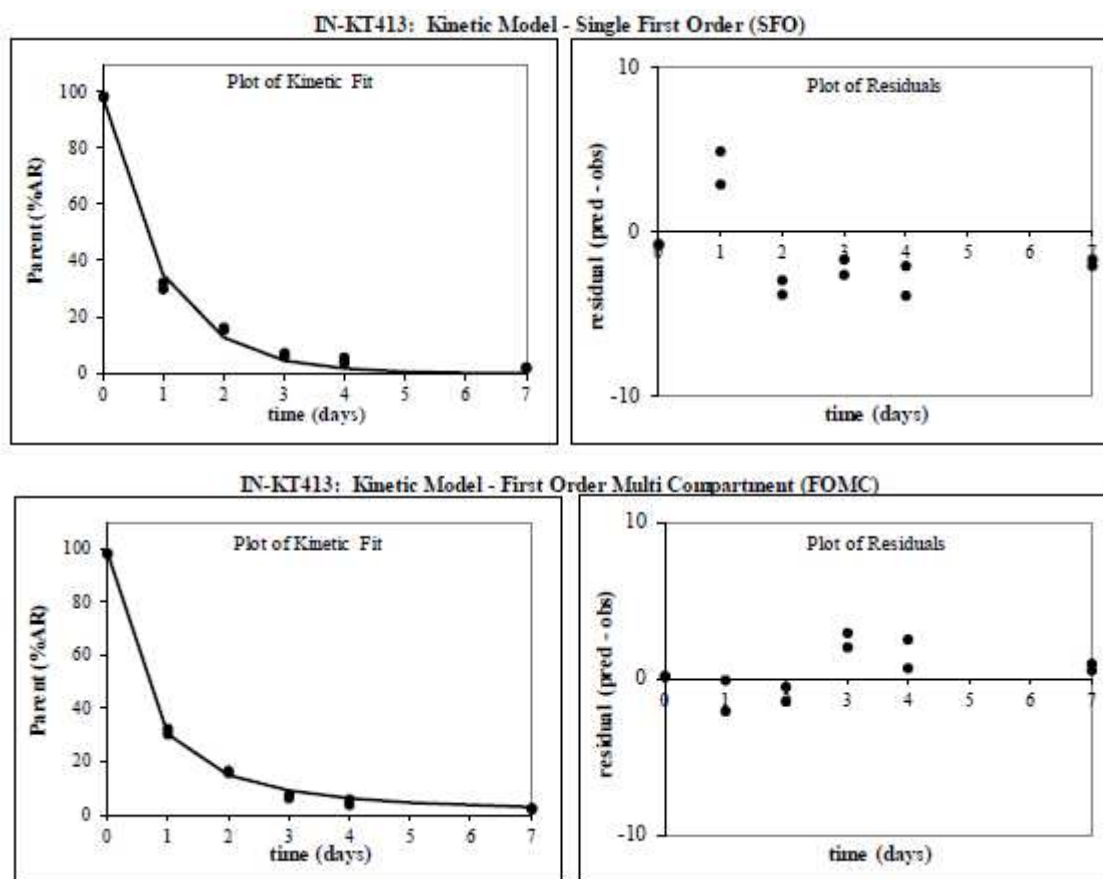
Lleida - HS

Mattapex soil**Table 8-81: Summary of kinetics and goodness of fit statistics for IN-KT413 (applied as parent) in Mattapex soil**

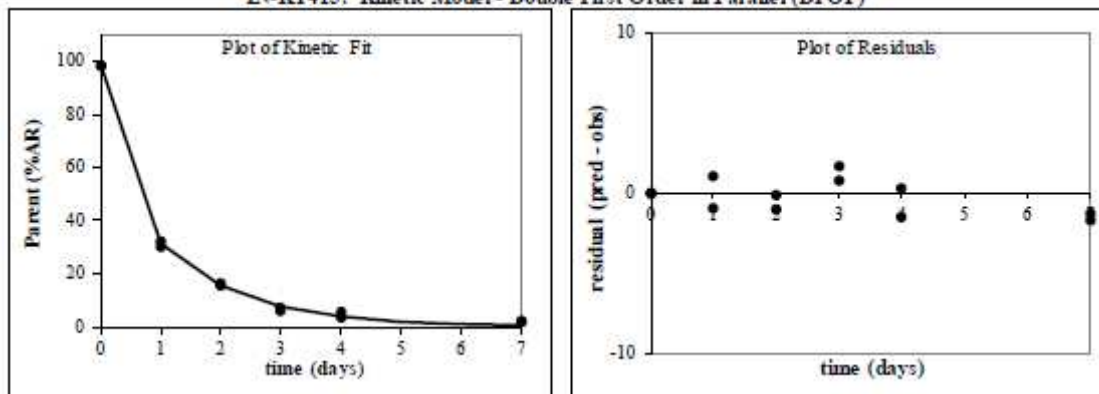
Soil	SFO			p (t-test)	FOMC				DFOP			p (t-test)	HS			p (t-test)
	DegT ₅₀	DegT ₉₀	χ^2		DegT ₅₀	DegT ₉₀	DegT ₉₀ /3.32	χ^2	DegT ₅₀	DegT ₉₀	χ^2		DegT ₅₀	DegT ₉₀	χ^2	
Mattapex	0.7	2.3	8	<0.05	0.6	2.6	0.8	5	0.5	2.7	3	p1 ns ^c ; p2<0.05	0.6	2.7	3	p1<0.05; p2<0.05

Persistence trigger: The FOMC model is the best-fit for this soil.

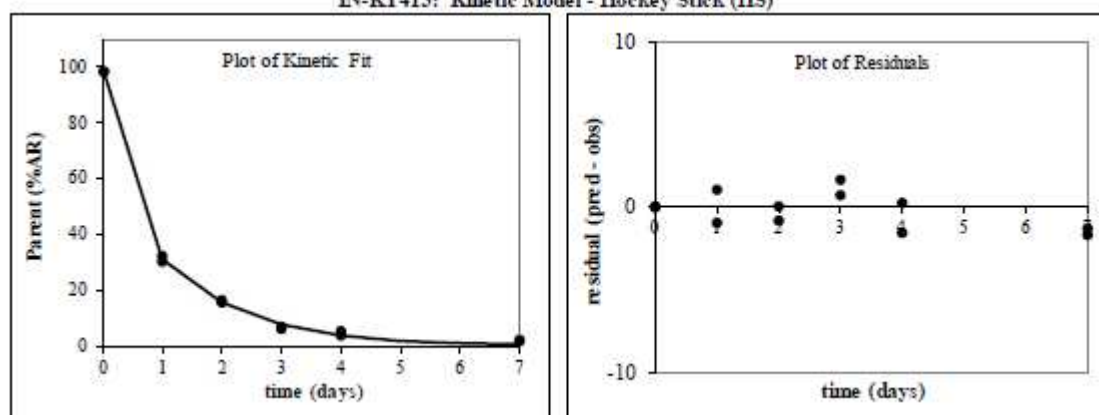
Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as visual and statistic assessment not too bad, and SFO more appropriate for modelling than any other models.

Visual fits and residuals for IN-KT413 in Mattapex soil

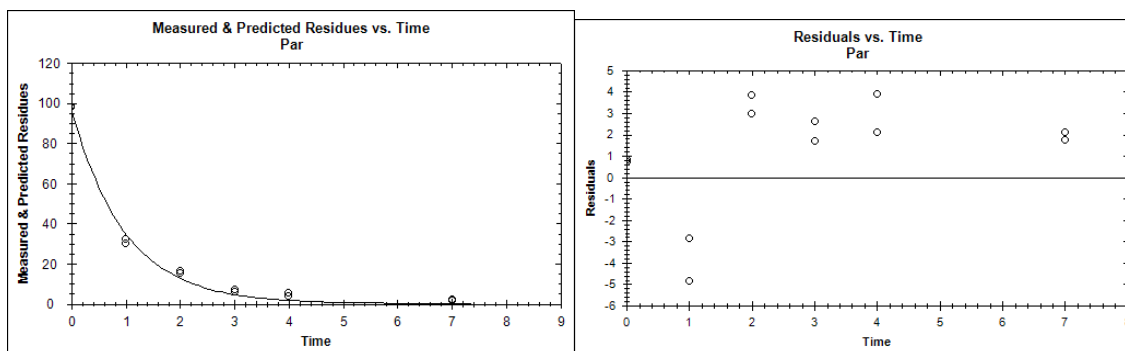
IN-KT413: Kinetic Model - Double First Order in Parallel (DFOP)



IN-KT413: Kinetic Model - Hockey Stick (HS)



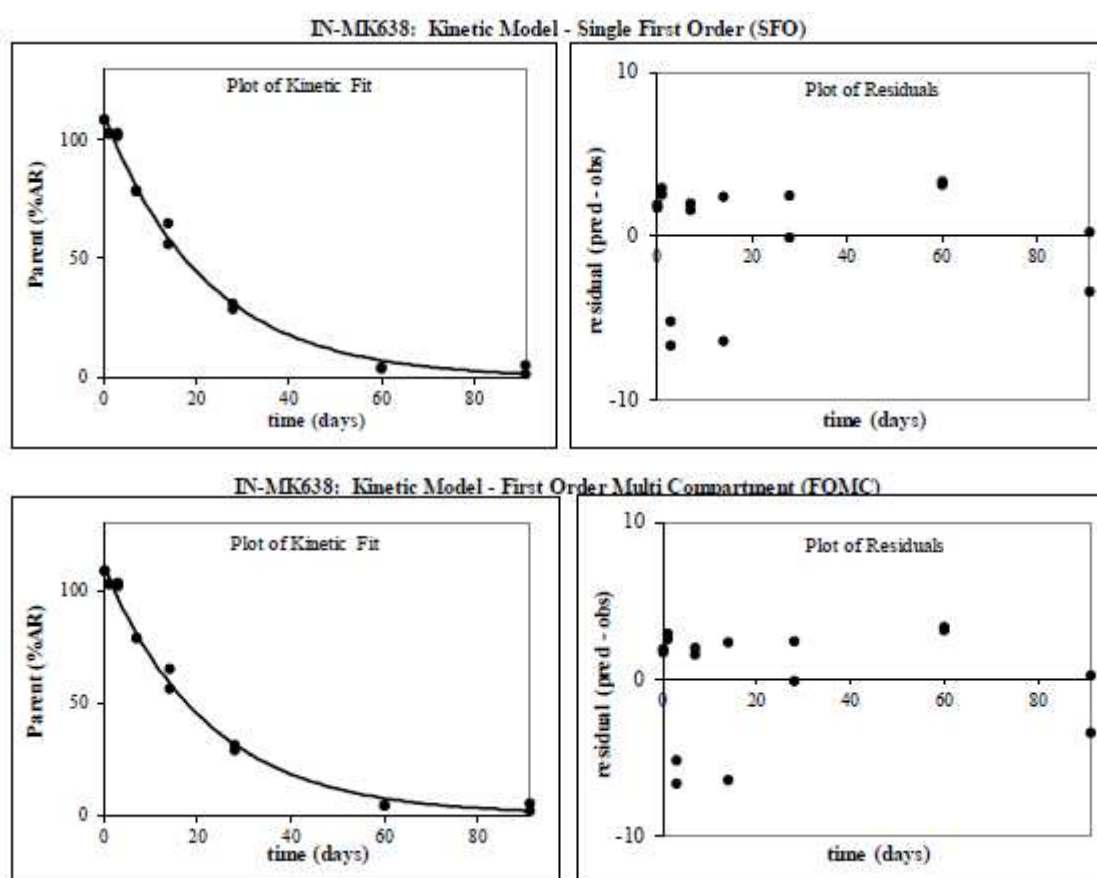
SFO – Mattapex (RMS)

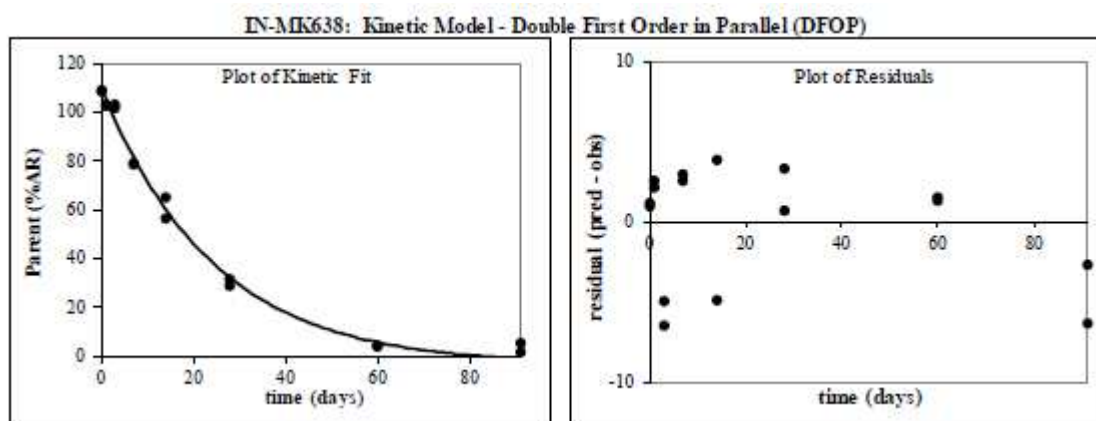


F. Metabolite IN-MK638 (from Hatzenbeler ,2002)**Table 8-82: Summary of kinetics and goodness of fit statistics for IN-MK638 (applied as parent) in five soils**

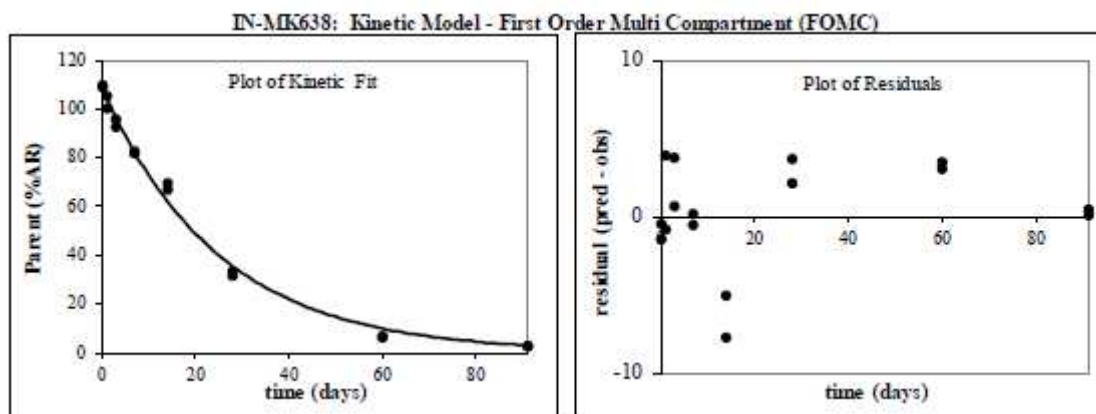
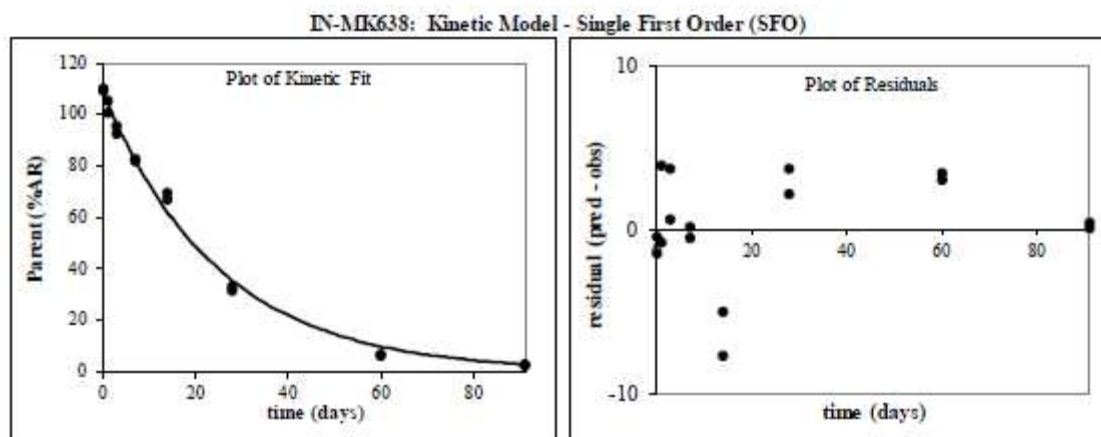
Soil	SFO				FOMC			DFOP			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
Speyer 2.2	15.4	51.0	4	<0.05	15.4	51.0	4	16.1	49.2	5	p1<0.05; p2<0.05
Mattapex	17.3	57.5	4	<0.05	17.3	57.5	4	17.8	54.1	4	p1 ns ^b ; p2 ns ^b
Pesaro	4.8	16.1	3	<0.05	4.8	16.1	3	4.8	16.2	3	p1<0.05; p2 ns ^b
Lleida	5.9	19.7	2	<0.05	5.7	21.8	2	5.6	21.9	2	p1<0.05; p2<0.05
Hidalgo	10.7	35.7	3	<0.05	10.7	35.7	3	10.8	35.2	4	p1<0.05; p2 ns ^b

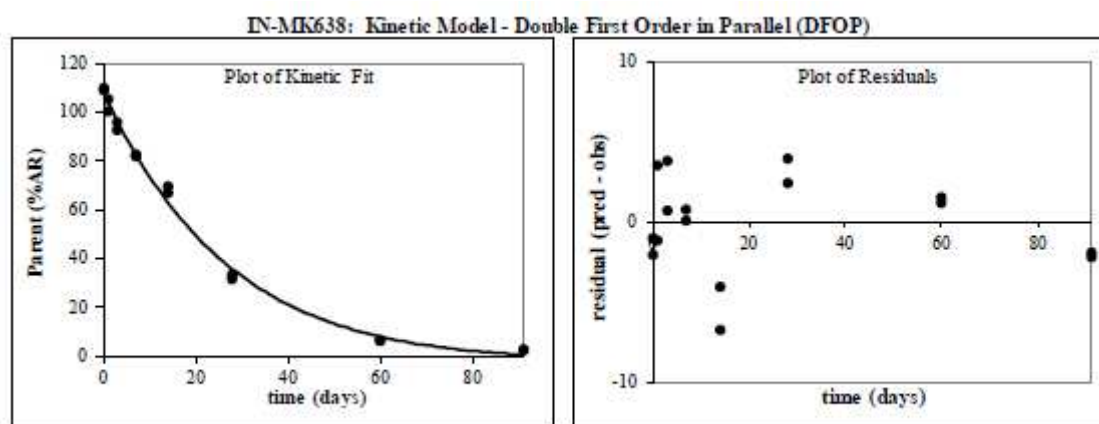
Persistence and modelling: SFO was considered best-fit and is retained for modelling in all soils. Visual plots are reported below.

Visual fits and residuals for IN-MK638 in Speyer 2.2 soil



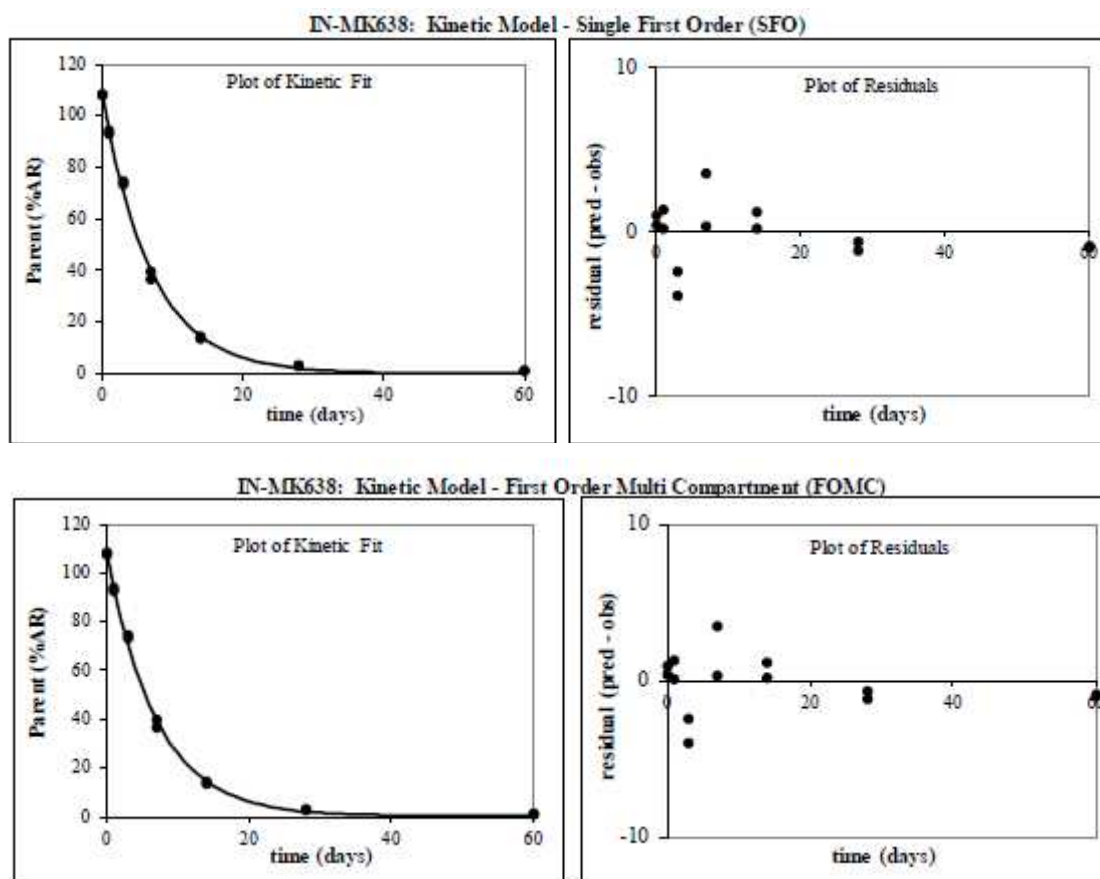
Visual fits and residuals for IN-MK638 in Mattapex soil

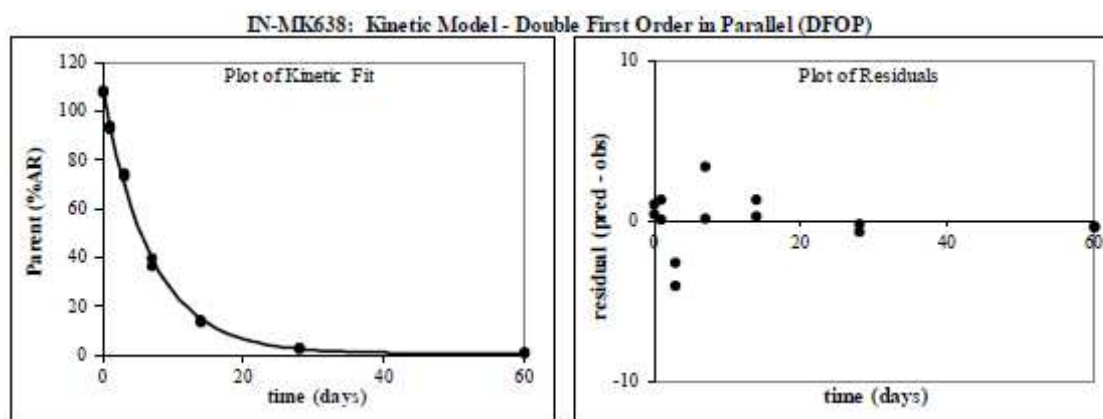




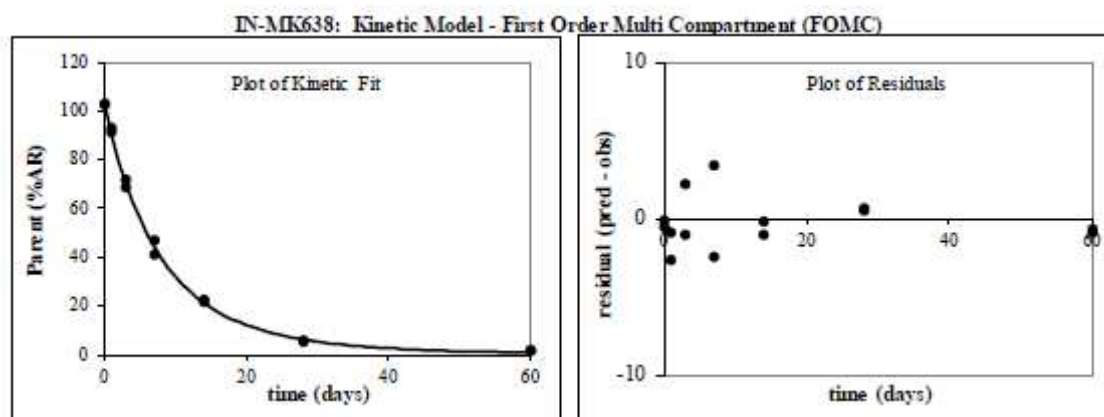
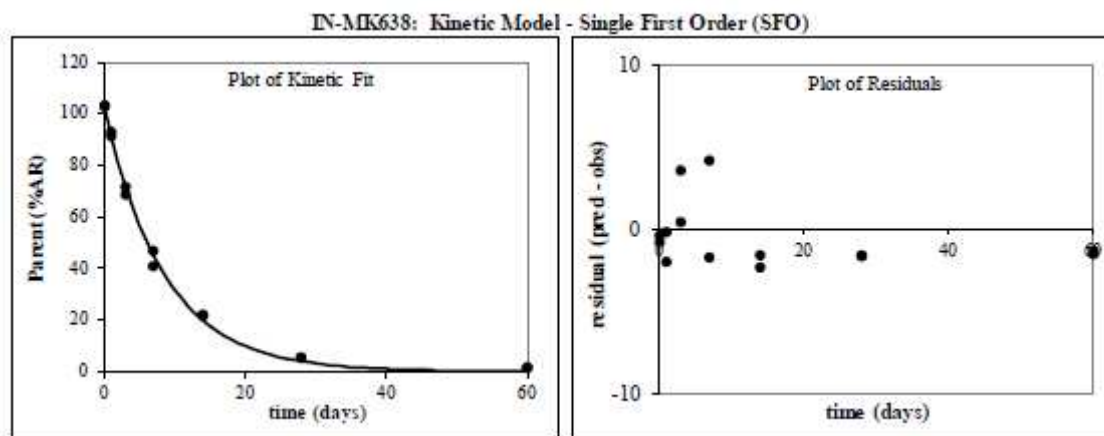
• DFOP model fit - $M0 = 108 \pm 1.5$, $k1 = 0.029 \pm 0.082$, and $k2 = 0.026 \pm 0.14$ ($g = 3.4$)

Visual fits and residuals for IN-MK638 in Pesaro soil

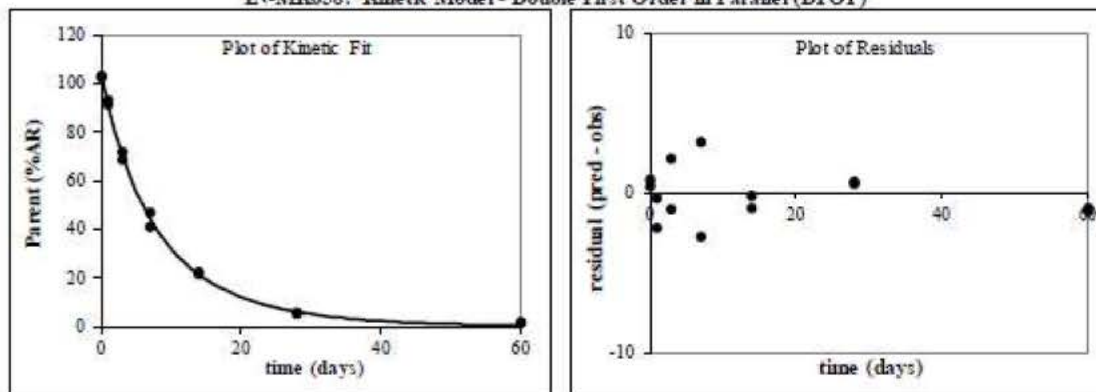




Visual fits and residuals for IN-MK638 in Lleida soil

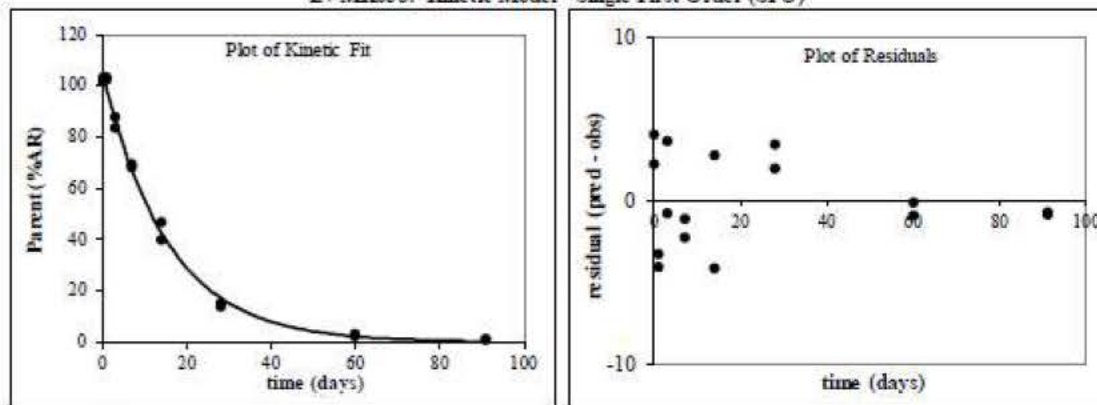


IN-MK638: Kinetic Model - Double First Order in Parallel (DFOP)

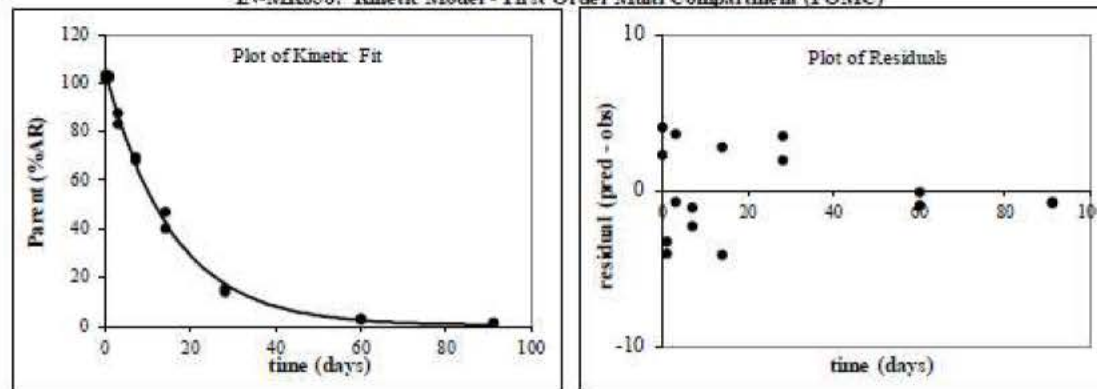


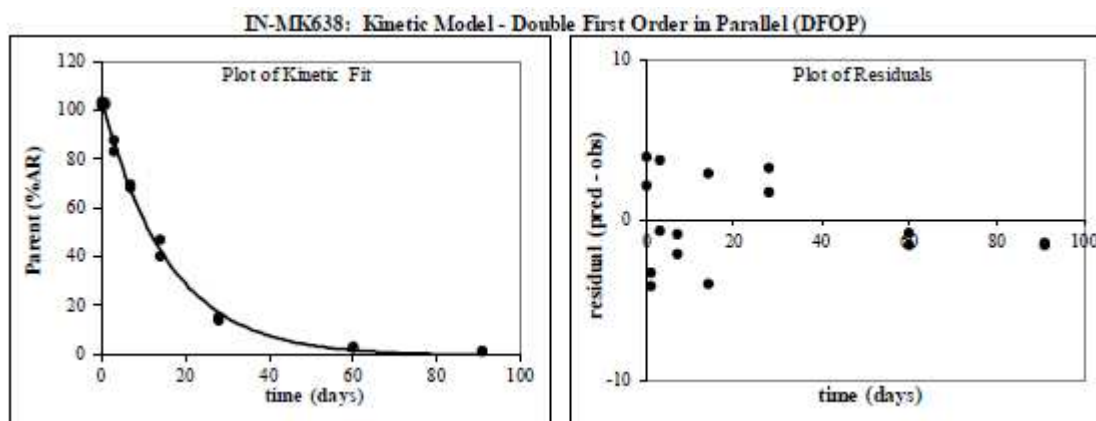
Visual fits and residuals for IN-MK638 in Hidalgo soil

IN-MK638: Kinetic Model - Single First Order (SFO)



IN-MK638: Kinetic Model - First Order Multi Compartment (FOMC)





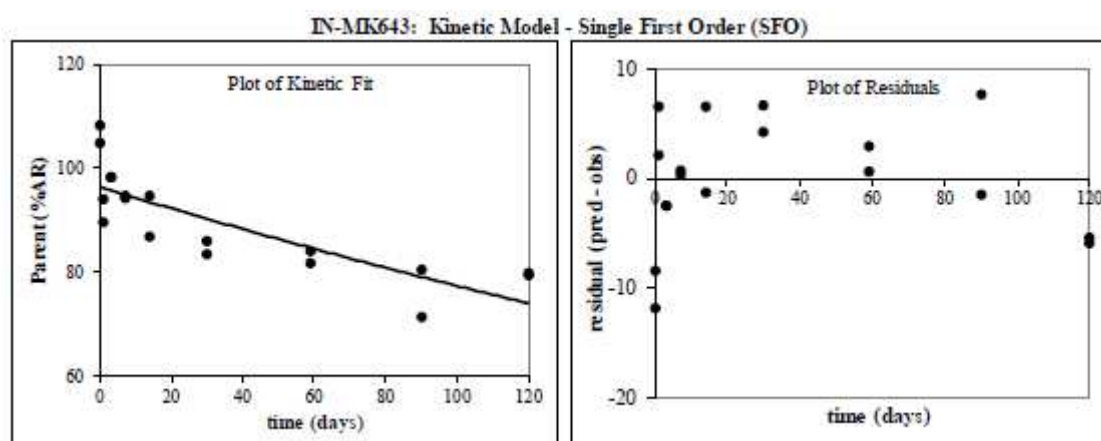
G. Metabolite IN-MK643 (from Caldwell, 2002)

Table 8-83: Summary of kinetics and goodness of fit statistics for IN-MK643 (applied as parent) in five soils

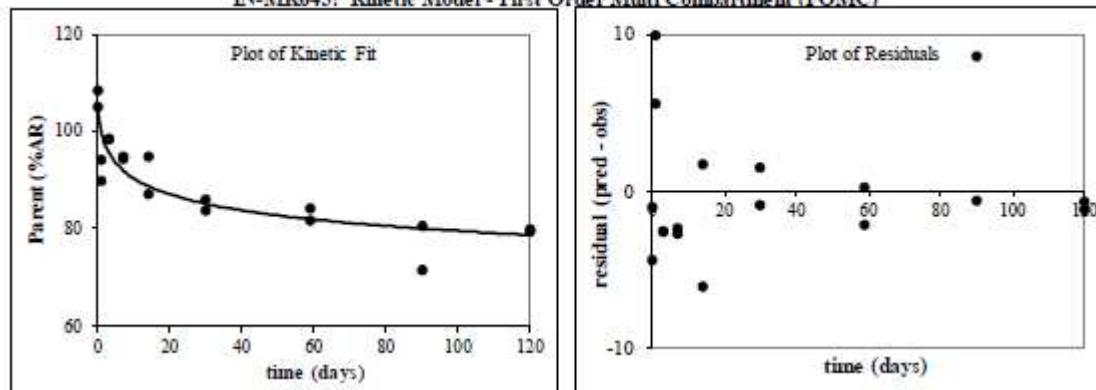
Soil	SFO				FOMC			DFOP			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
Speyer 2.2	314.2	1043.8	4	<0.05	1.8E+05	3.3E+17	3	1227.5	5241.8	4	p1 ns ^c ; p2 ns ^c
Mattapex	275.5	915.2	5	<0.05	2.9E+04	4.4E+14	2	694.8	3016.7	3	p1<0.1; p2 ns ^c
Pesaro	177.8	590.8	7	<0.05	721.0	5.8E+07	5	508.0	2829.8	6	p1 ns ^c ; p2 ns ^c
Lleida	199.4	662.3	8	<0.05	2286.8	2.7E+11	5	541.7	2863.6	5	p1<0.1; p2 ns ^c
Hidalgo	123.3	409.6	7	<0.05	174.8	3.6E+05	3	330.1	3296.8	4	p1<0.05; p2 ns ^c

Persistence and modelling: SFO was considered best-fit and is retained for modelling in all soils. Visual plots are reported below.

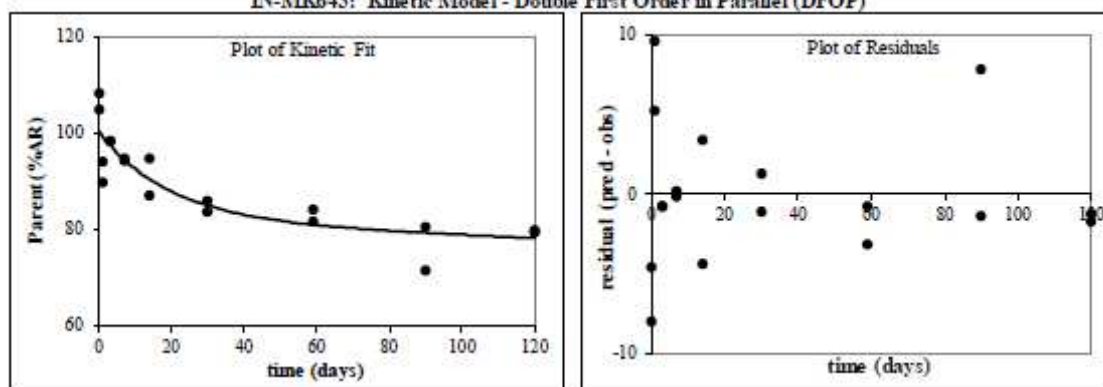
Visual fits and residuals for IN-MK643 in Speyer 2.2 soil



IN-MK643: Kinetic Model - First Order Multi Compartment (FOMC)

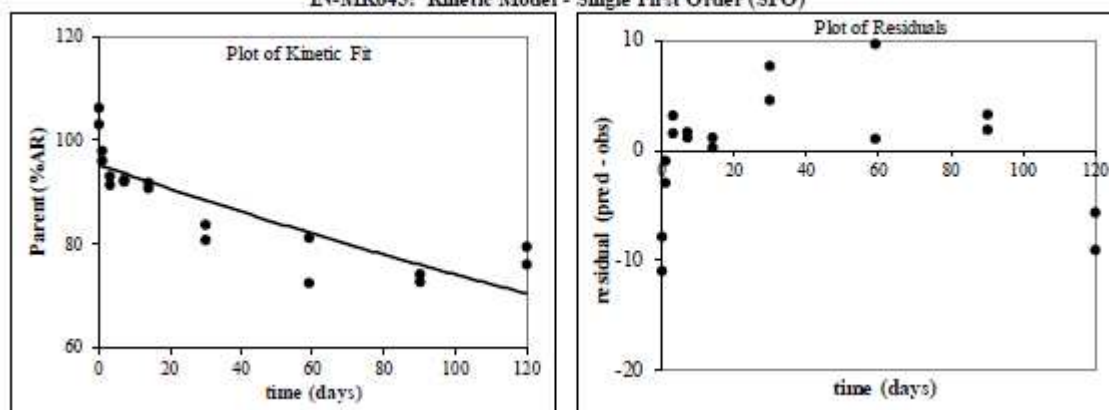


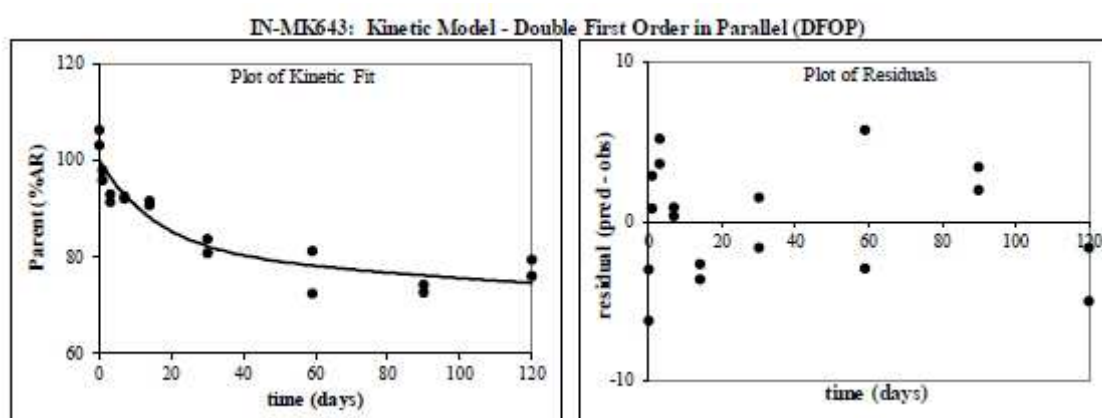
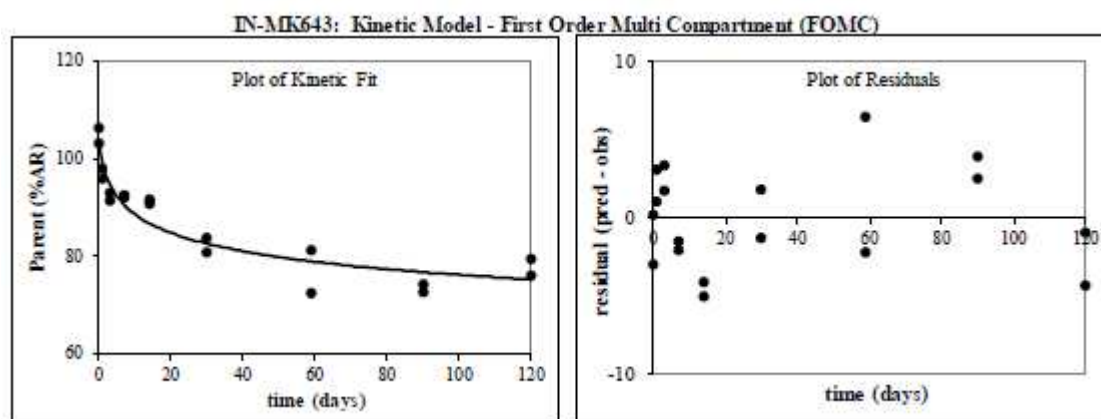
IN-MK643: Kinetic Model - Double First Order in Parallel (DFOP)



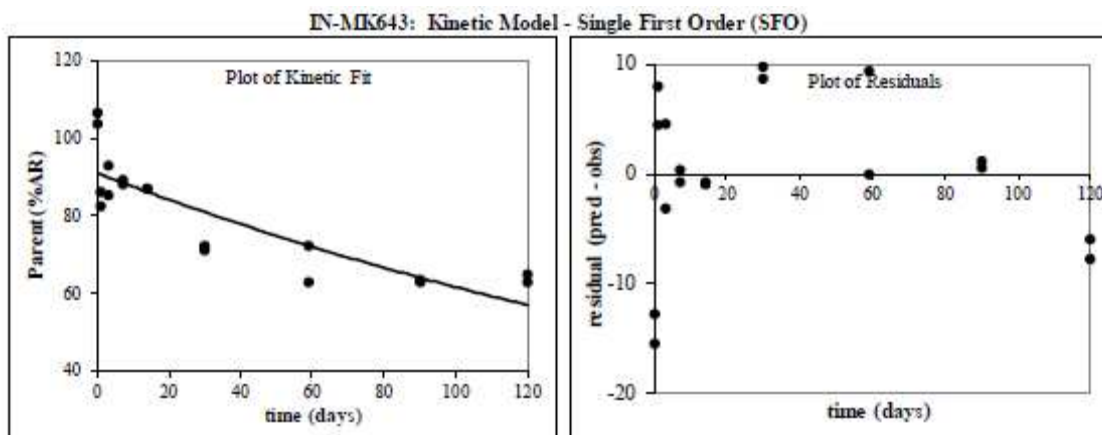
Visual fits and residuals for IN-MK643 in Mattapex soil

IN-MK643: Kinetic Model - Single First Order (SFO)

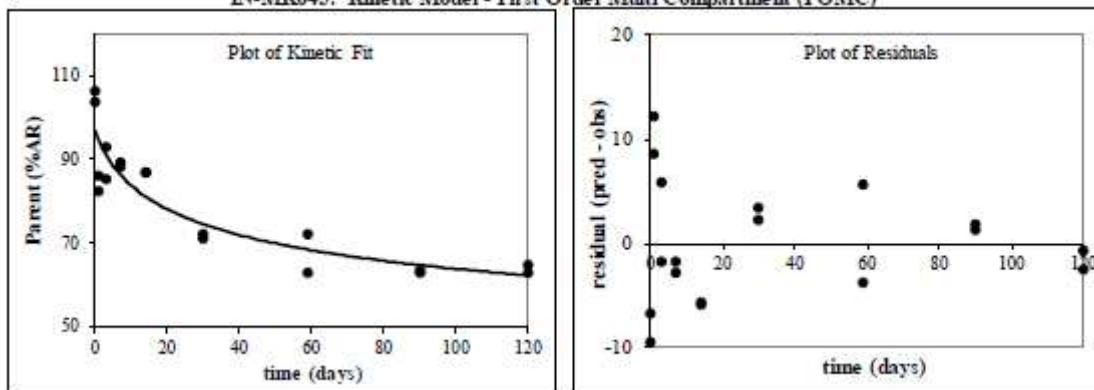




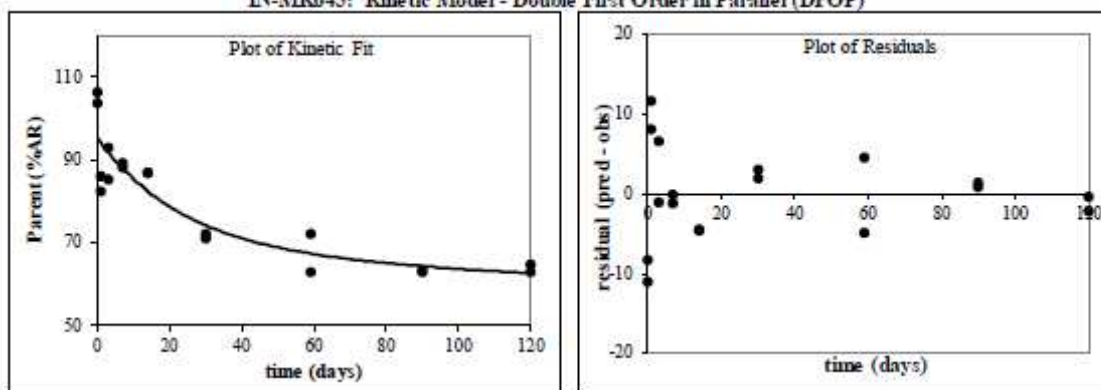
Visual fits and residuals for IN-MK643 in Pesaro soil



IN-MK643: Kinetic Model - First Order Multi Compartment (FOMC)

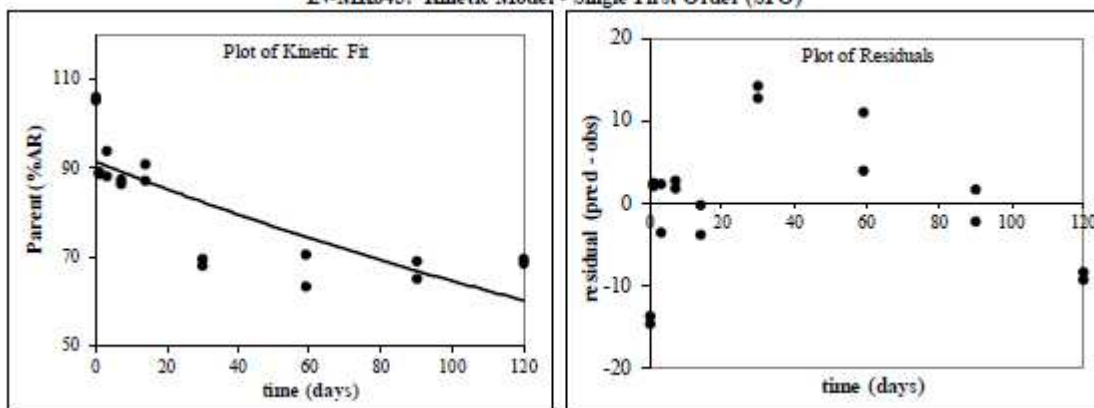


IN-MK643: Kinetic Model - Double First Order in Parallel (DFOP)

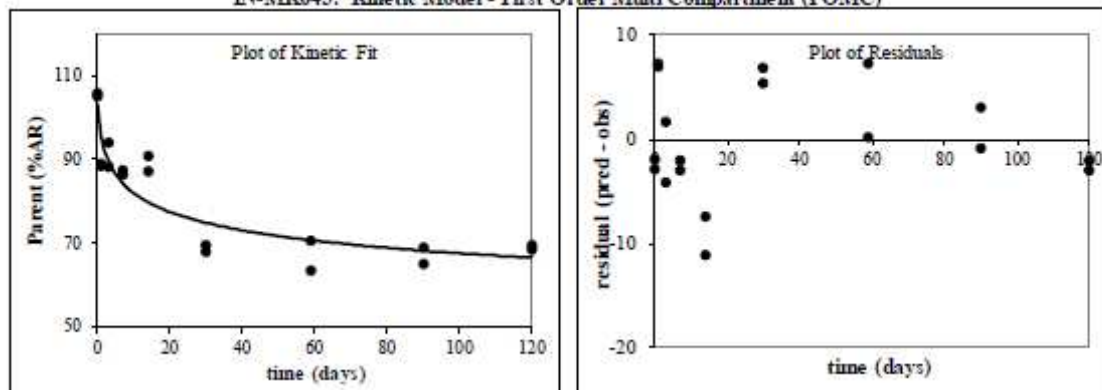


Visual fits and residuals for IN-MK643 in Lleida soil

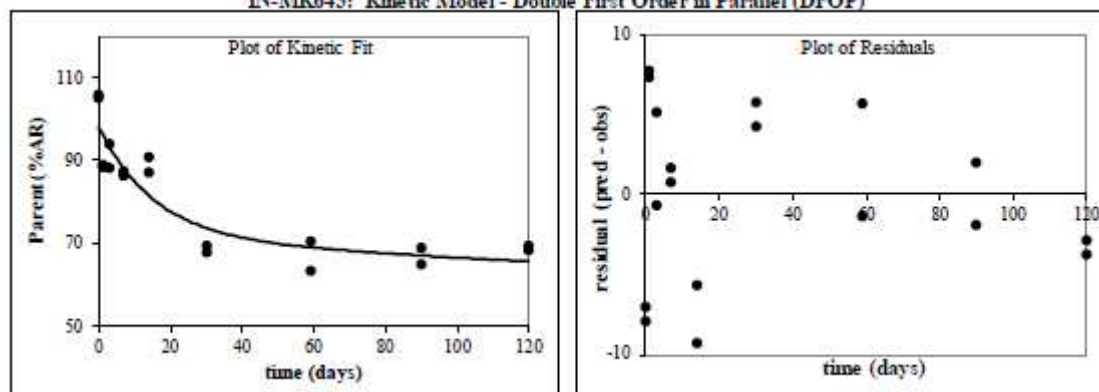
IN-MK643: Kinetic Model - Single First Order (SFO)



IN-MK643: Kinetic Model - First Order Multi Compartment (FOMC)

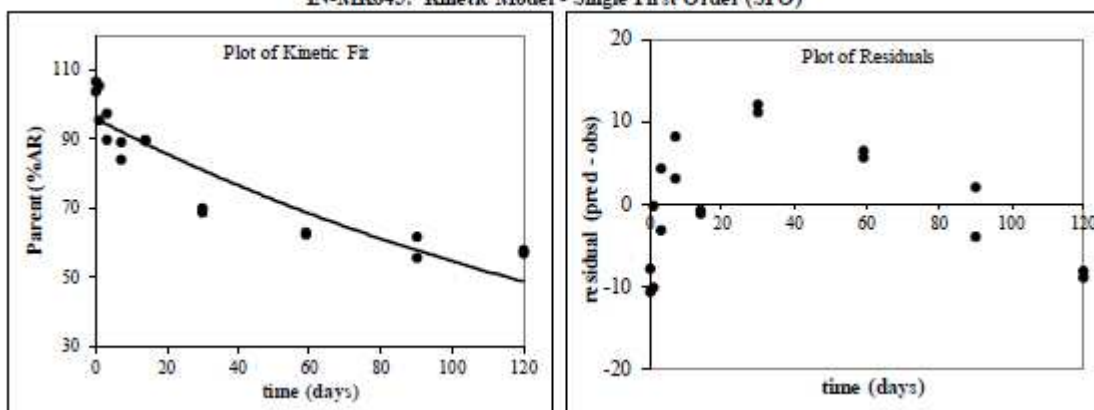


IN-MK643: Kinetic Model - Double First Order in Parallel (DFOP)

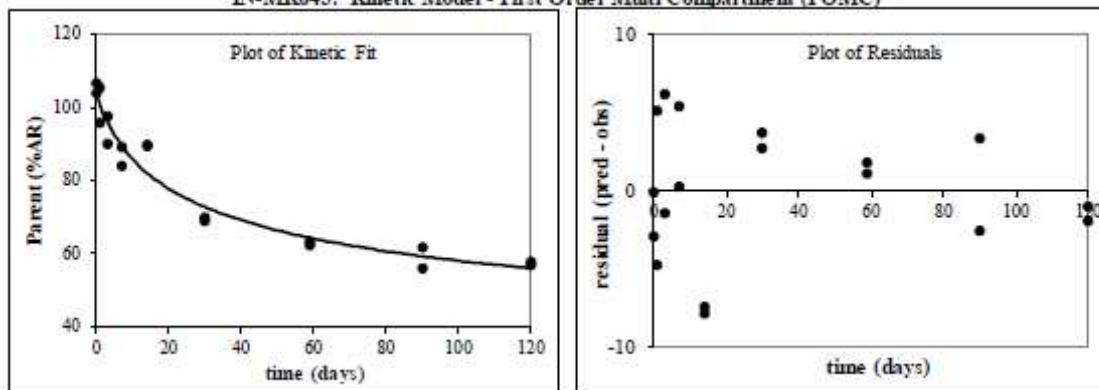


Visual fits and residuals for IN-MK643 in Hidalgo soil

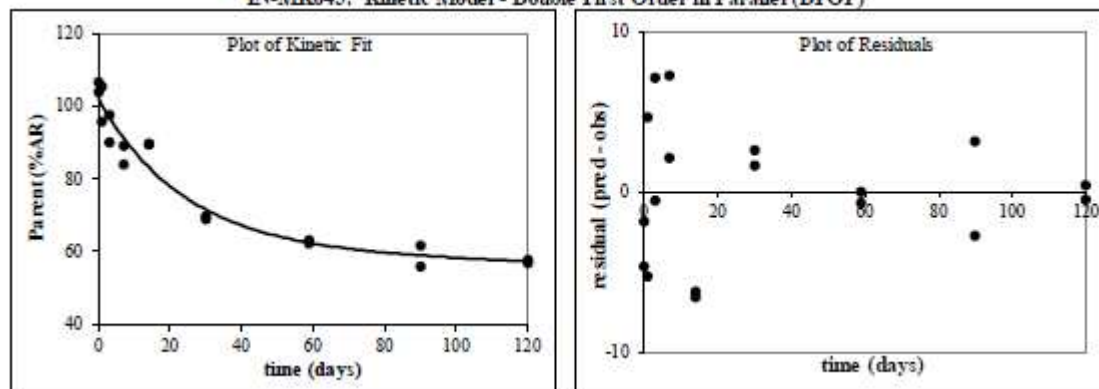
IN-MK643: Kinetic Model - Single First Order (SFO)



IN-MK643; Kinetic Model - First Order Multi Compartment (FOMC)



IN-MK643; Kinetic Model - Double First Order in Parallel (DFOP)

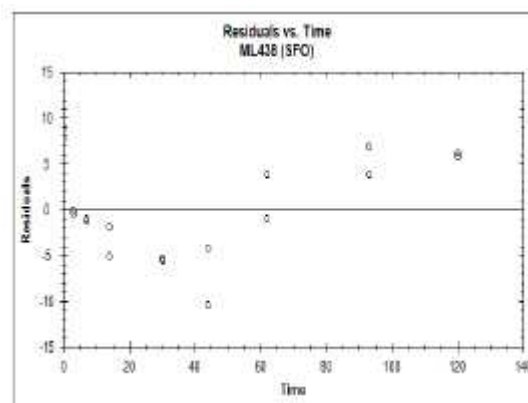
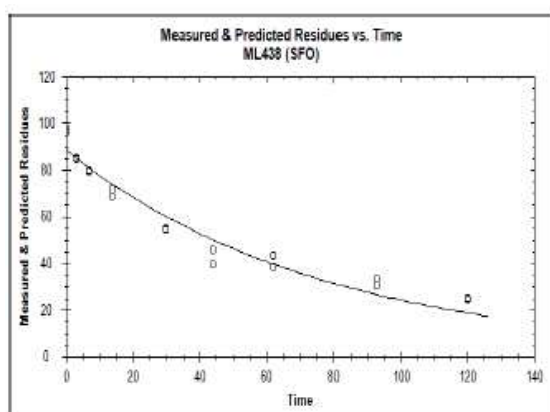


H. Metabolite IN-ML438 (from Allan, 2014)**Gross Umstadt soil****Table 8-84: Summary of kinetics and goodness of fit statistics for IN-ML438 (applied as parent) in Gross Umstadt soil**

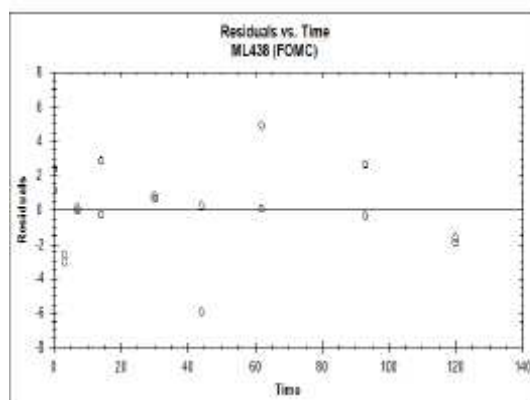
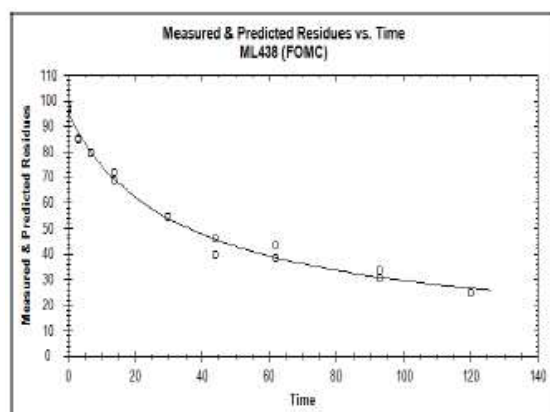
Soil	SFO				FOMC				DFOP				
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	Slow Phase DT ₅₀	χ^2	p (t-test)
Gross Umstadt	53.5	177.8	7.0	<0.05	40.1	556.8	2.7	β no	40.6	258.6	97.4	2.8	p1<0.05; p2<0.05

Persistence trigger: The FOMC model is the best-fit for this soil.

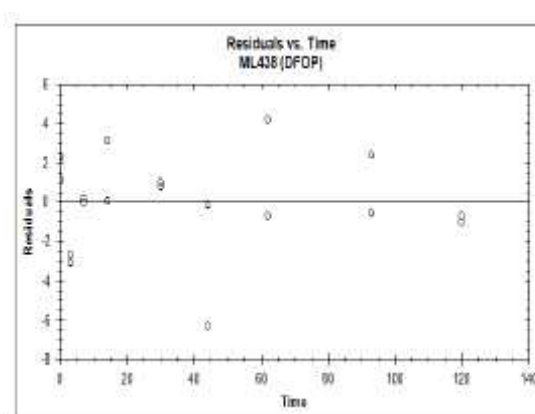
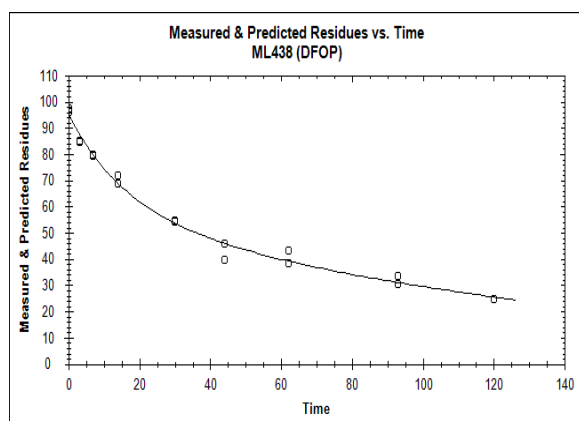
Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as more appropriate for modelling than any other models.

Visual fits and residuals for IN-ML438 in Gross Umstadt soil

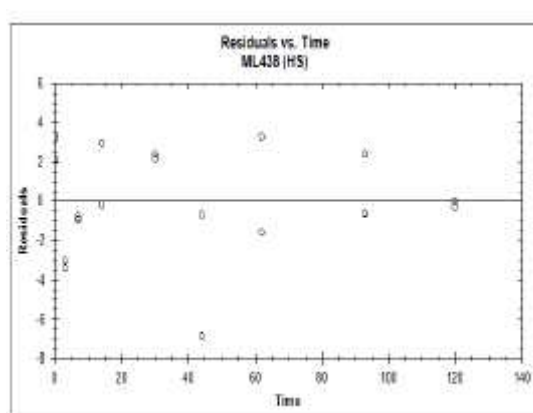
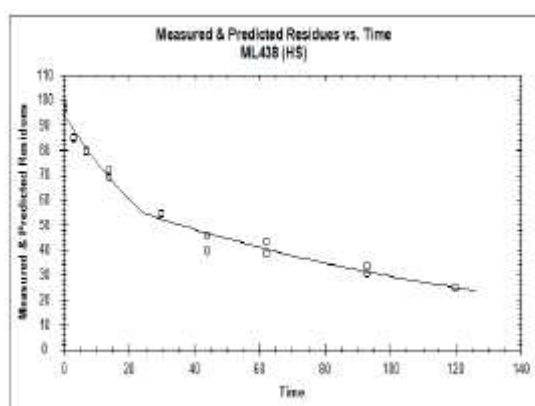
Gross Umstadt - SFO



Gross Umstadt - FOMC



Gross Umstadt - DFOP



Gross Umstadt - HS

Lleida soil

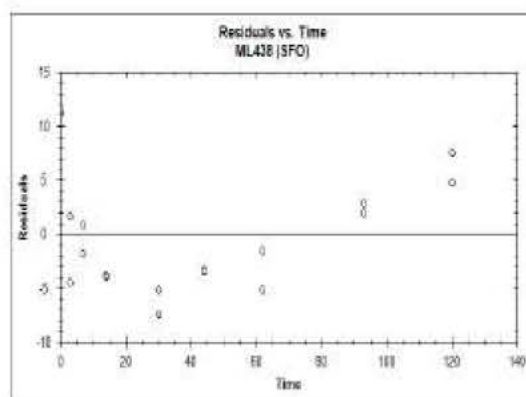
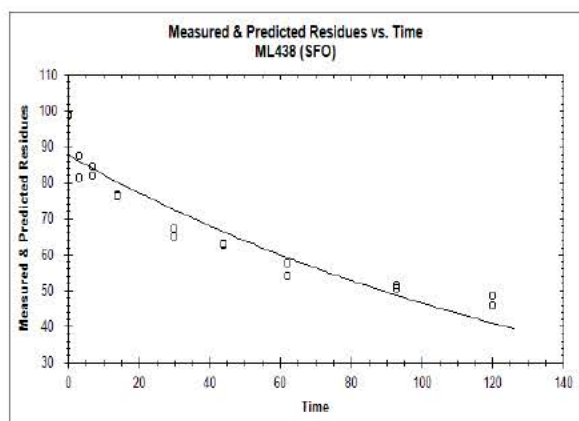
Table 8-85: Summary of kinetics and goodness of fit statistics for IN-ML438 (applied as parent) in Lleida soil

Soil	SFO				FOMC				DFOP				
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	Slow Phase DT ₅₀	χ^2	p (t-test)
Lleida	109.5	363.7	6.1	<0.05	121.8	>1000	2.5	β no	107.1	507.7	172.5	2.6	p1<0.05; p2<0.05

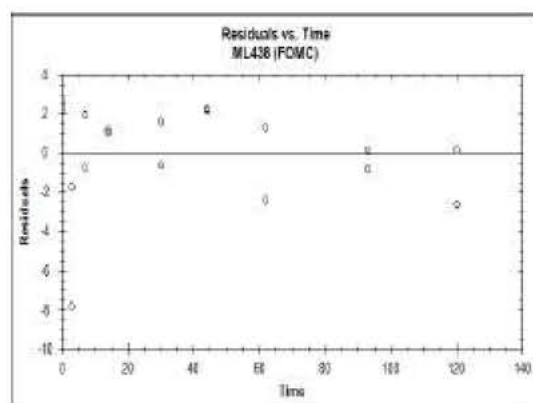
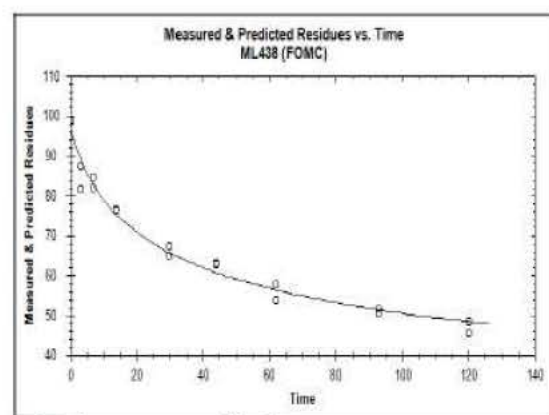
Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as more appropriate for modelling than any other models.

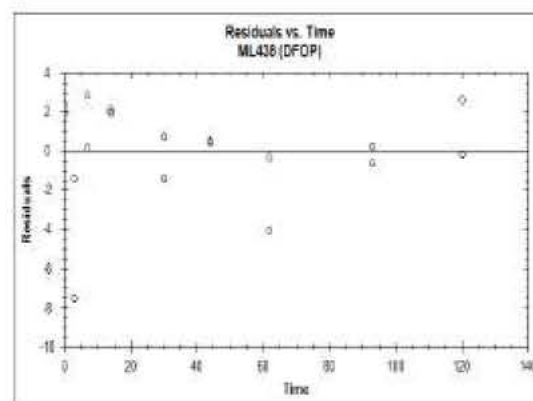
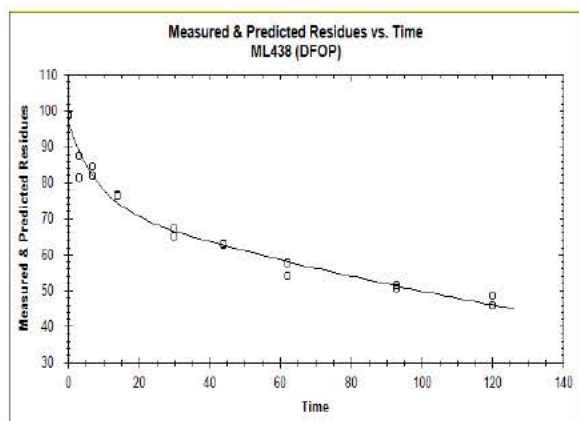
Visual fits and residuals for IN-ML438 in Lleida soil



Lleida - SFO



Lleida - FOMC



Lleida - DFOP

Nambsheim soil

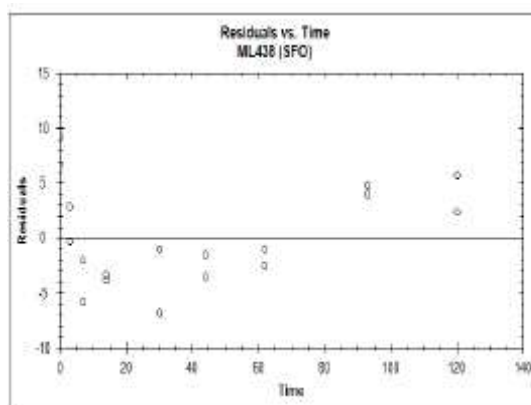
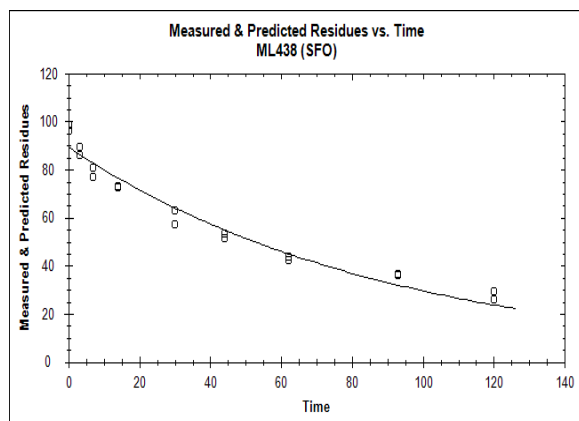
Table 8-86: Summary of kinetics and goodness of fit statistics for IN-ML438 (applied as parent) in Nambsheim soil

Soil	SFO				FOMC				DFOP				
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	Slow Phase DT ₅₀	χ^2	p (t-test)
Nambsheim	62.7	208.2	5.4	<0.05	51.3	682.9	2.6	β no	54.1	241.9	--	1.7	p1<0.05; p2<0.05

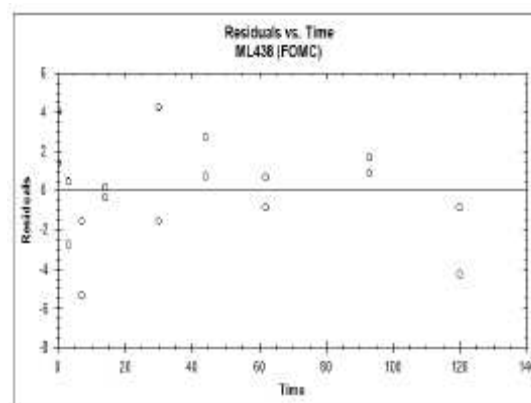
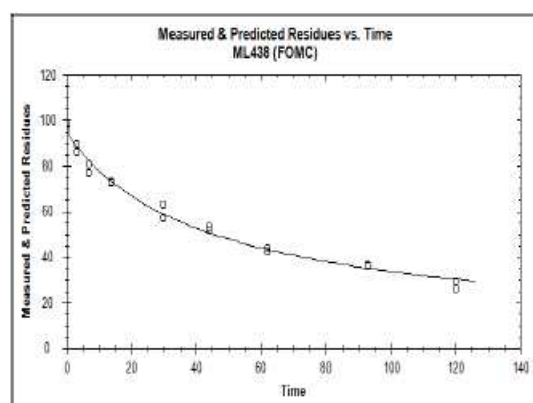
Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as more appropriate for modelling than any other models.

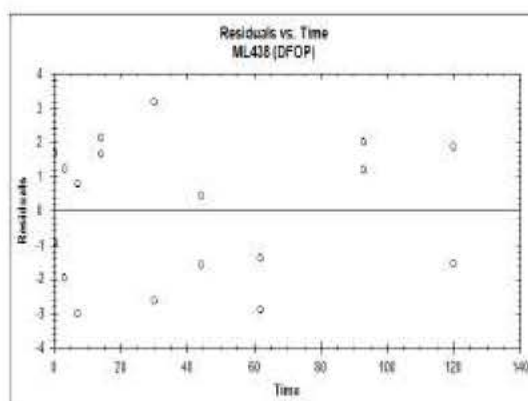
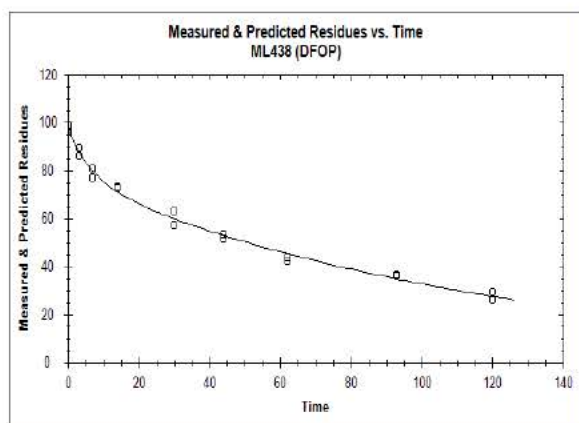
Visual fits and residuals for IN-ML438 in Nambsheim soil



Nambsheim - SFO



Nambsheim - FOMC



Nambasheim – DFOP

Sassafras soil

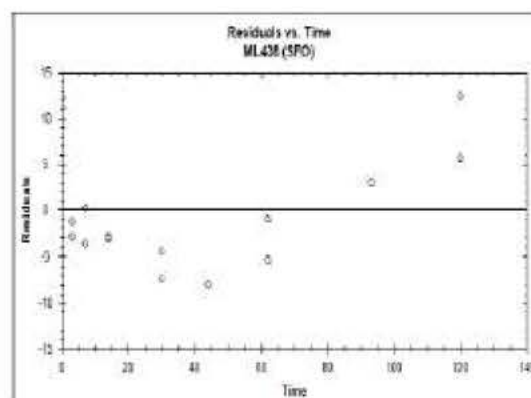
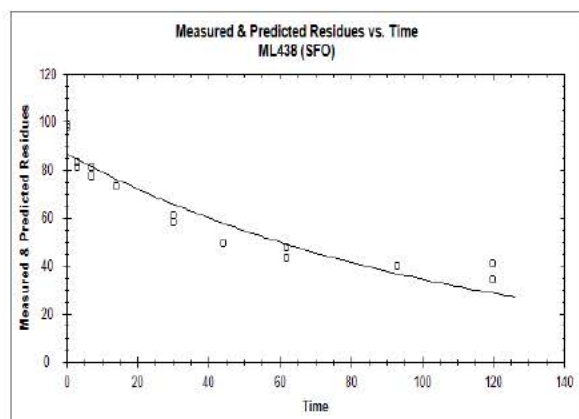
Table 8-87: Summary of kinetics and goodness of fit statistics for IN-ML438 (applied as parent) in Sassafras soil

Soil	SFO				FOMC				DFOP				
	DegT ₅₀	DegT ₉₀	χ^2	P (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	Slow Phase DT ₅₀	χ^2	P (t-test)
Sassafras ^a	74.9	248.9	8.0	<0.05	57.0	>1000	3.3	β no	59.7	486.2	186.5	3.8	p1<0.05; p2<0.05

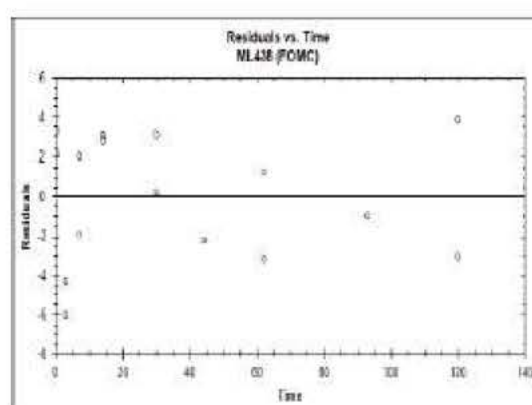
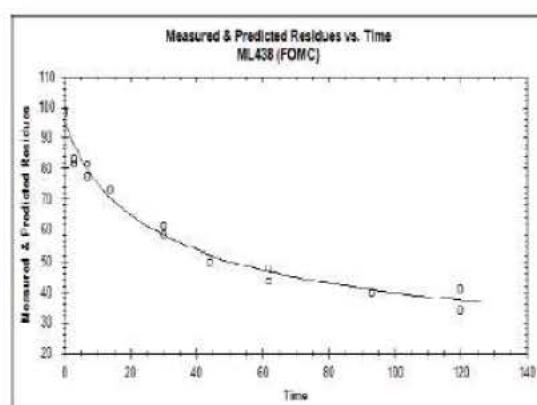
Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as visual and statistic assessment not too bad, and SFO more appropriate for modelling than any other models.

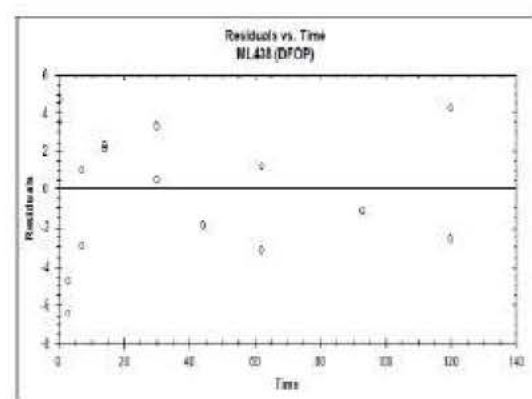
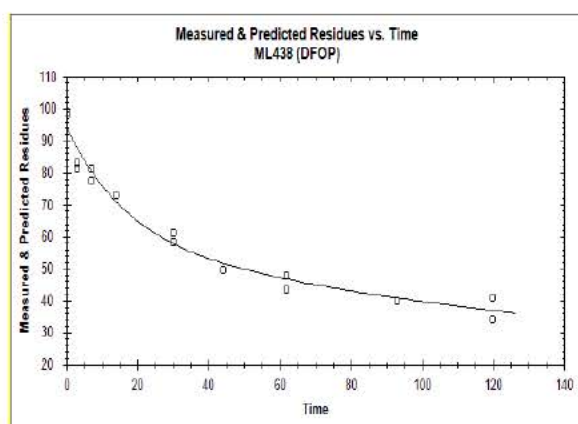
Visual fits and residuals for IN-ML438 in Sassafras soil



Sassafras – SFO



Sassafras – FOMC



Sassafras – DFOP

Tama soil

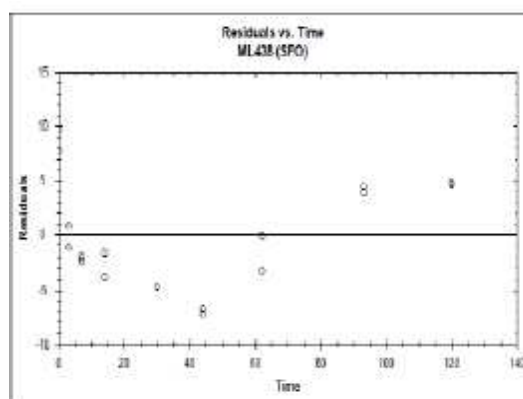
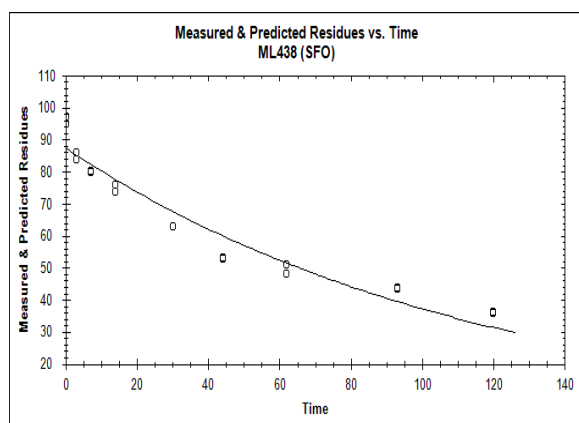
Table 8-88: Summary of kinetics and goodness of fit statistics for IN-ML438 (applied as parent) in Tama soil

Soil	SFO				FOMC				DFOP				
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	Slow Phase DT ₅₀	χ^2	p (t-test)
Tama ^b	81.1	269.3	5.8	<0.05	68.6	>1000	2.5	β no	72.2	384.7	--	2.5	p1<0.05; p2<0.05

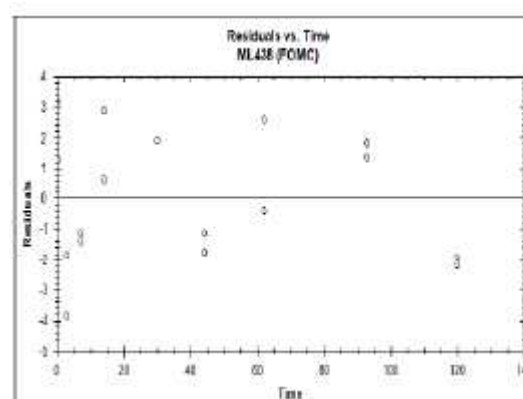
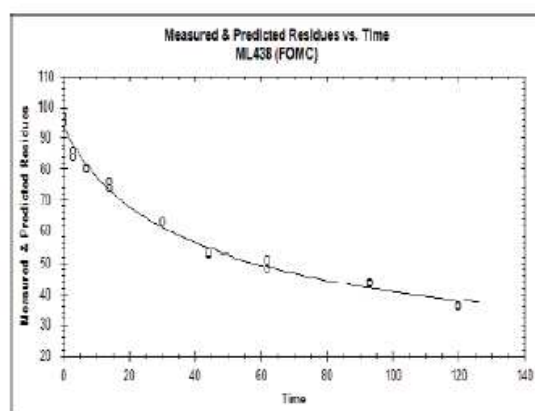
Persistence trigger: The DFOP model is the best-fit for this soil.

Modelling endpoint: The SFO DT₅₀ was retained by RMS for modelling, as visual and statistic assessment not too bad, and SFO more appropriate for modelling than any other models.

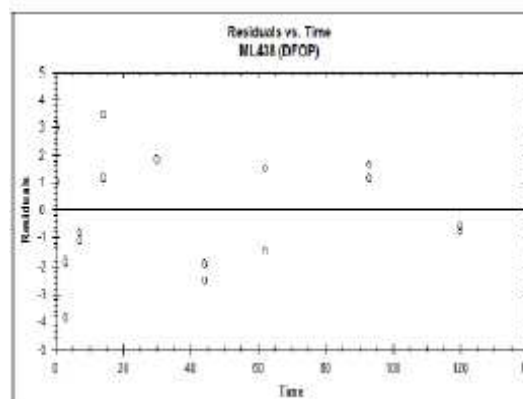
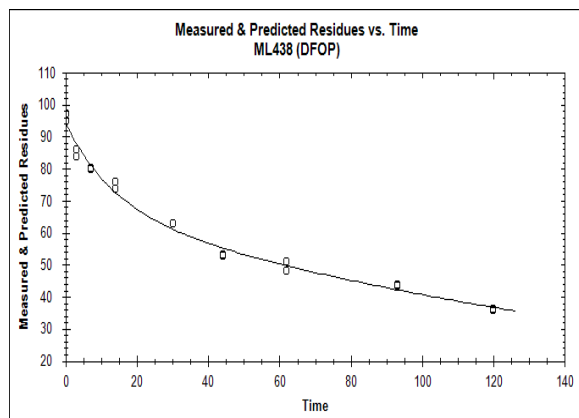
Visual fits and residuals for IN-ML438 in Tama soil



Tama - SFO



Tama - FOMC



Tama - DFOP

RMS (2016)

Applicant provided kinetic fittings following FOCUS Kinetic guidance.

This evaluation showed that indoxacarb and some of its major metabolites degradation are often better described with biphasic kinetic model. The first proposition of applicant was to retain bi-phasic kinetic when it showed better fit than SFO, and to select conservative pseudo-SFO DT_{50} for modelling, based on FOMC $DT_{50}/3.32$ or on the k_2 parameter of DFOP or HS. This was however not fully validated by RMS since it implies that the conservative choice made for one compound may not be conservative for the subsequent metabolite in the degradation scheme.

Given the complexity of the degradation scheme, RMS objectives were to perform a pragmatic modelling endpoint selection to ensure that the proposed degradation scheme is sufficiently conservative for each compound and for risk assessment of its subsequent metabolite.

In this purpose, RMS required that the ffm were set to 1 by default (in light of uncertainties in the fit of metabolite from indoxacarb applied studies) and that the DT₅₀ for metabolites were mostly taken from metabolite applied kinetics and/or fit from peak from parent applied studies, when the fit was acceptable. RMS also required selecting the SFO model as often as possible for metabolites (in accordance with FOCUS kinetics 2006 for modelling), even if the statistical and/or visual assesement did not show that 90% of the degradation was adequately described. This approach was followed by applicant except for the ffm of metabolite IN-JT333: applicant indeed proposed to keep the ffm of 0.24 for IN-JT333 obtained in Tama soil (Indanon label) as maximum peak was well represented in the fit. This was not accepted by RMS since the DT₅₀ for IN-JT333 derived together from this soil was not seen as reliable (SFO DT₅₀ derived together with the Ffm of 0.24 did not passed the χ^2 test and the fit was not visually acceptable due to non-random residuals in the decline phase). Ffm of 1 is retained by RMS for this metabolite as well.

For the active substance, kinetic fits clearly show a bi-phasic pattern, and SFO could not be considered providing a good description of the degradation pattern, for at least 3 soils out of 5. Applicant proposal following FOCUS guidance led to select various kind of kinetics for modelling, leading to an unhomogeneous final endpoint (see table below). RMS opinion is that the DFOP kinetic could have been selected in all soil as being the model also retained as best-fit for trigger persistence endpoints (see table below). The main issue about this solution is that DFOP degradation pattern cannot easily be implemented in GW models for metabolite simulation. Performing simulation with both DT₅₀ calculated from k1 and k2 parameter for metabolite simulation would lead to conduct 10 sets of simulations (5 degradations pathways are necessary to simulate all metabolites). This solution was eventually not seen as more reliable in this specific case.

It is also noted that attempts to fit parent and metabolite data in SFO-SFO models were not conducted by applicant. It is however considered by RMS was this would probably not have led to better parent-metabolite fit, given that the parent clearly does not follow a first-order degradation (in a least 3 out of 5 soils) and that the metabolites data from the original laboratory studies seemed not sufficiently robust to obtain reliable kinetic evaluation (parent/metabolite fit or fit from peak). Choice was made by RMS to select conservative ffm of 1 and DT₅₀ from metabolite dosed studies or from peak from parent studies when possible, to produce a consistent risk assessment for every metabolite.

The final endpoints retained as persistence endpoints, and for modelling for indoxacarb and its metabolites are the following:

INDOXACARB

Persistence endpoints

Table 8-89: Summary of final persistence endpoints selected for INDOXACARB

Soil type	pH ^{a)}	t. °C / % MWHC	DT ₅₀ /DT ₉₀ (d)	DT ₅₀ (d) 20 °C pF2/10kPa ^{b)}	St. (χ^2)	Method of calculat ion
Speyer 2.2 (both labels) – Loamy sand	6.2	20°C / 50% MWHC	2.4/216.9	-	5	FOMC
Tama (both labels) - Silt Loam	6.2	20°C / 75% MWHC	5.4/23.2	-	2	DFOP
Speyer 2.2 (TFMP) - Sandy loam	5.9	20°C / 50-60 % MWHC	10.3/404.7	-	6	DFOP
Nambsheim (TFMP) – Silt loam	7.7	20°C / 50-60 % MWHC	7.0/134.1	-	11	DFOP
Tama (Original) (both labels) – Silt loam	6.3	25°C / 75% pF2.5	3.4 ^c /15.7 ^c	-	12	DFOP
Geometric mean (if not pH dependent)				-		

Modelling endpoints

Table 8-90: Summary of final modelling endpoints selected for INDOXACARB

Soil type	pH	t. °C / % MWHC	DT ₅₀ /DT ₉₀ (d)	Modelling DT ₅₀ (d) 20°C	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Speyer 2.2 (both labels) – Loamy sand	6.2	20°C / 50% MWHC	2.4/216.9	65.3	65.3	5	FOMC (DT ₉₀ /3.32)
Tama (both labels) - Silt Loam	6.2	20°C / 75% MWHC	5.2/24.7	7.44	6.1	4	FOMC (DT ₉₀ /3.32)
Speyer 2.2 (TFMP) - Sandy loam	5.9	20°C / 50-60 % MWHC	10.5/322.9	164.5	164.5	6	HS (Slow phase DT ₅₀)
Nambsheim (TFMP) – Silt loam	7.7	20°C / 50-60 % MWHC	7.0/134.1	120.1	113.2	11	DFOP (Slow phase DT ₅₀)
Tama (Original) (both labels) – Silt loam	6.3	25°C / 75% pF2.5	2.0/11.8 ^f	5.6 ^g	4.6	14	FOMC (DT ₉₀ /3.32)
Geometric mean (if not pH dependent)					32.1		

Metabolite IN-JT333

Persistence endpoints

Table 8-91: Summary of final persistence endpoints selected for IN-JT333

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f /k _{dp}	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Gross Umstadt - Sandy loam	7.1	20°C / 50% MWHC	4.3/37.8	-	72.5	6.9	DFOP (Slow phase k2)
Lleida - Light clay	8.0	20°C / 50% MWHC	9.6/79.2	-	55.9	2.8	DFOP (Slow phase k2)
Nambsheim - Sandy loam	7.7	20°C / 50% MWHC	6.0/43.2	-	99.9	8.2	DFOP (Slow phase k2)
Speyer 2.2 - Sandy loam	5.6	20°C / 50% MWHC	7.9/228.8	-	147.5	4.8	DFOP (Slow phase k2)
Tama - Light clay	6.0	20°C / 50% MWHC	7.0/47.0	-	14.2	5.1	FOMC (DT90/3.32)
Speyer 2.2 (TFMP) – Loamy sand	6.2	20°C / 50% MWHC	11.5/149.2	-	45	13	FOMC (DT ₉₀ /3.32, fit from peak)
Tama (both labels) - Silt Loam	6.2	20°C / 75% MWHC	34.6/168.9	-	50.9	7	FOMC (DT ₉₀ /3.32, fit from peak)
Speyer 2.2 (TFMP) - Sandy loam	5.9	20°C / 50-60 % MWHC	11.3/65.2	-	19.6	9	FOMC (DT ₉₀ /3.32, fit from peak)
Nambsheim (TFMP) – Silt loam	7.7	20°C / 50-60 % MWHC	26.5/88.1	-	26.5	11	SFO(fit from peak)
Persistence endpoint					147.5		

Modelling endpoints

Table 8-92: Summary of final modelling endpoints selected for IN-JT333

Soil type	pH ^{a)}	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f /k _{dp}	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Gross Umstadt - Sandy loam	7.1	20°C / 50% MWHC	5.0/16.7	-	5.0	17.4	SFO
Lleida - Light clay	8.0	20°C / 50% MWHC	12.3/40.7	-	10.8	11.4	SFO
Nambsheim - Sandy loam	7.7	20°C / 50% MWHC	6.9/22.9	-	6.9	14.6	SFO
Speyer 2.2 - Sandy loam	5.6	20°C / 50% MWHC	6.2/57.2	-	111.0	4.1	HS (Slow phase DT ₅₀)
Tama - Light clay	6.0	20°C / 50% MWHC	9.7/32.3	-	9.7	12.2	SFO
Speyer 2.2 (TFMP) – Loamy sand	6.2	20°C / 50% MWHC	19.8/65.6	-	19.8	25	SFO
Tama (both labels) - Silt Loam	6.2	20°C / 75% MWHC	40.6/134.7	-	33.2	9	SFO (fit from peak)
Speyer 2.2 (TFMP) - Sandy loam	5.9	20°C / 50-60 % MWHC	12.4/41.3	-	12.4	11.3	SFO (fit from peak)
Nambsheim (TFMP) – Silt loam	7.7	20°C / 50-60 % MWHC	26.5/88.1	-	25.0	11	SFO (fit from peak)
Geometric mean (if not pH dependent)					16.3		
Arithmetic mean				1			

Metabolite IN-KT413

Persistence endpoints

Table 8-93: Summary of final persistence endpoints selected for IN-KT413

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f /k _{dp}	DT ₅₀ (d) 20 °C	St. (χ^2)	Method of calculation
Hidalgo – Sandy clay loam	8.1	20°C / 50% MWHC	4.0/20.5	-	10.4	1	DFOP (slow phase DT ₅₀)
Lleida – Clay loam	8.1	20°C / 50% MWHC	1.9/10.4	-	3.1	4	FOMC (DT ₉₀ /3.32)
Mattapex - Silt loam	6.7	20°C / 50% MWHC	0.6/2.6	-	0.8	3	FOMC (DT ₉₀ /3.32)
Persistence endpoint					10.4		

Modelling endpoints

Table 8-94: Summary of final modelling endpoints selected for IN-KT413

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f /k _{dp}	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Hidalgo – Sandy clay loam	8.1	20°C / 50% MWHC	4.6/15.3	-	3.7	6	SFO
Lleida – Clay loam	8.1	20°C / 50% MWHC	2.3/7.6	-	2.2	9	SFO
Mattapex - Silt loam	6.7	20°C / 50% MWHC	0.7/2.3	-	0.6	8	SFO
Geometric mean (if not pH dependent)					1.7		
Arithmetic mean				-			

Metabolite IN-KG433

Persistence endpoints

Table 8-95: Summary of final persistence endpoints selected for IN-KG433

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f /k _{dp}	DT ₅₀ (d) 20 °C	St. (χ^2)	Method of calculation
Speyer 2.2 – Loamy sand	6.2	20°C / 50% MWHC	1.9/57.8	-	17.4	5	FOMC (DT ₉₀ /3.32)
Mattapex – Silt loam	6.2	20°C / 50% MWHC	1.6/14.0	-		6	DFOP
Pesaro – Silty clay loam	8.5	20°C / 50% MWHC	2.5/13.1	-	3.95	8	FOMC (DT ₉₀ /3.32)
Lleida – Clay loam	8.2	20°C / 50% MWHC	1.7/13.1	-	3.95	2	FOMC (DT ₉₀ /3.32)
Hidalgo – Sandy clay loam	8.4	20°C / 50% MWHC	1.9/13.8	-	4.15	14	FOMC (DT ₉₀ /3.32)
Persistence endpoint					17.4		

Modelling endpoints

Table 8-96: Summary of final modelling endpoints selected for IN-KG433

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f / k _{dp}	Moisture correction factor	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Speyer 2.2 – Loamy sand	6.2	20°C / 50% MWHC	1.9/57.8	-	1	17.4	5	FOMC (DT ₉₀ /3.32)
Mattapex – Silt loam	6.2	20°C / 50% MWHC	1.6/10.4	-	0.86	2.7	8	FOMC (DT ₉₀ /3.32)
Pesaro – Silty clay loam	8.5	20°C / 50% MWHC	2.5/13.1	-	0.99	2.9	9	SFO
Lleida – Clay loam	8.2	20°C / 50% MWHC	1.7/13.1	-	0.98	3.8	2	FOMC (DT ₉₀ /3.32)
Hidalgo – Sandy clay loam	8.4	20°C / 50% MWHC	1.9/13.8	-	1	2.6	17	SFO
Geometric mean (if not pH dependent)						4.2		
Arithmetic mean				-				

Metabolite IN-JU873

Persistence endpoints

Table 8-97: Summary of final persistence endpoints selected for IN-JU873

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f / k _{dp}	DT ₅₀ (d) 20 °C	St. (χ^2)	Method of calculation
Speyer 2.2 – Loamy sand	6.2	20°C / 50% MWHC	32.8/186.1		66.1	4	DFOP (slow phase DT ₅₀)
Mattapex – Silt loam	6.2	20°C / 50% MWHC	19.0/242.5		103.5	5	DFOP (slow phase DT ₅₀)
Pesaro – Silty clay loam	8.5	20°C / 50% MWHC	10.0/66.4		24.8	4	DFOP (slow phase DT ₅₀)
Lleida – Clay loam	8.2	20°C / 50% MWHC	13.8/136.6		65.4	6	DFOP (slow phase DT ₅₀)
Hidalgo – Sandy clay loam	8.4	20°C / 50% MWHC	18.1/212.5		88.9	8	DFOP (slow phase DT ₅₀)
Persistence endpoint					103.5		

Modelling endpoints

Table 8-98: Summary of final modelling endpoints selected for IN-JU873

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f / k _{dp}	Moisture correction factor	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Speyer 2.2 – Loamy sand	6.2	20°C / 50% MWHC	47.2/156.8	-	1	47.2	10	SFO
Mattapex – Silt loam	6.2	20°C / 50% MWHC	42.4/140.9	-	0.86	36.7	14	SFO
Pesaro – Silty clay loam	8.5	20°C / 50% MWHC	15.7/52.2	-	0.99	15.6	13	SFO
Lleida – Clay loam	8.2	20°C / 50% MWHC	32.2/107.0	-	0.98	31.5	16	SFO
Hidalgo – Sandy clay loam	8.4	20°C / 50% MWHC	40.3/134.0	-	1	40.3	15	SFO
Geometric mean (if not pH dependent)						32.1		
Arithmetic mean				-				

Metabolite IN-KB687

Persistence endpoints

Table 8-99: Summary of final persistence endpoints selected for IN-KB687

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f /k _{dp}	DT ₅₀ (d) 20 °C	St. (χ^2)	Method of calculation
Sassafras - Loam	5.5	20°C / 50% MWHC	0.67/2.21	-	0.67	2	SFO
Tama – Silty clay loam	6.3	20°C / 50% MWHC	0.56/1.85	-	0.56	9	SFO
Persistence endpoint					0.67		

Modelling endpoints

Table 8-100: Summary of final modelling endpoints selected for IN-KB-687

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f / k _{dp}	Moisture correction factor	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Sassafras - Loam	5.5	20°C / 50% MWHC	0.67/2.21	-	1	0.67	2	SFO
Tama – Silty clay loam	6.3	20°C / 50% MWHC	0.56/1.85	-	0.91	0.51	9	SFO
Worst-case value						0.67		
Arithmetic mean				-				

Metabolite IN-ML438Persistence endpoints**Table 8-101: Summary of final persistence endpoints selected for IN-ML438**

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f / k _{dp}	DT ₅₀ (d) 20 °C	St. (χ^2)	Method of calculation
Gross Umstadt - Sandy loam	6.9	20°C / 50% MWHC	40.6/258.6		97.4		DFOP (slow phase DT ₅₀)
Lleida - Light clay	7.9	20°C / 50% MWHC	107.1/507.7		172.8		DFOP (slow phase DT ₅₀)
Nambsheim - Sandy loam	7.6	20°C / 50% MWHC	54.11/241.9		80.9		DFOP (slow phase DT ₅₀)
Sassafras – Sandy loam	6.0	20°C / 50% MWHC	59.73/586.2		186.5		DFOP (slow phase DT ₅₀)
Tama - Light clay	6.1	20°C / 50% MWHC	72.2/384.7		134.8		DFOP (slow phase DT ₅₀)
Tama (Original) (both labels) – Silt loam	6.3	25°C / 75% pF2.5	24.3 ^{u)} /315.5 ^{u)}		144.6 ^{u)}		DFOP, fit from peak (slow phase DT ₅₀)
Persistence endpoint					186.5		

Modelling endpoints**Table 8-102: Summary of final modelling endpoints selected for IN-ML438**

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f / k _{dp}	Moisture correction factor	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Gross Umstadt - Sandy loam	6.9	20°C / 50% MWHC	53.5/177.8	-	1	53.5	7.0	SFO
Lleida - Light clay	7.9	20°C / 50% MWHC	109.5/363.7	-	0.78	65.8	6.1	SFO
Nambsheim - Sandy loam	7.6	20°C / 50% MWHC	62.8/208.2	-	1	62.7	5.4	SFO
Sassafras – Sandy loam	6.0	20°C / 50% MWHC	74.9/248.9	-	1	74.9	8.0	SFO
Tama - Light clay	6.1	20°C / 50% MWHC	81.0/269.3	-	1	81.1	5.8	SFO
Tama (Original) (Indanon) – Silt loam	6.3	25°C / 75% pF2.5	24.3 ^{x)} /315.5 ^{x)}	-	0.8293	119.9	6	DFOP, fit from peak (slow phase DT ₅₀)
Geometric mean (if not pH dependent)						73.7		
Arithmetic mean				-				

Metabolite IN-MK643**Persistence endpoints****Table 8-103: Summary of final persistence endpoints selected for IN-MK643**

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f /k _{dp}	DT ₅₀ (d) 20 °C	St. (χ^2)	Method of calculation
Speyer 2.2 – Sand	6.3	20°C / 50% MWHC	314.2/1043.8	-	314.2	4	SFO
Mattapex –Loam	6.1	20°C / 50% MWHC	275.5/915.2	-	275.5	5	SFO
Pesaro – Clay loam	8.2	20°C / 50% MWHC	177.8/590.8	-	177.8	7	SFO
Lleida – Clay loam	8.0	20°C / 50% MWHC	199.4/662.3	-	199.4	8	SFO
Hidalgo – Sandy clay loam	8.1	20°C / 50% MWHC	123.3/490.6	-	123.3	7	SFO
Persistence endpoint					314.2		

Modelling endpoints**Table 8-104: Summary of final modelling endpoints selected for IN-MK643**

Soil type	pH ^{a)}	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f / k _{dp}	Moisture correction factor	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Speyer 2.2 – Sand	6.3	20°C / 50% MWHC	314.2/1043.8	-	1	314.2	4	SFO
Mattapex – Loam	6.1	20°C / 50% MWHC	275.5/915.2	-	0.73	201.1	5	SFO
Pesaro – Clay loam	8.2	20°C / 50% MWHC	177.8/590.8	-	0.84	149.0	7	SFO
Lleida – Clay loam	8.0	20°C / 50% MWHC	199.4/662.3	-	0.84	167.7	8	SFO
Hidalgo – Sandy clay loam	8.1	20°C / 50% MWHC	123.3/490.6	-	0.72	88.7	7	SFO
Geometric mean (if not pH dependent)						169.5		
Arithmetic mean				-				

Metabolite IN-MK638**Persistence endpoints****Table 8-105: Summary of final persistence endpoints selected for IN-MK638**

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f /k _{dp}	DT ₅₀ (d) 20 °C	St. (χ^2)	Method of calculation
Speyer 2.2 – Sand	6.3	20°C / 50% MWHC	15.4/51.0	-	15.4	4	SFO
Mattapex –Loam	6.1	20°C / 50% MWHC	17.3/57.5	-	17.3	5	SFO
Pesaro – Clay loam	8.2	20°C / 50% MWHC	4.8/16.1	-	4.8	7	SFO
Lleida – Clay loam	8.0	20°C / 50% MWHC	5.9/19.7	-	5.9	8	SFO
Hidalgo – Sandy clay loam	8.1	20°C / 50% MWHC	10.7/57.5	-	10.7	7	SFO
Persistence endpoint					17.3		

Modelling endpoints

Table 8-106: Summary of final modelling endpoints selected for IN-MK638

Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _f / k _{dp}	Moisture correction factor	DT ₅₀ (d) 20 °C pF2/10kPa	St. (χ^2)	Method of calculation
Speyer 2.2 – Loamy sand	6.3	20°C / 50% MWHC	15.4/51.0	-	1	15.4	4	SFO
Mattapex – Loam	6.2	20°C / 50% MWHC	17.3/57.5	-	0.92	16.0	5	SFO
Pesaro – Silty clay loam	8.1	20°C / 50% MWHC	4.8/16.1	-	0.84	4.0	7	SFO
Lleida – Clay loam	8.0	20°C / 50% MWHC	5.6/21.9	-	0.94	5.6	8	SFO
Hidalgo – Sandy clay loam	8.4	20°C / 50% MWHC	10.7/57.5	-	0.82	8.8	7	SFO
Geometric mean (if not pH dependent)						8.7		
Arithmetic mean				-				

B.8.1.1.2.2. Field studies**B.8.1.1.2.2.1. Soil dissipation studies**

The following studies were summarised in Indoxacarb DAR, Volume 3, B8, AD3, 2005. They are superseded by new studies submitted for the purpose of renewal (DuPont-34323, DuPont-34324, DuPont-34326 and DuPont-34892, summarized after.

Author(s)	Ruhl, J.C. (1997);
Title:	Field soil dissipation of [¹⁴ C]DPX-JW062 (racemic mixture of DPX-KN128 and IN-KN127) following application of DPX-JW062 experimental insecticide
Organisation:	
Document No:	AMR 3400-95, Revision No. 1

Author(s)	Smyser, B.P. (2002);
Title:	Field soil dissipation of [¹⁴ C]DPX-JW062 (racemic mixture of DPX-KN128 and IN-KN127) following application of DPX-JW062 experimental insecticide
Organisation:	
Document No:	AMR 3400-95, Revision No. 1, Supplement No. 2
Dates of experimental work	
Guidelines:	U.S. EPA 164-1
Deviations :	
GLP:	
Previous evaluation:	Yes
Acceptability:	Study superseded by 4 new studies (DuPont-34323, DuPont-34324, DuPont-34326 and DuPont-34892)

- Test material: ¹⁴C-DPX-JW062 30SE, ¹⁴C-DPX-JW062 60WG
 Lot/Batch #: [Indanone-1-¹⁴C]DPX-JW062 30SE, 3048-144,
 [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-JW062 30SE, 2995-250,
 [Indanone-1-¹⁴C]DPX-JW062 60WG, 23-25 OCT 95,
 [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-JW062 60WG, 21-28 DEC 95
 Purity: 35% DPX-JW062 (3048-144 and 2995-250);
 60% DPX-JW062 (23-25 OCT 95 and 21-28 DEC 95)

The field soil dissipation study AMR 3400-95, Revision No. 1, and AMR 3400-95, Revision No. 1, Supplement No. 2, originally submitted under EU Rev8 Point IIA 7.1.1.2.2 and conducted with test materials ¹⁴C-DPX-JW062 30 g/L SE, ¹⁴C-DPX-JW062 60WG, was conducted under guideline U.S. EPA 164-1.

A review of this study indicates that it partially meets the current guideline (OPPTS 835.6100, SETAC Europe (1995), SANCO/3029/99 rev. 4 (2000), EU 1607/VI/97 Rev 1 (1997), EU 7029/VI/1995 Rev 5 (1997)); deviation includes that some soil major metabolites (such as IN-KT413, IN-JU873, IN-KB687, IN-MK638, and IN-MK643) were not monitored due to analytical method limitation (LOQ of 7 µg/kg was used in old studies and LOQ of 1 µg/kg was used for new studies).

The results of rapid degradation and low leaching potential for indoxacarb from old studies are consistent with the new studies. AMR 3400-95, Revision No. 1 and Supplement No. 2 are considered supplemental and not relied upon, since the new studies (DuPont-34323, DuPont-34324, DuPont-34326 and DuPont-34892) adequately complete the understanding of soil dissipation and are relied upon for this submission.

Author(s)	Vincent, D.R., McCooley, K.T., Ruhl, J.C. (1997);
Title:	Field soil dissipation of DPX-JW062 (racemic mixture of DPX-KN128 [insecticidally active enantiomer] and IN-KN127) following application of DPX-JW062 experimental insecticide to bare ground
Organisation:	
Document No:	AMR 3402-95

Author(s)	Bonino, B., Ruhl, J.C., Smyser, B.P. (1997);
Title:	Field soil dissipation of DPX-JW062 (racemic mixture of DPX-KN128 [insecticidally active enantiomer] and IN-KN127) following application of DPX-JW062 experimental insecticide to bare ground

Author(s)	Smyser, B.P. (2002);
Title:	Field soil dissipation of DPX-JW062 (racemic mixture of DPX-KN128 [insecticidally active enantiomer] and IN-KN127) following application of DPX-JW062 experimental insecticide to bare ground
Organisation:	
Document No:	AMR 3402-95, Supplement No. 3
Dates of experimental work	
Guidelines:	U.S. EPA 164-1
Deviations :	
GLP:	
Previous evaluation:	Yes
Acceptability:	Study superseded by 4 new studies (DuPont-34323, DuPont-34324, DuPont-34326 and DuPont-34892)

- Test material: DPX-JW062 60WG
Lot/Batch #: JW062-135, JW062-91
Purity: 60% DPX-JW062

The field soil dissipation study AMR 3402-95, AMR 3402-95, Supplement No. 1 and AMR 3402-95, Supplement No. 3, conducted with test material DPX-JW062 60WG, was conducted under guideline U.S. EPA 164-1.

A review of this study indicates that it partially meets the current guideline (OPPTS 835.6100, SETAC Europe (1995), SANCO/3029/99 rev. 4 (2000), EU 1607/VI/97 Rev 1 (1997), EU 7029/VI/1995 Rev 5 (1997)); deviation includes that some soil major metabolites (such as IN-KT413, IN_JU873, IN-KB687, IN-MK638, and IN-MK643) were not monitored due to analytical method limitation (LOQ of 10 µg/kg was used in old studies and LOQ of 1 µg/kg was used for new studies). The results of rapid degradation and low leaching potential for indoxacarb from old studies are consistent with the new studies. AMR 3402-95 Supplement No. 3 is considered supplemental and not relied upon, since the new studies (DuPont-34323, DuPont-34324, DuPont-34326 and DuPont-34892) adequately complete the understanding of soil dissipation and are relied upon for this submission.

Author(s)	Zietz, E., Ruhl, J.C. (1999);
Title:	Field soil dissipation of DPX-KN128 together with IN-KN127 at European sites treated with DPX-MP062 WG season 1997-1998
Organisation:	
Document No:	AMR 4394-97, Revision No. 1
Dates of experimental work	
Guidelines:	SETAC Europe (1995)
Deviations :	
GLP:	
Previous evaluation:	Yes
Acceptability:	Study superseded by 4 new studies (DuPont-34323, DuPont-34324, DuPont-34326 and DuPont-34892)

1. Test material: DPX-MP062 30WG
Lot/Batch #: MP062-124
Purity: 300 g a.s./kg

The soil dissipation study AMR 4394-97, Revision No. 1, conducted with test material DPX-MP062 30WG, was conducted under guideline SETAC Europe (1995).

A review of this study indicates that it partially meets the current guidelines (OPPTS 835.6100, SETAC Europe (1995), SANCO/3029/99 rev. 4 (2000), EU 1607/VI/97 Rev 1 (1997), EU 7029/VI/1995 Rev 5 (1997)); deviation includes that some soil major metabolites (such as IN-KT413, IN-JU873, IN-KB687, IN-MK638, and IN-MK643) were not monitored due to analytical method limitation (LOQ of 10 µg/kg was used in old studies and LOQ of 1 µg/kg was used for new studies). The results of rapid degradation and low leaching potential for indoxacarb from old studies are consistent with the new studies. AMR 4394-97, Revision No. 1 is considered supplemental and not relied upon, since the new studies (DuPont-34323, DuPont-34324, DuPont-34326 and DuPont-34892) adequately complete the understanding of soil dissipation and are relied upon for this submission.

The following four studies were submitted to the EU for the first time for the purpose of renewal.

Data point:	CA 7.1.2.2.1/04
Author(s)	Doig, A. (2015d);
Title:	The field soil dissipation of indoxacarb (DPX-KN128) following a single application to bare ground - north France - 2012
Organisation:	Charles River Laboratories (UK), Tranent, Scotland, UK
Document No:	DuPont-34323
Dates of experimental work	18 April 2012 - 12 August 2014
Guidelines:	OPPTS 835.6100, SETAC Europe (1995), SANCO/3029/99 rev. 4 (2000), EU 1607/VI/97 Rev 1 (1997), EU 7029/VI/1995 Rev 5 (1997)
Deviations :	None
GLP:	Yes
Previous evaluation:	No
Acceptability:	The study is considered valid.

This report describes the soil dissipation of a single application of indoxacarb (DPX-KN128) to bare ground studied under field conditions in Douai, North France, for *ca.* 5 months after application on 14-May-2012.

The study design consisted of three replicate treated bare soil plots and a control (untreated) bare soil plot. The test site soil was characterised as silt loam in horizons 0–5, 5–15, 15–30, 30–50, 50–70, and 70–90 cm. The test item was applied at a nominal rate of 400 g a.s./ha, which was the highest proposed use rate for indoxacarb per year. Actual application based on the amount of spray solution applied and the output from calibrated spray equipment used indicated application at 98.2–100.7% of the targeted application rate in all three treated plots. The application method was representative of the proposed commercial use of this product.

Fresh fortified samples of control soil were analysed concurrently with each set of treated samples. Each analysis set included fresh fortifications ranging from the LOQ level up to 10 ppb. Residues were routinely detected above 10 ppb throughout the course of this study therefore an additional ‘high recovery’ batch containing two fortified control samples at 400 ppb (120 ppb for IN-KT413 converted as IN-MP819) was performed. The average recoveries of the fresh fortification samples analysed concurrently with the analysis of the field samples are summarised in the table below.

Analyte	Average recovery [%]	Relative standard deviation [%]
Indoxacarb (DPX-KN128)	108	10.8
IN-KG433	108	9.2
IN-JU873	100	9.3
IN-KT413	81.5	15.6
IN-JT333	97.7	11.4
IN-MK638	106	5.8
IN-MK643	110	5.1
IN-KB687	108	10.7

The LOQ and LOD were 1.0 and 0.3 ppb, respectively, for each component

The storage period between sampling in the field and analyte extraction did not exceed 352 days for all samples analysed. A separate storage stability study (DuPont-35167, Point CA 7.1.2.2.1) demonstrated that indoxacarb and its metabolites were stable during the maximum storage period, except IN-KT413.

MATERIALS AND METHODS

- Test material: Indoxacarb 30WG
 Lot/Batch #: KN128-298
 Purity: 300 g a.s./kg
 Description: White solid
 CAS#: 173584-44-6 for the active substance
 None for the formulation
 Stability of test compound: Shown to be stable under the conditions of the test
- Test site
 Test site description is detailed in Table 8-107. Soil samples collected to 90 cm depth were characterised and the soil characterisation data are included in Table 8-108.

Table 8-107: Test site description

Location:	Douai, Nord pas de Calais
Country:	France
GPS Coordinates	N 50° 23' 21.8" and E 003° 04' 14.2".
Representative Crop Region:	Northern Europe
Site Selection Criteria:	The field site was flat and level and allowed soil sampling down to 90 cm. The site had good security and was readily able to be remarked if required. The site was free from flooding risk.
Weather Station:	CWi technical/Meteo France on site weather station. Data gaps caused by a mechanical fault with the CWi weather station were filled with data from Meteo France.
Pre-treatment Exclusion Criteria:	No other chemical of similar structure applied during the past 3 years.
Plot History, Crops Grown	grass 2011, grass 2010, grass 2009.
Pesticides Used in preceding 3 years	2012: glyphosate, glufosinate ammonium 2011: none 2010: none
Location/Identification of weather station	CWi technical on site weather station.
Distance of weather station from test site	On site
Depth to ground water Table	Not defined

Table 8-108: Soil properties at Douai, Nord pas de Calais, France

Soil property	Soil depth (cm)					
	0-5	5-15	15-30	30-50	50-70	70-90
Sand % (0.05-2 mm) ^a	27	29	21	27	15	15
Silt % (0.05-0.002 mm) ^a	54	54	62	56	66	60
Clay % (<0.002 mm) ^a	19	17	17	17	19	25
pH (water, 1:1)	5.8	5.7	5.8	6.5	6.7	6.8
% Organic matter ^b	3.5	3.9	2.9	1.3	0.51	0.43
C.E.C [meq/100g] ^c	12.1	12.0	12.4	12.0	11.2	15.0
Bulk density (g cm ⁻³)	1.11	1.08	1.15	1.17	1.19	1.17
Moisture holding capacity at 1/3 bar (% of dry weight)	23.9	24.6	24.2	22.9	25.4	27.8
Moisture holding capacity at 15 bar (% of dry weight)	8.2	8.6	7.8	7.3	8.1	11.4
Soil classification ^d	Silt loam	Silt loam	Silt loam	Silt loam	Silt loam	Silt loam
Microbial biomass carbon (µg/g dry basis, 0–25cm depth)	21.1					

^a Particle size^b Walkley-Black method^c Cation Exchange Capacity (C.E.C)^d Soil classification according to USDA system**Experimental design**

The experimental details for the test substance application, application rate, application method, *etc.*, are included in Table 8-109 below.

Soil sampling

Soil sampling intervals and the sampling depths, and number of cores collected are listed in Table 8-109.

Description of analytical methods

Soil samples were analysed for residues of indoxacarb and all significant aerobic soil metabolites, IN-KG433, IN-JU873, IN-KB687, IN-KN125 (IN-JT333, a racemic mixture of IN-KN125 and IN-KN124, was used as reference standard for its S-enantiomer IN-KN125 analysis), IN-MK638, IN-MK643, and IN-KT413 (quantified as IN-MP819). Soil samples were extracted by a 3-step sequential extraction procedure using acetonitrile and 0.025% acetic acid solutions. The extracts were combined and diluted to 50 mL with acetonitrile. An aliquot was removed from each extract and transferred to a glass culture tube, capped and placed in a heating block set to 55°C for 1 hour to quantitatively convert IN-KT413 to IN-MP819. This was then evaporated to 0.5 mL, adjusted to 0.7 mL with acetonitrile and diluted to 3 mL with water prior to analysis. These samples were then analysed using reverse phase HPLC separation coupled to tandem mass spectrometry (LC-MS/MS). The Limit of Quantification (LOQ) for all analytes was 1.0 ppb, which was sufficient to quantify $\geq 0.2\%$ of the nominal applied amount.

The final purified extracts were quantified for indoxacarb and its metabolites by liquid chromatography with tandem mass spectrometry employing turbo ion spray ionisation in positive and negative mode.

The peak areas for indoxacarb, IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-MK638, IN-MK643, and IN-KB687 were calculated for the target ion for each of the calibration standards, quality control samples, control samples, and unknown test samples. A calibration curve was then obtained by weighted least squares linear regression analysis (1/x) of the plot peak area versus the concentration of indoxacarb, IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-MK638, IN-MK643, and IN-KB687 in each calibration standard. The concentrations (ppb) of indoxacarb and its degradation products were calculated using the calibration curve. The concentrations (ppb) of indoxacarb and its degradation products in treated field soil samples were calculated on a dry weight basis. The peak areas were calculated for target ion for indoxacarb (DPX-KN128), IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-MK638, IN-MK643, and IN-KB687, for each of the calibration standards, quality control samples, control samples and unknown test samples in one analytical run.

The limit of quantification (LOQ) for indoxacarb and its metabolites IN-KG433, IN-JU873, IN-KB687, IN-JT333, IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819) was 1.0 ppb since this was the lowest validated level. The limit of detection (LOD) was determined to be 0.3 ppb for indoxacarb and its metabolites IN-KG433, IN-JU873, IN-KB687, IN-JT333, IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819). The LOD was determined as the sample concentration equivalent to the lowest calibration standard (1.0 µg/kg).

Soil moisture was determined for each sample extracted by drying the sample to at 110°C, and determining the loss of weight. Moisture data were used to convert wet weight ppb residues into dry weight ppb.

The ppb residues for parent compound and each degradation product in each sample were converted to g/ha parent equivalents by multiplying the molar amounts of each analyte by the parent compound molecular weight to obtain parent equivalent mass. The parent equivalent masses were further multiplied by the total calculated soil in one hectare at each depth for conversion to g a.s./ha for the parent and each degradation product at each depth.

Table 8-109 : Experimental design, plot set up and application details

Details	Douai, France
Duration of study	357 days
Uncropped (bare) or cropped	Bare, maintained weed free
Controls used	Yes
Number of plot(s):	3 treated (Replicates I, II, and III) and 1 untreated control
Treated plot dimensions:	3 m × 30 m
Untreated control plot dimensions:	3 m × 7.5 m

Distance between control plot and treated plot	18 m
Distance between treated plots	3 m
Application rate used (g a.s./ha)	400 g a.s./ha, nominal, application by two passes in opposite directions
Was the maximum label rate per ha used in study?	Yes
Application date (s)	14-May-2012
Application method	Ground-directed boom broadcast spray
Type of spray equipment	Backpack sprayer with Lurmark 02F110 Flat Fan, 6 Spray nozzles, 3 m swath width.
Volume of spray solution applied/plot	393–403 L/ha
Identification and volume of carrier (e.g., water), if used	Water
Monthly weather reports included (yes/no)	Yes, also daily weather data
Pan evaporation data available?	No
Meteorological conditions during application	
Cloud cover (%)	0
Temperature (air)	17.8°C
Relative humidity (%)	49
Wind speed	0.6 meters/sec
Sunlight (hr) [time required for application]	Unknown
Irrigation to supplement natural precipitation (15-May-2012 to 08-May-2013)	71.0 mm
Rainfall (15-May-2012 to 08-May-2013)	764.1 mm
Verification of application	Plastic Petri dishes (approximately 9 cm diameter).
Field spikes (transit stability samples)	None; Day 0 sample and application monitor analyses confirmed transit stability
Additional modules added to study: run-off, leaching, volatilisation	None; however, test placed on flat site with little risk of flooding to control run-off. Soil sampling to 90 cm (36 in.) to measure movement in soil

Table 8-110: Soil sampling details

Details	Douai, France
Method of sampling (random or systematic)	Random
Sampling intervals (days)	-5 ^a , -0, +0 ^b , 3, 7, 10, 16, 22, 31, 53, 79, 101, 150, 205, 262, 309, and 357 ^c
Method of soil collection	The 0–5 cm segment was sampled using a metal cylinder with an inner diameter of 9.5 cm driven 5 cm into the soil and the soil was then scooped out by hand using a spoon. The metal cylinder remained in place during collection of the lower depths to prevent treated soil from falling onto the sampling area and potentially contaminating the lower depths. Soil cores for the 5–90 cm depths were taken with a Humax [®] coring system with an inner diameter of 5 cm. This allowed sampling of the lower depths in increments of 5–15, 15–30, 30–50, 50–70, and 70–90 cm segments.
Sampling depth	Nominally to 90 cm depth
Number of cores collected per plot	5 per replicate plot, 15 per time point total
Depth and diameter of segments	0–5 cm (9.5 cm diameter) 5–15 cm (5 cm diameter) 15–30 cm (5 cm diameter) 30–50 cm (5 cm diameter) 50–70 cm (5 cm diameter) 70–90 cm (5 cm diameter)
Storage conditions	Frozen

Maximum storage length	352 days
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^a Samples for soil characterisation and biomass

^b Just after application

^c Sample analysis was terminated early at Day 150 due to rapid dissipation of DPX-KN128 and its metabolites

RESULTS AND DISCUSSION

Application verification

Application was targeted at a rate of 400 g a.s./ha. The mean actual application rate was 399 g a.s./ha (99.8% of the intended application rate, calculated from the boom output). The test material application rate was monitored with the aid of Petri dishes placed in randomly chosen locations in each of the treated plots. The mean recovery of indoxacarb, as calculated from application monitors, was 347.9 g peq/ha, or 87.0% of target rate.

The residues in soil on Day 0 also served to confirm the actual application rate. Residues of indoxacarb in the 0–5 cm samples ranged from 164.4–309.2 peq/ha in the Day 0 soil samples. Averaged residue of indoxacarb in 0–5 cm soil on Day 0 was 250.1 g peq/ha in the three replicate soil samples, which represented 62.5% of the target application rate.

Residue Decline

Soil samples from all sampling events were generally analysed to the depth increment at which the residues found indicated no reasonable expectation of residues in lower depths. Residues were determined in ppb and then converted to g peq/ha for every sample analysed. Post application (Day 0) soil residues in the 0–5 cm samples ranged from 164.4–309.2 g peq/ha for indoxacarb.

Residues in ppb dry weight basis are listed in Table 8-111

Table 8-111: Average residues at each depth (ppb dry weight basis)

DAT (Days)	Rep	Depth (cm)	% Moist (dwb)	DPX- KN218 (ppb)	IN- KG43 3 (ppb)	IN- JU873 (ppb)	IN- KT413 (ppb)	IN- JT333 (ppb)	IN- MK638 (ppb)	IN- MK643 (ppb)	IN- KB687 (ppb)
0 ^a	I	0–5	23.9	416.1801	0.8143	0.0000	35.8938	5.6672	0.0000	0.0000	1.0598
	II	0–5	21.9	255.7462	0.6537	0.0000	19.9550	2.7330	0.0000	0.0000	0.7252
	III	0–5	22.7	481.7202	1.1293	0.0000	35.8407	6.7141	0.0000	0.0000	1.2761
	I	5–15	23.2	2.8287	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	23.9	1.6751	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	24.6	5.0812	0.0000	0.0000	0.4867	0.0000	0.0000	0.0000	0.0000
	I	15–30	22.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	23.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	23.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
3	I	0–5	23.2	479.9872	3.6640	0.0000	100.395	8.8113	0.8744	1.2029	4.7001
	II	0–5	22.9	325.5621	3.6083	0.0000	57.3820	7.9529	0.5669	0.6954	3.9279
	III	0–5	26.5	276.4025	2.3225	0.0000	79.1764	11.2889	0.6049	0.7207	2.6122
	I	5–15	25	8.8375	0.0000	0.0000	1.6688	0.0000	0.0000	0.0000	0.0000
	II	5–15	27.2	4.8145	0.0000	0.0000	1.0742	0.5457	0.0000	0.0000	0.0000
	III	5–15	26.6	20.7118	0.0000	0.0000	5.5628	1.4736	0.0000	0.0000	0.0000
	I	15–30	21.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	24.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	24.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
7	I	0–5	27.2	223.3632	2.7768	0.0000	72.9365	15.9509	1.3114	2.4041	5.7851
	II	0–5	26	280.2240	2.6548	0.0000	80.6274	10.1619	1.0248	1.6040	5.7229
	III	0–5	26.9	249.7392	3.2512	0.0000	75.7339	13.4641	1.0667	1.7487	4.7423
	I	5–15	24.3	2.5121	0.0000	0.0000	0.9744	0.9765	0.0000	0.0000	0.0000
	II	5–15	26.3	13.8551	0.0000	0.0000	2.7041	2.9087	0.0000	0.0000	0.0000
	III	5–15	29.5	2.9487	0.0000	0.0000	1.5786	0.7537	0.0000	0.0000	0.0000
	I	15–30	22.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	24	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.8878	0.0000
	III	15–30	25.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30–50	20.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	18.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	20.1	1.0785	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	50–70	22.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	50–70	22.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	50–70	22.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
10	I	0–5	23.9	245.817	3.0764	0.00	120.046	24.3835	2.6477	5.5259	5.9980
	II	0–5	28.8	125.412	2.1960	0.0000	89.0781	9.3818	1.5778	3.9838	3.8266

	III	0–5	31.2	196.406	2.5492	0.0000	146.156	21.3856	1.7712	3.8533	4.3047
	I	5–15	23.3	6.3204	0.0000	0.0000	2.3168	2.3735	0.0000	0.0000	0.0000
	II	5–15	23.9	1.3344	0.0000	0.0000	0.7538	0.4519	0.0000	0.0000	0.0000
	III	5–15	27.9	1.3404	0.0000	0.0000	1.4517	0.0000	0.0000	0.0000	0.0000
	I	15–30	22.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	23.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	25.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
16	I	0–5	13.8	82.1977	1.1790	0.0000	23.2835	15.3289	3.1659	6.4786	4.2208
	II	0–5	14.5	122.2860	2.3404	0.0000	27.0220	21.0566	3.6995	7.6578	5.9071
	III	0–5	14.7	146.3572	2.3055	0.0000	27.4936	16.5053	3.0717	6.2202	7.1355
	I	5–15	20.6	2.3517	0.0000	0.0000	0.5100	0.6130	0.0000	0.0000	0.0000
	II	5–15	23.4	1.0236	0.0000	0.0000	0.0000	0.5137	0.0000	0.0000	0.0000
	III	5–15	24	2.1365	0.0000	0.0000	0.8461	1.8141	0.0000	0.0000	0.5022
	I	15–30	21.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	22.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
22	III	15–30	24.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	0–5	23.6	115.9368	1.8330	0.0000	37.1665	21.2221	4.6177	13.2870	4.4298
	II	0–5	23.4	111.8374	1.5931	0.0000	40.0927	18.3372	3.4651	10.7087	5.5666
	III	0–5	22.5	97.3875	1.1907	0.0000	38.7835	19.6858	4.1871	13.4383	4.4566
	I	5–15	23.1	1.3960	0.0000	0.0000	1.1116	1.6545	0.0000	0.0000	0.0000
	II	5–15	23.3	0.9350	0.0000	0.0000	0.0000	0.7354	0.0000	0.0000	0.0000
	III	5–15	22.8	1.4380	0.0000	0.0000	0.4989	0.4544	0.0000	0.0000	0.0000
	I	15–30	22.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	22.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
31	III	15–30	23.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	0–5	23	46.7400	1.2817	0.0000	38.4867	13.1733	4.0209	15.1413	3.3948
	II	0–5	22.9	54.6045	1.1142	0.0000	36.6611	12.0061	4.1884	15.5100	3.0037
	III	0–5	22.8	54.2408	1.0508	0.0000	30.5404	13.8273	3.0896	10.5657	3.3193
	I	5–15	24.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	24.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	29.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15–30	23.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	24	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
53	III	15–30	24.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	0–5	26.9	9.0987	0.0000	0.0000	9.7345	4.0722	2.8235	11.5124	1.0969
	II	0–5	25.6	13.7281	0.0000	0.0000	8.0296	4.5241	1.6742	11.3392	1.4934
	III	0–5	25.8	14.8192	0.0000	0.0000	11.3874	5.7579	2.1210	9.3532	1.7687
	I	5–15	26.5	0.0000	0.0000	0.0000	0.8541	0.0000	0.0000	0.5113	0.0000
	II	5–15	24.1	0.0000	0.0000	0.0000	0.4356	0.0000	0.0000	0.0000	0.0000
	III	5–15	27.4	0.0000	0.0000	0.0000	0.6439	0.0000	0.0000	0.0000	0.0000
	I	15–30	25.4	0.0000	0.0000	0.0000	0.5291	0.0000	0.0000	0.0000	0.0000
	II	15–30	23.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
III	15–30	23.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

	I	30–50	20.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	19.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	22.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
79	I	0–5	17.8	3.6188	0.0000	0.0000	3.2360	1.9237	1.2852	8.8385	0.6764
	II	0–5	18.6	5.5754	0.0000	0.0000	5.0286	2.3293	1.2121	9.3291	1.1164
	III	0–5	18.7	5.4994	0.0000	0.0000	4.5581	2.2256	0.9370	8.4111	1.0843
	I	5–15	22.8	0.0000	0.0000	0.0000	0.5123	0.0000	0.0000	0.0000	0.0000
	II	5–15	24.4	0.0000	0.0000	0.0000	0.4858	0.0000	0.0000	0.0000	0.4213
	III	5–15	26.1	0.0000	0.0000	0.0000	0.4736	0.3962	0.0000	0.0000	0.0000
	I	15–30	21.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	23.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	23.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
101	I	0–5	26.6	4.7171	0.0000	0.0000	4.5158	2.1535	1.2133	8.3303	1.0472
	II	0–5	24.9	2.3481	0.0000	0.0000	1.6562	1.2977	0.6386	5.0497	0.8780
	III	0–5	27.1	5.5149	0.0000	0.0000	3.6554	2.9386	0.7181	6.4808	0.8494
	I	5–15	24.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	25	0.4030	0.0000	0.0000	0.0000	0.0000	0.0000	0.6113	0.0000
	III	5–15	24.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15–30	24.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	23.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	24.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
150	I	0–5	23.7	3.8372	0.0000	0.0000	1.6712	1.6205	0.5293	7.0126	0.8076
	II	0–5	23.7	2.5012	0.0000	0.0000	1.3261	0.8517	0.0000	6.2320	1.3211
	III	0–5	24.3	2.2585	0.0000	0.0000	1.0439	1.0211	0.0000	5.4978	0.7253
	I	5–15	25.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	25.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	28.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15–30	19.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	23.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	26.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

LOQ = 1.0 ppb

<LOD = <0.3 ppb

Quantifiable values >LOD but <LOQ are highlighted in bold.

Note: Values have been corrected for moisture content. Therefore, in some cases, values are highlighted in bold when >1.0 ppb. This is caused by detected values (uncorrected for moisture) at <1.0 ppb being corrected prior to inclusion in table.

Table 8-112 : Average residues summed for all depths in g/ha indoxacarb (DPX-KN128) (parent equivalent)

Days	Data in grams PEQ/ha							
	DPX-KN128	IN-JT333	IN-KG433	IN-KB687	IN-MK643	IN-JU873	IN-MK638	IN-KT413
0 ^a	281.1175	4.2328	0.5539	1.5814	0.0000	0.0000	0.0000	23.5066
	167.2878	1.9735	0.4300	1.0462	0.0000	0.0000	0.0000	12.6349
	316.8610	4.8423	0.7418	1.8386	0.0000	0.0000	0.0000	23.3856

3	368.0677	7.3356	2.7782	7.8173	2.1569	0.0000	1.5534	75.5940
	251.4001	7.5756	2.7745	6.6250	1.2644	0.0000	1.0214	43.9646
	212.9937	10.7571	1.5831	3.9057	1.1616	0.0000	0.9661	59.5979
7	163.2281	14.6670	2.0204	9.2331	4.1364	0.0000	2.2358	52.7745
	206.1492	12.5164	1.7940	8.4828	8.2028	0.0000	1.6225	56.5091
	161.5930	10.5967	2.0400	6.5271	2.5947	0.0000	1.5683	48.1748
10	170.1797	22.3972	2.0379	8.7153	8.6561	0.0000	4.1096	80.5479
	87.5944	8.0593	1.5274	5.8381	6.5522	0.0000	2.5713	60.9555
	127.2714	15.3357	1.6649	6.1670	5.9512	0.0000	2.7105	93.9416
16	56.2082	12.0750	0.7725	6.0666	10.0385	0.0000	4.8606	15.4513
	79.9086	15.9922	1.5368	8.5082	11.8907	0.0000	5.6918	17.0823
	100.9340	15.1885	1.5802	12.2584	10.0819	0.0000	4.9331	19.2738
22	73.6247	16.5786	1.1705	6.2049	20.0638	0.0000	6.9090	23.8497
	67.4664	13.2638	0.9660	7.4041	15.3553	0.0000	4.9231	23.4051
	67.4270	15.5593	0.8195	6.7283	21.8720	0.0000	6.7524	26.3560
31	29.6153	9.3780	0.8310	4.8281	23.2149	0.0000	6.1084	24.0236
	34.7030	8.5729	0.7246	4.2848	23.8521	0.0000	6.3822	22.9532
	34.1435	9.7793	0.6769	4.6899	16.0937	0.0000	4.6631	18.9389
53	6.3144	3.1752	0.0000	1.7087	20.8664	0.0000	4.6981	8.8797
	9.4790	3.5097	0.0000	2.3145	18.9456	0.0000	2.7717	5.9948
	9.8382	4.2948	0.0000	2.6357	15.0254	0.0000	3.3761	8.3463
79	2.3222	1.3869	0.0000	0.9743	13.7244	0.0000	1.9774	2.7904
	3.3517	1.5733	0.0000	2.7016	13.5710	0.0000	1.7471	3.5829
	3.4154	2.3303	0.0000	1.5116	12.6404	0.0000	1.3953	3.6036
101	3.1572	1.6194	0.0000	1.5733	13.4917	0.0000	1.9471	2.9776
	2.0973	0.9534	0.0000	1.2887	10.0523	0.0000	1.0012	1.0668
	3.6113	2.1620	0.0000	1.2485	10.2691	0.0000	1.1275	2.3581
150	2.6342	1.2499	0.0000	1.2445	11.6489	0.0000	0.8712	1.1302
	1.7620	0.6741	0.0000	2.0890	10.6233	0.0000	0.0000	0.9203
	1.4438	0.7334	0.0000	1.0407	8.5042	0.0000	0.0000	0.6574

^a Samples taken immediately after application had dried

Table 8-113: Residues in entire soil column, shown in percent of applied test substance

Days	Percent of the applied*							
	Indoxacarb (DPX- KN128)	IN- JT333	IN- KG433	IN- KB687	IN- MK643	IN- JU873	IN- MK638	IN- KT413
0	100.1566	1.5081	0.1973	0.5634	0.0000	0.0000	0.0000	8.3749
	59.6013	0.7031	0.1532	0.3727	0.0000	0.0000	0.0000	4.5015
	112.8913	1.7252	0.2643	0.6551	0.0000	0.0000	0.0000	8.3318
3	131.1352	2.6135	0.9898	2.7851	0.7685	0.0000	0.5534	26.9326
	89.5689	2.6990	0.9885	2.3603	0.4505	0.0000	0.3639	15.6637
	75.8854	3.8325	0.5640	1.3915	0.4139	0.0000	0.3442	21.2335

7	58.1549	5.2256	0.7198	3.2896	1.4737	0.0000	0.7966	18.8025
	73.4469	4.4594	0.6392	3.0223	2.9225	0.0000	0.5781	20.1331
	57.5724	3.7754	0.7268	2.3255	0.9244	0.0000	0.5588	17.1637
10	60.6317	7.9797	0.7261	3.1051	3.0840	0.0000	1.4642	28.6976
	31.2082	2.8714	0.5442	2.0800	2.3344	0.0000	0.9161	21.7172
	45.3443	5.4638	0.5932	2.1972	2.1203	0.0000	0.9657	33.4695
16	20.0259	4.3021	0.2752	2.1614	3.5765	0.0000	1.7317	5.5050
	28.4698	5.6977	0.5475	3.0313	4.2364	0.0000	2.0279	6.0861
	35.9608	5.4114	0.5630	4.3674	3.5920	0.0000	1.7576	6.8669
22	26.2310	5.9066	0.4170	2.2107	7.1483	0.0000	2.4615	8.4972
	24.0369	4.7256	0.3442	2.6379	5.4708	0.0000	1.7540	8.3388
	24.0229	5.5435	0.2920	2.3972	7.7926	0.0000	2.4058	9.3901
31	10.5513	3.3412	0.2961	1.7202	8.2710	0.0000	2.1763	8.5591
	12.3640	3.0544	0.2582	1.5266	8.4980	0.0000	2.2739	8.1778
	12.1646	3.4842	0.2412	1.6709	5.7339	0.0000	1.6614	6.7476
53	2.2497	1.1313	0.0000	0.6088	7.4343	0.0000	1.6739	3.1637
	3.3772	1.2504	0.0000	0.8246	6.7499	0.0000	0.9875	2.1358
	3.5052	1.5301	0.0000	0.9390	5.3533	0.0000	1.2028	2.9736
79	0.8274	0.4941	0.0000	0.3471	4.8897	0.0000	0.7045	0.9942
	1.1942	0.5605	0.0000	0.9625	4.8351	0.0000	0.6225	1.2765
	1.2168	0.8303	0.0000	0.5385	4.5035	0.0000	0.4971	1.2839
101	1.1249	0.5770	0.0000	0.5605	4.8068	0.0000	0.6937	1.0609
	0.7472	0.3397	0.0000	0.4591	3.5814	0.0000	0.3567	0.3801
	1.2866	0.7703	0.0000	0.4448	3.6587	0.0000	0.4017	0.8401
150	0.9385	0.4453	0.0000	0.4434	4.1503	0.0000	0.3104	0.4027
	0.6278	0.2402	0.0000	0.7443	3.7849	0.0000	0.0000	0.3279
	0.5144	0.2613	0.0000	0.3708	3.0299	0.0000	0.0000	0.2342

* Calculations based on a total g pec/ha value for parent and metabolites at Day 0, averaged across the 3 reps

Average residue of indoxacarb in the uppermost soil segment declined to about half the applied amount, 189.2 ppb by Day 10. Residue of indoxacarb in the upper depth declined from about 384.5 ppb on Day 0 to 2.9 ppb at the end of the study. Only a small amount, generally <12 ppb was found in the next depth (5-15 cm) segment, and only trace amounts, nearing the LOQ of 1.0 ppb in the 15–30 and 30–50 cm segment. No residues were detected below 50 cm.

Six of the metabolites monitored were detected during this study with only IN-JU873 undetected at any sampling interval. The first four metabolites in the sequence of degradation of indoxacarb, IN-JT333, IN-KG433, IN-KB687, and IN-KT413, were found immediately after the application. IN-JT333 reached an average level of 19.7 ppb in 0–5 cm depth by Day 22. It stayed near 2 ppb through Day 101 and then declined to about 1 ppb by the end of the study. IN-JT333 remained in the upper two depth segments with most of the residue remaining in the 0–5 cm segment. IN-KT413 reached its peak level of about 146.2 ppb by Day 10 and remained in the range 37–40 ppb through Day 22 before declining. IN-KG433 and IN-KB687 only reached a concentration of about 4 ppb by Day 3 and 7 ppb by Day 16, and never accounted for any significant portion of the residue. IN-MK643 reached a concentration of 15.5 ppb by Day 31. IN-MK638 reached a concentration of 4.6 ppb by Day 22. As stated earlier, IN-JU873 was not detected

Almost all of the applied test item and its degradation products remained in the upper 15 cm of soil. Detections below 15 cm were infrequent and seldom accounted for more than 1 ppb in any depth segment,

and for any individual component. No residues were detected in the depth segments below 50 cm at any sampling interval.

It can be concluded from these data that indoxacarb and its major metabolites were all degrading throughout this study at varying rates. In addition, very little residue moved to depths below 15 cm. Thus, loss of applied material via leaching did not contribute to the dissipation of residue in this study.

Mass balance

In order to quantify the rate of decline of the applied test item, the concentrations of indoxacarb as well as all metabolites, measured in ppb, were converted to mass in grams per unit area (g/ha parent equivalents) and is included in Table 8-112. The residues converted in percent of the applied are presented in Table 8-113.

A rapid degradation of the parent compound resulted in the indoxacarb residue declining to an average 177.0 g peq/ha by Day 7 and subsequently to around 3.0 g peq/ha by Day 79. Only 0.5% of the target application rate was remaining by the end of this study.

All degradation products except IN –JU873 were detected during the course of the study. IN-KT413 accounted for the largest proportion of the metabolites observed, reaching a maximum of 93.9 g peq/ha, or 33% of applied, on Day 10. IN-JT333 accounted for as much as 22.4 g peq/ha (about 6% of applied mass) at its peak, on Day 10. IN-KG433 accounted for 2.8 g peq/ha (0.7% of the applied mass) on Day 3. IN-KB687 accounted for 12.3 g peq/ha (3.1% of the applied mass) on Day 16. IN-MK643 and IN-MK638 also reached a maximum of 23.9 g peq/ha (6.0% of the applied mass) and 6.9 g peq/ha (1.7% of the applied mass), respectively, while IN-JU873 was not detected.

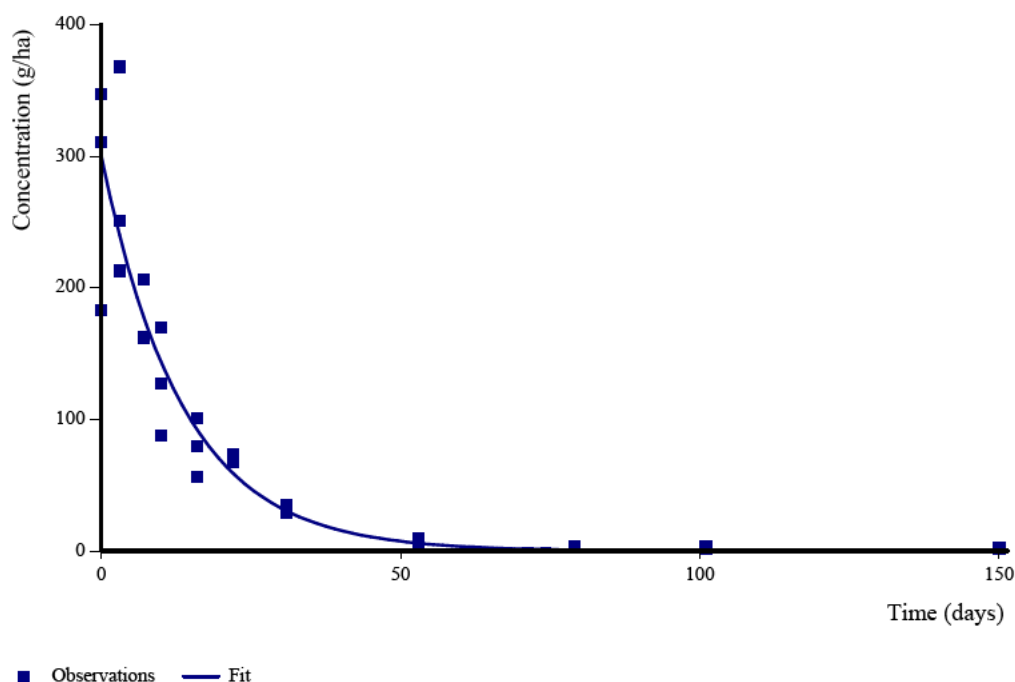
Decline of not only the parent compound, but all the metabolites observed underlines the degradation of all monitored components under field conditions.

Dissipation kinetics

The total soil column residues (Table 8-113) were analysed for the decline rates using CAKE version 2. The decline rate for indoxacarb using the single first order (SFO) kinetics model gave a DT_{50} of 9.4 days.

Kinetic model	χ^2 error	r^2	DT_{50} (days)	DT_{90} (days)
SFO	12.1	0.89	9.4	31.2

Figure 3 : Decline of indoxacarb (DPX-KN128) in Douai, France



III. CONCLUSIONS

There were no abnormal circumstances with respect to test site management, climate conditions or analysis which would compromise the conclusions drawn or the data collected.

The application monitors as well as the soil residues on Day 0 confirmed the nominal application rate. Averaged recoveries of indoxacarb on Day 0 were 87.0% based on the application monitor analysis.

A rapid degradation of the parent compound resulted in the indoxacarb residue declining from an average 255.1 g peq/ha on Day 0 to 177.0 g peq/ha by Day 7 and subsequently to less than 3.0 g peq/ha by Day 79. The parent compound had declined to less than 2 g peq/ha by the end of this study.

All degradation products except IN-JU873 were detected during the course of the study. IN-KT413 accounted for the largest proportion of the metabolites observed, reaching an average of 28.0% of the applied. IN-JT333 reached above 5 % and IN-MK643 reached an average of 7.5% of the applied mass. The remaining components did not exceed 5% of the applied mass.

Almost all of the applied test item and its degradation products remained in the upper 15 cm of soil. Loss of applied material via leaching did not contribute to the dissipation of residue in this study.

A DT_{50} of 9.4 days and a DT_{90} of 31.2 days was calculated for the parent compound.

Comments (RMS 2016)

This study was conducted with the active isomer DPX-KN128 as test material and is acceptable.

The level of residues observed at different depths confirm the rapid degradation of active substance (active isomer DPX-KN128) and the low potential of leaching of active substance and all its major metabolites, as none or very few residues of any compound were observed below 15 cm during the all course of the study.

No accumulation potential is detected for any of the compound, with the exception of IN-MK643 that seems to be quite persistent. However, this accumulation potential was already identified in the laboratory (with persistence DT_{50} of 314 days), and is taken into account in soil risk assessment with calculation of PECaccumulation.

It is noticeable that the metabolite IN-JU873 is not detected in this field trial although being a major metabolite in laboratory. However, laboratory data tend to show that this metabolite is quite transient (it is detected at level

> 10% at only one sampling time among all studies). As mentioned by applicant, it is believed that this metabolite may have formed in the field at level below the LOD.

Degradation rate were only provided for active substance. On the more no normalized DT₅₀ are available. This could have been done, since the study was conducted according to EFSA guidance (2010) to minimize surface processes (11 mm of irrigation applied to the test plot within 24 hours after 1st application).

As first approximation, it can be seen from the daily soil temperature monitored in field, and the moisture content of the samples that:

- Soil temperature was always < 20°C during the course of the study at the exception of the period between 13 and 23 August (max 22.2 °C), i.e 90 days after application
- Soil moisture was always < soil moisture at pF2.5, i.e soil correction factor from pF2 would certainly be <1.

This indicates that normalized DT₅₀ would certainly be shorter than the DT₅₀ based on non-normalised values.

Data point:	CA 7.1.2.2.1/03
Author(s)	Doig, A. (2015c);
Title:	The field soil dissipation of indoxacarb (DPX-KN128) following a single application to bare ground - north Spain - 2012
Organisation:	Charles River Laboratories (UK), Tranent, Scotland, UK
Document No:	DuPont-34324
Dates of experimental work	
Guidelines:	OPPTS 835.6100, SETAC Europe (1995), SANCO/3029/99 rev. 4 (2000), EU 1607/VI/97 Rev 1 (1997), EU 7029/VI/1995 Rev 5 (1997)
Deviations :	None
GLP:	Yes
Previous evaluation:	No
Acceptability:	The study is considered valid.

This report describes the soil dissipation of a single application of indoxacarb (DPX-KN128) to bare ground studied under field conditions in Termens, Spain, for *ca.* 5 months after application on 15-May-2012.

The study design consisted of three replicate treated bare soil plots and a control (untreated) bare soil plot. The test site soil was characterised as clay loam in horizons 0–5, 5–15, and 15–30 and clay in horizons 30–50, 50–70, and 70–90 cm. The test item was applied at a nominal rate of 400 g a.s./ha, which was the highest proposed use rate for indoxacarb per year. Actual application based on the amount of spray solution applied and the output from calibrated spray equipment used indicated application at 98.8–100.7% of the targeted application rate in all three treated plots. The application method was representative of the proposed commercial use of this product.

Fresh fortified samples of control soil were analysed concurrently with each set of treated samples. Each analysis set included fresh fortifications ranging from the LOQ level of 1 ppb up to 10 ppb. Residues were routinely detected above 10 ppb throughout the course of this study therefore an additional 'high recovery' batch containing two fortified control samples at 700 ppb (100 ppb for IN-KT413 converted as IN-MP819) was performed. The average recoveries of the fresh fortification samples analysed concurrently with the analysis of the field samples are summarised in the table below.

Analyte	Average recovery (%)	Relative standard deviation (%)
Indoxacarb (DPX-KN128)	102	8.1
IN-KG433	90.8	15.1
IN-JU873	91.3	12.9
IN-KT413	84.0	16.4

IN-JT333	96.0	10.5
IN-MK638	110	8.2
IN-MK643	112	7.2
IN-KB687	101	11.7

The LOQ and LOD were 1.0 and 0.3 ppb, respectively, for each component.

The storage period between sampling in the field and analyte extraction did not exceed 345 days for all samples analysed. Freezer storage stability of indoxacarb and its degradation products in frozen soil samples over 12 months is reported in another study (DuPont-35167, Point CA 7.1.2.2.1).

MATERIALS AND METHODS

- Test material: Indoxacarb 30WG
 Lot/Batch #: KN128-298
 Purity: 300 g a.s./kg
 Description: White solid
 CAS#: 173584-44-6 for indoxacarb the active substance
 None for the formulation
 Stability of test compound: Shown to be stable under the conditions of the test

2. Test Site

Test site description is detailed in Table 8-114. Soil samples collected to 90 cm depth were characterised and the soil characterisation data are included in Table 8-115.

Table 8-114: Test site description

Location:	Termens
Country:	Spain
GPS coordinates	N 41° 42' 20.9" and E 0° 47' 49.6".
Representative crop region:	Southern Europe
Site selection criteria:	The field site was flat and level and allowed soil sampling down to 90 cm. The site had good security and was readily able to be remarked if required. The site was free from flooding risk.
Weather station:	CWi technical on site weather station.
Pre-treatment exclusion criteria:	No other chemical of similar structure applied during the past 3 years.
Plot history, crops grown:	maize 2011, unused 2010, unused 2009.
Pesticides used in preceding 3 years:	2011: glyphosate 2010: glyphosate 2009: glyphosate.
Location/identification of weather station:	CWi technical on site weather station.
Distance of weather station from test site:	On site
Depth to ground water table:	Not defined

Table 8-115: Soil properties at Termens, Spain

Soil property	Soil depth (cm)					
	0–5	5–15	15–30	30–50	50–70	70–90
Sand % (0.05–2 mm) ^a	35	35	29	17	7	3
Silt % (0.05–0.002 mm) ^a	30	28	32	32	30	32
Clay % (<0.002 mm) ^a	35	37	39	51	63	65
pH (water, 1:1)	8.0	7.9	7.9	7.9	8.0	8.0
% Organic matter ^b	2.8	2.9	2.5	1.2	0.69	0.50
C.E.C [meq/100g] ^c	36.1	33.4	33.3	41.9	31.5	30.6
Bulk density (g cm ⁻³)	1.13	1.09	1.12	1.13	1.14	1.12

Moisture holding capacity at 1/3 bar (% of dry weight)	23.9	24.8	26.1	26.8	27.7	27.3
Moisture holding capacity at 15 bar (% of dry weight)	12.7	13.6	14.0	15.6	17.4	17.1
Soil classification ^d	Clay loam	Clay loam	Clay loam	Clay	Clay	Clay
Microbial biomass carbon (µg/g dry basis, 0–25cm depth)	341.5					

^a Particle size

^b Walkley-Black method

^c Cation Exchange Capacity (C.E.C)

^d Soil classification according to USDA system

METHODS

Experimental design

The experimental details for the test substance application, application rate, application method, *etc.*, are included in Table 8-116 below.

Soil sampling

Soil sampling intervals and the sampling depths, and number of cores collected are listed in Table 8-117.

Description of analytical methods

Soil samples were analysed for residues of indoxacarb and all significant soil metabolites, IN KG433, IN JU873, IN KB687, IN KN125 (IN JT333, a racemic mixture of IN-KN125 and IN-KN124, was used as reference standard for its S enantiomer IN KN125 analysis), IN MK638, IN MK643, and IN KT413 (quantified as IN MP819). Soil samples were extracted by a 3 step sequential extraction procedure using acetonitrile and 0.025% acetic acid solutions. The extracts were combined and diluted to 50 mL with acetonitrile. An aliquot was removed from each extract and transferred to a glass culture tube, capped and placed in a heating block set to 55° C for 1 hour to quantitatively convert IN KT413 to IN MP819. This was then evaporated to 0.5 mL, adjusted to 0.7 mL with acetonitrile and diluted to 3 mL with water prior to analysis. These samples were then analysed using reverse phase HPLC separation coupled to tandem mass spectrometry (LC MS/MS).

The Limit of Quantification (LOQ) for all analytes was 1.0 ppb, which was sufficient to quantify <0.2% of the nominal applied amount. The peak areas for indoxacarb, IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-MK638, IN-MK643, and IN-KB687 were calculated for the target ion for each of the calibration standards, quality control samples, control samples, and unknown test samples. A calibration curve was then obtained by weighted least squares linear regression analysis (1/x) of the plot peak area versus the concentration of indoxacarb, IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-MK638, IN-MK643, and IN-KB687 in each calibration standard. The concentrations (ppb) of indoxacarb and its degradation products were calculated using the calibration curve. The concentrations (ppb) of indoxacarb and its degradation products in treated field soil samples were calculated on a dry weight basis. The peak areas were calculated for target ion for indoxacarb, IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-MK638, IN-MK643, and IN-KB687, for each of the calibration standards, quality control samples, control samples and unknown test samples in one analytical run.

The limit of quantification (LOQ) for indoxacarb and its metabolites IN-KG433, IN-JU873, IN-KB687, IN-JT333, IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819) was 1.0 ppb since this was the lowest validated level. The limit of detection (LOD) was determined to be 0.3 ppb for indoxacarb and its metabolites IN-KG433, IN-JU873, IN-KB687, IN-JT333, IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819). The LOD was determined as the sample concentration equivalent to the lowest calibration standard (1.0 µg/kg).

Soil moisture was determined for each sample extracted by drying the sample to at 110°C, and determining the loss of weight. Moisture data were used to convert wet weight ppb residues into dry weight ppb.

The ppb residues for parent compound and each degradation product in each sample were converted to g/ha parent equivalents by multiplying the molar amounts of each analyte by the parent compound molecular weight to obtain parent equivalent mass. The parent equivalent masses were further multiplied by the total calculated soil in one hectare at each depth for conversion to g a.s./ha for the parent and each degradation product at each depth.

Table 8-116: Experimental design, plot set up and application details

Details	Termens, Spain
Duration of study	358 days
Uncropped (bare) or cropped	Bare, maintained weed free
Controls used	Yes
Number of plot(s)	3 treated (Replicates I, II, and III) and 1 untreated control
Treated plot dimensions	3 m × 30 m
Untreated control plot dimensions	3 m × 7.5 m
Distance between control plot and treated plot	10 m
Distance between treated plots	3 m
Application rate used (g a.s./ha)	400 g a.s./ha, nominal, application by two passes in opposite directions
Was the maximum label rate per ha used in study?	Yes
Application date(s)	15-May-2012
Application method	Ground-directed boom broadcast spray
Type of spray equipment	Backpack sprayer with Lurmark 03F110 Flat Fan, 6 Spray nozzles, 3 m swath width.
Volume of spray solution applied/plot	395–403 L/ha
Identification and volume of carrier (e.g., water), if used	Water
Monthly weather reports included (yes/no)	Yes, also daily weather data
Pan evaporation data available?	No
Meteorological conditions during application	
Cloud cover (%)	10
Temperature (air)	16.2°C
Relative humidity (%)	46
Wind speed	0.4 meters/sec
Sunlight (hr) [time required for application]	Unknown
Irrigation to supplement natural precipitation (15-May-2012 to 08-May-2013)	246.0 mm
Rainfall (15-May-2012 to 08-May-2013)	376.3 mm
Verification of application	Plastic Petri dishes (approximately 9 cm diameter).
Field spikes (Transit stability samples)	None; Day 0 sample and application monitor analyses confirmed transit stability
Additional modules added to study: run-off, leaching, volatilisation	None; however, test placed on flat site with little risk of flooding to control run-off. Soil sampling to 90 cm (36 in.) to measure movement in soil

Table 8-117: Soil sampling details

Details	Termens, Spain
Method of sampling (random or systematic)	Random
Sampling intervals (days)	-1 ^a , -0, +0 ^b , 3, 7, 10, 15, 21, 31, 50, 79, 97, 155, 203, 253, 307, and 358 ^c

Method of soil collection	The 0–5 cm segment was sampled using a metal cylinder with an inner diameter of 9.5 cm driven 5 cm into the soil and the soil was then scooped out by hand using a spoon. The metal cylinder remained in place during collection of the lower depths to prevent treated soil from falling onto the sampling area and potentially contaminating the lower depths. Soil cores for the 5–90 cm depths were taken with a Humax [®] coring system with an inner diameter of 5 cm. This allowed sampling of the lower depths in increments of 5–15, 15–30, 30–50, 50–70, and 70–90 cm segments.
Sampling depth	Nominally to 90 cm depth
Number of cores collected per plot	5 per replicate plot, 15 per time point total
Depth and diameter of segments	0–5 cm (9.5 cm diameter) 5–15 cm (5 cm diameter) 15–30 cm (5 cm diameter) 30–50 cm (5 cm diameter) 50–70 cm (5 cm diameter) 70–90 cm (5 cm diameter)
Storage conditions	Frozen
Maximum storage length	345 days

^a Samples for soil characterisation and biomass

^b Just after application

^c Sample analysis was terminated early at Day 155 due to rapid dissipation of indoxacarb (DPX-KN128) and its metabolites

RESULTS AND DISCUSSION

Application verification

Application was targeted at a rate of 400 g a.s./ha. The mean actual application rate was 399.6 g a.s./ha (99.9% of the intended application rate, calculated from the boom output). The test material application rate was monitored with the aid of Petri dishes placed in randomly chosen locations in each of the treated plots. The mean recovery of indoxacarb, as calculated from application monitors, was 472.0 g peq/ha, or 118% of target rate.

The residues in soil on Day 0 also served to confirm the actual application rate. Residues of indoxacarb in the 0–50 cm samples ranged from 444.7–506.3 peq/ha in the Day 0 soil samples. Averaged residue of indoxacarb in 0–5 cm soil on Day 0 was 444.6 g peq/ha in the three replicate soil samples, which represented 111% of the target application rate.

Residue decline

Residues in ppb dry weight basis are listed in Table 8-118.

Table 8-118: Average residues at each depth (ppb dry weight basis)

DAT (Days)	Rep	Depth (cm)	% Moist (dwb)	DPX-KN128 (ppb)	IN-KG433 (ppb)	IN-JU873 (ppb)	IN-KT413 (ppb)	IN-JT333 (ppb)	IN-MK638 (ppb)	IN-MK643 (ppb)	IN-KB687 (ppb)
0 ^a	I	0–5	11.8	717.0852	0.4076	0.0000	16.4458	2.5390	0.0000	0.0000	2.9079
	II	0–5	10.6	587.1754	0.4634	0.0000	11.3697	2.2109	0.0000	0.0000	2.9497
	III	0–5	11.8	666.4398	0.8247	0.0000	19.1513	3.5519	0.0000	0.0000	3.2992
	I	5–15	18	17.6174	0.0000	0.0000	1.1000	0.0000	0.0000	0.0000	0.0000
	II	5–15	17	15.7131	0.0000	0.0000	0.8002	0.0000	0.0000	0.0000	0.0000
	III	5–15	16.7	18.0068	0.0000	0.0000	0.7083	0.0000	0.0000	0.0000	0.0000
	I	15–30	20.3	0.7903	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	19.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

	III	15–30	19	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30–50	20.1	0.6727	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	20.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	18.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
3	I	0–5	20	375.1200	3.8160	0.0000	73.9560	10.8912	0.7135	0.7397	3.1116
	II	0–5	15.8	308.3754	5.2585	0.0000	77.7829	35.0874	1.4417	1.9501	5.5167
	III	0–5	19.5	356.7075	2.8130	0.0000	65.4980	9.1346	0.4909	0.5974	2.1665
	I	5–15	22.3	1.9458	0.0000	0.0000	0.7709	0.0000	0.0000	0.0000	0.0000
	II	5–15	19.9	13.8005	0.0000	0.0000	2.5898	0.0000	0.0000	0.0000	0.0000
	III	5–15	22.3	8.5965	0.0000	0.0000	1.6633	0.0000	0.0000	0.0000	0.0000
	I	15–30	20	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	19.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	20.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
7	I	0–5	14.7	256.9280	5.1443	0.0000	74.2912	14.3949	1.0266	1.6471	3.2414
	II	0–5	15.3	327.1061	7.0840	0.0000	71.8319	18.6901	0.9576	2.1446	3.2780
	III	0–5	13.9	290.7867	4.8806	0.0000	56.2324	18.2810	0.7886	2.1436	3.5913
	I	5–15	20.9	1.8256	0.0000	0.0000	0.7794	0.0000	0.0000	0.0000	0.0000
	II	5–15	19.4	20.2622	0.5195	0.0000	3.3313	0.8030	0.0000	0.0000	0.0000
	III	5–15	20.2	4.5904	0.0000	0.0000	1.1586	0.0000	0.0000	0.0000	0.0000
	I	15–30	21.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	19.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	20.9	0.8505	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30–50	20	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	19.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	20.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
10	I	0–5	11.3	256.8804	5.6407	0.0000	48.0705	33.1229	1.7496	4.0547	7.9746
	II	0–5	12.9	407.6819	5.0173	0.0000	65.3578	27.1412	1.4632	3.2809	6.1903
	III	0–5	12.7	294.7105	7.0460	0.0000	61.6131	30.7896	1.6499	2.7589	5.5843
	I	5–15	18.9	3.6110	0.0000	0.0000	1.1834	0.0000	0.0000	0.0000	0.0000
	II	5–15	16.9	5.4686	0.0000	0.0000	1.2017	0.4826	0.0000	0.0000	0.0000
	III	5–15	18.8	13.0680	0.3566	0.0000	2.2833	1.3971	0.0000	0.0000	0.0000
	I	15–30	20.4	1.3136	0.0000	0.0000	0.4336	0.0000	0.0000	0.0000	0.0000
	II	15–30	21	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	19.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30–50	19.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	21.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	18.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
15	I	0–5	19.2	0.0000 ^b	0.0000 ^b	0.0000 ^b	0.0000 ^b	0.0000 ^b	0.0000 ^b	0.0000 ^b	0.0000 ^b
	II	0–5	17.9	129.4542	3.7480	0.0000	38.8127	28.1781	0.9236	2.2825	2.9310
	III	0–5	19.9	185.6052	3.9183	0.0000	67.0601	34.7350	1.3681	2.8368	2.9807
	I	5–15	19.6	2.1982	0.0000	0.0000	0.8511	0.0000	0.0000	0.0000	0.0000
	II	5–15	19.5	3.2026	0.0000	0.0000	0.9094	0.6080	0.0000	0.0000	0.0000

	III	5–15	18.9	5.6347	0.0000	0.0000	0.9236	0.7927	0.0000	0.0000	0.0000
	I	15–30	18.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	18.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	18.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
21	I	0–5	13.7	91.8469	2.6231	0.0000	51.1764	36.1680	1.4599	3.7919	2.5219
	II	0–5	13.9	96.9289	2.8908	0.0000	65.0825	44.3413	1.5843	4.1972	2.0901
	III	0–5	13.6	58.2654	1.5518	0.0000	41.3163	26.0144	1.1564	3.5080	1.8721
	I	5–15	18.7	0.7532	0.0000	0.0000	0.6850	0.0000	0.0000	0.0000	0.0000
	II	5–15	18.1	0.7183	0.0000	0.0000	0.5352	0.0000	0.0000	0.0000	0.0000
	III	5–15	19	2.4621	0.0000	0.0000	1.2055	0.7841	0.0000	0.0000	0.0000
	I	15–30	19.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	17.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	20	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
31	I	0–5	12.2	45.3176	1.2241	0.0000	27.2085	37.1494	1.8850	3.7834	2.1284
	II	0–5	12.5	32.3100	0.8187	0.0000	19.0013	23.1525	1.0904	3.0634	1.5176
	III	0–5	10.8	51.0234	1.2044	0.0000	28.5421	40.7522	1.7196	3.6132	2.9639
	I	5–15	17.1	0.3836	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	17.9	0.5645	0.0000	0.0000	0.0000	0.3933	0.0000	0.0000	0.0000
	III	5–15	16.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15–30	16.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	18.4	0.3747	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	17.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30–50	20	0.5322	0.0000	0.0000	0.4841	0.0000	0.0000	0.0000	0.0000
	II	30–50	20.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	19.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	50–70	20.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	50–70	21	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	50–70	21.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
50	I	0–5	23.5	9.7861	0.0000	0.0000	8.4190	20.0194	0.8355	3.3320	0.6291
	II	0–5	21.2	7.8683	0.0000	0.0000	7.0502	17.5013	0.7440	2.0919	0.0000
	III	0–5	21.4	9.8601	0.0000	0.0000	9.4085	21.9491	0.7615	2.5676	0.4766
	I	5–15	20.5	0.0000	0.0000	0.0000	0.0000	0.3736	0.0000	0.0000	0.0000
	II	5–15	22.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	20	0.6416	0.0000	0.0000	0.5264	0.8934	0.0000	0.0000	0.0000
	I	15–30	18.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	19.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	18	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
79	I	0–5	15.7	3.8528	0.0000	0.0000	6.3242	18.6624	0.5879	2.6912	0.0000
	II	0–5	13.8	2.3090	0.0000	0.0000	3.2831	13.1780	0.5610	2.0586	0.0000
	III	0–5	15.4	2.4153	0.0000	0.0000	5.3973	14.4019	0.5750	2.3888	0.0000
	I	5–15	20.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	18.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

	III	5–15	17.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15–30	18.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	18.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	17.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
97	I	0–5	21.1	1.6203	0.0000	0.0000	2.7211	12.9456	0.4033	2.0672	0.0000
	II	0–5	22.1	1.6911	0.0000	0.0000	4.9402	14.7375	0.3827	1.8144	0.0000
	III	0–5	21	1.1324	0.0000	0.0000	4.4347	9.1839	0.0000	1.8767	0.0000
	I	5–15	21.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	18.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	19.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15–30	20.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	23.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	17.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
155	I	0–5	22.9	0.0000	0.0000	0.0000	0.0000	1.5866	0.0000	0.8012	0.0000
	II	0–5	23.2	0.0000	0.0000	0.0000	0.4717	1.2961	0.0000	0.7965	0.0000
	III	0–5	22.9	0.0000	0.0000	0.0000	0.8886	2.4555	0.0000	0.8865	0.0000
	I	5–15	22.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	21.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	22.1	0.0000	0.0000	0.0000	0.0000	1.4005	0.0000	0.0000	0.0000
	I	15–30	20.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	19.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	20.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

^a Sampled immediately after application had dried

^b Anomalous result, sample has been re-analysed to confirm.

LOQ = 1.0 ppb

<LOD = <0.3 ppb

Quantifiable values >LOD but <LOQ are highlighted in bold.

Note: Values have been corrected for moisture content. Therefore in some cases, results are highlighted when >1.0 ppb. This is caused by detected values (uncorrected for moisture) at <1.0 ppb being corrected prior to inclusion in table.

Table 8-119: Average residues summed for all depths in g/ha parent equivalents

Data in grams peq/ha								
Days	DPX-KN128	IN-KG433	IN-JU873	IN-KT413	IN-JT333	IN-MK638	IN-MK643	IN-KB687
0 ^a	446.1494	0.2444	0.0000	10.8023	1.6714	0.0000	0.0000	3.8244
	444.7427	0.3456	0.0000	9.0070	1.8103	0.0000	0.0000	4.8251
	506.3426	0.6150	0.0000	14.5505	2.9081	0.0000	0.0000	5.3964
3	271.8853	2.8012	0.0000	53.3532	8.7782	1.2272	1.2840	5.0103
	230.4486	3.7824	0.0000	56.3932	27.7112	2.4298	3.3170	8.7043
	276.0059	2.1174	0.0000	50.0592	7.5492	0.8658	1.0633	3.5771
7	166.3382	3.3596	0.0000	47.7032	10.3220	1.5708	2.5437	4.6435
	240.8676	5.4480	0.0000	50.6384	14.9311	1.5008	3.3924	4.8098
	202.6294	3.3469	0.0000	38.5330	13.7644	1.2672	3.4761	5.4020
10	157.4267	3.3579	0.0000	30.1348	21.6501	2.4405	5.7079	10.4134

Table 8-119: Average residues summed for all depths in g/ha parent equivalents

Data in grams peq/ha								
Days	DPX-KN128	IN-KG433	IN-JU873	IN-KT413	IN-JT333	IN-MK638	IN-MK643	IN-KB687
	304.1489	3.7474	0.0000	48.4205	22.9102	2.5607	5.7948	10.1420
	223.6039	5.5179	0.0000	45.5893	26.2844	2.8175	4.7548	8.9274
15	2.9923 ^b	0.0000 ^b	0.0000 ^b	1.1413 ^b	0.0000 ^b	0.0000 ^b	0.0000 ^b	0.0000 ^b
	92.5695	2.6332	0.0000	27.2840	22.5234	1.5204	3.7921	4.5168
	121.9338	2.5099	0.0000	42.2827	25.3382	2.0532	4.2970	4.1881
21	60.6333	1.7457	0.0000	33.5943	26.4289	2.2765	5.9676	3.6815
	57.7040	1.7368	0.0000	38.2271	29.2505	2.2303	5.9631	2.7544
	44.7542	1.1470	0.0000	30.6875	22.0671	2.0029	5.1318	3.0355
31	30.5757	0.7858	0.0000	18.3459	26.1833	2.8351	5.7430	2.9970
	22.5422	0.5450	0.0000	12.1789	17.4860	1.7009	4.8229	2.2163
	33.3579	0.8057	0.0000	18.3829	29.9344	2.6955	5.7161	4.3494
50	7.0238	0.0000	0.0000	5.9528	16.7343	1.4377	5.7869	1.0135
	6.0163	0.0000	0.0000	5.3106	15.0351	1.3640	3.8705	0.0000
	8.0420	0.0000	0.0000	7.4570	19.3841	1.3450	4.5767	0.7881
79	2.7888	0.0000	0.0000	4.5096	15.1773	1.0202	4.7137	0.0000
	1.6715	0.0000	0.0000	2.3414	10.7184	0.9738	3.6062	0.0000
	1.5190	0.0000	0.0000	3.3439	10.1762	0.8671	3.6352	0.0000
97	1.1651	0.0000	0.0000	1.9276	10.4589	0.6953	3.5969	0.0000
	1.1896	0.0000	0.0000	3.4236	11.6479	0.6454	3.0885	0.0000
	0.8176	0.0000	0.0000	3.1543	7.4502	0.0000	3.2789	0.0000
155	0.0000	0.0000	0.0000	0.0000	1.3111	0.0000	1.4259	0.0000
	0.0000	0.0000	0.0000	0.3561	1.1159	0.0000	1.4770	0.0000
	0.0000	0.0000	0.0000	0.6523	4.4474	0.0000	1.5985	0.0000

^a Samples taken immediately after application had dried^b Result considered to be an outlier, the results from this replicate have not been included in the kinetics evaluation.**Table 8-120: Residues in entire soil column, shown in percent of applied test substance**

Percent of the applied*								
Days	DPX-KN128	IN-KG433	IN-JU873	IN-KT413	IN-JT333	IN-MK638	IN-MK643	IN-KB687
0	92.1013	0.0505	0.0000	2.2300	0.3450	0.0000	0.0000	0.7895
	91.8109	0.0713	0.0000	1.8594	0.3737	0.0000	0.0000	0.9961
	104.5273	0.1270	0.0000	3.0038	0.6003	0.0000	0.0000	1.1140
3	56.1269	0.5783	0.0000	11.0140	1.8121	0.2533	0.2651	1.0343
	47.5729	0.7808	0.0000	11.6416	5.7206	0.5016	0.6847	1.7969
	56.9775	0.4371	0.0000	10.3340	1.5584	0.1787	0.2195	0.7384
7	34.3382	0.6935	0.0000	9.8477	2.1308	0.3243	0.5251	0.9586
	49.7237	1.1247	0.0000	10.4536	3.0823	0.3098	0.7003	0.9929
	41.8300	0.6909	0.0000	7.9546	2.8415	0.2616	0.7176	1.1152

10	32.4985	0.6932	0.0000	6.2209	4.4694	0.5038	1.1783	2.1497
	62.7873	0.7736	0.0000	9.9957	4.7295	0.5286	1.1963	2.0937
	46.1599	1.1391	0.0000	9.4113	5.4260	0.5816	0.9816	1.8429
15	0.6177	0.0000	0.0000	0.2356	0.0000	0.0000	0.0000	0.0000
	19.1097	0.5436	0.0000	5.6324	4.6496	0.3139	0.7828	0.9324
	25.1715	0.5181	0.0000	8.7287	5.2307	0.4239	0.8871	0.8646
21	12.5169	0.3604	0.0000	6.9351	5.4559	0.4700	1.2319	0.7600
	11.9122	0.3585	0.0000	7.8914	6.0384	0.4604	1.2310	0.5686
	9.2389	0.2368	0.0000	6.3350	4.5554	0.4135	1.2658	0.6266
31	6.3119	0.1622	0.0000	3.7873	5.4052	0.5853	1.1856	0.6187
	4.6535	0.1125	0.0000	2.5142	3.6097	0.3511	0.9956	0.4575
	6.8863	0.1663	0.0000	3.7949	6.1795	0.5565	1.1800	0.8979
50	1.4500	0.0000	0.0000	1.2289	3.4546	0.2768	1.1946	0.2092
	1.2420	0.0000	0.0000	1.0963	3.1038	0.2816	0.7990	0.0000
	1.6601	0.0000	0.0000	1.5394	4.0016	0.2777	0.9448	0.1627
79	0.5757	0.0000	0.0000	0.9309	3.1331	0.2106	0.9731	0.0000
	0.3451	0.0000	0.0000	0.4834	2.2127	0.2010	0.7444	0.0000
	0.3136	0.0000	0.0000	0.6903	2.1007	0.1790	0.7504	0.0000
97	0.2405	0.0000	0.0000	0.3979	2.1591	0.1435	0.7425	0.0000
	0.2456	0.0000	0.0000	0.7067	2.4045	0.1332	0.6376	0.0000
	0.1688	0.0000	0.0000	0.6512	1.5380	0.0000	0.6769	0.0000
155	0.0000	0.0000	0.0000	0.0000	0.2707	0.0000	0.2944	0.0000
	0.0000	0.0000	0.0000	0.0735	0.2304	0.0000	0.3049	0.0000
	0.0000	0.0000	0.0000	0.1347	0.9181	0.0000	0.3300	0.0000

* Calculations based on a total g peq/ha value for parent and metabolites at Day 0, averaged across the 3 reps: 484.41 g peq/ha

Average residues of indoxacarb in the uppermost soil segment (0–5 cm) were 656.9 ppb at Day 0. By Day 7 they had declined to 291.6 ppb, nearly 50% of the amount on Day 0. Indoxacarb residues were not detectable at the end of the study. Only a small amount of indoxacarb residues, <20 ppb, were detected in the next depth (5–15 cm) segment. Only trace amounts, nearing the LOQ of 1.0 ppb were detected in the 15–30 and 30–50 cm segments. No residues were detected below 50 cm.

The first four metabolites in the sequence of degradation of indoxacarb (DPX-KN128), IN-JT333, IN-KG433, IN-KB687, and IN-KT413, were found immediately after the application. IN-JT333 reached an average level of 35.5 ppb in 0–5 cm depth by Day 21. It stayed near 12 ppb through Day 97 and then declined to about 2 ppb by the end of the study. IN-JT333 remained in the upper two depth segments with most of the residue remaining in the 0–5 cm segment. IN-KT413 reached its peak level of about 72.4 ppb by Day 3 and remained in the range 53–67 ppb through Day 21 before declining. IN-KG433 and IN-KB687 only reached a concentration of about 6 ppb by Day 10, and never accounted for any significant portion of the residue. Likewise, IN-MK643 and IN-MK638 were also limited to near the LOQ levels during this whole study. Although IN-MK643 and IN-MK638 were anticipated to be somewhat mobile, no meaningful levels were ever encountered in the lower depths, especially below 5 cm. As stated earlier, IN-JU873 was not detected.

Almost all of the applied test item and its degradation products remained in the upper 15 cm of soil. Detections below 15 cm were infrequent and seldom accounted for more than 1 ppb in any depth segment, and for any individual component. No residues were detected in the depth segments below 50 cm at any sampling interval.

It can be concluded from these data that indoxacarb and its major metabolites were all degrading throughout this study at varying rates. In addition, very little residue moved to depths below 15 cm. Thus, loss of applied material via leaching did not contribute to the dissipation of residue in this study.

Mass balance

In order to quantify the rate of decline of the applied test item, the concentrations of indoxacarb as well as all metabolites, measured in ppb, were converted to mass in grams per unit area (g/ha parent equivalents) and is included in Table 8-119. The residues converted in percent of the applied are presented in Table 8-120.

The residue of indoxacarb expressed as total g peq/ha was averaged 465.7 g peq/ha on Day 0, which was 116% of the target application rate of 400 g a.s./ha. A rapid degradation of the parent compound resulted in the indoxacarb residue declining to an average 203.3 g peq/ha by Day 7 and subsequently to less than 7.0 g peq/ha by Day 50. The parent compound was not detectable by the end of this study.

All degradation products except IN-JU873 were detected during the course of the study. IN-KT413 accounted for the largest proportion of the metabolites observed, reaching a maximum of 56.4 g peq/ha, or 14% of the applied, on Day 3. IN-JT333 accounted for as much as 29.9 g peq/ha (about 7% of the applied mass) at its peak, on Day 31. IN-KG433 accounted for 5.5 g peq/ha (1% of the applied mass) on Day 10. IN-KB687 accounted for 10.4 g peq/ha (3% of the applied mass) on Day 10. IN-MK643 and IN-MK638 also reached a maximum of 5.7 g peq/ha (1.4% of the applied mass) and 2.7 g peq/ha (0.7% of the applied mass) respectively of the applied mass in the entire soil column at Days 21 and 31, respectively, while IN-JU873 was not detected.

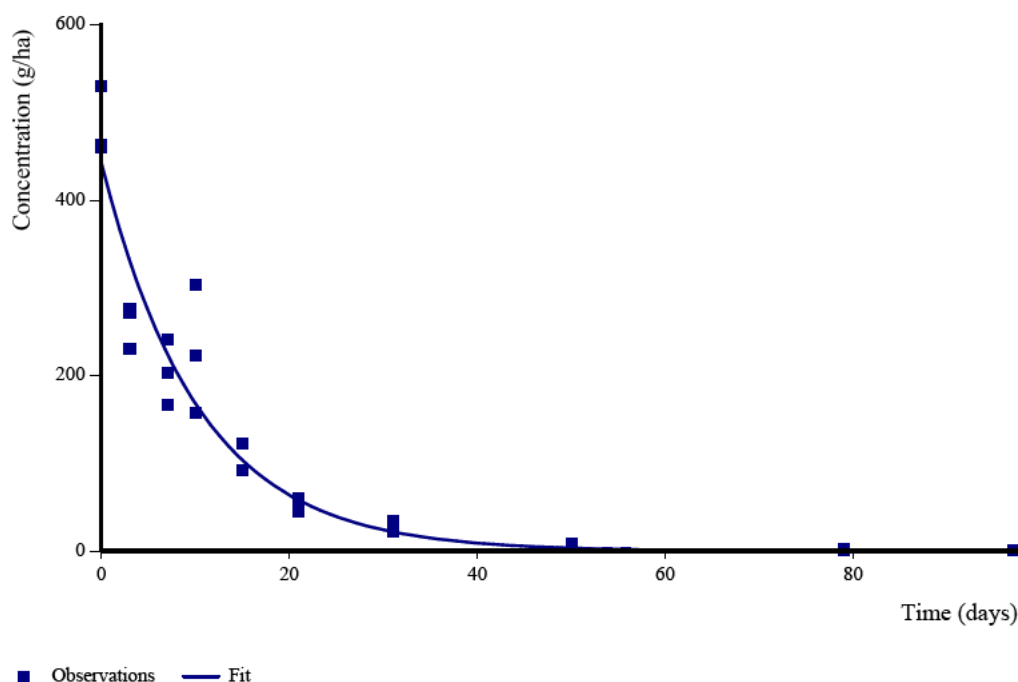
Decline of not only the parent compound, but all the metabolites observed underlines the degradation of all monitored components under field conditions.

Dissipation Kinetics

The total soil column residues in Table 8-120 were analysed for the decline rates using CAKE. The decline rate for indoxacarb using the single first order (SFO) kinetics model gave a DT_{50} of 7.16 days.

Kinetic model	χ^2 error	r^2	DT_{50} (days)	DT_{90} (days)
SFO	19.4	0.92	7.16	23.8

Figure 4: Decline of indoxacarb (DPX-KN128) in Termens, Spain



CONCLUSIONS

There were no abnormal circumstances with respect to test site management, climate conditions or analysis which would compromise the conclusions drawn or the data collected.

The application monitors as well as the soil residues on Day 0 confirmed the nominal application rate. Averaged recoveries of indoxacarb on Day 0 were 118% based on the application monitor analysis.

Indoxacarb declined rapidly to *ca* 50% of the initial concentration within the first 7 days after application and became undetectable by the end of the study (155 days).

All metabolites monitored (IN-KT413, IN-JU873, IN-JT333, IN-KG433, IN-KB687, IN-MK463, and IN-MK638) with the exception of IN-JU873 were detected at some sampling intervals during this study. IN-KT413 accounted for the largest proportion of the metabolites observed, reaching a maximum of 14% of the applied; IN-JT333 and IN-MK643 reached above 5% but less than 10% of the applied mass; the remaining components did not exceed 5% of the applied mass.

Almost all of the applied test item and its degradation products remained in the upper 15 cm of soil. Detections below 30 cm were infrequent and never accounted for more than 1% of the applied amount in any depth segment, and for any individual component. Thus, loss of applied material via leaching did not contribute to the dissipation of residue in this study.

A DT_{50} of 7.16 days and a DT_{90} of 23.8 days was calculated for the parent compound, demonstrating a rapid dissipation of indoxacarb under field conditions.

Comments (RMS 2016)

This study was conducted with the active isomer DPX-KN128 as test material and is acceptable.

The same comments as made for previous study (Doig 2015d) can be made and are repeated here:

The level of residues observed at different depths confirm the rapid degradation of active substance (active isomer DPX-KN128) and the low potential of leaching of active substance and all its major metabolites, as none or very few residues of any compound were observed below 15 cm during the all course of the study.

No accumulation potential is detected for any of the compound, with the exception of IN-MK643 that seems to be quite persistent. However, this accumulation potential was already identified in the laboraoty (with

persistence DT₅₀ of 314 days), and is taken into account in soil risk assessment with calculation of PEC_{accumulation}.

It is noticeable that the metabolite IN-JU873 is not detected in this field trial although being a major metabolite in laboratory. However, laboratory data tend to show that this metabolite is quite transient (it is detected at level > 10% at only one sampling time among all studies). As mentioned by applicant, it is believed that this metabolite may have formed in the field at level below the LOD.

Degradation rate were only provided for active substance. On the more no normalized DT₅₀ are available. This could have been done, since the study was conducted according to EFSA guidance (2010) to minimize surface processes (11 mm of irrigation applied to the test plot within 24 hours after 1st application).

As first approximation, from the daily soil temperature monitored in field, and the moisture content of the samples, it can be seen that:

- Soil temperature was always between 20 and 25°C during the first month (almost no residue after 30 days)
- Samples moisture was always < soil moisture at pF2.5, i.e soil correction factor from pF2 would always be <1.

If we consider as first approach that no moisture normalization is needed, and the the DT₅₀ could be normalised as worst-case to 25°C, the normalised DT₅₀ would be 11.3 days.

However, since irrigation was made after 1st sapling at days 0, normalised DT₅₀ should be derived from DAT3.

Data point:	CA 7.1.2.2.1/01
Author(s)	Doig, A. (2015a);
Title:	The field soil dissipation of indoxacarb (DPX-KN128) following a single application to bare ground - Italy - 2012
Organisation:	Charles River Laboratories (UK), Tranent, Scotland, UK
Document No:	DuPont-34346
Dates of experimental work	
Guidelines:	OPPTS 835.6100, SETAC Europe (1995), SANCO/3029/99 rev. 4 (2000), EU 1607/VI/97 Rev 1 (1997), EU 7029/VI/1995 Rev 5 (1997)
Deviations :	None
GLP:	Yes
Previous evaluation:	No
Acceptability:	The study is considered valid.

This report describes the soil dissipation of a single application of indoxacarb (DPX-KN128) to bare ground studied under field conditions in Graffignana, Italy, for *ca.* 5 months after application on 18-May-2012.

The study design consisted of three replicate treated bare soil plots and a control (untreated) bare soil plot. The test site soil was characterised as loam in horizons 0–5, 5–15, 15–30, and 30–50 cm, and sandy loam at 50–70 cm and clay loam at 70–90 cm. The test item was applied at a nominal rate of 400 g a.s./ha which was the highest proposed use rate for indoxacarb per year. Actual application based on the amount of spray solution applied and the output from calibrated spray equipment used indicated application at 97.2–103.4% of the targeted application rate in all three treated plots. The application method was representative of the proposed commercial use of this product.

Soil samples were analysed for residues of indoxacarb and all significant soil metabolites, IN-KG433, IN-JU873, IN-KB687, IN-KN125 (a racemic mixture IN-JT333 was used as reference standard for its S-enantiomer IN-KN125 analysis), IN-MK638, IN-MK643, and IN-KT413 (quantified as IN-MP819).

Fresh fortified samples of control soil were analysed concurrently with each set of treated samples. Each analysis set included fresh fortifications ranging from the LOQ level up to 10 ppb. Residues were routinely detected above 10 ppb throughout the course of this study therefore an additional ‘high recovery’ batch containing three fortified control samples at 700 ppb was performed. The average recoveries of the fresh

fortification samples analysed concurrently with the analysis of the field samples are summarised in the table below.

Analyte	Average recovery (%)	Relative standard deviation (%)
Indoxacarb (DPX-KN128)	101	12.5
IN-KG433	84.8	13.4
IN-JU873	98.5	9.4
IN-KT413	76.3	18.6
IN-JT333	99.0	10.0
IN-MK638	113	8.3
IN-MK643	114	8.7
IN-KB687	110	11.0

The LOQ and LOD were 1.0 and 0.3 ppb, respectively, for each component

Soil samples from all sampling events were generally analysed to the depth increment at which the residues found indicated no reasonable expectation of residues in lower depths. Residues were determined in ppb and then converted to g peq/ha for every sample analysed. Post application (Day 0) soil residues in the 0-5 cm samples ranged from 358.2–424.4 g peq/ha for indoxacarb.

Residues of indoxacarb declined rapidly throughout this study. Average residue (summed for all soil depths) declined to about half the applied amount 181.7 g peq/ha by Day 7 and to less than 5% of applied (17.2 g peq/ha) by Day 50. Beyond Day 76, average residues of indoxacarb were below 5 g peq/ha, declining to 1.0 g peq/ha by Day 145.

The storage period between sampling in the field and analyte extraction did not exceed 341 days for all samples analysed. A separate storage stability study (DuPont-35167, Point CA 7.1.2.2.1) demonstrated that indoxacarb and its metabolites were stable during the maximum storage period, except IN-KT413.

MATERIALS AND METHODS

- Test material: Indoxacarb 30WG
 Lot/Batch #: KN128-298
 Purity: 300 g a.s./kg
 Description: White solid
 CAS#: 173584-44-6 for indoxacarb the active substance
 None for the formulation
 Stability of test compound: Shown to be stable under the conditions of the test

2. Test Site

Test site description is detailed in Table 8-121. Soil samples collected to 90 cm depth were characterised and the soil characterisation data are included in Table 8-122.

Table 8-121: Test site description

Location:	Graffignana
Country:	Italy
GPS coordinates	N 45° 18.372' and E 009° 26.718'.
Representative crop region	Southern Europe
Site selection criteria	The field site was flat and level and allowed soil sampling down to 90 cm. The site had good security and was readily able to be remarked if required. The site was free from flooding risk.
Weather station	CWi technical on site weather station.
Pre-treatment exclusion criteria	No other chemical of similar structure applied during the

	past 3 years.
Plot history, crops grown	maize 2011, wheat 2009/2010, maize 2009.
Pesticides used in preceding 3 years	2012: glyphosate (360 g/L) 2011: s-metolachlor + terbuthazine (28.9% + 17.4%) 2010: MCPA (25%)
Location/identification of weather station	CWi technical on site weather station.
Distance of weather station from test site	On site
Depth to ground water table	Not defined

Table 8-122: Soil properties at Graffignana, Italy

Soil property	Soil depth (cm)					
	0–5	5–15	15–30	30–50	50–70	70–90
Sand % (0.05–2 mm) ^a	45	45	45	47	67	31
Silt % (0.05–0.002 mm) ^a	38	36	38	36	20	34
Clay % (<0.002 mm) ^a	17	19	17	17	13	35
pH (water, 1:1)	5.9	5.9	6.1	6.1	6.3	6.3
% Organic matter ^b	1.7	1.6	1.7	1.3	0.34	0.34
C.E.C [meq/100g] ^c	9.7	10.0	9.6	9.3	6.9	12.9
Bulk density (g cm ⁻³)	1.22	1.20	1.19	1.24	1.25	1.17
Moisture holding capacity at 1/3 bar (% of dry weight)	17.5	18.4	20.0	17.5	11.2	23.4
Moisture holding capacity at 15 bar (% of dry weight)	6.6	7.0	6.9	6.6	5.2	11.8
Soil classification ^d	Loam	Loam	Loam	Loam	Sandy loam	Clay loam
Microbial biomass carbon (µg/g dry basis, 0–25cm depth)	124.9					

^a Particle size^b Walkley-Black method^c Cation Exchange Capacity (C.E.C)^d Soil classification according to USDA system

Experimental design

The experimental details for the test substance application, application rate, application method, *etc.*, are included in Table 8-123 below.

Soil sampling

Soil sampling intervals and the sampling depths, and number of cores collected are listed in Table 8-124.

Description of analytical methods

Soil samples were analysed for residues of indoxacarb and all significant soil metabolites, IN-KG433, IN-JU873, IN-KB687, IN-KN125 (a racemic mixture IN-JT333 was used as reference standard for its S-enantiomer IN-KN125 analysis), IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819).

Soil samples were extracted by a 3 step sequential extraction procedure using acetonitrile and 0.025% acetic acid solutions. The extracts were combined and diluted to 50 mL with acetonitrile. An aliquot was removed from each extract and transferred to a glass culture tube, capped and placed in a heating block set to 55°C for 1 hour to quantitatively convert IN KT413 to IN MP819. This was then evaporated to 0.5 mL, adjusted to 0.7 mL with acetonitrile and diluted to 3mL with water prior to analysis. These samples were then analysed using reverse phase HPLC separation coupled to tandem mass spectrometry (LC MS/MS). The Limit of Quantification (LOQ) for all analytes was 1.0 ppb, which was sufficient to quantify □0.2% of the nominal applied amount.

The final purified extracts were quantified for indoxacarb (DPX-KN128) and its metabolites by liquid chromatography with tandem mass spectrometry employing turbo ion spray ionisation in positive and negative mode.

The indoxacarb (DPX-KN128), IN-KG433, IN-JU873, IN-KT413, IN-JT333, IN-MK638, IN-MK643, and IN-KB687 peak areas were calculated for the target ion for each of the calibration standards, quality control

samples, control samples, and unknown test samples. A calibration curve was then obtained by weighted least squares linear regression analysis ($1/x$) of the plot peak area versus the concentration of concentration of indoxacarb, IN-KG433, IN-JU873, IN-KT413, IN-JT333, IN-MK638, IN-MK643, and IN-KB687 in each calibration standard. The concentrations (ppb) of indoxacarb and its degradation products were calculated using the calibration curve. The concentrations (ppb) of indoxacarb and its degradation products in treated field soil samples were calculated on a dry weight basis. The peak areas were calculated for target ion for indoxacarb, IN-KG433, IN-JU873, IN-KT413, IN-JT333, IN-MK638, IN-MK643, and IN-KB687, for each of the calibration standards, quality control samples, control samples and unknown test samples in one analytical run.

The limit of quantification (LOQ) for indoxacarb and its metabolites IN-KG433, IN-JU873, IN-KB687, IN-JT333, IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819) was 1.0 ppb since this was the lowest validated level. The limit of detection (LOD) was determined to be 0.3 ppb for indoxacarb and its metabolites IN-KG433, IN-JU873, IN-KB687, IN-JT333, IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819). The LOD was determined as the sample concentration equivalent to the lowest calibration standard (1.0 $\mu\text{g/kg}$).

Soil moisture was determined for each sample extracted by drying the sample to at 110°C , and determining the loss of weight. Moisture data were used to convert wet weight ppb residues into dry weight ppb.

The ppb residues for parent compound and each degradation product in each sample were converted to g/ha parent equivalents by multiplying the molar amounts of each analyte by the parent compound molecular weight to obtain parent equivalent mass. The parent equivalent masses were further multiplied by the total calculated soil in one hectare at each depth for conversion to g a.s./ha for the parent and each degradation product at each depth.

Table 8-123: Experimental design, plot set up and application details

Details	Graffignana, Italy
Duration of study	356 days
Uncropped (bare) or cropped	Bare, maintained weed free
Controls used	Yes
Number of plot(s)	3 treated (Replicates I, II, and III) and 1 untreated control
Treated plot dimensions	3 m \times 30 m
Untreated control plot dimensions	3 m \times 7.5 m
Distance between control plot and treated plot	10 m
Distance between treated plots	3 m
Application rate used (g a.s./ha)	400 g a.s./ha, nominal, Application by two passes in opposite directions
Was the maximum label rate per ha used in study?	Yes
Application date(s)	18-May-2012
Application method	Ground-directed boom broadcast spray
Type of spray equipment	Backpack sprayer with Lurmark 02F110 Flat Fan, 6 Spray nozzles, 3 m swath width.
Volume of spray solution applied/plot	389-414 L/ha
Identification and volume of carrier (e.g., water), if used	Water
Monthly weather reports included (yes/no)	Yes, also daily weather data
Pan evaporation data available?	No
Meteorological conditions during application	
Cloud cover (%)	0
Temperature (air)	22.5 $^{\circ}\text{C}$
Relative humidity (%)	30
Wind speed	0.3 meters/sec
Sunlight (hr) [time required for application]	Unknown
Irrigation to supplement natural precipitation (17-May-2012 to 09-May-2013)	1074.0 mm
Rainfall (17-May-2012 to 09-May-2013)	838.6 mm

Verification of application	Plastic Petri dishes (approximately 9 cm diameter).
Field spikes (transit stability samples)	None; Day 0 sample and application monitor analyses confirmed transit stability
Additional modules added to study: run-off, leaching, volatilisation	None; however, test placed on flat site with little risk of flooding to control run-off. Soil sampling to 90 cm (36 in.) to measure movement in soil

Table 8-124: Soil sampling details

Details	Graffignana, Italy
Method of sampling (random or systematic)	Random
Sampling intervals (days)	-0, +0 ^a , 4, 7, 10, 15, 20, 31, 50, 76, 102, 145, 204, 252, 299, and 356 ^b
Method of soil collection	The 0–5 cm segment was sampled using a metal cylinder with an inner diameter of 9.5 cm driven 5 cm into the soil and the soil was then scooped out by hand using a spoon. The metal cylinder remained in place during collection of the lower depths to prevent treated soil from falling onto the sampling area and potentially contaminating the lower depths. Soil cores for the 5–90 cm depths were taken with a Humax [®] coring system with an inner diameter of 5 cm. This allowed sampling of the lower depths in increments of 5–15, 15–30, 30–50, 50–70, and 70–90 cm segments.
Sampling depth	Nominally to 90 cm depth
Number of cores collected per plot	5 per replicate plot, 15 per time point total
Depth and diameter of segments	0–5 cm (9.5 cm diameter) 5–15 cm (5 cm diameter) 15–30 cm (5 cm diameter) 30–50 cm (5 cm diameter) 50–70 cm (5 cm diameter) 70–90 cm (5 cm diameter)
Storage conditions	Frozen
Maximum storage length	341 days

^a Just after application^b Sample analysis was terminated early at Day 145 due to rapid dissipation of DPX-KN128 and its metabolites

RESULTS AND DISCUSSION

Application verification

Application was targeted at a rate of 400 g a.s./ha. The mean actual application rate was 399.81 g a.s./ha (100% of the intended application rate, calculated from the boom output). The test material application rate was monitored with the aid of Petri dishes placed in randomly chosen locations in each of the treated plots. The mean recovery of indoxacarb, as calculated from application monitors, was 467.1 g peq/ha, or 117% of target rate.

The residues in soil on Day 0 also served to confirm the actual application rate. Residues of indoxacarb in the 0–5 cm samples ranged from 358.2–414.4 peq/ha in the Day 0 soil samples. Averaged residue of indoxacarb in 0–5 cm soil on Day 0 was 377.4 g peq/ha in the three replicate soil samples, which represented 94.3% of the target application rate.

Residue decline

Residues in ppb dry weight basis are listed in Table 8-125.

Table 8-125: Average residues at each depth (ppb dry weight basis)

DAT (Days)	Rep	Depth (cm)	% Moist (dwb)	DPX- KN128 (ppb)	IN- KG433 (ppb)	IN- JU873 (ppb)	IN- KT413 (ppb)	IN- JT333 (ppb)	IN- MK638 (ppb)	IN- MK643 (ppb)	IN- KB687 (ppb)
0 ^a	I	0–5	5.7	692.2293	0.7516	0.0000	5.3653	7.0639	0.0000	0.0000	10.6863
	II	0–5	5	668.6400	0.5708	0.0000	5.4275	5.2658	0.0000	0.0000	9.5561
	III	0–5	3.7	749.7510	0.6757	0.0000	5.5065	4.9081	0.0000	0.0000	9.0955
	I	5–15	14.5	17.1636	0.0000	0.0000	0.6409	0.7201	0.0000	0.0000	0.4760
	II	5–15	12.8	14.9347	0.0000	0.0000	0.0000	0.4192	0.0000	0.0000	0.0000
	III	5–15	13.5	11.7586	0.0000	0.0000	0.6928	0.6245	0.0000	0.0000	0.0000
	I	15–30	16.4	0.6476	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	14.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	16.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30–50	15.1	0.3676	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	13.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	13.1	0.6856	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
4	I	0–5	22.9	455.5903	2.7247	0.0000	44.8093	24.9364	0.4057	0.0000	5.5465
	II	0–5	22.9	437.2782	2.8488	0.0000	70.1145	24.0761	0.3917	0.0000	6.2876
	III	0–5	24.4	342.3488	2.0725	0.0000	65.1980	21.0485	0.0000	0.0000	4.1139
	I	5–15	22.3	6.8464	0.0000	0.0000	1.5703	0.4965	0.0000	0.0000	0.0000
	II	5–15	23.7	9.4346	0.0000	0.0000	2.5173	0.7869	0.0000	0.0000	0.0000
	III	5–15	25.8	5.7340	0.0000	0.0000	2.4267	0.4651	0.0000	0.0000	0.0000
	I	15–30	22.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	20.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	23.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
7	I	0–5	12	322.1120	2.2579	0.0000	56.0784	47.4880	1.1514	2.8605	6.2877
	II	0–5	12.4	394.4116	2.7988	0.0000	68.2156	51.4118	1.4724	3.8418	4.9276
	III	0–5	10	313.8300	2.0031	0.0000	74.3050	40.2600	1.2518	3.6003	5.5517
	I	5–15	18	2.2573	0.0000	0.0000	0.5946	0.5196	0.0000	0.0000	0.0000
	II	5–15	18.5	1.2762	0.0000	0.0000	0.4709	0.0000	0.0000	0.0000	0.0000
	III	5–15	19.8	6.0355	0.0000	0.0000	0.9812	0.8190	0.0000	0.0000	0.0000
	I	15–30	18.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	19.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	19.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
10	I	0–5	9.3	391.4033	3.0396	0.0000	48.8571	56.1256	1.7324	6.0924	12.4493
	II	0–5	9.1	384.5775	2.6577	0.0000	51.3206	59.0231	1.9693	8.2250	9.6608
	III	0–5	10.6	260.0206	2.3646	0.0000	35.0713	39.5837	1.6833	6.5840	8.6567
	I	5–15	18.4	5.9792	0.0000	0.0000	0.9265	0.9886	0.0000	0.0000	0.0000
	II	5–15	15.8	16.7215	0.0000	0.0000	2.1794	2.9575	0.0000	0.3680	0.3688
	III	5–15	19.4	8.7568	0.0000	0.0000	0.9651	1.3170	0.0000	0.0000	0.0000
	I	15–30	18.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	18	0.4506	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	19.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

	I	30–50	18.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	18.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	18	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
15	I	0–5	7.7	210.5535	3.0835	0.4305	23.0478	49.2404	3.3215	13.3763	30.9961
	II	0–5	6.4	132.5744	1.7013	0.0000	9.7569	38.6445	1.6928	7.8406	11.5550
	III	0–5	7.7	145.3950	1.7943	0.0000	19.5583	45.3094	2.4749	8.2455	13.4087
	I	5–15	14	2.7314	0.0000	0.0000	0.5428	0.9332	0.0000	0.0000	0.0000
	II	5–15	14.9	1.0415	0.0000	0.0000	0.0000	0.3510	0.0000	0.0000	0.0000
	III	5–15	15.9	3.3901	0.0000	0.0000	0.5362	1.2529	0.0000	0.0000	0.5804
	I	15–30	17.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	14.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	16.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
20	I	0–5	9.5	157.7895	2.1309	0.0000	25.8420	52.6476	1.9885	9.1673	9.8747
	II	0–5	9	109.0000	1.5936	0.0000	8.1914	37.4197	2.0797	9.6781	5.7192
	III	0–5	9	98.9393	1.6470	0.0000	10.8837	34.8473	1.8476	8.7244	6.0560
	I	5–15	15.2	0.6139	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	5–15	14.4	2.2651	0.0000	0.0000	0.4464	1.1022	0.0000	0.0000	0.3851
	III	5–15	13.7	3.4872	0.0000	0.0000	0.5232	1.2200	0.0000	0.3680	0.0000
	I	15–30	16.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	17.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	17.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
31	I	0–5	5.5	84.3367	1.5962	0.0000	12.4596	42.6326	2.9614	13.9577	5.6527
	II	0–5	4.6	83.9833	1.2855	0.0000	10.5437	38.9217	2.5470	13.8595	5.4287
	III	0–5	2.7	58.6931	1.1112	0.0000	12.0981	31.8575	2.9896	15.9390	3.4723
	I	5–15	13.1	4.2333	0.0000	0.0000	0.7269	1.8662	0.0000	0.9308	0.0000
	II	5–15	11	0.8742	0.0000	0.0000	0.0000	0.4030	0.0000	0.0000	0.0000
	III	5–15	12.5	1.5480	0.0000	0.0000	0.6054	0.7967	0.0000	0.4869	0.0000
	I	15–30	13.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	11.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	13.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
50	I	0–5	10.4	40.4726	0.7975	0.0000	12.1330	26.3194	3.2336	12.6739	3.3396
	II	0–5	9.2	25.3016	0.4697	0.0000	7.5119	25.6511	2.3565	10.6459	1.6609
	III	0–5	8.5	24.7923	0.4489	0.0000	4.9183	24.5427	2.3946	10.2869	2.0365
	I	5–15	12.1	0.7318	0.0000	0.0000	0.0000	0.4671	0.0000	0.0000	0.0000
	II	5–15	10.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	9.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15–30	13.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	11.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	10.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
76	I	0–5	7.2	6.7611	0.0000	0.0000	5.5487	14.5578	0.9694	5.6473	0.4365
	II	0–5	7	6.8748	0.0000	0.0000	2.6215	9.5027	0.6928	4.5903	0.4474
	III	0–5	7.7	10.1087	0.0000	0.0000	5.8384	17.7597	1.4238	9.8449	0.5219

	I	5–15	13.2	0.0000	0.0000	0.0000	0.0000	0.3892	0.0000	0.9135	0.0000
	II	5–15	12.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.7790	0.0000
	III	5–15	12.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.7248	0.0000
	I	15–30	16.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	15.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	15.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
102	I	0–5	2.3	4.1503	0.0000	0.0000	1.5232	8.6791	0.9075	4.6812	1.5949
	II	0–5	1.8	4.2675	0.0000	0.0000	1.7153	6.7259	0.7969	6.1701	1.2145
	III	0–5	1.4	6.9611	0.0000	0.0000	2.8017	11.4582	1.3263	8.7630	1.3547
	I	5–15	7.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.7637	0.0000
	II	5–15	7.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.5741	0.0000
	III	5–15	7.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.3935	0.0000
	I	15–30	12.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	9.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	9.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
145	I	0–5	7.6	2.2155	0.0000	0.0000	0.8709	2.4866	0.0000	3.5637	0.3865
	II	0–5	5.2	0.9889	0.0000	0.0000	0.4565	1.5759	0.0000	2.0640	0.0000
	III	0–5	5.5	1.9307	0.0000	0.0000	0.8177	2.7198	0.0000	3.5754	0.0000
	I	5–15	12.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.4926	0.0000
	II	5–15	9.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	9.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15–30	11.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	9.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	9.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

^a Sampled immediately after application had dried

LOQ = 1.0 ppb

<LOD = <0.3 ppb

Quantifiable values >LOD but <LOQ are highlighted in bold.

Note: Values have been corrected for moisture content therefore in some cases, results are highlighted when >1.0 ppb. This is caused by detected values (uncorrected for moisture) at <1.0 ppb being corrected prior to inclusion in table.

Table 8-126: Average residues summed for all depths in g/ha parent equivalents

Data in grams peq/ha								
Days	DPX-KN128	IN-KG433	IN-JU873	IN-KT413	IN-JT333	IN-MK638	IN-MK643	IN-KB687
0 ^a	382.4642	0.3994	0.0000	3.5234	5.1192	0.0000	0.0000	13.7734
	379.2539	0.3129	0.0000	2.8646	3.8328	0.0000	0.0000	11.4916
	430.1098	0.3822	0.0000	3.8186	3.8912	0.0000	0.0000	11.2855
4	255.5940	1.5126	0.0000	25.8538	15.8867	0.1264	0.0000	6.7540
	270.0859	1.7169	0.0000	43.9794	17.1075	0.1325	0.0000	8.3119
	187.4177	1.1151	0.0000	36.8630	13.1100	0.0000	0.0000	4.8551
7	171.8143	1.2101	0.0000	29.7418	28.7489	1.4458	3.6251	7.3916
	192.3301	1.3845	0.0000	33.0905	27.9248	1.7067	4.4942	5.3470
	180.8705	1.1319	0.0000	41.6354	26.1326	1.6575	4.8110	6.8816

10	204.5621	1.5662	0.0000	25.3772	33.1417	2.0915	7.4230	14.0702
	173.6183	1.0766	0.0000	22.7087	30.4219	1.8691	8.9964	9.6232
	133.6377	1.1471	0.0000	17.5052	22.8360	1.9134	7.5530	9.2118
15	102.4860	1.4888	0.2342	11.3277	27.3087	3.7575	15.2723	32.8274
	78.8802	1.0197	0.0000	5.6296	25.8967	2.3772	11.1121	15.1907
	86.2570	1.0437	0.0000	11.5148	30.4361	3.3731	11.3415	18.4955
20	95.8202	1.3112	0.0000	15.3091	35.5706	2.8670	13.3396	13.3287
	60.4379	0.8611	0.0000	4.8201	23.7750	2.6332	12.3670	7.8771
	62.1526	0.9789	0.0000	6.9202	24.5827	2.5730	13.4585	7.8958
31	44.1599	0.7508	0.0000	6.5545	24.6887	3.2636	18.3948	5.8319
	40.7675	0.6194	0.0000	4.8907	21.2243	2.8754	15.7908	5.7375
	26.9238	0.4824	0.0000	5.8358	16.3553	3.0410	17.9028	3.3066
50	22.6252	0.4391	0.0000	6.4311	16.5195	4.1715	16.5008	4.0332
	15.3850	0.2922	0.0000	4.4998	17.5244	3.4356	15.6641	2.2669
	13.6245	0.2524	0.0000	2.6627	15.1536	3.1551	13.6793	2.5121
76	3.5141	0.0000	0.0000	2.8411	8.9764	1.2081	9.5048	0.5093
	3.4280	0.0000	0.0000	1.2877	5.3237	0.8283	7.7523	0.5007
	5.4956	0.0000	0.0000	3.1269	10.8478	1.8559	14.7615	0.6369
102	1.9375	0.0000	0.0000	0.7006	4.5524	1.0158	8.2189	1.6712
	2.0138	0.0000	0.0000	0.7975	3.5661	0.9016	9.6140	1.2864
	3.3414	0.0000	0.0000	1.3248	6.1794	1.5264	11.6314	1.4596
145	1.1923	0.0000	0.0000	0.4617	1.5035	0.0000	6.5062	0.4669
	0.6262	0.0000	0.0000	0.2848	1.1213	0.0000	3.1629	0.0000
	1.2593	0.0000	0.0000	0.5255	1.9932	0.0000	5.6433	0.0000

^a Samples taken immediately after application had dried

Table 8-127: Residues in entire soil column, shown in percent of applied test substance

Percent of the applied*								
Days	DPX-KN128	IN-KG433	IN-JU873	IN-KT413	IN-JT333	IN-MK638	IN-MK643	IN-KB687
0	91.6065	0.0957	0.0000	0.8439	1.2261	0.0000	0.0000	3.2990
	90.8376	0.0749	0.0000	0.6861	0.9180	0.0000	0.0000	2.7524
	103.0185	0.0915	0.0000	0.9146	0.9320	0.0000	0.0000	2.7031
4	61.2190	0.3623	0.0000	6.1924	3.8051	0.1264	0.0000	1.6177
	64.6901	0.4112	0.0000	10.5338	4.0975	0.1325	0.0000	1.9908
	44.8896	0.2671	0.0000	8.8293	3.1401	0.0000	0.0000	1.1629
7	41.1524	0.2898	0.0000	7.1237	6.8858	0.3463	0.8683	1.7704
	46.0662	0.3316	0.0000	7.9257	6.6884	0.4088	1.0764	1.2807
	43.3215	0.2711	0.0000	9.9724	6.2592	0.3970	1.1523	1.6483
10	48.9960	0.3751	0.0000	6.0783	7.9380	0.5009	1.7779	3.3701
	41.5845	0.2579	0.0000	5.4391	7.2866	0.4477	2.1548	2.3049
	32.0085	0.2748	0.0000	4.1928	5.4696	0.4583	1.8091	2.2064

15	24.5471	0.3566	0.0561	2.7132	6.5409	0.9000	3.6580	7.8627
	18.8931	0.2442	0.0000	1.3484	6.2027	0.5694	2.6615	3.6384
	20.6600	0.2500	0.0000	2.7580	7.2899	0.8079	2.7165	4.4300
20	22.9505	0.3141	0.0000	3.6668	8.5198	0.6867	3.1951	3.1924
	14.4759	0.2063	0.0000	1.1545	5.6945	0.6307	2.9621	1.8867
	14.8866	0.2345	0.0000	1.6575	5.8880	0.6163	3.2235	1.8912
31	10.5770	0.1798	0.0000	1.5699	5.9134	0.7817	4.4059	1.3968
	9.7645	0.1484	0.0000	1.1714	5.0836	0.6887	3.7822	1.3742
	6.4487	0.1155	0.0000	1.3978	3.9174	0.7284	4.2880	0.7920
50	5.4191	0.1052	0.0000	1.5403	3.9567	0.9991	3.9522	0.9660
	3.6850	0.0700	0.0000	1.0778	4.1974	0.8229	3.7518	0.5430
	3.2633	0.0605	0.0000	0.6378	3.6295	0.7557	3.2764	0.6017
76	0.8417	0.0000	0.0000	0.6805	2.1500	0.2894	2.2766	0.1220
	0.8211	0.0000	0.0000	0.3084	1.2751	0.1984	1.9047	0.1199
	1.3163	0.0000	0.0000	0.7489	2.5982	0.4445	3.5356	0.1525
102	0.4641	0.0000	0.0000	0.1678	1.0904	0.2433	1.9686	0.4003
	0.4824	0.0000	0.0000	0.1910	0.8542	0.2160	2.3027	0.3081
	0.8003	0.0000	0.0000	0.3173	1.4801	0.3656	2.7859	0.3496
145	0.2856	0.0000	0.0000	0.1106	0.3601	0.0000	1.5583	0.1118
	0.1500	0.0000	0.0000	0.0682	0.2686	0.0000	0.7576	0.0000
	0.3016	0.0000	0.0000	0.1259	0.4774	0.0000	1.3517	0.0000

* Calculations based on a total g peq/ha value for parent and metabolites at Day 0, averaged across the 3 reps: 417.6g peq/ha

Six of the seven metabolites monitored were detected at some sampling intervals during this study with only IN-JU873 undetected at any sampling interval. The first four metabolites in the sequence of degradation of indoxacarb (DPX-KN128), IN-JT333, IN-KG433, IN-KB687, and IN-KT413, were found immediately after the application. IN-KT413 accounted for the largest proportion of the metabolites observed, reaching a maximum of 9% of the applied; IN-JT333, IN-KB867, and IN-MK643 reached above 4% but less than 8% of the applied mass; the remaining components did not exceed 5% of the applied mass. IN-JT333 reached an average peak level of 28.8 g peq/ha by Day 10 and declined thereafter, IN-KG433 reached an average peak level of 1.4 g peq/ha by Day 4 and declined thereafter, IN-KB687 reached an average peak level of 22.2 g peq/ha by Day 15 and declined thereafter, IN-MK643 reached an average peak level of 17.4 g peq/ha by Day 31 and declined thereafter, IN-MK638 reached an average peak level of 3.6 g peq/ha by Day 50 and declined thereafter, while IN-KT413 reached its peak level of 35.6 g peq/ha by Day 4, and then declined. As stated earlier, IN-JU873 was not detected.

Almost all of the applied test item and its degradation products remained in the upper 15 cm of soil. Detections below 30 cm were infrequent and never accounted for more than 1% of the applied amount in any depth segment, and for any individual component. Residue analysis was not conducted below 50 cm.

Decline of not only the parent compound, but all the metabolites observed underlines the degradation of all monitored components under field conditions. Almost all of the applied test item and its degradation products remained in the upper 15 cm of soil. Detections below 15 cm were infrequent and seldom accounted for more than 1 ppb in any depth segment, and for any individual component. No residue analysis was conducted below 50cm.

It can be concluded from these data that indoxacarb and its major metabolites were all degrading throughout this study at varying rates. In addition, very little residue moved to depths below 15 cm. Thus, loss of applied material via leaching did not contribute to the dissipation of residue in this study.

Mass balance

In order to quantify the rate of decline of the applied test item, the concentrations of indoxacarb as well as all metabolites, measured in ppb, were converted to mass in grams per unit area (g/ha parent equivalents) and is included in Table 8-126. Residues in percent of the applied were converted in Table 8-127.

Residues of indoxacarb declined rapidly throughout this study. Average residue (summed for all soil depths) declined to about half the applied amount, 181.7 g peq/ha by Day 7 and to less than 5% of applied (17.2 g peq/ha) by Day 50. Beyond Day 76, average residues of indoxacarb were below 5 g peq/ha, declining to 1.0 g peq/ha by Day 145.

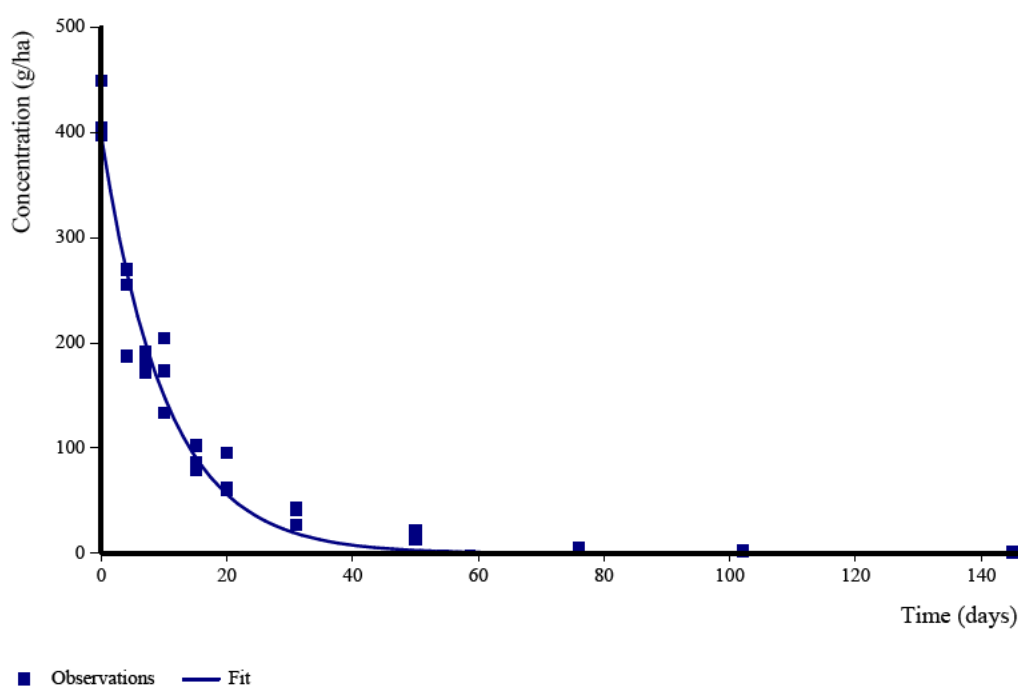
All degradation products except IN-JU873 were detected during the course of the study. IN-KT413 accounted for the largest proportion of the metabolites observed, reaching a maximum of 35.6 g peq/ha, or 8.9% of the applied, on Day 4. IN-JT333 accounted for as much as 28.8 g peq/ha (about 7.2% of the applied) at its peak, on Day 10. IN-KG433 accounted for 1.4 g peq/ha (0.35% of the applied mass) on Day 4. IN-KB687 accounted for 22.2 g peq/ha (5.6 % of the applied mass) on Day 15. IN-MK643 and IN-MK638 also reached a maximum of about 17.4 g peq/ha at Day 31 (*ca* 4.4% of the applied mass) and 3.6 g peq/ha at Day 50 (*ca* 1% of the applied mass) respectively. IN-JU873 was not detected.

Dissipation kinetics

The total soil column residues in Table 8-127 were analysed for the decline rates using CAKE. The decline rate for indoxacarb using the single first order (SFO) kinetics model gave a DT₅₀ of 7.08 days.

Kinetic model	χ^2 error	r^2	DT ₅₀ (days)	DT ₉₀ (days)
SFO	11.9	0.9662	7.08	23.5

Figure 5: Decline of indoxacarb (DPX-KN128) in Graffignana, Italy



CONCLUSIONS

There were no abnormal circumstances with respect to test site management, climate conditions or analysis which would compromise the conclusions drawn or the data collected.

The application monitors as well as the soil residues on Day 0 confirmed the nominal application rate. Averaged recoveries of indoxacarb on Day 0 were 117% based on the application monitor analysis.

A rapid degradation of the parent compound resulted in the indoxacarb residue declining from an average 397.6 g peq/ha on Day 0 to 181.7 g peq/ha by Day 7 and subsequently to less than 5.0 g peq/ha by Day 76. The parent compound had declined to 1 g peq/ha by the end of this study.

All metabolites monitored (IN-KT413, IN-JU873, IN-JT333, IN-KG433, IN-KB687, IN-MK463, and IN-MK638) with the exception of IN-JU873 were detected during the course of this study. IN-KT413 accounted for the largest proportion of the metabolites observed, reaching a maximum of 8.9% of the applied. IN-JT333 reached above 7% and IN-KB687 reached 5.6% of the applied mass. The remaining components did not exceed 5% of the applied mass.

Indoxacarb as well as the metabolites' residues found were generally confined to the upper soil segments (0-15 cm), with the highest concentration found in the 0–5 cm segment at every sampling. Loss of applied material via leaching did not contribute to the dissipation of residue in this study.

A DT_{50} of 7.08 days and a DT_{90} of 23.5 days was calculated for the parent compound, demonstrating a rapid dissipation of indoxacarb under field conditions.

Comments (RMS 2016)

This study was conducted with the active isomer DPX-KN128 as test material and is acceptable.

The same comments as made for previous study (Doig 2015d) can be made and are repeated here:

The level of residues observed at different depths confirm the rapid degradation of active substance (active isomer DPX-KN128) and the low potential of leaching of active substance and all its major metabolites, as none or very few residues of any compound were observed below 15 cm during the all course of the study.

No accumulation potential is detected for any of the compound, with the exception of IN-MK643 that seems to be quite persistent. However, this accumulation potential was already identified in the laboratory (with persistence DT_{50} of 314 days), and is taken into account in soil risk assessment with calculation of PEC_{accumulation}.

It is noticeable that the metabolite IN-JU873 is not detected in this field trial although being a major metabolite in laboratory. However, laboratory data tend to show that this metabolite is quite transient (it is detected at level > 10% at only one sampling time among all studies). As mentioned by applicant, it is believed that this metabolite may have formed in the field at level below the LOD.

Degradation rate were only provided for active substance. On the more no normalized DT_{50} are available. This could have been done, since the study was conducted according to EFSA guidance (2010) to minimize surface processes (11 mm of irrigation applied to the test plot within 24 hours after 1st application).

From the daily soil temperature monitored in field, and the moisture content of the samples, it can be seen that:

- Soil temperature was always < 22 °C during the first month
- Samples moisture was not always < soil moisture at pF2.5, i.e soil correction factor from pF2 would certainly be <1.

Since irrigation was made after 1st sapling at days 0, normalised DT_{50} should be derived from DAT3.

Data point:	CA 7.1.2.2.1/02
Author(s)	Doig, A. (2015b);
Title:	The field soil dissipation of indoxacarb (DPX-KN128) following a single application to bare ground - northern Germany - 2012
Organisation:	Charles River Laboratories (UK), Tranent, Scotland, UK
Document No:	DuPont-34892
Dates of experimental work	
Guidelines:	OPPTS 835.6100, SETAC Europe (1995), SANCO/3029/99 rev. 4 (2000), EU 1607/VI/97 Rev 1 (1997), EU 7029/VI/1995 Rev 5 (1997)
Deviations :	None
GLP:	Yes
Previous evaluation:	No
Acceptability:	The study is considered valid.

This report describes the soil dissipation of a single application of indoxacarb (DPX-KN128) to bare ground studied under field conditions in Bühren, North Germany, for *ca.* 5 months after application on 25-May-2012.

The study design consisted of three replicate treated bare soil plots and a control (untreated) bare soil plot. The test site soil was characterised as loam in horizons 0–5, 5–15, 15–30, and 30–50 cm, and sandy loam at 50–70 cm and sand at 70–90 cm. The test item was applied at a nominal rate of 400 g a.s./ha which was the highest proposed use rate for indoxacarb per year. Actual application based on the amount of spray solution applied and the output from calibrated spray equipment used indicated application at 101.4–102.8% of the targeted application rate in all three treated plots. The application method was representative of the proposed commercial use of this product.

Soil samples for soil characterisation and biomass were taken 5 days before application of the test item. Post treatment soil samples were collected on Days +0, 3, 7, 10, 15, 21, 30, 49, 73, 101, 148, 205, 251, 298, and 356 following application of the test item. Sample analysis was terminated early at Day 148 due to rapid dissipation indoxacarb and its metabolites. Five replicate cores were taken from each of the treated replicate areas at each sampling event. Soil cores were collected in the field at 0–5, 5–15, 15–30, 30–50, 50–70, and 70–90 cm soil depths (except Days 0 and 3, where samples down to 50 cm only were collected).

Fresh fortified samples of control soil were analysed concurrently with each set of treated samples. Each analysis set included fresh fortifications ranging from the LOQ level up to 10 ppb. Residues were routinely detected above 10 ppb throughout the course of this study therefore an additional ‘high recovery’ batch containing two fortified control samples at 800 ppb (100 ppb for IN-KT413, quantified using IN-MP819) was performed.

The average recoveries of the fresh fortification samples analysed concurrently with the analysis of the field samples are summarised in the table below.

Analyte	Average recovery (%)	Relative standard deviation (%)
Indoxacarb (DPX-KN128)	104	13.9
IN-KG433	102	8.1
IN-JU873	96.6	13.4
IN-KT413	70.9	16.1
IN-JT333	97.9	12.2
IN-MK638	109	8.0
IN-MK643	110	6.4
IN-KB687	105	9.3

The LOQ and LOD were 1.0 and 0.3 ppb, respectively, for each component

Soil samples from all sampling events were generally analysed to the depth increment at which the residues found indicated no reasonable expectation of residues in lower depths. Residues were determined in ppb and then converted to g peq/ha for every sample analysed. Post application (Day 0) soil residues in the 0-5 cm samples ranged from 258.0–449.5 g peq/ha for indoxacarb.

Residues of indoxacarb declined rapidly throughout this study. Average residue (summed for all soil depths) declined to about half the applied amount, 202.0 g peq/ha by Day 7 and to less than 5% of applied (12.7 g peq/ha) by Day 49. Beyond Day 73, average residues of indoxacarb were generally near or below 5 g peq/ha, declining to *ca* 3.13 g peq/ha by Day 148.

Six of the seven metabolites of indoxacarb were detected at various sampling intervals during this study, with only IN-JU873 undetected at any sampling interval. IN-JT333 reached an average peak level of 28.2 g peq/ha by Day 7 and declined thereafter, IN-KG433 reached an average peak level of 1.94 g peq/ha by Day 7 and declined thereafter, IN-KB687 was detected at an average peak level of 8.69 g peq/ha at Day 0 and declined at Day 3. This level increased to 7.16 g peq/ha at Day 7 then declined thereafter. IN-MK643 reached an average peak level of 20.8 g peq/ha by Day 21 and declined thereafter. IN-MK638 reached an average peak level of 1.91 g peq/ha by Day 21 and declined thereafter, while IN-KT413 reached its peak level of 50.6 g peq/ha by Day 10, and then declined. As stated earlier, IN-JU873 was not detected.

Almost all of the applied test item and its degradation products remained in the upper 15 cm of soil. Detections below 15 cm were infrequent and seldom accounted for more than 5% of the applied amount in any depth segment, and for any individual component. Only one residue just above the limit of detection was detected at 70–90 cm at Day 7.

The storage period between sampling in the field and analyte extraction did not exceed 350 days for all samples analysed. A separate storage stability study (DuPont-35167, CA 7.1.2.2.1)) demonstrated that indoxacarb and its metabolites were stable during the maximum storage period, except IN-KT413.

MATERIALS AND METHODS

- Test material: Indoxacarb 30WG
 Lot/Batch #: KN128-298
 Purity: 300 g a.s./kg
 Description: White solid
 CAS#: 173584-44-6 for indoxacarb the active substance
 None for the formulation
 Stability of test compound: Shown to be stable under the conditions of the test
- Test Site

Test site description is detailed in Table 8-128. Soil samples collected to 90 cm depth were characterised and the soil characterisation data are included in Table 8-129.

Table 8-128: Test Site Description

Location:	Bühren
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Country:	Germany
GPS coordinates	N 52° 48' 24" and E 08° 11' 19".
Representative crop region	Northern Europe
Site selection criteria	The field site was flat and level and allowed soil sampling down to 90 cm. The site had good security and was readily able to be remarked if required. The site was free from flooding risk.
Weather station	CWi technical on site weather station.
Pre-treatment exclusion criteria	No other chemical of similar structure applied during the past 3 years.
Plot history, crops grown	winter barley 2012, winter wheat 2011, winter barley 2010.
Pesticides used in preceding 3 years	2012: glyphosate (360 g/L) 2011: diflufenican + flufenacet (200 g/kg + 400 g/kg), pirimicarb (500 g/kg), lambda-Cyhalothrin (100 g/L), epoxiconazole + metconazole (37.5 g/L + 27.5 g/L), epoxiconazole + fenpropimorph + pyraclostrobine (43 g/L + 214 g/L + 114 g/L), tribenuron (482.3 g/kg), prothioconazole + bifxafen (150 g/L + 75 g/L), epoxiconazole + fenpropimorph (84 g/L + 250 g/L), chlormequat (558 g/L), trinexapac (222 g/L), 2010: diflufenican + flurtamone (100 g/L + 250 g/L), fluoxastrobilin + prothioconazole (100 g/L + 100 g/L), ethephon (660 g/L), spiroxamine + prothioconazole (300 g/L + 160 g/L), trinexapac (222 g/L)
Location/identification of weather station	CWi technical on site weather station.
Distance of weather station from test site	On site
Depth to ground water table	Not defined

Table 8-129: Soil properties at Bühren, Germany

Soil property	Soil depth (cm)					
	0–5	5–15	15–30	30–50	50–70	70–90
Sand % (0.05-2 mm) ^a	44	44	44	38	58	88
Silt % (0.05-0.002 mm) ^a	46	44	44	48	30	8
Clay % (<0.002 mm) ^a	10	12	12	14	12	4
pH (water, 1:1)	6.3	6.2	6.3	6.5	6.6	6.7
% Organic matter ^b	3.3	3.3	3.4	1.9	0.47	0.02
C.E.C [meq/100g] ^c	10.3	10.5	10.5	10.3	7.2	4.0
Bulk density (g cm ⁻³)	1.14	1.12	1.15	1.20	1.35	1.42
Moisture holding capacity at 1/3 bar (% of dry weight)	17.0	16.5	19.3	20.8	14.8	3.9
Moisture holding capacity at 15 bar (% of dry weight)	7.0	7.4	6.9	7.1	5.1	2.0
Soil classification ^d	Loam	Loam	Loam	Loam	Sandy loam	Sand
Microbial biomass carbon (µg/g dry basis, 0–25cm depth)	216.3					

^a Particle size^b Walkley-Black method^c Cation Exchange Capacity (C.E.C)^d Soil classification according to USDA system

Experimental design

The experimental details for the test substance application, application rate, application method, *etc.*, are included in Table 8-130 below.

Soil sampling

Soil sampling intervals and the sampling depths, and number of cores collected are listed in Table 8-131.

Description of analytical methods

Soil samples were analysed for residues of indoxacarb (DPX-KN128) and all significant soil metabolites, IN-KG433, IN-JU873, IN-KB687, IN-KN125 (a racemic mixture IN-JT333 was used as reference standard for its S-enantiomer IN-KN125 analysis), IN-MK638, IN-MK643, and IN-KT413.

The final purified extracts were quantified for indoxacarb and its metabolites by liquid chromatography with tandem mass spectrometry employing turbo ion spray ionisation in positive and negative mode.

The indoxacarb, IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-JT333, IN-MK638, IN-MK643, and IN-KB687 peak areas were calculated for the target ion for each of the calibration standards, quality control samples, control samples, and unknown test samples. A calibration curve was then obtained by weighted least squares linear regression analysis (1/x) of the plot peak area versus the concentration of indoxacarb, IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-MK638, IN-MK643, and IN-KB687 in each calibration standard. The concentrations (ppb) of indoxacarb and its degradation products were calculated using the calibration curve. The concentrations (ppb) of indoxacarb and its degradation products in treated field soil samples were calculated on a dry weight basis. The peak areas were calculated for target ion for indoxacarb, IN-KG433, IN-JU873, IN-MP819 (used to quantify IN-KT413), IN-JT333, IN-MK638, IN-MK643, and IN-KB687, for each of the calibration standards, quality control samples, control samples and unknown test samples in one analytical run.

The limit of quantification (LOQ) for indoxacarb, and its metabolites IN-KG433, IN-JU873, IN-KB687, IN-JT333, IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819) was 1.0 ppb since this was the lowest validated level. The limit of detection (LOD) was determined to be 0.3 ppb for indoxacarb and its metabolites IN-KG433, IN-JU873, IN-KB687, IN-JT333, IN-MK638, IN-MK643, and IN-KT413 (quantitatively converted as IN-MP819). The LOD was determined as the sample concentration equivalent to the lowest calibration standard (1.0 µg/kg).

Soil moisture was determined for each sample extracted by drying the sample to at 110°C, and determining the loss of weight. Moisture data were used to convert wet weight ppb residues into dry weight ppb.

The ppb residues for parent compound and each degradation product in each sample were converted to g/ha parent equivalents by multiplying the molar amounts of each analyte by the parent compound molecular weight to obtain parent equivalent mass. The parent equivalent masses were further multiplied by the total calculated soil in one hectare at each depth for conversion to g a.s./ha for the parent and each degradation product at each depth.

Table 8-130: Experimental design, plot set up and application details

Details	Bühren, Germany
Duration of study	356 days
Uncropped (bare) or cropped	Bare, maintained weed free
Controls used	Yes
Number of plot(s)	3 treated (Replicates I, II, and III) and 1 untreated control
Treated plot dimensions	3 m × 30 m
Untreated control plot dimensions	3 m × 10 m
Distance between control plot and treated plot	11 m
Distance between treated plots	3.5 m
Application rate used (g a.s./ha)	400 g a.s./ha, nominal, Application by two passes in opposite directions
Was the maximum label rate per ha used in study?	Yes
Application date (s)	25-May-2012
Application method	Ariel application horizontal
Type of spray equipment	Backpack sprayer with Lechler IDK 120-025 POM, 6 Spray nozzles, 3 m swath width.
Volume of spray solution applied/plot	400 L/ha
Identification and volume of carrier (e.g., water), if used	Water
Monthly weather reports included (yes/no)	Yes, also daily weather data
Pan evaporation data available?	No
Meteorological conditions during application	

Cloud cover (%)	0
Temperature (air)	21.0°C
Relative humidity (%)	60
Wind speed	0.0 meters/sec
Sunlight (hr) [time required for application]	Unknown
Irrigation to supplement natural precipitation (25 May 2012 - 06 May 2013)	161.2 mm
Rainfall (25 May 2012 – 06 May 2013)	683.8 mm
Verification of application	Plastic Petri dishes (approximately 9 cm diameter).
Field spikes (Transit stability samples)	None; Day 0 sample and application monitor analyses confirmed transit stability
Additional modules added to study: run-off, leaching, volatilisation	None; however, test placed on flat site with little risk of flooding to control run-off. Soil sampling to 90 cm (36 in.) to measure movement in soil

Table 8-131: Soil sampling details

Details	Bühren, Germany
Method of sampling (random or systematic)	Random
Sampling intervals (days)	-0, +0 ^a , 3, 7, 10, 15, 21, 30, 49, 73, 101, 148, 205, 251, 298, and 356 ^b
Method of soil collection	The 0–5 cm segment was sampled using a metal cylinder with an inner diameter of 9.5 cm driven 5 cm into the soil and the soil was then scooped out by hand using a spoon. The metal cylinder remained in place during collection of the lower depths to prevent treated soil from falling onto the sampling area and potentially contaminating the lower depths. Soil cores for the 5–90 cm depths were taken with a Humax [®] coring system with an inner diameter of 5 cm. This allowed sampling of the lower depths in increments of 5–15, 15–30, 30–50, 50–70, and 70–90 cm segments.
Sampling depth	Nominally to 90 cm depth
Number of cores collected per plot	5 per replicate plot, 15 per time point total
Depth and diameter of segments	0–5 cm (9.5 cm diameter) 5–15 cm (5 cm diameter) 15–30 cm (5 cm diameter) 30–50 cm (5 cm diameter) 50–70 cm (5 cm diameter) 70–90 cm (5 cm diameter)
Storage conditions	Frozen
Maximum storage length	350 days

^a Just after application^b Sample analysis was terminated early at Day 148 due to rapid dissipation of DPX-KN128 and its metabolites

RESULTS AND DISCUSSION

Application verification

Application was targeted at a rate of 400 g a.s./ha. The mean actual application rate was 409.1 g a.s./ha (102.3% of the intended application rate, calculated from the boom output). The test material application rate was monitored with the aid of Petri dishes placed in randomly chosen locations in each of the treated plots. The mean recovery of indoxacarb, as calculated from application monitors, was 398.8 g peq/ha, or 99.7% of target rate.

The residues in soil on Day 0 also served to confirm the actual application rate. Residues of indoxacarb in the 0–5 cm samples ranged from 188.6–422.0 peq/ha in the Day 0 soil samples. Averaged residue of indoxacarb in 0–5 cm soil on Day 0 was 290.2 g peq/ha in the three replicate soil samples, which represented 72.6% of the target application rate.

Residue decline

Residues in ppb dry weight basis are listed in Table 8-132.

Table 8-132: Average residues at each depth (ppb dry weight basis)

DAT (Days)	Rep	Depth (cm)	% Moist (dwb)	DPX- KN218 (ppb)	IN- KG433 (ppb)	IN- JU873 (ppb)	IN- KT413 (ppb)	IN- JT333 (ppb)	IN- MK638 (ppb)	IN- MK643 (ppb)	IN- KB687 (ppb)
0	I	0-5	14.3	837.3618	1.6356	0.0000	39.5592	18.7109	0.0000	0.0000	6.3642
	II	0-5	12.2	471.5766	1.2679	0.0000	16.5944	7.3581	0.0000	0.0000	7.6453
	III	0-5	14.3	523.1511	2.0505	0.0000	35.4673	20.2425	0.0000	0.0000	5.1801
	I	5-15	18.7	22.9091	0.0000	0.0000	1.6203	0.7551	0.0000	0.0000	0.4310
	II	5-15	18.7	44.7262	0.0000	0.0000	2.3930	1.1077	0.0000	0.0000	0.9132
	III	5-15	21.2	20.6525	0.0000	0.0000	0.8945	1.1850	0.0000	0.0000	0.6313
	I	15-30	23.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15-30	20.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15-30	20.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
3	I	0-5	17.1	198.3674	1.1874	0.0000	46.9688	16.5462	0.4849	1.4111	2.5258
	II	0-5	17.7	283.3039	1.6443	0.0000	98.1500	16.7369	0.5252	1.8867	2.8766
	III	0-5	16.0	177.9440	1.5544	0.0000	53.3948	15.9384	0.3631	1.1878	2.4847
	I	5-15	21.2	20.5434	0.0000	0.0000	4.6710	1.8374	0.0000	0.0000	0.5042
	II	5-15	19.9	15.4191	0.0000	0.0000	6.1784	1.0892	0.0000	0.0000	0.0000
	III	5-15	21.6	22.5446	0.0000	0.0000	6.7135	1.6647	0.0000	0.0000	0.0000
	I	15-30	23.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15-30	22.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15-30	24.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
7	I	0-5	26.1	318.4025	2.1777	0.0000	65.2694	38.3722	0.9787	4.9898	4.2584
	II	0-5	27.5	292.4850	2.8611	0.0000	86.1390	40.2645	1.5185	9.0857	5.4086
	III	0-5	24.7	308.5078	3.3195	0.0000	84.9706	38.7318	1.2507	5.5317	4.6214
	I	5-15	26.8	8.0049	0.0000	0.0000	2.2266	0.9816	0.0000	0.0000	0.0000
	II	5-15	25.7	14.1915	0.0000	0.0000	5.0557	1.2922	0.0000	0.0000	0.0000
	III	5-15	25.1	4.5349	0.0000	0.0000	1.2096	0.4313	0.0000	0.0000	0.0000
	I	15-30	24.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15-30	23.0	33.0009 ^a	0.5437^a	0.0000 ^a	5.9163 ^a	3.0898 ^a	0.0000 ^a	0.0000 ^a	0.9208^a
	III	15-30	23.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30-50	16.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30-50	16.7	0.9473	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30-50	17.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	50-70	13.8	0.0000	0.0000	0.0000	0.0000	0.6941	0.0000	0.0000	0.0000
	II	50-70	14.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	50-70	12.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	70-90	12.5	0.3482	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	70-90	12.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	70-90	12.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
10	I	0-5	25.9	180.4147	1.5826	0.0000	82.4016	34.8114	1.2691	6.3063	2.4865
	II	0-5	26.8	157.8660	1.4569	0.0000	87.6822	22.3675	1.0178	7.9199	2.1619
	III	0-5	25.9	231.9078	2.3166	0.0000	71.3475	28.6297	0.6998	4.5299	3.4106
	I	5-15	26.8	3.2816	0.0000	0.0000	1.4988	0.6618	0.0000	0.0000	0.4126
	II	5-15	26.3	1.1330	0.0000	0.0000	0.8057	0.0000	0.0000	0.0000	0.4356
	III	5-15	26.0	1.7791	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	15-30	25.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15-30	23.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.4672
	III	15-30	26.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30-50	15.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30-50	18.1	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30-50	20.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

15	I	0–5	27.1	126.1468	1.4972	0.0000	47.6498	21.8866	1.3523	9.1220	1.7718
	II	0–5	25.6	166.7968	2.5811	0.0000	84.0264	31.7140	1.4092	14.1174	1.9543
	III	0–5	24.8	142.8960	2.3949	0.0000	66.2688	23.5498	0.7117	7.5304	1.7435
	I	5–15	27.1	4.2401	0.0000	0.0000	1.8175	1.0736	0.0000	0.0000	0.6950
	II	5–15	25.6	16.1522	0.4128	0.0000	9.0721	3.5507	0.0000	1.3791	0.5379
	III	5–15	27.1	5.2441	0.0000	0.0000	2.3704	0.9774	0.0000	0.0000	0.0000
	I	15–30	26.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	22.5	0.7544	0.0000	0.0000	0.5285	0.0000	0.0000	0.0000	0.0000
	III	15–30	25.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30–50	14.8	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	16.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	24.4	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
21	I	0–5	22.4	99.2297	1.3476	0.0000	58.0910	22.9990	1.6757	13.0111	1.9474
	II	0–5	22.2	54.1102	0.7838	0.0000	46.5826	13.0632	1.3515	12.5499	1.4139
	III	0–5	23.4	99.9170	1.0659	0.0000	74.0153	26.8025	1.0925	15.7829	1.9633
	I	5–15	24.9	4.1279	0.0000	0.0000	1.7886	1.9759	0.0000	0.6973	0.0000
	II	5–15	27.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	5–15	22.6	5.3981	0.0000	0.0000	4.9751	1.7299	0.0000	1.1459	0.0000
	I	15–30	22.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	24.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	22.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
30	I	0–5	15.6	54.4938	0.4127	0.0000	39.0266	16.6348	1.3121	12.8432	0.5128
	II	0–5	16.2	26.6214	0.0000	0.0000	27.5278	7.8470	0.5737	7.9248	0.4586
	III	0–5	20.3	21.8224	0.0000	0.0000	15.3626	8.8433	0.3795	4.1227	0.3799
	I	5–15	22.1	3.8584	0.0000	0.0000	3.6813	1.5433	0.0000	0.9656	0.0000
	II	5–15	22.1	1.5946	0.0000	0.0000	1.7399	0.4013	0.0000	0.5907	0.0000
	III	5–15	23.2	0.0000	0.0000	0.0000	0.4992	0.0000	0.0000	0.0000	0.0000
	I	15–30	21.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	22.1	0.6752	0.0000	0.0000	0.6998	0.0000	0.0000	0.0000	0.0000
	III	15–30	23.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	I	30–50	19.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	18.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	20.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
49	I	0–5	20.4	15.6520	0.0000	0.0000	14.0146	7.5250	0.4492	10.7878	0.4445
	II	0–5	23.2	15.5478	0.0000	0.0000	14.1310	6.4261	0.3840	7.3784	0.0000
	III	0–5	27.3	21.3482	0.0000	0.0000	20.1516	10.2744	0.4851	7.7806	0.0000
	I	5–15	19.5	1.7650	0.0000	0.0000	1.3360	1.1918	0.0000	0.8053	0.0000
	II	5–15	21.1	1.3042	0.0000	0.0000	1.5113	0.4022	0.0000	0.8808	0.0000
	III	5–15	27.1	0.4970	0.0000	0.0000	0.6344	0.0000	0.0000	0.0000	0.0000
	I	15–30	20.7	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	23.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	23.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
73	I	0–5	16.2	8.8544	0.0000	0.0000	6.5641	3.9450	0.0000	9.0334	0.0000
	II	0–5	16.0	6.2594	0.0000	0.0000	7.1966	2.4928	0.0000	8.6339	0.0000
	III	0–5	16.7	8.3254	0.0000	0.0000	6.3987	4.7719	0.0000	5.4382	0.0000
	I	5–15	22.1	1.2271	0.0000	0.0000	1.0525	0.7733	0.0000	1.0349	0.0000
	II	5–15	21.3	0.5292	0.0000	0.0000	0.5558	0.0000	0.0000	0.7010	0.0000
	III	5–15	22.5	0.6440	0.0000	0.0000	0.0000	0.3697	0.0000	0.3985	0.0000
	I	15–30	21.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	21.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	23.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
101	I	0–5	17.5	4.5249	0.0000	0.0000	4.1736	1.7190	0.0000	5.2581	0.0000
	II	0–5	17.5	6.7645	0.0000	0.0000	4.8622	1.7719	0.0000	6.0947	0.0000
	III	0–5	18.2	4.7091	0.0000	0.0000	3.2907	1.6974	0.0000	3.7836	0.0000
	I	5–15	20.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.5786	0.0000

	II	5–15	21.0	0.3809	0.0000	0.0000	0.0000	0.6897	0.0000	0.3651	0.0000
	III	5–15	21.0	0.5330	0.0000	0.0000	0.5812	0.0000	0.0000	0.5967	0.0000
	I	15–30	21.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	21.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	20.6	0.5761	0.0000	0.0000	0.5299	0.0000	0.0000	0.6697	0.0000
	I	30–50	15.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	30–50	17.5	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	30–50	19.3	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
148	I	0–5	22.6	4.2640	0.0000	0.0000	2.3944	1.2861	0.0000	5.7806	0.0000
	II	0–5	22.4	4.9584	0.0000	0.0000	3.2681	1.4394	0.0000	3.2791	0.0000
	III	0–5	24.4	1.0298	0.0000	0.0000	0.9625	0.0000	0.0000	4.4025	0.0000
	I	5–15	23.3	0.5794	0.0000	0.0000	0.0000	0.0000	0.0000	0.5769	0.0000
	II	5–15	28.6	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.4318	0.0000
	III	5–15	23.9	1.0315	0.0000	0.0000	0.5750	0.0000	0.0000	1.0487	0.0000
	I	15–30	23.0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	II	15–30	22.9	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	III	15–30	25.2	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

LOQ = 1.0 ppb

<LOD = <0.3 ppb

Quantifiable values >LOD but <LOQ are highlighted in bold.

^a Anomalous result. Re-analysis was conducted to confirm.

Note: Values have been corrected for moisture content therefore in some cases, results are highlighted when >1.0 ppb. This is caused by detected values (uncorrected for moisture) at <1.0 ppb being corrected prior to inclusion in table.

Table 8-133: Average residues summed for all depths in g/ha parent equivalents

Days	Data in grams peg/ha							
	DPX-KN128	IN-JT333	IN-KG433	IN-KB687	IN-MK643	IN-JU873	IN-MK638	IN-KT413
0*	449.4681	11.6113	0.8436	8.3582	0.0000	0.0000	0.0000	21.5532
	257.9914	5.2372	0.5189	10.0432	0.0000	0.0000	0.0000	10.1957
	287.5923	13.0818	1.0428	7.6716	0.0000	0.0000	0.0000	18.5424
3	137.4261	13.0659	0.6728	4.6588	1.8908	0.0000	0.6438	31.8005
	169.6750	11.5511	0.8757	3.3604	2.3761	0.0000	0.6553	59.0984
	128.8762	12.3542	0.8408	2.9480	1.5193	0.0000	0.4601	38.0187
7	171.6245	25.9367	1.1070	4.7481	5.9978	0.0000	1.1656	35.3017
	235.7844	31.1169	2.6186	10.3139	10.1920	0.0000	1.6878	60.3554
	198.4884	27.7516	2.1061	6.4316	8.2993	0.0000	1.8593	53.7947
10	114.0367	24.7678	0.9815	4.7061	9.2489	0.0000	1.8442	51.3106
	100.4170	15.7151	0.9323	6.9319	11.9842	0.0000	1.5260	55.2056
	152.3860	20.7878	1.5319	4.9474	7.0838	0.0000	1.0842	45.4235
15	84.7544	17.1037	0.9504	4.8583	13.6931	0.0000	2.0114	31.8650
	105.2871	22.9559	1.9026	3.9622	21.2350	0.0000	1.5768	54.0677
	83.9535	15.7293	1.3095	2.0911	9.7371	0.0000	0.9119	38.2676
21	70.5713	20.1372	0.8926	2.8292	22.9716	0.0000	2.6004	39.7493
	33.2527	9.0196	0.4929	1.9503	18.6624	0.0000	1.9914	28.2015
	52.1525	16.1975	0.4801	1.9398	21.0083	0.0000	1.1530	39.5149
30	34.6875	12.4874	0.2258	0.6155	19.9778	0.0000	1.6822	25.7734
	20.3134	6.0796	0.0000	0.6297	13.9066	0.0000	0.8414	20.8330
	13.5232	6.1571	0.0000	0.5284	6.1821	0.0000	0.5639	10.0907
49	12.8447	7.5147	0.0000	0.6506	19.9347	0.0000	0.7023	10.9702

73	12.0502	5.3805	0.0000	0.0000	14.7243	0.0000	0.6055	11.2387
	13.3121	6.8357	0.0000	0.0000	11.1487	0.0000	0.6888	12.5989
	7.1302	3.9761	0.0000	0.0000	16.7628	0.0000	0.0000	5.4322
	4.5833	1.6686	0.0000	0.0000	15.1847	0.0000	0.0000	5.1076
	6.0621	3.9049	0.0000	0.0000	9.4991	0.0000	0.0000	3.8371
101	3.0714	1.3110	0.0000	0.0000	10.8224	0.0000	0.0000	2.7908
	4.6569	2.3725	0.0000	0.0000	10.2330	0.0000	0.0000	2.8898
	5.4107	1.3098	0.0000	0.0000	12.3281	0.0000	0.0000	4.3314
148	3.7054	0.9316	0.0000	0.0000	11.3224	0.0000	0.0000	1.5208
	3.3867	1.1046	0.0000	0.0000	6.9952	0.0000	0.0000	2.1990
	2.2852	0.0000	0.0000	0.0000	11.4387	0.0000	0.0000	1.5291

* Samples taken immediately after application had dried

Table 8-134: Residues in entire soil column, shown in percent of applied test substance

Days	Percent of the applied*							
	DPX-KN128	IN-JT333	IN-KG433	IN-KB687	IN-MK643	IN-JU873	IN-MK638	IN-KT413
0	122.2	3.2	0.2	2.3	0.0	0.0	0.0	5.9
	70.1	1.4	0.1	2.7	0.0	0.0	0.0	2.8
	78.2	3.6	0.3	2.1	0.0	0.0	0.0	5.0
3	37.4	3.6	0.2	1.3	0.5	0.0	0.2	8.6
	46.1	3.1	0.2	0.9	0.6	0.0	0.2	16.1
	35.0	3.4	0.2	0.8	0.4	0.0	0.1	10.3
7	46.6	7.0	0.3	1.3	1.6	0.0	0.3	9.6
	64.1	8.5	0.7	2.8	2.8	0.0	0.5	16.4
	53.9	7.5	0.6	1.7	2.3	0.0	0.5	14.6
10	31.0	6.7	0.3	1.3	2.5	0.0	0.5	13.9
	27.3	4.3	0.3	1.9	3.3	0.0	0.4	15.0
	41.4	5.7	0.4	1.3	1.9	0.0	0.3	12.3
15	23.0	4.6	0.3	1.3	3.7	0.0	0.5	8.7
	28.6	6.2	0.5	1.1	5.8	0.0	0.4	14.7
	22.8	4.3	0.4	0.6	2.6	0.0	0.2	10.4
21	19.2	5.5	0.2	0.8	6.2	0.0	0.7	10.8
	9.0	2.5	0.1	0.5	5.1	0.0	0.5	7.7
	14.2	4.4	0.1	0.5	5.7	0.0	0.3	10.7
30	9.4	3.4	0.1	0.2	5.4	0.0	0.5	7.0
	5.5	1.7	0.0	0.2	3.8	0.0	0.2	5.7
	3.7	1.7	0.0	0.1	1.7	0.0	0.2	2.7
49	3.5	2.0	0.0	0.2	5.4	0.0	0.2	3.0
	3.3	1.5	0.0	0.0	4.0	0.0	0.2	3.1
	3.6	1.9	0.0	0.0	3.0	0.0	0.2	3.4
73	1.9	1.1	0.0	0.0	4.6	0.0	0.0	1.5
	1.2	0.5	0.0	0.0	4.1	0.0	0.0	1.4
	1.6	1.1	0.0	0.0	2.6	0.0	0.0	1.0
101	0.8	0.4	0.0	0.0	2.9	0.0	0.0	0.8
	1.3	0.6	0.0	0.0	2.8	0.0	0.0	0.8
	1.5	0.4	0.0	0.0	3.4	0.0	0.0	1.2
148	1.0	0.3	0.0	0.0	3.1	0.0	0.0	0.4
	0.9	0.3	0.0	0.0	1.9	0.0	0.0	0.6
	0.6	0.0	0.0	0.0	3.1	0.0	0.0	0.4

* Calculations based on a total g peq/ha value for parent and metabolites at Day 0, averaged across the 3 reps

Average residue of indoxacarb in the uppermost soil segment declined to about half the applied amount, 307 ppb by Day 7. Residue in the upper depth declined from about 191 ppb on Day 10 to 3.41 ppb at the end of the study. Only a small amount, <10 ppb was found in the next depth (5–15 cm) segment, and only trace amounts,

nearing the LOQ of 1.0 ppb (except for Day 7 where the residue of indoxacarb for Replicate II was 33.0 ppb) in the 15–30 cm segment.

Six of the metabolites monitored were detected during this study with only IN-JU873 undetected at any sampling interval. The first three metabolites in the sequence of degradation of indoxacarb, IN-KT413, IN-JT333, and IN-KB687 were found almost immediately after the application. IN-JT333 reached an average level of 39.1 ppb in 0–5 cm depth by Day 7. It stayed near 20–28 ppb through Days 10–21 and then declined to an average of about 1.4 ppb by the end of the study. IN-JT333 remained in the upper two depth segments, apart from Day 7 where a residue was observed at 3.1 ppb in Replicate II from 15–30 cm depth. Most of the residue remained in the 0–5 cm segment. IN-KT413 reached its peak level of about 80.4 ppb by Day 10 and remained in the range 59.6–66.0 ppb through Days 15–21 before declining. IN-KB687 only reached a concentration of about 4.8 ppb by Day 7, and never accounted for any significant portion of the residue. Likewise, IN-MK643, IN-MK638, and IN-KG433 were also limited to near the LOQ levels during this whole study. As stated earlier, IN-JU873 was not detected.

Almost all of the applied test item and its degradation products remained in the upper 5 cm of soil. Detections below 15 cm were infrequent and seldom accounted for more than 1 ppb in any depth segment, and for any individual component.

It can be concluded from these data that indoxacarb and its major metabolites were all degrading throughout this study at varying rates. In addition, very little residue moved to depths below 15 cm. Thus, loss of applied material via leaching did not contribute to the dissipation of residue in this study.

Mass balance

In order to quantify the rate of decline of the applied test item, the concentrations of indoxacarb as well as all metabolites, measured in ppb, were converted to mass in grams per unit area (g/ha parent equivalents) and is included in Table 8-133. The residues converted in percent of the applied are presented in Table 8-134.

A rapid degradation of the parent compound resulted in the indoxacarb residue declining from an average 331.7 g peq/ha on Day 0 to 122.3 g peq/ha by Day 10 and subsequently to less than 6.0 g peq/ha by Day 73. The parent compound had declined to 3.12 g peq/ha (less than 1%) by the end of this study.

All degradation products except IN-JU873 were detected during the course of the study. IN-KT413 accounted for the largest proportion of the metabolites observed, reaching a maximum of 50.6 g peq/ha, or 13% of applied, on Day 10. IN-JT333 accounted for as much as 28.3 g peq/ha (about 7% of applied) at its peak, on Day 7. IN-KG433 accounted for 1.4 g peq/ha (0.35 % of the applied mass) on Day 15. IN-MK643 and IN-MK638 also reached a maximum of 20.9 g peq/ha (5% of the applied mass) and 1.91 g peq/ha (0.5% of the applied mass) at Day 21, while IN-JU873 was not detected.

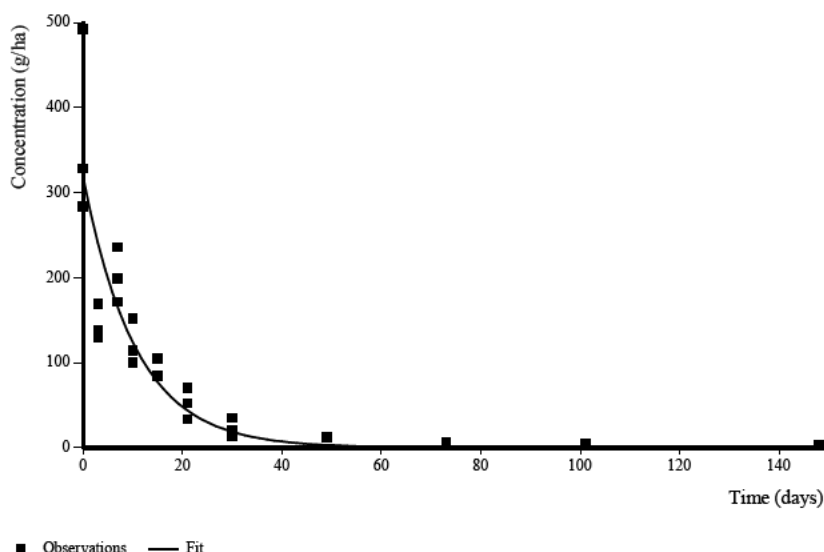
Decline of not only the parent compound, but all the metabolites observed underlines the degradation of all monitored components under field conditions.

Dissipation kinetics

The total soil column residues (Table 8-134) were analysed for the decline rates using CAKE. The decline rate for indoxacarb using the single first order [SFO] kinetics model gave a DT_{50} of 7.32 days, demonstrating a rapid dissipation of indoxacarb under field conditions.

Kinetic model	χ^2 error	r^2	DT_{50} (days)	DT_{90} (days)
SFO	29.9	0.8334	7.32	24.3

Figure 6: Decline of indoxacarb (DPX-KN128) in Bühren, Germany



CONCLUSIONS

There were no abnormal circumstances with respect to test site management, climate conditions or analysis which would compromise the conclusions drawn or the data collected.

The application monitors as well as the soil residues on Day 0 confirmed the nominal application rate.

A rapid degradation of the parent compound resulted in the indoxacarb residue declining from an average 331.7 g peq/ha on Day 0 to 122.3 g peq/ha by Day 10 and subsequently to less than 6.0 g peq/ha by Day 73.

All metabolites monitored (IN-KT413, IN-JU873, IN-JT333, IN-KG433, IN-KB687, IN-MK463, and IN-MK638) with the exception of IN-JU873 were detected during the course of the study.

Indoxacarb as well as the metabolites' residues found were generally confined to the upper soil segments (0–15 cm), with the highest concentration found in the 0–5 cm segment at every sampling. This demonstrates a low leaching potential for indoxacarb and its metabolites.

A DT_{50} of 7.32 days and a DT_{90} of 24.3 days was calculated for the parent compound, indicating a rapid dissipation of indoxacarb under field conditions.

Comment (RMS 2016)

This study was conducted with the active isomer DPX-KN128 as test material and is acceptable.

The same comments as made for previous study (Doig 2015d) can be made and are repeated here:

The level of residues observed at different depths confirm the rapid degradation of active substance (active isomer DPX-KN128) and the low potential of leaching of active substance and all its major metabolites, as none or very few residues of any compound were observed below 15 cm during the all course of the study.

No accumulation potential is detected for any of the compound, with the exception of IN-MK643 that seems to be quite persistent. However, this accumulation potential was already identified in the laboratory (with persistence DT_{50} of 314 days), and is taken into account in soil risk assessment with calculation of PECaccumulation.

It is noticeable that the metabolite IN-JU873 is not detected in this field trial although being a major metabolite in laboratory. However, laboratory data tend to show that this metabolite is quite transient (it is detected at level > 10% at only one sampling time among all studies). As mentioned by applicant, it is believed that this metabolite may have formed in the field at level below the LOD.

Degradation rate were only provided for active substance. On the more no normalized DT₅₀ are available. This could have been done, since the study was conducted according to EFSA guidance (2010) to minimize surface processes (11 mm of irrigation applied to the test plot within 24 hours after 1st application).

The data were not normalized and so no normalized DT₅₀ are available. At first approximation, from the daily soil temperature monitored in field, and the moisture content of the samples, it can be seen that:

- Soil temperature was always < 22°C during the course of the study
- Soil moisture was always < soil moisture at pF2.5, i.e soil correction factor from pF2 would certainly be <1.

This indicates that normalized DT₅₀ would have been shorter than the DT₅₀ based on non-normalised values. However, since irrigation was made after 1st sapling at days 0, normalised DT₅₀ should be derived from DAT3.

Study submitted to the EU for the first time in this submission and listed under “Documents Submitted”.

Data point:	CA 7.1.2.2.1/02
Author(s)	Woodmansey, L. (2014);
Title:	Freezer storage stability of indoxacarb (DPX-KN128) and metabolites (IN-MK643, IN-MK638, IN-KB687, IN-KT413, IN-KG433, IN-JU873 and IN-JT333) in soils
Organisation:	Charles River Laboratories (UK), Tranent, Scotland, UK, Charles River (France), Armancourt, France, Charles River Laboratories (Spain), Acala de Guadaira, Sevilla, 41500, Spain
Document No:	DuPont-35167
Dates of experimental work	
Guidelines:	OECD 506 (2007))
Deviations :	None
GLP:	Yes
Previous evaluation:	No
Acceptability:	The study is considered valid.

The frozen storage stability of indoxacarb (DPX-KN128) and its soil metabolites [IN-MK643, IN-MK638, IN-KB687, IN-KT413, IN-KG433, IN-JU873 and IN-JT333] was assessed in two representative soils obtained from the field dissipation study sites in North France [used for study DuPont-34323] and North Spain [used for study DuPont-34324].

The analytical method was that used in field dissipation studies.

The data demonstrated stability of residues in frozen soil for the 12-month duration of the study except for IN-KT413 in one site.

Summary of field dissipation trials

Field soil dissipation studies were conducted at 4 sites in Europe using Indoxacarb (DPX-KN128) 30WG: Bühren, Germany; Graffignana, Italy; Termens, Spain; and Douai, France. The metabolites were chosen based on the major metabolites observed from the laboratory metabolism studies. All metabolites monitored (IN-KT413, IN-JU873, IN-JT333, IN-KG433, IN-KB687, IN-MK463, and IN-MK638) with the exception of IN-JU873 were detected during the course of the study, which confirmed the degradation profile observed from the laboratory studies.

Indoxacarb as well as the metabolites' residues found were generally confined to the upper soil segments (0-15 cm), with the highest concentration found in the 0–5 cm segment at every sampling. This demonstrates a

low leaching potential for indoxacarb. These conclusions are consistent with its physical-chemical properties of low mobility (low solubility = 0.2 µg/ mL and high K_{ow} = 4.65).

The DT_{50} values (ranged from 7.08 to 9.4 days) were calculated for the parent compound, indicating a rapid dissipation of indoxacarb under field conditions. These field dissipation rates are also similar to the DT_{50} values (range from 2.4 to 10.3 days) estimated from laboratory study conditions at 20°C. No normalized DT_{50} were derived from these field data, although the trials were performed according to EFSA (2014)¹ guidance. At first approximation, RMS estimated from the field trials conditions (temperature and moisture) that the normalized DT_{50} should be in the same range, or shorter than DT_{50} derived from ambient conditions.

B.8.1.1.2.2. Soil accumulation studies

Not required

B.8.1.1.3. SUMMARY OF ROUTE AND RATE OF DEGRADATION IN SOIL

Route of degradation in laboratory

Under aerobic soil condition, the route of degradation of indoxacarb (DPX-KN128) was studied using radiolabelled [TFMP-¹⁴C]/[Ind-¹⁴C] DPX-JW062 and DPX-MP062 in a variety of aerobic soils, from four laboratory studies. These four laboratory studies were submitted in the original DAR, and no new studies were submitted for the purpose of renewal. Updated assessment of these studies revealed some uncertainties in the analytical results (unidentified radioactivity, variation of the isomeric ratio). They were still considered valid but a data gap is proposed by RMS for further investigation on the identification and characterization of unidentified polar fraction and further investigation on identity of metabolite IN-ML437-OH in the study of Singles (2002). It is RMS and co-RMS opinion that this data gap could be addressed with an additional soil metabolism study with active isomer DPX-KN128 on similar soil, with correct mass balance and peaks identification to confirm residue definition for risk assessment.

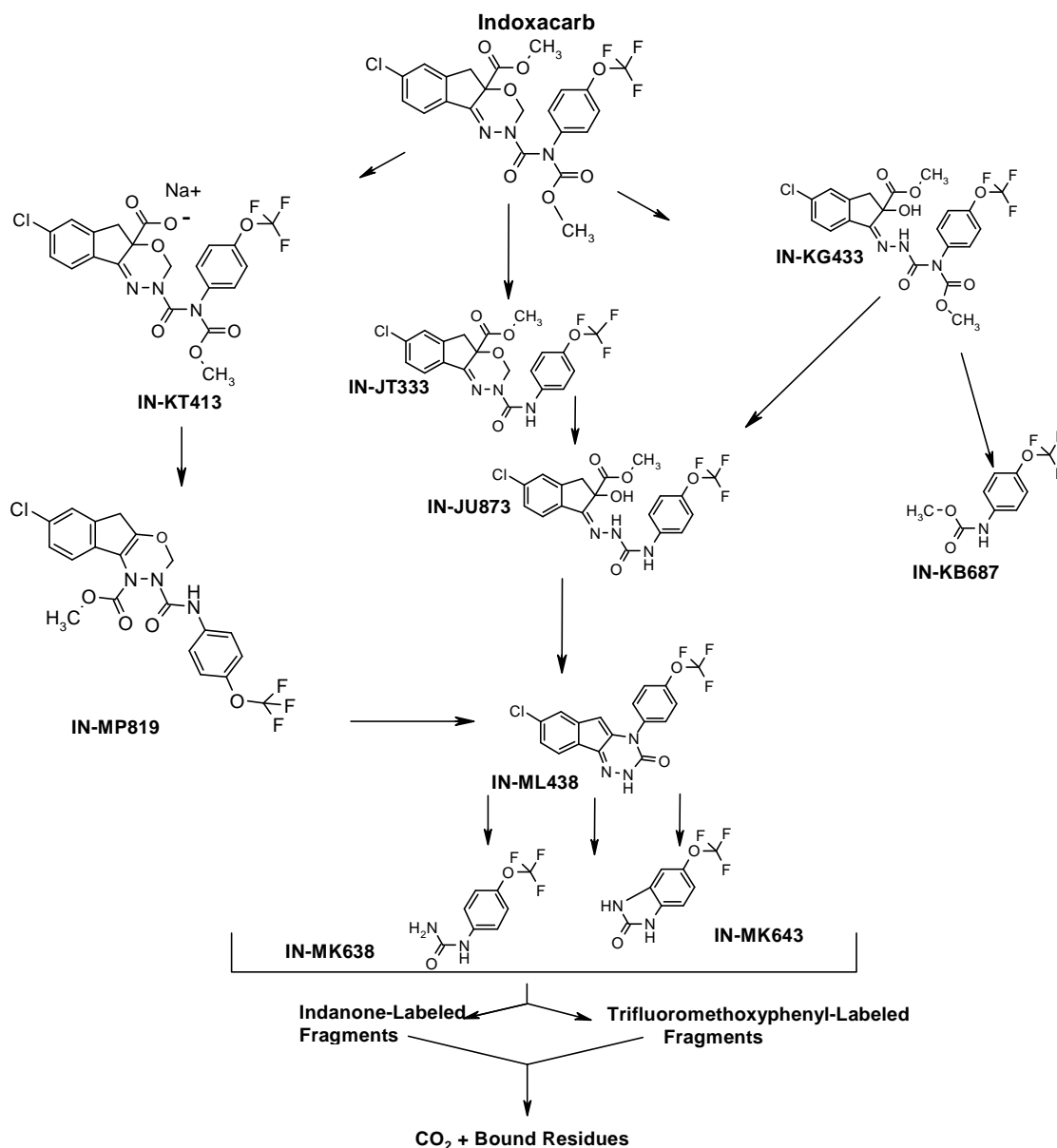
Some of the data were excluded from the kinetic evaluation for deriving degradation rate.

The proposed degradation pathway of indoxacarb in aerobic soil is shown in Figure 7. Degradation of indoxacarb proceeds by 3 major pathways: demethylation followed by N-decarboxylation to form IN-JT333, ester hydrolysis to form IN-KT413, and opening of the oxadiazine ring to form IN-KG433. These primary metabolites also degrade further. IN-JT333 undergoes additional transformation *via* opening of the oxadiazine ring to form IN-JU873. IN-JU873 proceeds through de-esterification and decarboxylation reactions and a ring closure to form IN-ML438. Both IN-JU873 and IN-ML438 are further transformed by bridge cleavage to form IN-MK643 and IN-MK638. IN-KG433 degraded *via* N-decarboxylation to form IN-JU873, and also cleavage of the urea bridge to form IN-KB687. IN-KT413 rearranged to form IN-MP819, which also rearranged to form IN-ML438. Mineralisation to ¹⁴CO₂ (maximum of 35.7% AR) and formation of non-extractable (bound) residues (maximum of 74.7% AR) were significant degradation processes.

The significance of the various metabolites varies in the different soils and is most likely due to variability in the composition of the microbial populations between soils. Based on the various soil metabolism studies, the overall maximum occurrences of IN-KT413, IN-KG433, IN-JT333, IN-JU873, IN-KB687, IN-ML438, IN-MK643, IN-MK638, and IN-MP819 were 18.4%, 39.7%, 18.6%, 12.9%, 6.9%, 9.7%, 12.0%, 28.1%, and 1.9% of the applied radioactivity (AR).

The major metabolites of indoxacarb in laboratory soils are IN-KT413, IN-KG433, IN-JT333, IN-JU873, IN-ML438, IN-MK643, and IN-MK638. IN-KB687 is a minor non transient metabolite. These eight metabolites are including in residue definition for risk assessment.

¹ EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662

Figure 7: Proposed degradation pathway of indoxacarb in aerobic soil**Discussion on the stability of the enantiomeric ratio of Indoxacarb and IN-JT333 in soil**

RMS had concern about the stability of the enantiomeric ratio of Indoxacarb and IN-JT333, since all laboratory degradation studies from the original DAR provided to support assessment of renewal of DPX-KN128 are made using DPX-JW062 (racemic mixture S/R) and DPX-MP062 (enriched mixture S/R 75/25). The data from chiral chromatography available does not provide conclusive evidence that the ratio is stable and that all data obtained with the racemic or 75/25 mixture can be transposed to DPX-KN128. This was also a concern raised by co-RMS during review.

For Indoxacarb and metabolite IN-JT333, data from chiral chromatography are available in two soils:

In the Tama soil from study of Spare 1997 the data collected from the chiral chromatography at day 14 and 21 tend to show that the R/S ratios of DPX-MP062 and IN-JT333 are stable throughout time (being approximatively 80:20 for indoxacarb and 90:10 for IN-JT333), indicating no preferential degradation of one isomer. It can

however be seen that active substance and metabolite do not have the same ratio (20/80 and 10/90 respectively), which is quite unexpected given that the degradation of indoxacarb to IN-JT333 does not involve the chiral center. Applicant further indicated that this could be due to small failure in fraction collection of IN-KN125 (S enantiomer of IN-JT333) which could not be easily isolated from DPX-KN128 (S enantiomer of DPX-MP062) as the peaks were very close. Peak of IN-KN125 (S) could be abnormally higher as containing small amount of DPX-KN128 (S).

In the Speyer 2.2 soil from the study of Mellor (2003), chiral chromatography was performed for sample treated with [^{14}C -Ind]label at several sampling times. It appears that the ratios were not stable with variation from 1/3 or 1/4 to 1/2 of 1/1 for indoxacarb and from 1/25 to 1/1 for metabolite IN-JT333. This is explained in the study being due to decreasing of radioactivity over time in each sample (for indoxacarb) and to the very low radioactivity present at each sampling time (for metabolite). However, RMS notes that this explanation is quite not reliable, as each item is detected at levels that are much higher than the theoretical LOQ (up to 15% AR as indoxacarb at the end of the study, and between 4 and 14% of AR for metabolite over time in each sample). The variations are more likely a result of the procedures used to isolate the peaks in preparation for chiral analyses.

The results from this chiral chromatography do not provide conclusive evidence of the stability of the ratio (see graph below). However, it does not either show a trend in the ratio evolution through time, which would reveal faster degradation of one isomer.

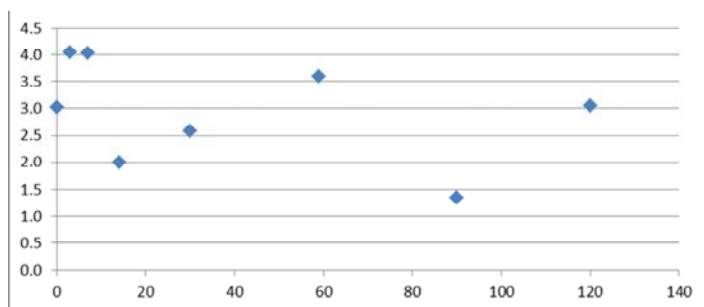


Figure 8: Evolution of the enantiomeric ratio of DPX-MP062 in the soil samples treated with ^{14}C -Ind in the study of Mellor (2003).

For IN-JT333, additional data on the enantiomeric ratio are available from the metabolite dosed study. It was not clear from the chiral chromatogram that the two peaks representing IN-KN125 and IN-KN124 (two enantiomers of IN-JT333) were identical. Applicant further provided the values of the peak area counted in dpm, which were shown to be nearly identical, indicating that there was no preferential degradation for the two enantiomers of IN-KN125 and IN-KN124 until day 7. It is however unfortunate that the ratio stability was not checked beyond 7 days.

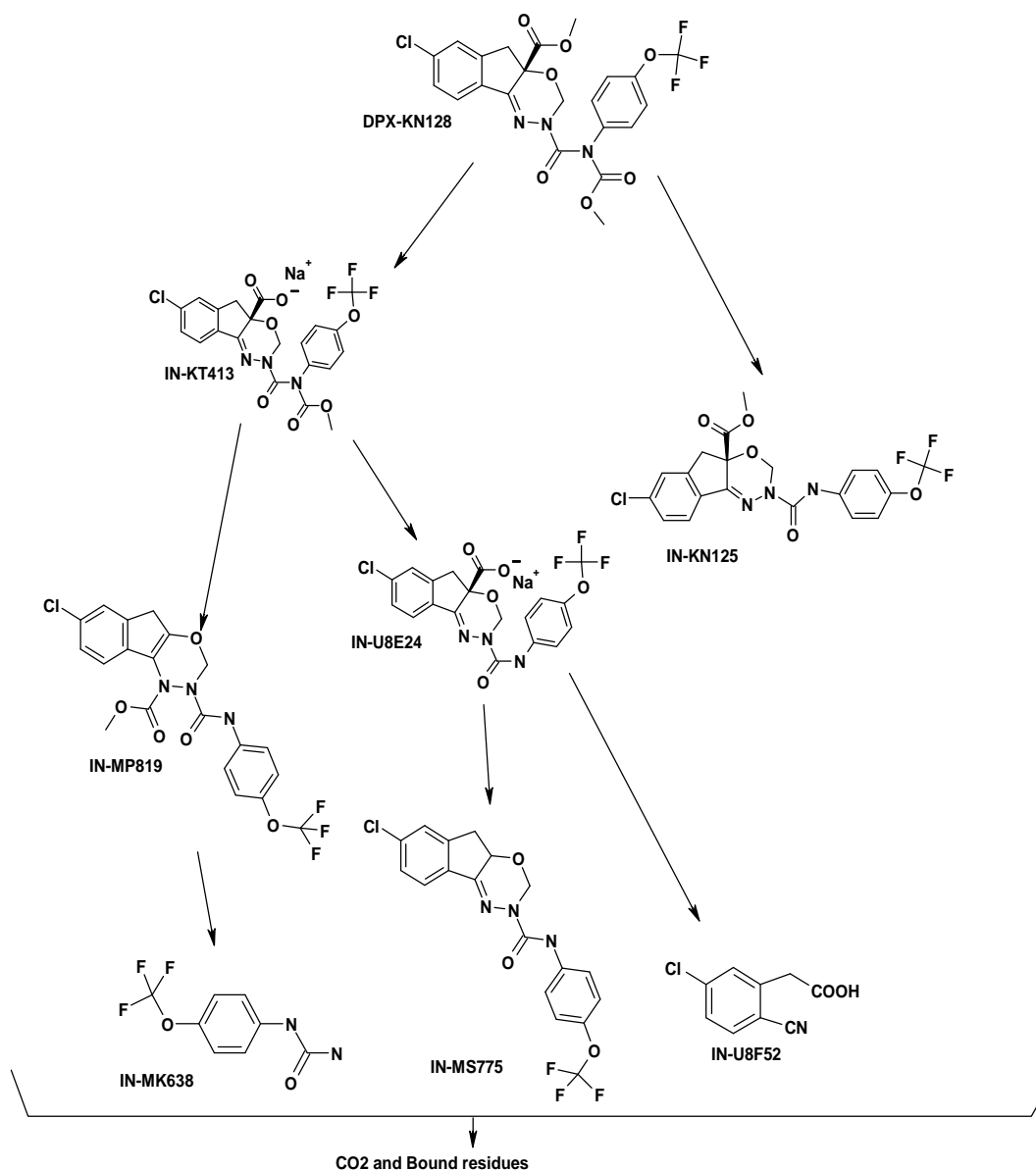
From all this data, it can be seen that no conclusive evidence of the stability of the active substance ratio is provided, as the data collected from the original laboratory studies seem to be uncertain due to analytical procedure. It is however noticeable that it does not provide clear evidence of a faster degradation of one of the isomers. RMS notes that new field trials were provided for the purpose of renewal, which were conducted with active S-isomer DPX-KN128 of the active substance. No normalised DT_{50} were derived from these trials, but this could give opportunity to check whether DT_{50} from field conducted with active isomer only are comparable to the DT_{50} of the mixture.

Under anaerobic conditions, the route of degradation of indoxacarb was studied using radiolabelled DPX-KN128 (S-enantiomer of Indoxacarb).

The major transformation products detected were IN-KT413, IN-U8E24, IN-MP819, IN-KN125, IN-MS775, IN-U8F52, and IN-MK638, with observed maximum concentrations of 25.2, 40.0, 5.9, 10.6, 35.4, 14.7, and 9.4% of the applied radioactivity (AR), respectively. It is noted that metabolite IN-U8E24 reached its maximum concentration during the anaerobic phase of the study (40.0%) but also reached 13.8% at DAT 2 during the preliminary aerobic phase of the study. It is thus considered as potential aerobic major metabolite and is included in the residue definition for risk assessment for soil and groundwater.

Proposed degradation pathway of indoxacarb in anaerobic soil is shown in Figure 9. Indoxacarb underwent ester hydrolysis to form IN-KT413 and IN-KN125 (S-enantiomer of IN-JT333; IN-JT333 is a mixture of IN-KN125 and IN-KN124, the break down product of IN-KN127) via demethylation N-decarboxylation. IN-KT413 also underwent decarboxylation and rearrangement of the N-methylester group to form IN-MP819. IN-MP819 further degraded to IN-MK638 through oxadiazine ring opening and bridge cleavage. IN-KT413 could degrade via demethylation N-decarboxylation to form IN-U8E24. Decarboxylation of IN-U8E24 led to the formation of the residue IN-MS775. IN-U8F52 was formed from IN-U8E24 via indanone ring opening. Formation of non-extractable (bound) residues (maximum of 37.3% AR) was also a significant degradation process.

RMS notes that this study revealed a new metabolite (IN-U8E24) that was detected at level >10% within the first aerobic phase of the study (max of 13.8% AR after 2.5 days). Applicant was thus requested to include this metabolite in the residue definition for risk assessment.



Note: IN-KN125 is S-enantiomer of IN-JT333

Figure 9: Proposed degradation pathway of indoxacarb in anaerobic soil

Soil photolysis of indoxacarb was studied using radiolabelled DPX-JW062. Under photolytic conditions, the main reaction was cleavage of the amide bond to form IN-KB687 (maximum of 22% of applied radioactivity). A minor reaction was the formation of IN-JT333 (maximum of 2.5% of the applied radioactivity) *via* N-decarboxylation. A small amount of CO₂ was also generated (maximum of 4.5% applied radiolabel). Soil photolysis is not expected to be a significant environmental degradation process, since the rate of degradation due to photolysis was essentially the same as the rate measured in the dark control.

Rates of degradation in laboratory

The rates of aerobic degradation of indoxacarb and its metabolites in the laboratory were calculated in a new kinetic evaluation which meets the current guidance of the FOCUS workgroup on degradation kinetics (FOCUS 2006).

Indoxacarb

The rate of aerobic degradation of indoxacarb was calculated in 5 different soils and conditions that were found to be reliable for kinetic purpose. DegT₅₀ and DegT₉₀ values for indoxacarb using FOMC and DFOP kinetics ranged from 2.4 to 10.3 days at 20°C and from 15.7 to 404.7 days, respectively. Normalised SFO or pseudo-SFO DegT₅₀ value ranged from 4.8 to 164.5 days and geomean of 32.4 days was retained for modelling purpose.

Metabolites

For metabolites, laboratory rate of degradation studies with metabolite directly applied were available for the following: IN-KT413, IN-KG433, IN-JT333, IN-JU873, IN-KB687, IN-ML438, IN-MK643 and IN-MK638. In addition, attempts were made to derive DT₅₀ data for every metabolite from the laboratory degradation studies performed with indoxacarb as the applied test material, but only some of the fits results for IN-JT333 and IN-ML438 were found reliable.

DegT₅₀ and DegT₉₀ values for the metabolite IN-JT333 using SFO, FOMC and DFOP kinetics ranged from 4.3 to 34.6 days and from 37.8 to 228.8 days, respectively. Normalised SFO or pseudo-SFO DegT₅₀ value ranged from 5.0 to 111 days and geomean of 16.3 days was retained for modelling purpose. The values were derived from metabolite applied studies and indoxacarb laboratory degradation studies.

DegT₅₀ and DegT₉₀ values for the metabolite IN-KG433 using FOMC and DFOP kinetics ranged from 1.6 to 2.5 days and from 13.1 to 57.8 days, respectively. Normalised SFO or pseudo-SFO DegT₅₀ value ranged from 2.6 to 17.4 days and geomean of 4.2 days was retained for modelling purpose. The values were derived from metabolite applied studies only.

DegT₅₀ and DegT₉₀ values for the metabolite IN-MK638 using SFO and DFOP kinetics ranged from 4.8 to 17.3 days and from 16.1 to 57.5 days, respectively. Normalised SFO or pseudo-SFO DegT₅₀ value ranged from 4.0 to 16.0 days and geomean of 8.0 days was retained for modelling purpose. The values were derived from metabolite applied studies only.

DegT₅₀ and DegT₉₀ values for the metabolite IN-MK643 using SFO kinetics ranged from 123.3 to 314.2 days and from 490.6 to 1043.8 days, respectively. Normalised SFO DegT₅₀ value ranged from 88.7 to 314.2 days and geomean of 169.5 days was retained for modelling purpose. The values were derived from metabolite applied studies only.

DegT₅₀ and DegT₉₀ values for the metabolite IN-ML438 using SFO and DFOP kinetics ranged from 40.6 to 107.1 days and from 241.9 to 507.7 days, respectively. Normalised SFO or pseudo-SFO DegT₅₀ value ranged from 80.9 to 172.8 days and geomean of 186.5 days was retained for modelling purpose. The values were derived from metabolite applied studies and indoxacarb laboratory degradation studies.

DegT₅₀ and DegT₉₀ values for the metabolite IN-JU873 using DFOP kinetics ranged from 10.0 to 32.8 days and from 66.4 to 242.5 days, respectively. Normalised SFO DegT₅₀ value ranged from 15.6 to 47.2 days and geomean of 32.1 days was retained for modelling purpose. The values were derived from metabolite applied study only.

DegT₅₀ and DegT₉₀ values for the metabolite IN-KB687 using SFO and FOMC kinetics were 0.67 and 0.56 days and from 2.21 to 1.85 days, respectively (only two reliable values). Normalised SFO DegT₅₀ value were 0.51 and 0.67 days and worst-case value of 0.67 days was retained for modelling purpose.

DegT₅₀ and DegT₉₀ values for the metabolite IN-KT413 using DFOP and FOMC kinetics ranged from 0.6 to 4.0 days and from 2.6 to 20.5 days, respectively. Normalised SFO DegT₅₀ value ranged from 0.6 to 3.7 days and geomean of 1.7 days was retained for modelling purpose. The values were derived from metabolite applied study only.

Based on the DT₅₀ values (2.4 to 10.3 days) measured under laboratory conditions, there is little chance of accumulation of indoxacarb under realistic environmental conditions. However, based on the DT₉₀ of indoxacarb and DegT₅₀ or DegT₉₀ of metabolites, field dissipation trials are triggered for the following items:

- Indoxacarb, with maximum persistence DT₉₀ of 404.7 d (DFOP)
- IN-JT333, with maximum persistence DT₉₀ of 228.8 d (DFOP)
- IN-JU873, with maximum persistence DT₉₀ of 156.8d (SFO)
- IN-ML438, with maximum persistence DT₅₀ and DT₉₀ of 109.5d and 363.7d (SFO)
- IN-MK643, with maximum persistence DT₅₀ and DT₉₀ of 314.2d and 1043.8d (SFO)

Field dissipation studies

Field soil dissipation studies were conducted at 4 sites in Europe using Indoxacarb (DPX-KN128) 30WG: Bühren, Germany; Graffignana, Italy; Termens, Spain; and Douai, France. The metabolites were chosen based on the major metabolites observed from the laboratory metabolism studies. All metabolites monitored (IN-KT413, IN-JU873, IN-JT333, IN-KG433, IN-KB687, IN-MK463, and IN-MK638) with the exception of IN-JU873 were detected during the course of the study, which confirmed the degradation profile observed from the laboratory studies.

Indoxacarb as well as the metabolites' residues found were generally confined to the upper soil segments (0-15 cm), with the highest concentration found in the 0–5 cm segment at every sampling. This demonstrates a low leaching potential for indoxacarb. These conclusions are consistent with high K_{oc} (K_{oc} = 5125 mL/g).

The DT₅₀ values (ranged from 7.08 to 9.4 days) were calculated for the parent compound, indicating a rapid dissipation of indoxacarb under field conditions. These field dissipation rates are also in the same range of the DT₅₀ values (range from 2.4 to 10.3 days) estimated from laboratory study conditions at 20°C.

No normalized DT₅₀ were derived from these field data, although the trials were performed according to EFSA (2014)² guidance. RMS is of the opinion that normalized DT₅₀ should be derived and would allow addressing some of remaining uncertainties concerning the stability of the isomeric ratio, and the robustness of the original laboratory data to derive DT₅₀. Since irrigation was made after 1st sampling at days 0, normalised DT₅₀ should be derived from DAT3.

² EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT₅₀ values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014;12(5):3662

B.8.1.2. ADSORPTION AND DESORPTION IN SOIL**B.8.1.2.1. ACTIVE SUBSTANCE**

Author(s)	Smyser, B.P. (2002);
Title:	Batch equilibrium study of DPX-JW062 (a racemic mixture of DPX-KN128 and IN-KN127) and IN-JT333
Organisation:	Critical Path Services, LLC, Newport, Delaware, USA
Document No:	AMR 3489-95, Revision No. 1
Dates of experimental work	
Guidelines:	USEPA 163-1
Deviations :	See RMS comments
GLP:	Yes
Previous evaluation:	Yes,
Acceptability:	See RMS comments

MATERIALS AND METHODS

2. Radiolabeled test material:	¹⁴ C-DPX-JW062 technical ¹⁴ C-IN-JT333 technical
Lot/Batch #:	[Indanone-1- ¹⁴ C]DPX-JW062: HOTC# 0428 [Trifluoromethoxyphenyl(U)- ¹⁴ C]DPX-JW062: HOTC# 0423 [Methylene- ¹⁴ C]IN-JT333: HOTC# 464
Radiochemical purity:	[Indanone-1- ¹⁴ C]DPX-JW062: 95% [Trifluoromethoxyphenyl(U)- ¹⁴ C]DPX-JW062: 93% [Methylene- ¹⁴ C]IN-JT333: 90%
Specific activity:	[Indanone-1- ¹⁴ C]DPX-JW062: 45.118 µCi/mg [Trifluoromethoxyphenyl(U)- ¹⁴ C]DPX-JW062: 54.03 µCi/mg [Methylene- ¹⁴ C]IN-JT333: 42.64 µCi/mg
Description:	White powder
Stability of test compound:	The test substances were not stable in the soil-water systems.

Study design

The adsorption characteristics of [trifluoromethoxyphenyl (U)-¹⁴C]DPX-JW062 and [methylene-¹⁴C]IN-JT333 on four US soils were investigated (Table 8-135). Initial concentrations of approximately 12 ng ¹⁴C-DPX-JW062 or ¹⁴C-IN-JT333 per mL were prepared in 0.01 M aqueous calcium chloride. Testing was conducted in duplicates (one [indanone-1-¹⁴C]indoxacarb label and one Trifluoromethoxyphenyl-¹⁴C(U)]indoxacarb label for DPX-JW062) with five soil/solution ratios varying from 0.2:25 to 5:25 (g:mL). This study design was used due to the low aqueous solubility of both DPX-JW062 and IN-JT333. The soil/solution mixtures were shaken at 24-26°C for one hour in the dark. Following equilibration, aqueous samples and soil extracts were analysed by LSC and by HPLC. Unextracted residues were quantitated by combustion analysis and LSC.

Mean adsorption coefficients, K_d , were calculated from the ratios of C_s to C_w , where C_s and C_w represent the test substance concentration in soil and in the aqueous phase at equilibrium, respectively. Linear sorption equations were generated by plotting the C_s values against the C_w and forcing the intercept through zero.

Table 8-135: Characteristics of U.S. test soils

Characteristic	Soil			
Soil Name or Designation	Myaka	Donna	Chino	Tama
Origin Location	Florida, USA	Texas, USA	California, USA	Illinois, USA
pH*	6.2	7.8	7.6	6.2
% Sand (2000-50 µm)	91.6	47.2	40.8	9.6
% Silt (<50-2 µm)	4.0	24.0	40.4	66.0
% Clay (<2 µm)	4.4	28.8	18.8	24.4
Texture ^a	Sand	Sandy clay loam	Loam	Silt loam
Organic matter (%)	1.0	1.4	1.7	2.4
Organic carbon (%) ^b	0.58	0.812	0.986	1.392
Cation exchange capacity	3.8	18.1	17.3	16.7

^a USDA soil classification system

^b organic carbon = organic matter/1.72

* Medium in which pH was measured is not precised in the report.

RESULTS AND DISCUSSION

Equilibration time

An equilibration time of 1 hour was used based on results from preliminary experiments.

Material balance

Total recoveries of radioactivity ranged from 72 to 116% and from 82 to 130% across all soils for DPX-JW062 and IN-JT333, respectively.

Adsorption

Mean adsorption coefficients for DPX-JW062 and IN-JT333 are listed in Table 8-136 and Table 8-137, respectively. The K_d values for DPX-JW062 ranged from 26 to 95 mL/g (average of 46 mL/g) and K_{oc} values ranged from 2500 to 9600 mL/g (average of 5125 mL/g). The K_d values for IN-JT333 ranged from 96 to 241 mL/g (average of 150 mL/g) and K_{oc} values ranged from 8200 to 25000 mL/g (average of 17300 mL/g). There was no clear correlation between adsorption and soil characteristics.

Desorption

Desorptions were not performed, since DPX-JW062 and IN-JT333 were not stable in the soil-water systems.

Table 8-136: Summary of mean soil adsorption coefficients for DPX-JW062

Soil	Texture ^a	pH	% Organic carbon ^b	K_d (mL/g)	K_{om} (mL/g)	K_{oc} (mL/g)
Myaka	Sand	6.2	0.58	29	2900	5100
Donna	Sandy clay loam	7.8	0.81	26	1900	3300
Chino	Loam	7.6	0.99	95	5600	9600
Tama	Silt loam	6.2	1.5	35	1500	2500

^a USDA classification

^b Organic matter/1.72

Table 8-137: Summary of mean soil adsorption coefficients for IN-JT333

Soil	Texture ^a	pH	% Organic carbon ^b	K _d (mL/g)	K _{om} (mL/g)	K _{oc} (mL/g)
Myaka	Sand	6.2	0.58	147	14700	25000
Donna	Sandy clay loam	7.8	0.81	96	6900	12000
Chino	Loam	7.6	0.99	241	14200	24000
Tama	Silt loam	6.2	1.5	114	46500	8200

^a USDA classification

^b Organic matter/1.72

CONCLUSION

DPX-JW062 and IN-JT333 strongly adsorbed to soil. The average K_{oc} values for DPX-JW062 and IN-JT333 were 5125 and 17300 mL/g, respectively. There was no clear correlation between adsorption and soil characteristics.

RMS (2016):

Definitive tests were limited to 1 hour as the two substances were not stable in the test system. Concentrations of test items were determined in both aqueous and solid phase.

The definitive test was not conducted with different test solution concentration but with 5 different soil/solution ratios. This implies that the values obtained are not determined according to an adsorption isotherm, which is a major deviation of the OECD 106 guideline.

This approach is justified by applicant by the fact that the limits of solubility of the 2 tested items being very low it was necessary to ensure sufficient concentration in aqueous phase for detection. This also allowed minimizing the adsorption effect on test vessels.

RMS notes that the LOD and LOQ were not indicated in the study report and applicant further indicated that they were the following:

	LOD	LOQ
[Indanone-1-14C]DPX-JW062	0.12 ppb	1.10ppb
[Trifluoromethoxyphenyl-(U)14C]DPX-JW062	LOD=0.11	0.92ppb

Physico-chemical studies indicate that the aqueous solubility was determined to be 15 ppb and 0.2 mg/L in two different studies. RMS is of the opinion that solubility of indoxacarb should have been tested in a new batch equilibrium study and attempts to get a freundlich K_{foc} value should have been made.

In the absence of any other updated adsorption study, and considering that the experimental data reflect strong adsorption of indoxacarb on soil, the arithmetic mean K_{oc} from this study with default 1/n value of 1 are kept for risk assessment

B.8.1.2.2. METABOLITES**IN-JT333**

Author(s)	Smyser, B.P. (2002);
Title:	Batch equilibrium study of DPX-JW062 (a racemic mixture of DPX-KN128 and IN-KN127) and IN-JT333
Organisation:	Critical Path Services, LLC, Newport, Delaware, USA
Document No:	AMR 3489-95, Revision No. 1
Dates of experimental work	
Guidelines:	USEPA 163-1
Deviations :	See RMS comments
GLP:	Yes
Previous evaluation:	Yes,
Acceptability:	See RMS comments

See study summary under previous point

IN-JU873

Author(s)	Hatzenbeler, C.J. (2002);
Title:	Adsorption/desorption of [¹⁴ C]IN-JU873, a metabolite of indoxacarb, in five soils
Organisation:	
Document No:	DuPont-6407
Dates of experimental work	
Guidelines:	U.S. EPA 163-1 (1982), OECD 106 (1999)
Deviations :	See RMS comments
GLP:	Yes
Previous evaluation:	Yes, in DAR addendum 2005
Acceptability:	Yes

- Test material: ¹⁴C-IN-JU873 radiolabeled technical metabolite
Lot/Batch #: HOTC 0572
Purity: 99%

MATERIALS AND METHODS

1. Radiolabeled test material:	[¹⁴ C]IN-JU873 technical metabolite
Lot/Batch #:	[¹⁴ C]IN-JU873: HOTC 0572
Radiochemical purity:	[¹⁴ C]IN-JU873: 99%
Specific activity:	[¹⁴ C]IN-JU873: 39.3 µCi/mg
Description:	White powder
Stability of test compound:	The test material was stable under the conditions of the study.

Study design

The adsorption/desorption characteristics of [¹⁴C]IN-JU873 were investigated on five different soils (Table 8-138). Nominal test solution concentrations of 0.005, 0.01, 0.025, 0.05, 0.075, and 0.1 µg/mL were prepared in 0.01 M CaCl₂. Testing was conducted in duplicate with soil-to-solution ratios of 1:20 (2 grams dry weight soil: 40 mL test solution). Samples were equilibrated for 24 hours *via* mechanical agitation at 20°C in the dark. After equilibrium was reached, samples were centrifuged and the supernatant was decanted. The supernatant was analysed by LSC and HPLC analysis with radiochemical detection was performed on one replicate at the highest concentration in each soil to verify stability. Two 24-hour desorption intervals were conducted on the 0.075 µg/mL samples following the adsorption by removing the supernatant following centrifugation and replacing with an equivalent volume of fresh 0.01 M CaCl₂ solution. After the second desorption, non-extractable soil residues were quantified by combustion and LSC.

Adsorption and desorption isotherm data were analysed using the log form of the Freundlich equation: $\log x/m = 1/n * \log C_e + \log K_f$. The constants K_f and $1/n$ were obtained by a least squares regression of a plot of $\log x/m$ versus $\log C_e$. K_d values were obtained by determining the mean ratio of x/m to C_e for each soil type. K_{oc} and K_{foc} values are equivalent to the K_d or K_f value divided by the fraction of organic carbon in the system. K_{om} and K_{fom} are equivalent to the K_d or K_f value divided by the fraction of organic matter in the soil.

Table 8-138: Characteristics of test soils

Characteristic	Soil				
Soil Name or Designation	Speyer 2.2	Mattapex (#25)	Pesaro	Lleida	Hidalgo 5-S
Origin	Germany	USA	Italy	Spain	USA
pH (in water)	6.7	5.2	8	8.1	8
% Sand (2000-50 µm)	73.2	45.2	20.8	32.8	55.2
% Silt (<50-2 µm)	20.0	44.0	48.8	36.8	22.0
% Clay (<2 µm)	6.8	10.8	30.4	30.4	22.8
Texture ^a	Sandy loam	Loam	Clay loam	Clay loam	Sandy clay loam
Organic matter	3.8	1.4	2.0	2.0	0.7
Organic carbon (%) ^b	2.2	0.8	1.2	1.2	0.4
Cation exchange capacity (mEq/100 g)	9.09	4.09	17.22	19.02	12.21
Maximum water-holding capacity (%)	47.8	41.9	58.3	42.6	36.0

^a USDA soil classification system

^b organic carbon = organic matter/1.724

II. RESULTS AND DISCUSSION

Equilibration time

Time to equilibration of IN-JU873 between soil and solution was judged to be 24 hours with a soil-to-solution ratio of 1:20.

Material balance

Recoveries of radioactivity from vessels were determined in all the soils after a 24 hour equilibration period. Recoveries of radioactivity after adsorption and two desorption equilibrations ranged from 95 to 102%.

After 24 hours of equilibration, greater than 87% of the radioactivity in the supernatant was IN-JU873 by HPLC analysis.

Adsorption

The linear adsorption coefficients for IN-JU873 are listed in Table 8-139. The K_d values ranged from 53 to 409 mL/g and the K_{oc} values ranged from 7535 to 18591 mL/g (average = 12816 mL/g). Freündlich sorption isotherm parameters are given in Table 8-140. The adsorption constant, K_f , ranged from 56 to 605 mL/g with K_{foc} values ranging from 5417 to 31750 mL/g (average = 16883 mL/g). The $1/n$ values ranged from 0.939 to 1.123 (average = 1.02).

Desorption

IN-JU873 could be desorbed from the soils. The average percentage of the adsorbed IN-JU873 which was desorbed during two desorption intervals is listed in Table 8-141. A total of 10 to 45% of the adsorbed IN-JU873 was removed in the two desorption intervals.

Table 8-139: Summary of the averaged linear soil adsorption coefficients for IN-JU873

Soil	Texture ^a	pH (water)	% Organic carbon ^b	K_d (mL/g)	K_{om} (mL/g)	K_{oc} (mL/g)
Speyer 2.2	Sandy loam	6.7	2.2	409	10763	18591
Mattapex (#25)	Loam	5.2	0.8	141	10042	17573
Pesaro	Clay loam	8.0	1.2	87	4354	7257
Lleida	Clay loam	8.1	1.2	90	4521	7535
Hidalgo	Sandy clay loam	8.0	0.4	53	7500	13125

^a USDA classification

^b Organic matter/1.72

Table 8-140: Summary of the Freündlich equation parameters for the IN-JU873 adsorption isotherms

Soil	Texture ^a	pH (water)	% Organic carbon ^b	K_f (mL/g)	$1/n$	K_{fom} (mL/g)	K_{foc} (mL/g)
Speyer 2.2	Sandy loam	6.7	2.2	605	1.061	15921	27500
Mattapex (#25)	Loam	5.2	0.8	254	1.123	18143	31750
Pesaro	Clay loam	8.0	1.2	69	0.954	3450	5750
Lleida	Clay loam	8.1	1.2	65	0.939	3250	5417
Hidalgo	Sandy clay loam	8.0	0.4	56	1.025	8000	14000

^a USDA classification

^b Organic matter/1.72

Table 8-141: Average percent of sorbed IN-JU873 desorbed during two desorption intervals

Soil	USDA texture	% Organic carbon	Percent of adsorbed IN-JU873 desorbed during the first desorption interval	Percent of adsorbed IN-JU873 desorbed during the second desorption interval	Total percent of adsorbed IN-JU873 desorbed
Speyer 2.2	Sandy loam	2.2	4.1	5.5	9.6
Mattapex (#25)	Loam	0.8	13.7	5.1	18.8
Pesaro	Clay loam	1.2	21.2	13.0	34.2
Lleida	Clay loam	1.2	15.9	17.6	33.4
Hidalgo	Sandy clay loam	0.4	25.5	19.3	44.7

RMS (2016)

Study still considered valid. Concentration of test item in soil was calculated from difference between total amount added and amount analysed in water. This can be accepted as the substance is strongly adsorbed to soil, and as preliminary tests showed that it was stable in solution, and did not adsorb to vessels.

As done during first review, K_{foc} value from Mattapex soil is excluded from the final endpoint calculation, since 1/n value of outside the acceptable range.

There was no clear correlation between adsorption and soil characteristics. Mean K_{foc} value of 13 167 mL/g (n=4) with 1/n value of 0.99 is retained for modelling.

IN-KG433

Data point:	CA 7.1.3.1.2
Author(s)	Hatzenbeler, C.J. (2002);
Title:	Adsorption/desorption of [¹⁴ C]IN-KG433, a metabolite of indoxacarb, in five soils
Organisation:	Ricerca LLC, Painesville, Ohio, USA
Document No:	DuPont-6408, Revision No. 2
Dates of experimental work	
Guidelines:	USEPA 163-1 (1982), OECD 106 (1999)
Deviations :	See RMS comments
GLP:	Yes
Previous evaluation:	Yes, in the indoxacarb DAR addendum 3 (2005)
Acceptability:	Yes

MATERIALS AND METHODS

- Radiolabeled test material: [¹⁴C]IN-KG433 technical metabolite
 Lot/Batch #: [¹⁴C]IN-KG433: HOTC 422
 Radiochemical purity: [¹⁴C]IN-KG433: 92.7%
 Specific activity: [¹⁴C]IN-KG433: 108.9 µCi/mg

Description:	White powder
Stability of test compound:	The test substance was considered stable over the 1 hour equilibration period.

Study design

The adsorption/desorption characteristics of [indanone-1-¹⁴C]IN-KG433 were investigated on five different soils (Table 8-142). Nominal test solution concentrations of 0.025, 0.05, 0.1, 0.5, and 1.0 µg/mL were prepared in 0.01 M CaCl₂. Testing was conducted in duplicate with soil-to-solution ratios of 1:2 (5 grams dry weight soil: 10 mL test solution). Samples were equilibrated for 1 hour *via* mechanical agitation at 20°C in the dark. After equilibrium was reached, samples were centrifuged and the supernatant was decanted. The supernatant was analysed by LSC and HPLC analysis with radiochemical detection was performed on one replicate at the highest concentration in each soil to verify stability. Two 24-hour desorption intervals were conducted on the 1.0 µg/mL samples following the adsorption by removing the supernatant following centrifugation and replacing with an equivalent volume of fresh 0.01 M CaCl₂ solution. After the second desorption, non-extractable soil residues were quantified by combustion and LSC.

Adsorption and desorption isotherm data were analysed using the log form of the Freundlich equation: $\log x/m = 1/n * \log C_e + \log K_f$. The constants K_f and $1/n$ were obtained by a least squares regression of a plot of $\log x/m$ versus $\log C_e$. K_d values were obtained by determining the mean ratio of x/m to C_e for each soil type. K_{oc} and K_{foc} values are equivalent to the K_d or K_f value divided by the fraction of organic carbon in the system. K_{om} and K_{fom} are equivalent to the K_d or K_f value divided by the fraction of organic matter in the soil.

Table 8-142: Characteristics of test soils

Characteristic	Soil				
Soil name or designation	Speyer 2.2	Mattapex #25	Pesaro	Lleida	Hidalgo 5-S
Origin	Germany	USA	Italy	Spain	USA
pH (in water)	6.7	5.2	8	8.1	8
% Sand (2000-50 µm)	73.2	45.2	20.8	32.8	55.2
% Silt (<50-2 µm)	20.0	44.0	48.8	36.8	22.0
% Clay (<2 µm)	6.8	10.8	30.4	30.4	22.8
Texture ^a	Sandy loam	Loam	Clay loam	Clay loam	Sandy clay loam
Organic matter	3.8	1.4	2.0	2.0	0.7
Organic carbon (%) ^b	2.2	0.8	1.2	1.2	0.4
Cation exchange capacity (mEq/100 g)	9.09	4.09	17.22	19.02	12.21
Maximum water-holding capacity (%)	47.8	41.9	58.3	42.6	36.0

^a USDA soil classification system

^b organic carbon = organic matter/1.724

II. RESULTS AND DISCUSSION

Equilibration time

Time for equilibration of IN-KG433 between soil and solution was judged to be 1 hour with a soil-to-solution ratio of 1:2.

Material balance

Recoveries of radioactivity from vessels were determined in the Speyer 2.2 and Hidalgo 5-S soils. Recoveries of radioactivity after adsorption and two desorption equilibrations were 106.1 and 102.0% in the Speyer and Hidalgo soils, respectively.

After 1 hour of equilibration, greater than 90% of the radioactivity in the supernatant was IN-KG433 by HPLC analysis.

Adsorption

The linear adsorption coefficients for IN-KG433 are listed in Table 8-143. The K_d values ranged from 1.4 to 11.4 mL/g and K_{oc} values ranged from 343 to 518 mL/g (average = 400 mL/g). Freündlich sorption isotherm parameters are given in Table 8-144. The adsorption constant, K_f , ranged from 1.2 to 8.7 mL/g with K_{foc} values ranging from 267 to 395 mL/g (average = 314 mL/g). The $1/n$ values ranged from 0.8774 to 0.9475 (average = 0.9132).

Desorption

IN-KG433 was moderately desorbed from the soils. The average percentage of the adsorbed IN-KG433 which was desorbed during two desorption intervals is listed in Table 8-145. A total of 37 to 63% of the adsorbed IN-KG433 was removed in the two desorption intervals.

Table 8-143: Summary of the averaged linear soil adsorption coefficients for IN-KG433

Soil	Texture ^a	pH (water)	% Organic carbon ^b	K_d (mL/g)	K_{om} (mL/g)	K_{oc} (mL/g)
Speyer 2.2	Sandy loam	6.7	2.2	11.4	300	518
Mattapex (#25)	Loam	5.2	0.8	2.9	206	360
Pesaro	Clay loam	8	1.2	5.2	260	433
Lleida	Clay loam	8.1	1.2	4.2	209	348
Hidalgo 5-S	Sandy clay loam	8	0.4	1.4	196	343

^a USDA classification

^b Organic matter/1.72

Table 8-144: Summary of the Freündlich equation parameters for the IN-KG433 adsorption isotherms

Soil	Texture ^a	pH (water)	% Organic carbon ^b	K_f (mL/g)	$1/n$	K_{fom} (mL/g)	K_{foc} (mL/g)
Speyer 2.2	Sandy loam	6.7	2.2	8.7	0.9154	229	395
Mattapex (#25)	Loam	5.2	0.8	2.4	0.9278	171	300
Pesaro	Clay loam	8	1.2	3.7	0.8774	185	308
Lleida	Clay loam	8.1	1.2	3.2	0.8979	160	267
Hidalgo 5-S	Sandy clay loam	8	0.4	1.2	0.9475	171	300

^a USDA classification

^b Organic matter/1.72

Table 8-145 : Average percent of sorbed IN-KG433 desorbed during two desorption intervals

Soil	USDA texture	% Organic carbon	Percent of adsorbed IN-KG433 desorbed during the first desorption interval	Percent of adsorbed IN-KG433 desorbed during the second desorption interval	Total percent of adsorbed IN-KG433 desorbed
Speyer 2.2	Sandy loam	2.2	21.9	15.2	37.1
Mattapex (#25)	Loam	0.8	43.0	19.8	62.7
Pesaro	Clay loam	1.2	38.8	20.4	59.2
Lleida	Clay loam	1.2	41.4	20.2	61.6
Hidalgo 5-S	Sandy clay loam	0.4	35.9	19.0	54.9

CONCLUSION

IN-KG433 is moderately sorbed to soil. The average linear K_{oc} value was 400 mL/g and the average Freundlich K_{foc} value was 314 mL/g. The average Freundlich $1/n$ value was 0.9132. The sorption was correlated to the organic carbon content of soil, so adsorption will be affected by soil type. Adsorbed IN-KG433 was moderately (37 to 63%) desorbed from test soils.

RMS (2016)

For Hidalgo soil, the soil/solution ratio used in the definitive test was different from the others (1:2 instead of 1:5) as no sufficient adsorption was observed in the preliminary test for this soil with 1:5 ratio. The study is considered acceptable.

There was no clear correlation between adsorption and soil characteristics. Mean K_{foc} value of 314 mL/g with $1/n$ value of 0.913 is retained for modelling.

IN-KT413

Author(s)	Walsh, K.J. (2003);
Title:	Adsorption/desorption of [^{14}C]IN-KT413, a metabolite of indoxacarb, in four soils
Organisation:	Ricerca LLC, Painesville, Ohio, USA
Document No:	DuPont-10500
Dates of experimental work	
Guidelines:	OECD 106 (2000), US EPA 163-1 (1982)
Deviations :	None
GLP:	Yes
Previous evaluation:	Yes
Acceptability:	Yes

MATERIALS AND METHODS

- Radiolabeled test material: [^{14}C]IN-KT413 technical
 Lot/Batch #: [^{14}C]IN-KT413 SMS#: 4000423
 Radiochemical purity: [^{14}C]IN-KT413: 91.6%
 Specific activity: [^{14}C]IN-KT413: 47.2 $\mu\text{Ci/mg}$
 Description: White powder
 Stability of test compound: Shown to be stable under the conditions of the test.

- Soils:

Table 8-146: Characteristics of test soils

Characteristic	Soil			
Soil Name or Designation	Speyer 2.2	Mattapex (#25)	Lleida	Hidalgo 5-S
Origin	Germany	USA	Spain	USA
pH (in water)	6.5	6.7	8.1	8.6
% Sand (2000-50 µm)	88.0	24.0	34.0	58.0
% Silt (<50-2 µm)	10.0	68.0	38.0	20.0
% Clay (<2 µm)	2.0	8.0	28.0	22.0
Texture ^a	Sand	Silt loam	Clay loam	Sandy clay loam
Organic matter	3.0	3.7	2.0	0.8
Organic carbon (%) ^b	1.7	2.2	1.2	0.5
Cation exchange capacity (mEq/100 g)	8.27	13.78	20.69	15.8
Maximum water-holding capacity (%)	43.1	60.9	45.2	38.1

^a USDA soil classification system

^b organic carbon = organic matter/1.724

Experimental conditions

The adsorption/desorption characteristics of [trifluoromethoxyphenyl(U)-¹⁴C]IN-KT413 were investigated on five different soils (Table 8-146). Nominal test solution concentrations of 0.1, 0.05, 0.025, 0.01, and 0.005 µg/mL were prepared in 0.01 M CaCl₂. Testing was conducted in duplicate with soil-to-solution ratios of 1:5 (5 grams dry-weight soil: 25 mL test solution). Samples were equilibrated for 18 hours *via* mechanical agitation at 20°C in the dark. After equilibrium was reached, samples were centrifuged and the supernatant was decanted. The supernatant was analysed by LSC and HPLC analysis with radiochemical detection was performed on one replicate at the highest concentration in each soil to verify stability. Two 18-hour desorption intervals were conducted on the 0.1 µg/mL samples following the adsorption by removing the supernatant following centrifugation and replacing with an equivalent volume of fresh 0.01 M CaCl₂ solution. After the second desorption, non-extractable soil residues were quantified by combustion and LSC.

Adsorption and desorption isotherm data were analysed using the log form of the Freundlich equation: $\log x/m = 1/n * \log C_e + \log K_f$. The constants K_f and $1/n$ were obtained by a least squares regression of a plot of $\log x/m$ versus $\log C_e$. K_d values were obtained by determining the mean ratio of x/m to C_e for each soil type. K_{oc} and K_{foc} values are equivalent to the K_d or K_f value divided by the fraction of organic carbon in the system. K_{om} and K_{fom} are equivalent to the K_d or K_f value divided by the fraction of organic matter in the soil.

RESULTS AND DISCUSSION

Equilibration time

Time for equilibration of IN-KT413 between soil and solution was judged to be 18 hours with a soil-to-solution ratio of 1:5.

Material balance

Recoveries of radioactivity from vessels were determined in all the soils after a 24 hour equilibration period. Recoveries of radioactivity after adsorption and two desorption equilibrations ranged from 92.3 to 101.4%.

After 18 hours of equilibration, greater than 92% of the radioactivity in the supernatant was IN-KT413 by HPLC analysis.

Adsorption

The linear adsorption coefficients for IN-KT413 are listed in Table 8-147. The K_d values ranged from 2.2 to 10.0 mL/g and K_{oc} values ranged from 364 to 453 mL/g (average of 422 mL/g). Freundlich sorption isotherm parameters are given in Table 8-148. The adsorption constant, K_f , ranged from 1.0 to 10.3 mL/g with K_{foc} values

ranging from 204 to 469 mL/g (average of 344 mL/g). The 1/n values ranged from 0.83 to 1.01 (average of 0.95).

Desorption

IN-KT413 could be desorbed from the soils. The average percentage of the adsorbed IN-KT413 which was desorbed during two desorption intervals is listed in Table 8-149. A total of 26 to 44% of the adsorbed IN-KT413 was removed in the two desorption intervals.

Table 8-147: Summary of the averaged linear soil adsorption coefficients for IN-KT413

Soil	Texture ^a	pH (water)	% Organic carbon ^b	K _d (mL/g)	K _{om} (mL/g)	K _{oc} (mL/g)
Speyer 2.2	Sand	6.5	1.7	7.3	244	431
Mattapex (#25)	Silt loam	6.7	2.2	10.0	269	453
Lleida	Clay loam	8.1	1.2	4.4	219	364
Hidalgo	Sandy clay loam	8.6	0.5	2.2	276	441

^a USDA classification

^b Organic matter/1.72

Table 8-148: Summary of the Freündlich equation parameters for the IN-KT413 adsorption isotherms

Soil	Texture ^a	pH (water)	% Organic carbon ^b	K _f (mL/g)	1/n	K _{fom} (mL/g)	K _{foc} (mL/g)
Speyer 2.2	Sand	6.5	1.7	6.1	0.96	203	358
Mattapex (#25)	Silt loam	6.7	2.2	10.3	1.01	279	469
Lleida	Clay loam	8.1	1.2	4.1	0.99	207	346
Hidalgo	Sandy clay loam	8.6	0.5	1.0	0.83	128	204

^a USDA classification

^b Organic matter/1.72

Table 8-149: Average percent of sorbed IN-KT413 desorbed during two desorption intervals

Soil	USDA texture	% Organic carbon	Percent of adsorbed IN-KT413 desorbed during the first desorption interval	Percent of adsorbed IN-KT413 desorbed during the second desorption interval	Total percent of adsorbed IN-KT413 desorbed
Speyer 2.2	Sand	1.7	25.9	12.4	38.3
Mattapex (#25)	Silt loam	2.2	17.2	8.8	26.0
Lleida	Clay loam	1.2	27.3	13.0	40.2
Hidalgo	Sandy clay loam	0.5	33.0	11.4	44.4

CONCLUSION

IN-KT413 is moderately sorbed to soil. The average linear K_{oc} value was 422 mL/g and the average Freündlich K_{foc} value was 344 mL/g. The average Freündlich 1/n value was 0.95. Adsorbed IN-KT413 was moderately desorbed (26 to 44%) from test soils.

Comments (RMS 2015)

The study is still considered valid.

There was no clear correlation between adsorption and soil characteristics. Mean K_{foc} value of 344 mL/g with 1/n value of 0.95 is retained for modelling.

IN-MK 638

Author(s)	Herczog, K.J.S. (2002);
Title:	Adsorption/desorption of [¹⁴C]IN-MK638, a metabolite of indoxacarb, in five soils
Organisation:	Ricerca LLC, Painesville, Ohio, USA
Document No:	DuPont-10279
Dates of experimental work	
Guidelines:	OECD 106 (2000), US EPA 163-1 (1982)
Deviations :	None
GLP:	Yes
Previous evaluation:	Yes
Acceptability:	Yes

MATERIALS AND METHODS

1. Radiolabeled test material: [¹⁴C]IN-MK638 technical
Lot/Batch #: [¹⁴C]IN-MK638 SMS#: 400271
Radiochemical purity: [¹⁴C]IN-MK638: 99%
Specific activity: [¹⁴C]IN-MK638: 45.01 µCi/mg
Description: White powder
Stability of test compound: Shown to be stable under the conditions of the test.

Experimental conditions

The adsorption/desorption characteristics of [carbonyl-¹⁴C]IN-MK638 were investigated on five different soils (Table 8-150). Nominal test solution concentrations of 0.005, 0.01, 0.025, 0.05, and 0.1 µg/mL were prepared in 0.01 M CaCl₂. Testing was conducted in duplicate with soil-to-solution ratios of 1:2 (5 grams dry-weight soil: 10 mL test solution). Samples were equilibrated for 24 hours *via* mechanical agitation at 20°C in the dark. After equilibrium was reached, samples were centrifuged and the supernatant was decanted. The supernatant was analysed by LSC and HPLC. Analysis with radiochemical detection was performed on one replicate at the highest concentration in each soil to verify stability. Two 24-hour desorption intervals were conducted on the 0.1 µg/mL samples following the adsorption by removing the supernatant following centrifugation and replacing with an equivalent volume of fresh 0.01 M CaCl₂ solution. After the second desorption, non-extractable soil residues were quantified by combustion and LSC.

Adsorption and desorption isotherm data were analysed using the log form of the Freundlich equation: $\log x/m = 1/n * \log C_e + \log K_f$. The constants K_f and $1/n$ were obtained by a least squares regression of a plot of $\log x/m$ versus $\log C_e$. K_d values were obtained by determining the mean ratio of x/m to C_e for each soil type. K_{oc} and K_{foc} values are equivalent to the K_d or K_f value divided by the fraction of organic carbon in the system. K_{om} and K_{fom} are equivalent to the K_d or K_f value divided by the fraction of organic matter in the soil.

Table 8-150: Characteristics of test soils

Characteristic	Soil				
Soil Name or Designation	Speyer 2.2	Mattapex (#25)	Pesaro	Lleida	Hidalgo 5-S
Origin	Germany	USA	Italy	Spain	USA
pH (in water)	6.3	6.2	8.1	8	8.4
% Sand (2000-50 μm)	87.6	32.0	19.6	25.6	58.0
% Silt (<50-2 μm)	7.2	46.0	43.2	37.2	16.0
% Clay (<2 μm)	5.2	22.0	37.2	37.2	26.0
Texture ^a	Loamy sand	Loam	Silty clay loam	Clay loam	Sandy clay loam
Organic matter	3.4	2.5	2.4	1.9	0.6
Organic carbon (%) ^b	2.0	1.5	1.4	1.1	0.3
Cation exchange capacity (mEq/100 g)	9.61	8.1	24.99	19.68	13.7
Maximum water-holding capacity (%)	40.4	51.6	54.0	46.0	38.3

^a USDA soil classification system

^b organic carbon = organic matter/1.724

RESULTS AND DISCUSSION

Equilibration time

Time for equilibration of IN-MK638 between soil and solution was judged to be less than 24 hours with a soil-to-solution ratio of 1:2. Therefore, a 24 hour equilibration time was chosen.

Material balance

Recoveries of radioactivity from vessels was determined in all the soils after a 24 hour equilibration period. Recoveries of radioactivity after adsorption and two desorption equilibrations ranged from 91.7 to 105.3%.

After 24 hours of equilibration, greater than 95% of the radioactivity in the supernatant was IN-MK638 by HPLC analysis.

Adsorption

The linear adsorption coefficients for IN-MK638 are listed in Table 8-151. The K_d values ranged from 1.2 to 5.6 mL/g and the K_{oc} values ranged from 145 to 463 mL/g (average = 322 mL/g). Freundlich sorption isotherm parameters are given in Table 8-152. The adsorption constant, K_f , ranged from 0.9 to 2.6 mL/g with K_{foc} values ranging from 67 to 300 mL/g (average = 151 mL/g). The $1/n$ values ranged from 0.76 to 0.94 (average = 0.84).

Desorption

IN-MK638 could be desorbed from the soils. The average percentage of the adsorbed IN-MK638 which was desorbed during two desorption intervals is listed in Table 8-153. A total of 32 to 50% of the adsorbed IN-MK638 was removed in the two desorption intervals.

Table 8-151: Summary of the averaged linear soil adsorption coefficients for IN-MK638

Soil	Texture ^a	pH (water)	% Organic carbon ^b	K _d (mL/g)	K _{om} (mL/g)	K _{oc} (mL/g)
Speyer 2.2	Loamy sand	6.3	2.0	5.6	163	278
Mattapex (#25)	Loam	6.2	1.5	2.2	87	145
Pesaro	Silty clay loam	8.1	1.4	4.6	189	325
Lleida	Clay loam	8.0	1.1	5.1	268	463
Hidalgo	Sandy clay loam	8.4	0.3	1.2	198	397

^a USDA classification

^b Organic matter/1.72

Table 8-152: Summary of the Freündlich equation parameters for the IN-MK638 adsorption isotherms

Soil	Texture ^a	pH (water)	% Organic carbon ^b	K _f (mL/g)	1/n	K _{fom} (mL/g)	K _{foc} (mL/g)
Speyer 2.2	Loamy sand	6.3	2.0	2.6	0.85	76	130
Mattapex (#25)	Loam	6.2	1.5	1.0	0.84	40	67
Pesaro	Silty clay loam	8.1	1.4	1.3	0.76	54	93
Lleida	Clay loam	8.0	1.1	1.8	0.80	95	164
Hidalgo	Sandy clay loam	8.4	0.3	0.9	0.94	150	300

^a USDA classification

^b Organic matter/1.72

Table 8-153: Average percent of sorbed IN-MK638 desorbed during two desorption intervals

Soil	USDA texture	% Organic carbon	Percent of adsorbed IN-MK638 desorbed during the first desorption interval	Percent of adsorbed IN-MK638 desorbed during the second desorption interval	Total percent of adsorbed IN-MK638 desorbed
Speyer 2.2	Loamy sand	2.0	19.1	14.0	33.1
Mattapex (#25)	Loam	1.5	27.6	17.7	45.2
Pesaro	Silty clay loam	1.4	21.4	11.4	32.8
Lleida	Clay loam	1.1	19.9	12.3	32.2
Hidalgo	Sandy clay loam	0.3	29.6	20.0	49.5

CONCLUSION

IN-MK638 is moderately sorbed to soil. The average linear K_{oc} value was 322 mL/g and the average Freündlich K_{foc} value was 151 mL/g. The average Freündlich 1/n value was 0.84. Adsorbed IN-MK638 was moderately desorbed (32 to 50%) from test soils.

Comments (RMS 2015)

The study is still considered valid.

There was no clear correlation between adsorption and soil characteristics. Mean K_{oc} value of 151 mL/g with 1/n value of 0.84 is retained for modelling.

IN-KB687

No study on adsorption behavior of IN-KB687 was submitted during first EU review, as this metabolite was not considered in risk assessment, being a minor non transient soil metabolite.

The following study is submitted to the EU for the first time for the purpose of renewal.

Data point:	
Author(s)	Allan, J. (2012);
Title:	¹⁴ C-IN-KB687: Batch equilibrium (adsorption/desorption) in five soils
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-31718
Dates of experimental work	
Guidelines:	OECD 106 (2000), OPPTS 835.1230 (2008)
Deviations :	See RMS comments.
GLP:	Yes
Previous evaluation:	No
Acceptability:	Yes

MATERIALS AND METHODS

- Radiolabelled test material: ¹⁴C-IN-KB687 technical metabolite
 Lot/Batch/Stock #: [Methoxy-¹⁴C]IN-KB687 Lot #: 3638094
 Radiochemical purity: 98.6%
 Specific activity: 41.06 µCi/mg
 Description: Not given
 Stability of test compound: Stable during the test

- Soils

The study was conducted with five different soil types (three European and two from the U.S.A). Air-dried soils were stored at ambient temperatures overnight prior to experimentation. A summary of the physical and chemical properties of the soils is provided in Table 8-154. The percent sand, silt, and clay are quoted on the basis of the USDA classification.

Table 8-154: Soil characteristics

Property	Speyer 2.2	Nambsheim	Lleida	Tama	Sassafras
Origin	Hanhofen, Rhein, Germany	Nambsheim, Alsace, France	Lleida, Catalunya, Spain	Stark County, Illinois, USA	Kent County, Maryland, USA
Soil texture ^a	Loamy Sand	Sandy Loam	Clay Loam	Silty Clay Loam	Sandy Loam
% Sand (2000-50 µm)	85	68	23	16	57
% Silt (<50-2 µm)	10	21	42	54	32
% Clay (<2 µm)	5	11	35	30	11
pH ^b	6.1	7.8	8.0	6.8	5.7
pH ^c	5.7	7.4	7.8	6.3	5.1
Organic carbon (%)	2.0	1.7	1.9	3.3	0.93
CEC (meq/100 g)	8.2	9.1	15.5	19.1	6.5
Moisture at 1/3 atm (%)	10.4	14.9	30.4	35.0	15.1
Bulk density (g/cm ³)	1.21	1.09	1.04	1.03	1.16

^a USDA soil classification system

^b 1:1 soil:water ratio

^c pH in 1:2 soil:0.01M CaCl₂ (aq)

Experimental conditions

Stock solutions of ¹⁴C-labelled IN-KB687 in acetonitrile were prepared and aliquots added to portions of 0.01 M CaCl₂ solution to give a concentration range of 0.05, 0.25, 0.50, 2.5, and 5.0 µg/mL. The appropriate solution to soil ratio was determined in preliminary testing at 1:10 (circa 20–80% adsorption). Portions of the test solution (2 mL) were shaken at 20°C with samples of test soil (2 g dry weight) for a 2-hour equilibration period in darkness. Following centrifugation (205 g for 10 minutes), the supernatant was decanted and triplicate aliquots were prepared for radioassay.

Immediately after removing the supernatant following the adsorption phase, an amount of fresh 0.01 M CaCl₂ solution equivalent to that removed following adsorption was added to each of the soil samples from the highest test substance solution concentration (nominal 0.5 µg/mL). The samples were weighed, the soil pellets re-suspended, and the samples were placed on the shaker. The samples were equilibrated at 20 ± 2°C for 2 hours.

After the 2-hour equilibration time, the samples were removed from the shaker and processed as described above. Triplicate 1-mL aliquots of the filtered supernatants were analysed by LSC.

Description of analytical procedures

Radioactivity was determined by LSC, and aqueous supernatants obtained after equilibration were analysed and confirmed for IN-KB687 by reverse phase HPLC of the highest test concentration (0.5 µg/mL) samples. Samples of soil residues were combusted in a biological oxidiser for four minutes, then analysed by LSC. Results were corrected for the overall average oxidiser efficiency and expressed as dpm/g. The limits of detection (LOD) for IN-KB687 were 1.02E-04 µg/mL (0.5 and 0.005 µg/mL adsorption supernatants); 3.96E-05 µg/mL (soil combustions); and 2.27E-04 µg/mL (0.5 and 0.005 µg/mL CaCl₂ HPLC analyses).

RESULTS AND DISCUSSION

Mass balance

The material balances ranged from 94.6 to 98.0%, which are within the recommended guideline range of 90–110% of the applied radioactivity.

Findings

Adsorption isotherm data were analysed using the log form of the Freundlich equation: $\log x/m = 1/n * \log C_e + \log K_F$ (Table 8-155).

Table 8-155: Adsorption and desorption constants of IN-KB687 in the soils

Soil	OC %	pH (CaCl ₂)	Adsorption				Desorption	
			K _F (mL/g)	1/n	r ²	K _{Foc} (mL/g)	K _d (mL/g)	K _{d, oc} (mL/g)
Speyer 2.2	2.0	5.7	4.83	0.8727	0.9990	244	8.25	417
Tama	3.3	6.3	5.45	0.7728	0.9993	164	10.1	305
Lleida	1.9	7.8	5.37	0.8740	0.9996	280	9.57	499
Sassafras	0.93	5.1	2.94	0.9035	0.9991	316	5.59	601
Nambsheim	1.7	7.4	3.07	0.8389	0.9987	182	5.75	341

K_F – Freundlich adsorption and desorption coefficients; 1/n – Slope of Freundlich adsorption/desorption isotherms

K_{Foc} - Coefficient adsorption per organic carbon (K_d or K × 100% organic carbon)

The adsorption K_F values ranged from 2.94 in the Sassafras soil to 5.45 in the Tama soil. The adsorption K_{Fom} values ranged from 96 in the Tama soil to 184 in the Sassafras soil. The adsorption K_{Foc} values ranged from 164 in the Tama soil to 316 in the Sassafras soil. The desorption coefficients, K_{d1}, K_{d2}, K_{d1,om}, K_{d1,oc}, K_{d2,om} and K_{d2,oc} were calculated for each soil at the highest test concentration. The desorption K_d values ranged from 5.59 in the Sassafras soil to 10.1 in the Tama soil. The desorption K_{d,om} values ranged from 177 in the Tama soil to 350 in the Sassafras soil. The desorption K_{d,oc} values ranged from 305 in the Tama soil to 601 in the Sassafras soil. The % adsorbed and desorbed IN-KB687 at each concentration is provided in Table 8-156 and Table 8-157, respectively.

Table 8-156: Concentration of IN-KB687 in the solid and liquid phases at the end of adsorption equilibration period

Concentration on soil (µg/mL)	Rep	Speyer 2.2			Tama			Lleida		
		On soil ^a (mg/kg)	In solution (µg/mL)	% Adsorbed ^b	On soil (mg/kg)	In solution (µg/mL)	% Adsorbed	On soil (mg/kg)	In solution (µg/mL)	% Adsorbed
0.0528	1	0.0270	0.00251	52.2	0.0374	0.00148	71.6	0.0292	0.00242	54.7
0.0528	2	0.0275	0.00256	51.9	0.0364	0.00161	69.4	0.0277	0.00251	52.8
0.0263	1	0.117	0.0144	45.3	0.159	0.0105	60.5	0.122	0.0138	47.2
0.0263	2	0.115	0.0150	43.6	0.154	0.0110	58.6	0.127	0.0139	47.7
0.0528	1	0.221	0.0304	42.2	0.297	0.0230	56.4	0.247	0.0283	47.1
0.0528	2	0.221	0.0302	42.3	0.306	0.0223	57.8	0.239	0.0279	46.3
2.61	1	1.06	0.159	40.5	1.21	0.137	47.0	1.02	0.154	39.9
2.61	2	0.926	0.162	36.9	1.20	0.139	46.7	1.06	0.157	40.9
5.30	1	1.90	0.337	36.3	2.13	0.303	41.3	2.06	0.326	38.9
5.30	2	1.90	0.334	36.4	2.15	0.308	41.4	2.02	0.327	38.5
Concentration on soil (µg a.s./mL)	Rep	Sassafras			Nambshheim					
		On soil ^a (mg/kg)	In solution (µg/mL)	% Adsorbed ^b	On soil (mg/kg)	In solution (µg/mL)	% Adsorbed			
0.0528	1	0.0181	0.0035	33.8	0.0235	0.00301	43.9			
0.0528	2	0.0179	0.0035	33.9	0.0241	0.00289	46.0			
0.0263	1	0.0810	0.0186	30.8	0.0995	0.0165	37.9			
0.0263	2	0.0823	0.0185	30.7	0.0904	0.0170	35.1			
0.0528	1	0.151	0.0378	28.7	0.182	0.0343	34.7			
0.0528	2	0.144	0.0376	28.0	0.183	0.0342	34.8			
2.61	1	0.629	0.197	24.3	0.763	0.186	29.4			
2.61	2	0.689	0.197	25.9	0.690	0.189	26.8			
5.30	1	1.42	0.397	26.4	1.47	0.388	27.4			
5.30	2	1.25	0.405	23.9	1.42	0.388	27.2			

^a The amount on soil residue is measured by dividing the mass in desorption soil by the initial dry soil weight.

^b % Adsorbed as the % of the applied.

Table 8-157: Concentration of IN-KB687 in the solid and liquid phases at the end of desorption

Concentration on soil (µg/mL)	Rep	Speyer 2.2			Tama			Lleida		
		On soil ^a (µg/g)	In solution (µg/mL)	% Desorbed as % of the adsorbed	On soil ^a (mg/kg)	In solution (µg/mL)	% Desorbed as % of the adsorbed	On soil ^a (mg/kg)	In solution (µg/mL)	% Desorbed as % of the adsorbed
5.30	1	0.954	0.115	49.8	1.23	0.122	42.1	1.20	0.123	41.6
5.30	2	0.951	0.116	49.9	1.26	0.124	41.5	1.16	0.123	42.7
Concentration on soil (µg/mL)	Rep	Sassafras			Nambenheim					
		On soil ^a (mg/kg)	In solution (µg/mL)	% Desorbed as % of the adsorbed	On soil ^a (mg a.s./kg)	In solution (µg/mL)	% Desorbed as % of the adsorbed			
5.30	1	0.647	0.104	54.4	0.643	0.108	56.2			
5.30	2	0.511	0.103	59.1	0.616	0.111	56.7			

^a The amount on soil residue is measured by dividing the mass in desorption soil by the initial dry soil weight.

^b % Adsorbed as the % of the applied.

CONCLUSION

The adsorption/desorption characteristics of ¹⁴C-IN-KB687 were studied in five soils (pH range of 5.1 to 7.8, organic carbon range of 0.93% to 3.3%). The adsorption K_F values ranged from 2.94 in the Sassafras soil to 5.45 in the Tama soil. The adsorption K_{Foc} values ranged from 164 in the Tama soil to 316 in the Sassafras soil.

RMS (2016)

Only one soil/solution ration of 1/10 was tested in the preliminary test, although multiple ratios should be tested according to OECD 106 guideline. However, as this soil solution ration gives satisfactory level of adsorption (between 20 and 80%); it is considered that it is appropriate to use this ratio.

The preliminary test to determine equilibrium time was conducted during 4 hours only, with 3 times of adsorption determination. It is quite difficult to confirm that equilibrium time is reached within these 4 hours, as adsorption level is increasing at each measured point.

Equilibrium time was determined to be 2 hours, although adsorption was higher after 4 hours for both tested soils. However, this can be considered providing a conservative estimation of K_{oc} value for risk assessment, as minimizing the adsorption potential.

The study results are accepted for risk assessment. There was no clear correlation between adsorption and soil characteristics. Mean K_{foc} value of 237 mL/g with 1/n value of 0.85 is retained for modelling.

IN-ML438

The following study was summarised in Indoxacarb DAR, addendum 3 (2005) but is not considered relied upon for this data requirement

Author(s)	Singles, S.K. (2002);
Title:	Rate of degradation and estimated K _{oc} of IN-ML438 in soil
Organisation:	
Document No:	
Dates of experimental work	
Guidelines:	OECD 121 (2001)
Deviations :	See below
GLP:	Yes
Previous evaluation:	No
Acceptability:	No

- | | |
|-------------------|-------------------------------|
| 1. Test material: | IN-ML438 technical metabolite |
| Lot/Batch #: | Not applicable |
| Purity: | Not applicable |

The study on adsorption and desorption of metabolite IN-ML438, DuPont-11433, originally submitted under EU Rev8 Point IIA 7.1.2 and was conducted under guideline OECD 121 (2001). However, it was conducted under non-GLP and the sorption coefficient was estimated using a HPLC method. DuPont-11433 will not be relied upon for Point CA 7.1.3.1.2, since the study has been superseded by DuPont-36992 which is summarised below.

The following study is submitted to the EU for the first time for the purpose of renewal.

Data point:	7.1.3.1.2/02
Author(s)	Allan, J. (2015);
Title:	[¹⁴ C]IN-ML438: Batch equilibrium (adsorption/desorption) in five soils
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-36692
Dates of experimental work	
Guidelines:	OECD 106 (2000), OPPTS 835.1230 (2008)
Deviations :	See RMS comments
GLP:	Yes
Previous evaluation:	No
Acceptability:	Yes

MATERIALS AND METHODS

- | | |
|---------------------------------|--|
| 1. Radiolabelled test material: | [¹⁴ C]IN-ML438 technical metabolite |
| Lot/Batch #: | [Indanone-1- ¹⁴ C]-IN-ML438 Lot #: 1723247
Abbreviated as [I- ¹⁴ C]IN-ML438 |
| Radiochemical purity: | 95.0% |
| Specific activity: | 31.3 µCi/mg |

Stability of test compound:

The test material was stable under the test conditions.

2. Soils

The study was conducted with five different soil types (three European and two from the U.S.A). Soils were pre-equilibrated overnight prior to experimentation. A summary of the physical and chemical properties of the soils is provided in Table 8-158. The percent sand, silt, and clay are quoted on the basis of the USDA classification.

Table 8-158: Soil characteristics

Property	Gross-Umstadt	Lleida	Nambsheim	Sassafras	Tama
Origin	Darmstadt, Hessen, Germany	Lleida, Cataluña, Spain	Nambsheim, Alsace France	Kent County, Maryland, USA	Stark County, Illinois, USA
Soil texture ^a	Loam	Clay	Sandy loam	Sandy loam	Silty clay loam
% Sand (2000-50 µm)	41	16	62	52	10
% Silt (<50-2 µm)	44	40	25	35	56
% Clay (<2 µm)	15	44	13	13	34
pH ^b	6.9	7.9	7.6	6.0	6.1
pH ^c	6.5	7.6	7.3	5.4	5.5
Organic carbon (%)	1.2	1.9	1.7	0.76	1.8
CEC (meq/100 g)	10.4	17.9	10.6	6.2	18.3
Moisture at 1/3 bar (%)	17.0	29.5	14.7	17.3	33.5
Bulk density (g/cm ³)	1.16	1.06	1.16	1.22	1.06

^a USDA soil classification system

^b 1:1 soil:water ratio

^c pH in 1:2 soil:0.01M CaCl₂ (aq)

Experimental conditions

A stock solution of ¹⁴C-labelled IN-ML438 in acetonitrile was prepared and determined to be 85.0 µg/mL. The appropriate solution to soil ratio was determined in preliminary testing for the definitive test to be 1:50. For each test soil, triplicate 0.8 g (dry weight equivalent) aliquots were weighed into tared, glass test vessels. A sufficient amount of 0.01 M CaCl₂ (aq) was added to bring the total volume of aqueous phase present to 40 mL for a 1:50 ratio in the soil samples. The soil samples were pre-equilibrated by mixing overnight on an end-over-end shaker before the experiment. After pre-equilibration, 5 µL of the 85.0 µg/mL was added via a Hamilton syringe to the test vessels. The samples were then shaken at 20 ± 2°C for a 6-hour equilibration period in darkness. A control experiment was also performed to assess potential adsorption to glass test vessels. The pH of the adsorption supernatant ranged from 7.480 to 8.426 after addition of the test substance. Following centrifugation (913 × g), the supernatant was decanted, and triplicate aliquots were prepared for radioassay.

Immediately after removing the supernatant following the adsorption phase, an amount of fresh 0.01 M CaCl₂ solution equivalent to that removed following adsorption was added to each of the soil samples to perform a desorption step. The samples were weighed, the soil pellets re-suspended and the samples were placed on the shaker. The samples were equilibrated at 20 ± 2°C for 6 hours, then the phases were separated and the supernatant radioassayed as above.

Following the desorption, the soils were extracted twice with 10 mL of acetonitrile. The extract was concentrated, filtered, and analysed by ¹⁴C-HPLC analysis. The remaining soil pellet was then combusted followed by LSC analysis. The replicate adsorption supernatants were combined, concentrated by SPE (C18 cartridges) and nitrogen blow down, and then analysed by ¹⁴C-HPLC analysis.

Description of analytical procedures

Radioactivity was determined by LSC, and aqueous supernatants obtained after equilibration were analysed and confirmed for IN-ML438 by reverse phase HPLC. Samples of the soil residues were combusted in a biological oxidiser for four minutes, then analysed by LSC. Results were corrected for the overall average oxidiser efficiency and expressed as dpm/g. The limits of detection (LOD) for IN-ML438 were 0.0323 and 0.0808 ng/mL for LSC analysis of the sorption supernatants and soil extracts, respectively; 0.00648 ng/mL for the soil combustion; and 0.0180 and 0.0106 ng/mL for HPLC analysis of the adsorption supernatants and soil extracts. These values correlated to limits of quantification (LOQ) of 0.125, 0.312, 0.0228, 0.0693, and 0.0408 ng/mL, respectively. These LOD and LOQ values were sufficiently lower than the nominal dose rate (10.0 ng/mL) and were sufficient for determining the sorption of IN-ML438 in this study.

RESULTS AND DISCUSSION

Mass balance

Mean material balances were 103.8, 102.4, 98.9, and 102.3% for the Gross-Umstadt, Lleida, Sassafras, and Tama soils, respectively, which are within the acceptable guideline range of 90–110% of the applied radioactivity. For the Nambenheim soil, two replicates were outside of acceptable range (<75%), while the third replicate was slightly high at 113.3%, which was used for characterising adsorption and desorption constants of IN-ML438.

Findings

Stability of IN-ML438 was confirmed in this study, as the percent of applied radioactivity (% AR) remained above 90% in the adsorption supernatants and the soil extracts. Therefore, no correction to the concentrations as determined by LSC analysis was necessary.

Given the high adsorption, low solubility, and sensitivity levels, the test was only performed at one concentration. Thus, the Freundlich isotherm testing could not be calculated. Instead, the sorption of IN-ML438 was characterised using one dose level of 10.0 ng/mL. The mean sorption characteristics determined are summarised in Table 8-159.

Table 8-159: Adsorption and desorption constants of IN-ML438 in the soils

Soil	OC %	pH ^a	Adsorption			Desorption		
			%	K _d	K _{oc}	%	K _{d1}	K _{d1,oc}
Gross-Umstadt	1.2	6.5	82.4	231	19908	11.8	363	31180
Lleida	1.9	7.6	88.7	381	20498	7.5	584	31370
Nambenheim	1.7	7.3	84.2	263	15082	10.9	395	22645
Sassafras	0.76	5.4	75.4	156	20667	18.4	223	29487
Tama	1.8	5.5	86.3	312	17332	9.7	449	24909

^a 1:2 soil: 0.01M CaCl₂ (aq) ratio

Adsorption K_{oc} values were high, showing that IN-ML438 was strongly bound to all five soils. The desorption constants were larger than those obtained for adsorption, indicating that once adsorbed, IN-ML438 is not as readily desorbed. The % adsorbed and desorbed IN-ML438 at each concentration is provided in Table 8-160 and Table 8-161, respectively.

Table 8-160: Concentration of IN-ML438 in the solid and liquid phases at the end of adsorption period

Soil	Rep	m ₀ (µg)	C _s (µg/g)	C _w (µg/mL)	% Ads	K _d (mL/g)	K _{om} (mL/g)	K _{oc} (mL/g)
Gross-Umstadt	1	0.425	0.432	0.00193	82.1	224	11204	19271
	2	0.425	0.439	0.00174	83.8	253	12654	21765
	3	0.425	0.430	0.00198	81.5	217	10866	18689
	Mean	0.425	0.434	0.00188	82.4	231	11575	19908
Lleida	1	0.425	0.459	0.00122	88.6	376	11741	20194
	2	0.425	0.466	0.0117	89.1	398	12438	21393
	3	0.425	0.463	0.00125	88.4	370	11573	19906
	Mean	0.425	0.463	0.00121	88.7	381	11917	20498
Nambsheim ^a	2	0.425	0.441	0.00168	84.2	263	8768	15082
Sassafras	1	0.425	0.395	0.00263	75.5	150	11538	19845
	2	0.425	0.389	0.00286	73.1	136	10470	18009
	3	0.425	0.432	0.00237	77.8	182	14038	24146
	Mean	0.425	0.405	0.00262	75.4	156	12016	20667
Tama	1	0.425	0.460	0.00144	86.4	318	10266	17658
	2	0.425	0.465	0.00147	86.2	316	10182	17513
	3	0.425	0.448	0.00148	86.2	303	9781	16823
	Mean	0.425	0.458	0.00147	86.3	312	10077	17332

^a Since mass balance from replicates 1 and 3 were low (<90%) and considered outliers, results only reported for replicate 2.

Note: Values calculated using unrounded numbers.

Table 8-161: Concentration of IN-ML438 in the solid and liquid phases at the end of desorption period

Soil	Rep	C _{s,D} (µg/g)	C _{w,D} (µg/mL)	% Des	K _{ds,D} (mL/g)	K _{om,D} (mL/g)	K _{oc,D} (mL/g)
Gross-Umstadt	1	0.379	0.00109	12.2	347	17344	29831
	2	0.391	0.00101	11.0	387	19342	33268
	3	0.378	0.00107	12.0	354	17699	30443
	Mean	0.383	0.00106	11.8	363	18128	31180
Lleida	1	0.425	0.000728	7.5	584	18245	31381
	2	0.432	0.000711	7.3	608	19008	32694
	3	0.426	0.000763	7.9	559	17463	30036
	Mean	0.428	0.000734	7.5	584	18238	31370
Nambsheim ^a	2	0.393	0.000996	10.9	395	13166	22645
Sassafras	1	0.320	0.00154	18.8	208	15976	27479
	2	0.308	0.00166	20.9	186	14296	24588
	3	0.364	0.00132	15.7	275	21159	36393
	Mean	0.331	0.00151	18.4	223	17143	29487
Tama	1	0.416	0.000904	9.5	461	14858	25556
	2	0.417	0.000976	10.3	427	13790	23719
	3	0.407	0.000886	9.3	459	14798	25453
	Mean	0.413	0.000922	9.7	449	14482	24909

^a Since mass balance from replicates 1 and 3 were low (<90%) and considered outliers, results only reported for replicate 2.

Note: Values calculated using unrounded numbers.

CONCLUSION

Adsorption K_d values ranged from 156 to 381 mL/g. Overall adsorption K_{oc} values ranged from 15082 to 20667 mL/g. On the basis of the results obtained, IN-ML438 has very low potential for soil mobility.

COMMENTS (RMS 2016)

Preliminary test control showed that potential adsorption on test vessel could occur. However, this adsorption seemed to be considerably lower in presence of soil, as mass balance with test soil showed to be > 90%, and that rinses of the test vessel showed %AR <5.2%.

The soil to solution ratio of the definitive test was set to 1:50 (lower than the tested ratio of the preliminary tests) as the results of the preliminary tests showed level of adsorption >90% for the two tested soil (ratio 1:10) and for one soil (ratio 1:40). This is considered being conservative for this substance.

Mass balances of the definitive tests were satisfactory except for two replicates of Nambenheim soil, which were not used in the calculations.

Definitive tests were not conducted with different solution concentrations. This implies that the values obtained are not determined according to an adsorption isotherm, which is a major deviation of the OECD 106 guideline. According to study report, this is due to the low solubility of the substance that did not allow testing different concentration. The LOQ is reported to be 0.125 ng/mL for the aqueous phase, but the limit of solubility of the compound is not reported.

However, the data clearly indicate that the metabolite IN-ML438 is strongly adsorbed to soil and it is considered that testing different solution concentrations would not have changed the class of mobility of this compound.

There was no clear correlation between adsorption and soil characteristics. Mean K_{foc} value of 19601 mL/g with default 1/n value of 1 is retained for modelling.

IN-ML643

Author(s)	Caldwell, E. (2002);
Title:	Adsorption/desorption of [¹⁴ C]IN-MK643, a metabolite of indoxacarb, in five soils
Organisation:	
Document No:	DuPont-9784
Dates of experimental work	
Guidelines:	SETAC-Europe, OECD 106 (January 2000), U.S. EPA 163-1 (1982)
Deviations :	See RMS comments
GLP:	Yes
Previous evaluation:	Yes
Acceptability:	Yes

1. Test material: ¹⁴C-IN-MK643 radiolabeled technical metabolite
 Lot/Batch #: BB8998
 Radiochemical purity: [Carbonyl ¹⁴C]IN-MK643 >95%

The study on adsorption and desorption of metabolite IN-MK643, DuPont-9784, originally submitted under EU Rev8 Point IIA 7.1.2 and conducted with test material ¹⁴C-IN-MK643, was conducted under guidelines SETAC-Europe, OECD 106 (January 2000), and U.S. EPA 163-1 (1982). A review of this study indicates that it fully meets the current guideline (OECD 106) and is relied upon.

2. Soils

The study was conducted with five different soil types. All soils were passed through a 2-mm sieve and air dried if necessary prior to use and were stored at ca. +4°C. Characterisation of the sieved soils is given in the table below.

Table 8-162: Soil characteristics

Property	Speyer	Mattapex	Pesaro	Lleida	Hidalgo
Origin	Germany	USA	Italy	Spain	USA
Soil texture ^a	Sand	Loam	Clay Loam	Clay Loam	Sandy Clay Loam
% Sand (2000-50 µm)	96.0	40.0	26.4	24.4	52.0
% Silt (<50-2 µm)	2.0	42.0	37.6	39.6	24.0
% Clay (<2 µm)	2.0	18.0	36.0	36.0	24.0
pH ^b	6.3	6.1	8.2	8.0	8.1
pH ^c	6.2	6.0	8.1	7.9	7.8
Organic carbon (%)	2.1	0.9	1.2	1.1	0.4
CEC (meq/100 g)	5.9	8.22	23.06	18.08	14.83
Moisture at 0 bar (%)	43.1	39.3	59.2	45.6	40.8
Moisture at 1/3 bar (%)					
Bulk density (g/cm ³)	1.22	1.26	1.23	1.27	1.16

^a USDA soil classification system

^b 1:1 soil:water ratio

^c pH in 1:2 soil:0.01M CaCl₂ (aq)

Experimental conditions

[14C]IN-MK643 was dissolved in acetonitrile to create a stock solution from which the treatment solutions were derived. Five treatment solutions were prepared in acetonitrile/0.01 M calcium chloride at nominal concentrations of 2.5, 1.25, 0.625, 0.25 and 0.125 mg/mL.

The treatment solutions were all prepared using [14C]IN-MK643 without radiodilution.

Triplicate aliquots (100 - 250 μ L) of each of the treatment solutions were taken for LSC to determine their concentration. An aliquot (1 mL) of each treatment solution was added to 0.01 M calcium chloride (24 mL) to give test solutions with final concentrations of 0.1, 0.05, 0.025, 0.01 and 0.005 μ g/mL.

Preliminary test

A soil-to-solution ratio of 1:1 was initially selected for the preliminary experiment. The tubes were pre-equilibrated *via* shaking at approximately 20-22°C for *ca.* 15 hours in darkness. Five of the six soil tubes were treated with 1.0 mL of a 2.5 g/mL test substance treatment solution. The remaining test vessel for each soil type was treated with 1.0 mL 0.01 M calcium chloride to provide radioassay blanks. The test substance in solution was equilibrated with the soil slurry (by shaking at approximately 20 - 22°C in darkness). After intervals of about 2, 4, 8, 18 and 24 hours, single tubes of each soil type were removed for analysis. The soil slurry was separated by centrifugation and the supernatant removed. After removal of the supernatant the soil was extracted with acetonitrile:water (8:2) by shaking for 20 minutes.

Following each extraction the soil and supernatant were separated by centrifugation at *ca.* 2800 rpm for 20 minutes. The supernatant was removed, the volume measured and duplicate aliquots (1.0 mL) were taken for radioassay.

The use of a soil-to-solution ratio of 1:1 resulted in unacceptably high levels of test substance adsorption for both soils. The experiment was repeated using a soil-to-solution ratio of 1:2 (12.5 g dry weight equivalent of soil) for all five soils. This resulted in high levels of adsorption for Speyer 2.2 soil and so the experiment was repeated using all soils and a soil-to-solution ratio of 1:5 (5 g dry weight equivalent of soil) and 24 hours equilibration time. This final soil-to-solution ratio and equilibration period was selected for use in the definitive experiments for all soil types.

Test substance stability and mass balance was measured for tubes at the selected soil-to-solution ratio (1 : 5) and following 24 hours equilibration in all soils.

The possibility of adsorption of the test substance to the tube surface was investigated in the preliminary experiments by shaking test solutions at the highest and lowest concentrations in tubes with no soil present for 24 hours at approximately 20 - 22°C then analysing the test solutions by LSC.

Definitive test

The soil in the tubes was pre-equilibrated by shaking for approximately 18 hours at *ca.* 20 - 22°C in darkness. After pre-equilibration the soil slurries were treated with their respective treatment solutions (1.0 mL) to achieve nominal concentrations of the test substance of 0.1, 0.05, 0.025, 0.01 and 0.005 g/mL.

At the end of the equilibration period, each soil slurry was centrifuged to separate the soil and solution. Following adsorption, centrifugation and separation of the solution and soil, the desorption process was initiated by adding a volume of fresh (0.01 M) calcium chloride solution (equal to that removed) to two vessels of each soil type from the highest initial concentration and the blank samples only. The soil slurry was shaken again for 24 hours under the same conditions as described for adsorption. The solution and soil were separated by centrifugation and the desorption process repeated once more. After each centrifugation the radioactivity concentration in the supernatant solution was measured by LSC of triplicate aliquots (1 mL). At the end of the second desorption, mass balances of radioactivity were obtained for samples at the highest concentration only.

The soils were solvent extracted (generally two or three extractions for all samples) and the radioactivity content of the extracts and non-extractable residue measured.

Non-extractable radioactive residue was measured by combustion and LSC. For each sample respective soil extracts were pooled (50% by volume). The extract pools were then concentrated and analysed. Adsorption supernatants were pooled for each soil type as were the two desorption supernatants (10% by volume). The supernatant pools were analysed by HPLC

Description of analytical procedure

Radioactivity was measured by LSC. Aliquots (up to 1 mL) of liquid samples were mixed with Ultima Gold scintillator cocktail (7 mL, Canberra-Packard Ltd., Pangbourne, Berkshire, UK) for measurement of radioactivity. Samples were generally counted for 10 minutes or 40,000 counts, whichever occurred first. Samples of soil residues after extraction were combusted in oxygen using a sample oxidiser (Harvey OX500, Laboratory Impex Ltd., Teddington, Middlesex, UK). Combustion products were absorbed into Oxysolve C-400 combined scintillator (Zinsser Analytic, Maidenhead, Berkshire, UK). The efficiency of the oxidiser was determined using carbon-14 standard solution (Spec Chec □ carbon- 14 check source, Canberra-Packard Ltd.) and was greater than 95%. Measurements of radioactivity were corrected for oxidiser efficiency. Radioactivity in amounts of less than twice background levels were generally considered to be below the limit of detection.

RESULTS AND DISCUSSION

Mass balance

Recoveries of radioactivity from samples set aside for the determination of the material balance upon completion of adsorption were in the range 104 - 107% of the amount applied. It was not possible to determine a material balance in all samples at this phase as some were required for desorption phases. No corrections were made for mass balance in the adsorption parameters. A material balance was also obtained after completion of the second desorption phase for all of the soil types tested (see Section 4.5.1).

Table 8-163: Recovery of radioactivity after 24 hours adsorption equilibration

SOIL (SOIL-TO-SOLUTION RATIO)	SPEYER 2.2 (1 : 5)	MATTAPEX # 25 (1 : 5)	PESARO (1 : 5)	LLEIDA (1 : 5)	HIDALGO (1 : 5)
Aqueous solution	38.2	55.2	39.1	41.1	64.3
Soil extracts	67.1	48.5	60.4	61.3	39.2
Non-extractable	1.3	1.3	4.7	3.9	2.6
Total recovered	106.6	105.0	104.2	106.3	106.1

Findings

Results of the HPLC analysis are shown in Table 3. IN-MK643 was shown to be stable in the presence of soil under these incubation conditions. IN-MK643 represented >95% sample radioactivity in both soil extracts and aqueous solutions. Actual concentrations of IN-MK643 in the aqueous solutions and soil extracts were calculated accounting for the proportion of the total radioactivity representing IN-MK643 as determined by HPLC analysis.

Table 8-164: Concentration of IN-MK643 in the solid and liquid phases at the end of adsorption period on the Speyer 2.2 soil – adsorption coefficient

NOMINAL INITIAL CONCENTRATION IN SOLUTION (C _o) (µG/ML)	CONCENTRATION AFTER EQUILIBRATION		ADSORPTION COEFFICIENTS		
	IN SOLUTION (C _{ad}) ^A (µG/ML)	ON SOIL (C _s) ^A (µG/G)	K _o (ML/G)	K _{ow} (ML/G)	K _{oc} (ML/G)
0.1	0.03896	0.2811	7.22	201	344
0.1	0.03969	0.2775	6.99	194	333
0.05	0.01961	0.1496	7.63	212	363
0.05	0.01955	0.1503	7.69	214	366
0.025	0.009204	0.07751	8.42	234	401
0.025	0.008622	0.08013	9.29	258	442
0.01	0.003199	0.03381	10.6	294	505
0.01	0.003101	0.03431	11.1	308	529
0.005	0.001329	0.01801	13.6	378	648
0.005	0.001501	0.01708	11.4	317	543
Mean			9.39	261	447

Table 8-165: Concentration of IN-MK643 in the solid and liquid phases at the end of adsorption period on the Mattapex soil – adsorption coefficient

NOMINAL INITIAL CONCENTRATION IN SOLUTION (C _o) (µG/ML)	CONCENTRATION AFTER EQUILIBRATION		ADSORPTION COEFFICIENTS		
	IN SOLUTION (C _{ad}) ^A (µG/ML)	ON SOIL (C _s) ^A (µG/G)	K _o (ML/G)	K _{ow} (ML/G)	K _{oc} (ML/G)
0.1	0.05756	0.1883	3.27	204	363
0.1	0.05494	0.2017	3.67	229	408
0.05	0.02631	0.1159	4.41	276	490
0.05	0.02834	0.1027	3.74	234	416
0.025	0.01287	0.05879	4.57	286	508
0.025	0.01248	0.06075	4.87	304	541
0.01	0.004660	0.02648	5.68	355	631
0.01	0.004643	0.02651	5.71	357	634
0.005	0.002149	0.01384	6.44	403	716
0.005	0.002149	0.01390	6.47	404	719
Mean			4.88	305	543

Table 8-166: Concentration of IN-MK643 in the solid and liquid phases at the end of adsorption period on the Pesaro soil – adsorption coefficient

NOMINAL INITIAL CONCENTRATION IN SOLUTION (C_o) ($\mu\text{G/mL}$)	CONCENTRATION AFTER EQUILIBRATION		ADSORPTION COEFFICIENTS		
	IN SOLUTION (C_{ad}) ^A ($\mu\text{G/mL}$)	ON SOIL (C_s) ^A ($\mu\text{G/G}$)	K_o (mL/G)	K_{om} (mL/G)	K_{oc} (mL/G)
0.1	0.04378	0.2578	5.89	280	491
0.1	0.04231	0.2652	6.27	299	523
0.05	0.02106	0.1423	6.76	322	563
0.05	0.008655	0.2043	23.6	1124	1967
0.025	0.008720	0.07981	9.15	436	763
0.025	0.008648	0.08018	9.27	441	773
0.01	0.003240	0.03361	10.4	495	867
0.01	0.003224	0.03361	10.4	495	867
0.005	0.001354	0.01781	13.2	629	1100
0.005	0.001436	0.01747	12.2	581	1017
Mean			10.7	510	893

Table 8-167: Concentration of IN-MK643 in the solid and liquid phases at the end of adsorption period on the Lleida soil – adsorption coefficient

NOMINAL INITIAL CONCENTRATION IN SOLUTION (C_o) ($\mu\text{G/mL}$)	CONCENTRATION AFTER EQUILIBRATION		ADSORPTION COEFFICIENTS		
	IN SOLUTION (C_{ad}) ^A ($\mu\text{G/mL}$)	ON SOIL (C_s) ^A ($\mu\text{G/G}$)	K_o (mL/G)	K_{om} (mL/G)	K_{oc} (mL/G)
0.1	0.04030	0.2751	6.83	359	621
0.1	0.03982	0.2755	6.92	364	629
0.05	0.01878	0.1538	8.19	431	745
0.05	0.01929	0.1515	7.85	413	714
0.025	0.008072	0.0828	10.3	542	936
0.025	0.01871	0.02943	1.57	82.6	143
0.01	0.003749	0.03099	8.27	435	752
0.01	0.003052	0.03445	11.3	595	1027
0.005	0.001304	0.01806	13.8	726	1255
0.005	0.001288	0.01810	14.1	742	1282
Mean			8.91	469	810

Table 8-168: Concentration of IN-MK643 in the solid and liquid phases at the end of adsorption period on the Hidalgo soil – adsorption coefficient

NOMINAL INITIAL CONCENTRATION IN SOLUTION (C_o) ($\mu\text{g/mL}$)	CONCENTRATION AFTER EQUILIBRATION		ADSORPTION COEFFICIENTS		
	IN SOLUTION (C_{Ag}) ^a ($\mu\text{g/mL}$)	ON SOIL (C_s) ^a ($\mu\text{g/g}$)	K_o (mL/g)	K_{oc} (mL/g)	K_{oc} (mL/g)
0.1	0.06314	0.1411	2.23	319	558
0.1	0.06655	0.1439	2.16	309	540
0.05	0.03237	0.08624	2.66	380	665
0.05	0.03283	0.08364	2.55	364	638
0.025	0.01538	0.04623	3.01	430	753
0.025	0.01562	0.04537	2.90	414	725
0.01	0.005521	0.02090	3.79	541	948
0.01	0.006226	0.01863	2.99	427	748
0.005	0.002765	0.01081	3.91	559	978
0.005	0.002617	0.01148	4.39	627	1098
Mean			3.06	437	765

Table 8-169: Summary of Freundlich adsorption constants of IN-MK643 in the soils

Soil	OC %	pH ^a	Adsorption			
			%	K_f	1/n	$K_{f_{oc}}$
Speyer	2.1	6.3	67.1	3.96	0.83	189
Mattapex	0.9	6.1	48.5	2.03	0.81	226
Pesaro	1.2	8.2	60.4	4.23	0.83	353
Lleida	1.1	8.0	61.3	2.67	0.77	243
Hidalgo	0.4	8.1	39.2	1.34	0.81	335
Mean				2.85	0.81	269.2

Overall adsorption $K_{f_{oc}}$ values ranged from 189 to 353 mL/g, with mean value of 269 mL/g and mean 1/n of 0.81.

RMS comments (2016)

The study is still valid.

There was no clear correlation between adsorption and soil characteristics. Mean K_{foc} value of 269 mL/g with 1/n value of 0.81 is retained for modelling.

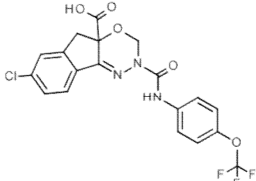
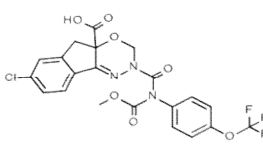
Metabolite IN-U8E24

This metabolite is a major anaerobic metabolite, which reaches more than 10 % AR (13.2% after 2 days) during the preliminary aerobic phase of the anaerobic study and has to be considered in risk assessment although not seen in the soil aerobic metabolism studies.

As no batch equilibrium study was available for this metabolite, applicant provided a K_{oc} determination from KOCWIN 2.0 from EPA EPI Suite 4.11:

The structural and physicochemical properties of IN-U8E24 are very similar to those of IN-KT413, the precursor of IN-U8E24. Several prediction models were used to compare the physicochemical and toxicological properties between IN-U8E24 and IN KT413. The model prediction results support that IN-U8E24 and IN KT413 are similar in the physicochemical properties and toxicity profiles (see the two summary tables and the attached

predictions summary file below). DuPont has also generated IN-U8E24 acute toxicity data for fish, daphnia and algae (see table summary below), showing that IN-U8E24 is the same or much less toxic than IN-KT413.

Parameters	IN-U8E24	IN-KT413	
Structure			Prediction model
MOL WT	455.78	513.82	
LogKow	4.776	4.317	EPISuite Kowwin v1.68
Wat. Sol (mg/L)	0.1142	0.1202	EPISuite WSKowwin v1.43
Koc (L/kg)	1910	1991	KOCWIN v2.00, MCI method
LogKoc	3.281	3.229	KOCWIN v2.00, MCI method

RMS (2016)

RMS agrees that the structural and physicochemical properties of IN-U8E24 are seen very similar to those of IN-KT413, and thus the Koc predicted by the model for both metabolites are similar. However, the batch equilibrium study for IN-KT413 resulted in the determination of a mean K_{foc} value of 344 mL/g, which is very different from the Koc value of 1991 L/kg predicted by the KOWWIN model for this metabolite.

Considering this, RMS is of the opinion that the K_{foc} value of 1910 L/kg predicted by the KOWWIN for metabolite IN-U8E24 cannot be considered reliable and a data gap for Koc determination from batch equilibrium study is proposed by RMS.

B.8.1.2.3. SUMMARY OF ADSORPTION IN SOIL

Adsorption of indoxacarb was measured in a batch equilibrium study on 4 soils. Adsorption constant was not determined according to Freundlich isotherm since definitive test was performed at a single water concentration. Linear Koc values ranged between 2500 and 9 600 mL/g (arithmetic mean: 5125 mL/g). In the absence of any updated study, and considering that this K_{doc} data however reflects strong adsorption to soil, this value was kept for risk assessment. According to McCall classification, indoxacarb is considered as slightly mobile to immobile in soil. No pH dependence was identified.

The batch equilibrium adsorption studies suggest that the major soil metabolites of indoxacarb are moderately to strongly sorbed to soil. IN-JT333 has an average K_{oc} of 17300 mL/g, IN-KT413 has an average K_{foc} of 344 mL/g, IN-KG433 has an average K_{foc} of 314 mL/g, IN-JU873 has an average K_{foc} of 16883 mL/g, IN-MK643 has an average K_{foc} of 269 mL/g, IN-MK638 has an average K_{foc} of 151 mL/g, IN-ML438 has an average K_{oc} of 18697 mL/g, and IN-KB687 had an average K_{foc} of 237.2 mL/g.

Koc value for metabolite IN-U8E24 was estimated to be 1910 mL/g with EPISuite, but this value was found to be probably overestimated by RMS, when comparing Koc value obtained with EPISuite and K_{foc} value obtained from batch equilibrium study for metabolite IN-KT413. This Koc value from EPISuite is thus not considered as reliable for risk assessment. A data gap for reliable Koc from batch equilibrium study is proposed.

The field soil dissipation studies performed in Europe support the mobility conclusions above. In general, nearly all residues including the parent and its major metabolites were confined at top two sampling layers (0-5 cm and 5-15 cm, no quantifiable residues (LOQ = 1 µg/kg) were detected at lower depths (30 cm) at any site

B.8.1.3. MOBILITY IN SOIL**B.8.1.3.1. COLUMN LEACHING**

See below

B.8.1.3.2. AGED COLUMN LEACHING

Data to address this point were presented in the dossier submitted for first inclusion in Annex I and were deemed acceptable following evaluation and peer review at EU level. No additional studies are submitted for the renewal.

Column leaching studies are not required as reliable adsorption coefficient values for indoxacarb were obtained from the available adsorption and desorption study.

Summary of the following study, as presented in the original DAR Indoxacarb DAR (2000) is reported below for information.

A review of this study indicates that it fully meets the current guideline (OECD 312). However the study is considered supplemental and not relied upon since reliable absorption coefficient values have been obtained in adsorption/desorption studies.

Data point:	
Author(s)	Fetterman, D.E., Chrzanowski, R.L. (1997);
Title:	Soil column leaching study of ¹⁴ C-DPX-MP062 (a 3:1 mixture of DPX-KN128 and IN-KN127) on four aged soils
Organisation:	
Document No:	AMR 3845-96
Dates of experimental work	
Guidelines:	U.S. EPA 163-1 (1982), Directive 91/414
Previous evaluation:	Yes
Acceptability:	Yes

- Test material: ¹⁴C-DPX-MP062
Lot/Batch #: [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-JW062EL: HOTC 462
Radiochemical purity: >95%

Description

An aged leaching study with indoxacarb (50:50) was performed. Indoxacarb was labelled in the TFM-position. Ageing experiment: Two flasks containing 60 g (dry weight equivalents) of each soil were treated with 131 µg ¹⁴C-labelled indoxacarb. Volatiles were trapped on ethylene glycol and NaOH solutions. The soils were incubated for 4 to 32 days at 20 °C. One of each soil type was extracted with acetonitrile:water 90:10 and acetone:water 90:10. Radioactivity in the extracts was quantified by ISC. Combined extracts were concentrated and analyzed by HPLC with radiochemical detection. The other was used for the column experiment.

Leaching experiment: Characteristics of column: I.D 5 cm, 30 cm untreated soil and c. 3 cm treated soil. The leachate was collected in hourly portions of c. 7-8 ml. The soil column was dismantled into 5 cm segments. Each segment was air dried and homogenized before combustion. Segments containing >5% of applied radioactivity were extracted as mentioned above. Detec. method: LSC, HPLC, combustion, and GC (recovery unknown). LOD in leachate was 0.18% of r.a. applied.

Results

Ageing study: Total recovery of radioactivity varied from 97 to 104% after ageing. 86-99 % of the radioactivity was extractable, distributed over indoxacarb, IN-JU873 and other metabolites. Other metabolites consisted of different compounds which individually did not exceed 3% a.r.. Bound residue amounted to 2- 13%.

Table 8-170: Distribution of ^{14}C -label in aged soil (% of applied).

Soil type	indoxacarb	IN-JU873	others	unextracted
sand	92	-	8	4
sandy clay loam	28	18	40	13
loam	90	-	5	2
silt loam	67	15	9	6

Leaching study: Total recovery of radioactivity applied to the soil column was 92% (range 82-97%). No significant amount of radioactivity appeared in the leachate.

49% or more of the applied radioactivity remained in the aged soil layer (average 70%, range 49-84%). Amounts of indoxacarb were a little lower than after ageing.

Table 8-171: Distribution of ^{14}C -label (% of a.r.) in soil column segments.

Soil type	aged soil	0-5 cm	5-10 cm	10-15 cm
sand	75	6	0.9	0.2
sandy clay loam	49	30	9	6
loam	73	18	0.01	0.05
silt loam	84	9	2	0.2
average	70	16	3	1.6

B.8.1.3.3. FIELD LEACHING / LYSIMETER STUDIES

A lysimeter study was not conducted with indoxacarb (DPX-KN128). Data from the adsorption/desorption studies, the aged residue soil column leaching study, and the aerobic soil degradation studies have clearly demonstrated that there is no reasonable expectation of any movement of indoxacarb or its degradation products from the top few centimetres of soil under normal use conditions.

The lack of mobility potential of indoxacarb in soil was demonstrated in the modeling done in support of the various proposed uses. In no case was there estimated to be detectable levels of indoxacarb in soil at a depth of 1 meter (see also Indoxacarb RAR_Volume_3CP_B8).

B.8.2. FATE AND BEHAVIOUR IN WATER AND SEDIMENT**B.8.2.1. ROUTE AND RATE OF DEGRADATION IN AQUATIC SYSTEMS (CHEMICAL AND PHOTOCHEMICAL DEGRADATION)****B.8.2.1.1. HYDROLYTIC DEGRADATION**

Data point:	CA 7.2.1.1/01
Author(s)	Clark, B. (2015);
Title:	Hydrolysis of ¹⁴ C-Indoxacarb (DPX-KN128) in buffer solutions at pH 4, 7, and 9
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-35853, Revision No. 1
Dates of experimental work	
Guidelines:	OECD guideline 111 (2004), U.S. EPA, OPPTS 835.2120 (2008)
Deviations:	None
Previous evaluation:	No, study submitted for AIR III
Acceptability:	Yes

MATERIALS AND METHODS

- Radiolabelled test material: ¹⁴C DPX-KN128

Lot/Batch #: [Indanone-1-¹⁴C]indoxacarb: 1643850
(abbreviated as [I-¹⁴C]indoxacarb
[4-Trifluoromethoxyphenyl-¹⁴C(U)]indoxacarb: 1643851A
(abbreviated as [TFMP-¹⁴C]indoxacarb

Radiochemical purity: [I-¹⁴C]indoxacarb: 98.8%
[TFMP-¹⁴C]indoxacarb: 99.5%

Specific activity: [I-¹⁴C]indoxacarb: 49.5 µCi/mg (1.83 Mbq/mg)
[TFMP-¹⁴C]indoxacarb: 46.3 µCi/mg (1.71 Mbq/mg)

Description: White powder

Stability of test compound: Stable during test
- Buffers:

0.1 M buffer solutions in HPLC grade water were prepared at pH 4, using acetate, at pH 7 using phosphate, and at pH 9 using borate.

Experimental conditions

Hydrolysis of radiolabelled indoxacarb was studied in the dark at 10, 20, and 30°C in sterile aqueous buffered solutions at pH 4 (0.01 M acetate), pH 7 (0.01 M phosphate), and pH 9 (0.01 M borate) for up to 30 days. The buffer solutions were sterilised by autoclaving and were placed in 100- to 200-mL glass flasks. Samples were analysed at the time intervals shown in Table 8-173 through Table 8-178 and the indoxacarb residues were analysed by LSC and HPLC. Identification of the transformation products was done by HPLC/UV with fraction collection. The limit of detection (LOD) for indoxacarb was 11 dpm. The limit of quantification (LOQ) for indoxacarb was 43 dpm.

RESULTS AND DISCUSSION**Mass balance**

Average recovery of radiolabel ranged from 96.2–106.9.0% for the [I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb labels.

Findings

Hydrolysis of indoxacarb occurred over the pH range 7–9 and was most rapid at pH 9. Hydrolysis rate increased substantially at the higher temperature (30°C). At test termination, the concentration of the parent compound decreased from 99.3% at Day 0 to 68.8%, 99.3 to 31.0%, and 99.3 to 10.1% of the applied radioactivity (AR) at 10, 20, and 30°C for pH 7, and from 97.6 to 12.8%, 98.0 to 10.8%, and 98.1 to 14.7% AR at 10, 20, and 30°C for pH 9. The first-order DT₅₀ values of indoxacarb were 68.9, 17.6, and 5.6 days at 10, 20, and 30°C for pH 7, respectively. The first-order DT₅₀ values of indoxacarb were 0.99, 0.37, and 0.14 days at 10, 20, and 30°C for pH 9, respectively. Arrhenius analysis was performed for each pH. The activation energy, E_a was calculated as 89.8 and 70.8 kJ/mol for pH 7 and 9, respectively. The coefficient of determination, R², was 0.9989 and 0.9992 for pH 7 and 9, respectively.

Table 8-172: Hydrolytic half-lives and rate constants for radiolabelled indoxacarb

pH	Temperature (°C)	Half-life (day)	k (day ⁻¹)	r ²	Method of calculation
4	—	Stable	Stable	—	First-order
7	10	68.9	0.0101	0.6180	
	20	17.6	0.0395	0.9406	
	30	5.57	0.124	0.9897	
9	10	0.99	0.700	0.8191	
	20	0.37	1.86	0.9943	
	30	0.14	5.09	0.9928	

At pH 7, the major transformation products detected were IN-KT413 and IN-MP819, with a maximum mean concentration of 66.9% AR and 16.2% AR, respectively, observed on the 30.0 day of incubation/at test termination and 15.0 day of incubation (Table 8-173 through Table 8-175). At pH 9, the major transformation product detected was IN-KT413, with a maximum mean concentration of 99.1% AR, observed on Day 1.2 of incubation/at test termination (Table 8-176 through Table 8-178). Minor components detected represented <4.3% of the applied radioactivity individually.

Table 8-173: Hydrolysis of radiolabelled indoxacarb at pH 7, 10°C (expressed as mean percentage of the applied radioactivity)

Compound ^a	Sampling times (days)						
	0.0	1.9	7.0	15.0	16.9	24.0	30.0
Indoxacarb (DPX-KN128)	96.7	92.0	101.1	93.5	90.7	74.4	70.5
IN-KT413	0.0	2.7	10.9	20.7	21.4	29.4	28.1
IN-MP819	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Unidentified radioactivity, if any	3.3	0.7	0.5	0.3	0.2	0.2	8.8
Total % recovery	100.0	95.4	112.4	114.6	112.4	104.0	107.4

^a Data were average from two labels ([I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb) including sampling intervals (round to one decimal place).

Table 8-174: Hydrolysis of radiolabelled indoxacarb at pH 7, 20°C (expressed as mean percentage of the applied radioactivity)

Compound ^a	Sampling times (days)							
	0.0	1.0	2.9	7.0	10.0	17.0	24.0	30.0
Indoxacarb (DPX-KN128)	96.7	85.9	94.6	80.9	67.2	44.3	34.3	33.2
IN-KT413	0.0	4.4	12.9	31.0	32.8	52.9	64.5	66.9
IN-MP819	0.0	0.0	0.0	0.0	4.1	11.7	7.4	11.8
Unidentified radioactivity, if any	3.3	0.9	3.0	0.6	4.5	2.0	0.9	0.8
Total % recovery	100.0	90.5	106.8	112.0	110.0	110.4	108.5	111.3

^a Data were average from two labels ([I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb) including sampling intervals (round to one decimal place).

Table 8-175: Hydrolysis of radiolabelled indoxacarb at pH 7, 30°C (expressed as mean percentage of the applied radioactivity)

Compound ^a	Sampling times (days)						
	0.0	1.0	2.9	5.9	10.0	15.0	17.0
Indoxacarb (DPX-KN128)	96.7	90.9	74.0	51.3	32.8	16.1	11.6
IN-KT413	0.0	12.9	30.5	51.6	58.1	67.9	58.7
IN-MP819	0.0	0.0	0.0	7.2	12.9	15.9	16.2
Unidentified radioactivity, if any	3.3	1.1	1.4	0.6	2.8	5.0	6.8
Total % recovery	100.0	104.9	105.9	110.8	106.6	105.0	93.4

^a Data were average from two labels ([I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb) including sampling intervals (round to one decimal place).

Table 8-176: Hydrolysis of radiolabelled indoxacarb at pH 9, 10°C
(expressed as mean percentage of the applied radioactivity)

Compound ^a	Sampling times (days)							
	0.0	0.1	0.1	0.2	1.0	1.0	1.2	2.9
Indoxacarb (DPX-KN128)	96.3	76.5	77.3	74.3	43.6	38.5	36.6	27.7
IN-KT413	3.3	9.9	17.6	21.8	53.5	54.3	60.9	66.6
Unidentified radioactivity, if any	0.4	0.4	0.0	0.6	0.0	1.6	0.2	0.2
Total % recovery	100.0	86.8	94.9	96.8	97.1	94.4	97.7	94.5

^a Data were average from two labels ([I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb) including sampling intervals (round to one decimal place).

Table 8-177: Hydrolysis of radiolabelled indoxacarb at pH 9, 20°C
(expressed as mean percentage of the applied radioactivity)

Compound ^a	Sampling times (days)							
	0.0	0.1	0.1	0.2	0.2	0.3	1.0	1.2
Indoxacarb (DPX-KN128)	97.6	92.9	79.8	76.0	68.9	54.5	15.0	12.1
IN-KT413	2.0	12.6	21.6	31.1	40.5	55.0	95.0	99.1
Unidentified radioactivity, if any	0.4	0.2	0.0	0.0	0.0	0.0	0.7	0.2
Total % recovery	100.0	105.8	101.3	107.0	109.4	109.5	110.7	111.4

^a Data were average from two labels ([I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb) including sampling intervals (round to one decimal place).

Table 8-178: Hydrolysis of radiolabelled indoxacarb at pH 9, 30°C
(expressed as mean percentage of the applied radioactivity)

Compound ^a	Sampling times (days)						
	0.0	0.1	0.1	0.2	0.2	0.3	0.4
Indoxacarb (DPX-KN128)	97.2	71.5	56.2	44.6	33.5	26.9	16.9
IN-KT413	2.3	20.5	39.1	53.7	66.7	78.1	89.9
Unidentified radioactivity, if any	0.5	0.0	0.0	0.0	0.0	0.0	0.2
Total % recovery	100.0	91.9	95.4	98.3	100.2	104.9	107.0

^a Data were average from two labels ([I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb) including sampling intervals (round to one decimal place).

CONCLUSION

The hydrolysis of indoxacarb (DPX-KN128) in sterile buffer solutions was temperature and pH dependent. Indoxacarb degraded most rapidly at pH 9, followed by pH 7. Indoxacarb was shown to be hydrolytically stable at acidic pH 4. At pH 7, the DT₅₀ values of indoxacarb were 68.9, 17.6, and 5.6 days for 10, 20, and 30°C, respectively. At pH 9, the DT₅₀ values of indoxacarb were 0.99, 0.37, and 0.14 days for 10, 20, and 30°C, respectively.

Hydrolysis products measured at greater than 10% of the applied were IN-KT413 and IN-MP819. The major pathway was ester hydrolysis to form significant IN-KT413 at pH7 and 9. IN-KT413 can also undergo decarboxylation and rearrangement of the N-methylester group to form IN-MP819 at pH 7.

RMS (2016)

The study is acceptable. It is noted that in the test at pH 7 and 30°C with both label, unidentified radioactivity is > 5% on two consecutive points and still increasing at the end of the study. However no additional information is deemed necessary since specific hydrolysis metabolites would not be included in the risk assessment for surface water, water/sediment studies being more representative of natural aquatic environments. On the more, as this

unidentified radioactivity is observed after 15 days, it is considered that other biotic degradation mechanism would have occurred in natural aquatic environment.

For IN-KT413, as the maximum occurrence of 99.1% is observed after 1.2 days at pH 9, this value is taken into account for PEC_{sw} calculation.

B.8.2.1.2. DIRECT PHOTOCHEMICAL DEGRADATION

The following study is a position paper submitted to the EU for the first time for the purpose of renewal.

Author(s)	Singles, S.K. (2003);
Title:	Photodegradation of DPX-KN128 in pH 5 buffer and natural water by simulated sunlight
Organisation:	
Document No:	DuPont-12943
Dates of experimental work	
Guidelines:	USEPA 161-2 (1982), SETAC (1995)
Deviations:	None
Previous evaluation:	Yes, in the Indoxacarb DAR addendum 3 (2005).
Acceptability:	

The photolysis of indoxacarb (DPX-KN128) was measured using radiolabelled DPX-MP062, which is a 3:1 mixture of indoxacarb (DPX-KN128) and IN-KN127. The enantiomeric ratio of DPX-MP062 was constant during the photolysis experiment and therefore, indoxacarb (DPX-KN128) degrades at the same rate as DPX-MP062. Indoxacarb (DPX-KN128) undergoes photodegradation in aqueous solution.

The photolytic half-life of indoxacarb (DPX-KN128) at pH 5 and 25°C was 4.5 natural sunlight days. Several degradation intermediates resulting from cleavage of the molecule were formed and further degraded to CO₂ and numerous minor polar components.

RMS (2016)

This document is a position paper summarizing the data obtained in the studies of Ferraro (1997) and Lentz (2002). It is noted that the study of Ferraro (1997), was considered superseded by the study of Lentz (2003) in the original DAR addendum 3 (2005) and this latter study is fully summarized below

See RMS comments on photolysis after study summary below.

Author(s)	Ferraro (1997)
Title:	Photodegradation of DPX-JW062 (a racemic mixture of DPX-KN128 and IN-KN127) in pH 5 buffer solution and natural water by simulated sunlight DuPont Experimental Station AMR 2788-93
Organisation:	DuPont Experimental Station.
Document No:	2788-93
Dates of experimental work	
Guidelines:	EEC 94/37; US EPA 161-2; MAFF 1995.

Deviations:	None
Previous evaluation:	Yes, in the Indoaxacarb DAR addendum 3 (2005).
Acceptability:	

The study of Ferraro was considered superseded by the study of Lentz 2003 in the DAR addendum 3 (2005).

Author(s)	Lentz, N.R. (2002);
Title:	Photodegradation of ¹⁴ C-DPX-MP062 in pH 5 buffer by simulated sunlight
Organisation:	Ricerca Biosciences, LLC, Concord, Ohio, USA
Document No:	DuPont-9801
Dates of experimental work	
Guidelines:	USEPA 161-2 (1982), SETAC (1995)
Deviations:	None
Previous evaluation:	Yes, in the Indoaxacarb DAR addendum 3 (2005).
Acceptability:	

Test Substance: ¹⁴C-DPX-MP062 **Batch:** SMS 3000462 and SMS 3000481

Purity: 96% (SMS 3000481), 99.9% (SMS 3000462)

Material and Methods:

The photolytic stability of DPX-MP062 (1) [indanone-1-¹⁴C] labeled (Batch no. DuPont SMS 3000481; specific activity 31.4 Ci/mg, radiochemical purity 96%) and (2) [trifluoromethoxyphenyl(U)-¹⁴C] labeled (Batch no. DuPont SMS 3000462; specific activity 48.4 Ci/mg, radiochemical purity 99.9%) was studied in pH 5 buffer. DPX-MP062 was dissolved in acetonitrile and an aliquot of each radiolabel was applied to test vessels containing the appropriate buffer (co-solvent concentration after application was less than 0.9%). The nominal concentration of DPX-MP062 in the test vessels was 0.1 g/mL (which is approximately one-half of the water solubility).

The test vessels were continuously irradiated for 15 days using a xenon arc simulated sunlight source (intensity equal to midday summer sunlight at a latitude of 52°N, equivalent to 22 days of sunlight) at 25°C under sterile conditions. Dark controls were also prepared and maintained at 25°C. Provisions were made to trap volatile radioactivity. Prior to analysis, the test vessels were rinsed with acetonitrile to ensure that all remaining DPX-MP062 was in solution. Single samples treated with each radiolabeled form were taken at each sampling time and the pH was measured. The test solutions were analysed by LSC and reversed phase HPLC with fraction collection and LSC of the eluate. Traps for volatile radioactivity were analysed by LSC. Metabolites were identified by co-chromatography with authentic standards and by LC/MS. In addition, selected samples were analysed by normal phase chiral HPLC to determine the amount of DPX-KN128 and IN-KN127 present in the DPX-MP062 peak. The quantum yield of DPX-MP062 was determined using chemical actinometry.

The DT₅₀ and DT₉₀ values of DPX-MP062 were calculated using non-linear first order regression using ModelManager[®] ver 1.1 (Cherwell Scientific, Oxford, UK).

Findings:

Material Balance. Recovery ranged from 93.9 to 105.9% (Table 117 to Table 120).

Degradation products: DPX-MP062 was extensively degraded under photolytic conditions and resulted in cleavage of the molecule and degradation of the central nucleus of the molecule. The major degradation products detected in the samples treated with [indanone-1-¹⁴C]DPX-MP062 were IN-MH304, IN-MA573, IN-C0639, and numerous minor components (none of which exceeded 7% of the applied radioactivity, Table 117). IN-MH304 reached a maximum concentration of 32.3% of the applied radioactivity and was further degraded to yield a dicarboxylic acid, IN-MA573, which reached a maximum of 19.9% of the applied radioactivity. IN-MA573 was further degraded to another dicarboxylic acid, IN-C0639, which reached a maximum concentration of 10.2% of

the applied radioactivity. The only other major degradation product was carbon dioxide, which reached a maximum concentration of 10.4% of the applied radiolabel. The major degradation products detected in the sterile pH 5 buffer irradiated samples treated with [trifluoromethoxyphenyl(U)- ^{14}C]DPX-MP062 were IN-KB687, IN-MF014, and numerous minor components (none of which exceeded 5.5% of the applied radioactivity, Table 118). IN-MF014, which was also found in the hydrolysis study, reached a maximum concentration of 37.6% of the applied radioactivity and was further degraded to IN-KB687 (maximum of 15% of the applied radioactivity). Carbon dioxide was also a major degradation product, reaching a maximum concentration of 12.1% of the applied radioactivity. Dark controls in pH 5 showed little detectable degradation.

Table 8-179: Distribution and mass balance of AR in irradiated pH 5 buffer samples treated with [Ind14C]DPX-MP062

Distribution and mass balance of radioactivity [indanone-1- ^{14}C]										
		Days post-treatment								
		0	0.25	0.5	1	2	3	7	10	15
DPX-MP062 (parent)	%AR ^a	93.6	84.5	80.3	75.2	52.5	42.1	21.6	7.2	6.3
Polars Total	%AR	0.6	2.7	3.2	4.4	11.9	16.6	29.1	35.5	36.2
IN-C0639	%AR	Nd ^d	Nd	Nd	0.4	Nd	Nd	7.0	6.0	10.2
IN-MA573	%AR	Nd	Nd	Nd	1.8	Nd	Nd	12.8	19.9	15.4
Polar Others ^b	%AR	Nd	Nd	Nd	2.2	Nd	Nd	9.3	9.6	10.6
IN-MH304	%AR	Na ^e	2.6	4.7	7.9	15.9	12.9	25.2	26.6	32.3
Nonpolar Others ^b	%AR	2.0	6.4	8.9	9.7	15.9	23.7	21.2	26.9	11.7
Total residue aqueous	%AR	96.2	96.2	97.1	97.1	96.2	95.2	97.1	96.2	86.5
CO ₂	%AR	Na	Na	Na	Na	Na	1.1	3.3	7.7	10.4
Total % recovery ^c	%AR	96.2	96.2	97.1	97.1	96.2	96.3	100.4	103.9	96.9

^a %AR = Percent of applied radioactivity (dosing solution = 0.104 $\mu\text{g/mL}$)

^b Others = components not identified. Individual polar and nonpolar other ^{14}C components detected by HPLC were less than 7% of the applied radioactivity.

^c Recovery of administered radioactivity as determined by LSC analyses of the dosing solution.

^d Nd = Not determined. The Day 2 and Day 3 samples were totally consumed for the chiral HPLC analysis. Day 2 and Day 3 samples were not available for the analysis of polars.

^e Na = Not analysed

Table 8-180: Distribution and mass balance of AR in irradiated pH 5 buffer samples treated with [TFMP ^{14}C]DPX-MP062

Distribution and mass balance of radioactivity [trifluoromethoxyphenyl(¹⁴ C)]										
		Days post-treatment								
		0	0.25	0.5	1	2	3	7	10	15
DPX-MP062 (parent)	%AR ^a	96.5	90.0	84.8	67.8	53.4	37.8	15.4	6.4	5.8
Polars ^b	%AR	0.2	2.1	3.0	7.3	12.6	18.6	21.8	27.3	19.6
IN-MF014	%AR	Nd ^e	1.9	3.0	8.0	15.6	16.1	25.0	27.8	37.6
IN-KB687	%AR	Nd	2.7	5.3	10.1	13.4	19.4	23.5	28.7	15.0
Others ^c	%AR	0.9	2.4	2.9	4.9	5.0	5.1	8.7	6.9	8.5
Total residue aqueous	%AR	97.6	99.0	99.0	98.1	100.0	97.1	94.2	97.1	86.5
CO ₂	%AR	Na ^f	Na	Na	Na	Na	1.9	6.1	8.8	12.1
Total % recovery ^d	%AR	97.6	99.0	99.0	98.1	100.0	99.0	100.3	105.9	98.6

^a %AR = Percent of applied radioactivity (dosing solution = 0.104 µg/mL)

^b Individual polar ¹⁴C components detected by HPLC were less than 4.5% of the applied radioactivity.

^c Others = Components not identified. Individual ¹⁴C components detected by HPLC were less than 5.5% of the applied radioactivity

^d Recovery of administered radioactivity as determined by LSC analyses of the dosing solution.

^e Nd = Not detected

^f Na = Not analysed

Table 8-181: Distribution and mass balance of AR in dark control sterile pH 5 buffer samples treated with [Ind¹⁴C]-DPX-MP062

Distribution and mass balance of radioactivity [indanone-1- ¹⁴ C]								
		Days post-treatment						
		0	1	3	7	15	21	30
DPX-MP062 (parent)	%AR ^a	96.0	98.4	97.6	90.9	99.8	94.5	94.8
Others ^b	%AR	2.8	5.2	2.3	3.0	1.9	4.7	3.9
Total % recovery ^c	%AR	98.8	103.6	99.9	93.9	101.7	99.2	98.7

^a %AR = Percent of applied radioactivity (dosing solution = 0.106 µg/mL)

^b Others = components not identified.

^c Recovery of administered radioactivity as determined by LSC analyses of the dosing solution.

Table 8-182: Distribution and mass balance of AR in dark control sterile pH 5 buffer samples treated with [TFMP¹⁴C]-DPX-MP062

Distribution and mass balance of radioactivity [trifluoromethoxyphenyl(U)- ¹⁴ C]								
		Days post-treatment						
		0	1	3	7	15	21	30
DPX-MP062 (parent)	%AR ^a	96.9	92.8	97.1	96.5	98.5	97.2	87.3
IN-MF014	%AR	Nd ^d	Nd	Nd	Nd	1.6	1.9	6.1
Others ^b	%AR	1.1	3.9	2.6	2.9	2.5	0.9	4.7
Total % recovery ^c	%AR	98.0	96.7	99.7	99.4	102.6	100.0	98.1

^a %AR = Percent of applied radioactivity (dosing solution = 0.107 µg/mL)

^b Others = Components not identified.

^c Recovery of administered radioactivity as determined by LSC analyses of the dosing solution.

^d Nd = Not detected

DT₅₀ and DT₉₀ values for DPX-MP062: DPX-MP062 was stable to hydrolysis at pH 5, so the DT₅₀ measured is due only to photolysis. DT₅₀ and DT₉₀ values under continuous irradiation were 3 and 9 days, respectively (Table 121). The corresponding photochemical half-life of DPX-MP062 in sunlight equivalent days was 4.5 days (based on a Wilmington, Delaware, USA summer day, latitude 39°40'N). The enantiomeric ratio of DPX-KN128 and IN-KN127 remained constant over time, showing that the enantiomers degraded at the same rate under photolytic conditions (Table 122).

Table 8-183: Degradation kinetics for samples in pH 5 buffer treated with[¹⁴C]-DPX-MP0602

Sample	DT ₅₀ (days)	DT ₉₀ (days)	k (day ⁻¹)	r ²	Method of Calculation
Continuous irradiation ^a	3	9	0.0265	0.991	Non-linear first order regression
Sunlight equivalent days ^b	4.5	---	---	---	

^a No contribution from hydrolysis at this pH.

^b Based on a Wilmington, Delaware, USA summer day, latitude 39°40'N

Table 8-184: Distribution of [Ind¹⁴C]-DPX-MP062 as a mixture of the enantiomers IN-KN127 and DPX-KN128 for the irradiated sterile pH5 buffer photolysis samples.

		Sample Day		
		0	2	3
DPX-MP062	%AR	93.6	52.5	42.1
IN-KN127 : DPX-KN128		1.0 : 3.3	1.0 : 3.3	1.0 : 3.0
IN-KN127	%AR	21.8	12.2	10.5
DPX-KN128	%AR	71.8	40.3	31.6

Quantum yield for DPX-MP062: The calculated quantum yield for DPX-MP062 was 0.00038.

Comments (RMS 2016)

The study of Lentz is acceptable. This study show that DPX-MP062 is rapidly degraded by photolysis in pH 5 sterile buffer, having a half-life of approximately 3 days (4.5 days considering sunlight equivalent days). This study showed that the enantiomeric ratio of DPX-KN128 and IN-KN127 remained constant over time, showing that the enantiomers degrade at the same rate under photolytic conditions.

The major degradation products detected in the sterile pH 5 buffer irradiated samples treated with [indanone- 1-¹⁴C]DPX-MP062 were IN-C0639, IN-MA573, IN-MH304, and numerous minor components. The major degradation products detected in the sterile pH 5 buffer irradiated samples treated with [trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062 were IN-KB687, IN-MF014, and numerous minor components.

RMS had concern on whether some of the photolysis metabolites should be included in risk assessment. As indicated in this position paper of Singles 2003 and in the study of Lentz 2003, aqueous photolysis would be a major contribution in the degradation of DPX-KN128 in the environment, with formation of 4 new major metabolites. However, these photolysis metabolites were not initially considered in risk assessment by applicant, arguing that photolysis would be insignificant under environmental conditions. RMS does not totally agree with this statement, because even if these metabolites reach their maximum occurrence at almost the end of the photolysis study (10 or 15 days), it can be seen that two of them are becoming major at DAT 2 and could probably be formed under natural conditions (IN-MH304, 15.9% and IN-MF014, 15.6%).

In response to RMS request, applicant provided the following argumentation:

“DuPont noticed that these two metabolites were detected above 10% at Day 2 under continuous irradiation. DuPont also noticed that the 2-day continuous irradiation actually equals to 4 days in sunlight-equivalent days. DuPont did an initial stage of the risk assessment as a follow up to predicted concentrations of these two metabolites in water under the natural conditions.

Based on our evaluation, these two metabolites would not exceed 10% AR under natural conditions in the surface water. Following is the summary of our evaluations:

DuPont-8417 water/sediment study shows that Indoxacarb was rapidly transferred from the water column to the sediment in water/sediment systems with DT50 of 0.48-0.96 days (Bury Pond system: DT50=0.58 days, Chatsworth system: DT50=0.48 days; DuPont-39061: Sand System: DT50=0.96 days, Clay loam system: DT50=0.76 days), on Day 1 at least 50% of indoxacarb is partitioned into sediment systems, which would not allow indoxacarb to be available to undergo photolytic decomposition.

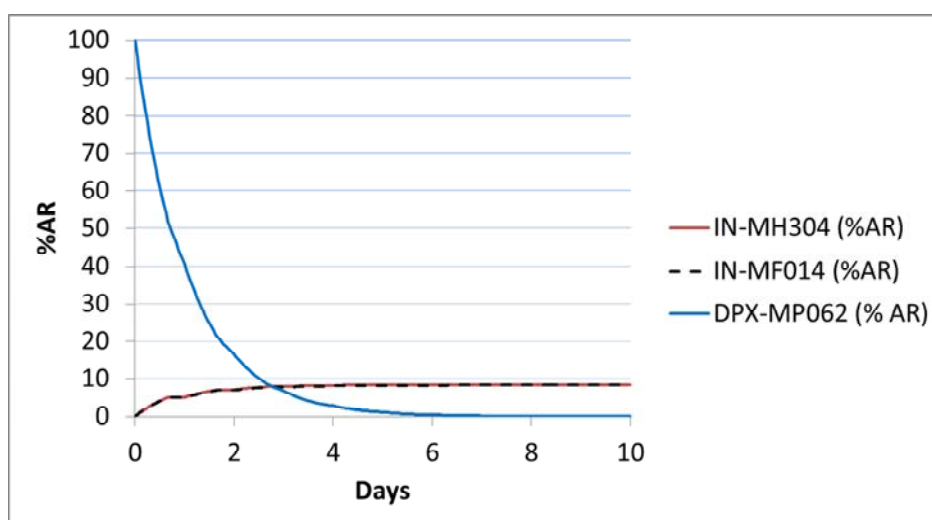
To demonstrate kinetically the surface water concentrations for IN-MH304 and IN-MF014, DuPont did further calculation based on data from the aqueous photolysis and water-sediment studies.

- 1. we estimated photolytic formation rate coefficients of IN-MH304 and IN-MF014 based on the photolytic degradation rate coefficient of indoxacarb (0.265 1/d) determined in irradiated sterile pH5 buffer (DuPont report 12943) and the formation of IN-MH304 and IN-MF014 observed in this study after 48 h (15.9 and 15.6 % of applied radioactivity, resp.), assuming first-order degradation of the parent and first-order formation of the metabolites. Photolytic formation rate coefficients of IN-MH304 and IN-MF014 were optimized manually until they matched the observed residues. The resulting formation rate coefficients were 0.1024 1/d for IN-MH304 and 0.1005 1/d for IN-MF014.*
- 2. we calculated the dissipation of indoxacarb and the formation of the two metabolites on an hourly basis, with the two processes “dark” dissipation (partitioning to sediment + non-photolytic degradation) and photolysis occurring in parallel as first-order processes. The calculations were performed using days with 12h sunlight and days with 16 h sunlight. We used:*
 - a “dark” dissipation half-life of 0.96 d (the longest) and 0.70 d (average from four systems)*
 - a photolytic degradation rate coefficient of 0.265 1/d (from the sterile pH5 buffer study)*
 - the photolytic formation rate coefficients of the metabolites estimated above: 0.1024 1/d for IN-MH304 and 0.1005 1/d for IN-MF014*

The calculations yield that both metabolites stay below 10 % of applied radioactivity even after 10 days:

When dissipation rate at 0.96 d (worst case)

- For days with 12 h sunlight we obtain 7.0 and 6.9 % of applied radioactivity after 10 days (about 0.1% parent left at Day 10) for IN-MH304 and IN-MF014, resp.
- For days with 16 h sunlight we obtain 8.4 and 8.3 % of applied radioactivity after 10 days (about 0.1% parent left at Day 10) for IN-MH304 and IN-MF014, respectively (as shown in the following graph).



When dissipation rate at 0.70 d (average value from four systems)

- For days with 12 h sunlight we obtain 5.6 and 5.5 % of applied radioactivity after 10 days (about 0.1% parent left at Day 10) for IN-MH304 and IN-MF014, respectively.
- For days with 16 h sunlight we obtain 6.7 and 6.6 % of applied radioactivity after 10 days (about 0.1% parent left at Day 10) for IN-MH304 and IN-MF014, respectively.

Based on the calculation above, the maximum occurrence of IN-MH304 and IN-MF014 in natural water-sediment systems will be below 10 % of applied parent, and therefore they were considered non-relevant metabolites. Consequently, DuPont believes that a model in STEPS1-2 for surface water is not warranted.

RMS (2016)

RMS does not fully agree with applicant's conclusion. Although demonstration is made that the maximum occurrence of photolysis metabolites is likely to be below 10% of applied parent, the results show that this maximum is > 5 % and increasing from day 1. They should be thus considered as relevant metabolites.

As first approach, and considering as worst-case a maximum occurrence of 10 % and a molar ratio of 0.55 (worst-case of the two metabolites), it is considered that max PEC_{sw} concentration covering both metabolites will be equal to 5.5 % of the PEC_{sw} for parent. Thus the risk assessment for metabolite is covered by risk assessment made for parent, if metabolite is considered 10 times more toxic.

B.8.2.1.3. INDIRECT PHOTOCHEMICAL DEGRADATION

No study on the indirect photolysis of indoxacarb (DPX-KN128) was performed. The photodegradation of indoxacarb was well defined in the direct photolysis. There is no evidence to suggest that indirect photolysis of indoxacarb would be different from that observed in the direct study.

B.8.2.2. ROUTE AND RATE OF BIOLOGICAL DEGRADATION IN AQUATIC SYSTEMS**B.8.2.2.1. READY BIODEGRADABILITY**

The following study is submitted to the EU for the first time for the purpose of renewal

Data point:	CA 7.2.2.1/01
Author(s)	Tunink, A. (2014);
Title:	DPX-KN128: Determination of ready biodegradability using the CO ₂ evolution method
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-36501
Dates of experimental work	
Guidelines:	OECD 301 B, OPPTS 850.3110
Deviations:	None
Previous evaluation:	No
Acceptability:	Yes

MATERIALS AND METHODS

- Test material: Indoxacarb (DPX-KN128) technical
 Lot/Batch #: KN128-215
 Purity: 98.4%
 Description: White powdered solid
 CAS#: 173584-44-6
 Stability of test compound: Stable during study period

- Inoculum

Activated sludge was collected from the Columbia Wastewater Treatment Plant in Columbia, Missouri, USA and used immediately without storage. Activated sludge micro-organisms were maintained in an aqueous mineral medium. The microbial evaluation data suggests that the test substance had no significant effect on the population of microbes, and the microbial populations in the inoculum were viable and acceptable for the study design

Experimental conditions

Samples were maintained in stirred bioreactors at a nominal temperature range of 20-24°C with CO₂-free aeration. The test concentration of indoxacarb was 20 mg/ L. Sodium benzoate was used as a positive control at 20 mg/L.

Sampling

Duplicate samples were taken for analysis at Days 2, 5, 7, 9, 12, 15, 19, 22, 28, and 29 after application.

Description of analytical procedures

The cultures were acidified in order to drive off soluble forms of inorganic carbon and final analysis was performed on Day 29. The CO₂ produced in the test systems was trapped in 0.2 N KOH solutions, which were

then analyzed for inorganic carbon (IC) content using a Teledyne Fusion Persulfate Total Organic Carbon (TOC) Analyzer.

RESULTS AND DISCUSSION

Table 8-185: Percent biodegradation levels

Treatment	Percent biodegradation			
	Day 2	Day 5	Day 15	Day 29
Indoxacarb (DPX-KN128) 20 mg/L	0.5	0.5	5.0	12.0
Sodium benzoate 20 mg/L	37.6	67.7	77.6	79.6

CONCLUSION

The mean percent theoretical CO₂ produced by the test substance, indoxacarb, was 12.0% by Day 29 of the study. Since the biodegradation values did not reach 60% theoretical CO₂ by the end of the study, the test substance cannot be classified as readily biodegradable. The percent theoretical CO₂ produced by the reference substance was 67.7% by Day 5 of the study, confirming the inoculum was viable.

Comments RMS

The study is acceptable.

B.8.2.2.2. AEROBIC MINERALISATION IN SURFACE WATER

The following study is submitted to the EU for the first time for the purpose of renewal

Data point:	CA 7.2.2.2/01
Author(s)	Allan, J. (2014);
Title:	DPX-KN128: Aerobic mineralization in surface water
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-34820
Dates of experimental work	
Guidelines:	OPPTS 835.3190, OECD Guideline 309 (2004)
Deviations :	None
GLP:	Yes
Previous evaluation:	No
Acceptability:	See RMS comments

Executive summary:**I. MATERIALS AND METHODS****A. MATERIALS**

1. Radiolabelled test material: [¹⁴C]-indoxacarb (DPX-KN128)
 Radiolabelled Lot/Batch #: [indanone-1-¹⁴C]indoxacarb: Lot # 1643850
 abbreviated as [I-¹⁴C]indoxacarb
 [4-trifluoromethoxyphenyl-¹⁴C]indoxacarb: Lot # 1643851A
 abbreviated as [TFMP-¹⁴C]indoxacarb
 Radiochemical purity: [I-¹⁴C]indoxacarb: 98.8%
 [TFMP-¹⁴C]indoxacarb: 99.5%
 Specific activity: [I-¹⁴C]indoxacarb: 49.50 µCi/mg
 [TFMP-¹⁴C]indoxacarb: 46.3 µCi/mg
 Stability of test compound: The test material was stable in the aqueous phase under the test conditions.

2. Surface Water:

The study was conducted using surface water collected from Chula, Georgia, USA. The water was clear, free of debris and used without filtration on the day of collection. A summary of the physical and chemical properties of the surface water is provided in Table 8-186.

Table 8-186: Surface water characteristics

Parameter	Value	Parameter	Value
Water Identity	Chula	Total nitrogen (ppm)	2.6
pH	7.4	Nitrate-nitrogen (ppm)	<0.1
Biochemical Oxygen Demand (mg-O ₂ /L)	8.5	Total phosphorus (ppm) (ppm)	2.1
Hardness (mg-equivalent CaCO ₃ /L)	100	Phosphate-P (ppm)	<0.1
Alkalinity (mg CaCO ₃ /L)	36	Total suspended solids (ppm)	46
Conductivity (mmhos/cm)	0.25	Total organic carbon (ppm)	9.9

B. STUDY DESIGN

The aerobic mineralisation of radiolabelled indoxacarb (DPX-KN128) was studied in one natural surface water system from North America under pelagic conditions at 20 ± 2°C in the dark. The pH, biological oxygen demand, and total suspended solids were 7.4, 8.5 mg-O₂/L, and 46 ppm, respectively.

1. Experimental conditions

Stock solutions of ¹⁴C-labelled indoxacarb in acetonitrile were prepared and aliquots were added to four bioreactors containing 700 mL of surface water to give targeted concentrations. Two concentrations of each radiolabel were tested consisting of bulk samples at nominal values of 20 µg/L (low rate) and 120 µg/L (high rate) of test substance.

For mineralisation testing, a sub-sample of the surface water was removed at each sampling time and assayed for radioactivity followed by acidification (pH 2–3 using concentrated hydrochloric acid) and purging with air to expel any CO₂. Decreases in radioactivity following acidification were evaluated as possible mineralisation.

The potential for biotransformation was determined by HPLC analysis of the surface water prior to acidification. Material balance was determined by direct measurement of the mass balance bioreactor flasks.

Eight additional bioreactors were similarly prepared for mass balance determinations at Day 0 and termination (Day 60).

Finally, to confirm microbial viability of the surface water, two additional bioreactors were prepared with a reference compound ([¹⁴C]benzoic acid) at 500 µg/L and were analysed in parallel for mineralisation.

2. Sampling

Sampling was performed following test substance application (zero time) and after the following intervals of incubation: 5, 14, 28, 45, and 60 days.

3. Description of analytical procedures

Radioactivity was determined by LSC. The mean limit of detection (LOD) was 0.056 µg/L, which corresponded to 0.27% and 0.048% AR for the low and high rates, respectively. The mean limit of quantification (LOQ) was 0.22 µg/L, which corresponded to 1.1% and 0.18% AR for the low and high rates, respectively.

Aliquots of the highest test concentration samples were analysed prior to acidification by reverse phase HPLC (Thermo Scientific, Polar Acclaim II C18 (250 mm × 4.6 mm × 5 µm id), eluted with a gradient of 0.01M ammonium acetate (aq) and acetonitrile. The mean detection limits LOD and LOQ were 1.1 µg/L (0.88% AR) and 2.11 µg/L (was 1.8% AR), respectively.

II. RESULTS AND DISCUSSION

A. MASS BALANCE

At termination, material balance in the low dose samples was 76.4% and 91.7% AR of the initially applied dose for the [I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb treated samples, respectively. Material balance in the high dose samples was 87.5% and 96.7% AR of the initially applied dose for the [I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb treated samples, respectively. The lower recoveries in the [I-¹⁴C]indoxacarb samples were attributed to the formation of ¹⁴CO₂, which was observed as dissolved carbonate in Day 60 samples at 15.2% AR prior to acidification.

B. MINERALISATION

At termination, the mean mineralisation was 24.6% (range: 5.8% to 43.4%) and 15.5% (range: 15.2% to 15.8%) for low and high dose samples, respectively. The reference compound (sodium benzoate) was mineralised up to a mean of 80.3% within the first 5 days of testing confirming the viability of the test system.

Mineralisation rate constants were calculated to be 88 and 162 day⁻¹ for the 20 µg/L and 71 and 52 day⁻¹ for 120 µg/L dose rates for the [I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb treatments, respectively. A summary of results are present in Table 8-187 through Table 8-189.

C. TRANSFORMATION OF PARENT COMPOUND

Following application of [I-¹⁴C]indoxacarb to the surface water system, the amount of parent present declined from 83.2% AR at Day 0 to undetectable levels by Day 45. One major degradation product was observed, which through co-chromatography with reference standards and mass spectrometry was identified as IN-KT413. IN-KT413 reached a maximum level of 81.0% AR in the surface water at Day 28 and then declined to 62.0% AR by Day 60. IN-MP819 was a minor degradation product reaching a maximum of 4.1% at Day 28 to Day 45 and then declined to 1.0% AR by Day 60. At Day 60, up to 15.2% AR was observed as a broad peak near the solvent front of the HPLC analysis. Acidification of this sample followed by HPLC analysis showed disappearance of this peak, which was evidence of dissolved carbonates. All other components were minor in the surface water accounting for ≤5% at two consecutive sampling intervals and not increasing at the end of the study.

Following application of [TFMP-¹⁴C]indoxacarb to the surface water system, the amount of parent present declined from 89.7% AR at Day 0 to undetectable levels by Day 45. Three major degradation products were observed, which through co-chromatography with reference standards and mass spectrometry were identified as IN-KT413, IN-MK638, and IN-P0036. IN-KT413 reached a maximum level of 88.6% AR in the surface at Day 28 and then declined to 79.3% AR by Day 60, while IN-MK638 reached a maximum of 8.5% AR by Day 60. IN-P0036 slowly increased during the study to a maximum of 5.4% AR by Day 60. IN-MP819 was a minor degradation product reaching a maximum of 4.9% at Day 45 and then declined to 3.2% AR by Day 60. All other components were minor in the surface water accounting for ≤5% at two consecutive sampling intervals and not increasing at the end of the study.

All remaining unidentified degradation products detected in the surface did not account for greater than a combined maximum of 12.6% and 6.5% AR at any sampling interval in the [I-¹⁴C]indoxacarb and [TFMP-¹⁴C]indoxacarb samples, respectively. All other components were minor in the surface water accounting for <5% at two consecutive sampling intervals and not increasing at the end of the study. No single component was ≥5% AR.

A summary of results is presented in Table 8-187 and Table 8-189.

Table 8-187: Mineralisation results of indoxacarb (DPX-KN128) (20 µg/L)

ABC pond surface water	Rep.	Sampling interval (days)					
		0	5	14	28	45	60
Percentage in surface water (%) ^a (pre-acidification)	[I- ¹⁴ C]indoxacarb	95.5	90.2	98.8	96.2	82.9	72.7
	[TFMP- ¹⁴ C]indoxacarb	92.3	87.5	97.6	98.2	96.3	93.5
	Mean	93.9	88.8	98.2	97.2	89.6	83.1
Percentage in surface water (%) (post-acidification)	[I- ¹⁴ C]indoxacarb	77.6	85.2	87.0	89.5	72.4	52.1
	[TFMP- ¹⁴ C]indoxacarb	74.2	81.2	91.9	89.0	87.7	86.5
	Mean	77.6	83.2	89.5	89.2	80.0	69.3
Mineralisation (%) ^b	[I- ¹⁴ C]indoxacarb	NA	10.3	8.5	6.0	23.1	43.4
	[TFMP- ¹⁴ C]indoxacarb	NA	11.1	0.4	3.4	4.6	5.8
	Mean	NA	10.7	4.4	4.7	13.9	24.6

^a Percentages are based on the concentration (dpm/mL) at each interval sampling relative to the dose control concentration.

^b Mineralisation is the calculated difference between the percentage in phase (pre-acidification) at Day 0 and the percentage in the water (post-acidification).

NA = Not Applicable, since mineralisation is unlikely until strong acid is added.

Table 8-188: Mineralisation results of indoxacarb (120 µg/L)

ABC pond surface water	Rep.	Sampling interval (days)					
		0	5	14	28	45	60
Percentage in surface water (%) ^a (pre-acidification)	[I- ¹⁴ C]indoxacarb	85.4	86.3	93.9	94.6	91.9	90.8
	[TFMP- ¹⁴ C]indoxacarb	89.7	88.0	96.7	99.6	99.9	100.5
	Mean	87.6	87.2	95.3	97.1	95.9	95.7
Percentage in surface water (%) (post-acidification)	[I- ¹⁴ C]indoxacarb	64.9	73.0	78.4	78.9	76.8	70.3
	[TFMP- ¹⁴ C]indoxacarb	74.1	75.6	84.3	83.0	85.7	73.9
	Mean	69.5	74.3	81.3	81.0	81.3	72.1
Mineralisation (%) ^b	[I- ¹⁴ C]indoxacarb	NA	12.4	7.0	6.5	8.6	15.2
	[TFMP- ¹⁴ C]indoxacarb	NA	14.1	5.5	6.7	4.0	15.8
	Mean	NA	13.3	6.2	6.6	6.3	15.5

^a Percentages are based on the concentration (dpm/mL) at each interval sampling relative to the dose control concentration.

^b Mineralisation is the calculated difference between the percentage in phase (pre-acidification) at Day 0 and the percentage in the water (post-acidification).

NA = Not Applicable, since mineralisation is unlikely until strong acid is added.

Table 8-189: Mineralisation results of reference compound [I-¹⁴C]-sodium benzoate (500 µg/L)

ABC pond surface water	Rep.	Sampling interval (days)					
		0	5	14	28	45	60
Percentage in surface water (%) ^a (pre-acidification)	1	100.0	70.3	37.6	31.0	23.6	17.5
	2	100.0	52.6	25.0	18.8	13.1	9.8
	Mean	100.0	61.4	31.3	24.9	18.4	13.7
Percentage in surface water (%) (post-acidification)	1	100.5	21.6	7.6	13.4	10.8	7.0
	2	87.5	17.9	14.5	12.1	8.2	6.0
	Mean	100.5	19.7	11.0	12.8	9.5	6.5
Mineralisation (%) ^b	1	NA	78.4	92.4	86.6	89.2	93.0
	2	NA	82.1	85.5	87.9	91.8	94.0
	Mean	NA	80.3	89.0	87.2	90.5	93.5

^a Percentages are based on the concentration (dpm/ mL) at each interval sampling relative to 100%.

^b Mineralisation is the calculated difference between 100% (pre-acidification) and the percentage in the water (post-acidification).

NA = Not Applicable, since mineralisation is unlikely until strong acid is added

Table 8-190 : Biotransformation of [¹⁴C]-indoxacarb, expressed as percentage of applied radioactivity, in surface water prior to acidification

Surface water dosed at 120 µg/L of [I- ¹⁴ C]indoxacarb						
Compound ^a	Sampling interval (days)					
	0	7	14	28	45	60
As indoxacarb (DPX-KN128)	83.2	47.4	25.1	6.0	0.0	0.0
As IN-KT413	0.0	37.1	65.6	81.0	76.8	62.0
As IN-MP819	0.0	0.0	0.0	4.1	4.1	1.0
As unassigned ^c	2.2	1.9	3.2	3.6	11.0	27.8 ^b
Total recovered residue ^c	85.4	86.3	93.9	94.6	91.9	90.8
Overall mean = 90.5%; Standard deviation = ± 3.8%						
Surface water dosed at 120 µg/L of [TFMP- ¹⁴ C]indoxacarb						
As indoxacarb (DPX-KN128)	89.7	47.5	21.3	2.5	0.0	0.0
As IN-KT413	0.0	39.4	70.5	88.6	81.3	79.3
As IN-MP819	0.0	0.0	0.0	3.8	4.9	3.2
As IN-MK638	0.0	0.0	0.0	3.1	4.0	8.5
As IN-P0036	0.0	0.0	2.6	1.6	3.2	5.4
As unassigned ^c	0.0	1.1	2.3	0.0	6.5	4.1
Total recovered residue	89.7	88.0	96.7	99.6	99.9	100.5
Overall mean = 95.8%; Standard deviation = ± 5.5%						

^a Relative to dose control samples prepared in parallel

^b 15.2% determined to be dissolved carbonates.

^c No individual unidentified % peak accounted for ≥5%, except for the dissolved carbonates

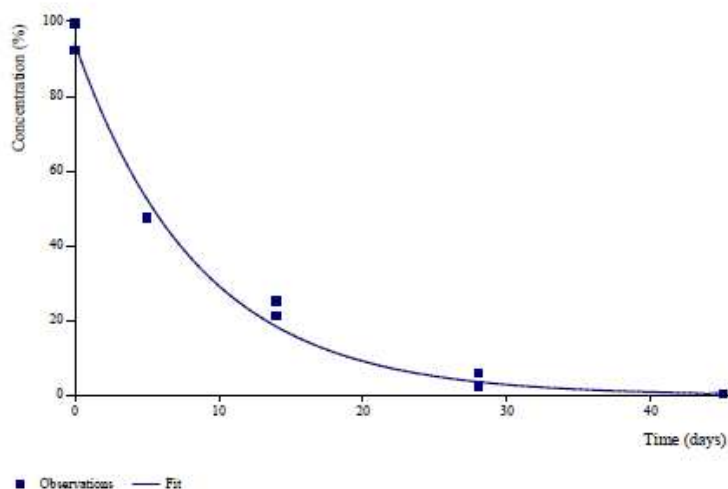
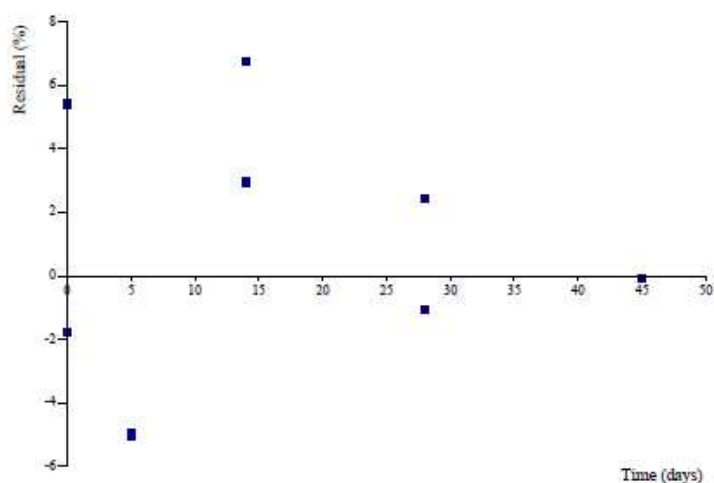
Table 8-191: Biotransformation of [¹⁴C]-indoxacarb, expressed as ppm parent equivalent, in surface water prior to acidification

Surface water dosed at 120 µg/L of [I- ¹⁴ C]indoxacarb						
Compound ^a	Sampling interval (days)					
	0	7	14	28	45	60
As indoxacarb (DPX-KN128)	0.097	0.055	0.029	0.007	0.000	0.000
As IN-KT413	0.000	0.043	0.076	0.094	0.089	0.072
As IN-MP819	0.000	0.000	0.000	0.005	0.005	0.001
As unassigned ^b	0.003	0.002	0.004	0.004	0.013	0.032
Total recovered residue	0.099	0.101	0.109	0.110	0.107	0.106
Surface water dosed at 120 µg/L of [TFMP- ¹⁴ C]indoxacarb						
As indoxacarb (DPX-KN128)	0.109	0.058	0.026	0.003	0.000	0.000
As IN-KT413	0.000	0.048	0.085	0.107	0.098	0.096
As IN-MP819	0.000	0.000	0.000	0.005	0.006	0.004
As IN-MK638	0.000	0.000	0.000	0.004	0.005	0.010
As IN-P0036	0.000	0.000	0.003	0.002	0.004	0.007
As unassigned ^b	0.000	0.001	0.003	0.000	0.008	0.005
Total recovered residue	0.109	0.107	0.117	0.121	0.121	0.122

^a Relative to dose control samples prepared in parallel

^b No individual unidentified % peak accounted for ≥5%

Kinetic analysis of the data

A. Observations and Fitted Model**B. Residual****C. Estimated Values**

COMPONENTS MODELED	MODEL	OPTIMIZED PARAMETERS ± STANDARD ERROR	χ^2	R^2	DT ₅₀ (DAYS)	DT ₉₀ (DAYS)
Surface Water (Chula)	SFO	MO (%AR) = 94.08 ± 2.899 k (d ⁻¹) = 0.1168 ± 0.00884	7.57	0.9886	5.93	19.7

III. CONCLUSION

Results indicated that mineralisation of indoxacarb was 24.6% and 15.5% for the 20 µg/L and 120 µg/L dose rates, respectively over the study duration. DT₅₀ and DT₉₀ values for indoxacarb in surface water were 5.93 and 19.7 days, respectively. The major metabolite observed >10% AR in this study was IN-KT413. The major pathway was ester hydrolysis to form IN-KT413 via demethylation N-decarboxylation. IN-KT413 can also undergo decarboxylation and rearrangement of the N-methylester group to form IN-MP819. IN-MP819 further degrades to IN-MK638 and IN-P0036 through oxadiazine ring opening and bridge cleavage.

RMS (2016)

It is noted that the two test concentrations are both higher than those recommended in the OECD 309.

The pH and the temperature of the water were not determined at collection. Thus the degradation could not be normalized to the temperature of sampling.

B.8.2.2.3. WATER/SEDIMENT STUDY

The following study was summarised in original Indoxacarb DAR (2000) but is not relied upon.

Author(s)	McFetridge, R.D., Houben, K.L. (1997)
Title:	Degradability and fate of DPX-JW062 in the aerobic aquatic environment (water/sediment system)
Organisation:	
Document No:	(DuPont Report No) AMR 3523-95, Revision No. 1
Dates of experimental work	
Guidelines:	U.S. EPA 162-4 (1982)
Deviations :	See below
GLP:	Yes
Previous evaluation:	Yes, in Indoxacar DAR (2000)
Acceptability:	No

- Test material: ^{14}C -DPX-JW062
 Lot/Batch #: [Indanone-1- ^{14}C]DPX-MP062: HOTC 451,
 [Trifluoromethoxyphenyl(U)- ^{14}C]DPX-MP062: HOTC 429
 Radiochemical purity: >95% (HOTC 451), >95% (HOTC 429)

The water/sediment study AMR 3523-95, Revision No. 1, originally submitted under EU Rev8 Point IIA 7.2.1.3.2 and conducted with test material ^{14}C -DPX-JW062, was conducted under guideline U.S. EPA 162-4 (1982). A review of this study indicates that it partially meets the current guideline (OECD 308); deviations include AR recoveries below 90% and all unidentified compound that might have been > 5%. This study is considered supplemental and not relied upon, since there are studies available with test materials of DPX-MP062 (DuPont-8417) and DPX-KN128 (DuPont-39061).

Author(s)	Shaw, D. (2002)
Title:	¹⁴ C-DPX-MP062 (a 3:1 mixture of DPX-KN128 and IN-KN127): Degradability and fate in the water/sediment system
Organisation:	Huntingdon Life Sciences Ltd., Huntingdon, Cambridgeshire, England, UK
Document No:	DuPont-8417
Dates of experimental work	
Guidelines:	SETAC 1995, USEPA 162-4 (1982)
Deviations :	
GLP:	Yes
Previous evaluation:	Yes
Acceptability:	

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: DPX-MP062 technical
 Lot/Batch #: MP062-160
 Purity: 99.4%
 Description: Off-white solid
 CAS#: 144171-61-9
 Stability of test compound: Shown to be stable under the conditions of the test
2. Radiolabelled test material: [Indanone-1-¹⁴C]DPX-MP062
 [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062
 Lot/Batch #: [Indanone-1-¹⁴C]DPX-MP062: HOTV 481
 [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062: HOTC 462
 Radiochemical purity: [Indanone-1-¹⁴C]DPX-MP062: >95%
 [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062: >95%
 Specific activity: [Indanone-1-¹⁴C]DPX-MP062: 31.4 µCi/mg
 [Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062: 48.4 µCi/mg
 Description: White powder
 Stability of test compound: <Shown to be stable under the conditions of the test
3. Water/Sediment
 Two freshly collected water/sediment systems were used, one from a pond, Bury Pond, Cambridshire, UK, and the other from a lake, Emperor Lake, Derbyshire, UK (Table 8-201). Prior to use, the water was filtered through a 0.2-mm sieve, and the sediment was sieved through a 2.0-mm screen.

Table 8-192: Physiochemical parameters of the water/sediment systems

Sediment parameter	System 1	System 2
Geographic location	Bury, Cambridgeshire, United Kingdom	Chatsworth, Derbyshire, United Kingdom
Texture class	Clay loam	Loamy sand
Sand	44.00%	79.95%
Silt	29.56%	11.85%
Clay	26.45%	8.19%
pH (in water)	8.1	7.6
pH (in M CaCl ₂)	7.8	7.1
Organic carbon	1.7%	3.1%
Soil biomass Initial	<0.05 mg C/kg	<0.05 mg C/kg
Final	545.9 mg C/kg	1683.4 mg C/kg
Cation exchange capacity (CEC)	27.2 meq/100 g	23.4 meq/100 g
Nitrogen, Total	1148.1 mg/kg	2365.7 mg/kg
Phosphorus, Total	610.0 mg/kg	708.9 mg/kg
Water parameter	System 1	System 2
pH	7.9	6.9
Hardness (CaCO ₃)	461.0 mgCaCO ₃ /L	56.0 mgCaCO ₃ /L
Dissolved organic carbon	50.2 mg/L	27.8 mg/L
Nitrogen, total	<0.05 mg/L	7.0 mg/L
Phosphorus, total	0.7 mg/L	<0.05 mg/L

B. STUDY DESIGN

1. Experimental conditions

The study was performed in an air flow-through system using Teflon[®] vessels containing 100 mL of water and either 46.1 g of pond sediment or 49.5 g of lake sediment. Vessels were filled to a height of about 6 cm for water and a depth of 2.0–2.5 cm for the sediment layer, which were then allowed to equilibrate for 24 days before application of the test material.

The test systems were maintained at $20 \pm 2^\circ\text{C}$ for the experimental period. Untreated controls were similarly maintained. One set of treated flasks was ventilated with CO₂ free air with simultaneous gentle agitation of the water column by stirring from the top with a suspended magnetic stirrer. Radiolabelled DPX-MP062 was applied to the surface of both systems at a rate of 0.5 µg/g of water. The study was conducted in the dark over a 100-day incubation period.

2. Sampling

Volatile compounds were collected in ethylene glycol traps and CO₂ in 2 N NaOH traps. A single sample was collected at sampling intervals 0, 1, 7, 14, 28, 42, 56, 70, 84 and 102 days. For each radiolabelled form of the test substance, a single high level sample was taken after 7, 31, and 98 days of incubation.

3. Description of analytical procedures

Water and sediment layers were separated by centrifugation and decantation. Sediment samples were extracted three times with acetonitrile/water (4/1, v/v), and in some cases additionally twice with acetone/water (1/1, v/v). The water layers were analysed directly by LSC and reversed-phase HPLC. Portions of the pooled extracts were concentrated and analysed by LSC and reversed-phase HPLC. Transformation products were identified variously by co-chromatography with authentic standards using reversed phase HPLC, normal phase (chiral) HPLC, and reversed phase TLC, as well as UV diode array spectroscopy and LC/MS. Extracted sediment was separated into the humin, humic acid, and fulvic acid fractions by alkaline fractionation to determine the amount of residual radioactivity associated with each fraction by LSC and/or combustion of residues.

The relative proportions of the enantiomers of DPX-MP062 in the extracts of the sediment treated with [Ind-¹⁴C] in both systems were determined.

LOD was below 0.1%. LOQ was not indicated in the study report.

II. RESULTS AND DISCUSSION

A. MASS BALANCE

Apart from one sample with a very low recovery (and which was not analysed), the overall recovery from all samples ranged from 89.8 to 128.9% of the applied radiolabel (Table 8-193 and Table 8-194).

B. FINDINGS

1. Distribution between water and sediment

The applied radiolabel dissipated rapidly from the water phase of both systems. Total ^{14}C -residues in the water of Bury Pond systems declined from 65.3% of the applied radiolabel at zero time to 4.2% after 102 days for the indanone label, and 48.8% of the radiolabel at Day 0 to 6.6% after 102 days in the trifluoromethoxyphenyl label (Table 8-193). Total radioactivity in the water of Chatsworth systems declined from 75.2% at zero time to 2.7% after 102 days for the indanone label, and 35.9% of the applied radiolabel at Day 0 to 2.9% after 102 days for the trifluoromethoxyphenyl label (Table 8-194).

Table 8-193

Percent distribution of applied radioactivity and mass balance in the Bury Pond water/sediment systems treated with DPX-MP062

Day	% of Radiolabel					
	Volatile organics	Labelled CO_2	Water	Sediment extractable	Sediment NER	Total recovered
[Indanone-1-^{14}C]DPX-MP062						
0	ns ^a	ns	65.3	55.1	0.1	120.5
1	0.2	nd ^b	47.7	63.4	0.5	111.8
7	2.5	1.0	24.6	61.0	2.3	91.4
14	3.5	2.7	29.8	54.6	3.9	94.5
28	5.8	2.8	17.5	55.7	8.0	89.8
42	4.9	2.2	9.9	59.0	15.6	91.6
56	5.7	4.0	7.7	52.4	23.9	93.7
70	4.4	6.3	8.2	59.0	17.9	95.8
84	8.8	7.4	6.2	53.8	19.2	95.4
102	1.9	9.6	4.2	52.4	28.6	96.7
[Trifluoromethoxyphenyl(U)-^{14}C]DPX-MP062						
0	ns	ns	48.8	62.5	0.1	111.4
1	<0.1	nd	42.3	61.9	0.3	104.5
7	1.4	0.2	34.8	60.3	2.6	99.3
14	12.7	0.1	24.1	56.2	2.8	95.9
28	14.0	0.8	15.2	50.2	12.2	92.4
42	6.4	0.7	13.7	50.7	19.5	91.0
56	11.7	0.7	9.0	51.5	22.2	95.1
70	8.5	1.0	8.6	57.4	22.7	98.2
84	12.8	1.3	6.4	57.7	20.1	98.3
102	17.7	1.5	6.6	47.3	16.7	89.8

^a Not sampled

^b Not detected

Table 8-194: Percent distribution of applied radioactivity and mass balance in the Chatsworth water/sediment systems treated with DPX-MP062

Day	% of Radiolabel					
	Volatile organics	Labelled CO ₂	Water	Sediment extractable	Sediment NER	Total recovered
[Indanone-1-¹⁴C]DPX-MP062						
0	ns ^a	ns	75.7	52.5	0.7	128.9
1	<0.1	nd ^b	38.3	64.6	1.3	104.2
7	0.2	nd	4.5	48.6	7.6	60.9
14	1.6	4.7	11.9	55.4	17.5	91.1
28	1.9	13.4	2.3	44.9	29.4	91.9
42	1.3	7.9	5.1	37.1	42.2	93.6
56	3.0	13.2	2.5	32.0	50.4	101.1
70	1.1	20.6	2.6	30.4	39.9	94.6
84	2.0	22.8	2.3	26.3	42.1	95.5
102	1.5	25.8	2.7	22.6	43.7	96.3
[Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062						
0	ns	ns	35.9	71.6	0.8	108.3
1	0.2	nd	25.6	81.5	1.1	108.4
7	1.8	0.2	19.4	65.5	9.7	96.6
14	2.1	0.3	21.1	66.8	10.6	100.9
28	1.5	0.8	8.4	55.6	34.5	100.8
42	4.4	1.4	4.5	35.4	44.7	90.4
56	2.5	1.9	2.2	28.6	65.4	100.6
70	3.1	3.1	2.7	35.6	63.7	108.2
84	2.7	3.2	1.5	35.9	54.9	98.2
102	3.8	6.8	2.9	22.8	62.3	98.6

^a Not sampled

^b Not detected

2. Non-extractable residues (NER)

Non-extractable residues in the sediment increased from 0.1% of the applied radiolabel at zero time to 22.7% after 102 days in Bury Pond systems and from 0.8% at zero time to 53.0% after 102 days in Chatsworth systems (mean values, Table 8-193 and Table 8-194).

The Days 42 and 102 extracted solids were fractionated by alkaline hydrolysis to the fulvic acid, humic acid, and humin fractions (Table 8-195). Radioactivity was primarily associated with the humin fraction.

Table 8-195: Distribution of non-extractable components in soil organic matter

System	Day	Soil fraction	% of Applied radioactivity	
			[Indanone-1- ¹⁴ C] DPX-MP062	[Trifluoromethoxyphenyl(U)- ¹⁴ C] DPX-MP062
Bury Pond	42	Fulvic acid	2.4	3.6
		Humic acid	0.4	1.0
		Humin	12.8	14.9
	102	Fulvic acid	4.4	2.4
		Humic acid	0.8	0.4
		Humin	23.4	13.8
Chatsworth	42	Fulvic acid	5.5	4.0
		Humic acid	12.2	14.9
		Humin	24.4	25.8
	102	Fulvic acid	7.4	8.7
		Humic acid	13.6	23.0
		Humin	22.7	30.6

3. Major metabolites

The only major metabolite in water was IN-KT413 (maximum of 25.5% of applied radiolabel in Bury Pond systems and 18.3% in Chatsworth systems, Table 8-196 and Table 8-197). In Bury Pond sediment, the major degradation products were IN-KT413 (maximum of 16.6% of applied radiolabel), IN-MS775 (maximum of 14.7% of applied radiolabel), and IN-MP819 (maximum of 10.3% applied radiolabel) (Table 8-198). The other identified products in Bury Pond sediment were IN-JT333 (maximum of 6.0% of applied radiolabel) and IN-KG433 (maximum of 5.8% applied radiolabel). In Chatsworth sediment, the major degradation products were IN-KT413 (maximum of 13.1% of applied radiolabel) and IN-JT333 (maximum of 25.7% of applied radiolabel) (Table 8-199). The other identified products in Chatsworth sediment were IN-KG433 (maximum of 7.7% of applied radiolabel), IN-MS775 (maximum of 5.2% of applied radiolabel), and IN-ML438 (maximum of 3.6% of applied radiolabel) (Table 8-199). IN-MP819 was found only in Bury Pond sediment and IN-ML438 was found only in Chatsworth sediment. Of the other degradation products detected in the sediment, none individually accounted for more than 8% of the applied radiolabel. There were no observed radiolabel differences; *i.e.*, no metabolites were formed that contained either the [indanone-1-¹⁴C] radiolabel or the [trifluoromethoxyphenyl(U)-¹⁴C] radiolabel only.

In Bury Pond systems treated with [indanone-1-¹⁴C]DPX-MP062, volatile organic radioactivity accounted for a maximum of 8.8% of applied radioactivity and ¹⁴CO₂ accounted for a maximum of 9.6% of applied radioactivity (Table 8-193). In Bury Pond systems treated with [trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062, volatile organic radioactivity accounted for a maximum of 17.7% of applied radioactivity and ¹⁴CO₂ accounted for a maximum of 1.5% of applied radioactivity. In Chatsworth systems treated with [indanone-1-¹⁴C]DPX-MP062, volatile organic radioactivity accounted for a maximum of 3.0% of applied radioactivity and ¹⁴CO₂ accounted for a maximum of 25.8% of applied radioactivity (Table 8-194). In Chatsworth systems treated with [trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062, volatile organic radioactivity accounted for a maximum of 4.4% of applied radioactivity and ¹⁴CO₂ accounted for a maximum of 6.8% of applied radioactivity.

Table 8-196: Percent distribution of applied radioactivity in the water phase of the Bury Pond water/sediment system treated with ¹⁴C-DPX-MP062

Day	% of Radiolabel	
	DPX-MP062	IN-KT413
[Indanone-1-¹⁴C]DPX-MP062		
0	63.5	1.8
1	37.3	10.4
7	4.3	19.9
14	3.4	25.5
28	1.4	15.2
42	0.6	6.7
56	0.8	5.6
70	0.3	5.9
84	0.2	3.3
102	0.2	2.3
[Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062		
0	46.2	0.9
1	36.2	5.5
7	10.1	20.8
14	2.5	20.2
28	0.7	13.0
42	0.6	10.6
56	0.3	6.3
70	0.2	4.6
84	0.5	3.4
102	nd ^a	4.3

^a Not detected

Table 8-197: Percent distribution of applied radioactivity in the water phase of the Chatsworth water/sediment system treated with ¹⁴C-DPX-MP062

Day	% of Radiolabel	
	DPX-MP062	IN-KT413
[Indanone-1-¹⁴C]DPX-MP062		
0	75.2	0.5
1	32.0	6.3
7	na ^a	na
14	0.2	9.2
28	0.3	0.6
42	0.2	4.5
56	0.1	0.7
70	0.6	1.5
84	na	1.0
102	0.1	1.1
[Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062		
0	35.1	0.6
1	22.5	2.7
7	0.9	17.4
14	1.1	18.3
28	0.3	4.8
42	0.3	3.0
56	0.1	0.9
70	0.1	2.3
84	nd ^b	0.3
102	0.1	1.2

^a Not analysed

^b Not detected

Table 8-198: Percent distribution of applied radioactivity in the sediment phase of the Bury Pond water/sediment system treated with ¹⁴C-DPX-MP062

Day	% of Radiolabel					
	DPX-MP062	IN-KT413	IN-KG433	IN-MP819	IN-JT333	IN-MS775
[Indanone-1-¹⁴C]DPX-MP062						
0	55.0	nd ^a	nd	nd	nd	nd
1	58.6	0.4	nd	nd	0.3	nd
7	52.8	0.1	1.5	nd	0.8	nd
14	30.3	16.6	nd	2.9	2.4	1.1
28	29.4	7.5	5.8	2.1	3.5	1.3
42	28.9	nd	5.7	9.1	4.4	6.2
56	10.0	5.9	1.4	6.2	2.3	11.3
70	21.5	0.9	5.1	8.0	6.0	6.1
84	12.4	2.2	3.2	10.3	3.6	11.5
102	7.9	4.7	1.4	6.6	2.0	10.0
[Trifluoromethoxyphenyl(U)-¹⁴C]DPX-MP062						
0	62.3	nd	nd	nd	0.2	nd
1	60.5	0.1	nd	nd	0.3	nd
7	27.9	12.0	0.2	nd	2.8	2.6
14	32.8	10.7	0.7	nd	5.0	2.8
28	25.3	6.6	4.7	3.7	3.2	2.1
42	15.6	8.1	5.5	5.5	2.9	3.8
56	15.5	11.5	1.2	0.7	2.3	3.0
70	11.9	6.5	1.8	10.2	3.3	14.7
84	21.5	7.3	2.1	8.9	2.7	12.8
102	13.7	10.0	1.6	7.9	2.0	2.8

^a Not detected

Table 8-199: Percent distribution of applied radioactivity in the sediment phase of the Chatsworth water/sediment system treated with ^{14}C -DPX-MP062

Day	% of Radiolabel					
	DPX-MP062	IN-KT413	IN-KG433	IN-ML438	IN-JT333	IN-MS775
[Indanone-1-^{14}C]DPX-MP062						
0	49.9	nd ^a	0.6	nd	1.7	nd
1	51.7	0.8	0.5	0.6	10.6	nd
7	na ^b	na	na	na	2	na
14	7.4	8.9	0.8	1.2	25.7	nd
28	7.7	1.2	1.7	3.6	21.1	2.0
42	8.2	2.1	1.9	3.1	13.1	2.0
56	3.6	4.8	1.0	2.0	9.5	1.6
70	4.8	1.3	1.5	1.9	8.7	1.8
84	4.2	1.4	2.1	2.1	6.3	2.5
102	3.8	2.3	1.1	0.8	3.9	0.5
[Trifluoromethoxyphenyl(U)-^{14}C]DPX-MP062						
0	70.5	nd	nd	nd	0.4	nd
1	77.8	0.3	0.1	0.2	2.4	nd
7	20.3	6.6	1.1	1.0	21.4	0.3
14	5.5	13.1	7.7	1.0	16.0	0.5
28	14.1	5.7	4.4	nd	17.7	3.4
42	6.7	2.9	1.5	3.0	10.8	3.4
56	4.2	3.8	0.4	2.4	5.9	5.2
70	2.8	2.9	1.9	1.6	12.7	0.4
84	3.2	4.8	2.4	3.0	6.4	2.2
102	3.1	2.2	1.5	nd	3.1	0.8

^a Not detected^b Not analysed

4. Degradation pathway

The degradation pathway of DPX-MP062 in water was the same in both systems and IN-KT413 was the only major metabolite in water. IN-KT413 was formed from DPX-MP062 *via* ester hydrolysis. In the sediment, the route of degradation of DPX-MP062 was dependent on the oxygen content (redox potential) of the sediment. The Bury Pond sediment remained anaerobic throughout the incubation while Chatsworth sediment was more aerobic.

In the anaerobic sediment (Bury Pond), DPX-MP062 degraded *via* two major pathways. IN-JT333 was formed *via* demethylation followed by N-decarboxylation (minor metabolite under anaerobic conditions), and IN-JT333 was then degraded *via* ester hydrolysis and decarboxylation at the chiral centre to form IN-MS775, a major metabolite. The second pathway involved ester hydrolysis of DPX-MP062 to form IN-KT413, a major metabolite in sediment. IN-KT413 underwent rearrangement to IN-MP819, which was also a major metabolite. IN-KG433 was a minor metabolite formed *via* oxadiazine ring cleavage of DPX-MP062.

In the aerobic sediment (Chatsworth), DPX-MP062 degraded *via* two major pathways. IN-JT333 was formed *via* demethylation followed by N-decarboxylation to become a major metabolite in aerobic sediment. IN-MS775 was a minor metabolite under aerobic conditions. The second pathway involved ester hydrolysis of DPX-MP062 to form IN-KT413, a major metabolite in sediment. IN-KG433 was a minor metabolite formed *via* oxadiazine ring cleavage of DPX-MP062. The conversion of IN-JT333 to IN-MS775 occurred to a greater extent in the anaerobic sediment. Formation of IN-MP819 occurred only in the anaerobic sediment. IN-ML438 was also detected only in the aerobic sediment as a minor metabolite. IN-ML438 could be formed *via* rearrangement of IN-JT333, IN-KT413, and IN-KG433. Both enantiomers (DPX-KN128 and IN-KN127) degraded at the same rate in either sediment, regardless of redox potential.

III. CONCLUSION

The rate and route of degradation of DPX-MP062 were studied in two water/sediment systems. All principal degradation products contained both [indanone-1-¹⁴C] and [trifluoromethoxyphenyl(U)-¹⁴C] radiolabels. The only major product (>10% of applied radiolabel) in the water was IN-KT413. The major products in sediment were IN-JT333, IN-KT413, IN-MP819, and IN-MS775. Other identified products were IN-KG433 and IN-ML438. IN-MP819 was formed only in Bury Pond sediment and IN-ML438 was formed only in Chatsworth sediment. Levels of some of the other products also differed between sediment type. Such differences were most likely attributable to the oxidation state of the sediment: Bury Pond sediment remained anaerobic throughout the incubation while Chatsworth sediment was more aerobic. Non-extractable residues (mostly associated with the humin fraction) and ¹⁴CO₂ also exceeded 10% of applied radiolabel.

RMS comments (2016)

This study was conducted under guidelines SETAC 1995 and U.S. EPA 162-4 (1982). A review of this study indicates that it partially meets the current guideline (OECD 308); deviations include an unidentified metabolite at >5% AR. However, together with new study of Allan (2012) summarized below, both studies adequately completes the understanding of water/sediment study. This study is therefore still relied upon.

As raised during first review of this study, the initial biomass measurements in sediment by fumigation/extraction method were considered unreliable by the lab performing the analyses. This was then interpreted as a failure in the biomass analysis, rather than an indication of no biomass in the sediments. On the more, based on data of biomass measurements via plate counting of colonies at day 55 and at the end of the study, it can be seen that there was measurable biomass in the sediment and it remained essentially constant, at study termination.

This study was conducted with DPX MP062 (enriched mixture, 75:25 S:R), and RMS has concern about the stability of the isomeric ratio of indoxacarb and of IN-JT333. In both system, the ratio of R and S-enantiomer of indoxacarb in sediment was variable (see data below), and it was explained in the study that these differences may be due to experimental variability since only one replicate was available at each sampling interval. The low level of total indoxacarb radioactivity in the Chatsworth sediment (less than 10% at third sampling point) might also explain the variability of measurement of individual enantiomer.

However, the variability of the ratio does not show a trend that would reveal a preferential degradation of one of the isomer.

Table 8-200: Proportion of enantiomers of DPX-MP062 as percentage of applied radioactivity, in Bury Pond and Chatsworth sediment extract from samples treated with [Indanon-1-14C]DPX-MP062

	SAMPLING TIMES (DAYS)									
	0	1	7	14	28	42	56	70	84	102
BURY POND										
R-enantiomer	13.9	14.5	9.0	4.5	6.5	6.6	2.1	4.2	2.5	1.6
S-enantiomer	41.1	44.1	43.8	25.8	22.9	22.3	7.9	17.3	9.9	6.3
Total radioactivity	55.0	58.6	52.8	30.3	29.4	28.9	10.0	21.5	12.4	7.9
Enantiomeric ratio (R:S)	1:3.0	1:3.0	1:4.9	1:5.7	1:3.5	1:3.4	1:3.8	1:4.1	1:4.0	1:3.9
CHATSWORTH										
R-enantiomer	12.8	6.1	a	1.7	1.1	1.3	0.7	1.1	0.7	0.8
S-enantiomer	37.1	45.6	a	5.7	6.6	6.9	2.9	3.7	3.5	3.0
Total radioactivity	49.9	51.7	a	7.4	7.7	8.2	3.6	4.8	4.2	3.8
Enantiomeric ratio (R:S)	1:2.9	1:7.5	a	1:3.4	1:6.0	1:5.3	1:4.1	1:3.4	1:5.0	1:3.8

a Not analysed (anomalous sample)

The following study is submitted to the EU for the first time for the purpose of renewal

Data point:	KCA 7.2.2.3/01
Author(s)	Allan, J. (2014);
Title:	Aerobic aquatic metabolism of [14C]DPX-KN128 (indoxacarb) in two water-sediment systems
Organisation:	ABC Laboratories, Inc. (Missouri), Columbia, Missouri, USA
Document No:	DuPont-39061
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Guidelines:	OECD Guideline 308 (2002), OPPTS 835.4300 (2008),
Deviations :	No
GLP:	Yes
Previous evaluation:	No
Acceptability:	Yes

I. MATERIALS AND METHODS

A. MATERIALS

- Radiolabelled test material:** ¹⁴C indoxacarb (DPX-KN128) technical
 Lot/Batch #: [Indanone-1-¹⁴C]indoxacarb: 1643850
 abbreviated as [I-¹⁴C]indoxacarb
 [Trifluoromethoxyphenyl-¹⁴C (U)]indoxacarb: 1643851A
 abbreviated as [TFMP-¹⁴C]indoxacarb samples
 Radiochemical purity: [i-¹⁴C]indoxacarb: 98.8%
 [TFMP-¹⁴C (U)]indoxacarb: 99.5%
 Specific activity: [I-¹⁴C]indoxacarb: 49.50 µCi/mg
 [TFMP-¹⁴C (U)]indoxacarb: 46.3 µCi/mg
 Stability of test compound: Stable during study

- Water/Sediment**

Two freshly collected water/sediment systems were used, one from a river (Table 8-201, System 1), and the other from a pond (Table 8-201, System 2). The bulk water was observed to be free of debris greater than 2-mm and was therefore used unfiltered. The sediment was sieved through a 2-mm screen.

Table 8-201: Physiochemical parameters of the water/sediment systems

Sediment parameter	System 1 (from river)		System 2 (from pond)	
Geographic location	Grand Forks, North Dakota, USA		Tift County, Georgia, USA	
Sediment name	Goose River		Chula	
Texture class (USDA)	Clay Loam		Sand	
% Sand (2000–50 µm)	27%		98%	
% Silt (<50–2 µm)	38%		2%	
% Clay (<2 µm)	35%		0%	
pH (1:1 soil:water ratio)	7.6		6.7	
Organic matter (Walkley Black)	6.9%		1.3%	
Organic carbon ^a	4.0		0.75	
Soil biomass Initial (µg C/g dry soil)	452.9		356.5	
Final (µg C/g dry soil)	512.1		383.6	
Cation exchange capacity (CEC)	23.7 meq/100g		3.1 meq/100g	
Moisture at 0.33 bar	57.3%		3.7%	
Moisture at 15 bar	27.6%		2.9%	
Bulk density (disturbed)	0.86 g/cc		1.28 g/cc	
Redox potential (Eh-mV)	Initial	Final	Initial	Final
	-137	-114	-73	-155
Water parameter	System 1		System 2	
Temperature (°C)	20 ± 2°C		20 ± 2°C	
pH	8.6		7.4	
Hardness (CaCO ₃)	804		100	
Electrical conductivity (mmhos/cm)	1.74		0.25	
Oxygen concentration (mg/L)	8.58		7.04	
Organic carbon Initial	14.4 ppm		8.2 ppm	
Final	18.4 ppm		8.4 ppm	
Redox potential (Eh-mV)	Initial	Final	Initial	Final
	297	323	245	398

^a % organic carbon = % organic matter/1.72

B. STUDY DESIGN

1. Experimental conditions

The study was performed in an open gas flow system using glass vessels containing 335 mL of the corresponding water. Flasks were filled to a height of about 10 cm for water and a depth of ~2.5 cm for the sediment layer, which were then allowed to equilibrate for 12 days before application of the test material.

The test systems were maintained at 20 ± 2°C for the experimental period. Untreated controls were similarly maintained, but were equipped with a dedicated redox probe permanently positioned in the sediment via a custom side arm. Radiolabelled indoxacarb was applied just beneath the water surface of both systems at a rate of 0.20 mg a.s./L corresponding to a field rate of 400 g a.s./ha based on a surface water depth of 20 cm. The study was conducted in the dark over a 100-day incubation period.

2. Sampling

Volatile compounds were collected in Supelco ORBO™ 32 tubes and CO₂ in two 1 N KOH traps. Duplicate samples were collected at sampling intervals 0, 1, 3, 7, 14, 28, 52, 74, and 100 days.

3. Description of analytical procedures

The water and sediment were separated by decanting. Any water remaining in the sediment was thereafter treated as sediment. The water phase was analysed directly without concentration by LSC and reverse phase HPLC (Thermo Scientific, Polar Acclaim II C18 (250 mm × 4.6 mm × 5 µm id) and eluted with a gradient of 0.01M ammonium acetate (aq) and acetonitrile.

After removal of the water phase, the sediment was exhaustively extracted at room temperature three times with acetonitrile reagent: water (4:1, v:v). The samples were shaken, centrifuged, and the supernatants combined. A

sub-sample of the combined sediment extract was passed through a solid phase extraction column (C-18) to remove interferences, concentrated, and analyzed by HPLC.

Sediment samples from Days 28, 52, and 100 were submitted to fractionation into humin, humic and fulvic acids. Post-extracted sediment samples from Day 100 were further extracted using a harsh method (Soxhlet).

The limit of detection (LOD) for indoxacarb in the water phase and sediment extracts was 0.052% AR. For HPLC analyses, the limit of detection (LOD) for indoxacarb in the water phase and concentrated sediment extracts was 0.479% and 0.034% AR, respectively. The limit of quantification (LOQ) for indoxacarb in the water phase and sediment extracts was 0.199% AR. For HPLC analyses, the limit of quantification (LOQ) for indoxacarb in the water phase and concentrated sediment extracts was 1.44% and 0.101% AR, respectively.

II. RESULTS AND DISCUSSION

A. MASS BALANCE

The mean recoveries of radioactivity for the systems were 107.3% (92.0–115.6%) for the Goose River (clay loam) system and 106.1% (96.9–116.7%) for the Chula (sand) system. A summary of the recoveries and the distribution of the residues expressed as applied radioactivity and as mg/kg (ppm) at each sampling time interval is provided in Table 8-202 to Table 8-205.

B. FINDINGS

The level of radioactivity in Goose River (clay loam) water decreased from 101.2% of the applied radioactivity at Day 0 to 25.9% at Day 100, and in Chula (sand) water it decreased from 105.3 to 22.5% over the same period.

In Goose River (clay loam) sediment, the level of radioactivity increased from 1.2% of the applied radioactivity at Day 0 to 67.9% of the applied radioactivity at Day 100, and in Chula (sand) sediment from 1.0% of the applied radioactivity to 67.7% of the applied radioactivity in the same period. Volatile substances (CO₂ or organic volatile compounds) never exceeded 7.0% of the applied radioactivity in any test system. Mineralisation occurs to a greater extent from the [I-¹⁴C]indoxacarb samples as compared to [TFMP-¹⁴C]indoxacarb samples.

Overall, in the Goose River (clay loam) system (water plus sediment) the amount of indoxacarb decreased from 92.0 to 1.5% of applied radioactivity after 100 days incubation, and in the total Chula (sand) system decreased from 97.1 to 1.8% after 100 days incubation.

Once in sediment, residues remained tightly bound. Further harsh extraction (Soxhlet) did not extract any additional parent compound.

There was no significant difference in the distribution pattern for metabolites between the two systems with the seven metabolites present in each in similar proportions. In the total system, IN-KT413 was detected in both Goose River (clay loam) and Chula (sand) systems comprising 83.0 and 75.2% of the applied radioactivity at Day 7 and 14, while IN-MP819 (metabolite 2) comprised 9.3 and 21.3% of applied radioactivity at Day 52 and 74, IN-U8E24 (metabolite 3) comprised 24.3 and 13.0% of applied radioactivity at Day 28 and 52, IN-KN125 (metabolite 4) comprised of 2.3 and 4.4% of applied radioactivity at Day 7 and 14, IN-U8F52 (metabolite 5) comprised of 4.5 and 4.6% of applied radioactivity at Day 28 and 52, IN-UYG24 (metabolite 6) comprised of 3.2 and 31.6% of applied radioactivity at Day 28 and 52, and IN-MS775 (metabolite 7) comprised of 3.8 and 6.0% of applied radioactivity at Day 74 and 100, respectively. The major degradation products observed were IN-KT413, IN-U8E24, IN-MP819, IN-MS775, IN-UYG24, and IN-MK638; and the minor metabolites were IN-KN125 and IN-U8F52. A summary of the distribution of the residues expressed as % AR and mg/kg at each sampling time interval is provided in Table 8-202 to Table 8-205.

In aerobic aquatic sediment systems, the degradation pathway of indoxacarb was the same in both systems. Indoxacarb underwent ester hydrolysis to form IN-KT413 as the most significant metabolite in water, and indoxacarb was also transformed to IN-KN125 (S-enantiomer of IN-JT333) via demethylation N-decarboxylation as minor metabolite in sediment. IN-KT413 further degraded to IN-U8E24 via demethylation N-decarboxylation, and IN-U8E24 then degraded to IN-MS775, IN-UYG24, and IN-U8F52 via decarboxylation, bridge cleavage, and indanone ring opening, respectively. IN-KT413 also underwent decarboxylation and rearrangement of the N-methylester group to form IN-MP819, and IN-MP819 further degraded to IN-MK638 through oxadiazine ring opening and bridge cleavage. Both newly identified metabolites

(IN-U8E24, and IN-UYG24) were not stable, especially the transitory metabolite IN-UYG24 that spiked from 5.3 to 31.6% AR and quickly dropped back to 2.1% AR within three short consecutive sampling intervals in water phase from only one system. Formation of non-extractable (bound) residues (maximum of 66.1% AR) was also a significant degradation process.

The degradation rate was re-evaluated in DuPont-34821 EU according to FOCUS (2006, 2011) guidelines. (see point B.8.1.1.2.1.3.)

Table 8-202: Biotransformation of [I-¹⁴C]indoxacarb, expressed as percentage of applied radioactivity, in the Goose River (clay loam) system

Compound	Matrix	Sampling times (days)								
		0	1	3	7	14	28	52	74	100
Indoxacarb (DPX-KN128)	Water	83.7	30.4	11.8	2.4	0.0	0.0	0.0	0.0	0.0
	Sediment	8.3	31.3	21.1	14.3	7.6	1.4	2.2	1.3	1.5
	Total	92.0	61.6	32.9	16.7	7.6	1.4	2.2	1.3	1.5
IN-KT413	Water	0.0	40.3	57.8	66.1	47.9	27.3	15.2	6.5	1.7
	Sediment	0.3	2.4	6.0	9.8	9.3	6.4	4.1	2.2	2.1
	Total	0.3	42.7	63.8	75.9	57.3	33.7	19.3	8.8	3.8
IN-MP819	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.4	0.0	0.0
	Sediment	0.0	0.4	0.8	2.0	2.7	3.0	8.2	8.2	9.0
	Total	0.0	0.4	0.8	2.0	2.7	3.0	8.7	8.2	9.0
IN-U8E24	Water	0.0	0.0	0.0	0.0	4.4	8.2	2.6	1.8	0.7
	Sediment	0.0	0.0	1.1	5.7	7.7	12.4	12.8	8.8	12.2
	Total	0.0	0.0	1.1	5.7	12.2	20.7	15.4	10.6	12.9
IN-KN125	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.4	0.8	2.3	1.5	0.9	0.9	0.8	0.6
	Total	0.0	0.4	0.8	2.3	1.5	0.9	0.9	0.8	0.6
IN-U8F52	Water	0.0	0.0	0.0	0.0	0.0	1.8	0.0	0.0	0.0
	Sediment	0.0	0.0	0.2	0.8	2.0	2.7	2.1	3.7	2.0
	Total	0.0	0.0	0.2	0.8	2.0	4.5	2.1	3.7	2.0
IN-UYG24	Water	0.0	0.0	0.0	0.0	1.7	3.2	1.0	0.3	0.0
	Sediment	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Total	0.0	0.0	0.0	0.0	1.7	3.2	1.0	0.3	0.0
IN-MS775	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.0	0.0	0.0	0.0	1.5	2.8	3.5	2.9
	Total	0.0	0.0	0.0	0.0	0.0	1.5	2.8	3.5	2.9
Unidentified radioactivity ^a	Water	2.7	2.3	1.0	2.3	0.0	1.7	4.5	3.4	4.0
	Sediment	0.0	0.0	0.0	0.5	1.2	1.8	3.2	6.7	6.3
	Total	2.7	2.3	1.0	2.8	1.2	3.5	7.7	10.1	10.3
Total extractable residues ^b	Water	86.4	73.0	70.6	70.8	54.1	42.1	23.7	12.0	6.4
	Sediment	8.5	34.5	30.0	35.3	32.1	30.1	36.2	35.2	36.6
	Total	95.0	107.4	100.7	106.1	86.2	72.3	60.0	47.2	43.0
CO₂		N/A	0.0	0.0	0.2	0.5	2.0	4.5	6.1	7.0
Non-extractable residue		0.3	1.4	2.9	7.4	17.9	31.5	45.1	54.0	60.5
Total mass balance		95.3	108.8	103.6	113.7	104.6	105.8	109.5	107.3	110.5

^a Unidentified radioactivity consisted of multiple peaks, none of which were ≥5% AR.

^b Total values may differ slightly from the sum of the individual values due to rounding.

Table 8-203: Biotransformation of [trifluoromethoxyphenyl-¹⁴C(U)]indoxacarb, expressed as percentage of applied radioactivity, in the Goose River (clay loam) system

Compound	Matrix	Sampling times (days)								
		0	1	3	7	14	28	52	74	100
Indoxacarb (DPX-KN128)	Water	72.9	48.6	20.7	8.0	0.0	0.0	0.0	0.0	0.0
	Sediment	16.9	31.3	18.8	13.2	3.7	1.2	1.3	0.9	1.3
	Total	89.7	79.9	39.4	21.3	3.7	1.2	1.3	0.9	1.3
IN-KT413	Water	0.0	23.5	54.4	74.7	62.1	35.9	17.0	7.2	1.4
	Sediment	0.3	0.9	4.3	8.3	10.7	8.0	4.3	4.5	1.5
	Total	0.3	24.5	58.7	83.0	72.8	43.9	21.3	11.7	2.9
IN-MP819	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.2	0.5	1.5	2.7	4.5	9.3	8.9	7.8
	Total	0.0	0.2	0.5	1.5	2.7	4.5	9.3	8.9	7.8
IN-U8E24	Water	0.0	0.0	0.0	0.0	4.6	8.3	4.5	3.1	1.7
	Sediment	0.0	0.0	0.6	2.9	9.8	16.0	15.7	9.3	13.9
	Total	0.0	0.0	0.6	2.9	14.4	24.3	20.2	12.3	15.5
IN-MK638	Water	0.0	0.0	0.0	0.0	0.0	0.0	1.5	0.8	0.0
	Sediment	0.0	0.0	0.0	0.8	1.8	1.2	1.7	0.0	1.9
	Total	0.0	0.0	0.0	0.8	1.8	1.2	3.2	0.8	1.9
IN-KN125	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.0	0.7	0.9	0.8	0.7	0.5	0.5	0.6
	Total	0.0	0.0	0.7	0.9	0.8	0.7	0.5	0.5	0.6
IN-MS775	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.0	0.0	0.0	0.0	1.8	3.3	3.8	3.3
	Total	0.0	0.0	0.0	0.0	0.0	1.8	3.3	3.8	3.3
Unidentified radioactivity ^a	Water	1.7	0.6	1.4	1.4	1.9	2.1	3.3	4.7	5.5
	Sediment	0.0	0.0	0.0	0.4	0.7	1.3	5.2	8.8	6.9
	Total	1.7	0.6	1.4	1.8	2.6	3.4	8.5	13.5	12.4
Total Extractable residues ^b	Water	74.6	72.7	76.5	84.1	68.6	46.3	26.3	15.8	8.6
	Sediment	17.2	32.5	24.8	28.1	30.1	35.0	41.3	36.8	37.2
	Total	91.8	105.2	101.4	112.1	98.7	81.2	67.6	52.5	45.7
CO₂		N/A	0.0	0.0	0.0	0.2	0.5	1.0	1.3	1.8
Non-extractable residue		0.2	0.3	3.4	3.5	10.6	26.6	45.2	55.0	66.1
Total mass balance		92.0	105.5	104.8	115.6	109.4	108.4	113.9	108.9	113.7

^a Unidentified radioactivity consisted of multiple peaks, none of which was ≥5% AR.

^b Total values may differ slightly from the sum of the individual values due to rounding.

Table 8-204: Biotransformation of [indanone-1-¹⁴C]indoxacarb, expressed as percentage of applied radioactivity, in the Chula (sand) system

Compound	Matrix	Sampling times (days)								
		0	1	3	7	14	28	52	74	100
Indoxacarb (DPX-KN128)	Water	89.6	56.8	24.4	9.5	0.6	0.0	0.0	0.0	0.0
	Sediment	5.3	24.8	31.0	29.5	11.8	3.4	1.6	1.2	1.0
	Total	94.9	81.5	55.4	38.9	12.4	3.4	1.6	1.2	1.0
IN-KT413	Water	0.0	15.5	38.5	60.8	69.1	58.0	22.4	1.7	2.0
	Sediment	0.0	0.4	2.4	5.2	6.1	9.1	5.7	1.9	1.0
	Total	0.0	15.9	40.9	66.0	75.2	67.1	28.0	3.7	3.0
IN-MP819	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.2	0.6	2.5	4.9	6.4	8.3	15.4	11.9
	Total	0.0	0.2	0.6	2.5	4.9	6.4	8.3	15.4	11.9
IN-U8E24	Water	0.0	0.0	0.0	0.0	3.7	7.0	10.5	2.5	0.3
	Sediment	0.0	0.0	0.0	0.9	0.4	4.5	2.5	1.8	2.3
	Total	0.0	0.0	0.0	0.9	4.1	11.5	13.0	4.3	2.6
IN-KN125	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.2	0.8	1.9	2.5	1.0	0.5	0.4	0.4
	Total	0.0	0.2	0.8	1.9	2.5	1.0	0.5	0.4	0.4
IN-U8F52	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.0	0.0	0.3	1.7	1.8	4.6	4.3	4.1
	Total	0.0	0.0	0.0	0.3	1.7	1.8	4.6	4.3	4.1
IN-UYG24	Water	0.0	0.0	0.0	0.0	2.1	5.3	31.6	2.1	1.8
	Sediment	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Total	0.0	0.0	0.0	0.0	2.1	5.3	31.6	2.1	1.8
IN-MS775	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.0	0.0	0.0	0.5	1.1	3.6	4.4	4.2
	Total	0.0	0.0	0.0	0.0	0.5	1.1	3.6	4.4	4.2
Unidentified radioactivity ^a	Water	1.8	2.7	1.6	0.0	0.0	0.0	0.0	32.5	34.6
	Sediment	0.2	0.0	0.0	0.0	1.0	1.4	3.1	9.4	8.4
	Total	2.0	2.7	1.6	0.0	1.0	1.4	3.1	41.9	43.0
Total extractable residues ^b	Water	91.4	75.0	64.5	70.3	75.5	70.3	64.4	38.8	38.7
	Sediment	5.5	25.5	34.8	40.3	28.9	28.6	29.9	38.8	33.3
	Total	96.9	100.5	99.3	110.6	104.3	98.9	94.3	77.6	72.0
CO₂		N/A	0.0	0.0	0.1	0.3	1.0	2.7	4.5	6.2
Non-extractable residue		0.0	0.5	1.4	1.9	2.7	6.2	11.8	25.3	35.3
Total mass balance		96.9	100.9	100.7	112.6	107.3	106.1	108.8	107.3	113.4

^a Unidentified radioactivity consisted of multiple peaks, none of which was ≥5% AR.

^b Total values may differ slightly from the sum of the individual values due to rounding.

Table 8-205: Biotransformation of [trifluoromethoxyphenyl-¹⁴C(U)]indoxacarb, expressed as percentage of applied radioactivity, in the Chula (sand) system

Compound	Matrix	Sampling times (days)								
		0	1	3	7	14	28	52	74	100
Indoxacarb (DPX-KN128)	Water	89.3	40.9	28.9	8.9	0.0	0.0	0.0	0.0	0.0
	Sediment	7.9	43.5	29.3	40.1	14.6	4.4	1.7	1.4	1.8
	Total	97.1	84.4	58.2	49.0	14.6	4.4	1.7	1.4	1.8
IN-KT413	Water	0.0	22.7	41.2	54.3	66.1	58.8	36.5	1.4	0.7
	Sediment	0.0	0.3	2.3	5.3	6.1	8.2	6.6	1.7	0.7
	Total	0.0	23.0	43.5	59.7	72.2	67.0	43.1	3.1	1.4
IN-MP819	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.4	0.6	2.8	4.2	7.6	12.1	21.3	17.9
	Total	0.0	0.4	0.6	2.8	4.2	7.6	12.1	21.3	17.9
IN-U8E24	Water	0.0	0.0	0.0	0.0	3.4	6.9	1.2	0.6	0.2
	Sediment	0.0	0.0	0.0	0.7	2.9	4.2	5.2	1.3	1.6
	Total	0.0	0.0	0.0	0.7	6.3	11.1	6.5	1.9	1.8
IN-MK638	Water	0.0	0.0	0.0	0.0	0.0	0.0	2.0	1.9	4.0
	Sediment	0.0	0.0	0.0	0.0	2.0	1.3	1.6	4.0	5.0
	Total	0.0	0.0	0.0	0.0	2.0	1.3	3.6	5.9	9.0
IN-KN125	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.4	1.1	2.4	4.4	1.2	0.6	0.4	0.0
	Total	0.0	0.4	1.1	2.4	4.4	1.2	0.6	0.4	0.0
IN-MS775	Water	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Sediment	0.0	0.0	0.0	0.0	1.2	1.7	4.0	5.7	6.0
	Total	0.0	0.0	0.0	0.0	1.2	1.7	4.0	5.7	6.0
Unidentified radioactivity ^a	Water	3.5	1.4	0.0	0.0	1.6	3.5	14.9	25.7	18.3
	Sediment	0.3	0.0	0.0	0.0	2.5	2.4	2.8	9.9	8.3
	Total	3.8	1.4	0.0	0.0	4.1	5.9	17.7	35.6	26.6
Total extractable residues ^b	Water	92.7	64.9	70.0	63.2	71.0	69.2	54.6	29.6	23.2
	Sediment	8.1	44.5	33.3	51.3	37.9	31.0	34.6	45.6	41.2
	Total	100.9	109.5	103.3	114.5	109.0	100.2	89.2	75.2	64.4
CO ₂		N/A	0.0	0.0	0.0	0.1	0.2	0.3	0.7	0.9
Non-extractable residue		0.1	1.0	1.2	2.2	3.1	6.1	15.2	25.4	32.3
Total mass balance		101.0	110.4	104.5	116.7	112.1	106.5	104.6	101.2	97.6

^a Unidentified radioactivity consisted of multiple peaks, none of which was ≥5% AR.

^b Total values may differ slightly from the sum of the individual values due to rounding.

III. CONCLUSION

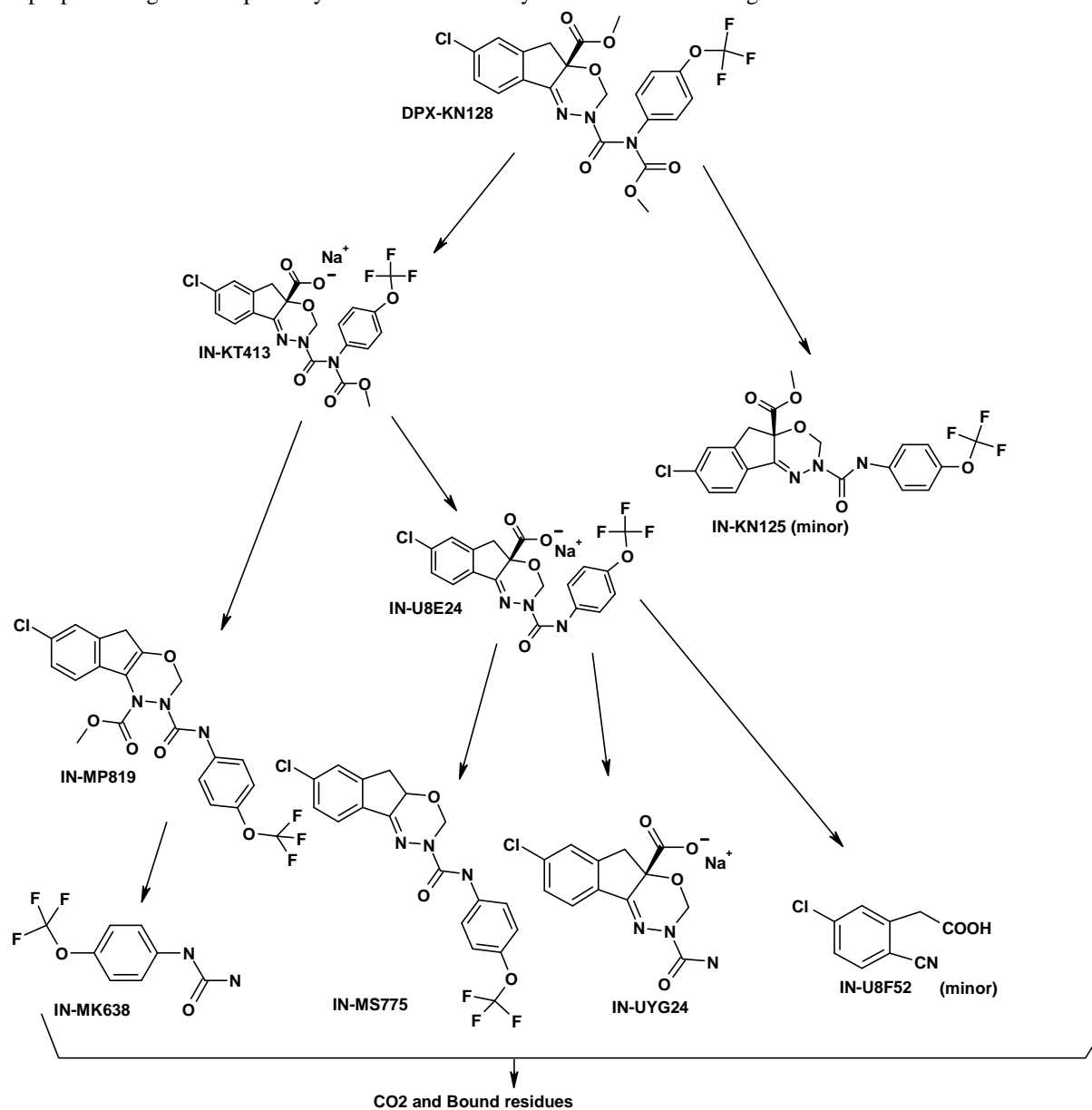
The study provided evidence that indoxacarb degrades rapidly in water bodies through degradation to polar metabolites and through binding to sediment. It can be anticipated that in viable streams degradation will be most rapid at recommended use rates of indoxacarb. It is unlikely to result in any significant environmental loading of the aquatic environment.

RMS (2016)

The study is acceptable

Both water/sediment systems contain water at pH ranging between 7.4 and 8.6. Considering that indoxacarb hydrolysis is pH-dependant (no hydrolysis in acidic water), it could be expected that degradation in water/sediment systems containing more acidic water would be slower. Ideally, a more acidic water/sediment system could have been tested, and would have provided a more complete overview of behavior of indoxacarb under natural conditions.

A proposed degradation pathway in water-sediment systems is outlined in Figure 10 below.



(Note: IN-KN125 is S- enantiomer of IN-JT333)

Figure 10: Proposed degradation pathway of indoxacarb (DPX-KN128) in water/sediment systems

DEGRADATION RATE IN WATER/SEDIMENT STUDIES:

The following study is submitted to the EU for the first time for the purpose of renewal

Data point:	CA 7.1.2/01
Author(s)	Partsch, S., Khanjio, I., Price, K., Ball, M. (2015)
Title:	Degradation of indoxacarb and its metabolites IN JT333 (IN-KN125), IN-JU873, IN-KB687, IN-KG433, IN-KT413, IN-MK638, IN-MK643, IN-ML438, IN MP819, IN-MS775, IN-UYG24, IN-U8E24, and IN-U8F52 in soil and water/sediment systems - kinetic calculations following Focus kinetics
Organisation:	Dr. Knoell Consult GmbH, Mannheim, Germany
Document No:	DuPont-34821 EU
Guidelines:	Focus, 2006, 2011
Deviations :	None
GLP:	N.a.
Previous evaluation:	No, study submitted for AIR 3 renewal
Acceptability:	Yes

Two aquatic degradation studies have been conducted to investigate the rate of degradation of indoxacarb (DPX-KN128) and its metabolites (DuPont-39061 and DuPont-8417 see Points CA 7.2.2.3 and CA 7.2.2.4). Since the studies do not contain a kinetic evaluation of the data according to recent FOCUS recommendations, a re-evaluation of the test results was conducted in DuPont-34821 EU.

MATERIAL AND METHOD

Data

The degradation of indoxacarb and its metabolites were evaluated in two studies four water-sediment systems - Bury Pond and Chatsworth system, and Chula and Goose River - under laboratory conditions at 20°C (Shaw, 2002; Allan, 2014b).

Table 8-206: Summary of reference and origin of the study data retained for kinetic fitting

Study reference	Substance applied	System	Susbtances observed	Origin
Shaw, 2002	Indoxacarb (DPX-MP062)	Bury Pond	Indaxacarb IN-JT333 IN-KT413 IN-KG433 IN-MP819 IN-MS775	DAR AD3 2005
		Chatsworth	Indoxacarb IN-JT333 IN-KT413 IN-KG4333 IN-ML438 IN-MS775	
Allan, 2014b	Indoxacarb (DPX-KN128)	Chula	Indaxacarb, IN-JT333(IN-KN125) IN-KT413 IN-MK638 (TFMP label only)	New study submitted for AIR III
		Goose river	IN-MP819 IN-MS775 IN-UYG24 (Indanon label only) IN-U8E24, IN-U8F52 (Indanon label only)	

Data handling

The studies were conducted with two label position (Indanon and TFMP). The indanone and TFMP labels were treated as replicates for parent kinetics and treated separately for metabolite kinetic analysis.

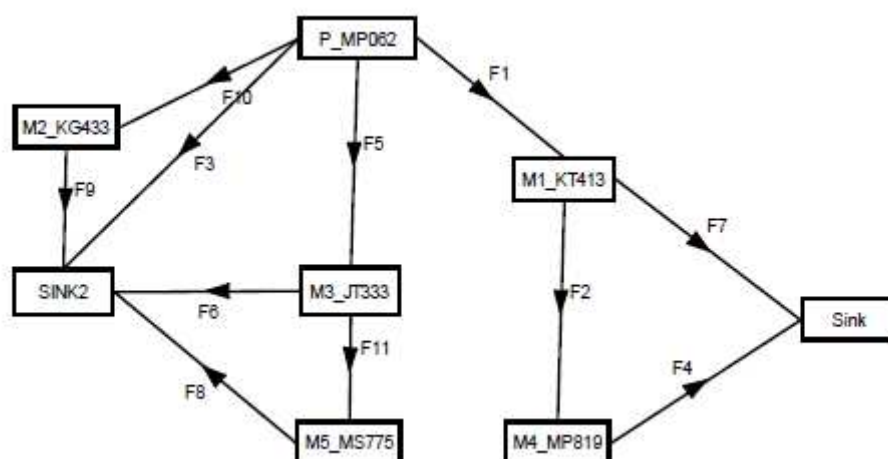
The available data from the studies and the implementation of FOCUS kinetics guidelines for treatment of initial (Day 0) and adjustments for levels below LOQ/LOD are found in Appendix I.

Kinetic model used and degradation model

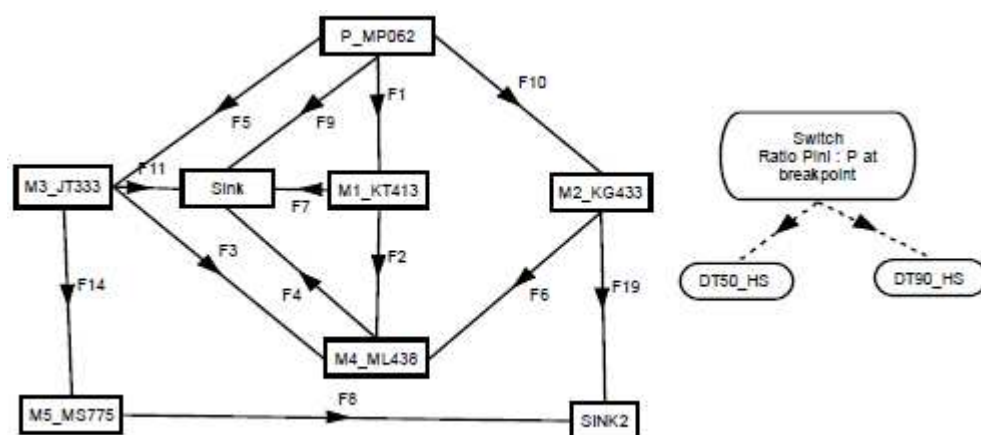
Kinetic calculations and optimizations were performed using the fitting program Model Maker version 4.0 (Cherwell Scientific Publishing, The Magdalene Centre, Oxford OX4 4 UK) and KINGUI software tool version 2.2012.209.845 (Bayer Crop Science, 2011).

The kinetic evaluation of one of the water-sediment studies (Burry Pond and Chatsworth) was done at two levels, while the evaluation of the second study was done at one level only. Level I consisted of the derivation of total-system, water phase and sediment half-lives for indoxacarb (P-I) and its metabolites (M-I). Level II comprised a two-compartmental approach and yielded separate DegT_{50} values for indoxacarb (P-II) for the water and sediment layers.

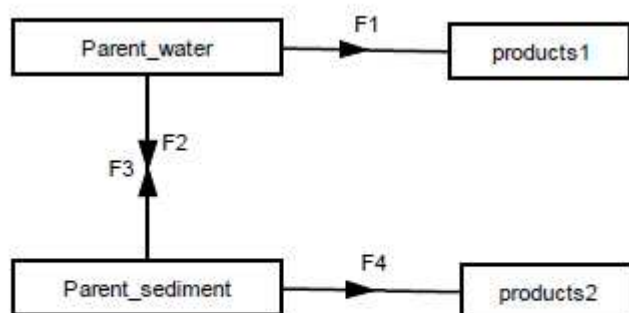
Degradation model used are described below



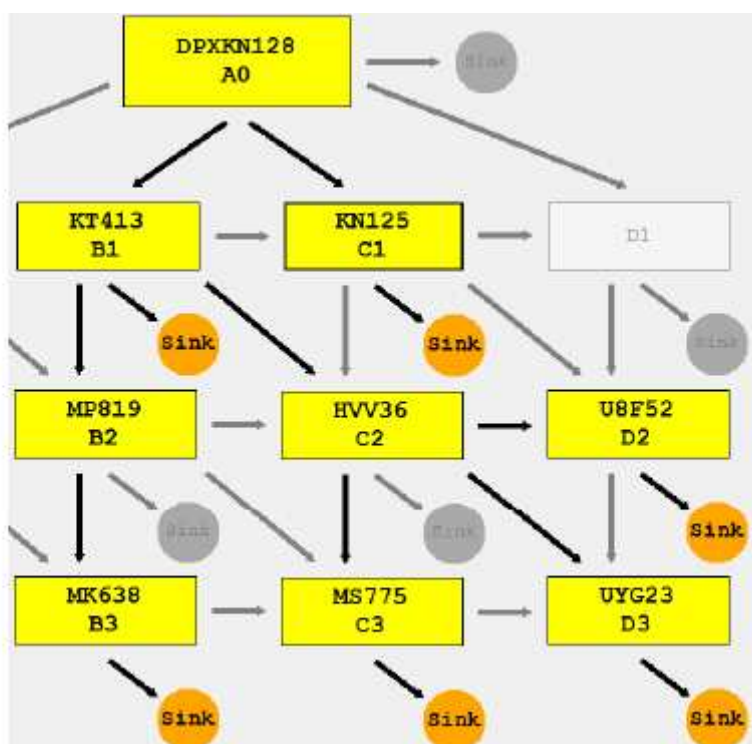
DFOP-SFO Kinetic Model for DPX-MP062 and Five Metabolites in Bury Pond Water Sediment System– Indanone and TFMP Label (Model Maker)



HS-SFO Kinetic Model for DPX-MP062 and Five Metabolites in Chatsworth Pond Water Sediment System– Indanone and TFMP Label (Model Maker)



SFO Kinetic Model, P-II Water/Sediment Studies (Model Maker)



Kinetic Model used in KinGUI v2.1 for Indoxacarb and its Metabolites in Water-Sediment (Level M-I Degradation)

The results of the evaluation referring to either the active substance or one of its aerobic metabolites are reported below and are not split into different subsections. This was done for the sake of clarity and easier reading.

DETAILED RESULTS

A. Indoxacarb

Level P-I

Bury pond system

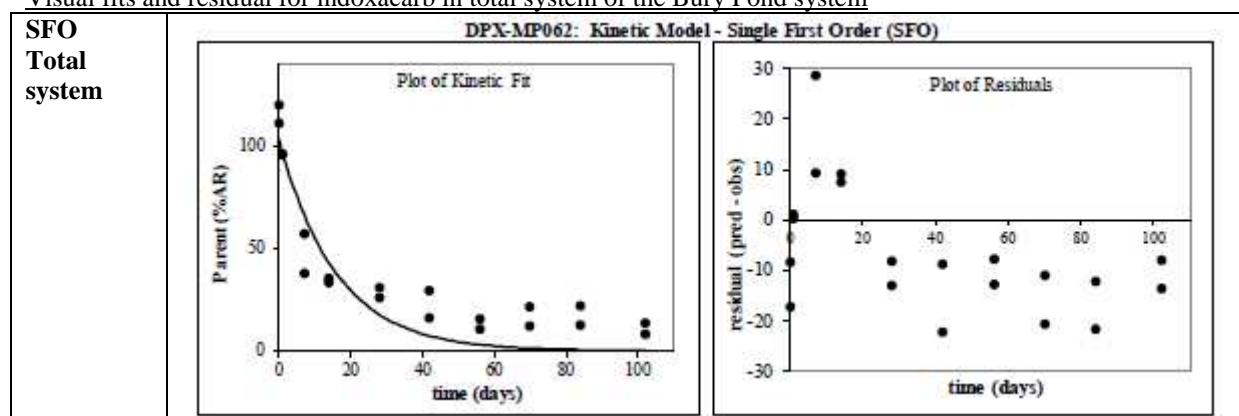
Table 8-207: Summary of kinetics and goodness of fit Statistics of P-I kinetics for indoxacarb in Bury pond system

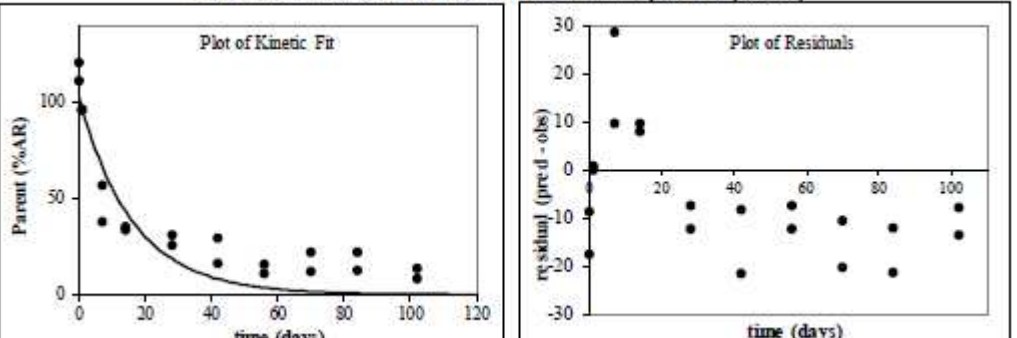
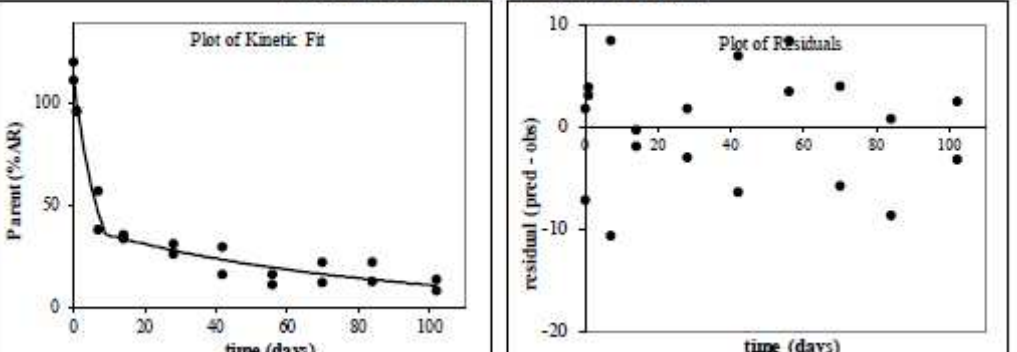
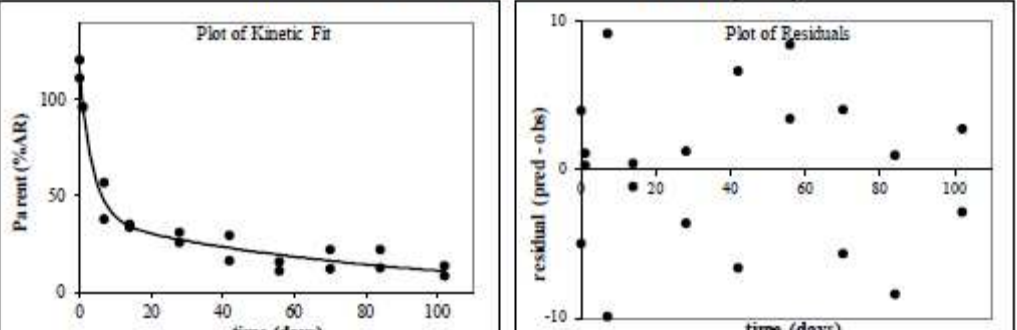
compartment	SFO				FOMC				HS				DFOP			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
Total System	11.1	36.7	26	<0.05	11.3	38	27	Not available	5.5	97.1	6	p1<0.05; p2<0.05	4.8	97.6	5	p1<0.05; p2<0.05
Water	0.6	2.0	12	<0.05	Could not be optimized				0.6	2.5	2	p1<0.05; p2<0.05	0.6	3.2	2	p1<0.05; p2<0.05
Sediment	36.2	120.2	16	<0.05	16.7	491.7	8	Not available	22.0	136.6	10	p1 ns [†] ; p2<0.05	16.1	159.5	8	p1=0.102; p2<0.05

Persistence: DFOP is best fit for total system, for water and for sediment phase

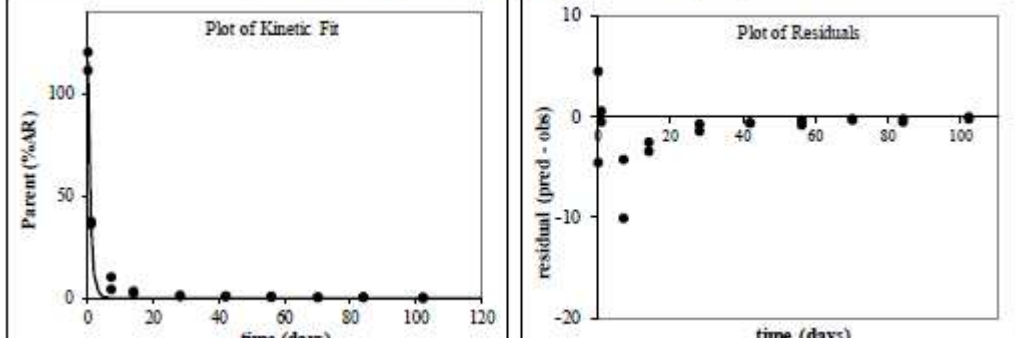
Modelling: SFO model did not result in an acceptable fit. Endpoint calculated from DFOP DT₉₀/3.32 from total system is retained for modelling.

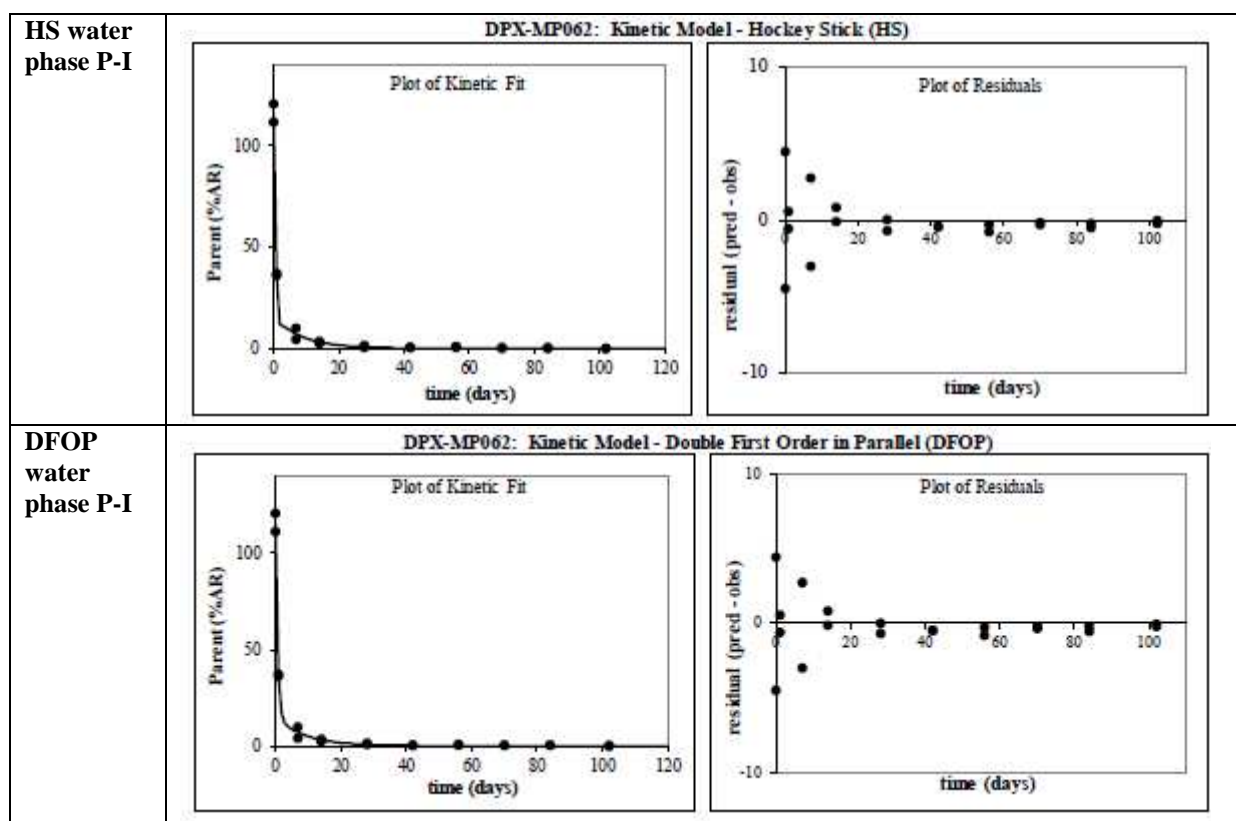
Visual fits and residual for indoxacarb in total system of the Bury Pond system



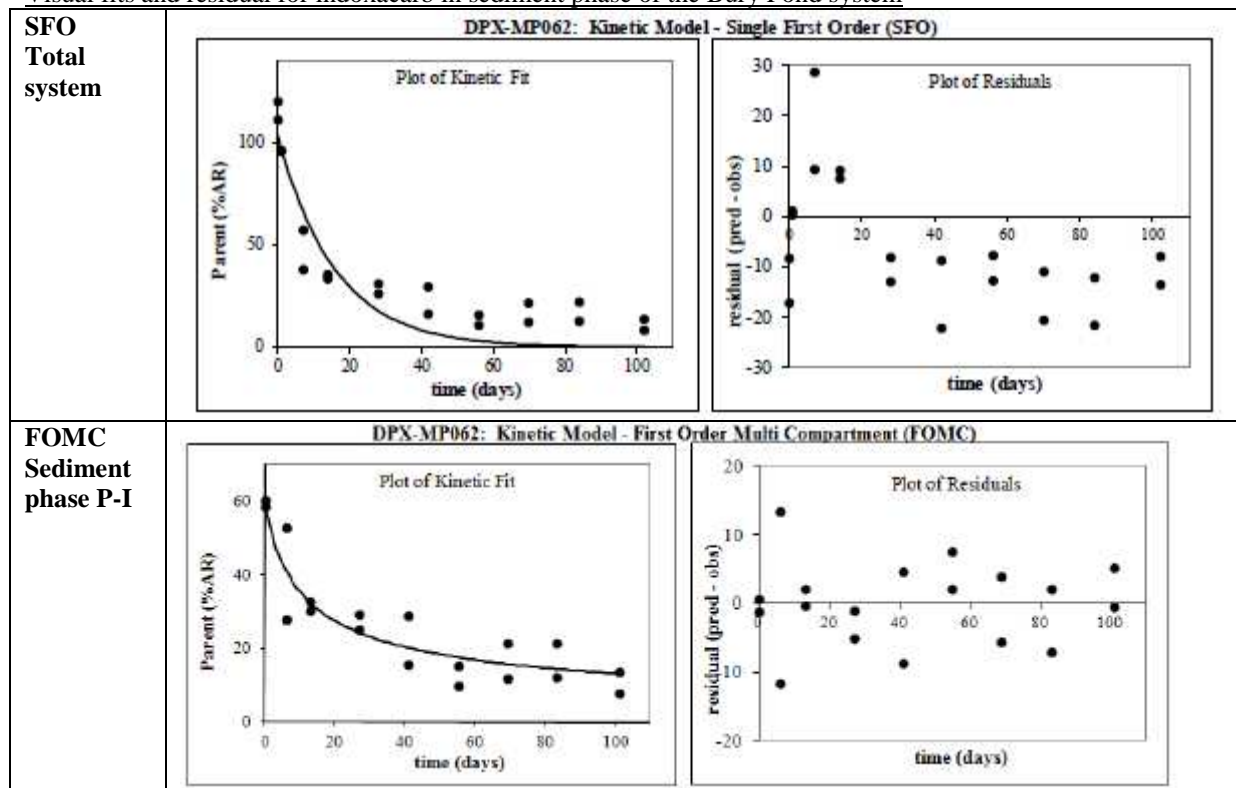
FOMC Total system	<p align="center">DPX-MP062: Kinetic Model - First Order Multi Compartment (FOMC)</p> 
HS Total system	<p align="center">DPX-MP062: Kinetic Model - Hockey Stick (HS)</p> 
DFOP Total system	<p align="center">DPX-MP062: Kinetic Model - Double First Order in Parallel (DFOP)</p> 

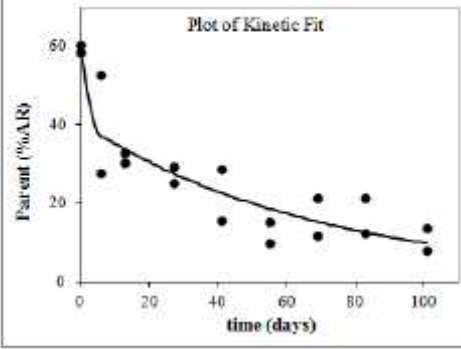
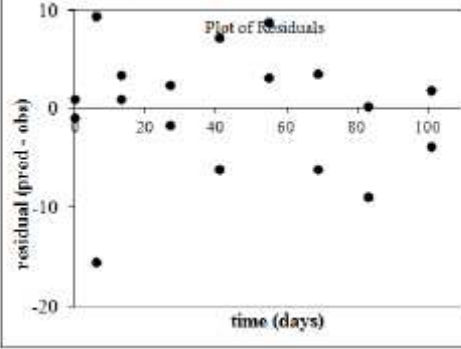
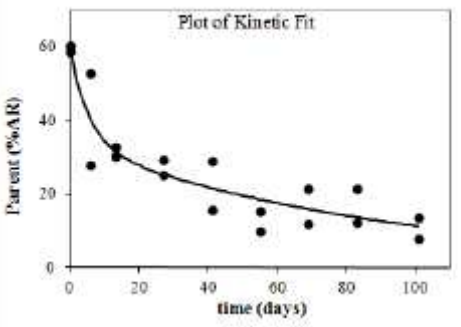
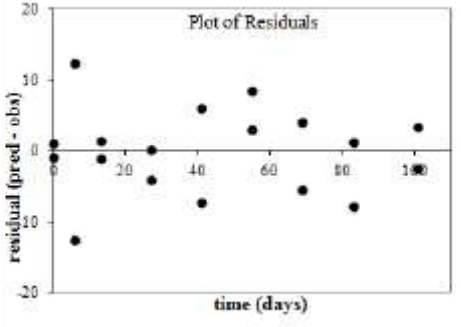
Visual fits and residual for indoxacarb in water phase of the Bury Pond system

SFO Water phase P-I	<p align="center">DPX-MP062: Kinetic Model - Single First Order (SFO)</p> 
FOMC Water phase P-I	Could not be optimized



Visual fits and residual for indoxacarb in sediment phase of the Bury Pond system



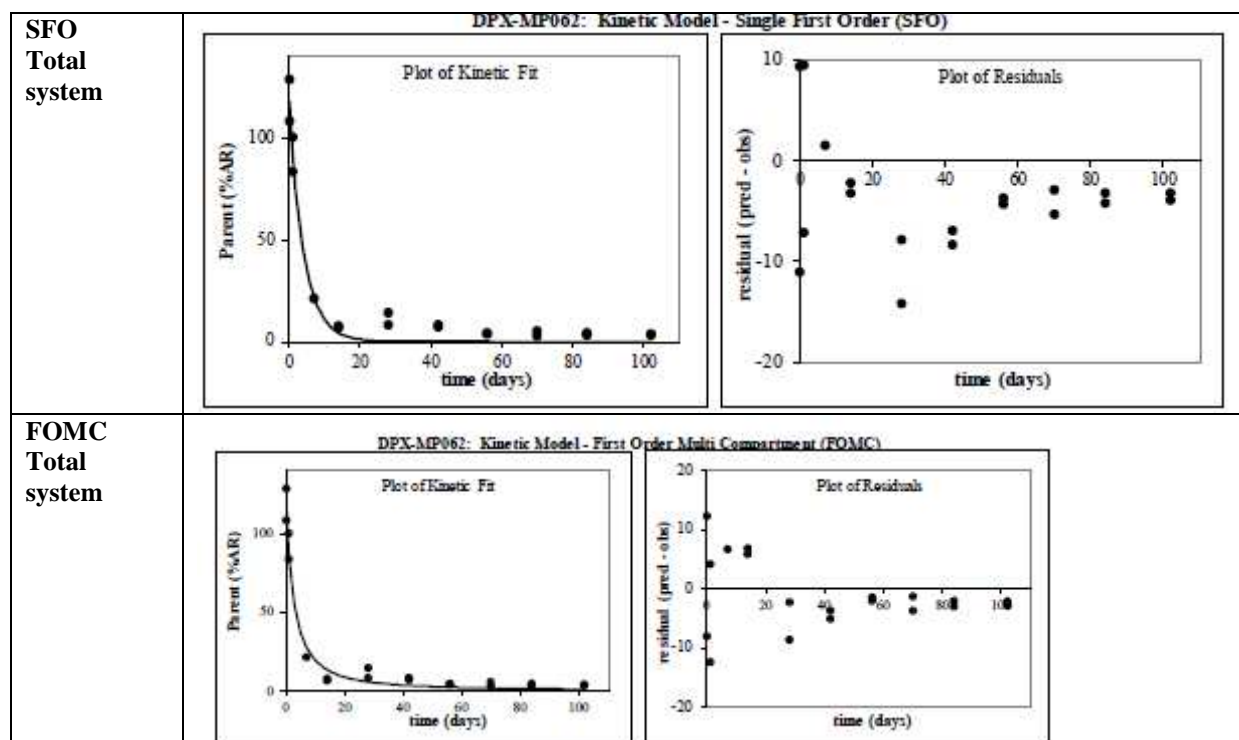
HS Sediment phase P-I	<p style="text-align: center;">DPX-MP062: Kinetic Model - Hockey Stick (HS)</p> <div><p>Plot of Kinetic Fit</p></div> <div><p>Plot of Residuals</p></div>
DFOP Sediment phase P-I	<p style="text-align: center;">DPX-MP062: Kinetic Model - Double First Order in Parallel (DFOP)</p> <div><p>Plot of Kinetic Fit</p></div> <div><p>Plot of Residuals</p></div>

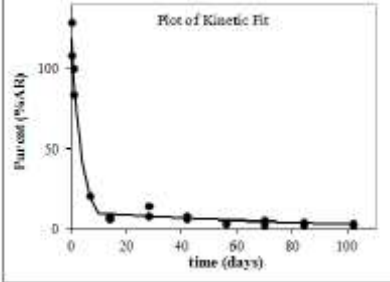
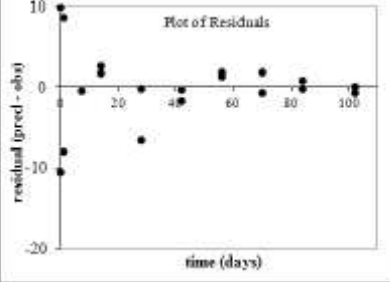
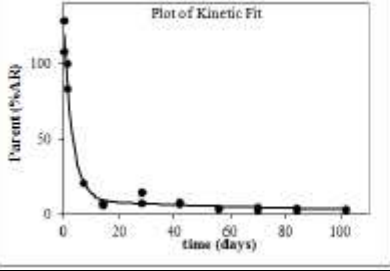
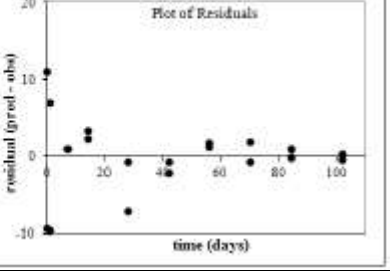
Chartsworth system**Table 8-208: Summary of kinetics and goodness of fit Statistics of P-I kinetics for indoxacarb in Chatsworth system**

compartment	SFO				FOMC				HS			DFOP				
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
Total System	3.0	9.8	15	<0.05	2.5	15.4	13	Not available	2.8	9.3	5	p1<0.05; p2=0.104	2.6	11.6	6	p1<0.05; p2=0.16
Water	0.5	1.6	2	<0.05	0.4	1.9	1	Not available	0.5	1.6	1	p1<0.05; p2 ns ^f	0.5	1.6	1	p1<0.05; p2 ns ^f
Sediment	4	13.2	29	<0.05	1.6	34.9	14	Not available	3.6	40.2	10	p1<0.05; p2=0.14	3.0	39.6	12	p1<0.05; p2 ns ^f

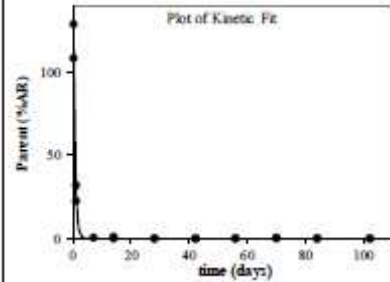
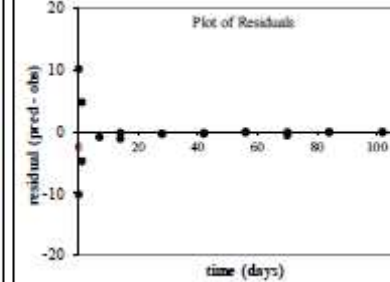
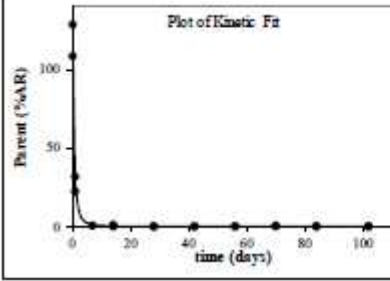
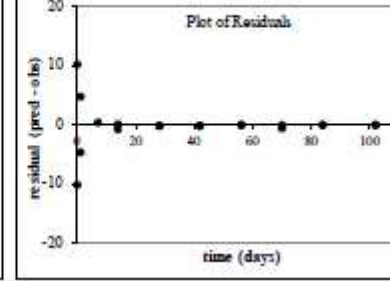
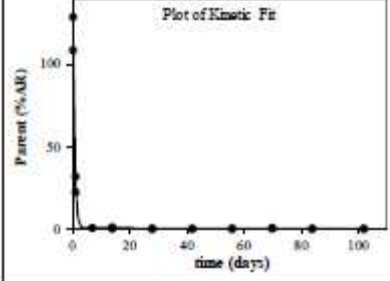
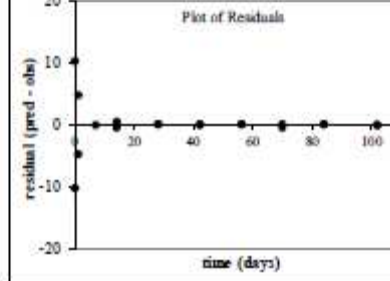
Persistence: HS is best fit for total system and for sediment phase (although HS k-rate failed significance test at P=0.14, it is close to passing P value of 0.10 for sediment kinetics and is the best visual fit, it was selected as best fit model). SFO is best-fit for water phase.

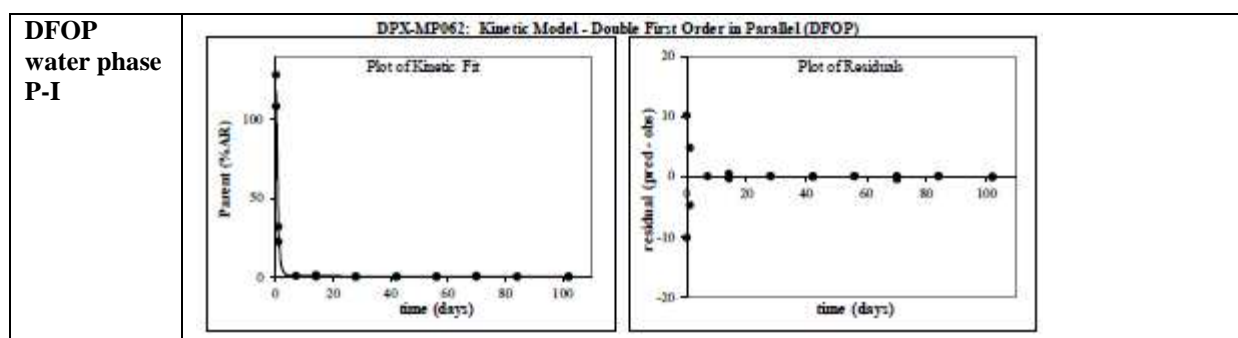
Modelling: SFO model did not result in an acceptable fit. Endpoint calculated from HS DT₉₀/3.32 from total system is retained for modelling.

Visual fits and residual for indoxacarb in total system of the Chatsworth system

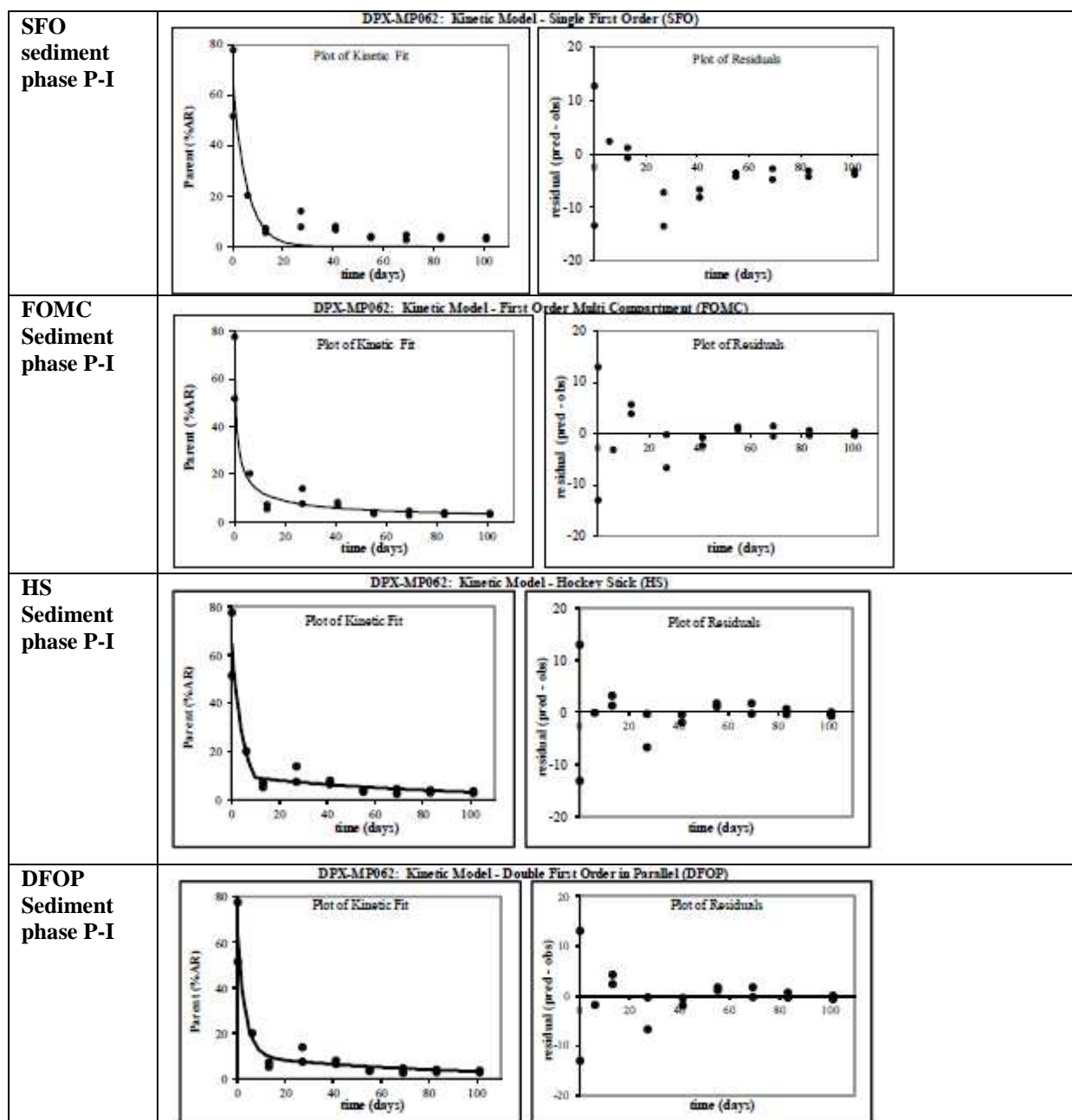
HS Total system	<p style="text-align: center;">DPX-MP062: Kinetic Model - Hockey Stick (HS)</p> <div style="display: flex; justify-content: space-around;">   </div>
DFOP Total system	<p style="text-align: center;">DPX-MP062: Kinetic Model - Double First Order in Parallel (DFOP)</p> <div style="display: flex; justify-content: space-around;">   </div>

Visual fits and residual for indoxacarb in water phase of the Chatsworth system

SFO Water phase P-I	<p style="text-align: center;">DPX-MP062: Kinetic Model - Single First Order (SFO)</p> <div style="display: flex; justify-content: space-around;">   </div>
FOMC Water phase P-I	<p style="text-align: center;">DPX-MP062: Kinetic Model - First Order Multi Compartment (FOMC)</p> <div style="display: flex; justify-content: space-around;">   </div>
HS water phase P-I	<p style="text-align: center;">DPX-MP062: Kinetic Model - Hockey Stick (HS)</p> <div style="display: flex; justify-content: space-around;">   </div>



Visual fits and residual for indoxacarb in sediment phase of the Chatsworth system

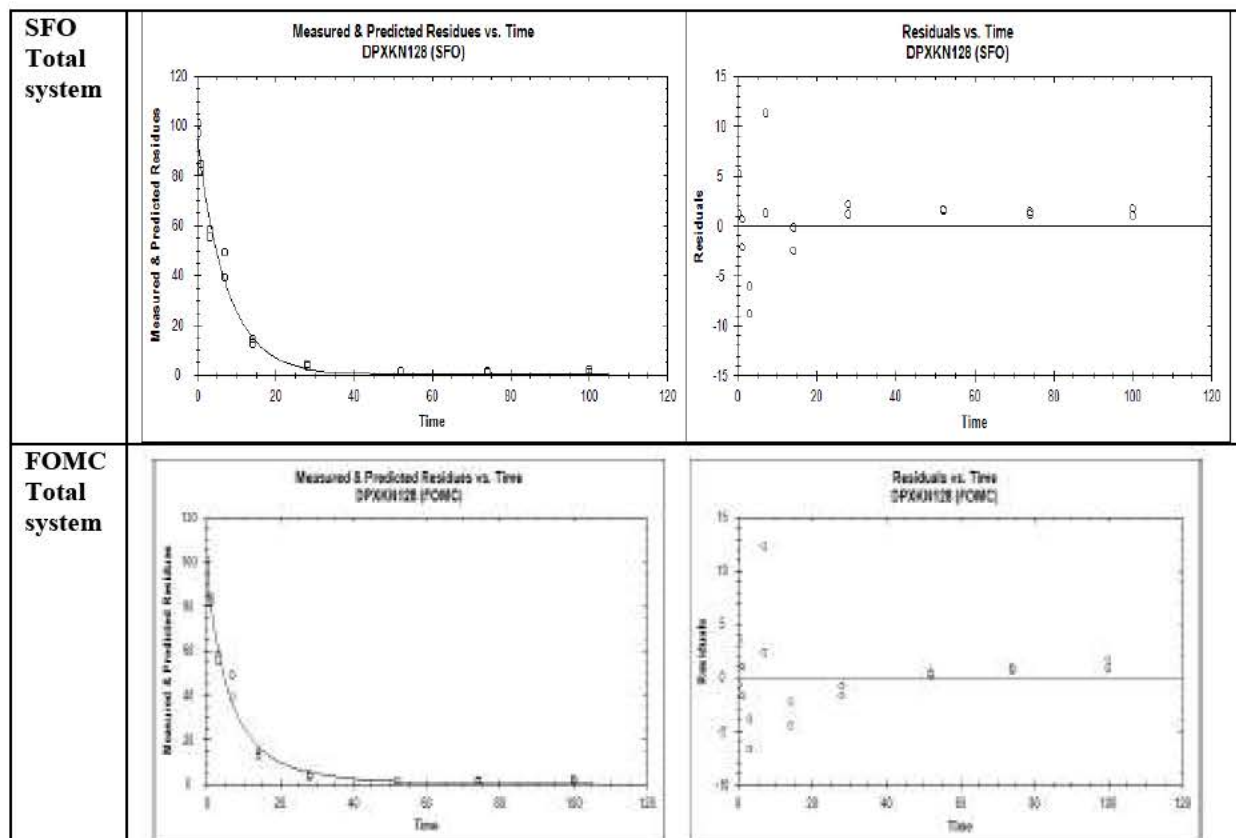


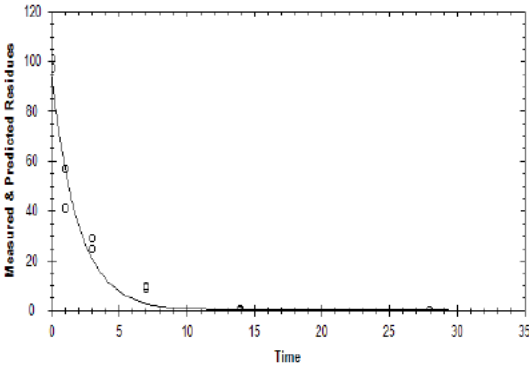
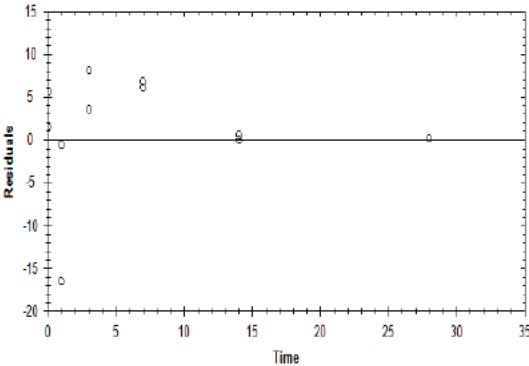
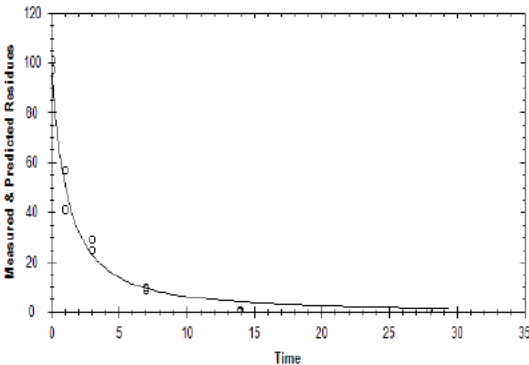
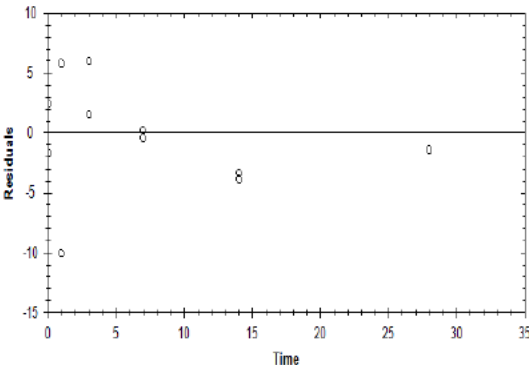
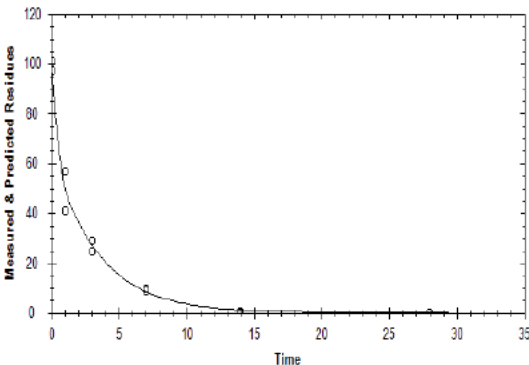
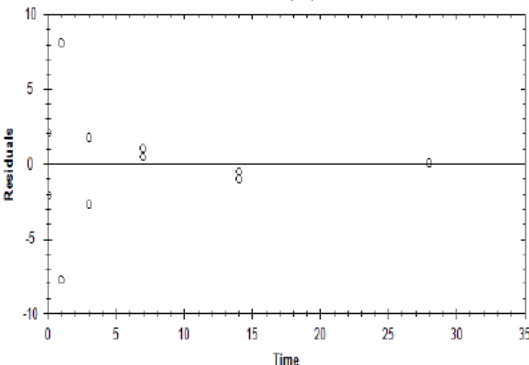
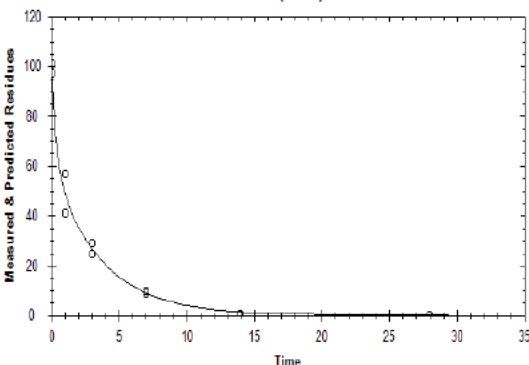
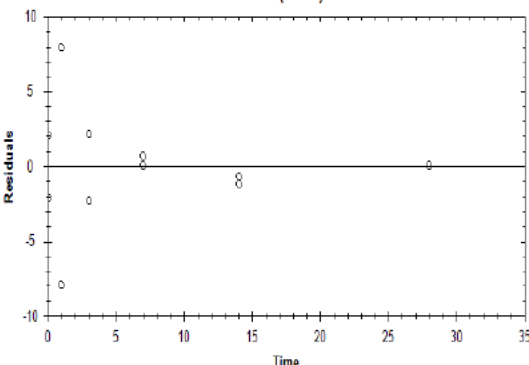
Chula system**Table 8-209: Summary of kinetics and goodness of fit Statistics of P-I kinetics for indoxacarb in Chula system**

Compartment	SFO				FOMC				HS				DFOP			
	DegT ₅₀	DegT ₉₀	χ^2	P (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	χ^2	P (t-test)	DegT ₅₀	DegT ₉₀	χ^2	P (t-test)
Total System	5.2	17.3	8.5	<0.05	4.8	20.0	8.3	β yes	5.2	17.2	9.2	p1<0.05; p2=0.289	5.1	18.3	9.1	p1<0.05; p2=0.363
Water	1.4	4.5	13.5	<0.05	1.1	6.7	6.8	β yes	1.0	6.5	1.6	p1<0.05; p2<0.05	1.0	6.6	1.3	p1=0.284; p2<0.05
Sediment	5.4	17.9	10.6	<0.05	4.5	26.1	4.2	β yes	3.8	24.3	9.2	p1<0.05; p2<0.05	4.9	21.8	2.3	p1<0.05; p2=0.349

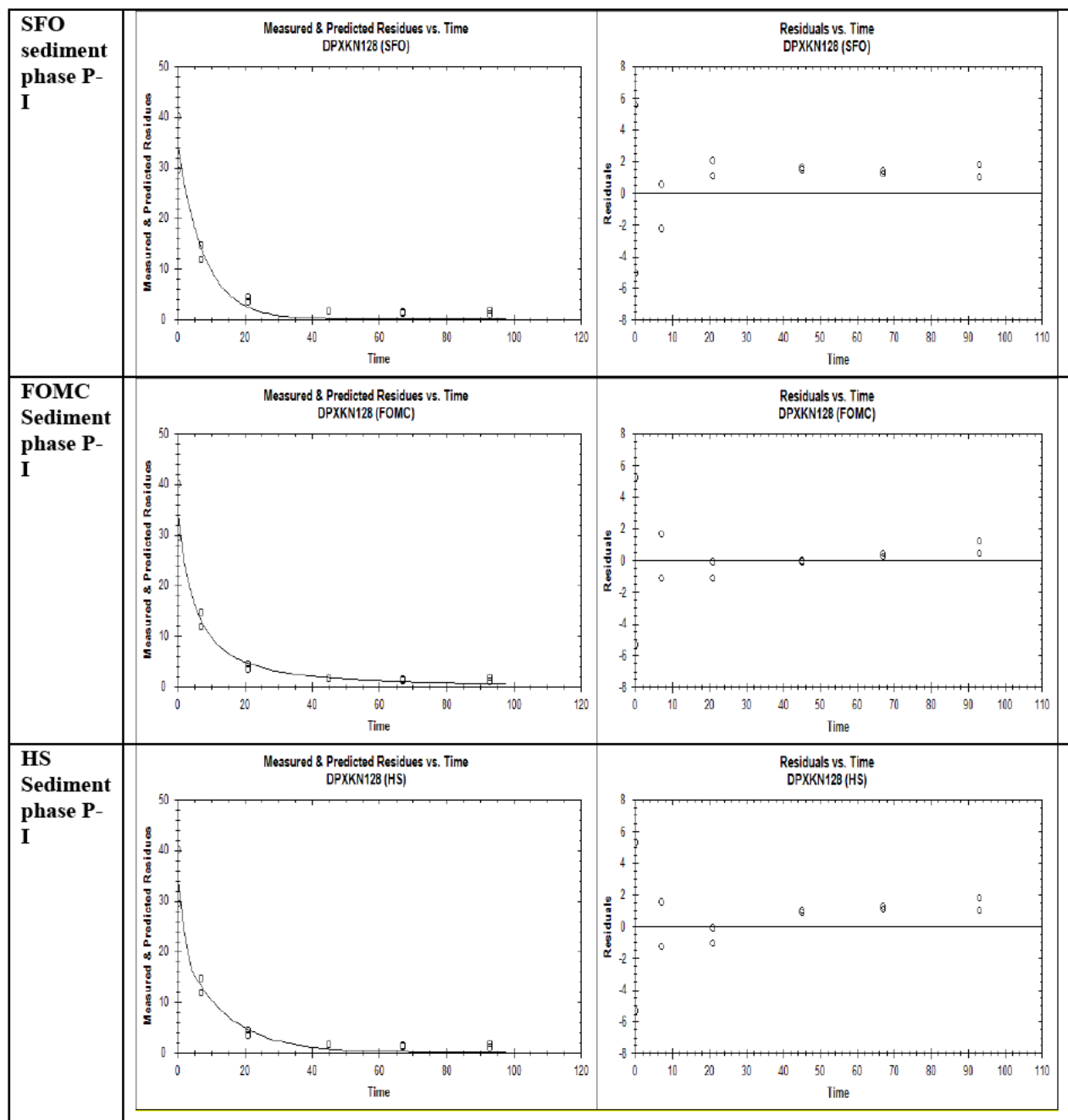
Persistence: SFO is best fit for total system (FOMC did not improve the fit very much). HS is best fit for water phase (HS was selected since k1 of DFOP was not significant.), DFOP is best-fit for sediment phase (k-rate not significant; still the model provided the best visual fit).

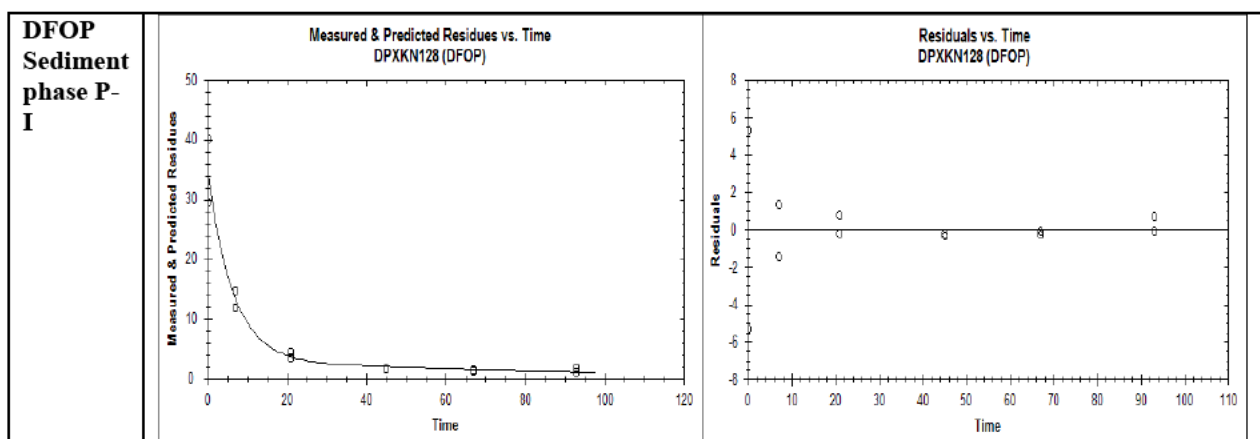
Modelling: SFO DT₅₀ from total system is retained for modelling.

Visual fits – Total system**Visual fits – Water phase**

SFO Water phase P-I	<p>Measured & Predicted Residues vs. Time DPXKN128 (SFO)</p> 	<p>Residuals vs. Time DPXKN128 (SFO)</p> 
FOMC Water phase P-I	<p>Measured & Predicted Residues vs. Time DPXKN128 (FOMC)</p> 	<p>Residuals vs. Time DPXKN128 (FOMC)</p> 
HS water phase P-I	<p>Measured & Predicted Residues vs. Time DPXKN128 (HS)</p> 	<p>Residuals vs. Time DPXKN128 (HS)</p> 
DFOP water phase P-I	<p>Measured & Predicted Residues vs. Time DPXKN128 (DFOP)</p> 	<p>Residuals vs. Time DPXKN128 (DFOP)</p> 

Visual fits – Sediment phase



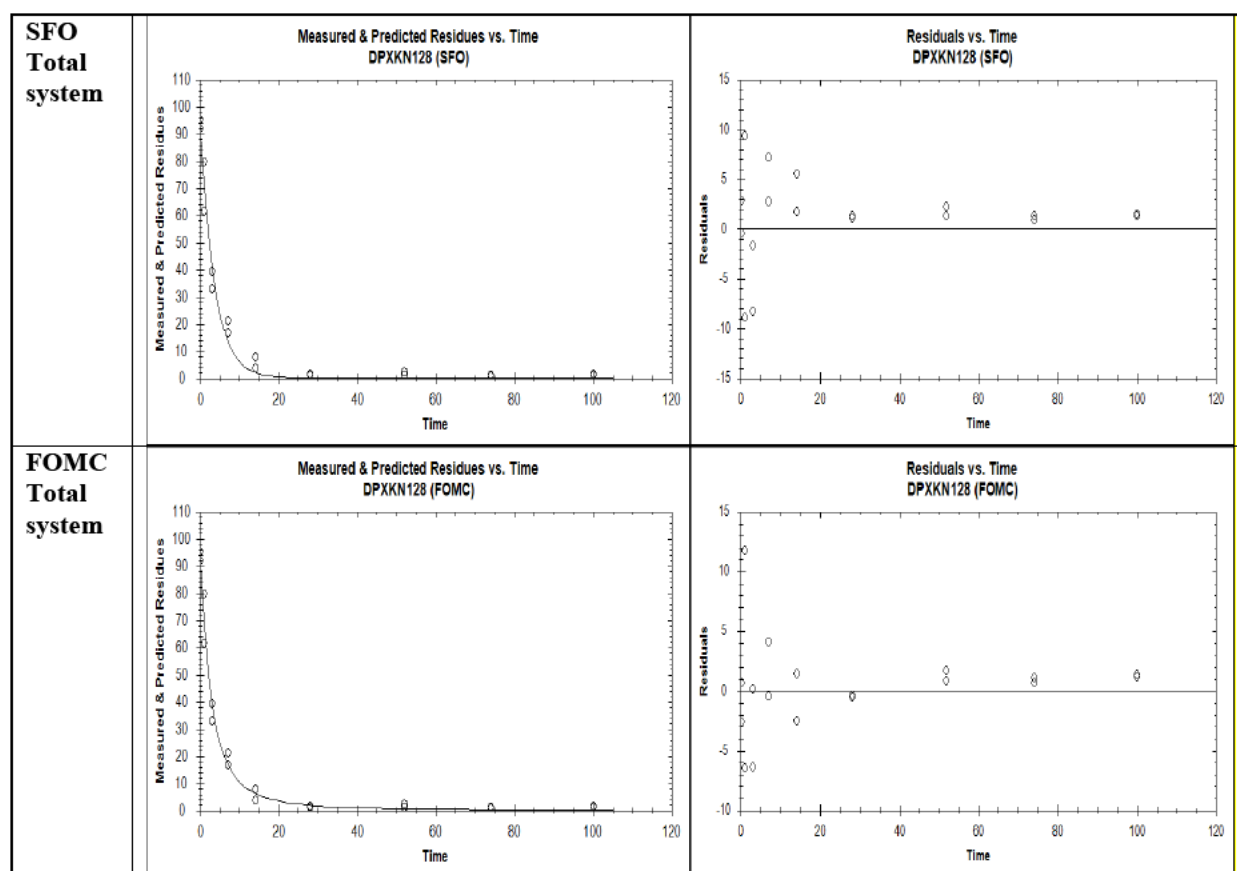


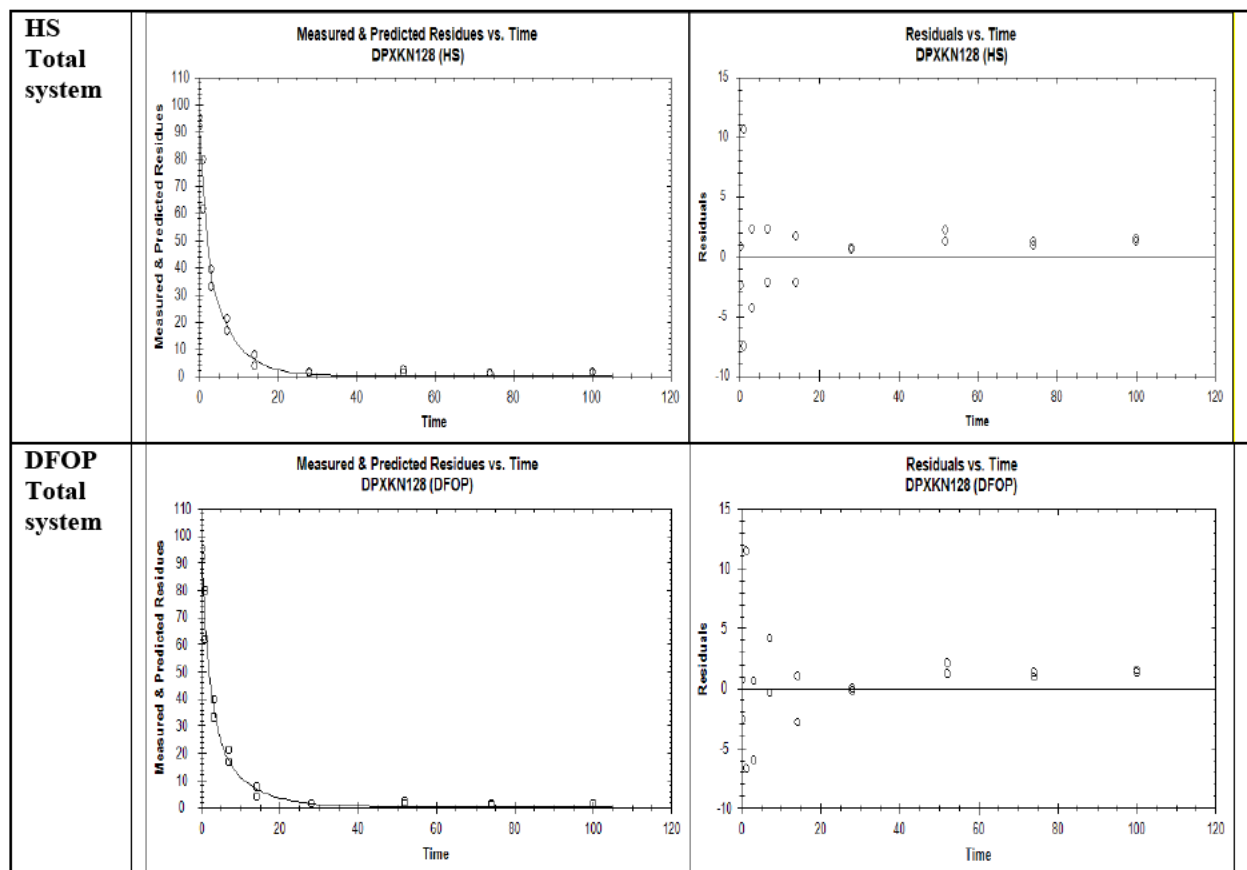
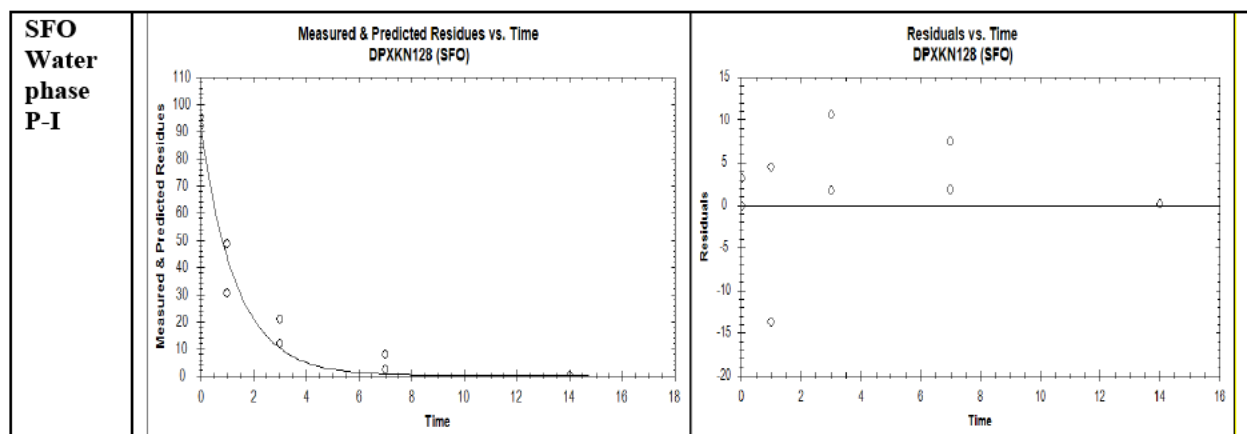
Goose river**Table 8-210: Summary of kinetics and goodness of fit Statistics of P-I kinetics for indoxacarb in Goose River system**

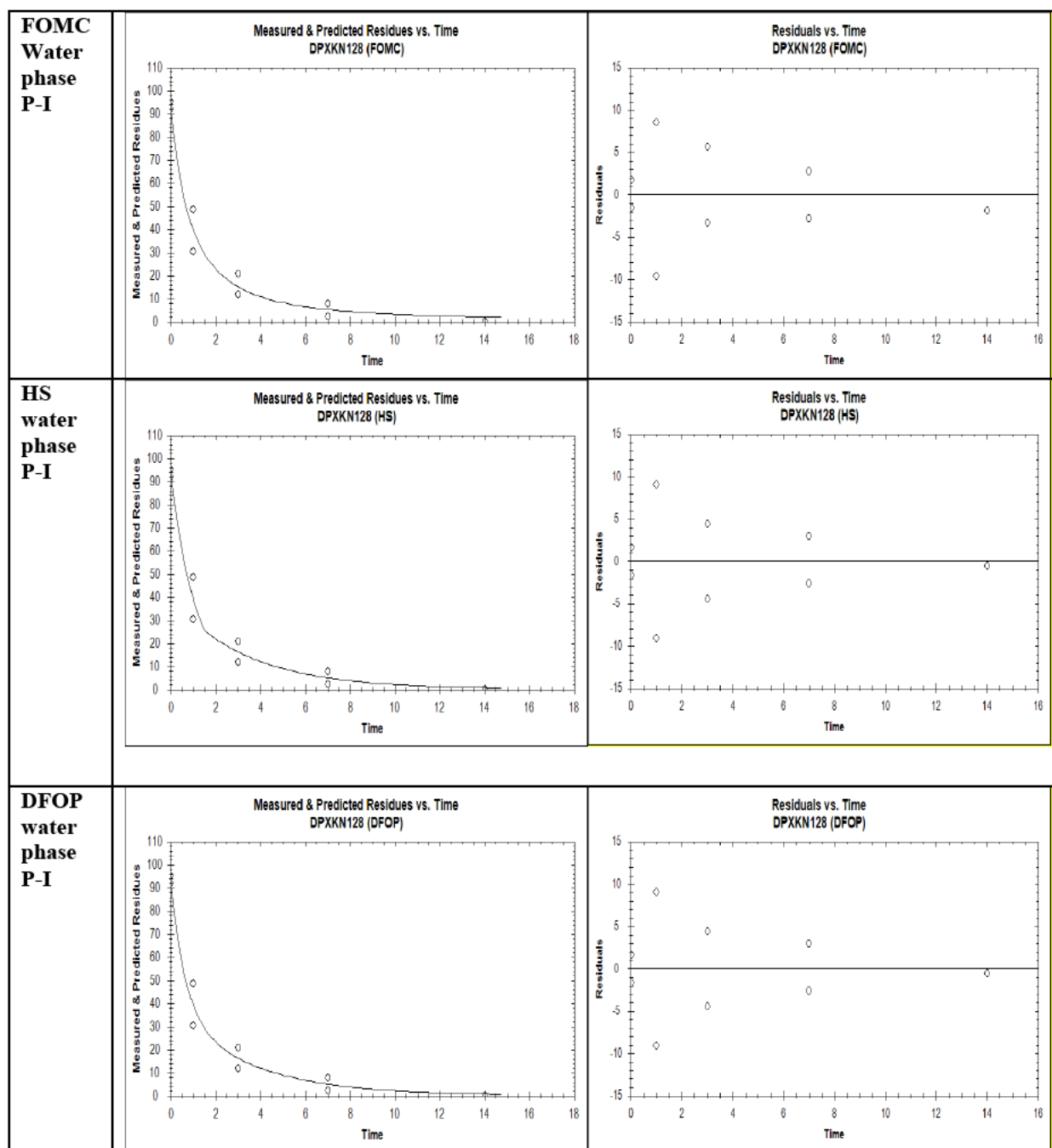
compartment	SFO				FOMC				HS			P (t-test)	DFOP			
	DegT ₅₀	DegT ₉₀	χ^2	P (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	DegT ₅₀	DegT ₉₀	χ^2		DegT ₅₀	DegT ₉₀	χ^2	P (t-test)
Total System	2.6	8.5	8.8	<0.05	2.3	10.8	5.6	β yes	2.2	11.2	3.9	p1<0.05; p2<0.05	2.3	11.1	5.7	p1<0.05; p2=0.111
Water	0.9	3.1	10.5	<0.05	0.8	4.5	3.0	β yes	0.8	4.9	0.9	p1<0.05; p2=0.109	0.8	4.8	1.0	p1=0.139; p2=0.137
Sediment	5.0	16.7	12.1	<0.05	4.0	24.5	9.0	β no	4.6	25.6	13.0	p1<0.05; p2<0.05	4.7	19.1	10.4	p1<0.05; p2=0.373

Persistence: HS is best fit for total system and for water phase. FOMC is best-fit for sediment phase (k-rate not significant; still the model provided the best visual fit).

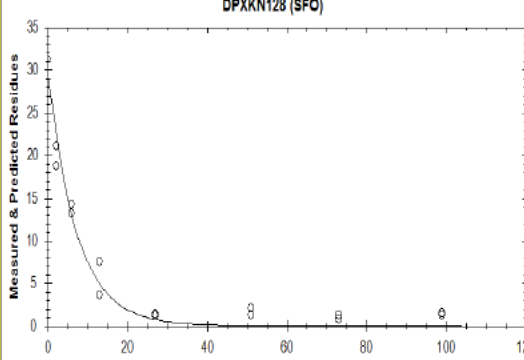
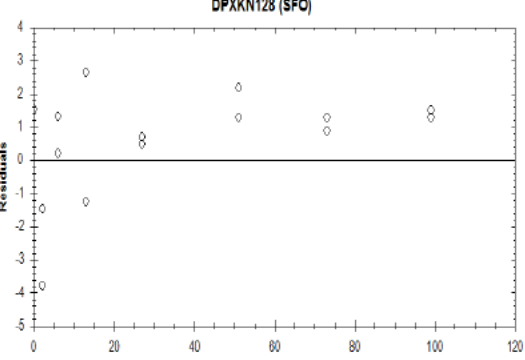
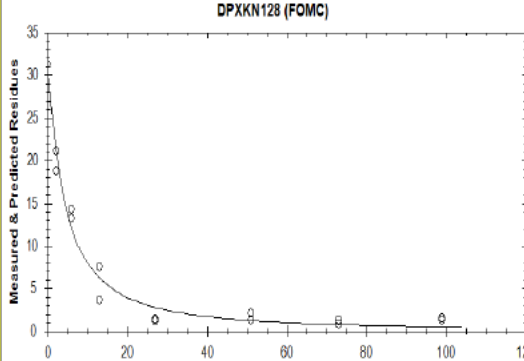
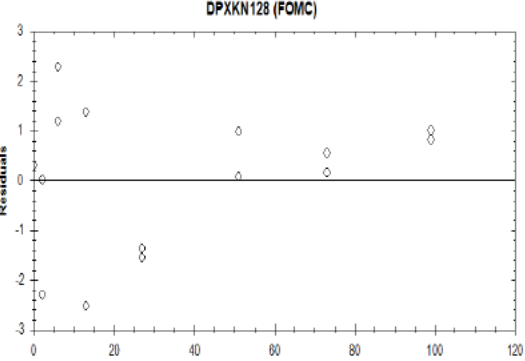
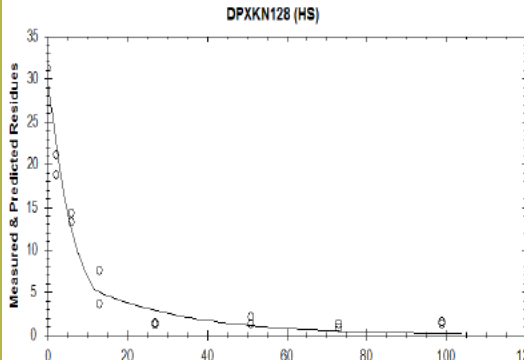
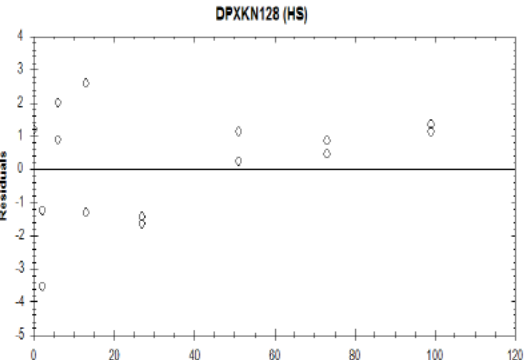
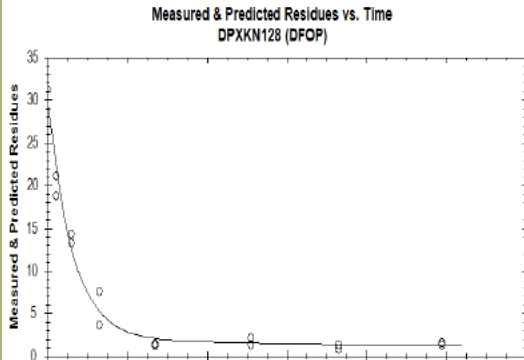
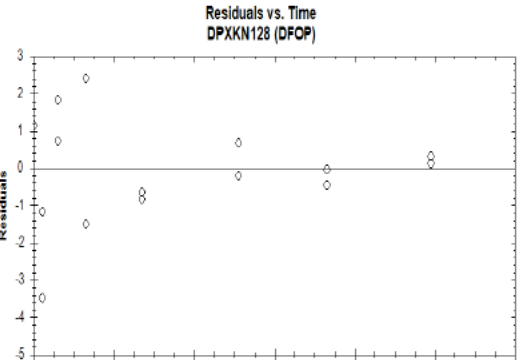
Modelling: SFO DT₅₀ from total system is retained for modelling.

Visual fits – Total system

Visual fits – Water phase



Visual fits – Sediment phase

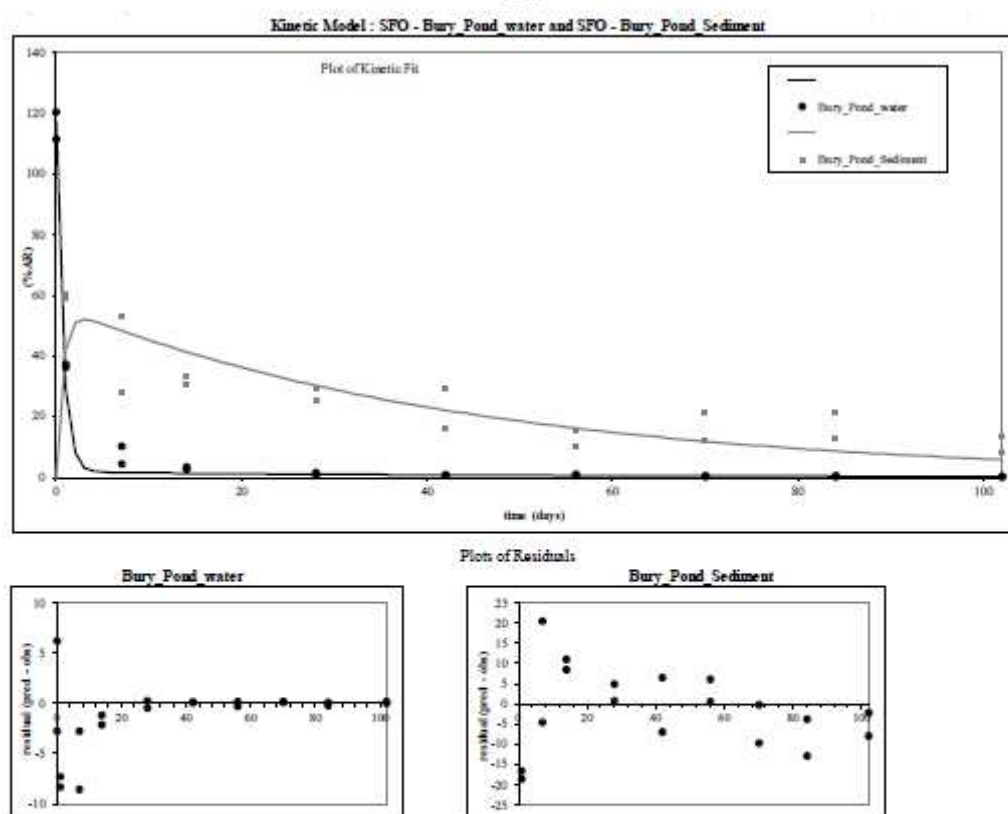
SFO sediment phase P-I	<p>Measured & Predicted Residues vs. Time DPXKN128 (SFO)</p> 	<p>Residuals vs. Time DPXKN128 (SFO)</p> 
FOMC Sediment phase P-I	<p>Measured & Predicted Residues vs. Time DPXKN128 (FOMC)</p> 	<p>Residuals vs. Time DPXKN128 (FOMC)</p> 
HS Sediment phase P-I	<p>Measured & Predicted Residues vs. Time DPXKN128 (HS)</p> 	<p>Residuals vs. Time DPXKN128 (HS)</p> 
DFOP Sediment phase P-I	<p>Measured & Predicted Residues vs. Time DPXKN128 (DFOP)</p> 	<p>Residuals vs. Time DPXKN128 (DFOP)</p> 

Level P-IIBury pond system**Table 8-211: Summary of kinetics of P-II kinetics for indoxacarb in Bury pond system**

Bury Pond level P-II	Water phase (SFO)			Sediment phase (SFO)				
	DT ₅₀	DT ₉₀	t-test	DT ₅₀	DT ₉₀	t-test	rsw	t-test
	0.9	3.1	0.000	6995.8	23239.7	0.4334	0.6891	0.0000

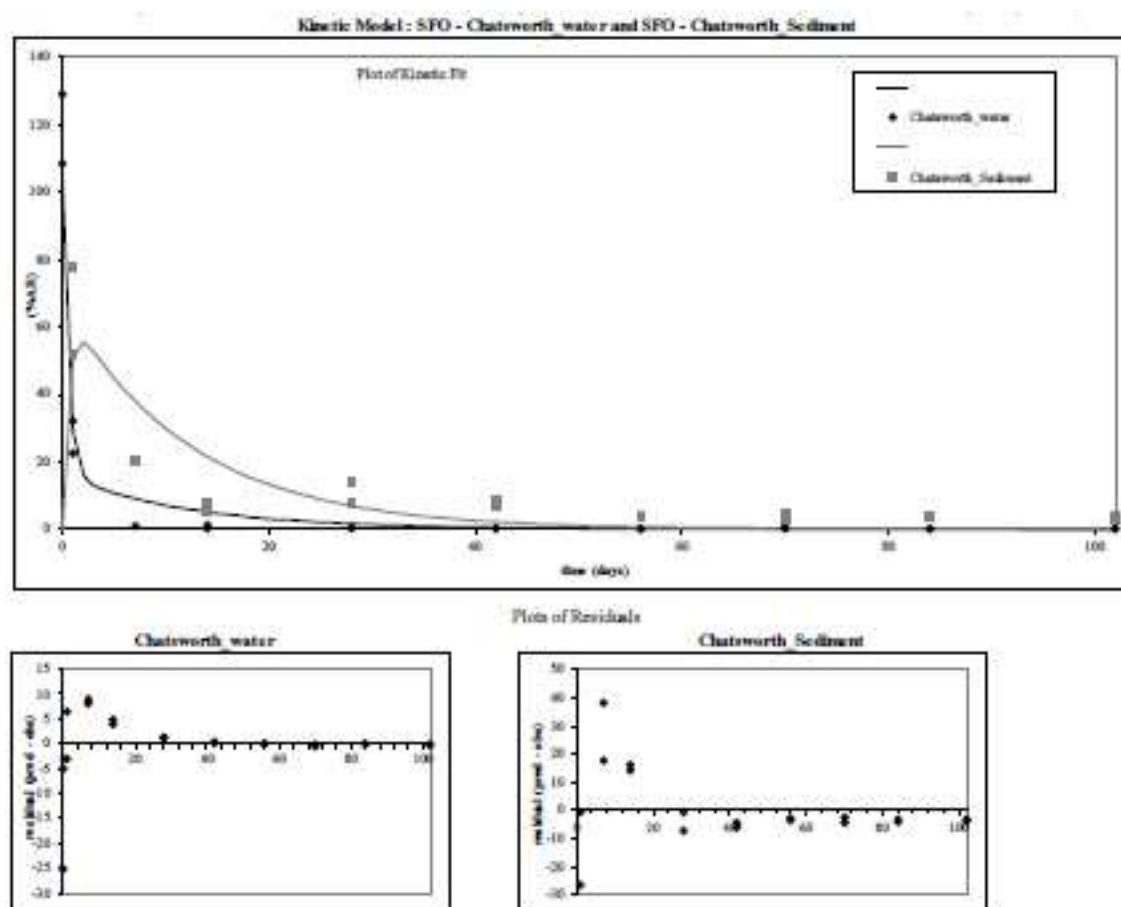
The kinetic evaluation revealed neither a visually nor statistically acceptable fit for the sediment compartment. Therefore, the evaluation at Level P-II was not pursued further.

Figure 160
Optimised SFO Kinetic Model of Indoxacarb and Transfer in Bury Pond: Water and Sediment Phase, P-II

Chatsworth system**Table 8-212: Summary of kinetics of P-II kinetics for indoxacarb in Chatsworth system**

Chartsworth level P-II	Water phase (SFO)			Sediment phase (SFO)				
	DT ₅₀	DT ₉₀	t-test	DT ₅₀	DT ₉₀	t-test	rws	t-test
	1.7	5.5	0.0470	645.9	2045.8	0.4957	0.34	0.3298

The kinetic evaluation revealed neither a visually nor statistically acceptable fit for the water and for the sediment compartment. Therefore, the evaluation at Level P-II was not pursued further.



For both system, F_{sed} test passed but one of the P-II degradation rates failed t-test. Then only degradation rates from P-I level are kept for modelling.

Chula system

P-II was not evaluated; degradation in water faster than in sediment.

Goose river system

P-II was not evaluated; degradation in water faster than in sediment.

No P-II endpoints were reliable for any of the systems. Only P-I level endpoint are kept and are summarized below.

Summary of selected endpoint total system, water column and sediment phase for indoxacarb

Table 8-213: Total system degradation persistence endpoint derived at level P-I for indoxacarb

Compound	Level	System	Selected model	DissT ₅₀ (days)	DissT ₉₀ (days)
Indoxacarb	P-I	Bury Pond	DFOP	4.8	97.6
		Chatsworth	HS	2.8	9.3
		Chula	SFO	5.2	17.3
		Goose river	HS	2.2	11.2

Table 8-214: Total system degradation modelling endpoints derived at levels P-I for indoxacarb

Compound	Level	System	Selected model	DegT ₅₀ (days)
Indoxacarb	P-I	Bury Pond	DFOP (DT ₉₀ /3.32)	29.4
		Chatsworth	HS (DT ₉₀ /3.32)	2.8
		Chula	SFO	5.2
		Goose river	SFO	2.6
		Geometric mean:	-	5.8

Table 8-215: Water column dissipation persistence endpoint derived at level P-I for indoxacarb

Compound	Level	System	Selected model	DissT ₅₀ (days)	DissT ₉₀ (days)
Indoxacarb	P-I	Bury Pond	DFOP	0.6	3.2
		Chatsworth	SFO	0.5	1.6
		Chula	HS	1.0	6.5
		Goose river	HS	0.8	4.9

Table 8-216: Sediment dissipation persistence endpoint derived at level P-I for indoxacarb

Compound	Level	System	Selected model	DissT ₅₀ (days)	DissT ₉₀ (days)
Indoxacarb	P-I	Bury Pond	DFOP	16.1	159.5
		Chatsworth	HS	3.6	40.2
		Chula	DFOP	4.9	21.8
		Goose river	FOMC	4.0	24.5

Summary of selected endpoint total system, water column and sediment phase for indoxacarb at level P-II**Table 8-217: Total system degradation persistence endpoint derived at level P-II for indoxacarb**

Compound	Level	System	Selected model	DissT ₅₀ (days)	DissT ₉₀ (days)
Indoxacarb	P-II	Bury Pond	Not reliable		
		Chatsworth	Not reliable		
		Chula	Not evaluated		
		Goose river	Not evaluated		

B. IN-JT333**Fit parent-metabolite**

A first attempt to fit data in a parent (best-fit)-metabolite (SFO) model was done, but only the run with the chatsworth (TFMPlabel) data resulted in an acceptable fit. Summary of statistics obtained for all fits are summarized below but only the visual fits of chatsworth system are reported below. All other visuals are reported in appendix II to keep the document clear.

Table 8-218: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-JT333/IN-KN125 derived from indoxacarb water sediment studies

Study	Soil/Label	IN-JT333/IN-KN125 via Indoxacarb Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction	
DuPont-8417	Bury Pond (Replicates)	24.5 ^a	81.4 ^a	53	0.09	DFOP-SFO
	Bury Pond (Indanone)	23.5 ^a	78.2 ^a	72	0.1	DFOP-SFO
	Bury Pond (TFMP)	23.2 ^a	77.0 ^a	42	0.09	DFOP-SFO
	Chatsworth (Replicates)	36.6	121.4	11	0.24	HS-SFO
	Chatsworth (Indanone)	53.4 ^b	177.5 ^b	19	0.20	HS-SFO
	Chatsworth (TFMP)	38.3	127.4	22	0.22	HS-SFO
DuPont-39061	Chula (Replicates)	14.0 ^c	46.4 ^c	28.6	0.05 ^c	SFO-SFO
	Chula (Indanone)	16.3 ^c	54.3 ^c	23.2	0.04 ^c	SFO-SFO
	Chula (TFMP)	12.4 ^c	41.3 ^c	34.1	0.06 ^c	SFO-SFO
	Goose River (Replicates)	52.2 ^c	173.5 ^c	28.5	0.02 ^c	HS-SFO
	Goose River (Indanone)	46.9 ^c	155.7 ^c	26.0	0.02 ^c	FOMC-SFO
	Goose River (TFMP)	77.6 ^c	257.6 ^c	14.7	0.01 ^c	SFO-SFO

^a. Endpoints considered unreliable due to overestimation of the peak and non-random residual errors at the tail end

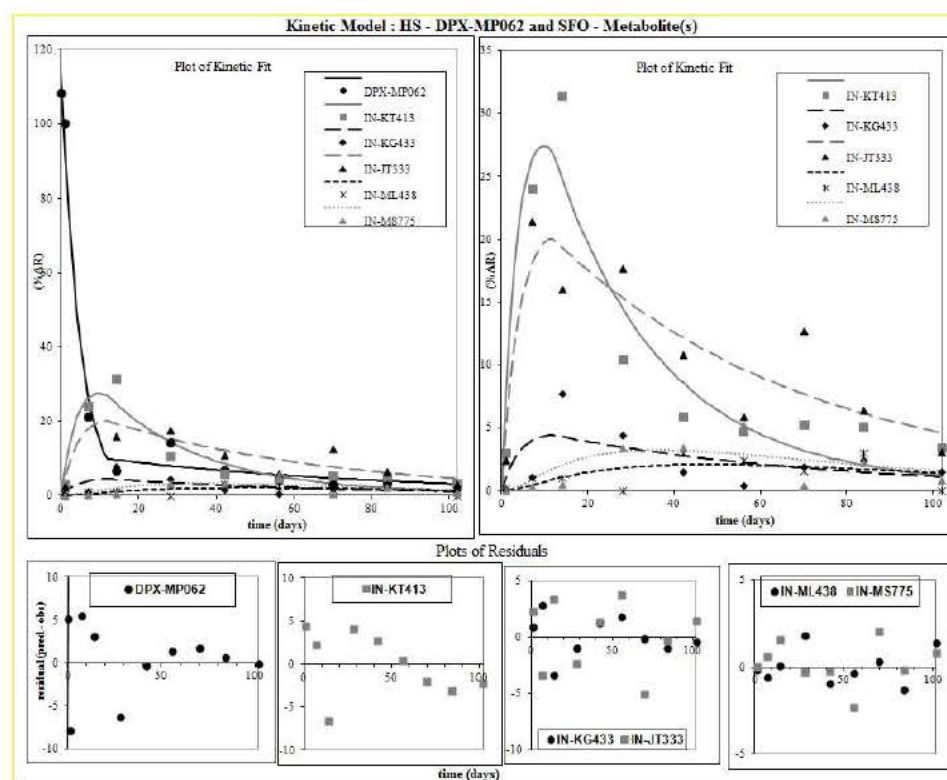
^b. Endpoints considered unreliable due to underestimation of the peak and non-random residual errors at the tail end

^c. Endpoint considered unreliable due to underestimation of the peak; due to high correlation of residue data, k and ff where estimated in a parent and IN-KN125 only fit and fixed when further metabolites were added to pathway fit.

Visual fits

Only the visual fit of Chatsworth system are reported below as it is the only fit that resulted in acceptable statistical assessment and was retained for modelling. All other visual fits are reported in appendix II.

Optimised HS-SFO kinetic model of indoxacarb and metabolites in Chatsworth Pond: Total system TFMP label, M-I



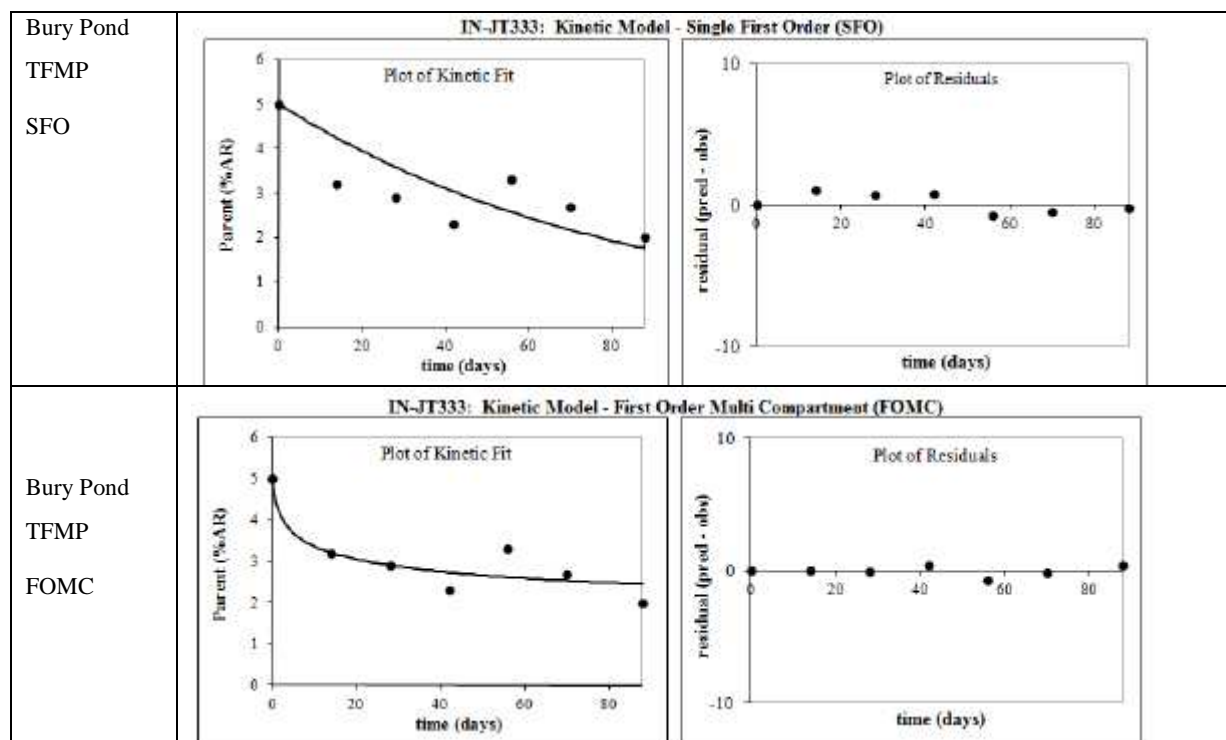
Fit from peak

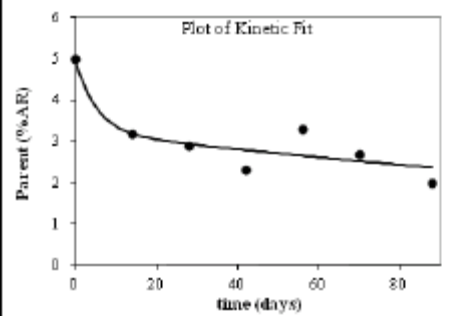
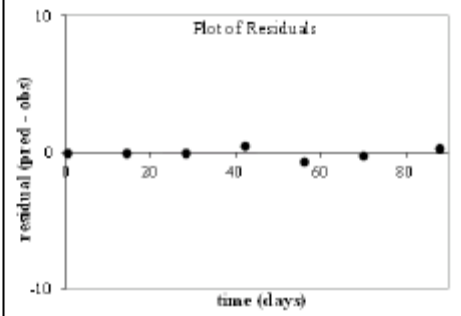
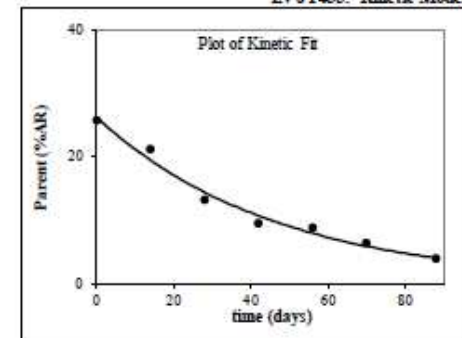
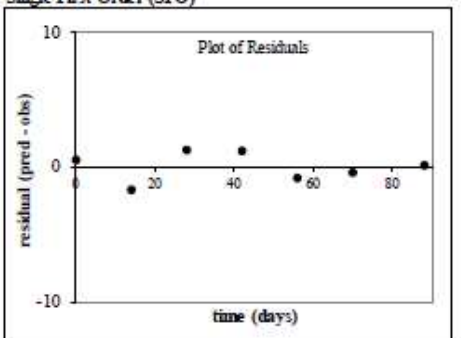
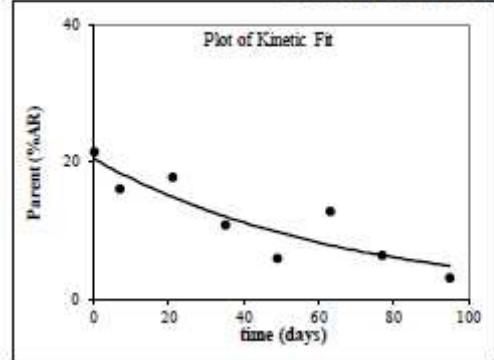
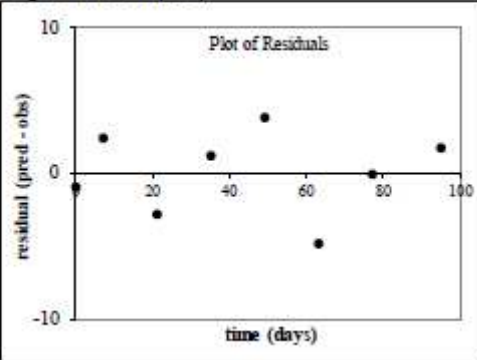
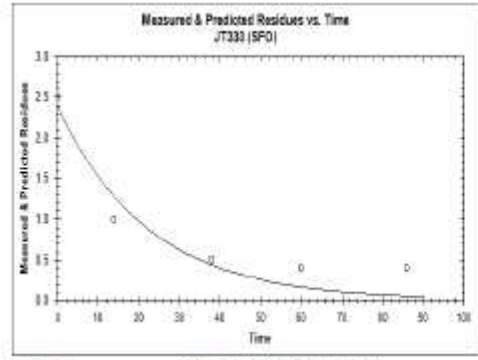
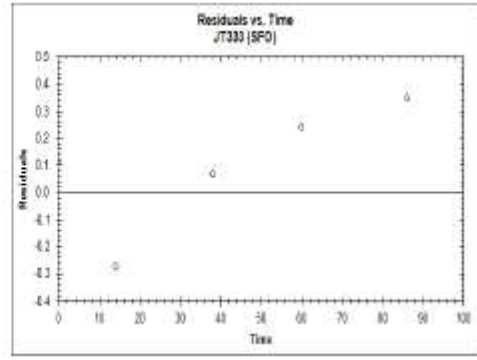
In the four system, metabolite IN-JT333 was not observed in the water phase. DegT₅₀ derived from the data are thus corresponding to the total system and the sediment phase.

The data from the Indanon label of the Bury pond system were not fitted as no clear decline was observed.

System	SFO				FOMC			DFOP			HS		
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	95% CI contains 0	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Bury Pond TFMP	58.5	194.2	17	<0.05	78.8	3.6E+6	-	73.1	519.1	p1 ns ^b ; p2 ns	93.1	500.6	p1 ns; p2 ns
Chatsworth Indanon	32.4	107.7	6	<0.05	32.1	110	-	Not required			Not required		
Chatsworth TFMP	45.6	151.5	18	<0.05	44.8	160.1	-	Not required			Not required		
Chula Indanon	15.5	51.4	19.4	<0.05	8.3	134.7	β no	10.1	336.1	p1<0.05; p2=0.290	10.6	172.8	p1<0.05; p2=0.170
Chula TFMP	8.5	28.3	15.7	<0.05	5.6	45.9	β yes	0.7	50.2	p1<0.05; p2<0.05	7.1	50.2	p1<0.05; p2<0.05
Goose River Indnon	41.3	137.3	18.9	<0.05	15.6	1959.0	β yes	13.3	319.5	p1=0.054; p2=0.145	11.4	302.1	p1<0.05; p2=0.056
Goose River TFMP	112.6	374.1	10.0	<0.05	170.5	>>1000	β yes	>>1000	>>1000	p1=0.290; p2=0.500	>>1000	>>1000	p1=0.075; p2=0.500

Visual fits – fit from peak IN-JT333 - sediment and total system



Bury Pond TFMP DFOP	<p>IN-JT333: Kinetic Model - Double First Order in Parallel (DFOP)</p> <div>   </div>
Chatsworth Indanon SFO	<p>IN-JT433: Kinetic Model - Single First Order (SFO)</p> <div>   </div>
Chatsworth TFMP SFO	<p>IN-JT333: Kinetic Model - Single First Order (SFO)</p> <div>   </div>
Chula Indanon SFO	<div>   </div>

Chula Indanon FOMC	<p>Measured & Predicted Residues vs. Time JT333 (FOMC)</p> <p>This graph shows the measured and predicted residues of Indanon over time (0 to 120 hours) using the FOMC model. The y-axis represents Measured & Predicted Residues (0.0 to 3.0), and the x-axis represents Time (0 to 120). The data points show a rapid initial decline followed by a slower approach to a residual level around 0.5.</p> <p>Residuals vs. Time JT333 (FOMC)</p> <p>This graph shows the residuals for the Indanon FOMC model over time (0 to 120 hours). The y-axis represents Residuals (-0.08 to 0.08), and the x-axis represents Time (0 to 120). The residuals are scattered around zero, indicating a good fit of the model to the data.</p>
Chula Indanon DFOP	<p>Measured & Predicted Residues vs. Time JT333 (DFOP)</p> <p>This graph shows the measured and predicted residues of Indanon over time (0 to 100 hours) using the DFOP model. The y-axis represents Measured & Predicted Residues (0.0 to 3.0), and the x-axis represents Time (0 to 100). The data points show a rapid initial decline followed by a slower approach to a residual level around 0.5.</p> <p>Residuals vs. Time JT333 (DFOP)</p> <p>This graph shows the residuals for the Indanon DFOP model over time (0 to 100 hours). The y-axis represents Residuals (-0.020 to 0.020), and the x-axis represents Time (0 to 100). The residuals are scattered around zero, indicating a good fit of the model to the data.</p>
Chula TFMP SFO	<p>Measured & Predicted Residues vs. Time JT333 (SFO)</p> <p>This graph shows the measured and predicted residues of TFMP over time (0 to 100 hours) using the SFO model. The y-axis represents Measured & Predicted Residues (0 to 5), and the x-axis represents Time (0 to 100). The data points show a rapid initial decline followed by a slower approach to a residual level around 0.5.</p> <p>Residuals vs. Time JT333 (SFO)</p> <p>This graph shows the residuals for the TFMP SFO model over time (0 to 100 hours). The y-axis represents Residuals (-0.2 to 0.5), and the x-axis represents Time (0 to 100). The residuals are scattered around zero, indicating a good fit of the model to the data.</p>
Chula TFMP FOMC	<p>Measured & Predicted Residues vs. Time JT333 (FOMC)</p> <p>This graph shows the measured and predicted residues of TFMP over time (0 to 120 hours) using the FOMC model. The y-axis represents Measured & Predicted Residues (0 to 5), and the x-axis represents Time (0 to 120). The data points show a rapid initial decline followed by a slower approach to a residual level around 0.5.</p> <p>Residuals vs. Time JT333 (FOMC)</p> <p>This graph shows the residuals for the TFMP FOMC model over time (0 to 120 hours). The y-axis represents Residuals (-0.20 to 0.10), and the x-axis represents Time (0 to 120). The residuals are scattered around zero, indicating a good fit of the model to the data.</p>

Chula TFMP DFOP	<p>Measured & Predicted Residues vs. Time JT333 (DFOP)</p> <p>This graph shows the measured and predicted residues of JT333 over time using the DFOP model. The y-axis represents 'Measured & Predicted Residues' from 0 to 5, and the x-axis represents 'Time' from 0 to 100. Data points are open circles, and a solid line represents the model fit. The residues decrease rapidly from approximately 2.5 at time 0 to near 0 by time 100.</p>	<p>Residuals vs. Time JT333 (DFOP)</p> <p>This graph shows the residuals for the DFOP model. The y-axis represents 'Residuals' from -0.08 to 0.08, and the x-axis represents 'Time' from 0 to 100. Data points are open circles, and a horizontal line at y=0 represents the zero residual line. The residuals are mostly within the range of -0.04 to 0.06.</p>
Goose river Indanon SFO	<p>Measured & Predicted Residues vs. Time JT333 (SFO)</p> <p>This graph shows the measured and predicted residues of JT333 over time using the SFO model. The y-axis represents 'Measured & Predicted Residues' from 0.0 to 2.5, and the x-axis represents 'Time' from 0 to 120. Data points are open circles, and a solid line represents the model fit. The residues decrease from approximately 2.0 at time 0 to about 0.5 at time 120.</p>	<p>Residuals vs. Time JT333 (SFO)</p> <p>This graph shows the residuals for the SFO model. The y-axis represents 'Residuals' from -0.6 to 0.5, and the x-axis represents 'Time' from 0 to 120. Data points are open circles, and a horizontal line at y=0 represents the zero residual line. The residuals range from approximately -0.5 to 0.2.</p>
Goose river Indanon FOMC	<p>Measured & Predicted Residues vs. Time JT333 (FOMC)</p> <p>This graph shows the measured and predicted residues of JT333 over time using the FOMC model. The y-axis represents 'Measured & Predicted Residues' from 0.0 to 2.5, and the x-axis represents 'Time' from 0 to 120. Data points are open circles, and a solid line represents the model fit. The residues decrease from approximately 2.0 at time 0 to about 0.5 at time 120.</p>	<p>Residuals vs. Time JT333 (FOMC)</p> <p>This graph shows the residuals for the FOMC model. The y-axis represents 'Residuals' from -0.20 to 0.10, and the x-axis represents 'Time' from 0 to 120. Data points are open circles, and a horizontal line at y=0 represents the zero residual line. The residuals range from approximately -0.15 to 0.07.</p>
Goose river Indanon DFOP	<p>Measured & Predicted Residues vs. Time JT333 (DFOP)</p> <p>This graph shows the measured and predicted residues of JT333 over time using the DFOP model. The y-axis represents 'Measured & Predicted Residues' from 0.0 to 2.5, and the x-axis represents 'Time' from 0 to 120. Data points are open circles, and a solid line represents the model fit. The residues decrease from approximately 2.0 at time 0 to about 0.5 at time 120.</p>	<p>Residuals vs. Time JT333 (DFOP)</p> <p>This graph shows the residuals for the DFOP model. The y-axis represents 'Residuals' from -0.15 to 0.10, and the x-axis represents 'Time' from 0 to 120. Data points are open circles, and a horizontal line at y=0 represents the zero residual line. The residuals range from approximately -0.10 to 0.07.</p>

Goose river Indanon HS	<p>Measured & Predicted Residues vs. Time JT333 (HS)</p> <p>This graph shows measured residues (open circles) and predicted residues (solid line) over time for JT333 (HS). The y-axis is 'Measured & Predicted Residues' ranging from 0.0 to 2.5. The x-axis is 'Time' ranging from 0 to 120. The predicted curve starts at approximately 2.4 and decreases to about 0.6 at time 120.</p>	<p>Residuals vs. Time JT333 (HS)</p> <p>This graph shows the residuals (open circles) over time for JT333 (HS). The y-axis is 'Residuals' ranging from -0.08 to 0.08. The x-axis is 'Time' ranging from 0 to 120. The residuals are scattered around zero, with a horizontal line at y=0.</p>
Goose river TFMP SFO	<p>Measured & Predicted Residues vs. Time JT333 (SFO)</p> <p>This graph shows measured residues (open circles) and predicted residues (solid line) over time for JT333 (SFO). The y-axis is 'Measured & Predicted Residues' ranging from 0.4 to 1.0. The x-axis is 'Time' ranging from 0 to 120. The predicted curve starts at approximately 0.9 and decreases to about 0.4 at time 120.</p>	<p>Residuals vs. Time JT333 (SFO)</p> <p>This graph shows the residuals (open circles) over time for JT333 (SFO). The y-axis is 'Residuals' ranging from -0.20 to 0.20. The x-axis is 'Time' ranging from 0 to 120. The residuals are scattered around zero, with a horizontal line at y=0.</p>
Goose river TFMP FOMC	<p>Measured & Predicted Residues vs. Time JT333 (FOMC)</p> <p>This graph shows measured residues (open circles) and predicted residues (solid line) over time for JT333 (FOMC). The y-axis is 'Measured & Predicted Residues' ranging from 0.4 to 1.0. The x-axis is 'Time' ranging from 0 to 120. The predicted curve starts at approximately 0.9 and decreases to about 0.4 at time 120.</p>	<p>Residuals vs. Time JT333 (FOMC)</p> <p>This graph shows the residuals (open circles) over time for JT333 (FOMC). The y-axis is 'Residuals' ranging from -0.15 to 0.15. The x-axis is 'Time' ranging from 0 to 120. The residuals are scattered around zero, with a horizontal line at y=0.</p>
Goose river TFMP DFOP	<p>Measured & Predicted Residues vs. Time JT333 (DFOP)</p> <p>This graph shows measured residues (open circles) and predicted residues (solid line) over time for JT333 (DFOP). The y-axis is 'Measured & Predicted Residues' ranging from 0.4 to 1.0. The x-axis is 'Time' ranging from 0 to 120. The predicted curve starts at approximately 0.9 and decreases to about 0.4 at time 120.</p>	<p>Residuals vs. Time JT333 (DFOP)</p> <p>This graph shows the residuals (open circles) over time for JT333 (DFOP). The y-axis is 'Residuals' ranging from -0.08 to 0.10. The x-axis is 'Time' ranging from 0 to 120. The residuals are scattered around zero, with a horizontal line at y=0.</p>

Summary of selected endpoint total system for IN-JT333

Table 8-219: Total system degradation modelling endpoints derived at level M-I for IN-JT333

System	FOCUS Step	Value(s)	Kinetic level and type
Bury Pond (TFMP)	Step 1-2	156	M-I, system decline DFOP/3.32
	Step 3	156	As no reliable fit was obtain from M-I, parent – metabolite, M-I system decline as default
Chatsworth (Indanone)	Step 1-2	32.4	M-I, system decline SFO
	Step 3	38.3	Value of 38.3 days obtained with M-I, HS-SFO with both label
Chatsworth (TFMP)	Step 1-2	45.6	M-I, system decline SFO
	Step 3	38.3	M-I, HS-SFO with both label, System Degradation
Chula (Indanone)	Step 1-2	101	M-I, system decline DFOP/3.32
	Step 3	101	As no reliable fit was obtain from M-I, parent – metabolite, M-I system decline as default (DFOP worst-case)
Chula (TFMP)	Step 1-2	15.1	M-I, system decline HS $DT_{90}/3.32$, (as 10% of maximum measured concentration reached)
	Step 3	15.1	As no reliable fit was obtain from M-I, parent – metabolite, M-I system decline as default
Goose River (Indanone)	Step 1-2	137.5	M-I, system decline Slow Phase HS (as 10% of maximum measured concentration not reached)
	Step 3	137.5	As no reliable fit was obtain from M-I, parent – metabolite, M-I system decline as default
Goose River (TFMP)	Step 1-2	--	M-I, No reliable fit
	Step 3	: --	M-I, No reliable fit
Geomean	STEP 1&2	60.3	n=6
	STEP 3	66.2	n=5

C. Metabolite IN-KT413

Parent –metabolite fit

A first attempt to fit data in a parent (best-fit)-all metabolite (SFO) model was done, but none of the fits resulted in an acceptable assessment (underestimation of peak). The visual fits are not reported here to keep document as clear as possible. All visuals are reported in appendix II.

Table 8-220: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-KT413 derived from indoxacarb water sediment studies

Study	Soil/Label	IN-KT413 via Indoxacarb Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction	
DuPont-8417	Bury Pond (Replicates)	24.4	81.0	16	0.5	DFOP-SFO
	Bury Pond (Indanone)	17.2	57.0	31	0.59	DFOP-SFO
	Bury Pond (TFMP)	36.0	119.7	14	0.44	DFOP-SFO
	Chatsworth (Replicates)	15.6	51.7	24	0.31	HS-SFO
	Chatsworth (Indanone)	44.8	148.7	51	0.10	HS-SFO
	Chatsworth (TFMP)	17.2	57.0	27	0.36	HS-SFO
DuPont-39061	Chula (Replicates)	29.9 ^a	99.2 ^a	20.9	0.95 ^a	SFO-SFO
	Chula (Indanone)	32.0 ^a	106.2 ^a	23.8	0.96 ^a	SFO-SFO
	Chula (TFMP)	28.4 ^a	94.5 ^a	22.1	0.94 ^a	SFO-SFO
	Goose River (Replicates)	24.1 ^a	80.1 ^a	13.1	0.98 ^a	HS-SFO
	Goose River (Indanone)	25.9 ^a	80.1 ^a	16.8	0.98 ^a	FOMC-SFO
	Goose River (TFMP)	25.5	84.7	11.2	0.99	SFO-SFO

^a Endpoint considered unreliable due to underestimation of peak and systematic error of residuals.

Fits from decline

Table 8-221: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-KT413 derived from indoxacarb water sediment studies

System	compartment	SFO				FOMC			DFOP			HS		
		DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Bury Pond	Total System (Indanone)	17.9	59.6	22	<0.05	12.4	100.2	16	12.9	625.3	p1 ns ^f ; p2 ns	9.8	79.01	p1 ns ^f ; p2 ns
	Total System (TFMP)	53.0	176.2	12	<0.05	42.3	656.1	10	38.9	1453.3	p1 ns ^f ; p2 ns	42.3	244.3	p1<0.05; p2<0.1
Chatsworth	Total System (Indanone)	23.4	77.9	13	<0.05	17.0	117.3	9	10.4	96.6	p1 ns ^f ; p2 ns	9.3	98.8	p1 ns ^f ; p2 ns
	Total System (TFMP)	12.7	42.2	25	<0.05	5.3	113.8	6	7.9	150.7	p1 ns ^f ; p2 ns	4.8	87.02	p1 ns ^f ; p2 ns

System	compartment	SFO				FOMC			DFOP			HS		
		DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	95% CI contains 0	DegT ₅₀	DegT ₉₀	p (t-test)	DegT ₅₀	DegT ₉₀	p (t-test)
Chula	Total System (Indanone)	23.6	78.5	18.4	<0.05	23.6	78.5	β no	23.6	78.5	p1=0.211; p2=0.134	23.6	78.5	p1=0.132; p2<0.05
	Total System (TFMP)	27.9	92.5	23.5	<0.05	27.9	92.5	β no	27.9	92.5	p1=0.170; p2=0.188	27.9	92.5	p1=0.170; p2<0.05
Goose River	Total System (Indanone)	20.6	68.5	4.7	<0.05	18.6	76.1	β yes	18.3	74.8	p1=0.215; p2<0.05	17.2	75.6	p1<0.05; p2<0.05
	Total System (TFMP)	22.7	75.5	4.3	<0.05	22.7	75.5	β no	22.7	75.5	p1<0.05; p2<0.05	23.8	72.7	p1<0.05; p2<0.05

Summary of selected endpoint total system for IN-KT413

Table 8-222: Total system degradation modelling endpoints derived at level M-I for IN-KT413

Compound	Level	System	Selected model	DegT ₅₀ (days)
IN-KT413	P-I	Bury Pond (Indanone)	M-I, system decline, FOMC DT ₉₀ /3.32	30.12
		Bury Pond (TFMP)	M-I, system decline,, SFO	53.0
		Chatsworth (Indanone)	M-I, system decline, SFO	23.4
		Chatsworth (TFMP)	M-I, system decline, FOMC DT ₉₀ /3.32	34.3
		Chula (Indanone)	M-I, system decline, SFO	23.6
		Chula (TFMP)	No data reliable	-
		Goose River (Indanone)	M-I, system decline, SFO	20.6
		Goose River (TFMP)	M-I, system decline, SFO	22.7
		Geomean		

D. Metabolite IN-KG433

Parent –all metabolite fit

A first attempt to fit data in a parent (best-fit)-all metabolite (SFO) model was done, but none of the fits resulted in an acceptable assessment. The visual fits are not reported here to keep document as clear as possible. All visuals are reported in appendix II.

Table 8-223: Summary of kinetics and goodness of fit statistics of M-I kinetics for IN-KG433 derived from indoxacarb water sediment studies

Study	Soil/Label	IN-KG433 via Indoxacarb Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction	
DuPont-8417	Bury Pond (Replicates)	177.6 ^a	589.9 ^a	60	0.03	DFOP-SFO
	Bury Pond (Indanone)	190.7 ^a	633.6 ^a	56	0.04	DFOP-SFO
	Bury Pond (TFMP)	151.2 ^a	502.2 ^a	70	0.03	DFOP-SFO
	Chatsworth (Replicates)	60.4 ^a	200.6 ^a	40	0.03	HS-SFO
	Chatsworth (Indanone)	2000 ^a	6644 ^a	26	0.01	HS-SFO
	Chatsworth (TFMP)	40.6 ^a	134.9 ^a	60	0.05	HS-SFO

^a Endpoints considered unreliable as significance test fails at P=0.10 level and unacceptable visual fit as shown by chi-square>15%

Fits from decline

Table 8-224: Summary of kinetics and goodness of fit statistics of M-I kinetics for IN-KG433 derived from indoxacarb water sediment studies

System	compartment	SFO				FOMC			DFOP			HS		
		Deg T ₅₀	Deg T ₉₀	χ^2	p (t-test)	Deg T ₅₀	Deg T ₉₀		Deg T ₅₀	Deg T ₉₀	p (t-test)	Deg T ₅₀	Deg T ₉₀	p (t-test)
Bury Pond	Total System and Sediment (TFMP)	17.8	59.2	33	<0.1	Not optimised			2.1	245.4	p1 ns; p2 ns	2.9	276.6	p1 ns; p2 ns
Chatsworth	Total System and Sediment (TFMP)	19.1	63.4	31	<0.05	11.7	154.7		12.4	970.4	p1 ns; p2 ns	14.2	1076	p1<0.05; p2 ns

ns : not significant

None of the models resulted in acceptable fits. The visual fits are not reported to keep document clear. Default DT₅₀ of 1000 days will be used in modelling.

Summary of selected endpoint total system for IN-KG433

Table 8-225: Total system degradation modelling endpoints derived at level M-I for IN-KG433

Compound	Level	System	Selected model	DegT ₅₀ (days)
IN-KG433	P-I	Bury Pond	No reliable fit from decline could be obtain	
		Chatsworth		
		Chula		
		Goose river		
		Geometric mean:	1000 (default)	

E. Metabolite IN-MK638

Parent –all metabolite fit

A first attempt to fit data in a parent (best-fit)-all metabolite (SFO) model was done, but none of the fits resulted in an acceptable assessment. The visual fits are not reported here to keep document as clear as possible. All visuals are reported in appendix II.

Table 8-226: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-MK638 derived from indoxacarb water sediment studies

Study	Soil/Label	IN-MK638 via IN-KT413 and MP819 Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction MP819>MK638	
DuPont-39061	Chula (Replicates)	212.6 ^a	706.1 ^a	4.3	1.00	SFO-SFO
	Chula (Indanone)	Not observed in Indanone Label				
	Chula (TFMP)	182.1 ^a	605.0 ^a	4.3	1.00	SFO-SFO
	GooseRiver Replicates)	139.1 ^b	462.0 ^b	68.0	1.00	HS-SFO
	GooseRiver (Indanone)	Not observed in Indanone Label				
	GooseRiver (TFMP)	28.6 ^b	95.0 ^b	62.4	1.00	SFO-SFO

^a Endpoints considered unreliable as significance test fails at P=0.10 level though good visual fit as shown by chi-square.

^b Endpoints considered unreliable as significance test fails at P=0.10 level and poor visual fit as shown by chi-square >15%.

Fits from decline

No decline was observed in any of the systems, so no fits from decline were made. Default DT50 of 1000 days is retained for modelling.

Summary of selected endpoint total system for IN-MK638

Table 8-227: Total system degradation modelling endpoints derived at level M-I for IN-MK638

Compound	Level	System	Selected model	DegT ₅₀ (days)
IN-MK638	P-I	Bury Pond	No reliable fit could be obtain	
		Chatsworth		
		Chula		
		Goose river		
		Geometric mean:	1000 (default)	

F. Metabolite IN-ML438

Parent –all metabolite fit

A first attempt to fit data in a parent (best-fit)-all metabolite (SFO) model was done, but none of the fits resulted in an acceptable assessment. The visual fits are not reported here to keep document as clear as possible. All visuals are reported in appendix II.

Table 8-228: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-ML438 derived from indoxacarb water sediment studies

Study	Soil/Label	IN-ML438 via IN-JT333, KT413, and KG433 Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction	
DuPont-8417	Chatsworth (Replicates)	11.6 ^a	38.7 ^a	30	0, 0, 0.54	HS-SFO
	Chatsworth (Indanone)	9.7 ^a	32.3 ^a	28	0.35, 0.37, 0.71	HS-SFO
	Chatsworth (TFMP)	22.8 ^a	75.9 ^a	53	0, 0, 0.31	HS-SFO

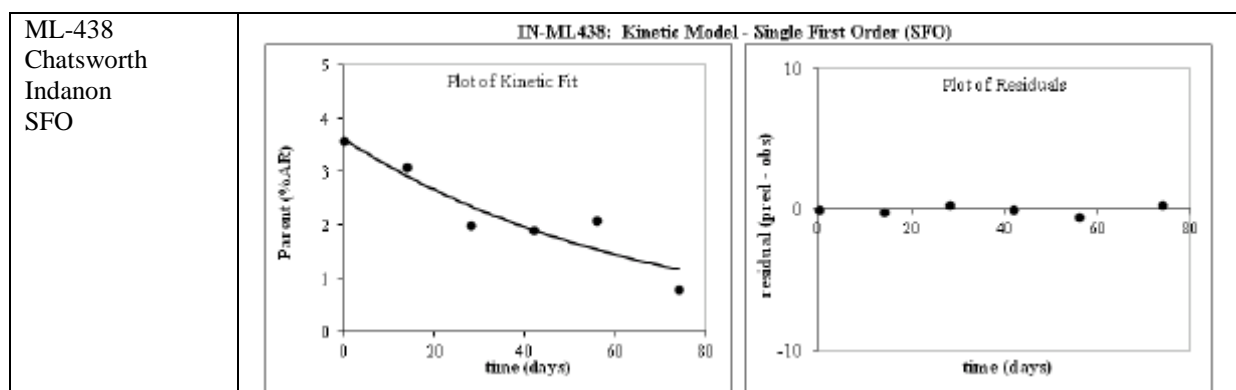
^a Endpoints considered unreliable as significance test fails at P=0.10 level and unacceptable visual fit as shown by chi-square>15%.

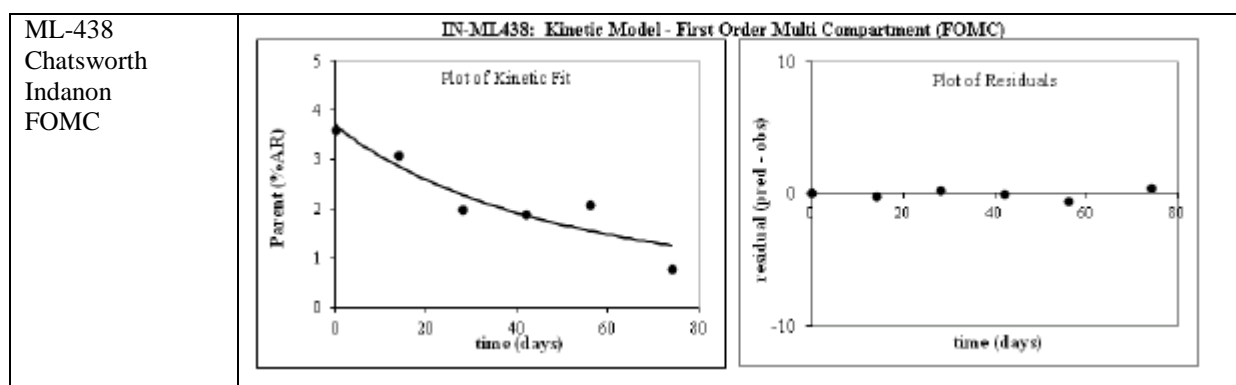
Fits from decline

Only data from Chatsworth Indanon label were fitted. No clear decline could be observed in the TFMP label.

Table 8-229: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-ML438 from decline derived from indoxacarb water sediment studies

Study	System	compartment	SFO				FOMC				Best Fit
			DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0	
DuPont-8417	Chatsworth	Total System and Sediment (Indanone)	45.4	150.9	11	<0.05	43.1	288.8	13		SFO

Visual fits



Summary of selected endpoint total system, water column and sediment phase for IN-MK638

Total system degradation modelling endpoints derived at level M-I for IN-MK638

Compound	Level	System	Selected model	DegT ₅₀ (days)
IN-MK638	P-I	Chatsworth (Indanon)	M-I, decline, SFO	45.4
		Chatsworth (TFMP)	M-I, no decline was observed, default DT50	1000
		Geomean		213.1

G. Metabolite IN-MS775

Parent –all metabolite fit

A first attempt to fit data in a parent (best-fit)-all metabolite (SFO) model was done. Results are provided below. Visual fits are not reported here to keep document as clear as possible. All visuals are reported in appendix II.

Table 8-230: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-MS775 derived from indoxacarb water sediment studies

From monosaccharide water sediment studies						
Study	Soil/Label	IN-MS775 via IN-JT333 and via KT413 and U8E24 ^d Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction	
DuPont-8417	Bury Pond (Replicates)	1000 ^a	3322 ^a	31	1.0	DFOP-SFO
	Bury Pond (Indanone)	1000 ^a	3322 ^a	30	1.0	DFOP-SFO
	Bury Pond (TFMP)	1000 ^a	3322 ^a	59	1.0	DFOP-SFO
	Chatsworth (Replicates)	14.7 ^a	48.8 ^a	38	0.46	HS-SFO
	Chatsworth (Indanone)	24.5 ^a	81.4 ^a	32	0.29	HS-SFO
	Chatsworth (TFMP)	13.4 ^a	44.6 ^a	53	0.69	HS-SFO
DuPont-39061	Chula (Replicates)	132.7 ^b	440.9 ^b	6.9	0.12	SFO-SFO
	Chula (Indanone)	66.4	220.6	7.7	0.13	SFO-SFO
	Chula (TFMP)	373.2 ^c	1239.8 ^c	8.4	0.12	SFO-SFO
	Goose River (Replicates)	40.1	133.1	6.8	0.11	HS-SFO
	Goose River (Indanone)	46.6	154.9	7.8	0.09	FOMC-SFO
	Goose River (TFMP)	35.6	118.1	6.1	0.12	SFO-SFO

^a Endpoints considered unreliable as significance test fails at P=0.10 level and unacceptable visual fit as shown by chi-square>15%.

^b Endpoints considered reliable as significance test fails only with P=0.11 and CI is very small; good visual fit as shown by chi-square <15%.

^c Endpoints considered unreliable as significance test fails at P=0.10 level.

^d Pathway considered in Allan (2014b).

Fits from decline

No clear decline was observed in any of the test systems.

Summary of selected endpoint total system, water column and sediment phase for IN-MK638**Table 8-231: Total system degradation modelling endpoints derived at level M-I for IN-MK638**

Compound	Level	System	Selected model	DegT ₅₀ (days)
IN-MS775	P-I	Bury Pond	M-I, no decline was observed in any system	
		Chatsworth		
		Chula		
		Goose river		
		Geometric mean:	1000 (default)	

H. Metabolite IN-MP819

A first attempt to fit data in a parent (best-fit)-all metabolite (SFO) model was done, but none of the fits resulted in an acceptable assessment. The visual fits are not reported here to keep document as clear as possible. All visuals are reported in appendix II.

Table 8-232: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-MP819 derived from indoxacarb water sediment studies

Study	Soil/Label	IN-MP819 via IN-KT413 Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction	
DuPont-8417	Bury Pond (Replicates)	1000 ^a	3322 ^a	27	0.19	DFOP-SFO
	Bury Pond (Indanone)	222.3 ^a	738.4 ^a	25	0.17	DFOP-SFO
	Bury Pond (TFMP)	1000 ^a	3322 ^a	38	0.24	DFOP-SFO
DuPont-39061	Chula (Replicates)	76.4 ^b	253.7 ^b	22.2	0.30	SFO-SFO
	Chula (Indanone)	110.6 ^a	367.3 ^a	21.2	0.24	SFO-SFO
	Chula (TFMP)	86.8 ^b	288.5 ^b	22.4	0.32	SFO-SFO
	Goose River (Replicates)	171.6	570.1	13.5	0.13	HS-SFO
	Goose River (Indanone)	557.9 ^c	1853.2 ^c	15.7	0.12	FOMC-SFO
	Goose River (TFMP)	97.4	323.4	12.8	0.14	SFO-SFO

^a Endpoints considered unreliable as significance test fails at P=0.10 level and unacceptable visual fit as shown by chi-square>15%.

^b Endpoints considered unreliable due to poor visual fit as shown by chi-square>15%.

^c Endpoints considered unreliable as significance test fails at P=0.10 level.

Fits from decline

No clear decline was observed in any of the test systems. Default DT50 of 1000 days is retained modelling.

Summary of selected endpoint total system, water column and sediment phase for IN-MS775

Table 8-233: Total system degradation modelling endpoints derived at level M-I for IN-MP819

Compound	Level	System	Selected model	DegT ₅₀ (days)
IN-MP819	P-I	Bury Pond	M-I, no decline was observed in any system	
		Chatsworth		
		Chula		
		Goose river		
		Geometric mean:	1000 (default)	

I. Metabolite IN UYG24

A first attempt to fit data in a parent (best-fit)-all metabolite (SFO) model was done, but none of the fits resulted in an acceptable assessment. The visual fits are not reported here to keep document as clear as possible. All visuals are reported in appendix II.

This metabolite was only seen in the Indanone labelled experiment.

Table 8-234: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-UYG24 derived from indoxacarb water sediment studies

Study	Soil/Label	IN-UYG24 via IN-KT413 and IN-U8E24 Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction	
DuPont-39061	Chula (Indanone)	18.5 ^a	61.6 ^a	109.9	0.66	SFO-SFO
	Goose River (Indanone)	3.8 ^a	12.6 ^a	62.8	0.32	FOMC-SFO

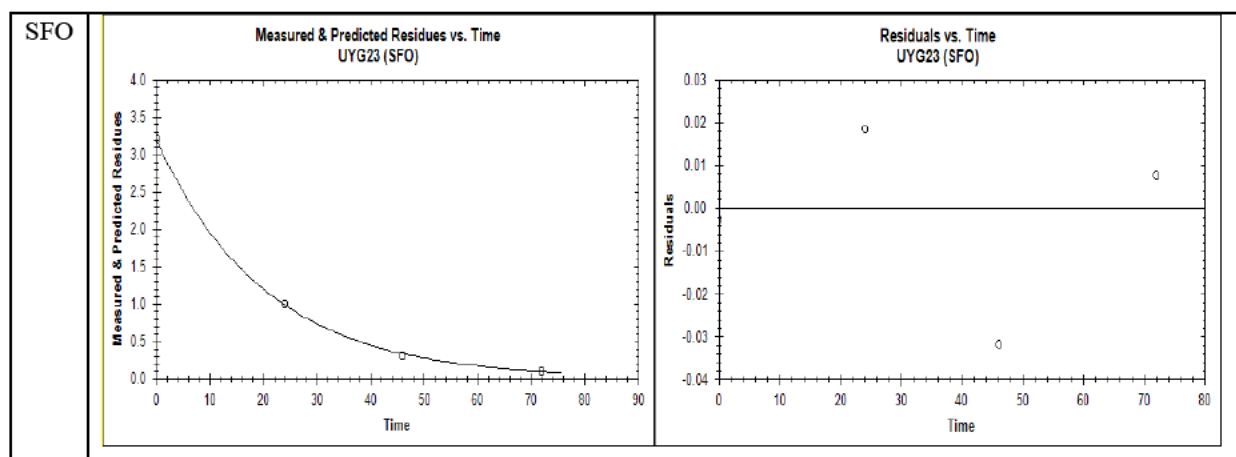
^a Endpoint considered unreliable as significance test fails at P=0.10 level and due to poor visual fit as shown by chi-square>15%.

Fits from decline

Fit from decline was performed in the Goose river system. No clear decline was observed in the Chula system.

Table 8-235: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-UYG24 derived from indoxacarb water sediment studies

Study	System	compartment	SFO			
			DegT ₅₀	DegT ₉₀	χ^2	p (t-test)
DuPont-39061	Goose River	Total System and Water (Indanone)	14.1	46.7	1.3	<0.05



Summary of selected endpoint total system, water column and sediment phase for IN-UYG24

Table 8-236: Total system degradation modelling endpoints derived at level M-I for IN-UYG24

Compound	Level	System	Selected model	DegT ₅₀ (days)
IN-UYG24	P-I	Chula	M-I, no decline was observed, default DT50	1000
		Goose river	M-I, decline, SFO	14.1
		Geometric mean:	118.7	

J. Metabolite IN-U8E24

Fit parent-metabolite

A first attempt to fit data in a parent (best-fit)-all metabolite (SFO) model was done, but none of the fits resulted in an acceptable assessment, due to lack of robustness of the data. The visual fits are not reported here to keep document as clear as possible. All visuals are reported in appendix II (metabolite code is HVV36 for this metabolite)

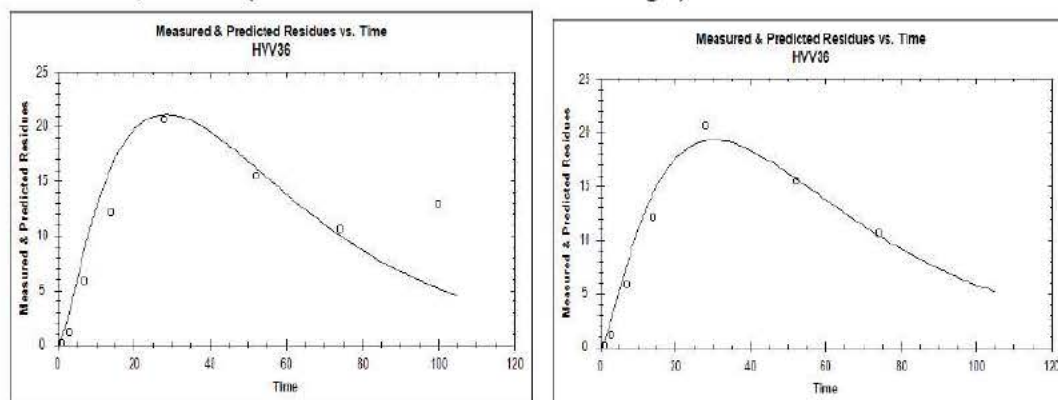
Table 8-237: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-U8E24 derived from indoxacarb water sediment studies

Study	Soil/Label	IN-U8E24 via IN-KT413 Best-Fit Kinetics				Best-Fit Kinetic Representation
		DegT ₅₀	DegT ₉₀	χ^2	Formation Fraction	
DuPont-39061	Chula (Indanone)	9.6	31.8	32.8	0.76	SFO-SFO
	Chula (TFMP)	6.8 ^a	22.5 ^a	27.3	0.68	SFO-SFO
	Goose River (Indanone)	12.6	42.0	11.1	0.88	FOMC-SFO
	Goose River (TFMP)	15.6	51.7	14.0	0.86	SFO-SFO

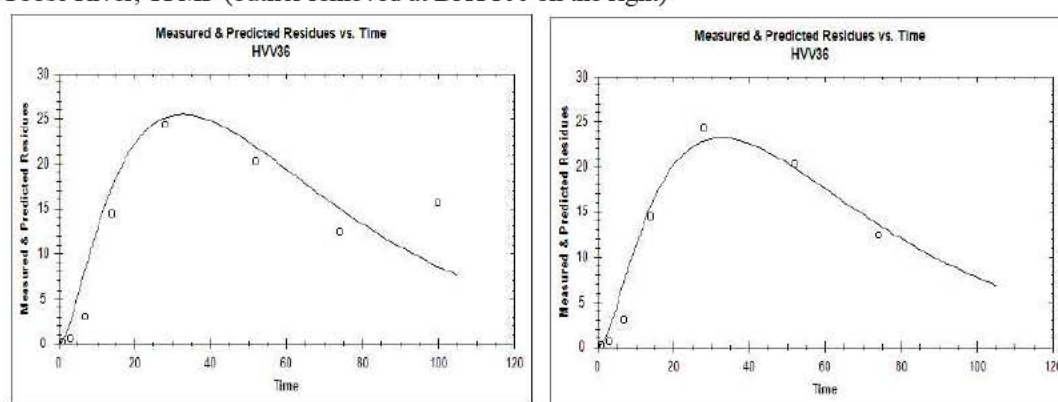
^a Endpoint considered unreliable as peak concentration is not met.

RMS notes that the fit for Goose River was done removing the last data point, considered as an outlier by applicant. As this was not further justified, RMS did not validate the fits (see below visual fits with ou without the outlier at DAT 100 removed)

Goose River, Indanon (outlier removed at DAT100 on the right)



Goose River, TFMP (outlier removed at DAT100 on the right)



Fit from decline

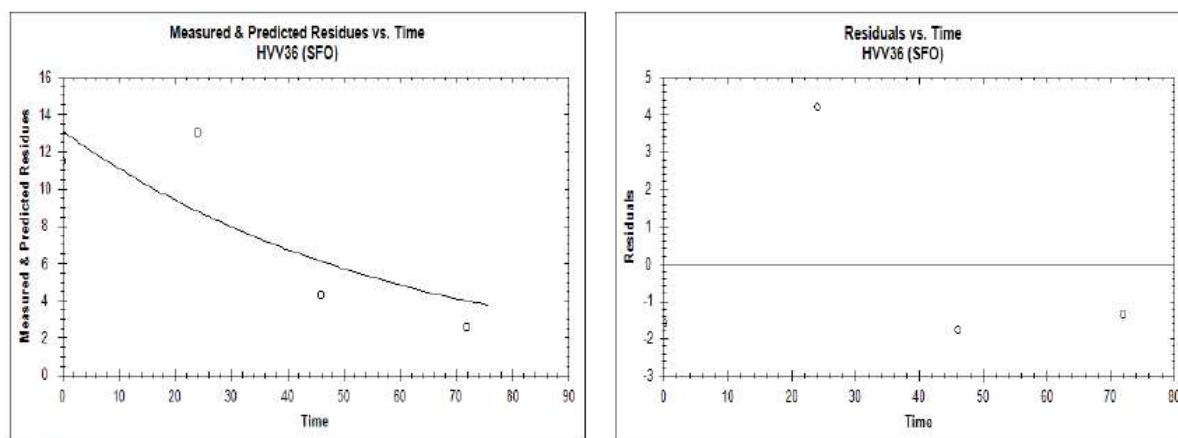
Table 8-238: Summary of kinetics and goodness of fit statistics of M-I Kinetics for IN-U8E24 derived from indoxacarb water sediment studies – Chula and Goose river system – Fit from decline.

compartment	SFO				FOMC			
	DegT ₅₀	DegT ₉₀	χ^2	p (t-test)	DegT ₅₀	DegT ₉₀	χ^2	95% CI contains 0
Chula Total System (Indanone)	41.7	138.6	26.2	0.117	41.7	138.6	32.7	β no
Chula Total System (TFMP)	23.9	79.5	10.8	<0.05	23.9	79.5	13.4	β no
Goose river Total System (Indanone)	80.0	265.6	10.1	<0.1	125.9	>>1000	9.2	β yes
Goose river Total System (TFMP)	82.5	273.9	10.5	<0.1	105.4	>1000	11.8	β yes

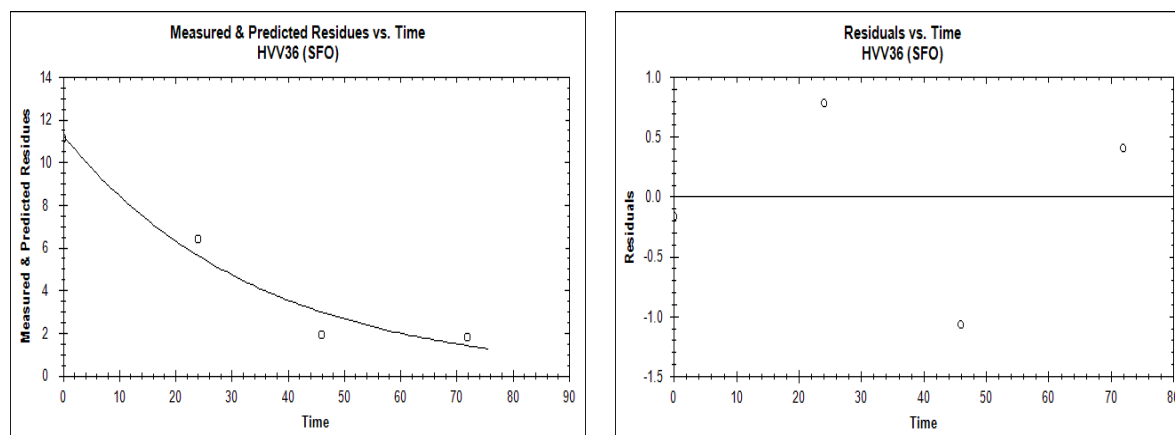
Only the data from Chula total system (TFMP labelled) could be fitted in a visually acceptable fit.

Visual fits (SFO only reported)

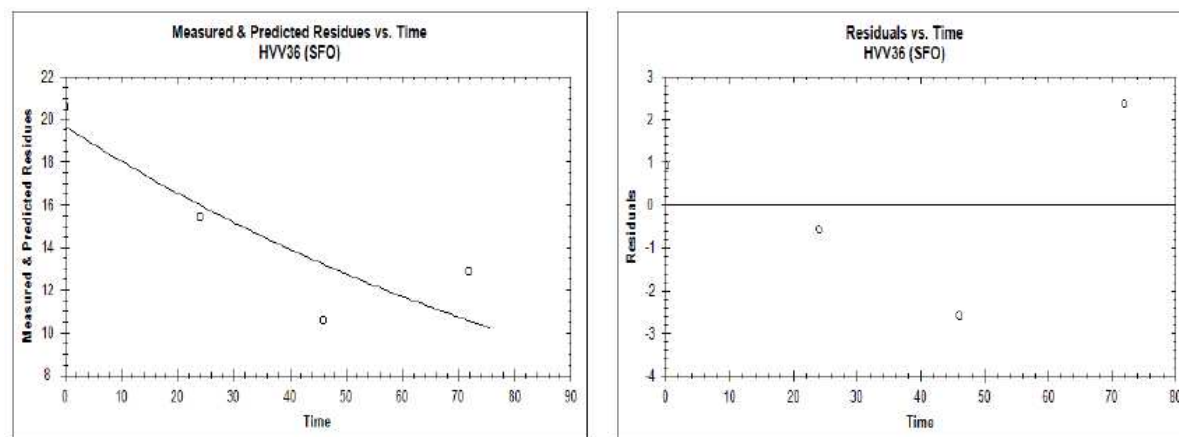
Optimised SFO kinetic model of IN-U8E24 Degradation in Chula: Water+sediment (total system), Indanon label, M-I



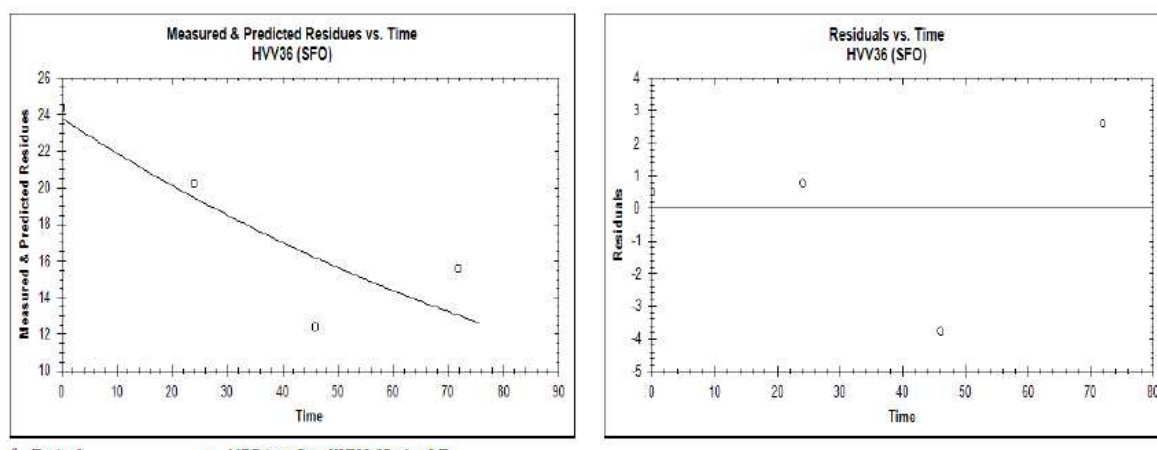
Optimised SFO kinetic model of IN-U8E24 Degradation in Chula: Water+sediment (total system), TFMP label, M-I



Optimised SFO kinetic model of IN-U8E24 Degradation in Goose River: Water+sediment (total system), Idanon label, M-I



Optimised SFO kinetic model of IN-U8E24 Degradation in Goose River: Water+sediment (total system), TFMP label, M-I



Summary of selected endpoint total system, water column and sediment phase for IN-U8E24

Table 8-239: Total system degradation modelling endpoints derived at level M-I for IN-U8E24

Compound	Level	System	Selected model	DegT ₅₀ (days)
IN-U8E24	P-I	Chula	M-I, decline, SFO	23.9
		Goose river	M-I, no reliable fit, default DT ₅₀	1000
		Geometric mean:	393.2	

Comments RMS 2016

Applicant provided a very complete kinetic evaluation of the data from the four water/sediment systems, and proposed persistence and modelling endpoint for indoxacarb and all its metabolites, for whole system and for water column and sediment compartment when possible. However, to simplify the approach, for metabolites, RMS focused on the evaluation of the modelling endpoints, since trigger endpoints are not used in the risk assessment.

On the more, as recommended in the FOCUS kinetic guidance document, only DT₅₀ from the whole system will be used for risk assessment at STEP 1-2. RMS thus also focused on the whole system decline for all metabolites, as no fits from parents could be obtained for any system and that only STEP 1-2 modelling were needed (with the exception of IN-JT333).

RMS considers that the following values should be used for PEC_{sw} modelling:

For indoxacarb

- At FOCUS Step 1-2: the geomean whole system DT₅₀ of 5.8 days will be used in whole system, water and sediment compartments, as recommended in the FOCUS kinetic guidance document.
- At FOCUS Step 3-4: Since no reliable fit was obtained at level P-II, RMS recommends the use of the geomean whole system DT₅₀ of 5.8 days in one compartment and the FOCUS default value of 1000 days for the other compartment.

Details of persistence endpoint for indoxacarb

Parent – persistence endpoint	Distribution (max in water 0.2 after 120 d. Max. sed 60.5 % after 1 d)
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Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Bury pond	7.9	8.1	20°C	4.8/97.6						DFOP
Chatsworth	6.9	7.6	20°C	2.8/9.3						HS
Chula	8.6	7.6	20°C	5.2/17.3						SFO
Gosse river	7.4	6.7	20°C	2.2/11.2						HS

^{a)} Measured in water

^{b)} Normalised using a Q10 of 2.58

Details of modelling endpoint for innoxacarb

Parent – modelling endpoints	Distribution (max in water 0.2 after 120 d. Max. sed 60.5 % after 1 d)									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Bury pond	7.9	8.1	20°C	4.8/97.6 (29.4*)						DFOP (DT ₉₀ /3.32)
Chatsworth	6.9	7.6	20°C	2.8/9.3 (2.8*)						HS (DT ₉₀ /3.32)
Chula	8.6	7.6	20°C	5.2/17.3						SFO
Gosse river	7.4	6.7	20°C	2.6/8.5						SFO
Geometric mean at 20°C ^{b)}				5.8						

^{c)} Measured in water

^{d)} Normalised using a Q10 of 2.58

* The DT₅₀ value into brackets corresponds to pseudo-SFO value calculated with method indicated in last column and included in the mean calculation

For IN-JT333

- At FOCUS Step 1-2: the geomean whole system DT₅₀ of 60.3 days (geomean including only whole system fits from decline only) will be used in for all compartments, as recommended in the FOCUS kinetic guidance document.
- At FOCUS Step 3: the geomean whole system DT₅₀ of 66.3 days (geomean including one fit from parent value) will be used in one compartment and the FOCUS default value of 1000 days for the other compartment.

Details of modelling endpoint for IN-JT333

Metabolite IN-JT333	Distribution (max in water 0 % after 100 d. Max. sed 25.7 % after 14 d). Max in total system 25.7 % after 14 days, kinetic formation fraction (k_f/k_{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Bury Pond (Indanone)	7.9	8.1	20° C	-		-		-		-
Bury Pond (TFMP)				73.1/519.1 (156*)		-			DFOP slow phase, from decline	
Chatsworth (both labels)	6.9	7.6	20° C	38.3/127.4		-		-		From parent, HS-SFO For step 3
Chatsworth (Indanone)	6.9	7.6	20° C	32.4/107.7		-		-		SFO, from decline For step 2
Chatsworth (TFMP)				45.6/151.5		-		-		SFO, from decline For step 2
Chula (Indanone)	8.6	7.6	20° C	10.1/336 (101*)		-		-		DFOP, from decline
Chula (TFMP)				7.1/50.2 (15.1*)		-		-		HS (DT ₉₀ /3.32), from decline
Goose River (Indanone)	7.4	6.7	20° C	11.4/302.1 (137.5*)		-		-		HS (slow phase), from decline
Goose River (TFMP)				-		-		-		
Geometric mean at 20°C ^{b)} (n=6) for step 1-2				60.3						
Geometric mean at 20°C ^{b)} (n=5) for step 3				66.2 (step 3)						

For all other metabolites

- At FOCUS Step 1-2: the geomean whole system DT₅₀ when available or default DT₅₀ of 1000 will be used for all compartments.

Details of modelling endpoint for all other metabolites:

Metabolite IN-KT413	Distribution (max in water 69.1% after 14 d. Max. sed 10.7 % after 14 d). Max in total system 83.0% after 7 days, kinetic formation fraction (k _f /k _{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ ²)	DT ₅₀ /DT ₉₀ water	St. (χ ²)	DT ₅₀ /DT ₉₀ sed	St. (χ ²)	Method of calculation
Bury Pond (Indanone)	7.9	8.1	20° C	12.4/100.2 (30.12*)		-		-		FOMC (DT ₉₀ /3.32), from decline
Bury Pond (TFMP)				53.0/176.2		-		-		SFO, from decline
Chatsworth (Indanone)	6.9	7.6	20° C	23.4/77.9		-		-		SFO, from decline
Chatsworth (TFMP)				5.3/113.8 (34.3*)		-		-		FOMC (DT ₉₀ /3.32), from decline
Chula (Indanone)	8.6	7.6	20° C	23.6/78.5		-		-		SFO, from decline
Chula (TFMP)				-		-		-		
Goose River (Indanone)	7.4	6.7	20° C	20.6/68.5		-		-		SFO, from decline
Goose River (TFMP)				22.7/75.5		-		-		SFO, from decline
Geometric mean at 20°C ^{b)}				28		-		-		

^{a)} Measured in [medium to be stated, usually calcium chloride solution or water]

^{b)} Normalised using a Q10 of 2.58

* The DT₅₀ value into brackets corresponds to pseudo-SFO value calculated with method indicated in last column and included in the mean calculation

Metabolite IN-KG433	Distribution (max in water 0 % after 102 d. Max. sed 7.7% after 14 d). Max in total system 7.7 % after 14 days. kinetic formation fraction (k_f/k_{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Bury pond	7.9	8.1	20° C	No reliable DT ₅₀		-		-		-
Chatsworth	6.9	7.6	20° C	No reliable DT ₅₀		-		-		-
Geometric mean at 20°C ^{b)}				1000 (default)						

Metabolite IN-ML438	Distribution (max in water 0 % after 102 d. Max. sed 3.6% after 28 d). Max in total system 3.6 % after 28 days. kinetic formation fraction (k_f/k_{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Bury pond	7.9	8.1	20° C	1000 (default)		-		-		-
Chatsworth	6.9	7.6	20° C	45.4/150.9		-		-		SFO, from decline
Geometric mean at 20°C ^{b)}				213.1						

Metabolite IN-MK638	Distribution (max in water 4.0 % after 100 d. Max. sed 5 % after 100 d). Max in total system 9 % after 100 days, and sill increasing at the end of the study. kinetic formation fraction (k_f/k_{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Chula	8.6	7.6	20° C	No reliable DT ₅₀		-		-		-
Gosse river	7.4	6.7	20° C	No reliable DT ₅₀		-		-		-
Geometric mean at 20°C ^{b)}				1000 (default)						

Metabolite IN-MP819	Distribution (max in water 0.4% after 52 d. Max. sed 21.3 % after 74 d). Max in total system 21.3% after 74 days, kinetic formation fraction (k_f/k_{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Bury pond	7.9	8.1	20° C	No reliable DT ₅₀		-		-		-
Chatsworth	6.9	7.6	20° C	No reliable DT ₅₀		-		-		-
Chula	8.6	7.6	20° C	No reliable DT ₅₀		-		-		-
Gosse river	7.4	6.7	20° C	No reliable DT ₅₀		-		-		-
Geometric mean at 20°C ^{b)}				1000 (default)						

Metabolite IN-U8E24	Distribution (max in water 10.5 % after 52 d. Max. sed 16.0 % after 28 d). Max in total system 24.3 % after 28 days, kinetic formation fraction (k_f/k_{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Chula	8.6	7.6	20° C	23.9/79.5		-		-		SFO, from decline
Gosse river	7.4	6.7	20° C	1000 (default)		-		-		-
Geometric mean at 20°C ^{b)}				393.2						

Metabolite IN-UYG24	Distribution (max in water 31.6 % after 52 d. Max. sed 0 % after 100 d). Max in total system 31.6 % after 52 days, kinetic formation fraction (k_f/k_{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Chula	8.6	7.6	20° C	1000 (default)		-		-		-
Gosse river	7.4	6.7	20° C	14.1/46.7		-		-		SFO, from decline
Geometric mean at 20°C ^{b)}				118.7						

Metabolite IN-MS775	Distribution (max in water 0 % after 100 d. Max. sed 14.7 % after 70 d). Max in total system 14.7 % after 70 days, kinetic formation fraction (k_f/k_{dp}): no reliable data									
Water / sediment system	pH water phase	pH sed ^{a)}	t. °C	DT ₅₀ /DT ₉₀ whole sys.	St. (χ^2)	DT ₅₀ /DT ₉₀ water	St. (χ^2)	DT ₅₀ /DT ₉₀ sed	St. (χ^2)	Method of calculation
Bury pond	7.9	8.1	20° C	No reliable DT ₅₀						
Chatsworth	6.9	7.6	20° C	No reliable DT ₅₀						
Chula	8.6	7.6	20° C	No reliable DT ₅₀		-		-		-
Gosse river	7.4	6.7	20° C	No reliable DT ₅₀		-		-		-
Geometric mean at 20°C ^{b)}				1000 (default)						

B.8.2.2.4. IRRADIATED WATER/SEDIMENT STUDY

Rapid hydrolysis and fast transfer from water to sediment phase are two major processes within natural environmental water/sediment conditions. Photodegradation was not expected to become significant and therefore an irradiated water/ sediment study was not conducted. Irradiated water/sediment studies are higher tier studies and were not required.

B.8.2.3. DEGRADATION IN THE SATURATED ZONE

No data submitted.

Modelling adequately assesses the potential for indoxacarb and its soil metabolites to move to the saturated zone (1 m depth). PEC_{gw} calculations show that indoxacarb (DPX-KN128) and its major and minor soil metabolites do not exceed 0.1 µg/L at a 1 m depth in the relevant FOCUS groundwater scenarios. Therefore, there is no scientific rationale for conducting degradation studies in the saturated zone with either indoxacarb or any of its degradation products.

B.8.2.4. SUMMARY OF FATE AND BEHAVIOUR IN WATER

The proposed degradation pathway of indoxacarb in irradiated and non-irradiated buffered systems is presented in Figure 11. The hydrolysis of indoxacarb in sterile buffer solutions is pH-dependent. At 20°C, indoxacarb (DPX-KN128) was stable at pH 4 and degraded at a moderate rate at pH 7 (DT_{50} of 17.6 days). At pH 9, degradation was the fastest (DT_{50} of 0.37 days at 20°C). The significant product detected in the sterile pH 7 and 9 sterile buffer samples was IN-KT413. At 20°C, IN-KT413 was detected at a maximum mean concentration of 66.9% AR and 99.1% AR from pH 7 and pH 9 samples, respectively. In the pH 7 samples, IN-KT413 can further undergo decarboxylation and rearrangement of the N-methylester group to form IN-MP819 with a maximum mean concentration of 11.8% AR at 20°C.

The aqueous photodegradation of indoxacarb was investigated in pH 5 buffer at 25°C under simulated sunlight (xenon arc light). Indoxacarb is rapidly degraded by photolysis in pH 5 sterile buffer (DT_{50} of approximately 3 days under continuous irradiation and 4.5 days when adjusted to sunlight-equivalent days). The major degradation products were IN-C0639 (maximum of 10.2% AR), IN-MA573 (maximum of 19.9% AR), IN-MH304 (maximum of 32.3% AR), IN-KB687 (maximum of 15% AR), IN-MF014 (maximum of 37.6% AR), and numerous minor components.

The aquatic degradation of indoxacarb was studied in the laboratory in four water/sediment systems. As in soil conditions, indoxacarb dissipates rapidly under water/sediment systems. The DT_{50} values of indoxacarb in four water/sediment systems ranged from 0.5 to 1.0 days in the water phase, 3.6 to 16.1 days in the sediment phase and 2.2 to 5.2 days in the total system.

The proposed major degradation pathway of indoxacarb in the four systems (two system from old study and two systems in new study) is demonstrated in Figure 12 where indoxacarb is basically degraded via 3 major pathways. The degradation pathway of indoxacarb in water was the same for all four systems and indoxacarb hydrolysed to form IN-KT413 as the most significant metabolite in water. In sediment (similar to aerobic soil condition), indoxacarb was transformed to IN-JT333/IN-KN125 (S-enantiomer of IN-JT333) via demethylation followed by N-decarboxylation, and to IN-KG433 via oxadiazine ring cleavage of indoxacarb. IN-KT413 underwent decarboxylation and rearrangement of the N-methylester group to form IN-MP819 in sediment. IN-KT413 degraded via demethylation N-decarboxylation to form IN-U8E24. IN-MP819 further degraded to IN-MK638 through oxadiazine ring opening and bridge cleavage. Decarboxylation and cleavage of IN-U8E24 led to the formation of the residue IN-MS775 and IN-UYG24, respectively. IN-JT333 could also be transformed to IN-MS775 via demethylation followed by decarboxylation.

The major degradation pathway between the old and the new study was similar. However, much more hydrolytical metabolite IN-KT413 was detected from the new study, which could be caused by the dose rate. The water/sediment system from previous study was dosed at a nominal rate of 0.5 µg/mL in water (greater than

the water solubility of indoxacarb, 0.2 µg/mL) and the dose rate for new study DuPont-39061 was 0.2 µg/mL in water (equal to the water solubility). When dosed at rates above solubility (DuPont-8417), the test material dissipated rapidly from the water phase of both systems (DT_{50} in water phase ranged from 0.5 to 0.6 days) with 55.1 to 62.5% AR indoxacarb extracted from sediment phase at Day 0, resulting in more metabolites formed in sediment including IN-JT333, IN-KG433, and IN-MS775. While dosed at the solubility of 0.2 µg/mL (DuPont-39061), a relatively slow transfer rate (DT_{50} in water phase ranged from 0.8 to 1.0 days) was observed from both systems with nearly 90% AR indoxacarb remained in water phase, resulting in significant hydrolytical metabolite IN-KT413 formed (maximum of 83.0% AR, with maximum of 74.7% AR in water), and then further degraded to IN-MP819, IN-U8E24, and transient water metabolite IN-UYG24.

While the rate of photolytic degradation of indoxacarb was rapid in sterile buffers (DT_{50} of approximately 3 days under continuous irradiation and 4.5 days in sunlight-equivalent days), the dissipation of indoxacarb from the water column in water/sediment systems was even more rapid (DT_{50} of 0.5-1.0 days). The rapid partitioning behaviour was expected since the average K_{oc} of indoxacarb was 5125 mL/g. The rapid partitioning into sediment would greatly decrease the amount of indoxacarb in the water column of a natural water body that would be available to undergo photolytic decomposition.

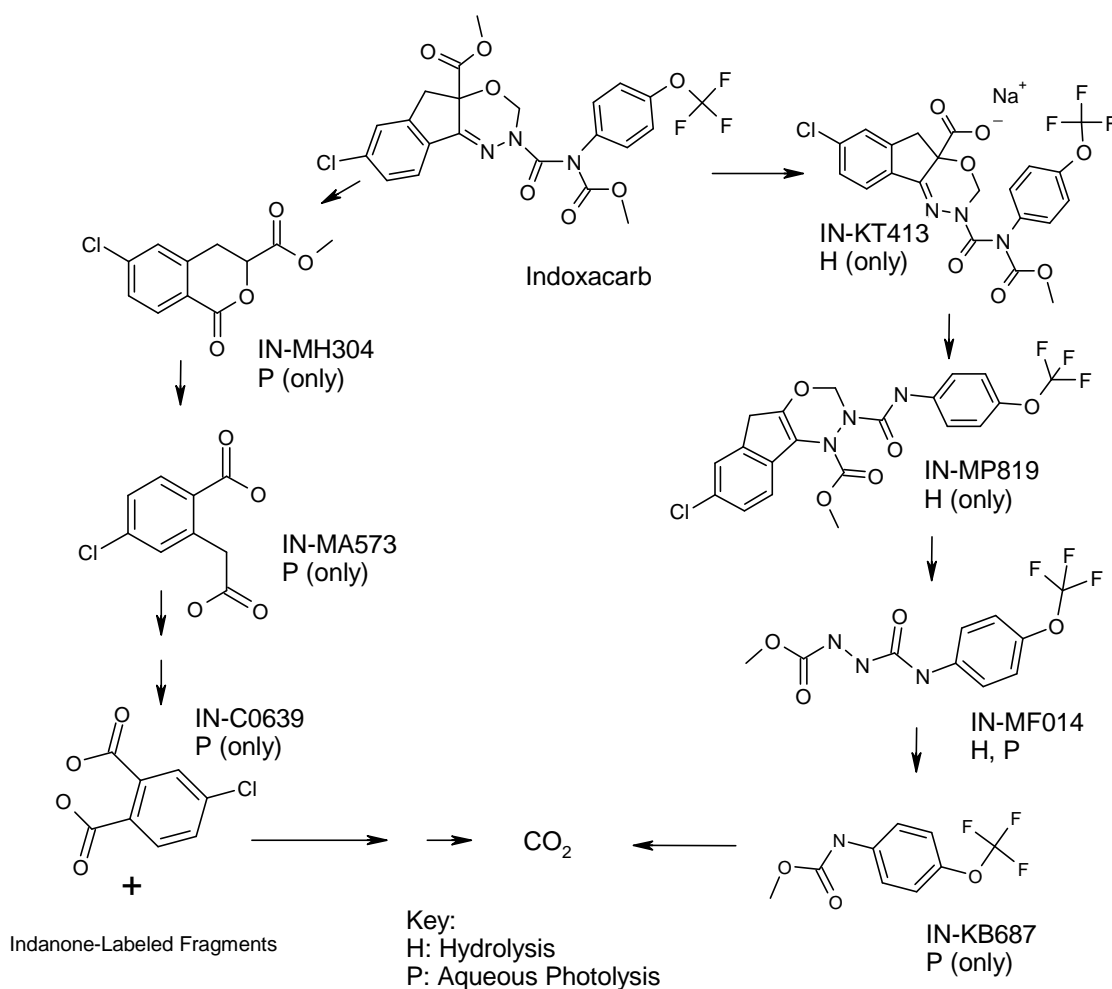
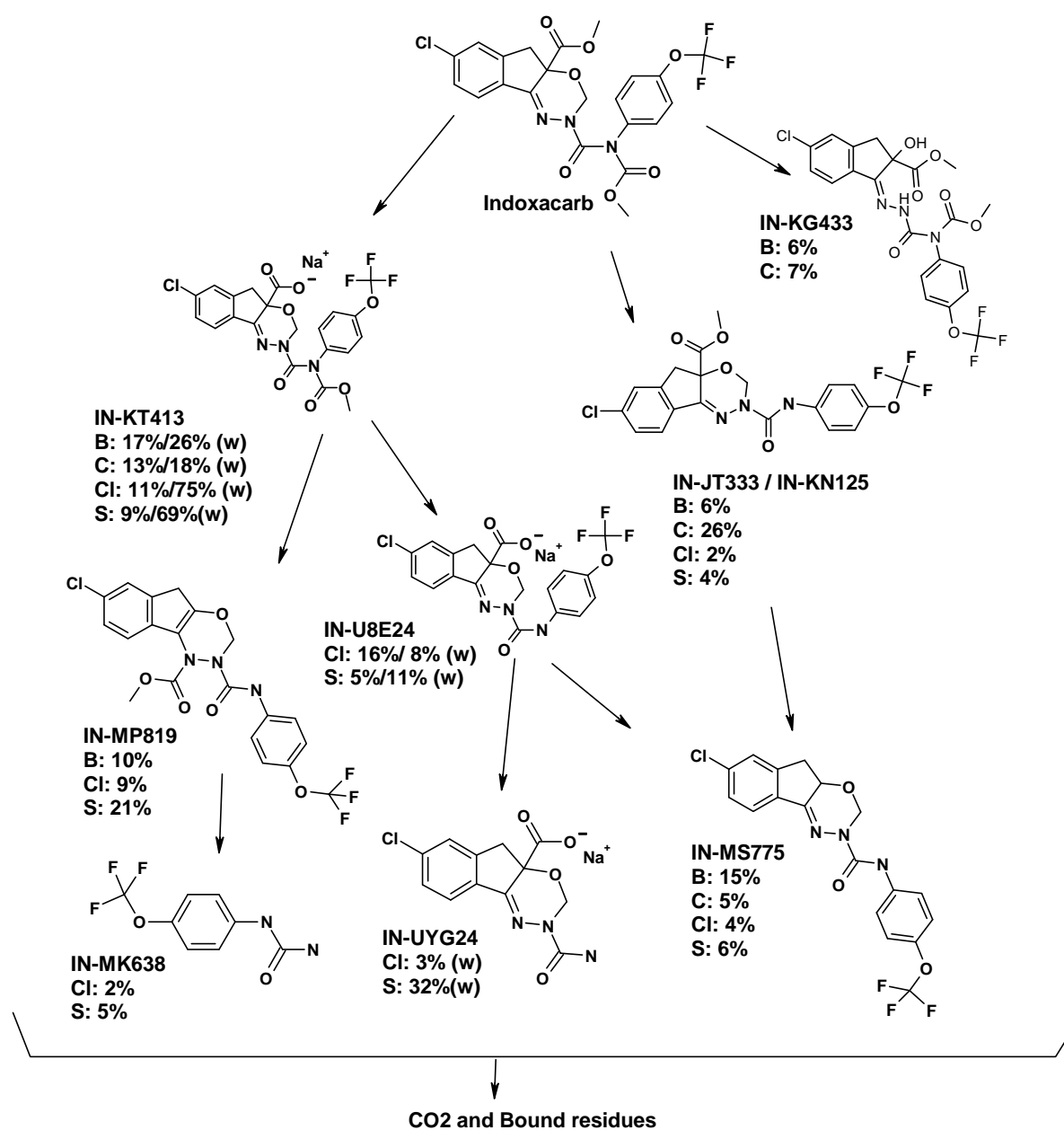


Figure 11: Proposed degradation pathway for indoxacarb in irradiated and non-irradiated buffers



Note:

B: Bury Pond Sediment

C: Chatsworth Sediment

Cl: Clay Loam (Goose River) sediment

S: Sand (Chula) Sediment

(w): the residue percentage with (w) represents that the residue is from water phase. For example, B: 17%/26%(w) indicates that 17% residue is from Bury Pond Sediment and 26% residue is from water phase

Minor metabolites (<5% AR in total system, IN-ML438 and IN-U8F52) were not shown in this proposed major degradation pathway

Figure 12: Proposed major degradation pathway for indoxacarb in water/sediment systems

B.8.3. FATE AND BEHAVIOUR IN AIR

B.8.3.1. IMPACT ON WATER TREATMENT PROCESSES

Information on the effect of water treatment processes on the nature of residues when surface water is abstracted for drinking water are needed according to Article 4(3) of Regulation (EC) No 1107/2009 which requires that 'it

shall have no immediate or delayed harmful effects on human health, including that of vulnerable groups, or animal health,....through drinking water (taking into account substances resulting from water treatment)'.

No information was provided by applicant. It is RMS and co-RMS opinion that a data gap should be identified. In the first instance, a consideration of the processes of ozonation and chlorination would appear appropriate. If an argumentation is made that concentrations at the point of abstraction for drinking water purposes will be low, this argumentation should cover metabolites predicted to be in surface water, as well as the active substance. Should this consideration indicate novel compounds might be expected to be formed from water treatment, the risk to human or animal health through the consumption of drinking water containing them would need to be addressed.

RMS however highlights that although this point is mentioned in Regulation 1107/2009 under Article 4, it is not further mentioned in Regulations 283/2013 and 284/2013 setting out the data requirements for active substances and plant protection products, respectively. No test method is proposed, and no guidance document is available on this issue.

B.8.3.2. ROUTE AND RATE OF DEGRADATION IN AIR

Neither indoxacarb (DPX-KN128) nor any of its principal degradation products have significant volatility. The vapour pressure of indoxacarb has been measured at 9.8×10^{-9} Pa at 20°C. The Henry's law constant for indoxacarb has been calculated as 6×10^{-5} Pa · m³/mol at 25°C (AMR 4169-96, summarised in Indoxacarb DAR, Volume 3, B2, 2000). The Henry's law constant for indoxacarb is lower than the Henry's law constant for water (3×10^{-2} Pa · m³/mol). Thus, indoxacarb can be considered to be non-volatile.

B.8.3.3. TRANSPORT VIA AIR

Since indoxacarb (DPX-KN128) and its metabolites are considered to be non-volatile, the transport via air of indoxacarb and its metabolites should not be expected as a meaningful pathway in environments, and thus no study has been conducted for this purpose.

B.8.3.4. LOCAL AND GLOBAL EFFECTS

Indoxacarb (DPX-KN128) is a chemical insecticide intended for use against plant pests of agricultural and horticultural significance, therefore its use should be very targeted and limited and thus should not produce any local or global effects. The vapour pressure and Henry's law constant of indoxacarb indicate that it has no potential to volatilize and therefore could not have any global warming potential (GWP), ozone depleting potential (ODP), photochemical ozone creation potential (POCP) or be expected to accumulated in the troposphere. The limited use of indoxacarb will not lead to significant production of nitrates or phosphates into soil and water, and thus has no acidification potential (AP) and eutrophication potential (EP).

B.8.4. RESIDUE DEFINITION FOR RISK ASSESSMENT

The following residue definition for risk assessment (pending additional information from applicant, see data gap proposed) and monitoring is proposed.

Soil

Definition for risk assessment: Indoxacarb, IN-JT333, IN-KG433, IN-KT413, IN-JU873, IN-ML438, IN-MK638, IN-KB687, IN-MK643, and IN-U8E24.

Definition for monitoring: Indoxacarb

Groundwater

Definition for exposure assessment: Indoxacarb, IN-JT333, IN-KG433, IN-KT413, IN-JU873, IN-ML438, IN-MK638, IN-KB687, IN-MK643, and IN-U8E24.

Definition for monitoring: Indoxacarb

Surface water

Definition for risk assessment: Indoxacarb, IN-JT333, IN-KG433, IN-KT413, IN-JU873, IN-ML438, IN-MK638, IN-KB687, IN-MK643, IN-MP819, IN-MS775, IN-U8E24, and IN-UYG24.

Definition for monitoring: Indoxacarb

Sediment

Definition for risk assessment: Indoxacarb, IN-JT333, IN-KG433, IN-KT413, IN-ML438, IN-MP819, and IN-MS775.

Definition for monitoring: Indoxacarb

Air Indoxacarb

B.8.5. MONITORING DATA CONCERNING FATE AND BEHAVIOUR OF THE ACTIVE SUBSTANCE, METABOLITES, DEGRADATION AND REACTION PRODUCTS

No data submitted. Monitoring studies with indoxacarb (DPX-KN128) were not conducted. The environmental characteristics of indoxacarb are such that monitoring studies would provide little, if any, useful information. Indoxacarb is strongly sorbed to soil and there is little likelihood that it could leach through the soil profile as demonstrated from the field dissipation studies. If it were to enter the aquatic environment, it would rapidly degrade prior to or after partitioning into sediment.

B.8.6. REFERENCES RELIED ON**B.8.6.1. LITERATURE REVIEW**

A literature review was provided by applicant and is summarized below.

Source

The applicant performed a literature search in 4 world wide databases (AGRICOLA, BIOSIS, CABA, CAPlus. This search considered studies published since 2005.

Relevance criteria

Table 8-240 lists the selection criteria applied to the results of the search for peer reviewed open literature relevant to indoxacarb and relevant metabolites.

Table 8-240: Relevance criteria

Data requirement(s) (indicated by the correspondent data point number(s) as identified in Commission Regulation (EU) 283/2013)	Criteria for relevance
All Data Points	1. The dose levels or application rates reflect the proposed GAP.
	2. The test system, target crop, or species are prescribed by Regulation (EC) No 1107/2009 or the relevance is explained if not standard.
	3. Well identified test material, including its purity and impurity profile, is described.
	4. Study design and/or execution are consistent with relevant study guidelines.
	5. The endpoint is relevant to an EU data point as prescribed by Regulations (EU) No 283/2013 and 284/2013
Fate and behaviour in the environment	6. The model is appropriate for European regulatory requirements.
	7. The input parameter selection is appropriate based on European regulatory requirements.
	8. The pedoclimatic conditions are appropriate.

Search strategies

The search ranged up to 10 years and within 6 months of the submission date. The initial search is a single concept search capturing all data points using search terms and synonyms for the active substance. If a large number of search results are returned from the single concept search making assessment for relevance impractical, a separate, focussed search is conducted for grouped data points. A separate single concept search is also conducted for each relevant metabolite.

Details of literature search strategy for indoxacarb and its metabolites

Indoxacarb/DPX-KN128 173584-44-6 (initial search)	
	Databases Searched in STN: AGRICOLA, BIOSIS, CABA, CAPlus, Efate
Justification for using these sources:	AGRICOLA – A bibliographic database containing selective worldwide coverage of agriculture and related fields. (4.2+ million records) BIOSIS - Contains information on life sciences, including biological and biomedical areas. (18.7+ million records) CABA – Covers worldwide literature from all areas of agriculture and related applied and life sciences. (5.3+ million records) CAPlus – Covers worldwide literature from all areas of chemistry, biochemistry, chemical engineering, and related sciences. (28.6+ million records)
Date of the search:	March 1, 2013
Date range of the search:	2005-2013
Search strategies used:	<ol style="list-style-type: none"> 1. 83120 s 173584-44-6, avant, avatar, indoxacarb mp, steward, activyl, explicit, provaunt 2. 39751 s L1 and 2005-2013/py 3. 38957 s L2 not p/dt 4. 2063 s L3 and (pesticide? Or herbicide? Or fungicide? Or insecticide?) 5. 1432 dup rem L4 (631 duplicates removed) 6. 88 s L5 and (WATER OR AIR OR SOIL OR GROUNDWATER) AND (EFATE OR FATE OR MODEL? OR SEDIMENT? OR LEACH? OR RUN-OFF OR RUNOFF OR HYDROLYSIS OR PHOTOLYSIS OR METABOL? OR EXPOSURE OR KINETIC? OR DEGRAD?)
Total number of original records retrieved:	88

Indoxacarb/DPX-KN128 173584-44-6 (Final search)

Databases Searched	Databases Searched in STN: AGRICOLA, BIOSIS, CABA, CAPlus, Efate
Date of the final search:	18 November 2014
Date range for final search	2012-2014
Search strategies used:	FILE 'CAPLUS, CABA, BIOSIS, AGRICOLA' ENTERED AT 15:43:50 ON 18 NOV 2014 L1 3481 S INDOXACARB OR KN128 OR 173584-44-6 L2 793 S L1 AND 2013-2014/PY L3 427 S L2 NOT P/DT L4 401 S L3 AND (PESTICID? OR HERBICID? OR INSECTICID? OR FUNGICID?) L5 280 DUP REM L4 (121 DUPLICATES REMOVED) L6 19 S L5 AND (WATER OR AIR OR SOIL OR GROUNDWATER) AND (EFATE OR FATE OR MODEL? OR SEDIMENT? OR LEACH? OR RUN-OFF OR RUNOFF OR HYDROLYSIS OR PHOTOLYSIS OR METABOL? OR EXPOSURE OR KINETIC? OR DEGRAD?)
Total number of original records retrieved:	19

DPX-JW062 144171-61-9 (Initial search)	
Data requirement(s) captured in the search	Databases Searched in STN: AGRICOLA, BIOSIS, CABA, CPlus, Efate
Justification for using these sources:	AGRICOLA – A bibliographic database containing selective worldwide coverage of agriculture and related fields. (4.2+ million records) BIOSIS - Contains information on life sciences, including biological and biomedical areas. (18.7+ million records) CABA – Covers worldwide literature from all areas of agriculture and related applied and life sciences. (5.3+ million records) CPlus – Covers worldwide literature from all areas of chemistry, biochemistry, chemical engineering, and related sciences. (28.6+ million records)
Date of the search:	March 1, 2013
Date range of the search:	2005-2013
Search strategies used:	<ol style="list-style-type: none"> 1. 3371 S 144171-61-9, DPX-JW062, Tornado 2. 2433 S L1 and 2005-2013/py 3. 1947 s L2 not p/dt 4. 1334 Dup rem l3 (613 duplicates removed) 5. 1016 s L4 and (pesticide? Or herbicide? Or fungicide? Or insecticide?) 6. 40 s L5 and (water or air or soil or groundwater) and (efate or fate or model? or sediment or leach? Or runoff or run(w)off or hydrolysis or photolysis or metabol? Or exposure or kinetic or degrad?)
Total number of original records retrieved:	40

IN-KN127 185608-75-7 (First search)	
Databases Searched	Databases Searched in STN: AGRICOLA, BIOSIS, CABA, CPlus, Efate
Justification for using this source:	<p>AGRICOLA – A bibliographic database containing selective worldwide coverage of agriculture and related fields. (4.2+ million records)</p> <p>BIOSIS - Contains information on life sciences, including biological and biomedical areas. (18.7+ million records)</p> <p>CABA – Covers worldwide literature from all areas of agriculture and related applied and life sciences. (5.3+ million records)</p> <p>CPlus – Covers worldwide literature from all areas of chemistry, biochemistry, chemical engineering, and related sciences. (28.6+ million records)</p>
Date of the search:	March 1, 2013
Date range of the search:	2005-2013/py
Search strategies used:	<ol style="list-style-type: none"> 1. 17 s 185608-75-7, DPX-KN127 2. 8 s L1 and 2005-2013/py 3. 8 Dup Rem L2 (0 duplicates removed)
Total number of records retrieved:	8

DPX-JW062 144171-61-9 and IN-KN127 185608-75-7 (Final search)	
Databases Searched	Databases Searched in STN: AGRICOLA, BIOSIS, CABA, CAPlus, Efaté
Date of the final search:	18 November 2014
Date range for final search	2012-2014
Search strategies used:	FILE 'CAPLUS, CABA, BIOSIS, AGRICOLA' ENTERED 15:59:38 ON 18 NOV 2014 L1 94 S 144171-61-9 OR JW062 L2 21 S 185608-75-7 OR KN127 L3 107 S L1 OR L2 L4 8 S L3 AND 2013-2014/PY L5 4 S L4 NOT P/DT L6 4 DUP REM L5 (0 DUPLICATES REMOVED)
Total number of records retrieved:	4

The published literature searches for DPX-KN128 and DPX-JW062 created a lot of duplicate responses which were removed giving the following grand totals:

Grand Total (both searches, DPX-KN128, IN-JW062 and IN-KN1127)	147 after removing duplicates 64
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Results – assessment of relevance

Literature included in the dossier are classified and summarized in the applicable data point in the Indoxacarb Renewal EU Renewal Dossier for indoxacarb. Studies are classified in the dossier in the following categories:

- Studies that provide data for establishing or refining risk assessment parameters. These studies are summarized in detail following the OECD guidance and can be found in an Appendix to the applicable data point.
- Studies that are relevant to the data requirement but only supply supplementary information for the risk assessment parameters. A justification for this decision is given in an Appendix to the applicable data point.
- Studies that remain of unclear relevance. An explanation as to why relevance of such studies could not be definitively determined is in an Appendix to the applicable data point.

No literature met the criteria for unclear relevance or relevance for environmental fate. Details are provided in the Table 8-241. Table 8-242 summarises the results of the selection process including the number of summary records and full text documents assessed.

Table 8-241: Literature search results: Environmental Fate

Data requirement(s) captured in the search	Number
Total number of summary records retrieved after all searches of peer-reviewed literature (excluding duplicates)	64
Number of summary records excluded from the search results after rapid assessment for relevance	64
Total number of full-text documents assessed in detail	0
Number of studies excluded from further consideration after detailed assessment for relevance	0
Number of studies not excluded for relevance after detailed assessment (<i>i.e.</i> , relevant studies and studies of unclear relevance)	0

Table 8-242 : Literature excluded by rapid assessment: Environmental Fate

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Ateyyat, M. A. [Reprint Author]	2005	Efficacy of some insecticides against the small red belted clearwing borer, <i>Synanthedon myopaeformis</i> (Borkh.) (Lepidoptera: Sessiidae), in apple orchards in Jordan.	Communications in Agricultural and Applied Biological Sciences	2
Li, Changfang; He, Qiang; Xu, Weisong; Yang, Qunhua; Jiang, Yanling; Li, Guiying	2005	Residue and dynamic degradation studies of indoxacarb in cabbage and soil	Nongyao Kexue Yu Guanli	2
Stevens, M. M.; Helliwell, S.; Hughes, P. A.	2005	Toxicity of <i>Bacillus thuringiensis</i> var. <i>Israelensis</i> formulations, spinosad, and selected synthetic insecticides to <i>Chironomus tepperi</i> larvae	Journal of the American Mosquito Control Association	2
Galvan, Tederson L.; Koch, Robert L.; Hutchison, William D.	2006	Toxicity of indoxacarb and spinosad to the multicolored asian lady beetle, <i>Harmonia axyridis</i> (Coleoptera: Coccinellidae), via three routes of exposure	Pest Management Science	2
Omote, M.; Harayama, K.; Sasaki, T.; Mochizuki, N.; Yamashita, H.	2006	Analysis of simultaneous screening for 277 pesticides in malt and beer by liquid chromatography with tandem mass spectrometry	Journal of the American Society of Brewing Chemists	2
Suess, Angelika; Bischoff, Gabriela; Mueller, Axel C. W.; Buhr, Liselotte	2006	Chemical and biological monitoring of the load of plant protection products and of zoocenoses in ditches of the orchard region "Altes Land"	Nachrichtenblatt des Deutschen Pflanzenschutzdienstes (Braunschweig, Germany)	2
Not given	2007	Indoxacarb; pesticide tolerance	Federal Register, Environmental Protection Agency EPA, Environmental Protection Agency, Washington, DC, MD, 20460-0001, USA	2
Mojtahedi, Mohammad Majid; Chalavi, Sohila; Ghassempour, Alireza; Tabar-Heydar, Kourosh; Sharif, Seyed Javad Ghotb; Malekzadeh, Maryam; Aboul-Enein, Hassan Y.	2007	Chiral separation of three agrochemical toxins enantiomers by high-performance liquid chromatography on a vancomycin crystalline degradation products-chiral stationary phase	Biomedical Chromatography	2
Muhammetoglu, A.; Uslu, B.	2007	Application of environmental impact quotient model to Kumluca region, Turkey to determine environmental impacts of pesticides	Water Science and Technology	10

Table 8-242 : Literature excluded by rapid assessment: Environmental Fate

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Andaloro, John T.; Portillo, Hector E.; Marcon, Paula G.; Barefoot, Aldos	2008	Indoxacarb's fit in global IPM programs	Abstracts of Papers, 236th ACS National Meeting, Philadelphia, PA, United States, August 17-21, 2008 (2008), AGRO-187. American Chemical Society: Washington, D. C. CODEN: 69KXQ2	2
Crossan, Angus N.; Kennedy, Ivan R.	2008	Calculation of pesticide degradation in decaying cotton gin trash	Bulletin of Environmental Contamination and Toxicology	2
Dong, Feng-shou; Cao, Qiao; Liu, Xin-gang; Zheng, Yong-quan; Li, Chong-jiu	2008	Enantiomeric separation of indoxacarb by HPLC with amylose chiral column	Huaxue Shiji	2
Hintzen, Emily P.; Lydy, Michael J.; Belden, Jason B.	2008	Occurrence and potential toxicity of pyrethroids and other insecticides in bed sediments of urban streams in central Texas	Environmental Pollution (Oxford, United Kingdom)	2
Roembke, Joerg; Waichman, Andrea V.; Garcia, Marcos V. B.	2008	Risk assessment of pesticides for soils of the Central Amazon, Brazil: comparing outcomes with temperate and tropical data	Integrated Environmental Assessment and Management	2, 10
Schenck, Frank J.; Brown, Amy N.; Podhorniak, Lynda V.; Parker, Alesia; Reliford, Michelle; Wong, Jon W.	2008	A rapid multiresidue method for determination of pesticides in fruits and vegetables by using acetonitrile extraction/partitioning and solid-phase extraction column cleanup	Journal of AOAC International	2
Warner, John; Yang, Rou-Ling; Scheffrahn, Rudolf H.	2008	Efficacy of selected bait and residual toxicants for control of bigheaded ants, Pheidole megacephala (Hymenoptera: Formicidae), in large field plots	Florida Entomologist	2
Zhou, Fengxia; Li, Pei	2008	Study on degradation dynamics of indoxacarb in the soil	Huanjing Kexue Yu Guanli	4
Not given	2009	Indoxacarb; pesticide tolerances	Federal Register, Environmental Protection Agency EPA, Office of Pesticide Programs, Environmental Protection Agency, Washington D. C., DC, 20460, USA	2

Table 8-242 : Literature excluded by rapid assessment: Environmental Fate

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Deihimfard, Reza; Zand, Eskandar; Soufizadeh, Saeid; Kambouzia, Jafar; Mirzaei Talarposhti, Reza; Ebrahimi, Meysam	2009	Evaluating the release-weighted risk of insecticides under rainy conditions: A case study in Iran	Archives of Agronomy and Soil Science	2
Karanjkar, A. S.; Naik, R. L.	2009	Acute toxicity: novel mode of pesticides on earthworm.	International Journal of Plant Protection	2
Rose, Gavin; Lane, Simon; Jordan, Robert	2009	The fate of fungicide and insecticide residues in Australian wine grape by-products following field application	Food Chemistry	2
Singh, J. P.; Jaiswal, A. K.; Monobrullah, Md.; Bhattacharya, A.	2009	Response of some selected insecticides on neuropteran predator (<i>Chrysopa lacciperda</i>) of lac insect (<i>Kerria lacca</i>)	Indian Journal of Agricultural Sciences	2
Spomer, Neil A.	2009	Environmental fate of chlorantraniliprole and indoxacarb termiticides and bioefficacy against eastern subterranean termites, <i>Reticulitermes flavipes</i> (Kollar)	URCE:	2
Bernard, Martina B.; Cole, Peter; Kobelt, Amanda; Home, Paul A.; Altmann, James; Wratten, Stephen D.; Yen, Alan L.	2010	Reducing the impact of pesticides on biological control in Australian vineyards: pesticide mortality and fecundity effects on an indicator species, the predatory mite <i>Euseius victoriensis</i> (Acari: Phytoseiidae)	Journal of Economic Entomology	2
Haith, Douglas A.	2010	Ecological Risk Assessment of Pesticide Runoff from Grass Surfaces	Environmental Science & Technology	2
Kafle, Lekhnath; Wu, Wen-Jer; Shih, Cheng-Jen [Reprint Author]	2010	A new fire ant (Hymenoptera: Formicidae) bait base carrier for moist conditions.	Pest Management Science	2
Karanasios, Evangelos; Tsiropoulos, Nikolaos G.; Karpouzas, Dimitrios G.; Ehaliotis, Constantinos	2010	Degradation and Adsorption of Pesticides in Compost-Based Biomixtures as Potential Substrates for Biobeds in Southern Europe	Journal of Agricultural and Food Chemistry	2, 4
Karanasios, Evangelos; Tsiropoulos, Nikolaos G.; Karpouzas, Dimitrios G.; Ehaliotis, Constantinos	2010	Degradation and Adsorption of Pesticides in Compost-Based Biomixtures as Potential Substrates for Biobeds in Southern Europe	Journal of agricultural and food chemistry	2, 4

Table 8-242 : Literature excluded by rapid assessment: Environmental Fate

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Schummer, Claude; Mothiron, Elodie; Appenzeller, Brice M. R.; Wennig, Robert; Millet, Maurice	2010	Gas/particle partitioning of currently used pesticides in the atmosphere of Strasbourg (France)	Air Quality, Atmosphere & Health	4
Zhou, Ruqiong; Fan, Hangqing; He, Binyuan	2010	Residues of pesticides and antibiotics in a mangrove area suffering aquaculture drainages	Guangxi Zhiwu	2
Not given	2011	Reasoned opinion of EFSA: review of the existing maximum residue levels (MRLs) for indoxacarb according to Article 12 of Regulation (EC) No 396/2005.	EFSA Journal, European Food Safety Authority (EFSA), Parma, Italy.; Italy, European Food Sa	2
Haith, Douglas A.	2011	National Assessment of Pesticide Runoff Loads from Grass Surfaces	Journal of Environmental Engineering (Reston, VA, United States)	4, 10, 11
Schafer, Ralf B.; Pettigrove, Vincent; Rose, Gavin; Allinson, Graeme; Wightwick, Adam; von der Ohe, Peter C.; Shimeta, Jeff; Kuhne, Ralph; Kefford, Ben J.	2011	Effects of pesticides monitored with three sampling methods in 24 sites on macroinvertebrates and microorganisms	Environmental Science & Technology	2
Su, Jianfeng; Lu, Shengyu; Chen, Jing; Chen, Jinxing; Liang, Zhen; Liu, Jianjun	2011	Multi-residue determination of 289 pesticides in garlic by gas chromatography and gas chromatography/mass spectrometry	Sepu	2
Yang, Liu; Chen, Shaohua; Hu, Meiyang; Hao, Weining; Geng, Peng; Zhang, Yanbo	2011	Biodegradation of carbofuran by Pichia anomala strain HQ-C-01 and its application for bioremediation of contaminated soils	Biology and Fertility of Soils	2
Not given	2012	Indoxacarb; pesticide tolerances	Federal Register, Environmental Protection Agency EPA, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, Washington, DC, 20460-0001, USA	2

Table 8-242 : Literature excluded by rapid assessment: Environmental Fate

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Dewey, K. A.; Gaw, S. K.; Northcott, G. L.; Lauren, D. R.; Hackenburg, S.	2012	The effects of copper on microbial activity and the degradation of atrazine and indoxacarb in a New Zealand soil	Soil Biology & Biochemistry	2
Ibtissem, Sbartaï; Houria, Berrebbah; Rachid, Rouabhi; Hana, Sbartaï; Reda, Djebar Mohammed	2012	Induction of oxidative stress in a freshwater ciliated microorganism <i>Paramecium</i> sp., after treatment with Indoxacarb	BioTechnology: An Indian Journal	2, 4
Karanasios, Evangelos; Karpouzas, Dimitrios G.; Tsiropoulos, Nikolaos G.	2012	Key parameters and practices controlling pesticide degradation efficiency of biobed substrates	Journal of Environmental Science and Health, Part B: Pesticides, Food Contaminants, and Agricultural Wastes	2, 4
Madureira, Fernando Diniz; Oliveira, Fabiano Aurelio da Silva; de Souza, Wesley Robert; Pontelo, Ana Paula; Goncalves de Oliveira, Mauro Lucio; Silva, Gilsara	2012	A multi-residue method for the determination of 90 pesticides in matrices with a high water content by LC-MS/MS without clean-up	Food Additives & Contaminants, Part A: Chemistry, Analysis, Control, Exposure & Risk Assessment	2
Mota-Sanchez, David; Cregg, Bert; Hoffmann, Eric; Flore, James; Wise, John C.	2012	Penetrative and Dislodgeable Residue Characteristics of ¹⁴ C-Insecticides in Apple Fruit	Journal of Agricultural and Food Chemistry	2
Mudaraddi, Tulasigiriappa Y.; Potadar, Rajeev R.; Kaliwal, Basappa B.	2012	Indoxacarb induces liver oxidative stress in Swiss albino mice	European Journal of Experimental Biology	2
Neoh, Kok-Boon; Hu, Jian; Yeoh, Boon-Hoi; Lee, Chow-Yang	2012	Toxicity and horizontal transfer of chlorantraniliprole against the Asian subterranean termite <i>Coptotermes gestroi</i> (Wasmann): effects of donor:recipient ratio, exposure duration and soil type	Pest Management Science	2
Quarcoo, Franklin Y.; Hu, Xing Ping; Appel, Arthur G.	2012	Effects of non-repellent termiticides on the tunneling and walking ability of the eastern subterranean termite (Isoptera: Rhinotermitidae)	Pest Management Science	2

Table 8-242 : Literature excluded by rapid assessment: Environmental Fate

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Sun, Dali; Qiu, Jing; Wu, Yijun; Liang, Hongwu; Liu, Chenglan; Li, Li	2012	Enantioselective Degradation of Indoxacarb in Cabbage and Soil under Field Conditions	Chirality	2,4
Bundschuh, Mirco; Zubrod, Jochen P.; Klemm, Patricia; Elsaesser, David; Stang, Christoph; Schulz, Ralf	2013	Effects of peak exposure scenarios on <i>Gammarus fossarum</i> using field relevant pesticide mixtures	Ecotoxicology and Environmental Safety	2
Elsaesser, David; Stang, Christoph; Bakanov, Nikita; Schulz, Ralf	2013	The Landau stream mesocosm facility: pesticide mitigation in vegetated flow-through streams	Bulletin of Environmental Contamination and Toxicology	4, 10, 11
Leskey, Tracy C.; Wright, Starker E.; Saguez, Julien; Vincent, Charles	2013	Impact of insecticide and fungicide residue contact on plum curculio, <i>Conotrachelus nenuphar</i> (Herbst), mobility and mortality: implications for pest management	Pest Management Science	2
Liao, Dan; Ma, Ming; Liang, Ji; Chen, Li-hua; Chen, Jiu-xing; Huang, Hua; Yang, Cheng-hu	2013	Determination of indoxacarb residue in rice field by HPLC	Jingxi Huagong Zhongjianti	2
Lopez-Velasco, G.; Tomas-Callejas, A.; Diribsa, D.; Wei, P.; Suslow, T. V.	2013	Growth of <i>Salmonella enterica</i> in foliar pesticide solutions and its survival during field production and postharvest handling of fresh market tomato	Journal of Applied Microbiology	2
Peng, Xiao; Gong, Dao-xin	2013	Residual dynamics of indoxacarb in paddy field	Nongyao	2
Reemtsma, Thorsten; Alder, Lutz; Banasiak, Ursula	2013	Emerging pesticide metabolites in groundwater and surface water as determined by the application of a multimethod for 150 pesticide metabolites	Water Research	10, 11
Schaefer, Ralf B.; Gerner, Nadine; Kefford, Ben J.; Rasmussen, Jes J.; Beketov, Mikhail A.; de Zwart, Dick; Liess, Matthias; von der Ohe, Peter C.	2013	How to Characterize Chemical Exposure to Predict Ecologic Effects on Aquatic Communities?	Environmental Science & Technology	2
Sun DaLi; Pang JunXiao; Qiu Jing; Li Li; Liu ChengLan; Jiao BiNing; Sun, D. L.; Pang, J. X.; Qiu, J.; Li, L.; Liu, C. L.; Jiao, B. N.	2013	Enantioselective degradation and enantiomerization of indoxacarb in soil.	Journal of Agricultural and Food Chemistry	4

Table 8-242 : Literature excluded by rapid assessment: Environmental Fate

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Wang, Jing; Liu, Zheng-zheng; Zhong, Guang-jian	2013	Determination of carbamates in soil and sediment using UPLC-MS/MS	Zhongguo Huanjing Jiance	2
Wong, Hywel; Haith, Douglas A.	2013	Volatilization of pesticides from golf courses in the United States: mass fluxes and inhalation health risks	Journal of Environmental Quality	2
Zhang, Xin-zhong; Luo, Feng-jian; Chen, Zong-mao; Liu, Guang-ming; Lou, Zheng-yun; Wang, Fang; Wu, Lu-chao	2013	Residue determination of epoxiconazole, indoxacarb and difenoconazole in tea, tea infusion and soil using ultra high performance liquid chromatography coupled with tandem mass spectrometry	Fenxi Huaxue	2
Fantke, Peter; Gillespie, Brenda W.; Juraske, Ronnie; Jolliet, Olivier	2014	Estimating Half-Lives for Pesticide Dissipation from Plants	Environmental Science & Technology	10, 11
Fenoll, J.; Vela, N.; Garrido, I.; Perez-Lucas, G.; Navarro, S.	2014	Abatement of spinosad and indoxacarb residues in pure water by photocatalytic treatment using binary and ternary oxides of Zn and Ti	Environmental Science and Pollution Research	2, 4
Liang, Hongwu; Qiu, Jing; Wang, Chengju; Li, Xuefeng; Qiu, Lihong; Zhou, Zhiqiang	2014	Enantioselectivity bioaccumulation and toxic effects of indoxacarb in zebrafish (<i>Danio rerio</i>)	Abstracts of Papers, 248 th ACS National Meeting & Exposition, San Francisco, CA, United States, August 10-14, 2014 (2014), AGRO-649. American Chemical Society: Washington, D. C. CODEN: 69SZG4	2
Nowell, Lisa H.; Norman, Julia E.; Moran, Patrick W.; Martin, Jeffrey D.; Stone, Wesley W.	2014	Pesticide Toxicity Index-A tool for assessing potential toxicity of pesticide mixtures to freshwater aquatic organisms	Science of the Total Environment	2
Zhang YuPing; Hu DeYu; Ling HuRong; Zhong Lei; Huang AnXiang; Zhang KanKan; Song BaoAn; Zhang, Y. P.; Hu, D. Y.; Ling, H. R.; Zhong, L.; Huang, A. X.; Zhang, K. K.; Song, B. A.	2014	Comparative study of the selective degradations of two enantiomers in the racemate and an enriched concentration of indoxacarb in soils.	Journal of Agricultural and Food Chemistry	4

Table 8-242 : Literature excluded by rapid assessment: Environmental Fate

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Zhang YuPing; Zhang KanKan; Song BaoAn; Ling HuRong; Li ZhiNing; Li MeiChuan; Hu DeYu; Zhang, Y. P.; Zhang, K. K.; Song, B. A.; Ling, H. R.; Li, Z. N.; Li, M. C.; Hu, D. Y.	2014	Enantiomeric separation of indoxacarb on an amylose-based chiral stationary phase and its application in study of indoxacarb degradation in water.	Biomedical Chromatography	2, 4
Zhang, Xinzhong; Luo, Fengjian; Lou, Zhengyun; Lu, Meiling; Chen, Zongmao	2014	Simultaneous and enantioselective determination of cis-epoxiconazole and indoxacarb residues in various teas, tea infusion and soil samples by chiral high performance liquid chromatography coupled with tandem quadrupole-time-of-flight mass spectrometry	Journal of Chromatography A	2

RMS (2016)

Applicant was requested to provide more detailed of the assesment relevance and the criteria used to exclude the following studies, and to provide their abstracts.

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Zhou, Fengxia; Li, Pei	2008	Study on degradation dynamics of indoxacarb in the soil	Huanjing Kexue Yu Guanli	4
ABSTRACT: Indoxacarb is a broad-spectrum, effective, low-toxic, less-persistent and carbamic pesticide. In this paper, we analyzed the residue and degradation dynamics of indoxacarb in the soil using gas chromatog. and field test method. We found that indoxacarb was quickly degraded in the soil and the degradation curve was conformed to the first-order dynamic equation. The half-life of indoxacarb is 7.6 days in the soil. The results indicated that indoxacarb could be quickly degraded in the environment and was safe for the production.				
Detailed reason for non-inclusion (4). Only collected 1-15 cm surface soil samples with no run-off or leaching informtion. No complete data of other conditions such as the weather or irrigation, soil properties and verification of application. No metabolites were monitored.				

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Sun, Dali; Qiu, Jing; Wu, Yijun; Liang, Hongwu; Liu, Chenglan; Li, Li	2012	Enantioselective Degradation of Indoxacarb in Cabbage and Soil under Field Conditions	Chirality	2,4

ABSTRACT: The enantioselective degradation of indoxacarb in cabbage and soil has been investigated in Beijing and Anhui under open conditions. Indoxacarb enantiomers in samples were extracted with acetonitrile, cleaned up by florisil SPE column, separated on high performance liquid chromatography with a cellulose-tris-(3, 5-dimethylphenylcarbamate)-based chiral stationary phase (CDMPC-CSP), and determined by a photodiode array detector. The validation of the developed method by fortification rac-indoxacarb in cabbage and soil showed good accuracy and precision. The results of field trials indicated that the dissipation of indoxacarb enantiomers followed pseudo-first-order kinetics or first-order kinetics in cabbage and soil at two locations. The half-lives of two enantiomers in cabbage ranged from 2.8 to 4.6d which were shorter than those in soil ranging from 23 to 35d. The changes of enantiomeric fraction values proved that enantioselective degradation of indoxacarb happened in cabbage and soil. The (-)-indoxacarb showed faster degradation in the Beijing cabbage, whereas in the Anhui cabbage, (+)-indoxacarb preferentially degraded. In soil, preferential degradation of (+)-indoxacarb was observed at two locations. Chirality 24:628633, 2012. (c) 2012 Wiley Periodicals, Inc.

Detailed reason for non-inclusion (2, 4). The HPLC method was not validated. It has been well established that the chiral column can separate the R- and S- Indoxcarb isomer but the chiral column maynot separate the indoxacarb from its metabolites in the chiral column without method optimization. The authors should have used the reverse phase HPLC to isolate the indoxacarb peak before using the chiral separation for quantitaion. Furthermore, no metabolites were used to check the chiral separations of metabolites from the parent enantiomers. Therefore, the conclusion on enantioelective metabolism is questionable.

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
Sun DaLi; Pang JunXiao; Qiu Jing; Li Li; Liu ChengLan; Jiao BiNing; Sun, D. L.; Pang, J. X.; Qiu, J.; Li, L.; Liu, C. L.; Jiao, B. N.	2013	Enantioselective degradation and enantiomerization of indoxacarb in soil.	Journal of Agricultural and Food Chemistry	4
<p>ABSTRACT: In this study, the enantioselective degradation and enantiomerization of indoxacarb were investigated in two soils under nonsterilized and sterilized conditions using a chiral OD-RH column on a reversed-phase HPLC. Under nonsterilized conditions, the degradation of indoxacarb in two soils was enantioselective. In acidic soil, the half-lives of R-(–)- and S-(+)-indoxacarb were 10.43 and 14.00 days, respectively. Acidic soil was preferential to the degradation of R-(–)-indoxacarb. In alkaline soil, the half-lives of R-(–)- and S-(+)-indoxacarb were 12.14 and 4.88 days, respectively. S-(+)-Indoxacarb was preferentially degraded. Under sterilized conditions, approximately 5–10% of the initial concentration degraded after 75 days of incubation in acidic soil, whereas in alkaline soil, approximately half of the initial concentration degraded due to chemical hydrolysis under alkaline conditions. Enantiomerization was also discovered in acidic and alkaline soils. The results showed that mutual transformation existed between two enantiomers and that S-(+)-indoxacarb had a significantly higher inversion rate to R-(–)-indoxacarb than its antipode.</p>				
Reason for non-inclusion (4). This publication was not included for the same reason as described above in response 2.				

Author(s)	Year	Title	Source	Reason(s) for non-inclusion
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Zhang YuPing; Zhang KanKan; Song BaoAn; Ling HuRong; Li ZhiNing; Li MeiChuan; Hu DeYu; Zhang, Y. P.; Zhang, K. K.; Song, B. A.; Ling, H. R.; Li, Z. N.; Li, M. C.; Hu, D. Y.	2014	Enantiomeric separation of indoxacarb on an amylose-based chiral stationary phase and its application in study of indoxacarb degradation in water.	Biomedical Chromatography	2, 4
<p>ABSTRACT: Direct semipreparative enantioseparation of indoxacarb was performed on a semipreparative Chiralpak IA column using normal-phase high-performance liquid chromatography (HPLC) with n-hexane–isopropanol–ethyl acetate (70:20:10) mixture as mobile phase. Degradation of indoxacarb (2.33S + 1R) and its two enantiopure isoforms in three aqueous buffer solutions and four water samples collected from natural water sources was then elucidated by HPLC analysis on Chiralpak IA column. Degradation of all three indoxacarbs complied with first-order kinetics and demonstrated linearity with regression coefficients $R^2 > 0.88$. Indoxacarb (2.33S + 1R) underwent enantioselective degradation in river water, rain water, and buffer solution of pH 7.0. Enantiopure S-(+)-indoxacarb and R-()-indoxacarb were both found to be configurationally stable in water.</p>				
Reason for non-inclusion (2, 4). This publication was not included for the same reason as described above in response 2.				

Applicant's reasons for non inclusion are agreed by RMS.

B.8.6.2. REFERENCE RELIED ON

Data Point	Author (s)	Year	Title Compagny 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	Spare, W.C.	1997	Aerobic soil metabolism of DPX-MP062, an ~3:1 mixture of DPX-KN128 and IN-KN127 Agriseach, Inc. AMR 3633-95 Published: No	N	N		DuPont	Yes, in the 2000 DAR.
CA, 7.1.1.1	Singles S.K.	1997	Aerobic soil metabolism of DPX-MP062, an ~3:1 mixture of DPX-KN128 and IN-KN127 Agriseach, Inc. AMR 3633-95, Supplement No. 1 Published: No	N	N		DuPont	Yes, in the 2000 DAR.
CA, 7.1.1.1	Mellor, S.J.	2003	¹⁴ C-DPX-MP062 (a 3:1 mixture of DPX-KN128 and IN-KN127): Aerobic soil metabolism Huntingdon Life Sciences Ltd. DuPont-8516 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.1.1	Singles, S.K.	2002	Aerobic soil metabolism of ¹⁴ C-DPX-JW062 DuPont Experimental Station AMR 2803-93, Revision No. 1 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.1.1	Singles, S.K.	2003	Measurement of the enantiomeric ratio of IN-JT333 in soil DuPont Stine-Haskell Research Center	N	N		DuPont	Yes, in the 2005 DAR addendum 3..

			DuPont-12971 Published: No					
CA, 7.1.1.2 /01	Allan, J.	2015	¹⁴ C-Indoxacarb (DPX-KN128): Anaerobic degradation in soil ABC Laboratories, Inc. (Missouri) DuPont-35049 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier.	DuPont	No, submitted for the purpose of renewal
CA, 7.1.1.3	Berg, D.S.	1997	Photodegradation of radiolabeled DPX-JW062, a racemic mixture of DPX-KN128 and IN-KN127, on soil under simulated sunlight DuPont Experimental Station AMR 2818-93 Published: No	N	N		DuPont	Yes, in the 2000 DAR.
CA, 7.1.2/0 1	Partsch, S., Khanijo, I., Price, K., Ball, M.	2015	Degradation of indoxacarb and its metabolites IN-JT333 (IN-KN125), IN-JU873, IN-KB687, IN-KG433, IN-KT413, IN-MK638, IN-MK643, IN-ML438, IN-MP819, IN-MS775, IN-UYG24, IN-U8E24, and IN-U8F52 in soil and water/sediment systems - kinetic calculations following Focus kinetics Dr. Knoell Consult GmbH DuPont-34821 EU GLP: No Published: No	N	N		DuPont	No, submitted for the purpose of renewal
CA, 7.1.2.1 .1	Rhodes, B.C.	1997	Degradation rates of DPX-MP062 in soil DuPont Experimental Station AMR 4251-96 Published: No	N	N		DuPont	Yes, in the 2000 DAR.

CA, 7.1.2.1 .1	Smyser, B.P.	2002	Degradation rates of DPX-MP062 in soil DuPont Experimental Station AMR 4251-96, Supplement No. 1 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .1	Mellor, S.J.	2003	¹⁴ C-DPX-MP062 (a 3:1 mixture of DPX-KN128 and IN-KN127): Aerobic soil metabolism Huntingdon Life Sciences Ltd. DuPont-8516 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .1	Singles, S.K.	2002	Aerobic soil metabolism of ¹⁴ C-DPX-JW062 DuPont Experimental Station AMR 2803-93, Revision No. 1 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .1	Spare, W.C.	1997	Aerobic soil metabolism of DPX-MP062, an ~3:1 mixture of DPX-KN128 and IN-KN127 Agriseach, Inc. AMR 3633-95 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .2	Aikens, P.J.	2002	Degradation rates of [¹⁴ C]IN-KG433 in five soils Huntingdon Life Sciences Ltd. DuPont-8117 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .2	Caldwell, E.	2002	Degradation rates of [¹⁴ C]IN-MK643 in five soils Huntingdon Life Sciences Ltd. DuPont-9783 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .2	Hatzenbeler , C.J.	2002	Rates of degradation of [¹⁴ C]IN-MK638 in five soils Ricerca Biosciences, LLC DuPont-10278 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.

CA, 7.1.2.1 .2	Lentz, N.R.	2003	Rates of degradation of [¹⁴ C]IN-KT413 in three soils Ricerca Biosciences DuPont-10499 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .2	Mellor, S.J.	2002	Degradation rates of [¹⁴ C]IN-JU873 in five soils Huntingdon Life Sciences Ltd. DuPont-8137 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .2	Singles, S.K.	2002	Rate of degradation and estimated K _{oc} of IN-ML438 in soil DuPont Stine-Haskell Research Center DuPont-11433 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .2	Singles, S.K.	2003	Measurement of the enantiomeric ratio of IN-JT333 in soil DuPont Stine-Haskell Research Center DuPont-12971 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.2.1 .2/01	Allan, J.	2012	¹⁴ C-IN-KB687: Rate of degradation in five aerobic soils ABC Laboratories, Inc. (Missouri) DuPont-31717 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.1.2.1 .2/02	Allan, J.	2014	Rate of degradation of ¹⁴ C-IN-ML438 in five aerobic soils ABC Laboratories, Inc. (Missouri) DuPont-36691 GLP: Yes	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data	DuPont	No, submitted for the purpose of renewal

			Published: No			protection has not expired at the time of submission of this dossier		
CA, 7.1.2.1.2/03	Clark, B.	2014	¹⁴ C-IN-JT333: Rate of degradation in five aerobic soils ABC Laboratories, Inc. (Missouri) DuPont-35168 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.1.2.1.3/01	Allan, J.	2015	¹⁴ C-Indoxacarb (DPX-KN128): Anaerobic degradation in soil ABC Laboratories, Inc. (Missouri) DuPont-35049 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.1.2.1.4/01	Allan, J.	2015	¹⁴ C-Indoxacarb (DPX-KN128): Anaerobic degradation in soil ABC Laboratories, Inc. (Missouri) DuPont-35049 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.1.2.2.1/01	Doig, A.	2015a	The field soil dissipation of indoxacarb (DPX-KN128) following a single application to bare ground - Italy - 2012 Charles River Laboratories (UK) DuPont-34346	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously	DuPont	No, submitted for the purpose of renewal

			GLP: Yes Published: No			protected the period of data protection has not expired at the time of submission of this dossier		
CA, 7.1.2.2.1/02	Doig, A.	2015b	The field soil dissipation of indoxacarb (DPX-KN128) following a single application to bare ground - northern Germany - 2012 Charles River Laboratories (UK) DuPont-34892 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.1.2.2.1/03	Doig, A.	2015c	The field soil dissipation of indoxacarb (DPX-KN128) following a single application to bare ground - north Spain - 2012 Charles River Laboratories (UK) DuPont-34324 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.1.2.2.1/04	Doig, A.	2015d	The field soil dissipation of indoxacarb (DPX-KN128) following a single application to bare ground - north France - 2012 Charles River Laboratories (UK) DuPont-34323 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.1.2.2.1/05	Woodmans ey, L.	2014	Freezer storage stability of indoxacarb (DPX-KN128) and metabolites (IN-MK643, IN-MK638, IN-KB687, IN-KT413, IN-KG433, IN-JU873 and IN-JT333) in soils	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been	DuPont	No, submitted for the purpose of renewal

			Charles River Laboratories (UK), Charles River (France), Charles River Laboratories (Spain) DuPont-35167 GLP: Yes Published: No			protected or if previously protected the period of data protection has not expired at the time of submission of this dossier		
CA, 7.1.3.1.1	Smyser, B.P.	2002	Batch equilibrium study of DPX-JW062 (a racemic mixture of DPX-KN128 and IN-KN127) and IN-JT333 DuPont Experimental Station, Harris Laboratories Inc. AMR 3489-95, Revision No. 1 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.3.1.2	Caldwell, E.	2002	Adsorption/desorption of [¹⁴ C]IN-MK643, a metabolite of indoxacarb, in five soils Huntingdon Life Sciences Ltd. DuPont-9784 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.3.1.2	Hatzenbeler, C.J.	2002	Adsorption/desorption of [¹⁴ C]IN-KG433, a metabolite of indoxacarb, in five soils Ricerca LLC DuPont-6408, Revision No. 2. Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.3.1.2	Hatzenbeler, C.J.	2002	Adsorption/desorption of [¹⁴ C]IN-JU873, a metabolite of indoxacarb, in five soils Ricerca Inc. (USA) DuPont-6407 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.1.3.1.2	Herczog, K.J.S.	2002	Adsorption/desorption of [¹⁴ C]IN-MK638, a metabolite of indoxacarb, in five soils Ricerca Biosciences, LLC DuPont-10279 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA,	Walsh, K.J.	2003	Adsorption/desorption of [¹⁴ C]IN-KT413, a	N	N		DuPont	Yes, in the 2005

7.1.3.1 .2			metabolite of indoxacarb, in four soils Ricerca Biosciences, LLC DuPont-10500 Published: No					DAR addendum 3.
CA, 7.1.3.1 .2/01	Allan, J.	2012	¹⁴ C-IN-KB687: Batch equilibrium (adsorption/desorption) in five soils ABC Laboratories, Inc. (Missouri) DuPont-31718 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.1.3.1 .2/02	Allan, J.	2015	[¹⁴ C]IN-ML438: Batch equilibrium (adsorption/desorption) in five soils ABC Laboratories, Inc. (Missouri) DuPont-36692 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.2.1.1 /01	Clark, B.	2015	Hydrolysis of ¹⁴ C-Indoxacarb (DPX-KN128) in buffer solutions at pH 4, 7, and 9 ABC Laboratories, Inc. (Missouri) DuPont-35853, Revision No. 1 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.2.1.2 /01	Singles, S.K.	2003	Photodegradation of DPX-KN128 in pH 5 buffer and natural water by simulated sunlight DuPont Stine-Haskell Research Center DuPont-12943	N	N		DuPont	No, submitted for the purpose of renewal

			GLP: No Published: No					
CA, 7.2.2.1 /01	Tunink, A.	2014	DPX-KN128: Determination of ready biodegradability using the CO ₂ evolution method ABC Laboratories, Inc. (Missouri) DuPont-36501 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.2.2.2 /01	Allan, J.	2014	DPX-KN128: Aerobic mineralization in surface water ABC Laboratories, Inc. (Missouri) DuPont-34820 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this dossier	DuPont	No, submitted for the purpose of renewal
CA, 7.2.2.3	Shaw, D.	2002	¹⁴ C-DPX-MP062 (a 3:1 mixture of DPX-KN128 and IN-KN127): Degradability and fate in the water/sediment system Huntingdon Life Sciences Ltd. DuPont-8417 Published: No	N	N		DuPont	Yes, in the 2005 DAR addendum 3.
CA, 7.2.2.3 /01	Allan, J.	2014	Aerobic aquatic metabolism of [¹⁴ C]DPX-KN128 (indoxacarb) in two water-sediment systems ABC Laboratories, Inc. (Missouri) DuPont-39061 GLP: Yes Published: No	N	Y	The study is necessary for the regulatory decision, conducted according to GLP and has not previously been protected or if previously protected the period of data protection has not expired at the time of submission of this	DuPont	No, submitted for the purpose of renewal

						dossier		
CA, 7.2.2.3 /02	Partsch, S., Khanijo, I., Price, K., Ball, M.	2015	Degradation of indoxacarb and its metabolites IN-JT333 (IN-KN125), IN-JU873, IN-KB687, IN- KG433, IN-KT413, IN-MK638, IN-MK643, IN-ML438, IN-MP819, IN-MS775, IN-UYG24, IN-U8E24, and IN-U8F52 in soil and water/sediment systems - kinetic calculations following Focus kinetics Dr. Knoell Consult GmbH DuPont-34821 EU GLP: No Published: No	N	N		DuPont	No, submitted for the purpose of renewal

APPENDIX 1: Study data summary for soil kinetic evaluation (from Partsch, 2015)

I. Data from Mellor (2003) – degradation of indoxacarb.

Percent Applied Radioactivity of Indoxacarb and Metabolites in Speyer 2.2 Soil after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset (Indanone Label)

Sampling Times (days)	DPX-MP062	IN-JT333	IN-KT413	IN-ML438	IN-KG433	IN-JU873
0	97.3a	0.0	0.0	0.0	0.0	0.0
3	43.9	10.4	18.4	-	4.1	-
7	36.7	14.3	17.1	-	8.6	0.55b
14	30.0	11.8	11.1	0.55b	2.0	4.0
30	17.2	4.0	7.9	3.2	4.7	0.55b
59	16.1	2.5	12.5	8.9	0.8	1.0
90	16.9	4.8	0.7	3.9	0.55b	0.55b
120	15.8	3.2	1.9	4.1	2.7	-
162	16.2	4.0	0.8	9.1	0.55b	-
220	8.3	2.1	0.55b	9.0	-	-
269	6.4	2.1	2.6	6.9	-	-
365	9.7	2.4	0.55b	7.8	-	-

a Sum of indoxacarb, others, and unextracted residues (Total % recovery)

b Half of Limit of Detection (LOD)

Percent Applied Radioactivity of Indoxacarb and Metabolites in Speyer 2.2 Soil after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset (TFMP Label)

Sampling Times (days)	DPX-MP062	IN-JT333	IN-KT413	IN-ML438	IN-MK638	IN-KG433	IN-JU873
0	97.1a	0.0	0.0	0.0	0.0	0.0	0.0
3	42.9	10.4	10.7	-	1.0	2.8	7.3
7	38.2	18.6	13.3	-	2.9	0.35b	0.35b
14	23.9	11.2	11.9	0.35b	0.35b	2.2	1.3
30	18.6	7.5	4.3	6.2	0.35b	0.352	0.35b
59	15.1	2.9	2.4	4.7	0.4	0.8	0.8
90	10.0	1.9	1.4	7.6	1.8	1.7	0.35b
120	7.5	3.1	4.0	3.7	1.7	2.8	-
162	7.6	0.8	1.2	8.7	0.7	0.35b	-
220	12.8	1.6	0.8	3.7	0.7	-	-
269	6.0	1.4	2.2	3.9	0.6	-	-
365	7.8	2.1	0.35b	7.6	0.35b	-	-

a Sum of indoxacarb, others, and unextracted residues (Total % recovery)

b Half of Limit of Detection (LOD)

II. Data from Spare (1997) - Degradation of indoxacarb.

Percent Applied Radioactivity of Indoxacarb and Metabolites in Tama Soil after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset (Indanon label, replicate)

Sampling Times (days)	DPX-MP062	IN-JT3333	IN-KG4333	IN-JU8733
0	104.3 ^a	0.0	0.0	0.0
0	103.9 ^a			
1	85.7	5.2	1.9	2.0
1	93.6			
3	70.9	10.6	6.0	2.0
3	69.4			
7	39.4	14.5	23.5	5.0
7	46.1	14.6	19.2	
14	18.8	13.3	23.0	7.0
14	20.2	13.6	19.7	
21	13.0	11.9	14.3	8.0
21	12.7	11.5	15.3	
30	7.1	8.7	14.2	5.0
30	8.0	9.4	13.0	
60	4.9	5.2	10.9	3.0
60	4.4	4.3	13.8	
90	2.9	3.2	7.6	4.0
90	3.1	3.6	6.1	
120	2.7	3.0	10.3	4.0
120	2.8	3.4	9.6	
180	1.9	1.9	9.8	5.0
180	2.1	2.3	8.0	
270	1.4	0.3	13.9	5.0
270	1.7		12.7	
365	0.05 ^b	0.05 ^b	9.1	2.0
365	0.05 ^b	0.05 ^b	8.4	

^a Sum of indoxacarb, others, and unextracted residues (Total % recovery)

^b Half of Limit of Detection (LOD)

^c Replicates were used where reported in the study

III. Data from Rhodes (1997) - Degradation of indoxacarb.

Percent Applied Radioactivity of Indoxacarb and Metabolites in Speyer 2.2 Soil after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset (TFMP Label)

Sampling Times (days)	DPX-MP062	IN-JT333	IN-ML438	IN-JU873	IN-KG433	IN-KB687	IN-MK638	IN-MK643
0	111.2a	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	100.0	0.25b	-	-	-	-	-	-
3	88.5	7.6	0.25b	0.25b	-	-	-	-
7	72.4	0.25b	1.4	5.1	0.25b	-	0.25b	0.25b
10	46.6	10.2	8.9	2.2	1.2	-	1.1	1.0
14	49.6	11.2	8.0	0.25b	0.25b	-	0.25b	1.0
24	41.0	6.5	9.7	0.25b	0.8	0.25b	0.25b	1.2
30	34.6	4.0	9.6	1.0	0.6	0.6	0.7	2.5
62	32.5	1.1	7.0	0.25b	0.25b	0.5	1.9	1.9
90	28.4	1.5	7.9	-	-	2.4	0.25b	0.25b
120	26.3	0.7	6.7	-	-	3.0	-	-

a Sum of indoxacarb, others, and unextracted residues (Total % recovery)
b Half of Limit of Detection (LOD)

Percent Applied Radioactivity of Indoxacarb and Metabolites in Nambenheim Soil after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset (TFMP Label)

Sampling Times (days)	DPX-MP062	IN-JT333	IN-ML438	IN-JU873	IN-KG433	IN-MK638	IN-MK643
0	108.1a	0.0	0.0	0.0	0.0	0.0	0.0
1	108.3	0.8	-	-	0.25b	-	1
3	97.5	1.0	-	0.25b	1.5	-	-
7	70.2	4.9	0.25b	2.7	15.2	0.25b	0.25b
10	38.3	8.7	1.5	3.8	24.7	2.4	9.7
14	39.3	9.8	0.25b	1.3	27.8	2.8	5.1
24	27.0	8.9	1.4	6.5	29.6	5.4	5.1
30	21.8	6.3	2.0	12.9	14.1	0.25b	9.5
62	19.1	2.0	2.6	0.25b	22.0	3.8	3.3
90	13.7	2.2	5.6	-	29.4	0.6	0.5
120	13.4	0.6	4.8	-	20.8	1.4	0.25b

a Sum of indoxacarb, others, and unextracted residues (Total % recovery)
b Half of Limit of Detection (LOD)

IV. Data from singles (2002) – Degradation of indoxacarb

Percent Applied Radioactivity of Indoxacarb and Metabolites in Tama Soil after Application and Incubation Under Aerobic Conditions at 25°C – Original Kinetic Calculation Dataset (Indanone Label)

Sampling Times (days) c	DPX-JW062	IN-JT333	IN-ML438	IN-JU873	IN-KG433
0	102.0a	0.0	0.0	0.0	0.0
2	53.3	10.6	-	0.1	9.9
3	39.8	16.7	7.6	6.8	6.1
7	17.4	7.0	6.3	1.3	1.7
15	8.2	6.2	3.8	0.9	2.1
21	6.0	8.1	3.9	1.1	1.8
30	3.9	4.5	2.9	0.8	3.5
60	4.2	3.4	2.5	1.0	2.2
90	2.4	1.8	1.7	0.3	1.4
120	0.03b	0.03b	0.03b	0.03b	0.03b

a Sum of indoxacarb, others, and unextracted residues (Total % recovery)
b Half of Limit of Detection (LOD)

c Data points after Day 120 (day 180, 270 and 365) were omitted from kinetic calculation as chemical is largely dissipated and values were below LOQ.

Applied Radioactivity of Indoxacarb and Metabolites in Tama Soil after Application and Incubation Under Aerobic Conditions at 25°C – Original Kinetic Calculation Dataset (TFMP Label)

Sampling Times (days)3	DPX-JW062	IN-JT333	IN-ML438	IN-JU873	IN-KG433	IN-KB687	IN-MK638	IN-MK643
0	104.0a	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	66.6	12.9	-	7.5	7.4	5.0	0.1	-
3	24.6	11.3	3.8	5.9	16.9	5.6	3.8	5.6
7	14.6	9.6	2.5	1.9	1.7	6.9	6.7	4.4

15	8.1	10.5	4.1	1.2	0.7	0.7	4.1	5.6
21	7.7	6.3	4.8	1.1	0.8	0.03b	7.0	3.7
30	6.2	7.5	5.8	1.4	1.9	1.2	3.6	3.6
60	4.2	2.5	3.5	0.1	2.1	0.03b	0.03b	0.03b
90	4.7	2.1	4.2	0.032	2.4	2.1	2.9	3.7
120	0.03b	0.03b	0.03b	-	0.03b	1.5	2.1	4.8

a Sum of indoxacarb, others, and unextracted residues (Total % recovery)

b Half of Limit of Detection (LOD)

c Data points after Day 120 (day 180, 270 and 365) were omitted from kinetic calculation as residues started to increase indicating decline in soil microbial activity.

V. Data from Lentz 2003 – Degradation of IN-KT413

Percent Applied Radioactivity of IN-KT413 in three soils after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset

Sampling Times (days)	Hidalgo	Lleida	Mattapex
0	100.5a	100.0a	98.2a
0	98.0a	99.8a	98.3a
1	81.6	66.5	32.1
1	82.2	64.8	30.1
2	67.4	47.1	15.5
2	71.2	50.0	16.4
3	59.2	37.9	6.2
3	59.2	39.9	7.1
4	47.7	27.8	3.7
4	48.7	29.5	5.5
7	33.9	14.6	1.8
7	31.9	13.5	2.2
14	19.0	10.6	
14	13.7	9.8	
21	8.9	7.5	
21	11.3	7.4	
28	4.4	3.9	
28	5.5	4.7	
35	3.8		
35	3.8		

a Total % Recovery

VI. Data from Aikens (2002) – Degradation of IN-KG433 in Five Soils

Table 89 Percent Applied Radioactivity of IN-KG433 in five soils after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset

IN-KG433

Sampling Times (days)	Speyer 2.2	Mattapex	Pesaro	Lleida	Hidalgo
0	101.0a	100.4a	-	102.1a	101.5a
0	102.6a	101.0a	102.4a	101.8a	106.3a
0.5	76.3	80.5	84.4	81.4	80.2
0.5	79.0	79.4	74.5	74.9	69.6
1	67.9	65.0	72.2	62.9	54.1
1	63.4	64.0	75.2	67.1	65.3
2	49.6	52.6	55.7	47.2	60.7
2	57.2	43.1	55.5	47.8	58.9
3	38.6	26.4	49.1	37.4	34.5
3	37.5	24.3	50.0	33.5	41.5
5	32.4	23.0	27.2	22.4	25.5
5	27.9	18.2	25.7	23.4	26.9
7	28.5	15.9	18.9	18.8	17.5
7	29.6	14.8	18.7	17.1	19.1
14	17.5	9.2	9.2	8.5	5.6
14	22.3	9.7	8.9	10.4	8.7
30	14.3	5.3	3.9	4.5	3.3
30	16.3	4.4	2.9	4.3	3.5
45	11.4	3.6	3.8	3.6	2.6
45	12.4	4.7	3.7	3.7	1.9
59	12.6	4.2	2.7	2.9	2.0
59	10.8	4.0	2.8	3.9	1.8
90	10.4				
90	10.9				
120	8.0				
120	7.9				

a Total % Recovery

I. Data from Mellor (2002) – Degradation of IN-JU873

Table 94 Percent Applied Radioactivity of IN-JU873 in fives soils after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset

	IN-JU873				
Sampling Times (days)	Speyer	Mattapex	Lleida	Pesaro	Hidalgo
0	100.9a	98.3a	101.0a	99.5a	102.0a
0	101.3a	101.1a	99.5a	100.1a	103.5a
3	85.0	83.9	74.0	81.0	83.6a
3	82.5	75.7	72.5	69.7	81.1
7	79.8	71.8	60.5	57.4	67.6
7	69.1	65.5	51.3	71.0	76.3
14	60.4	59.3	48.9	48.1	80.2
14	60.6	57.7	43.6	54.4	32.6
30	57.6	48.4	27.5	39.0	32.4
30	51.7	29.4	21.2	26.8	47.5
45	45.9	36.9	17.1	25.7	40.6
45	35.3	32.1	20.4	37.0	23.0
60	36.0	33.7	10.6	38.1	40.4
60	44.3	39.0	13.2	26.9	47.4
91	28.6	34.2	5.0	23.0	30.0
91	29.1	25.8	5.9	15.6	22.6

120	20.5	12.8	4.5	9.5	18.7
120	15.6	25.4	6.2	15.4	15.3

a Total % Recovery

II. Data from Allan (2012) – Degradation of IN-KB687 in Five Soils

Table 99 Percent Applied Radioactivity of IN-KB687 in Lleida Soil after Application and Incubation Under Aerobic Conditions at 20°C– Kinetic Calculation Dataset

	IN-KB687				
Sampling Times (hours)	Lleida	Sassafras	Nambsheim	Speyer 2.2	Tama
0	100.3a	97.1a	102.7a	100.1a	95.4a
0	100.1a	94.9a	102.2a	102.1a	96.6a
24	18.4	36.9	15.2	44.9	29.6
24	19.3	28.4	-	42.3	24.3
48	3.2	14.2	2.0	4.4	6.7
48	3.2	13.2	2.4	2.7	9.9
72		3.9			3.4
72		3.7			3.6

a Total % Recovery

III. Data from Caldwell (2002) – Degradation of IN-MK643 in Five Soils

Table 104 Percent Applied Radioactivity of IN-MK643 in Speyer 2.2 Soil after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset

	IN-MK643				
Sampling Times (days)	Speyer 2.2 soil	Mattapex soil	Pesaro	Lleida	Hidalgo
0	104.9a	106.3a	106.4a	105.1a	103.8a
0	108.3a	103.1a	103.7a	106.0a	106.6a
1	89.7	96.0	82.5	89.0	105.5
1	94.1	98.0	86.1	88.6	95.6
3	98.3	91.4	85.3	88.1	89.9
3	98.3	93.0	93	93.9	97.5
7	94.7	92.5	88.1	87.3	84.0
7	94.3	92.0	89.2	86.4	89.1
14	87.0	91.7	86.8	87.2	89.4
14	94.8	90.8	87.0	90.8	89.8
30	86.0	80.7	72.2	68.0	68.9
30	83.6	83.8	71.1	69.5	69.9
59	84.1	81.1	72.2	70.4	62.4
59	81.7	72.4	62.8	63.4	63.1
90	71.4	74.1	63.4	69.0	55.8
90	80.6	72.7	62.8	65.1	61.7
120	79.4	76.1	62.9	68.5	57.8
120	79.9	79.5	64.7	69.4	56.9

a Total % Recovery

IV. Data from Hatzenbeler (2002) – Degradation of IN-MK638 in Five Soils

Table 109 Percent Applied Radioactivity of IN-MK638 in Hidalgo Soil after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset

Sampling Times (days)	IN-MK638				
	Hidalgo soil	Lleida soil	Mattapex	Pesaro	Speyer 2.2 soil
0	101.5a	102.7a	110.0a	107.7a	108.7a
0	103.3a	103.1a	109.0a	108.3a	108.5a
1	103.0	93.0	100.4	92.8	102.6
1	102.2	91.2	105.1	94.0	103.0
3	87.7	71.6	92.5	73.1	103.1
3	83.3	68.4	95.6	74.6	101.6
7	68.2	46.8	82.5	39.5	78.9
7	69.4	40.9	81.8	36.3	78.5
14	39.9	21.4	69.6	14.4	65.1
14	46.8	22.2	66.9	13.4	56.3
28	15.3	5.5	31.6	2.6	31.3
28	13.8	5.4	33.1	3.1	28.7
60	3.1	1.6	6.7	1.0	4.2
60	2.3	1.4	6.3	0.9	4.0
91	1.1		2.7		5.2
91	1.0		2.4		1.6

a Total % Recovery

V. Data from Clark (2014) – Degradation of IN-JT333 in Five Soils

Table 114 Percent Applied Radioactivity of IN-JT333 in five soils after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset

Sampling Times (days)	IN-JT333				
	Gross Umstadt	in Lleida Soil	Nambsheim	Speyer soil	2.2 Tama soil
0	96.9a	96.1a	96.1a	95.0a	96.9a
0	95.8a	99.7a	97.5a	97.1a	95.0a
3	55.2	74.7	65.5	69.2	73.9
3	61.9	79.4	68.3	70.5	61.6
7	35.0	63.0	44.9	56.9	46.0
7	34.5	57.5	48.0	51.1	27.4b
15	9.3	32.2	13.7	31.8	23.7
15	13.3	35.3	17.9	25.5	35.8
21	14.0	28.0	20.3	26.8	24.7
21	16.6	29.4	19.2	35.1	23.2
31	12.3	22.2	12.5	23.0	14.8
31	12.5	19.0	13.3	26.6	13.1
52	7.2	17.1	6.4	21.5	6.1
52	6.3	12.1	7.7	23.4	5.1
91	5.5	9.0	6.2	18.2	4.9
91	6.3	8.0	5.2	20.3	5.0
122	5.3	6.3	8.1	16.5	3.8
122	3.5	4.3	5.7	13.3	4.4

a Total % Recovery

b Outlier, excluded during kinetic evaluation

VI. Data from Allan (2014a) – Degradation of IN-ML438 in Five Soils

Table 119 Percent Applied Radioactivity of IN-ML438 in five soils after Application and Incubation Under Aerobic Conditions at 20°C – Kinetic Calculation Dataset

Sampling Times (days)	IN-ML438				
	Gross Umstadt Soil	Lleida Soil	Nambsheim Soil	Sassafras soil	Tama
0	96.2a	99.0a	96.0a	97.8a	95.1a
0	97.4a	98.6a	98.6a	99.0a	97.0a
3	85.0	81.4	86.0	81.3	83.9
3	84.6	87.5	89.2	83.0	85.9
7	79.5	84.6	80.6	77.5	80.2
7	79.7	81.9	76.8	81.4	79.9
14	68.7	76.4	73.1	73.1	75.9
14	71.8	76.2	72.6	72.9	73.6
30	54.4	67.2	57.2	61.1	55.8b
30	54.6	65.0	63.0	58.3	62.9
44	45.8	62.8	51.3	49.7	53.3
44	39.6	62.9	53.3	42.7b	52.7
62	38.5	53.9	43.9	47.8	48.2
62	43.4	57.6	42.4	43.4	51.2
93	30.4	50.5	35.9	48.2b	43.3
93	33.4	51.4	36.7	39.7	43.8
120	24.8	45.7	26.0	41.1	36.1
120	24.5	48.5	29.4	34.2	35.9

a Total % Recovery

b Outlier, excluded during kinetic evaluation

APPENDIX 2: Study data summary for water/sediment kinetic evaluation (from Partsch, 2015)

Percent Applied Radioactivity of Indoxacarb and Metabolites at 20°C in Bury Pond (Indanone Label) – Kinetic Dataset

Sampling Times (days) {Sediment decline}	DPX-MP062 Water Phase	DPX-MP062 Sediment phase	DPX-MP062 Total System	IN-KT413 Total System	IN-KG433 Total System ^c	IN-MP819 Total System ^c	IN-JT333 Total System ^c	IN-MS775 Total System ^c
0	65.3	55.2	120.5 ^a	0.0	0.0	0.0	0.0	0.0
1 {0}	37.3	58.6	95.9	10.8	0.03 ^b	0.0	0.3	0.0
7 {6}	4.3	52.8	57.1	20.0	1.5	0.03 ^b	0.8	0.03 ^b
14 {13}	3.4	30.3	33.7	42.1	0.03 ^b	2.9	2.4	0.1
28 {27}	1.4	29.4	30.8	22.7	5.8	2.1	3.5	1.3
42 {41}	0.6	28.9	29.5	6.73	5.7	9.1	4.4	6.2
56 {55}	0.8	10	10.8	11.5	1.4	6.2	2.3	11.3
70 {69}	0.3	21.5	21.8	6.8	5.1	8.0	6.0	6.1
84 {83}	0.2	12.4	12.6	5.5	3.2	10.3	3.6	11.5
102 {101}	0.2	7.9	8.1	7.0	1.4	6.6	2.0	10.0

^a Includes parent in sediment and water and metabolite in sediment and water

^b Half of Limit of Detection (LOD)

^c Only observed in sediment.

Percent Applied Radioactivity of Indoxacarb and Metabolites at 20°C in Bury Pond (TFMP Label) – Kinetic Dataset

Sampling Times (days) {Sediment decline}	DPX-MP062 Water Phase	DPX-MP062 Sediment phase	DPX-MP062 Total System	IN-KT413 Total System	IN-KG433 Total System ^c	IN-MP819 Total System ^c	IN-JT333 Total System ^c	IN-MS775 Total System ^c
0 {0}	48.8	62.7	111.5 ^a	0.0	0.0	0.0	0.0	0.0
1 {1}	36.2	60.5	96.7	5.6	0.03 ^b	0.0	0.3	0.03 ^b
7 {7}	10.1	27.9	38	32.8	0.2	0.0	2.8	2.6
14 {14}	2.5	32.8	35.3	30.9	0.7	0.03 ^b	5.0	2.8
28 {28}	0.7	25.3	26	19.6	4.7	3.7	3.2	2.1
42 {41}	0.6	15.6	16.2	18.7	5.5	5.5	2.9	3.8
56 {56}	0.3	15.5	15.8	17.8	1.2	0.7	2.3	3.0
70 {70}	0.2	11.9	12.1	11.1	1.8	10.2	3.3	14.7
84 {84}	0.5	21.5	22	10.7	2.1	8.9	2.7	12.8
102 {102}	0.03 ^b	13.7	13.73	14.3	0.8	7.9	2.0	2.8

^a Includes parent in sediment and water and metabolite in sediment and water

^b Half of Limit of Detection (LOD)

^c Only observed in sediment.

TABLE 120
Percent Applied Radioactivity of Indoxacarb and Metabolites at 20°C in Chatsworth Pond (Indanone Label) – Kinetic Dataset

Sampling Times (days) {Sediment decline}	DPX-MP062 Water Phase	DPX-MP062 Sediment phase	DPX-MP062 Total System	IN-KT413 Total System	IN-KG433 Total System ^c	IN-ML438 Total System ^c	IN-JT333 Total System ^c	IN-MS775 Total System ^c
0 {0}	75.7	53.2	128.9 ^a	0.0	0.0	0.0	0.0	0.0
1 {1}	32	51.7	83.7	7.1	0.5	0.6	10.6	0.0
14 {14}	0.2	7.4	7.6	18.1	0.8	1.2	25.7	0.03 ^b
28 {28}	0.3	7.7	8	1.8	1.7	3.6	21.1	2.0
42 {41}	0.2	8.2	8.4	6.6	1.9	3.1	13.1	2.0
56 {56}	0.1	3.6	3.7	5.5	1.0	2.0	9.5	1.6
70 {70}	0.6	4.8	5.4	2.8	1.5	1.9	8.7	1.8
84 {84}	0.03 ^b	4.2	4.23	2.4	2.1	2.1	6.3	2.5
102 {102}	0.1	3.8	3.9	3.4	1.1	0.8	3.9	0.5

^a Includes parent in sediment and water and metabolite in sediment and water

^b Half of Limit of Detection (LOD)

^c Only observed in sediment.

**Percent Applied Radioactivity of Indoxacarb and Metabolites at 20°C in Chatsworth Pond (TFMP Label)
– Kinetic Dataset**

Sampling Times (days) {Sediment decline}	DPX-MP062 Water Phase	DPX-MP062 Sediment phase	DPX-MP062 Total System	IN-KT413 Total System	IN-KG433 Total System ³	IN-ML438 Total System ³	IN-JT333 Total System ³	IN-MS775 Total System ³
0 {0}	36	72.5	108.5 ^a	0.0	0.0	0.0	0.0	0.0
1 {1}	22.5	77.8	100.3	3.0	0.1	0.2	2.4	0.03 ^b
7 {7}	0.9	20.3	21.2	24.0	1.1	1.0	21.4	0.3
14 {14}	1.1	5.5	6.6	31.4	7.7	1.0	16.0	0.5
28 {28}	0.3	14.1	14.4	10.5	4.4	0.03 ^b	17.7	3.4
42 {41}	0.3	6.7	7	5.9	1.5	3.0	10.8	3.4
56 {56}	0.1	4.2	4.3	4.7	0.4	2.4	5.9	5.2
70 {70}	0.1	2.8	2.9	5.2	1.9	1.6	12.7	0.4
84 {84}	0.03 ^b	3.2	3.23	5.1	2.4	3.0	6.4	2.2
102 {102}	0.1	3.1	3.2	3.4	1.5	0.03	3.1	0.8

^a Includes parent in sediment and water and metabolite in sediment and water

^b Half of Limit of Detection (LOD)

^c Only observed in sediment.

**Percent Applied Radioactivity of Indoxacarb and Metabolites at 20°C in System Chula (Indanone and
TFMP Label) – Kinetic Dataset**

Sampling Times (days) {Sediment decline}	DPX-KN128 Water Phase	DPX-KN128 Sediment phase	DPX-KN128 Total System	IN-KN125 Total System ^c	IN-KT413 Total System	IN-MK638 Total System	IN-MP819 Total System ^c	IN-MS775 Total System ^c
0	96.9	5.3	96.9 ^a	0.0	0.0	0.0	0.0	0.0
0	101.0	7.9	101.0 ^a	0.0	0.0	0.0	0.0	0.0
1	56.8	24.8	81.6	0.2	15.9	NaN	0.2	NaN
1	40.9	43.5	84.4	0.4	23.0	0.0	0.4	NaN
3	24.4	31.0	55.4	0.8	40.9	NaN	0.6	NaN
3	28.9	29.3	58.2	1.1	43.5	0.0	0.6	NaN
7 {0}	9.5	29.5	39.0	1.9	66.0	NaN	2.5	0.05 ^b
7 {0}	8.9	40.1	49.0	2.4	59.6	0.1	2.8	0.05 ^b
14 {7}	0.6	11.8	12.4	2.5	75.2	NaN	4.9	0.50
14 {7}	0.05 ^b	14.6	14.7	4.4	72.2	2.0	4.2	1.20
28 {21}	0.05 ^b	3.4	3.5	1.0	67.1	NaN	6.4	1.10
28 {21}	NaN	4.4	4.4	1.2	67.0	1.4	7.6	1.70
52 {45}	NaN	1.6	1.6	0.5	28.1	NaN	8.3	3.60
52 {45}	NaN	1.7	1.7	0.6	43.1	3.6	12.1	4.00
74 {67}	NaN	1.2	1.2	0.4	3.6	NaN	15.4	4.40
74 {67}	NaN	1.4	1.4	0.4	3.1	5.9	21.3	5.70
100 {93}	NaN	1.0	1.0	0.4	3.0	NaN	11.9	4.20
100 {93}	NaN	1.8	1.8	0.05 ^b	1.4	9.0	17.9	6.00

^a Includes parent in sediment and water and metabolite in sediment and water

^b Half of Limit of Detection (LOD)

^c Only observed in sediment.

^d Requested by KinGUI software to indicate blanks ("Not a Number")

Percent Applied Radioactivity of Indoxacarb and Metabolites at 20°C in System Chula (Indanone and TFMP Label) – Kinetic Dataset (continued)

Sampling Times (days) {Sediment decline}	IN-UYG24 Total System ^e	IN-U8E24 Total System	IN-U8F52 Total System ^c
0	0.0	0.0	0.0
0	0.0	0.0	0.0
1	NaN	NaN	NaN
1	NaN	NaN	NaN
3	NaN	0.05 ^b	0.05 ^b
3	NaN	0.05 ^b	NaN
7 {0}	0.05 ^b	0.95	0.30
7 {0}	NaN	0.75	NaN
14 {7}	2.10	4.10	1.70
14 {7}	NaN	6.30	NaN
28 {21}	NaN	11.50	1.80
28 {21}	NaN	11.10	NaN
52 {45}	31.60	13.00	4.60
52 {45}	NaN	6.40	NaN
74 {67}	2.10	4.30	4.30
74 {67}	NaN	1.90	NaN
100 {93}	1.80	2.60	4.10
100 {93}	NaN	1.80	NaN

^a Includes parent in sediment and water and metabolite in sediment and water

^b Half of Limit of Detection (LOD)

^c Only observed in sediment.

^d Requested by KinGUI software to indicate blanks ("Not a Number")

^e Only observed in water.

Percent Applied Radioactivity of Indoxacarb and Metabolites at 20°C in System Chula (Indanone and TFMP Label) – Kinetic Dataset

Sampling Times (days) {Sediment decline}	DPX-KN128 Water Phase	DPX-KN128 Sediment phase	DPX-KN128 Total System	IN-KN125 Total System ^c	IN-KT413 Total System	IN-MK638 Total System	IN-MP819 Total System ^c	IN-MS775 Total System ^c
0	95.3	0.0	95.3 ^a	0.0	0.0	0.0	0.0	0.0
0	92.0	0.0	92.0 ^a	0.0	0.0	0.0	0.0	0.0
1 {0}	30.4	31.3	61.7	0.4	42.7	NaN	0.4	NaN
1 {0}	48.6	31.3	79.9	0.05 ^b	24.4	NaN	0.2	NaN
3 {2}	11.8	21.1	32.9	0.8	63.8	NaN	0.8	NaN
3 {2}	20.7	18.8	39.5	0.7	58.7	0.05 ^b	0.5	NaN
7 {6}	2.4	14.3	16.7	2.3	75.9	NaN	2.0	NaN
7 {6}	8.0	13.2	21.2	0.9	83.0	0.8	1.5	NaN
14 {13}	0.05	7.6	7.7	1.5	57.2	NaN	2.7	0.05 ^b
14 {13}	0.05	3.7	3.8	0.8	72.8	1.8	2.7	0.05 ^b
28 {27}	NaN	1.4	1.4	0.9	33.7	NaN	3.1	1.5
28 {27}	NaN	1.2	1.2	0.7	43.9	1.3	4.5	1.8
52 {51}	NaN	2.2	2.2	0.9	19.3	NaN	8.6	2.8
52 {51}	NaN	1.3	1.3	0.5	21.3	3.2	9.3	3.3
74 {73}	NaN	1.3	1.3	0.8	8.7	NaN	8.3	3.5
74 {73}	NaN	0.9	0.9	0.5	11.7	0.8	8.9	3.8
100 {99}	NaN	1.5	1.5	0.6	3.8	NaN	9.0	2.9
100 {99}	NaN	1.3	1.3	0.6	2.9	1.9	7.8	3.3

^a Includes parent in sediment and water and metabolite in sediment and water

^b Half of Limit of Detection (LOD)

^c Only observed in sediment.

^d Requested by KinGUI software to indicate blanks ("Not a Number")

Percent Applied Radioactivity of Indoxacarb and Metabolites at 20°C in System Chula (Indanone and TFMP Label) – Kinetic Dataset (continued)

Sampling Times (days) {Sediment decline}	IN-UYG24 Total System ^e	IN-U8E24 Total System	IN-U8F52 Total System ^c
0	0.0	0.0	0.0
0	0.0	0.0	0.0
1 {0}	NaN	0.05 ^b	0.05 ^b
1 {0}	NaN	0.05 ^b	NaN
3 {2}	NaN	1.1	0.2
3 {2}	NaN	0.6	NaN
7 {6}	0.05 ^b	5.8	0.8
7 {6}	NaN	2.9	NaN
14 {13}	1.7	12.1	2.1
14 {13}	NaN	14.4	NaN
28 {27}	3.2	20.6	4.5
28 {27}	NaN	24.3	NaN
52 {51}	1.0	15.4	2.2
52 {51}	NaN	20.2	NaN
74 {73}	0.3	10.6	3.7
74 {73}	NaN	12.4	NaN
100 {99}	0.05 ^b	12.9	2.0
100 {99}	NaN	15.6	NaN

^a Includes parent in sediment and water and metabolite in sediment and water

^b Half of Limit of Detection (LOD)

^c Only observed in sediment.

^d Requested by KinGUI software to indicate blanks ("Not a Number")

^e Only observed in water.

APPENDIX 3

Visual assessment of water/sediment kinetics

Figure 13

Optimised DFOP-SFO kinetic model of indoxacarb and metabolites in Bury Pond: Total system with replicates, M-I

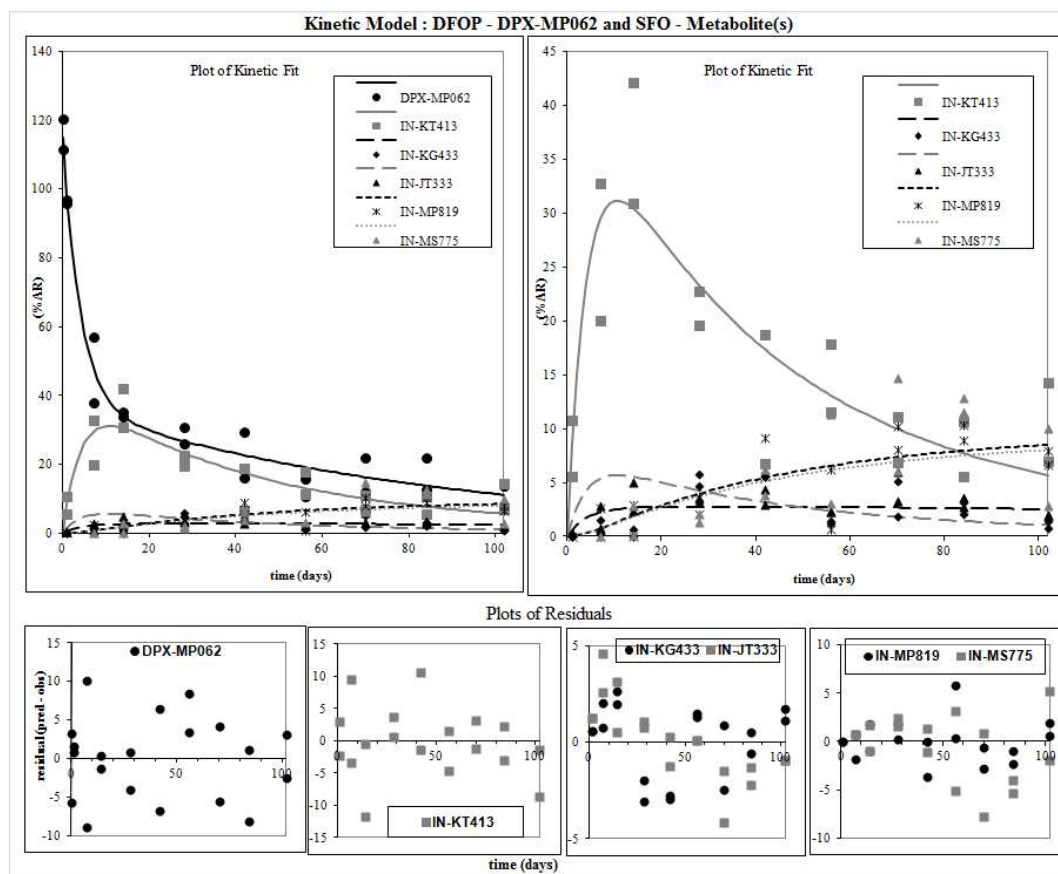


Figure 14

Optimised DFOP-SFO kinetic model of indoxacarb and metabolites in Bury Pond: Total system, indanone Label, M-I

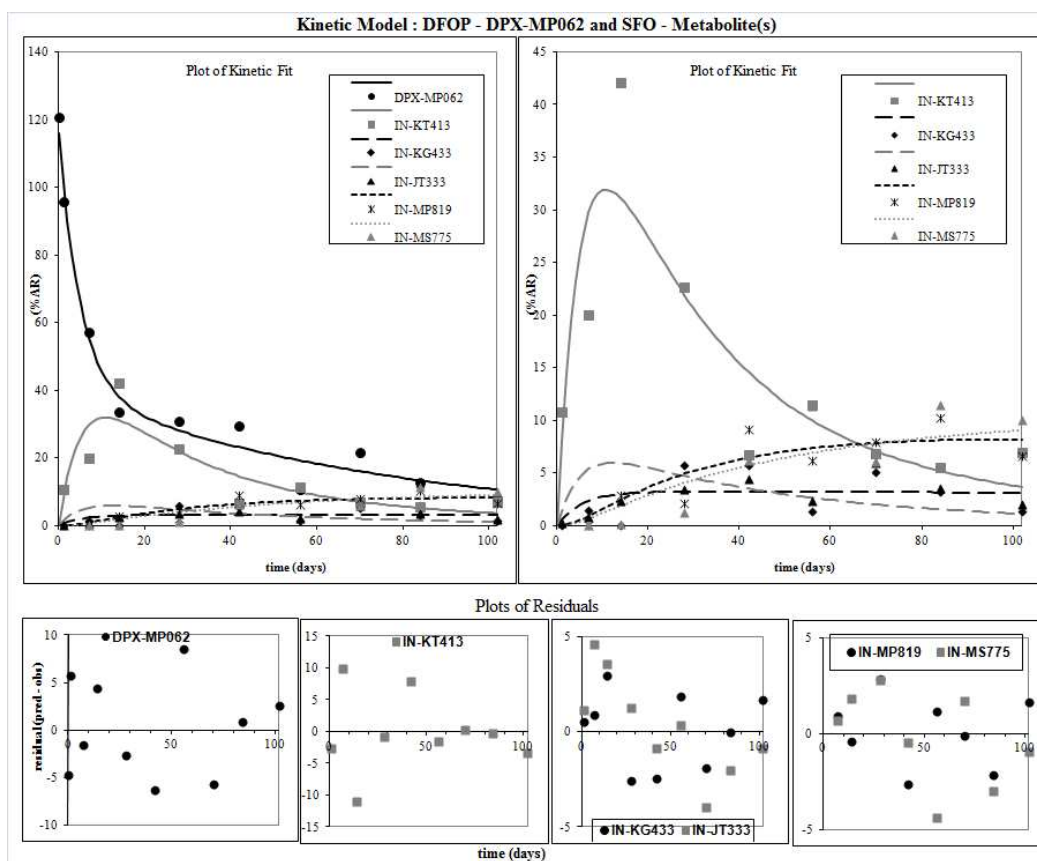


Figure 15
Optimised DFOP-SFO kinetic model of indoxacarb and metabolites in Bury Pond: Total System, TFMP label, M-I

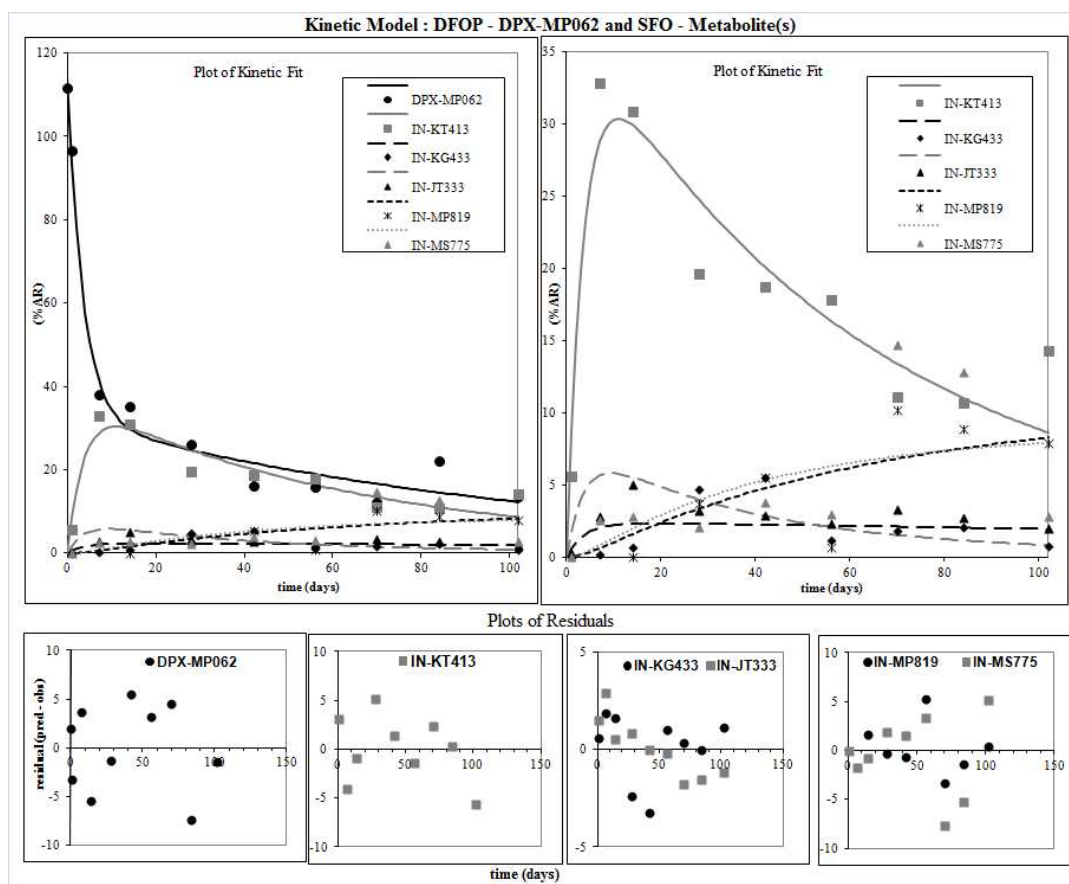


Figure 16
Optimised HS-SFO kinetic model of indoxacarb and metabolites in Chatsworth Pond: Total system with replicates, M-I

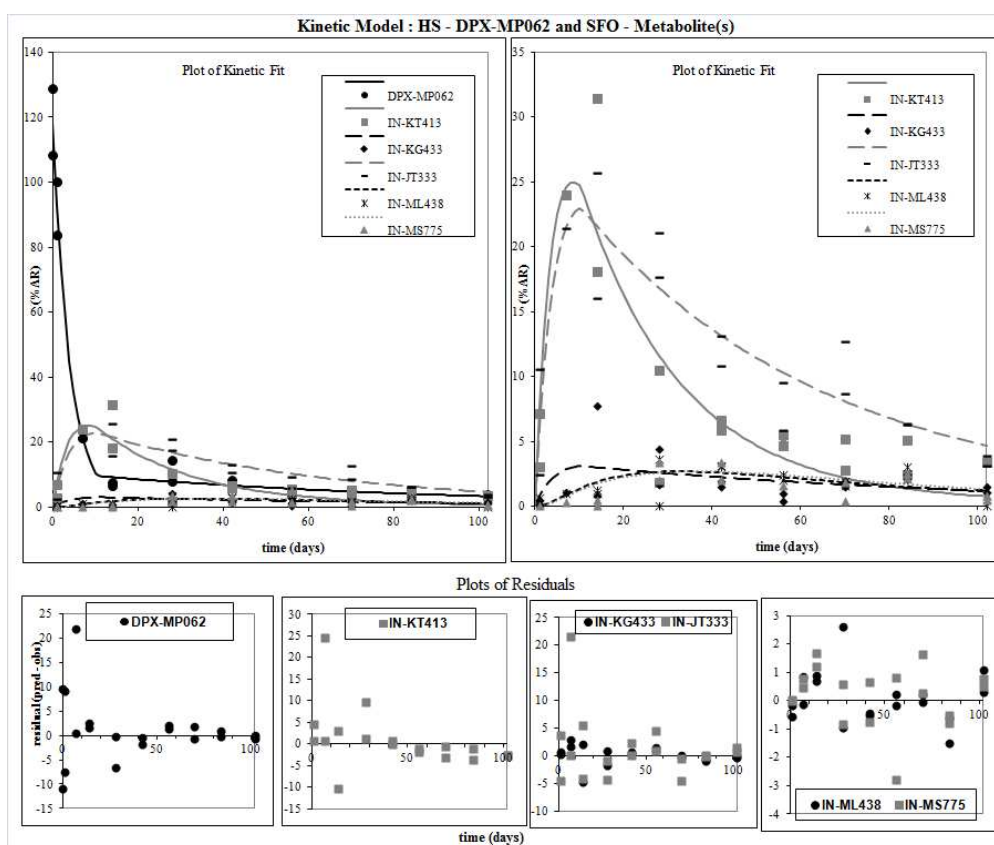


Figure 17
Optimised HS-SFO kinetic model of indoxacarb and metabolites in Chatsworth Pond: Total system indanone label, M-I

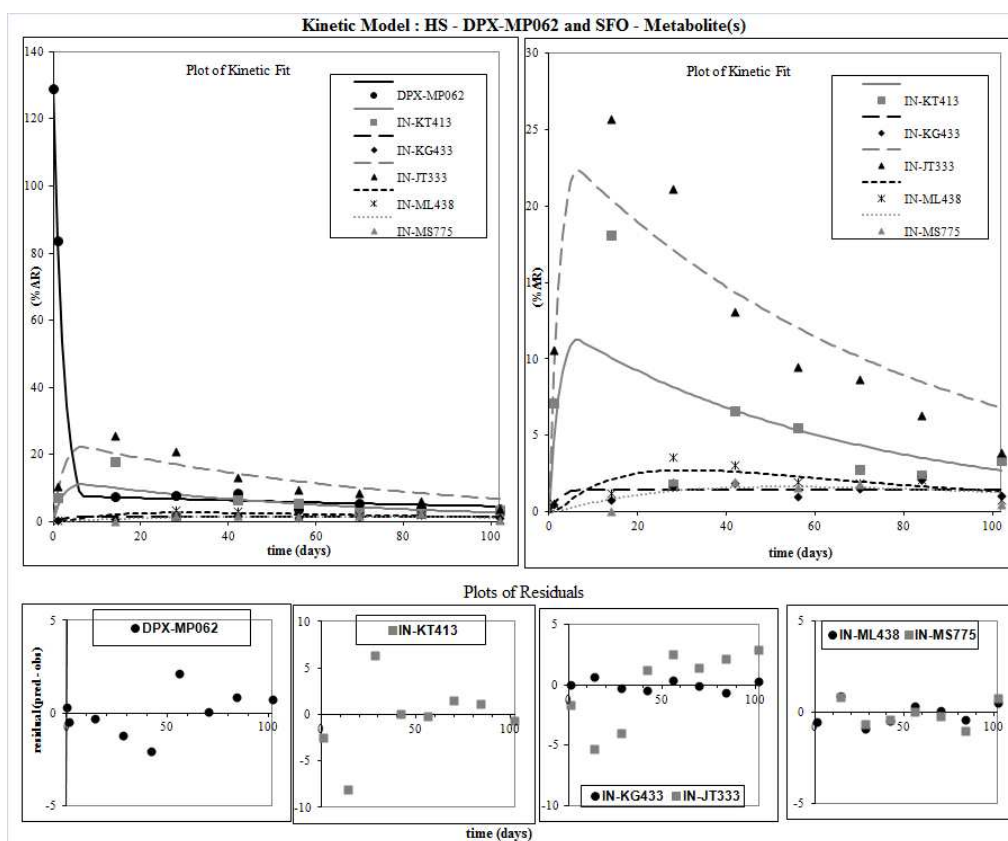


Figure 18
Optimised HS-SFO kinetic model of indoxacarb and metabolites in Chatsworth Pond: Total system
TFMP label, M-I

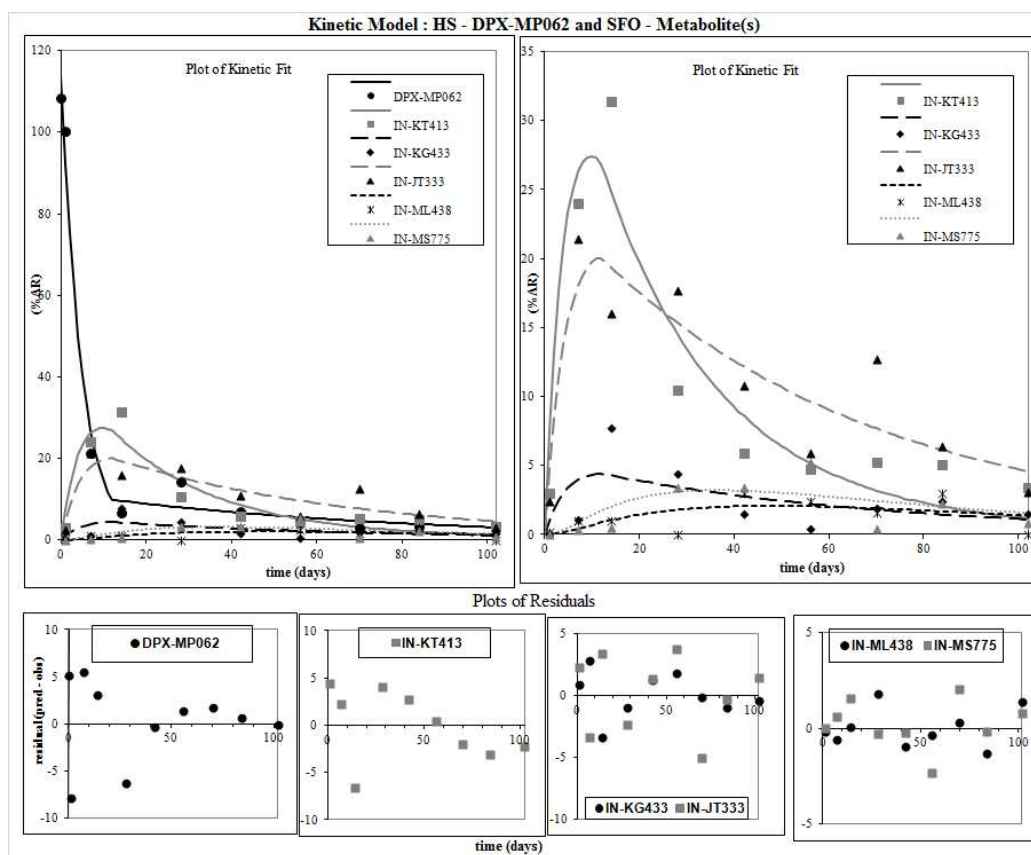


Figure 19
Optimised SFO-SFO kinetic model of indoxacarb and metabolites in Chula: Total system with replicates,
M-I

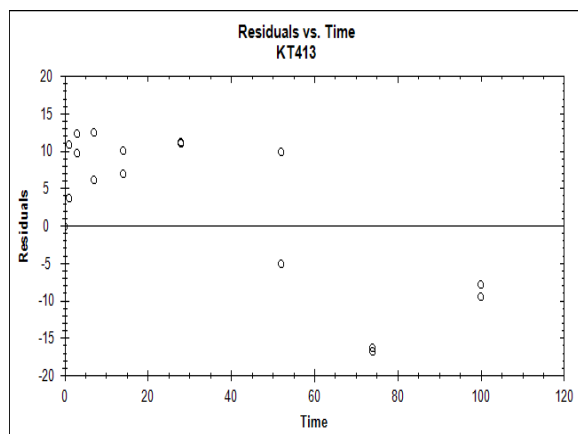
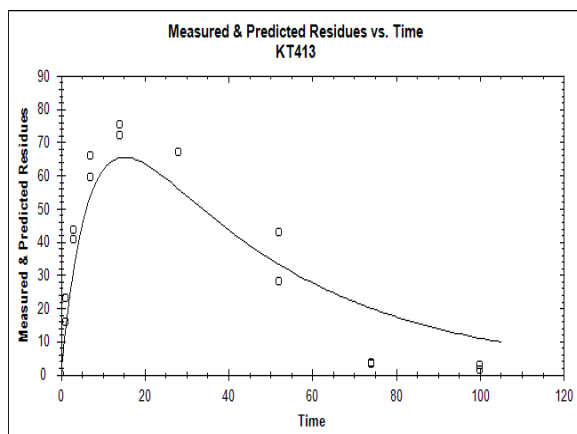
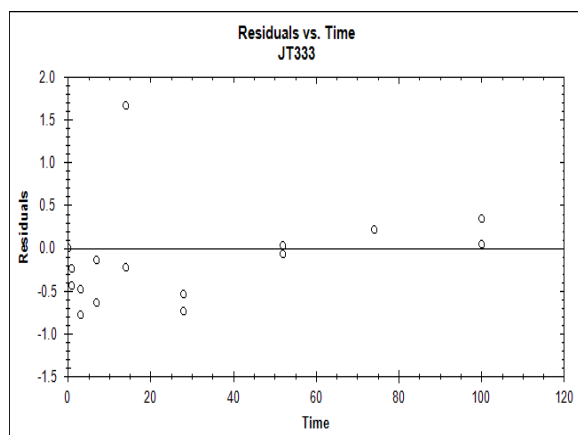
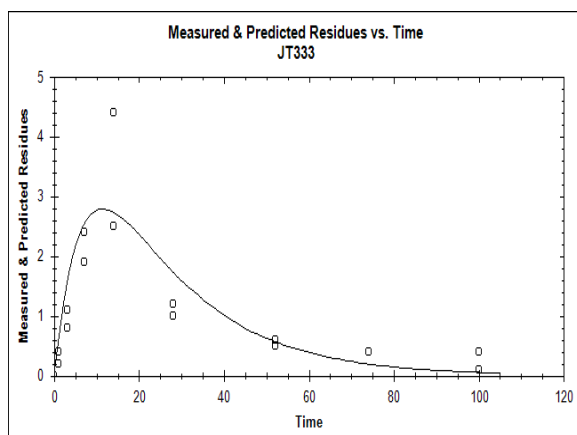
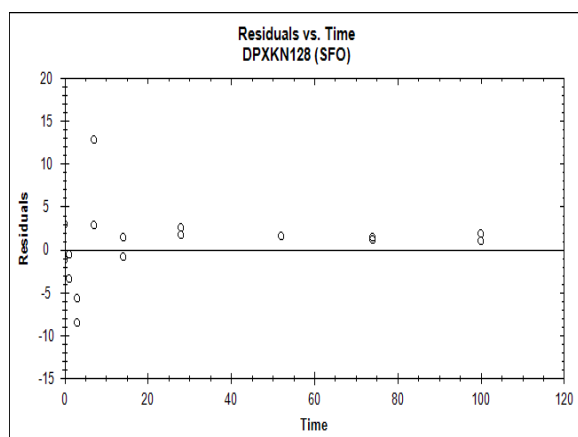
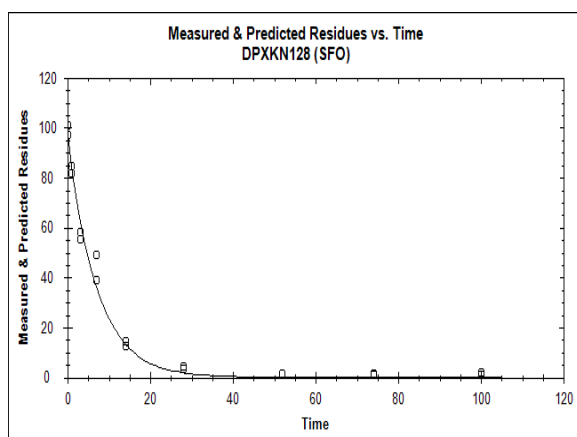


Figure 19
Optimised SFO-SFO kinetic model of indoxacarb and metabolites in Chula: Total system with replicates, M-I (continued)

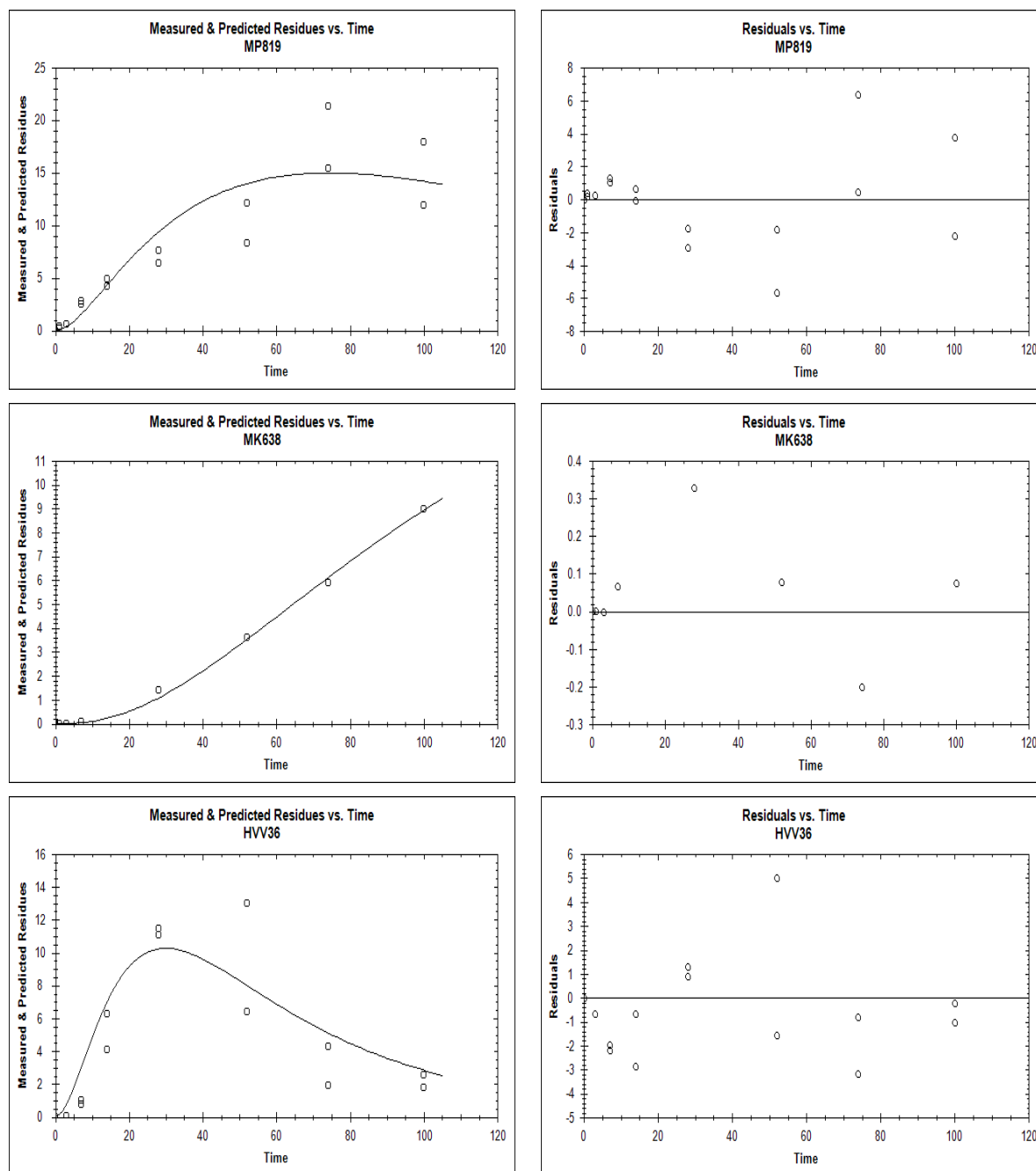


Figure 19
Optimised SFO-SFO kinetic model of indoxacarb and metabolites in Chula: Total system with replicates, M-I (continued)

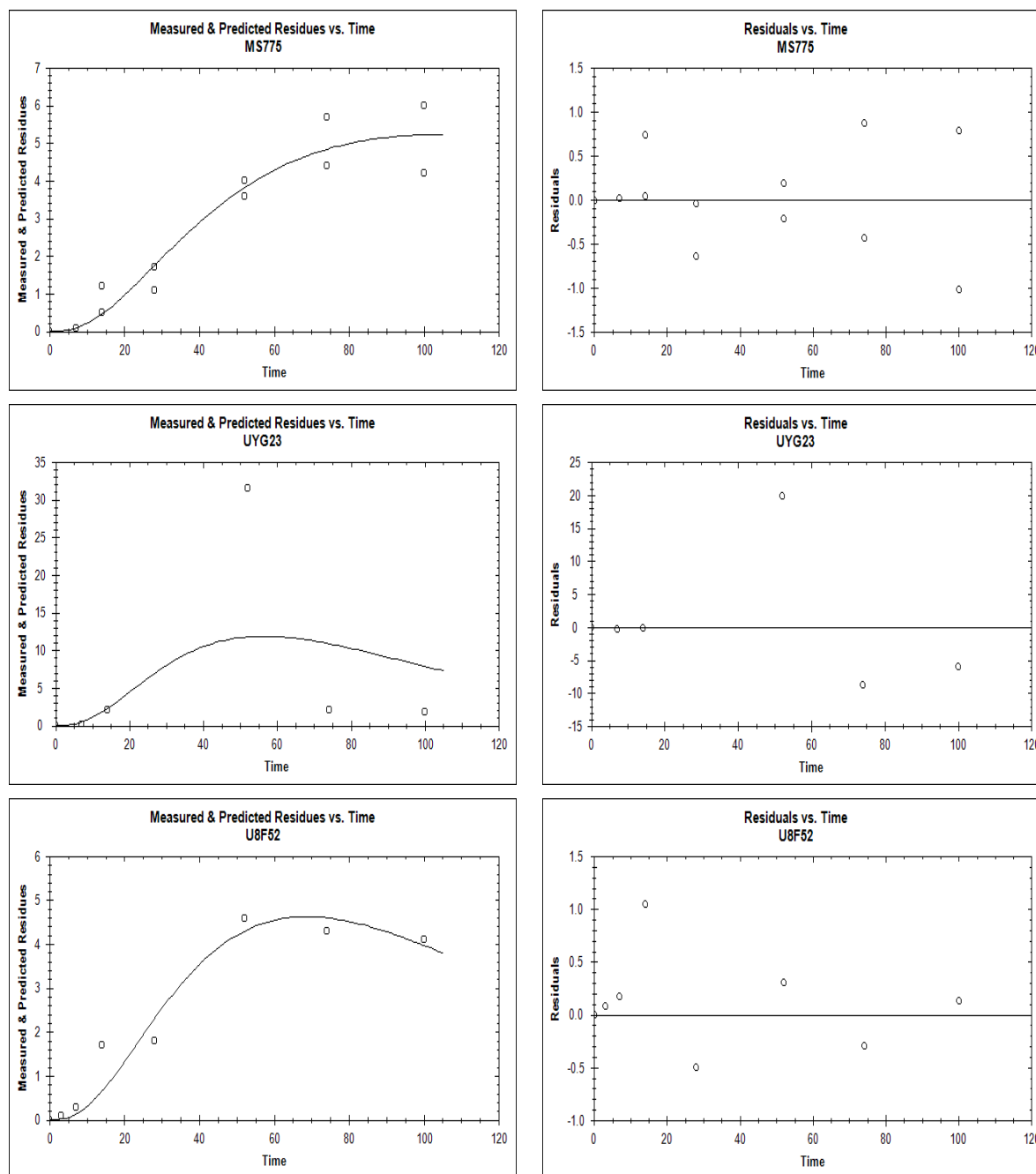


Figure 20
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Chula: Total system, indanone label, M-I

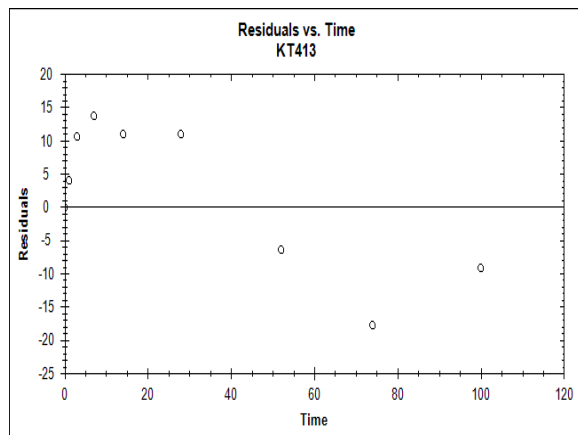
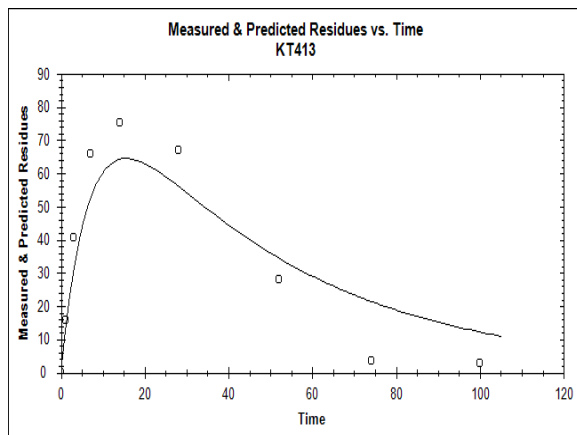
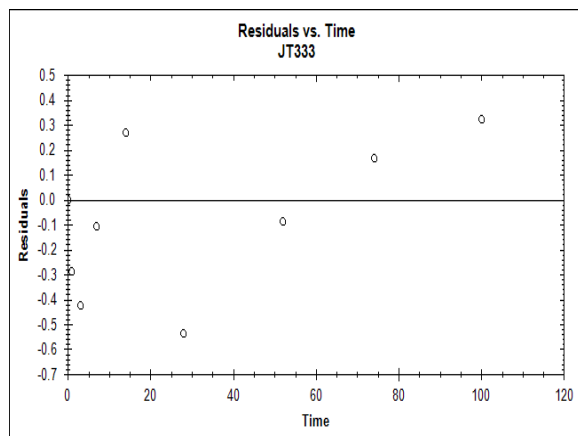
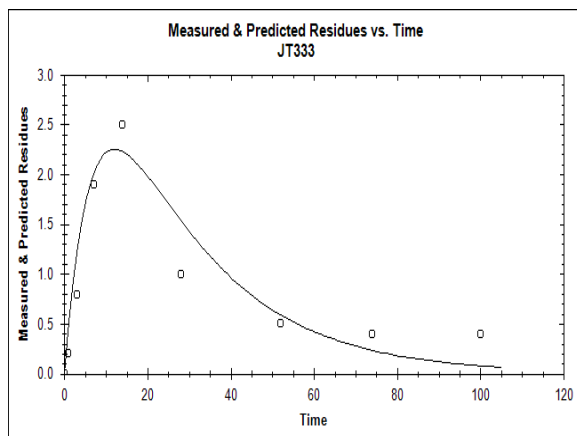
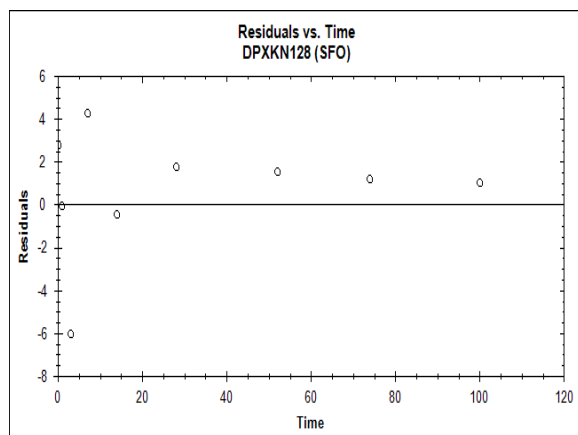
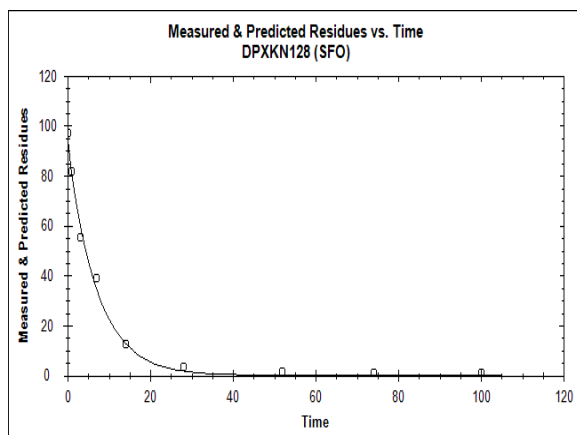


Figure 20
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Chula: Total system, indanone label, M-I (continued)

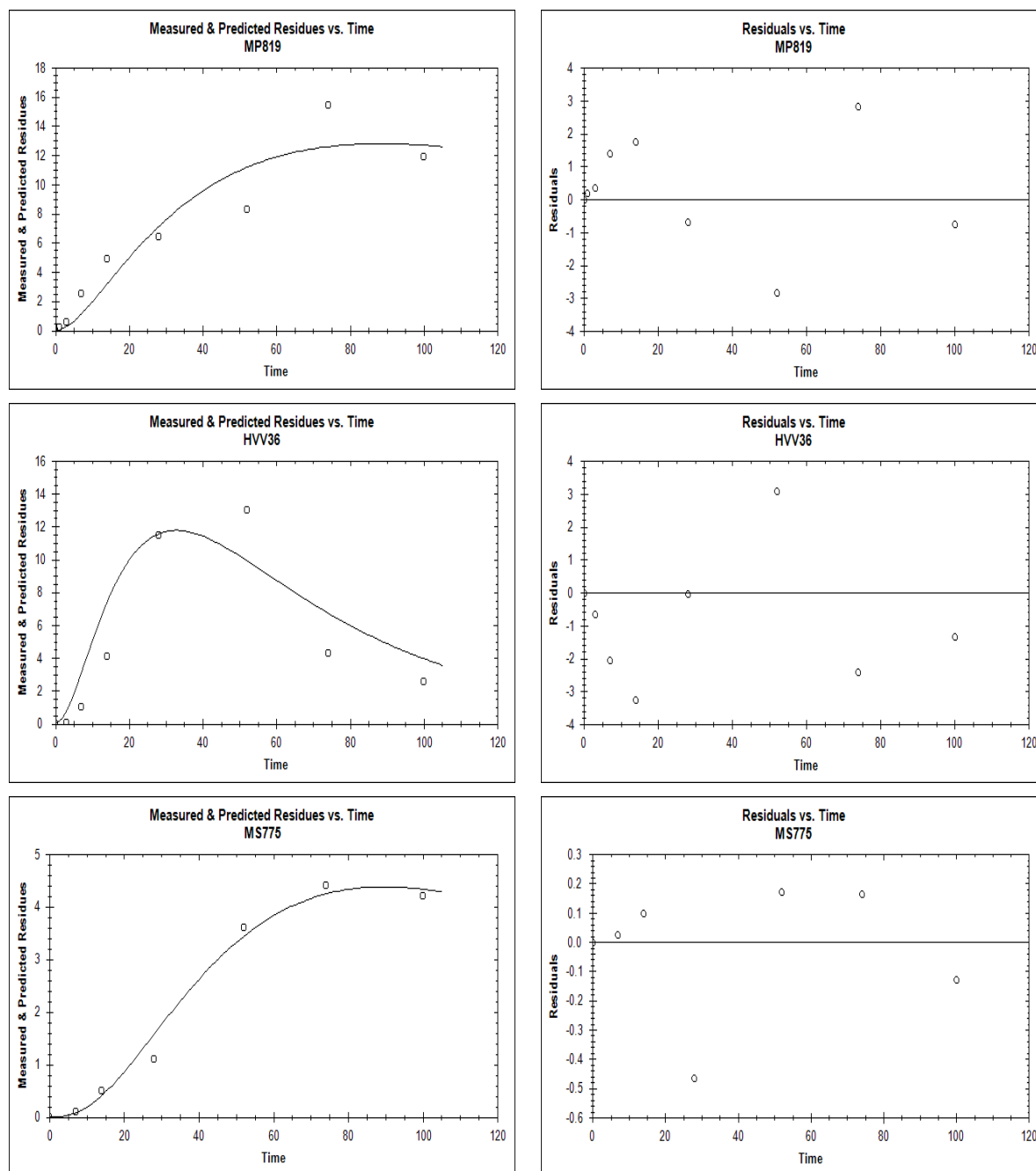


Figure 20
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Chula: Total system, indanone label, M-I (continued)

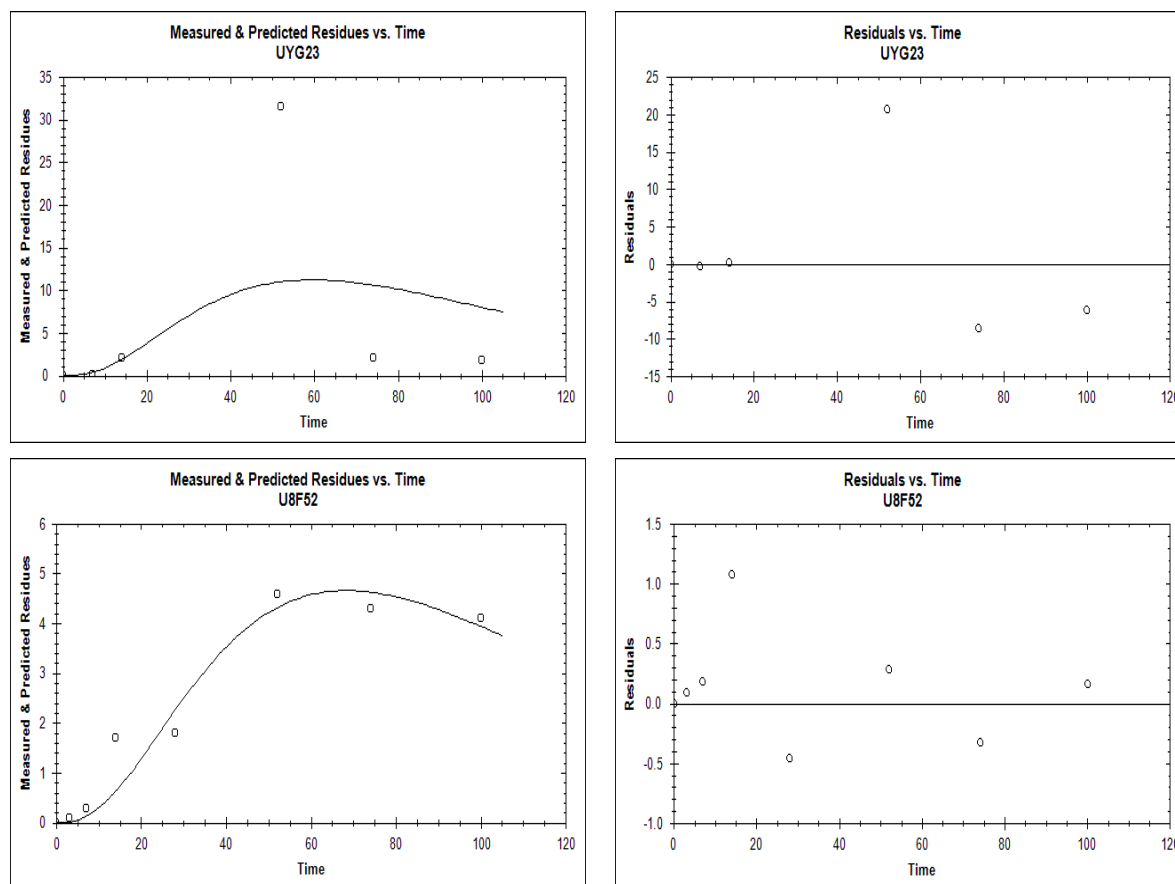


Figure 21
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Chula: Total System, TFMP label, M-I

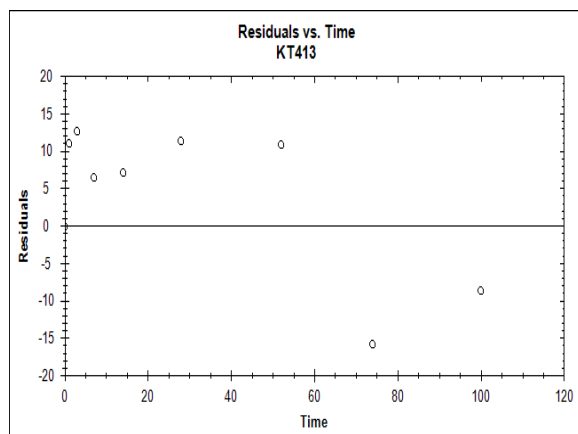
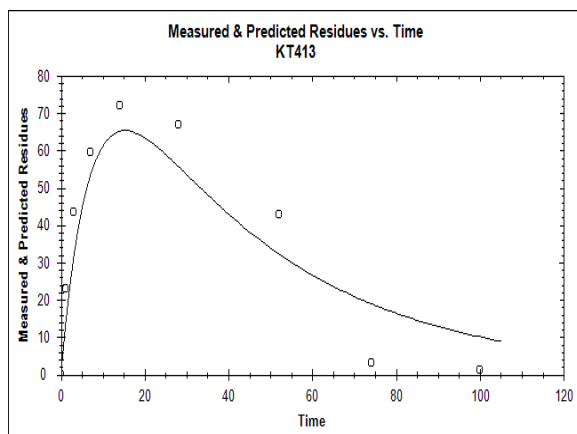
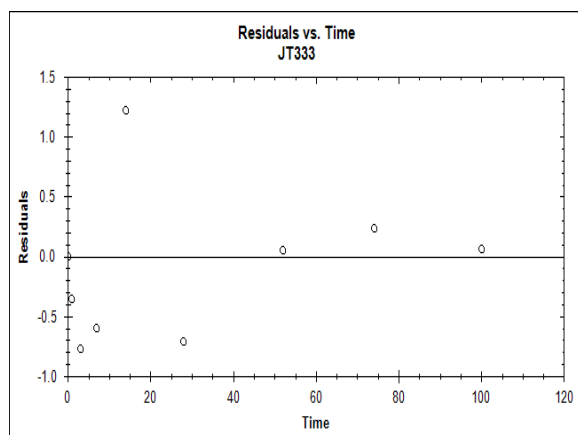
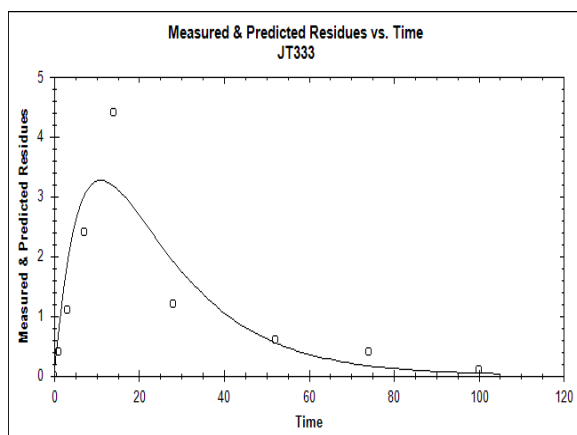
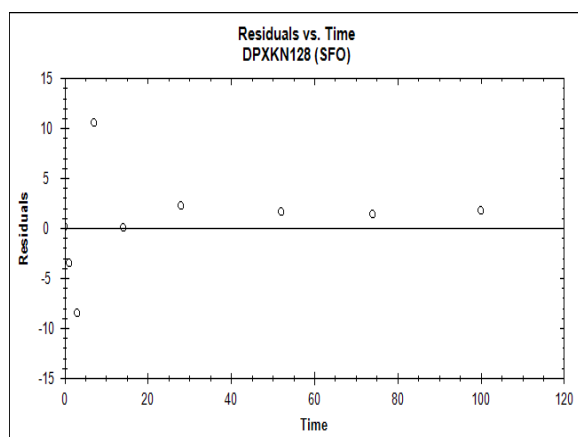
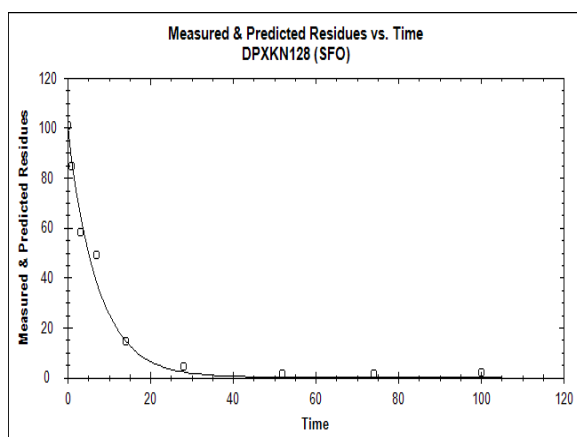


Figure 21
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Chula: Total System, TFMP label, M-I (continued)

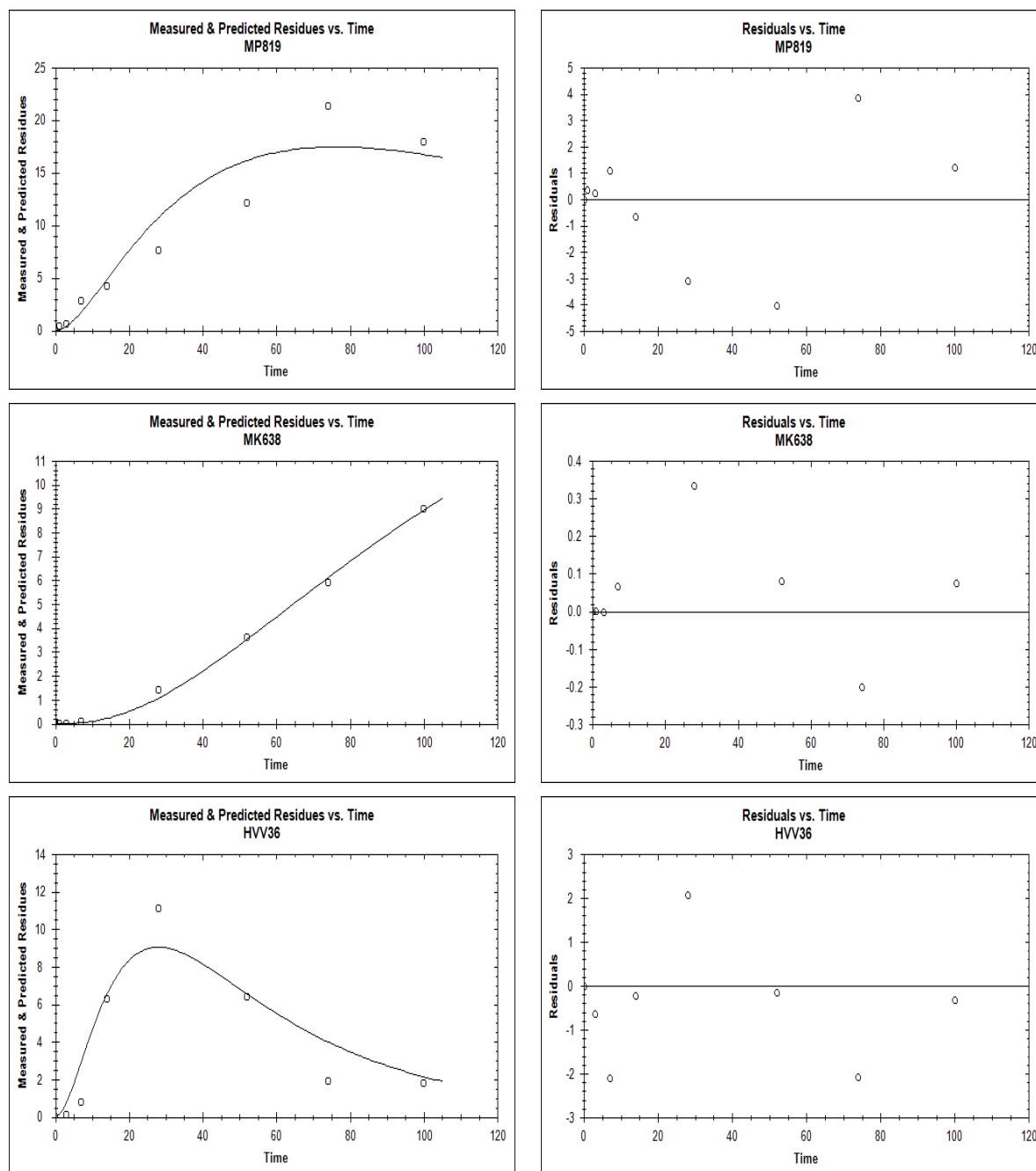


Figure 21
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Chula: Total System, TFMP label, M-I (continued)

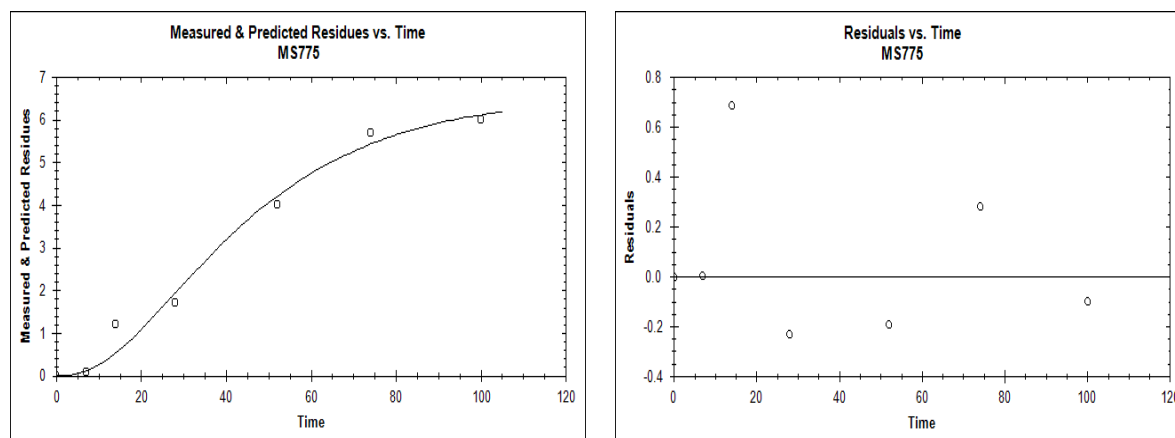


Figure 22
Optimised HS-SFO kinetic model of indoxacarb and metabolites in Goose River: Total system with replicates, M-I

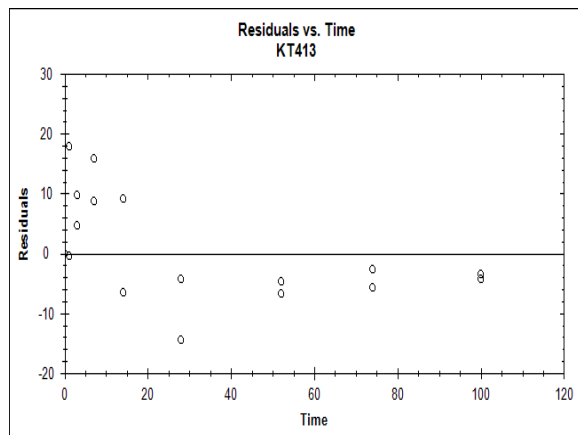
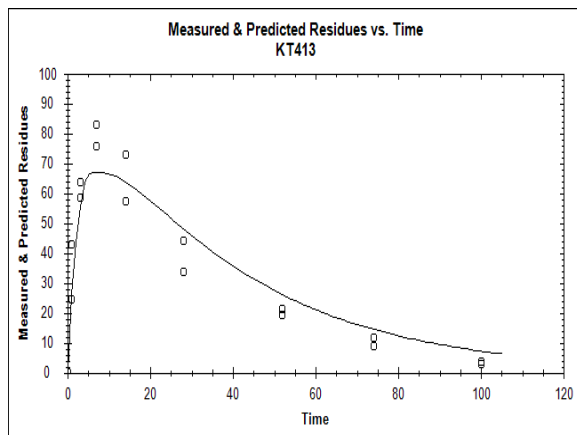
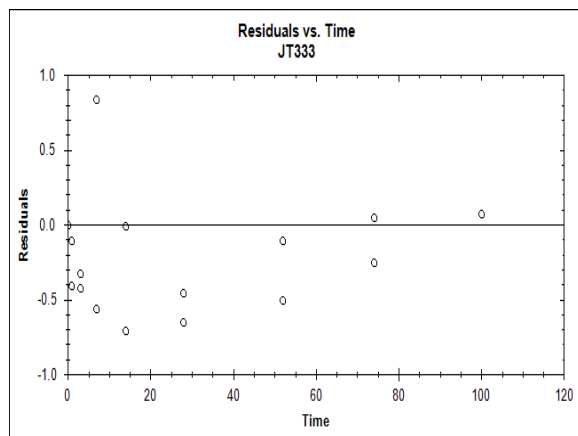
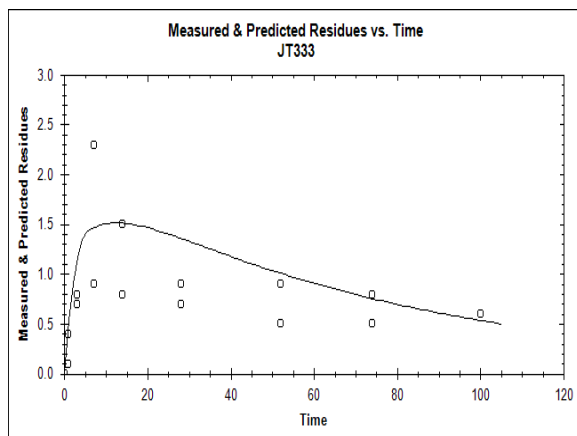
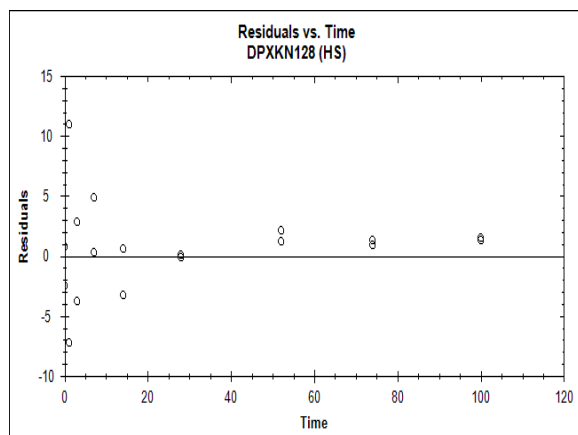
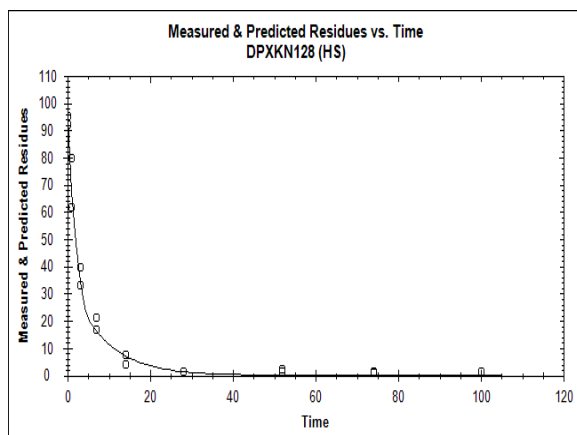


Figure 22
Optimised HS-SFO kinetic model of indoxacarb and metabolites in Goose River: Total system with replicates, M-I (continued)

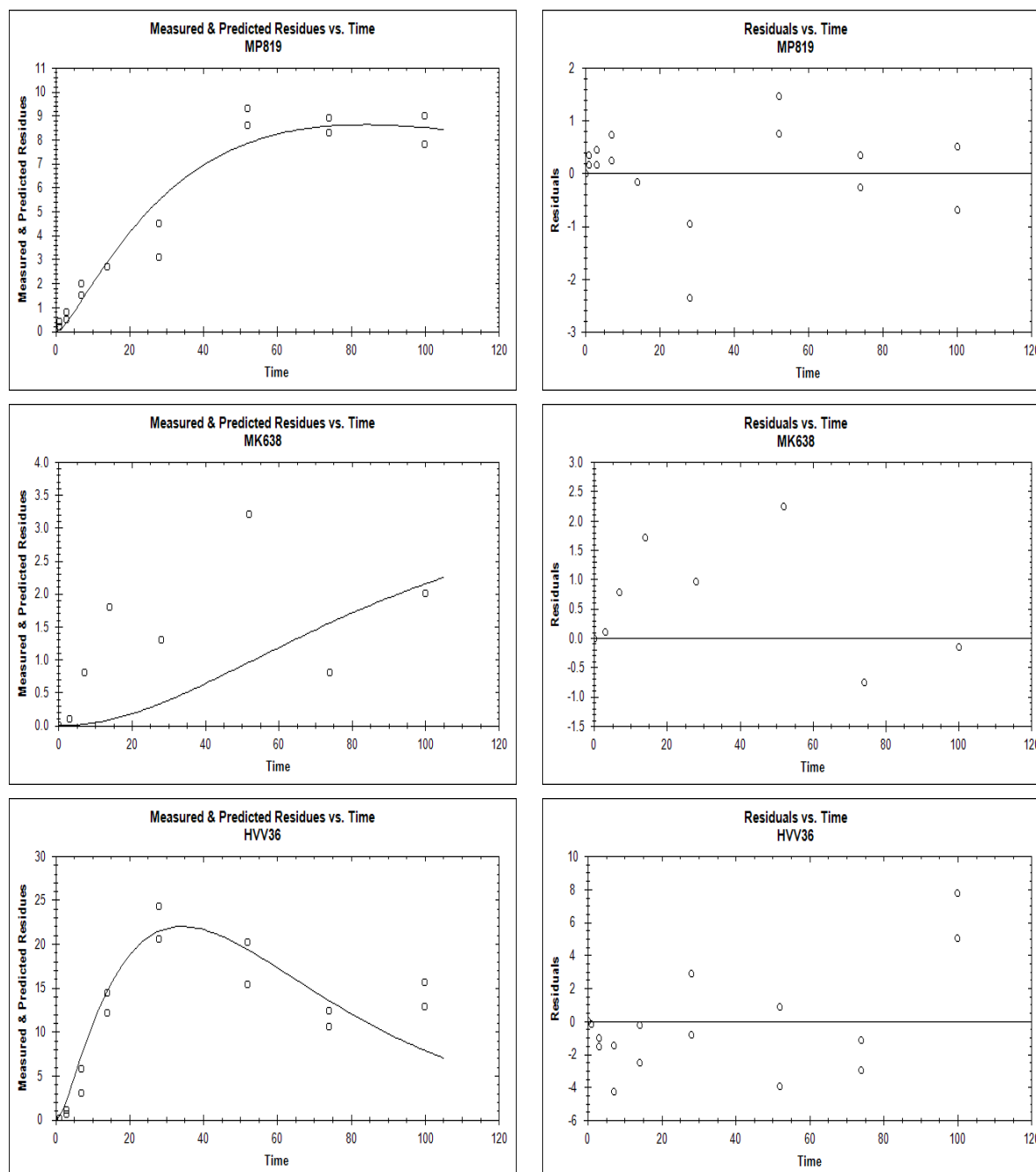


Figure 22
Optimised HS-SFO kinetic model of indoxacarb and metabolites in Goose River: Total system with replicates, M-I (continued)

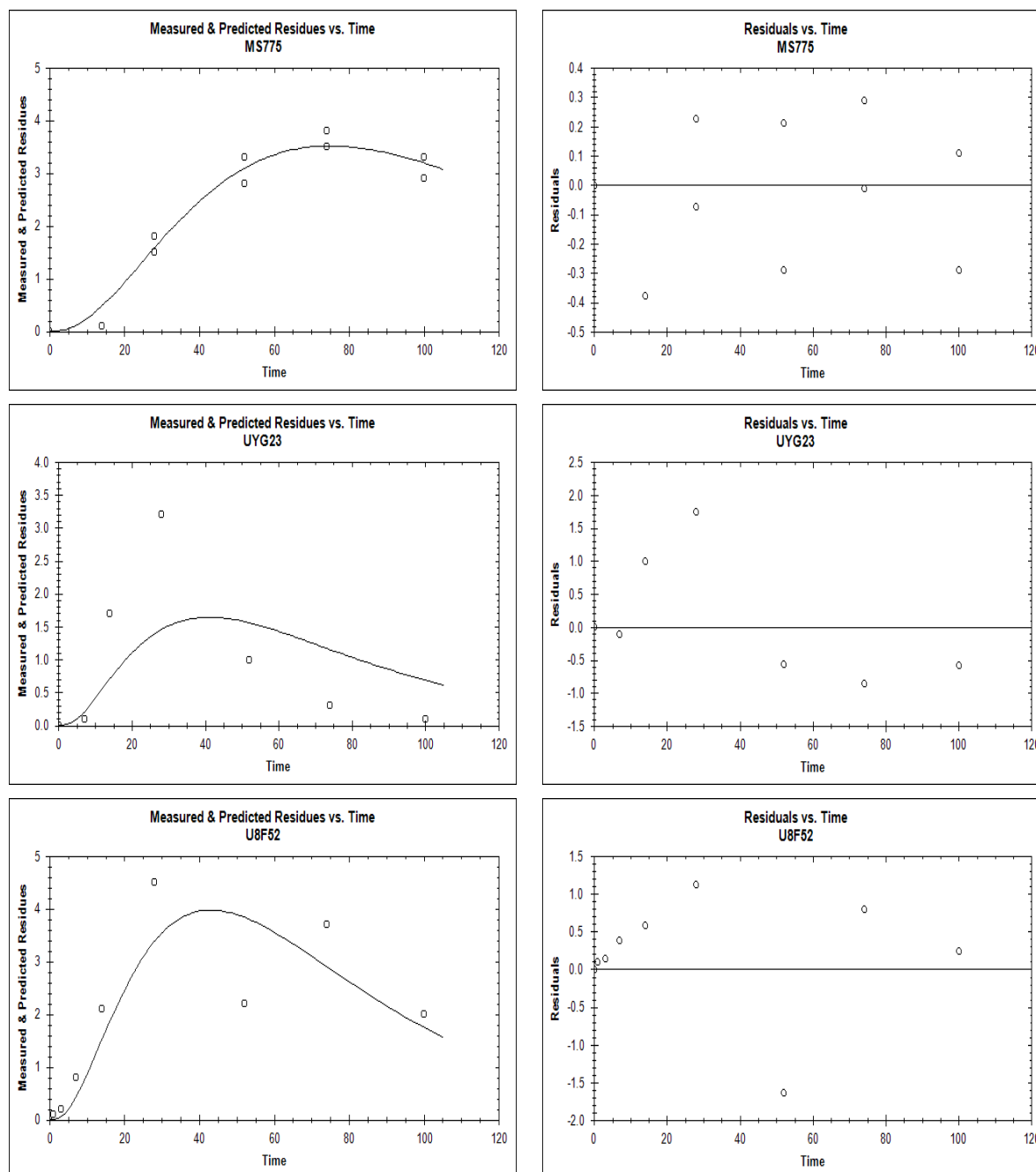


Figure 23
Optimised FOMC -SFO kinetic model of indoxacarb and metabolites in Goose River: Total system, indanone label, M-I

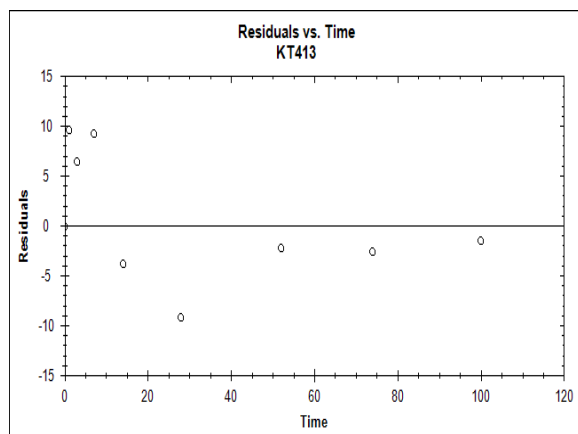
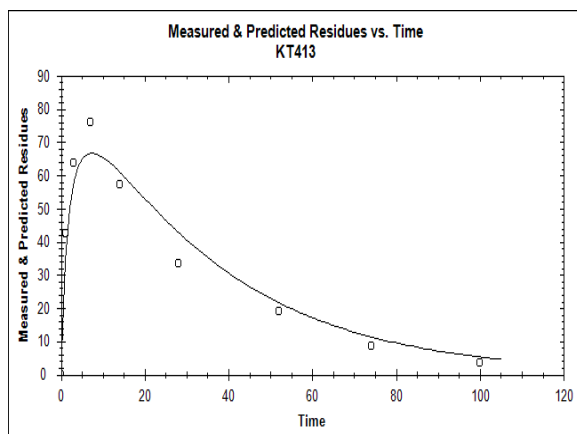
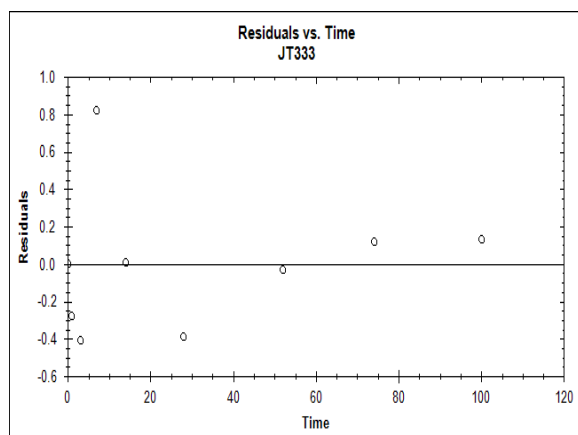
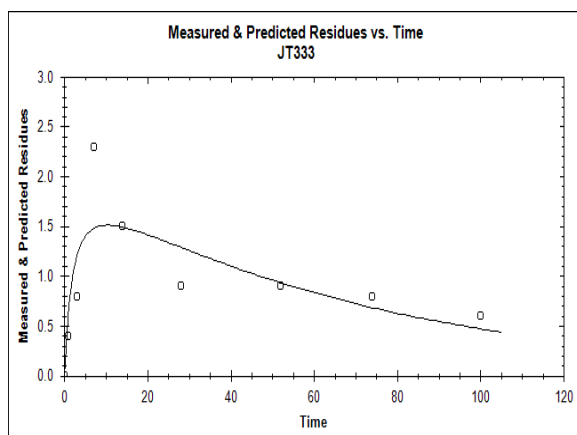
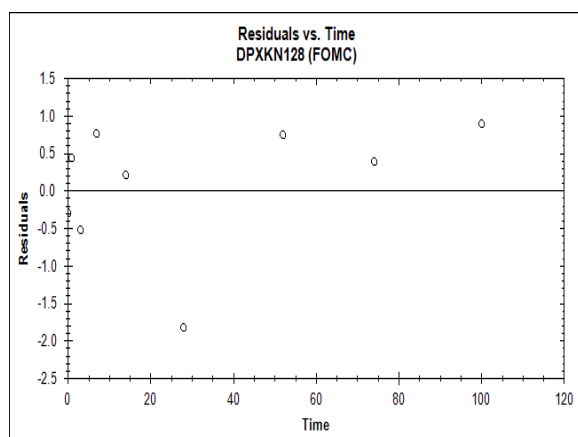
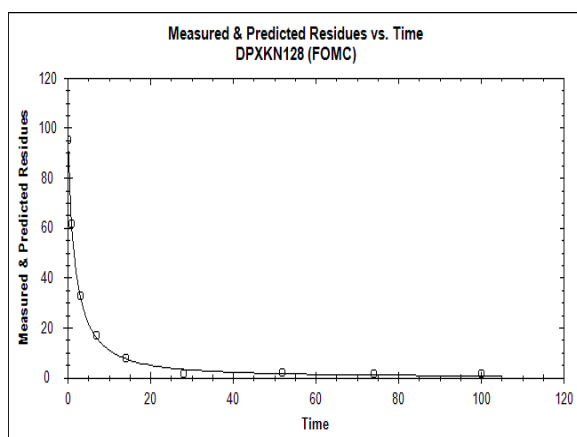


Figure 23
Optimised FOMC -SFO kinetic model of indoxacarb and metabolites in Goose River: Total system, indanone label, M-I (continued)

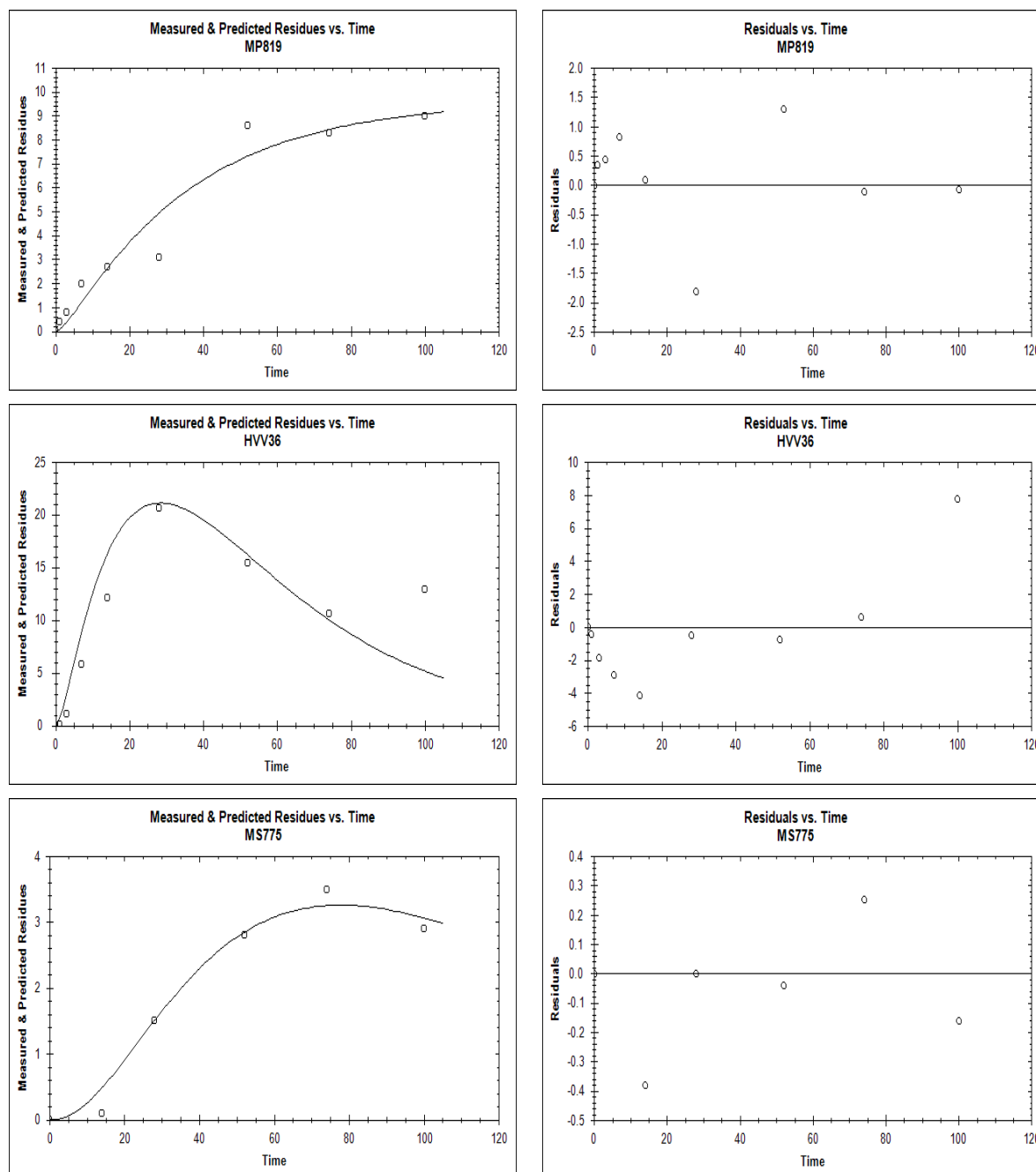


Figure 23
Optimised FOMC -SFO kinetic model of indoxacarb and metabolites in Goose River: Total system, indanone label, M-I (continued)

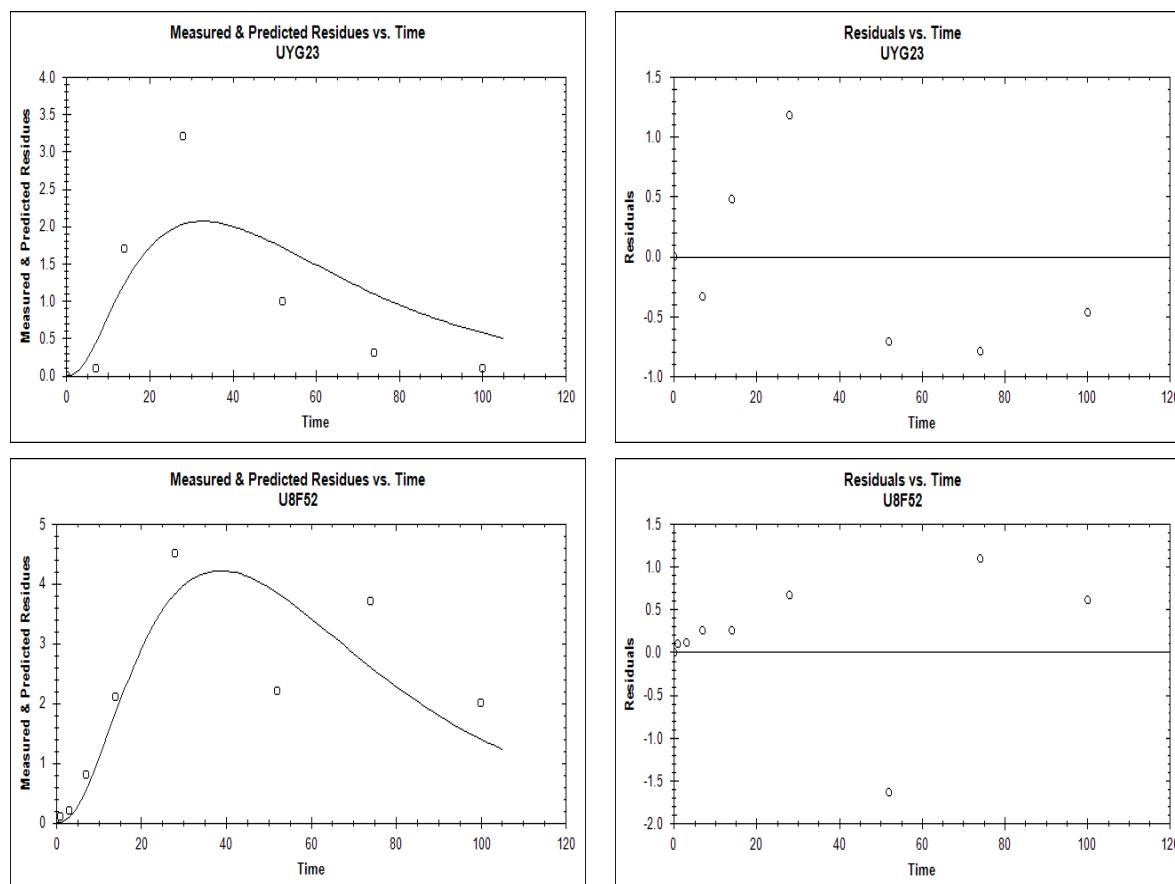


Figure 24
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Goose River: Total system, TFMP Label, M-I

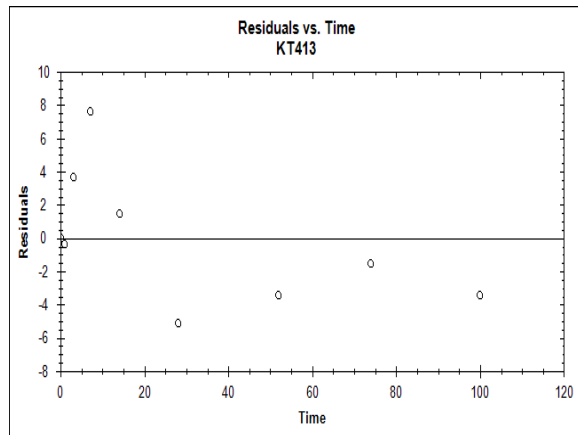
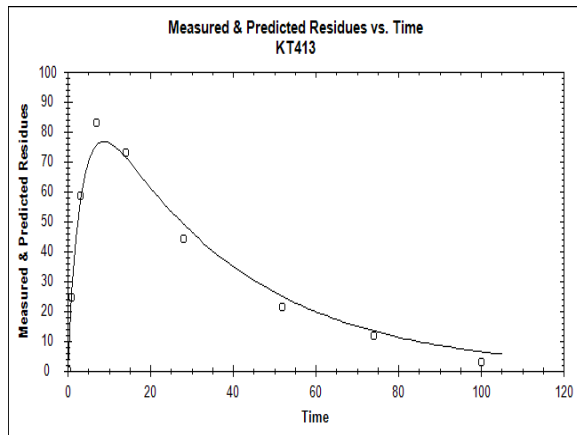
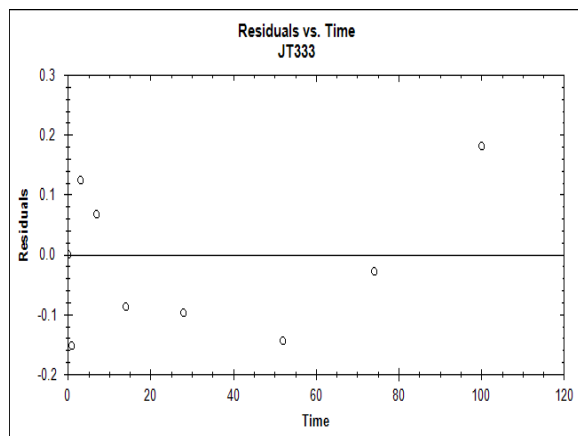
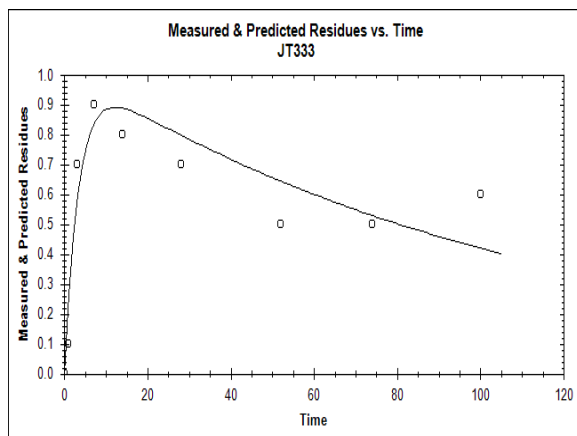
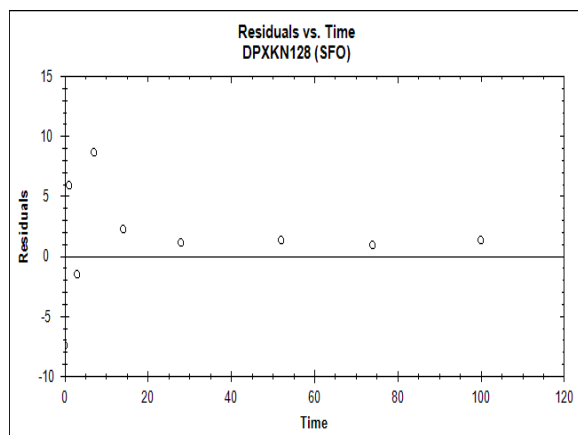
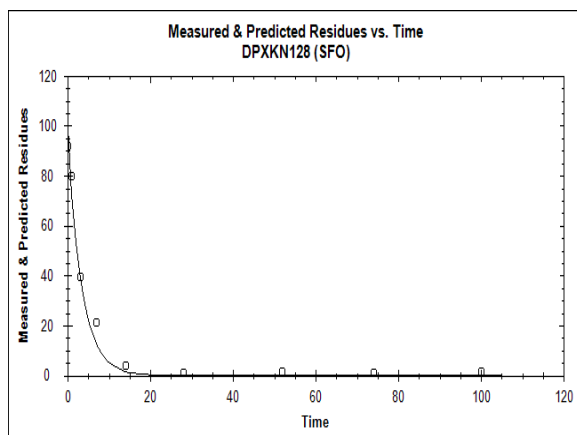


Figure 24
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Goose River: Total system, TFMP Label, M-I (continued)

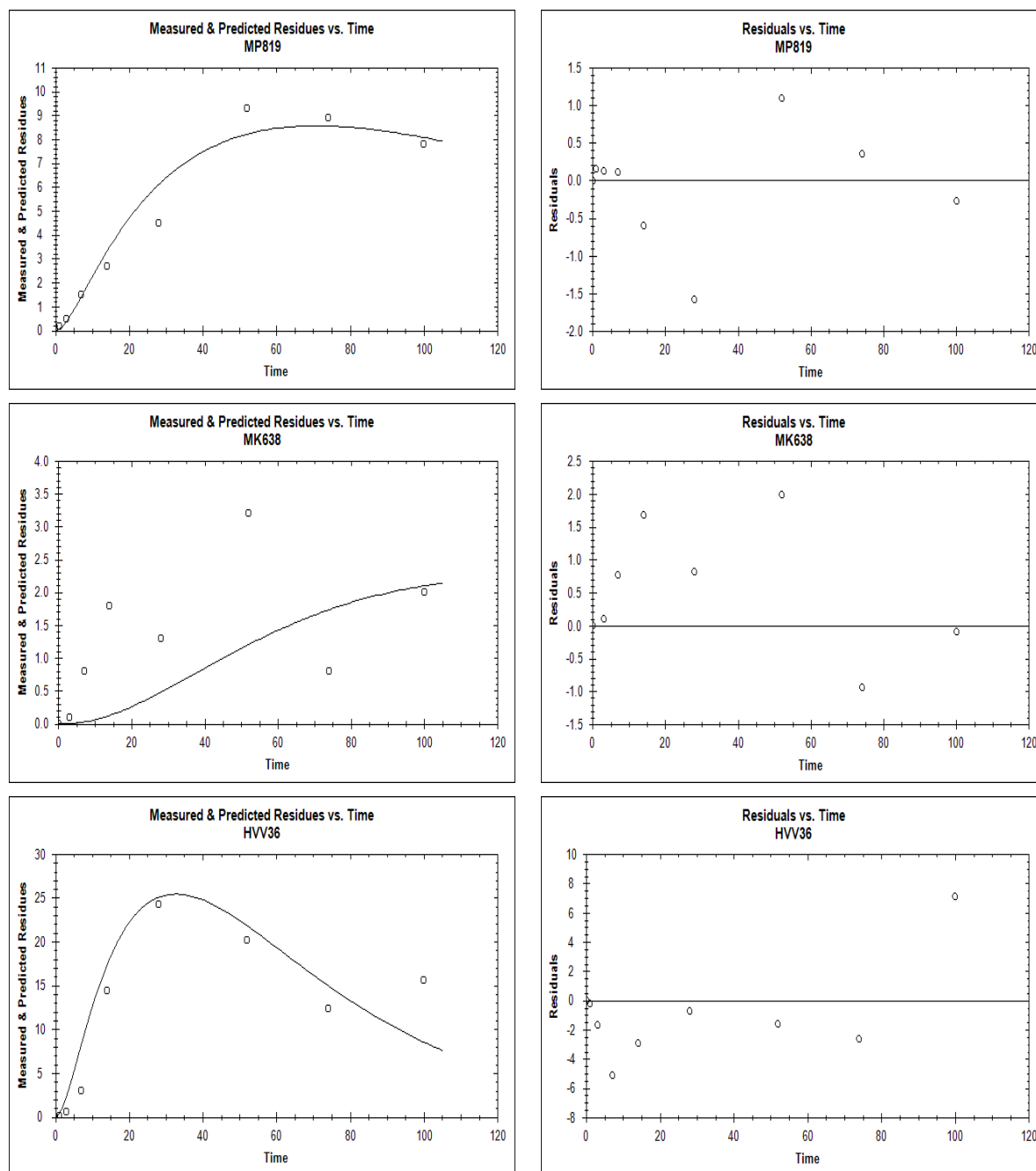


Figure 24
Optimised SFO -SFO kinetic model of indoxacarb and metabolites in Goose River: Total system, TFMP
Label, M-I (continued)

