Data Evaluation Report on the aerobic biotransformation of XDE-742 (pyroxsulam) in soil

PMRA Submission Number 2006-4727; EPA MRID Number 46908329; APVMA ATS 40362

Data Requirement:	PMRA DATA CODE:	8.2.3.4.2
	EPA DP Barcode:	332118
	OECD Data Point:	IIA 7.1.1, IIA 7.2.1
	EPA Guideline:	Subdivision N, §162-1 Aerobic Soil Metabolism

Common name:	XDE-742 (pyroxsulam)
Chemical name:	
IUPAC	*N*-(5,7-dimethoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide
CAS name	N-(5,7-dimethoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide
CAS No.	422556-08-9
Synonyms	XDE-742/BAS770H, XR-742
SMILES string:	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(cc3OC)OC)(=O)=O

Primary Reviewer:	Hemendra Mulye (PMRA)	**Date:** February 5, 2007
Secondary Reviewers:	J. Catherine Evans (PMRA)	**Date:** March 9, 2007
	David McAdam (AUS DEW)	**Date:** 29 May 2007
	D. Murphy for David McAdam	November 2, 2007
	Greg Orrick (USEPA)	**Date:** June 18, 2007
	Electronic for Greg Orrick	October 25, 2007
	Émilie Larivière (PMRA)	**Date:** October 19, 2007
	Émilie Larivière	October 19, 2007

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CITATION: Yoder, R. N., Meitl, T. J., Balcer, J. L., and Linder, S.J., 2005. Aerobic Soil Degradation of ^{14}C-XDE-742 in Four European Soils, Dow AgroSciences LLC, 9330 Zionsville Road, Indianapolis, IN 46268, 030013, M. D. Culy, January 12, 2006. PMRA # 1283157.

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EXECUTIVE SUMMARY:

The biotransformation of radiolabeled XDE-742 was studied in one French and three German soils; a Charentilly light clay (France), a LUFA 3A clay loam, a Borstel loamy sand, and a Bruch West sandy loam for 133 days after treatment (DAT). Samples were treated separately with ^{14}C-XDE-742 radiolabeled at the 2 and 6 positions of the pyridine ring or at the 2-position of the triazolopyrimidine ring. XDE-742 was applied at the rate of 0.033 mg a.i./kg soil (equivalent to 25 g a.i./ha). Samples were incubated under aerobic conditions in the dark (20°C and 40% moisture holding capacity) for up to 4 months after treatment. The study was conducted in accordance with the European Commission Directive 91/414/EEC (as amended by Directive 94/37/EEC) and SETAC Part 1 Section 1. This study was designed to meet Good Laboratory Practices standards, 40 CFR Part 160.

The test system consisted of two-chambered biometer flasks; one chamber containing 0.2 N NaOH for the collection of CO_2, and the other contained the treated soil. Samples were analysed at 0, 1, 3, 7, 14, 21, 29, 63, 94, and 133 days after treatment. One sample of each radiolabel was analysed at each time point. The soil samples were extracted three times with 90:10 acetonitrile: 1.0 N HCl and XDE-742 residues were analysed by HPLC. Five transformation products reaching concentrations of greater than 5% of the applied radioactivity were identified by a LC/MS comparison with authentic standards.

Average material balance values for the four tested soils were 99-101% of applied radioactivity. Several individual samples with recoveries less than 90% or greater than 110% of the applied radiocarbon were not used to determine transformation rates and their results were not reported. The concentration of the parent compound decreased from approximately 100% at 0 DAT to less than 5% of the applied radioactivity at the end of study period.

XDE-742 aerobic soil transformation rates were calculated for all four tested soils. Half-lives ranged from 2 to 10 days on the four soils tested in this study. The corresponding $t_{9/10s}$ ranged from 7 to 33 days.

Five transformation products reaching concentrations of greater than 5% of the applied radiocarbon were identified. The 5-OH-XDE-742 reached at a maximum concentration of 24% of the applied radiocarbon in the LUFA 3A clay loam at 3 DAT. The other four transformation products were observed at their maximum concentrations in the Charentilly light clay. The 7-OH-XDE-742 was observed at 13% of applied and the 6-Cl-7-OH-XDE-742 was observed at 26% of applied at 7 DAT. The transformation products cyanosulfonamide (CSF) and the pyridine sulfonic acid (PSA) reached their respective maximum concentrations of 8% and 6% of the applied at the 21-DAT and 1-month time points. All transformation products were observed at declining concentrations in all soil types at the end of the study period.

At the end of the study period, between 5 and 15% of the applied radioactivity was recovered in

the gas traps and was identified as CO_2. Non-extractable residues (NER) accounted for up to 94% of the applied radioactivity, with 60-90% at study termination. The unidentified radioactivity was made up of several small, extractable transformation products in total accounting for less than 5% of the applied radiocarbon.

The degradation of ^{14}C-XDE-742 at 10°C was studied on one soil, the Charentilly light clay. At 10°C, the DT_{50} was 14 days compared to 4 days at 20 °C. XDE-742 degradation was greatly reduced on Charentilly light clay soil samples sterilized with gamma irradiation. In sterilized soil at 20 °C, XDE-742 was projected to have a DT_{50} greater than 450 days (extrapolated beyond test duration of 133 days), indicating that the transformation of XDE-742 in the soil was microbially-mediated. Results in the Charentilly light clay soil also demonstrate a correlation between the rate of transformation of the parent and the formation of the NER. The NER is a result of incorporation of the radiocarbon into the soil biomass. After four months, the slower transformation rate at 10°C still led to essentially complete transformation of the parent and incorporation of the radiocarbon into the soil NER pool (parent was 2.1-2.6% and NER was 46.3-53.3%), while the untransformed parent was still readily extractable in the sterile soil (between 83.8 and 89.7% of the applied radioactivity remained as parent, while only 10.0 to 10.5% was NER).

A supplementary aerobic soil biotransformation study using exhaustive extraction methods was submitted as part of a clarification request to provide further evidence that the soil nonextractable residues are not from failure to extract pyroxsulam or any of its transformation products. Study conditions were similar (same soils, application rate, temperature, etc.). Samples were collected after 0, 1, 4, 7, 14, 29, 42, 63, 82, 100 and 118 days. Samples with more than 10% of the applied radioactivity unextracted after the initial extraction procedure with 90:10 acetonitrile:1 N HCl were subjected to additional extractions. Samples were sequentially extracted twice with 90:10 methanol:5 N HCl, twice with a borate aqueous buffer (pH approximately 10) and twice with 90:10 methanol: 2 N NaOH. Up to 28.8% of the applied that remained unextracted after the initial extraction were extracted under the additional extraction procedures. One major transformation product, not observed in the original study, was identified by LC/MS and comparison with an authentic standard of the XDE-742 sulfonamide. Maximum concentrations ranged from 1.9 to 13.2% of the applied radioactivity. Apart from the Borstel loamy sand, where maximum concentrations were observed at study termination (118 days), concentrations of this transformation product were declining by the end of the study. The other results of the supplemental study were relatively consistent with those of this study: the half-lives ranged from 2 to 15 days, transformation products were similar except for the above-noted exception, and NER accounted for 30-80% of the applied radioactivity, even after the exhaustive extraction procedures. Results of the supplementary study combined with those of the original study indicate that the majority of NER is a result of incorporation of the radiocarbon into the soil biomass and not from inability to extract pyroxsulam.

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Results Synopsis:

Soil type	Half-life (days)	$t_{9/10}$ (days)
Charentilly	3.8	12.6
LUFA 3A	2.1	6.8
Borstel	10.0	33.3
Bruch West	2.7	9.1

Major transformation products: 5-OH-XDE-742, 7-OH-XDE-742, 6-Cl-7-OH-XDE-742 (XDE-742 sulfonamide, formed in the supplementary study submitted).
Minor transformation products: cyanosulfonamide (CFS) and pyridine sulfonic acid (PSA).

Study Acceptability: PMRA and DEW: This study, in combination with the supplementary aerobic soil biotransformation study using exhaustive methods, is classified acceptable and satisfies the guideline requirement for an aerobic biotransformation study in soil.

USEPA: This study is classified as **supplemental** and does not satisfy the Subdivision N §162-1 guideline requirement. Multiple solvent systems were not employed in a reasonable extraction attempt; non-extractable [^{14}C]residues were measured at >10% of the applied by day 1, 3 or 7, were as high as 94%, and remained at 59-90% at study termination. A following study confirmed that multiple extraction procedures extracted up to 28.8% of the applied more than the extraction procedure of this study alone, which indicates that the results of this study are uncertain and should be superseded by those of the following study (Yoder *et al.*, 2007).

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted to fulfill the European Commission Directive 91/414/EEC (as amended by Directive 94/37/EEC) and SETAC Part 1 Section 1. There were no deviations from the guidelines.

COMPLIANCE: This study was conducted to meet Good Laboratory Practices standards, 40 CFR Part 160. Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

A. MATERIALS:

1. **Test Material:** Because XDE-742 contains two separate ring systems, two radiolabeled forms of the technical product were used to study the degradation of XDE-742 on soil.

Figure 1. XDE-742 TP test material

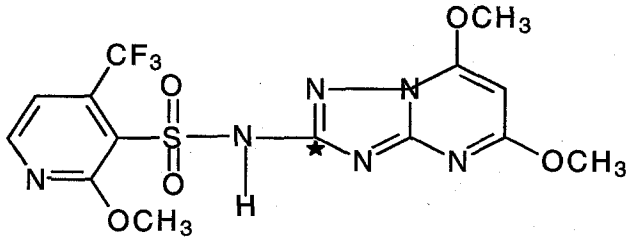
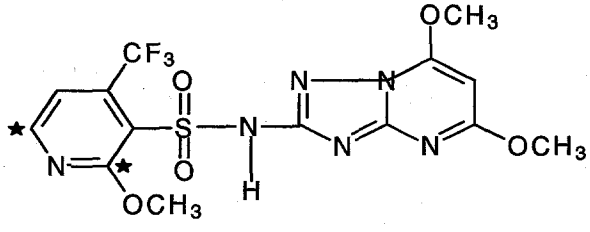
Common Name	TP-XDE-742		
	 * indicates position of radiolabel		
Synonyms	^{14}C-XDE-742-TP, X666742-Het-2-^{14}C		
Inventory#	INV1901	**Description**	Radiolabeled test material
Formula	$C_{14}H_{13}F_3N_6O_5S$	**MW**	434.4 g/mole
Purity (^{14}C)	100% (May 1, 2003)	**Specific Activity**	36.6 mCi/mmole
Storage	Stable during freezer storage		

Figure 2. XDE-742 PY test material

Common Name	PY-XDE-742		
	 * indicates position of radiolabel		
Synonyms	^{14}C-XDE-742-PY, XDE-742-pyridine-2,-6-^{14}C		
Inventory#	INV1905	**Description**	Radiolabeled test material
Formula	$C_{14}H_{13}F_3N_6O_5S$	**MW**	434.4 g/mole
Purity (^{14}C)	100% (May 1, 2003)	**Specific Activity**	43.7 mCi/mmole
Storage	Stable during freezer storage		

Physico-chemical properties of XDE-742

Parameter	Values	Comments
Water solubility	16.4 mg/L at pH 4 and 20 °C 3.20 x 10^3 mg/L at pH 7 and 20 °C 1.37 x 10^4 mg/L pH 9 and 20 °C 62.6 mg/L at 20 °C (unbuffered)	(1)

Parameter	Values	Comments
Vapour pressure/ volatility	$< 10^{-7}$ Pa $<8 \times 10^{-10}$ torr	(2)
pKa	4.51 (25 °C)	Probe data (3)
Kow : Log D	1.080 at pH 4 -1.010 at pH 7 -1.600 at pH 9	(4)
Stability of compound at room temperature, if provided	Not available	

2. Soil Characteristics

Following sampling, each soil was handled at all times in accordance with ISO/DIS 10381-6.

Table 1: Description of soil collection and storage.

Soil Type	Charentilly light clay
Parameter	Description
Geographic Location	Loire Valley, France
Site Description	Fallow
Pesticide Use History	Glyphosate last two years
Collection Date	March 19, 2003
Collection Procedures	Soil was collect at several points with a common garden spade
Sampling depth (cm)	Approximately 18 cm
Shipping Date	March 19, 2003
Shipping Conditions	Fresh (ambient temperature)
Storage Conditions at Facility	4 °C
Storage Length prior to use	2 months
Soil Preparation prior to use	Sieved, 2 mm
Soil Type	LUFA 3A clay loam
Parameter	Description
Geographic Location	Baden-Wurtemberg, Germany
Site Description	Fallow
Pesticide Use History	none past two years
Collection Date	February 25, 2003
Collection Procedures	Spade used to transfer soil to plastic box

Sampling depth (cm)	20 cm
Shipping Date	March 13, 2003
Shipping Conditions	Couriered, conditions not available
Storage Conditions at Facility	4 °C
Storage Length prior to use	3 months
Soil Preparation prior to use	Sieved, 2 mm
Soil Type	Borstel loamy sand
Parameter	Description
Geographic Location	Borstel, Germany
Site Description	cropped, winter rye.
Pesticide Use History	no pesticides listed in previous two years
Collection Date	March 6, 2003
Sampling depth (cm)	0-25 cm
Shipping Date	April 8, 2003
Shipping Conditions	Refrigerated in the dark
Storage Conditions at Facility	4 °C
Storage Length prior to use	2 ½ months
Soil Preparation prior to use	Sieved, 2 mm
Soil Type	Bruch West sandy loam
Parameter	Description
Geographic Location	Bruch West, Limburgerhof, Germany
Site Description	grass covering
Pesticide Use History	no pesticides used since 1997
Collection Date	February 17, 2003
Sampling depth (cm)	0-25 cm
Shipping Date	April 8, 2003
Shipping Conditions	Refrigerated in the dark
Storage Conditions at Facility	4 °C
Storage Length prior to use	3 months
Soil Preparation prior to use	Sieved, 2 mm

Table 2: Properties of the soils

Parameter	Results			
Study Designation	M641	M642	M661	M662
Geographic Location	France	Germany	Germany	Germany
Soil Series	Charentilly	LUFA 3A	Borstel	Bruch West
Texture Class	Clay loam	Sandy loam	Sand	Sandy loam
International Class [a]	Light Clay	Clay Loam	Loamy Sand	Sandy Loam
% Sand [a]	45	63	89	76
% Silt [a]	28	20	7	12
% Clay [a]	27	17	4	12
pH [b]	6.2	7.8	5.7	7.9
% Organic Carbon [c]	1.0	2.1	1.4	1.4
Initial Soil Biomass (µg/g) [d]	87	513	56	145
Final Soil Biomass(µg/g) [d]	131	379	54	136
CEC (meq/100g) [e]	17.0	14.5	6.7	9.9
% Moisture at 0 Bar [f]	68.2	62.8	35.8	49.3
40% MHC	27.3	25.1	14.3	19.7
% Moisture at 1/10 Bar [g]	33.6	35.5	13.9	22.9
% Moisture at 1/3 Bar [g]	20.6	22.0	8.9	12.6
% Moisture at 1 Bar [h]	16.7	17.6	5.9	10.3
% Moisture at 15 Bar [h]	10.4	10.4	3.8	7.3
Bulk Density (disturbed) [i]	1.1	1.2	1.4	1.3

[a] % Texture Analytical Procedure.

[b] pH Analytical Procedure-1:1 soil:water Method

[c] Organic Carbon (Walkley Black Method with Heat)

[d] Determination of Soil Microbial Biomass

[e] Cation Exchange Capacity-NH_4 Displacement Method

[f] Water Holding Capacity at 0 bar

[g] Water Holding Capacity (0.1 & 1/3 bar tension)

[h] Water Holding Capacity (1 & 15 bar tension)

[i] Bulk Density Analytical Procedure - Disturbed Samples

B. EXPERIMENTAL CONDITIONS:

1) Preliminary experiments: No preliminary experiments were conducted.

2) Experimental conditions:

Table 3: Experimental design.

Parameter		Description
Duration of test		Up to 4 months post treatment
Soil conditions		40% MHC, 20°C
Soil sample weight		50 g (oven dry) moist equivalent
Test concentrations	mg ai./kg soil	0.033 µg/g
	g ai./ha	25 g a.i./ha
Control conditions (if used)		Treated with ^{14}C-DCBA at experimental initiation. Incubated at 20°C for 8 DAT.
Number of replicates	Treatments	Duplicates of each soil type at each time point
	Control	Duplicate controls at 8 DAT
Test apparatus		2-chambered biometer flask
Traps for CO_2 and organic volatiles		0.2 N NaOH in biometer side-arm
Test material application	Identity of solvent	water
	Volume of solution	1 mL
	Application method	Drop-wise with syringe to soil surface
	Evaporation of solvent	N/A, dosing solutions in water
Test material sorption to walls of apparatus?		N/A
Experimental conditions	Temperature °C	20 ± 2°C; Additional samples incubated at 10 ± 2°C
	Moisture content	40% MHC
	Moisture maintenance method	Moisture checked at each time point gravimetrically
	Continuous darkness	Yes
Other details		N/A

3. **Aerobic conditions** Biometers were connected via an expansion bulb in the caustic trap to an O_2 manifold in an incubator to sustain aerobic conditions during incubation.

4. **Supplementary experiments:** ^{14}C-DCBA (dichlorobenzoic acid) was used to characterize soil microbial viability. Initial soil microbial activity was measured by dosing control samples with ^{14}C-DCBA. Control flasks for each soil type were prepared in an identical manner and at the same time as the samples used to measure the rate of XDE-742 transformation but were not dosed with XDE-742.

   At study initiation, control samples were dosed with ^{14}C-DCBA at a nominal rate of 0.05 µg/g. Dose checks were taken before and after fortification to verify the DCBA application rate. After incubation at 20°C under aerobic conditions for 8 days, a portion of the caustic trapping solution was collected and triplicate aliquots were analyzed by LSC. Soil samples were then extracted twice with 90:10 acetonitrile: 1 N HCl. All extractable radioactivity was assumed to be DCBA.

5. Sampling:

Table 4: Sampling details.

Parameter		Description
Sampling intervals		0, 1, 3, 7, 14, 21 DAT, and 1, 2, 3, and 4 months after treatment for 20°C samples. 0, 4, 7, 13 DAT and 1, 2, 3, and 4 months of incubation at 10°C. 0, 4, 7, 14 DAT and 1, 2, 3, and 4 months for sterile samples.
Soil sampling procedures		Soil samples extracted 3X with 90:10 acetonitrile: 1.0 N HCl. Extracts concentrated prior to reverse-phase HPLC analysis.
Collection of CO_2 and volatile organics		Aspiration of NaOH trap, followed by LSC counting of triplicate 1-mL aliquots
Sampling interval times	Moisture content	Determined gravimetrically with each sample
	Sterility checks	N/A
	Redox potential/Other	N/A
Sample storage before analysis		Samples extracted on day of sampling. Sample extracts stored in freezer or refrigerator prior to HPLC analysis, generally for less than 1 week. Re-analysis of various extracts showed stability during storage.
Other observations	Microbial Activity	Soil biomass determined prior to study initiation and after completion of incubation period.

C. ANALYTICAL METHODS

1. **Sample Preparation and Processing:** The caustic trapping solution was removed from the biometer side arm. The entire soil sample was transferred to a labeled, weighed centrifuge bottle for extraction. The bottle weight plus soil was also recorded to determine the final sample moisture.

2. **Organic Solvent Extraction:** Extraction solvent (90:10 acetonitrile: 1 N HCl) was added to each soil sample before extraction on a horizontal shaker. The sample was then centrifuged and the extract decanted into a labeled jar. Fresh solvent was added to the soil pellet, vortexing, shaking and centrifuging as before. The extracts were combined and the extraction process was repeated once more for a total of 3 extractions. Triplicate aliquots were assayed for radioactivity by LSC. The extracted soil pellet was allowed to air dry in a hood prior to combustion analysis to determine the amount of non-extractable residues present.

3. **Preparation of Samples for HPLC Analysis:** Concentration of the organic extracts was necessary prior to HPLC analysis. An aliquot of each organic extract was brought to a pH between 6 and 8 (as determined using pH paper) with 1 N NaOH. The neutralized solution was then centrifuged and the supernatant was transferred to a centrifuge tube.

The procedure then varied by soil type and time point. Later time points for the Charentilly light clay and the Borstel loamy sand were prepared for HPLC analysis as follows. The precipitate remaining after decanting the neutralized extract was washed with 50:50 water: acetonitrile containing 1% acetic acid, then placed on a horizontal shaker for ½ hour. The washed precipitate was then centrifuged. The rinse was combined with the neutralized extract, and the combined extract was concentrated to small volume using a Turbovap evaporator. The concentrated extract was analyzed by HPLC. The remaining precipitate was dissolved in 90:10 acetonitrile: 1 N HCl and aliquots counted by LSC. The amount of radioactivity in the precipitate was corrected for when determining the percent of applied radioactivity in each HPLC peak. The radioactivity in the precipitate was extracted with strongly acidified organic solvent, but components could not be identified and quantified as the radioactivity would not remain in solution in the HPLC mobile phase (see Table 5).

LUFA 3A clay loam and Bruch West sandy loam extracts (plus earlier time points for the other two soils) were neutralized as above. The neutralized extracts were concentrated under a stream of nitrogen to dryness using a Turbovap evaporator. Samples were reconstituted with 1 mL of 50:50 acetonitrile: water containing 1% acetic acid and analyzed by HPLC.

4. **Combustion of Extracted Soil Samples:** Extracted, air-dried soil samples were combusted to determine the amount of non-extractable residues. Sub-samples of each extracted soil pellet were combusted using a Harvey biological oxidizer. The generated $^{14}CO_2$ was then collected in Harvey scintillation cocktail and assayed by LSC.

5. **Non-Extractable Residue Characterization:** Sub-samples of previously extracted, air-dried soil were extracted with 0.5 M NaOH. The sample was centrifuged and the supernatant transferred to a centrifuge tube. The sample was mixed with another aliquot of 0.5 M NaOH and again centrifuged; the supernatant was combined with the original extract. The soil pellet was then rinsed with deionized water, again centrifuging and combining the supernatant with the original extract.

   The supernatant was transferred to a centrifuge tube, acidified to pH 2 and allowed to stand at room temperature overnight. The sample was then centrifuged and the supernatant was decanted, transferred to a volumetric flask and diluted to volume using deionized water. Triplicate aliquots of the supernatant (fulvic acid) were assayed for ^{14}C by LSC. The precipitate (humic acid) was re-dissolved in 5 mL of 0.5 M NaOH. Triplicate aliquots of the humic acid fraction were assayed by LSC. Fulvic acid is defined as the acid/base soluble portion, while humic acid is the segment soluble in base but not in acid. The humin fraction is the material remaining in the soil phase after extraction with base.

6. **Metabolite Identification Procedures:** Transformation product identification was performed by comparison of chromatographic retention times and mass spectra of generated transformation products and authentic standards using LC/MS.

7. **Determination of Radioactivity:** Radioactive material in solution was quantified by a liquid scintillation counter. With the exception of HPLC fractions and humic acid determination samples, ScintiSafe Plus 50% scintillation cocktail was added to each sample before counting. The TopCount LSC was set-up to analyze samples in 96-well microplates for reconstruction of HPLC chromatograms. MicroScint 40 scintillation cocktail was added to the plates. Radioactive material remaining in the soil pellet after extraction was quantified by oxidative combustion.

8. **Chromatographic and Spectroscopic Procedures:** Table 5 lists the reverse phase HPLC method used for sample analysis. Fractions were collected for all radiolabeled samples. The collected fractions were counted by TopCount LSC and used to generate reconstructed radiochromatograms. A direct spike of each sample analyzed by HPLC was compared to the sum of the radioactivity eluted from the column and used to determine chromatographic recovery. A UV detector at 254 nm wavelength was used to determine the retention times of non-radiolabeled standards and a RAM flow-through detector was used in conjunction with the fraction collector to characterize the radioactivity in solution.

Table 5: HPLC Conditions

Time (minutes)	Solvent Ratio	Comment
0.0	95:5 A:B	Initial Conditions
5.0	95:5 A:B	Aqueous Hold
20.0	5:95 A:B	Linear Gradient
24.2	5:95 A:B	Organic Hold
30.0	95:5 A:B	Initial Conditions
35.0	95:5 A:B	Re-equilibration

Column: Column:Zorbax SB-C18
Flow rate: 1mL/min
Solvent A: Water +1% acetic acid
Solvent B: Acetonitrile + 1% acetic acid

Typical Retention Times (in minutes) for Analytical Standards and Metabolites

Compound	Standard (UV)	Sample (^{14}C Fraction)
XDE-742	N/A	17.7
6-Cl	16.1	16.3
5-OH	15.8	15.8
7-OH	14.9	15.2
5,7-OH	14.4	NA
CSF	14.4	14.3
PSA	12.4	12.4

9. **Definitions of Detection Limits:** Using the method of Currie (5), the quantitation limit of ^{14}C for the sub-samples (e.g., caustic traps, organic extracts, combustions) and HPLC analyses were 3% or less of applied radiocarbon for each process. Limits of quantitation and detection for each sub-sample as a percentage of the applied radiocarbon are given in Table 6.

Table 6: Limits of Detection and Quantitation

Sub-sample Identification	Radio-Label	% of Applied ^{14}C	
		LOD	LOQ
Caustic Trap	TP	0.3	1.3
Caustic Trap	PY	0.3	1.1
Organic Extracts	TP	0.7	2.7
Organic Extracts	PY	0.6	2.3
Soil Combustions	TP	0.4	1.4
Soil Combustions	PY	0.3	1.2
HPLC Analyses – Organic Extracts	TP	0.04	0.17
HPLC Analyses – Organic Extracts	PY	0.04	0.15

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: Aerobic conditions were maintained via connection to an oxygen manifold during the incubation period. Samples were maintained in the dark at 10 or 20 °C for up to 4 months after treatment. Gravimetric determination of soil moisture at each time point showed no significant loss of moisture during sample incubation. Soil biomass was ascertained at study initiation and termination; results are presented in Table 2.

Roughly 60-80% of the applied radioactivity was recovered in the DCBA caustic traps after 8 days of incubation, indicating that all the soils tested were able to mineralize DCBA. Results of the DCBA analysis coupled with the initial and final biomass values confirm that all the tested soils (other than the sterilized Charentilly light clay) were viable.

B. MATERIAL BALANCE: Material balance results are contained in Table 7 through Table 12. Samples with recoveries less than 90% or greater than 110% of the applied radiocarbon were not used to determine transformation rates and are not reported in the listed tables.

Table 7. Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)— **Charentilly Light Clay** (100.3 ± 4.1%)

DAT	Label	CO_2	Extract	NER	Total
0	PY	N/A	107.2	1.1	108.3
1	TP	0.2	98.1	3.1	101.3
1	PY	0.0	97.5	2.4	99.9
3	TP	1.6	88.0	11.3	100.8
3	PY	0.1	91.0	6.1	97.3
7	TP	4.4	75.0	23.6	103.0
7	PY	0.2	75.2	26.2	101.6
14	TP	8.1	44.5	49.7	102.3
14	PY	1.8	53.4	46.4	101.7
21	TP	10.8	48.4	50.5	109.7
21	PY	2.5	49.5	47.4	99.4
29	TP	9.7	40.5	48.2	98.4
29	PY	3.5	39.3	58.1	100.9
63	TP	14.2	37.3	44.0	95.5
94	TP	14.8	24.5	56.0	95.2
94	PY	12.9	28.5	52.7	94.1
133	TP	15.6	23.7	59.1	98.4
133	PY	14.9	23.4	58.9	97.2

Table 8. Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)— **LUFA 3A Clay Loam** (99.0 ±1.8%)

DAT	Label	CO_2	Extract	NER	Total
0	TP	N/A	99.1	1.0	100.2
0	PY	N/A	100.1	0.7	100.8
1	TP	0.0	90.4	10.7	101.2
1	PY	0.0	88.4	11.3	99.8
3	TP	0.5	62.9	35.5	99.0
3	PY	0.1	63.7	36.3	100.1
7	TP	1.2	25.1	73.1	99.4
7	PY	0.2	24.8	75.3	100.3
14	TP	2.1	8.0	91.7	101.8
14	PY	1.2	10.3	87.5	99.0
21	TP	2.5	4.7	91.7	98.9
21	PY	2.3	6.0	92.7	100.9
29	TP	2.7	3.6	91.2	97.5
29	PY	2.5	4.9	92.5	99.9
63	TP	3.7	2.9	88.5	95.0
63	PY	4.6	3.8	90.7	99.2
94	TP	4.1	2.7	88.9	95.7
94	PY	5.3	2.9	88.4	96.7
133	TP	4.1	2.1	91.6	97.8
133	PY	5.7	2.5	89.3	97.6

Table 9. Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)— **Borstel Loamy Sand** (100.5 ± 4.1%)

DAT	Label	CO_2	Extract	NER	Total
0	TP	N/A	103.5	0.8	104.3
0	PY	N/A	100.3	0.5	100.8
1	TP	0.0	97.6	2.3	100.0
1	PY	0.0	99.4	1.7	101.1
3	TP	0.2	92.8	5.9	98.9
3	PY	0.1	92.6	5.3	98.1
7	TP	0.6	82.9	16.8	100.3
7	PY	0.0	86.7	13.9	100.6
14	TP	1.1	65.8	34.7	101.6
14	PY	1.3	69.9	34.1	105.3
21	TP	3.3	53.3	51.4	108.0
21	PY	0.4	56.6	43.0	100.0
29	TP	3.8	43.5	53.8	101.1
29	PY	0.3	50.2	56.7	107.2
63	TP	6.7	31.5	59.4	97.6
63	PY	1.2	40.6	48.8	90.5
94	TP	7.7	28.8	58.8	95.4
94	PY	1.7	37.4	55.7	94.8
133	TP	8.1	25.7	68.5	102.4
133	PY	2.1	36.7	62.8	101.7

Table 10. Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)— **Bruch West Sandy Loam** (99.3 ±2.2%)

DAT	Label	CO_2	Extract	NER	Total
0	TP	N/A	101.4	0.6	101.9
0	PY	N/A	101.1	0.4	101.5
1	TP	0.1	93.6	5.0	98.6
1	PY	0.0	93.2	5.2	98.5
3	TP	0.2	80.4	19.4	99.9
3	PY	0.1	74.2	24.7	99.0
7	TP	0.8	29.3	68.8	98.9
7	PY	0.1	30.9	68.3	99.3
14	TP	0.3	9.0	92.6	101.9
14	PY	0.5	11.0	90.7	102.3
21	TP	1.8	6.4	89.6	97.8
21	PY	1.1	7.9	88.5	97.5
29	TP	1.9	5.4	94.0	101.2
29	PY	1.6	6.7	94.1	102.4
63	TP	2.7	4.0	93.1	99.9
63	PY	3.0	5.4	88.4	96.9
94	TP	3.7	4.3	90.4	98.3
94	PY	3.7	5.5	87.4	96.6
133	TP	4.3	3.0	87.0	94.3
133	PY	4.7	4.0	89.6	98.3

Table 11. Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)— **Charentilly Light Clay, 10 °C Samples** (99.7 ± 4.9%)

DAT	Label	CO_2	Extract	NER	Total
0	2	N/A	109.8	0.7	110.5
4	1	0.0	99.2	3.4	102.6
4	2	0.1	97.6	3.2	100.9
7	1	0.1	95.0	6.2	101.2
7	2	0.1	91.6	6.2	97.9
13	2	0.1	90.5	13.7	104.4
31	1	0.4	69.0	22.6	92.0
66	1	1.4	50.3	46.3	98.0
66	2	1.5	50.5	46.1	98.1
94	1	3.0	45.9	46.7	95.7
94	2	2.5	48.2	44.7	95.4
122	1	4.8	45.6	53.3	103.6
122	2	4.3	45.4	46.3	96.1

Table 12. Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)— **Charentilly Light Clay, Sterile Samples** (102.2 ± 2.0%)

DAT	Label	CO_2	Extract	NER	Total
0	2	N/A	104.4	0.0	104.5
4	2	0.6	102.4	1.2	104.3
7	1	0.5	98.9	1.9	101.3
7	2	0.3	100.0	1.7	102.0
14	1	0.6	101.3	2.8	104.7
14	2	0.3	100.7	3.1	104.0
33	1	0.0	93.7	5.5	99.2
33	2	0.1	94.1	5.5	99.7
62	1	1.1	91.5	8.1	100.6
62	2	0.0	90.9	8.4	99.3
92	1	0.5	93.8	10.1	104.3
92	2	0.5	91.0	9.4	100.8
124	1	1.0	91.2	10.5	102.7
124	2	1.0	92.2	10.0	103.2

C. TRANSFORMATION OF PARENT COMPOUND: The concentration of the parent compound decreased from 100% at 0 DAT, to less than 2% of the applied radioactivity at the end of the study period in three of the four tested soils. XDE-742 concentrations decreased from 100% to less than 5% of the applied radioactivity in the Borstel loamy sand (Table 13 through Table 16).

The concentration of XDE-742 decreased from approximately 100% of the applied radioactivity to less than 5% in the Charentilly light clay samples incubated at 10 °C (Table 17). Approximately 90% XDE-742 remained in the sterilized Charentilly light clay samples at the end of the study period (Table 18). About 2% of the applied radioactivity was recovered as parent XDE-742 in the

non-sterile Charentilly light clay samples incubated at 20 °C (Table 13).

Table 13. Transformation Product Concentrations as Percent of Applied Radioactivity with Time
Charentilly Light Clay

DAT	Label	PSA	CSF	7-OH	5-OH	6-Cl	XDE-742	Other [a]
0	PY	0.0	0.0	0.0	0.0	0.0	107.2	0.0
1	TP	N/A	0.0	6.6	2.2	1.7	86.8	0.9
1	PY	0.0	0.0	6.1	1.9	2.0	86.4	1.0
3	TP	N/A	0.0	**13.7**	**6.4**	6.4	60.8	0.6
3	PY	0.0	0.0	12.0	3.7	10.5	63.5	1.3
7	TP	N/A	3.9	13.0	2.7	19.5	32.4	3.5
7	PY	1.6	3.1	11.9	2.2	**26.2**	27.3	2.9
14	TP	N/A	3.8	5.7	1.8	16.1	5.1	3.1
14	PY	3.4	4.9	5.6	0.0	23.7	4.6	2.5
21	TP	N/A	**8.1**	8.2	2.6	11.1	5.8	2.7
21	PY	5.3	5.5	4.4	1.5	16.1	3.7	2.8
29	TP	N/A	3.6	5.2	1.4	16.3	3.1	1.3
29	PY	**5.9**	2.9	4.2	1.7	9.8	2.6	3.4
63	TP	N/A	7.9	7.9	3.0	4.4	2.4	3.4
94	TP	N/A	3.2	1.9	3.6	4.3	1.0	2.2
94	PY	2.3	5.3	5.0	1.4	4.3	1.0	1.0
133	TP	N/A	3.7	2.4	3.5	1.8	2.2	2.6
133	PY	0.6	4.1	1.2	4.2	2.9	1.4	0.7

[a] Other includes the sum of several metabolites, none of which individually accounted for more than 5% of the applied radiocarbon.
Maximum concentrations are highlighted with **bold** text.

Table 14. Transformation Product Concentrations as Percent of Applied Radioactivity with Time
LUFA 3A Clay Loam

DAT	Label	PSA	CSF	7-OH	5-OH	6-Cl	XDE-742	Other [a]
0	TP	N/A	0.0	0.0	0.0	0.0	98.3	0.8
0	PY	0.0	0.0	0.5	0.0	0.0	97.4	2.2
1	TP	N/A	0.0	**2.6**	9.9	0.0	73.8	4.1
1	PY	0.0	0.0	2.5	11.0	0.0	75.0	0.0
3	TP	N/A	0.0	2.5	22.1	0.0	37.6	0.7
3	PY	0.0	0.0	2.4	**24.1**	0.0	37.2	0.0
7	TP	N/A	0.4	0.6	18.5	1.1	3.9	0.6
7	PY	0.9	0.5	0.0	19.0	0.0	3.3	1.0
14	TP	N/A	0.5	0.6	4.5	0.5	1.5	0.2
14	PY	**1.1**	**0.5**	0.6	4.0	**1.9**	1.3	1.0
21	TP	N/A	0.5	0.5	1.7	0.5	1.0	0.5
21	PY	0.7	0.5	0.3	1.5	1.2	1.0	0.7
29	TP	N/A	0.3	0.5	1.3	0.4	0.9	0.1
29	PY	0.5	0.4	0.5	1.0	1.1	0.8	0.6
63	TP	N/A	0.4	0.2	0.6	1.3	0.3	0.0
63	PY	0.4	0.4	0.1	0.5	1.7	0.5	0.2

[a] Other includes the sum of several metabolites, none of which individually accounted for more than 5% of the applied radiocarbon.
Maximum concentrations are highlighted with **bold** text.

Table 15. Transformation Product Concentrations as Percent of Applied Radioactivity with Time
Borstel Loamy Sand

DAT	Label	PSA	CSF	7-OH	5-OH	6-Cl	XDE-742	Other [a]
0	TP	N/A	0.0	0.0	0.0	0.0	103.5	0.0
0	PY	0.0	0.0	0.0	0.0	0.0	100.3	0.0
1	TP	N/A	0.0	3.8	0.7	0.0	93.1	0.0
1	PY	0.0	0.0	3.7	1.1	0.0	94.4	0.3
3	TP	N/A	0.0	6.9	1.0	0.8	83.1	0.9
3	PY	0.0	0.0	7.5	1.7	2.4	80.9	0.2
7	TP	N/A	0.7	9.6	**1.9**	4.7	64.1	1.8
7	PY	1.2	0.8	9.9	1.9	5.5	65.5	2.0
14	TP	N/A	1.3	**12.1**	0.0	7.2	38.3	1.8
14	PY	1.7	1.6	11.5	0.7	10.0	38.5	1.2
21	TP	N/A	2.1	10.6	1.3	8.6	22.8	2.6
21	PY	1.9	2.7	11.2	0.0	11.8	21.1	1.5
29	TP	N/A	2.6	9.7	0.6	9.7	13.6	1.0
29	PY	2.2	2.5	10.5	0.7	14.3	13.4	1.1
63	TP	N/A	**3.8**	8.2	0.0	9.3	3.2	1.1
63	PY	**3.2**	2.7	6.4	0.0	**17.0**	5.5	0.0
94	TP	N/A	2.4	5.4	0.0	8.1	4.1	1.8
94	PY	2.8	2.9	5.9	0.0	14.2	3.7	0.7
133	TP	N/A	3.7	4.1	0.0	5.9	3.5	1.1
133	PY	2.8	2.9	4.8	0.0	14.9	4.1	0.7

[a] Other includes the sum of several metabolites, none of which individually accounted for more than 5% of the applied radiocarbon.
Maximum concentrations are highlighted with **bold** text.

Table 16. Transformation Product Concentrations as Percent of Applied Radioactivity with Time
Bruch West Sandy Loam

DAT	Label	PSA	CSF	7-OH	5-OH	6-Cl	XDE-742	Other a
0	TP	N/A	0.0	0.0	0.0	0.0	101.4	0.0
0	PY	0.0	0.0	0.0	0.0	0.0	100.2	0.9
1	TP	N/A	0.0	4.7	4.6	0.0	84.2	0.1
1	PY	0.0	0.0	4.1	4.9	0.0	82.6	1.6
3	TP	N/A	0.0	**9.1**	10.3	1.3	58.5	1.2
3	PY	0.0	0.0	8.9	**10.9**	1.3	52.8	0.4
7	TP	N/A	0.8	5.8	9.4	3.9	8.9	0.4
7	PY	0.6	0.8	5.2	9.1	**6.8**	8.4	0.0
14	TP	N/A	**1.1**	0.9	1.9	3.6	1.3	0.2
14	PY	**1.4**	1.1	0.6	2.0	4.6	1.2	0.2
21	TP	N/A	1.1	0.7	0.9	2.6	0.9	0.2
21	PY	1.4	0.9	0.7	0.7	3.2	0.8	0.2
29	TP	N/A	1.0	0.5	0.4	1.4	0.4	0.4
29	PY	1.3	0.6	0.5	0.7	2.7	0.6	0.4
63	TP	N/A	1.3	0.7	0.7	0.9	0.4	0.0
63	PY	1.4	1.0	0.6	0.6	1.1	0.3	0.4

[a] Other includes the sum of several metabolites, none of which individually accounted for more than 5% of the applied radiocarbon.
Maximum concentrations are highlighted with **bold** text.

Table 17. Transformation Product Concentrations as Percent of Applied Radioactivity with Time **Charentilly Light Clay, 10 °C**

DAT	Label	PSA	CSF	7-OH	5-OH	6-Cl	XDE-742	Other [a]
0	2	0.0	0.0	0.0	0.0	0.0	109.2	0.7
4	1	0.0	0.0	4.2	0.8	2.6	91.1	0.6
4	2	0.0	0.0	4.2	0.8	2.1	89.4	1.2
7	1	0.0	0.0	8.2	2.6	4.8	78.7	0.7
7	2	0.0	0.0	7.6	2.1	5.8	75.6	0.5
13	2	0.7	2.3	**35.9**	**3.5**	14.2	32.7	1.3
31	1	2.5	3.9	9.9	0.0	**28.1**	22.8	1.9
66	1	4.6	5.0	6.1	1.0	25.0	5.1	3.6
66	2	4.9	**6.0**	6.0	1.6	24.8	4.7	2.5
94	1	4.8	5.0	6.2	0.0	16.6	3.6	2.6
94	2	**5.1**	6.0	6.5	0.0	15.1	4.5	4.5
122	1	2.3	3.5	3.7	0.0	10.8	2.1	6.6
122	2	3.7	4.8	3.8	0.0	12.3	3.6	5.1

[a] Other includes the sum of several metabolites, none of which individually accounted for more than 5% of the applied radiocarbon.
Maximum concentrations are highlighted with **bold** text.

Table 18. Transformation Product Concentrations as Percent of Applied Radioactivity with Time **Charentilly Light Clay, Sterile Samples**

DAT	Label	PSA	7-OH	5-OH	XDE-742	Other [a]
0	2	0.0	0.0	0.0	104.4	0.0
4	2	0.0	0.0	0.0	102.4	0.0
7	1	0.0	0.0	0.0	98.9	0.0
7	2	0.0	0.0	0.0	100.0	0.0
14	1	0.0	0.0	2.0	99.2	0.0
14	2	0.0	0.0	1.9	98.8	0.0
33	1	0.0	0.0	8.4	85.3	0.0
33	2	0.0	0.0	**8.7**	85.4	0.0
62	1	2.7	**1.2**	0.0	87.6	0.0
62	2	**3.0**	0.0	0.0	87.9	0.0
92	1	0.0	0.0	1.1	90.9	1.8
92	2	0.0	0.0	1.6	88.3	1.0
124	1	0.0	1.2	4.7	83.8	1.5
124	2	0.0	0.0	0.0	89.7	2.5

[a] Other includes the sum of several metabolites, none of which individually accounted for more than 5% of the applied radiocarbon.
Maximum concentrations are highlighted with **bold** text.

HALF-LIFE: Transformation rates for XDE-742 on the four soils tested here were calculated by the registrant with simple first order or first order multi-compartment kinetics using Modelmaker 4.0, as presented in Table 19. DT_{50} values between 2 and 10 days were calculated and DT_{90} values ranged from 7 to 33 days.

The PMRA does not have ModelMaker. The PMRA reviewer verified the dissipation of XDE-742 with a simple first order model using SigmaPlot, and half-lives are shown in Table 20.

Untransformed data were used in the dissipation calculations. The statistical output and figures are presented in Appendix 1. The models fit the data well and the r^2 ranged from 0.986 to 0.996 for all soils. The half-lives calculated by the reviewer confirm those reported in the study report.

The half-life of XDE-742 in the Charentilly light clay at 10 °C and in sterile samples were also calculated with Modelmaker 4.0 (Table 21) using simple first order kinetics. As expected, the half-life of XDE-742 at 10 °C was longer, 14 days vs. 4 days at 20 °C. The half-life of XDE-742 under sterile conditions was longer than the 133-d study time and was extrapolated as approximately 450 days, indicating that the transformation of XDE-742 in aerobic soil takes place primarily by biotic means.

Table 19. Transformation Rates of XDE-742 and Major Transformation Products in Four European Soils

Soil/Compound	k (day^{-1})	k total (day^{-1})	DT_{50} (days)	DT_{90} (days)
Charentilly				
XDE-742		0.182	3.8	12.6
k_1 (742 to Other)	0.091			
k_2 (742 to 7-OH)	0.091			
7-OH-XDE-742		0.321	2.2	7.2
k_4 (7-OH to 6-Cl)	0.321			
7-OH-6-Cl-XDE-742		0.094	7.4	24.4
k_5 (6-Cl to Other)	0.094			
LUFA 3A				
XDE-742		0.338	2.1	6.8
k_1 (742 to Other)	0.173			
k_2 (742 to 5-OH)	0.165			
5-OH-XDE-742		0.205	3.4	11.2
k_3 (5-OH to Other)	0.205			
Borstel				
XDE-742		0.069	10.0	33.3
k_1 (742 to Other)	0.049			
k_2 (742 to 7-OH)	0.020			
7-OH-XDE-742		0.047	14.7	49.0
k_4 (7-OH to 6-Cl)	0.047	48.9	162.3	
6-Cl-7-OH-XDE-742				
k_5 (6-Cl to Other)	0.014	0.014		
Bruch West				
XDE-742		0.253	2.7	9.1
k_1 (742 to 5-OH)	0.070			
k_2 (742 to Other)	0.114			
k_3 (742 to 7-OH)	0.068			
5-OH-XDE-742		0.254	2.7	9.1
k_4 (5-OH to other)	0.254			

Soil/Compound	k (day^{-1})	k total (day^{-1})	DT_{50} (days)	DT_{90} (days)
7-OH-XDE-742		0.382	1.8	6.0
k_5 (7-OH to other)	0.260			
k_6 (7-OH 6-Cl)	0.122		9.2	30.7
6-Cl-7-OH-XDE-742		0.075		
k_7 (6-Cl to Other)	0.075			
Arithmetic Mean		0.210	4.7	15.5
SD			3.7	12.1
Geometric Mean		0.181	3.8	12.7
Maximum			10.0	33.3
Minimum			2.1	6.8

Only transformation products that reached concentrations of greater than 10% of applied in at least one soil type were used in Modelmaker 4.0.

Table 20. PMRA-calculated half-lives of XDE-742 in Four European Soils.

Soil Series	Half-life (days)	$t_{9/10}$ (days)	Regression equation	r^2
Charentilly	3.7	12.4	y = 98.8458*exp(-0.1841*x)	0.996
LUFA 3A	2.1	6.8	y = 101.7645*exp(-0.3395*x)	0.995
Borstel	9.7	33	y = 98.0666*exp(-0.0691*x)	0.996
Bruch West	2.8	9.2	y = 102.8585*exp(-0.2532*x)	0.986

Untransformed data were fit using the simple first order model y = a*exp(-b*x).

Table 21. Degradation Rates of XDE-742 in the Charentilly light clay at Low Temperature and Sterile Conditions

Conditions	k total (day^{-1})	DT_{50} (days)	DT_{90} (days)	r^2
20 °C, non-sterile	0.182	3.8	12.6	0.981
10 °C	0.050	14	46	0.975
Sterile	0.001	478	1589	0.552

TRANSFORMATION PRODUCTS: Transformation product concentrations with time as a function of soil type are reported in Table 13 through Table 18. The concentration of each product varied greatly by soil type.

The pyridine sulfonic acid (PSA) and cyanosulfonamide (CSF) product were observed above 5% of the applied radiocarbon only in the Charentilly light clay soil. PSA reached a maximum of approximately 6% of applied at the 1-month time point while CSF was observed at a maximum of 8% of applied at 21 DAT. Both products had declined to less than 5% of applied at the 4-month time point. Neither product accounted for more than 4% of the applied radiocarbon in any of the other soil types.

The 5-OH-XDE-742 accounted for 24% of the applied radioactivity at 3 DAT in the LUFA 3A clay loam. The 5-OH reached 6% and 11% at 3 DAT in the Charentilly light clay and Bruch West sandy loam, respectively and only accounted for a maximum of 2% in the Borstel loamy sand. The 5-OH-XDE-742 declined to concentrations less than 5% of applied in all four soils at the end of the study.

The 7-OH-XDE-742 and 6-Cl-7-OH-XDE-742 reached levels greater than 5% of applied in all soil types except the LUFA 3A clay loam, where neither product accounted for more than 3% of applied radioactivity. At 7 DAT the 7-OH and 6-Cl products accounted for a maximum of 14% and 26% of the applied radioactivity, respectively, in the Charentilly light clay. The 7-OH declined to less than 5% of the applied radioactivity at the 4-month time point in all tested soils. By the end of the study, the 6-Cl product had decreased from a maximum concentration of 17% of applied at 2 months to 6 and 15% (TP amd PY labels, respectively) in the Borstel loamy sand and had declined to less than 3% of applied in the other soil types.

Degradation rates for the transformation products were calculated for the non-sterile soils at 20 °C and are presented in Table 19.

NON-EXTRACTABLE AND EXTRACTABLE RESIDUES: Non-extractable [^{14}C]residues were measured at >10% by day 1, 3 or 7 and were as high as 94%. At the end of the 4-month incubation period, 90% of the applied radioactivity was recovered by combustion of the extracted soils in both the LUFA 3A clay loam and Bruch West sandy loam samples. The non-extractable residues present in the Charentilly light clay and Borstel loamy sand accounted for 59% and 68% of the applied radioactivity present at the 4-month sample point.

The non-extractable residues were divided into the fulvic, humic and humin acid fractions. The humin fraction accounted for 65-70% of the NER in the LUFA 3A clay loam and Bruch West sandy loam soils. That is, the majority of the NER was not extractable even under basic conditions. Approximately 30% of the Charentilly light clay NER was associated with fulvic acid fraction (soluble in acid and base) with 40-60% unextractable with basic solution (humin fraction). The NER from the Borstel loamy sand was about equally divided between the fulvic, humic (base soluble, acid insoluble) and humin fractions.

Examination of the results from the sterile soil and 10°C incubation study using the Charentilly light clay soil demonstrate that the majority of NER is a result of incorporation of the radiocarbon into the soil biomass, and not from inability to extract pyroxsulam.

If the NER was formed from failure to extract pyroxsulam, then one could expect to see higher NER in sterile soil due to the higher residues of the parent available in the soil. Instead, significantly less formation of NER is observed. A comparison of the % NER observed in the Charentilly light clay soil at (nominal) 30 DAT in sterile soil, microbially-active 10°C soil, and microbially active 20°C soil is provided in Table 22.

Table 22. Comparison of the pyroxsulam (XDE-472) and non-extractable residues (NER) as percent of applied radioactivity observed in the Charentilly light clay soil under different conditions over time.

Soil Series	Days after treatement	Label	Study-report DT_{50} (days)	NER (% applied radioactivity)	XDE-742 (% applied radioactivity)
Sterile, 20°C	33	PY PY	478	5.5 5.5	85.3 85.4
Viable, 10°C	31	PY	14	22.6	22.8
Viable, 20°C	29	TP PY	3.8	48.2 58.1	3.1 2.6
Sterile, 20°C	124	PY PY	478	10.5 10.0	83.8 89.7
Viable, 10°C	122	PY PY	14	53.3 46.3	2.1 3.6
Viable, 20°C	133	TP PY	3.8	59.1 58.9	2.2 1.4

The data demonstrate a correlation between the rate of transformation of the parent and the formation of the NER. After four months, the slower transformation rate at 10°C still led to essentially complete transformation of the parent and incorporation of the radiocarbon into the soil NER pool, while the untransformed parent is still readily extractable in the sterile soil.

These data demonstrate that microbial viability is a prerequisite for formation of NER, indicating that the NER results from incorporation of transformation products into the soil matrix rather than from any inability to extract pyroxsulam. Aged residues of pyroxsulam itself are readily extractable from soil using the 90:10 acetonitrile:1 N HCl extraction solvent.

VOLATILIZATION: Mineralization to CO_2 accounted for up to 15% of the applied radioactivity in the Charentilly light clay soil at the end of the incubation period. The amount of radioactivity recovered in the caustic traps of the other three soils increased steadily over time, but accounted for less than 10% of the applied radioactivity at the end of the study.

The identity of CO_2 in the caustic traps was confirmed using a saturated $BaCl_2$ solution. As the radioactivity recovered in traps reached its maximum at the end of the incubation period, the traps from each 4-month kinetics sample were selected to confirm the presence of CO_2 in the traps. Virtually all the radioactivity in the traps was confirmed to be $^{14}CO_3^{-2}$ by precipitation with $BaCl_2$ to form insoluble $Ba^{14}CO_3$. Therefore, no significant transformation products other than CO_2 (as CO_3^{-2}) were present in the caustic traps.

Approximately 5% of the applied radioactivity was recovered in the caustic traps of the 10 °C samples at the 4-month time point. Only 1% of the applied radiocarbon was found in the caustic traps of the sterile samples at the end of the incubation period.

TRANSFORMATION PATHWAY: The proposed first step in XDE-742 aerobic soil transformation is de-methylation of one of the two methoxy groups on the TP ring to 5-OH- or 7-OH-XDE-742. Each hydroxy metabolite is then further transformed to CO_2 and bound residues. The proposed transformation pathway is shown below.

Figure 3. Proposed Transformation Pathway for XDE-742 in Soil under Aerobic Conditions

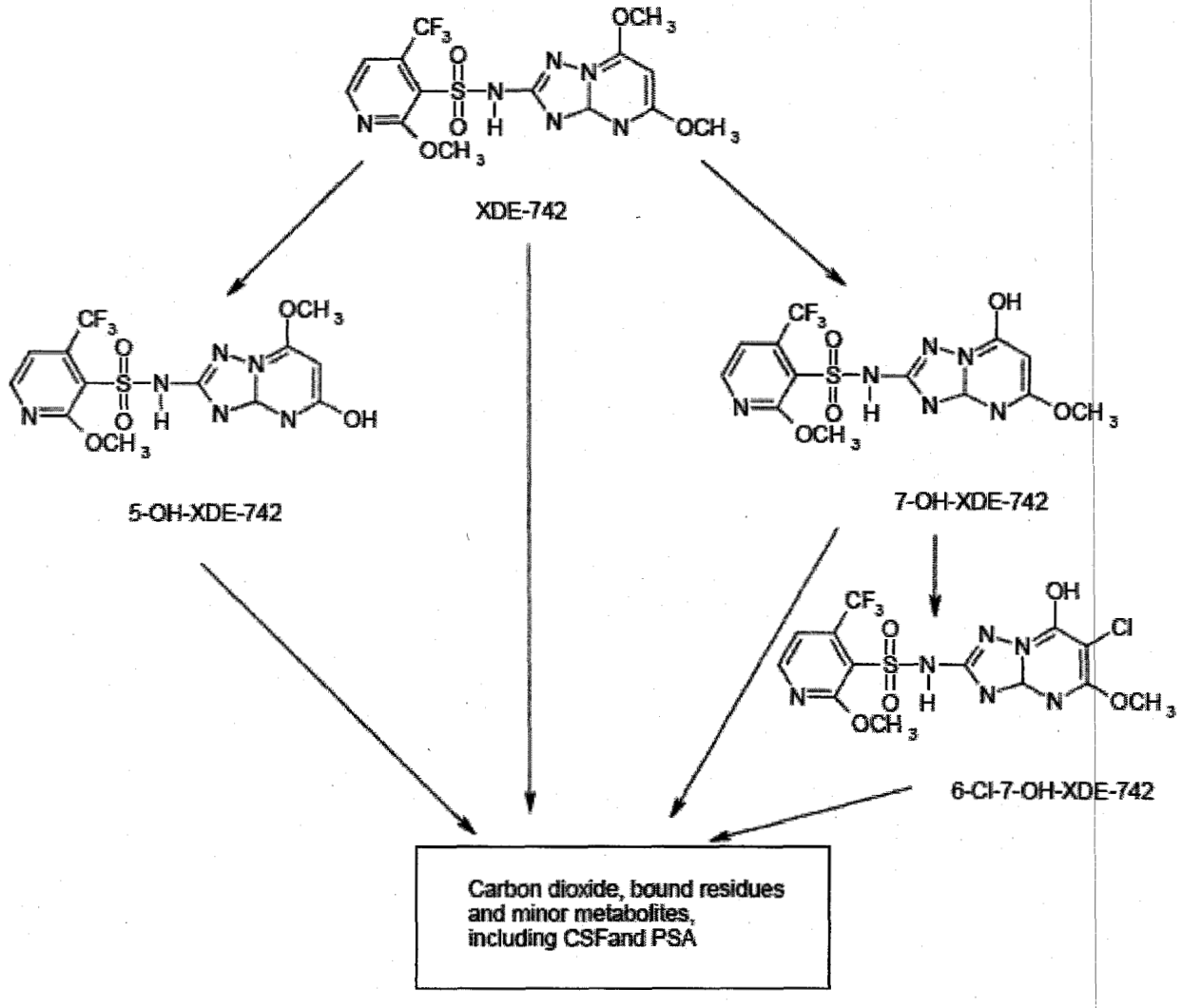
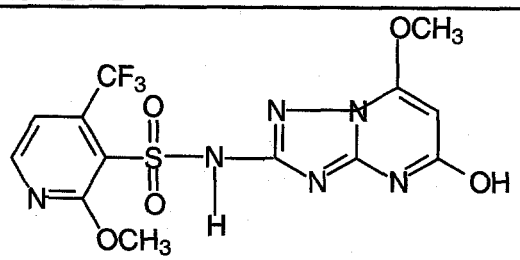
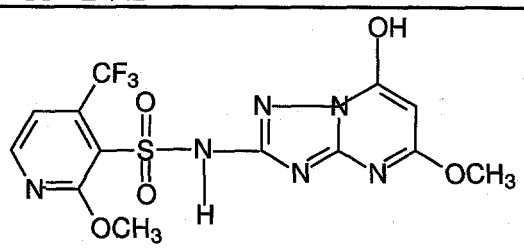


Table 23: Chemical names and CAS numbers for the transformation products of XDE-742

Common Name	5-OH-XDE-742		
			
IUPAC Chemical Name	*N*-(5-hydroxy-7-methoxy[1,2,4]triazolo [1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide		
CAS #	N/A	**SMILES String**	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(cc3OC)O)(=O)=O
Formula	$C_{13}H_{11}F_3N_6O_5S$	**MW**	420.3 g/mol

Common Name	7-OH-XDE-742		
			
IUPAC Chemical Name	*N*-(7-hydroxy-5-methoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide		
CAS #	N/A	**SMILES String**	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(cc3O)OC)(=O)=O
Formula	$C_{13}H_{11}F_3N_6O_5S$	**MW**	420.3 g/mol

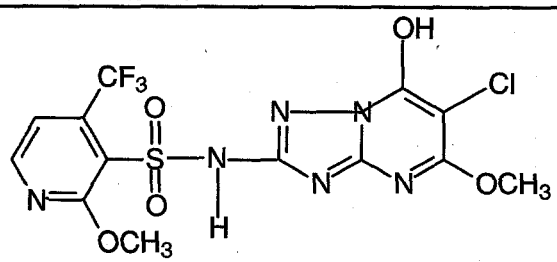
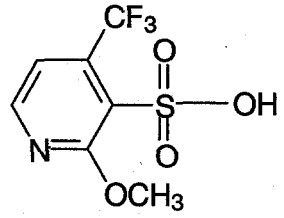
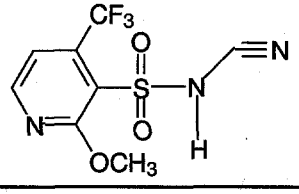
Common Name	7-OH-6-Cl-XDE-742		
			
IUPAC Chemical Name	*N*-(6-chloro-7-hydroxy-5-methoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide		
CAS #	N/A	**SMILES String**	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(c(c3O)Cl)OC)(=O)=O
Formula	$C_{13}H_{10}ClF_3N_6O_5S$	**MW**	454.77 g/mol

Table 22: Chemical names and CAS numbers for the transformation products of XDE-742 (continued)

Common Name	XDE-742 pyridine sulfonic acid (PSA)		
			
IUPAC Chemical Name	2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonic acid		
CAS #	N/A	**SMILES String**	c1(c(ccnc1OC)C(F)(F)F)S(O)(=O)=O
Formula	$C_7H_6F_3NO_4S$	**MW**	257.19 g/mol

Common Name	XDE-742 Cyanosulfonamide (CSF)		
			
IUPAC Chemical Name	N-cyano-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide		
CAS #	N/A	**SMILES String**	c1(c(ccnc1OC)C(F)(F)F)S(NC#N)(=O)=O
Formula	$C_8H_6F_3N_3O_3S$	**MW**	281.21 g/mol

III. STUDY DEFICIENCIES:

1. Only one extraction system was employed, leaving 59-90% of the applied unextracted at study termination. Therefore, attempts to identify the major degradates and establish the degradation kinetics of XDE-742 and its degradates were not reasonable for the USEPA.

A supplemental aerobic soil biotransformation study using exhaustive extraction methods (Yoder *et al.*, 2007) was submitted as part of a clarification request to provide further evidence that the soil non-extracted residues are not from failure to extract pyroxsulam or any of its transformation products. A brief summary of the study is attached in Appendix 3. Samples with more than 10% of the applied radioactivity unextracted after the initial extraction procedure with 90:10 acetonitrile:1 N HCl were subjected to additional extractions. Samples were sequentially extracted twice with 90:10 methanol:5 N HCl, twice with a borate aqueous buffer (pH approximately 10) and twice with 90:10 methanol: 2 N NaOH. The results of the supplemental study indicate that up to 28.8% of the applied that were not extracted in the original study were extractable with exhaustive extraction procedures, which invalidates the results of the original

study. NER accounted for 30-80% of the applied radioactivity in the supplemental study, even after the exhaustive extraction procedures. The PMRA reviewer feels that the extraction attempts of the two studies combined were adequate to demonstrate that NER is a result of incorporation of the radiocarbon into the soil biomass, and not from inability to extract pyroxsulam or its transformation products.

IV. REVIEWER'S COMMENTS:

PMRA Reviewer Comments: The PMRA reviewer agrees with the conclusions stated in the Study Profile Template. No significant deviations from good scientific practices were noted by the reviewer.

A supplemental aerobic soil biotransformation study using exhaustive extract methods (Yoder *et al.* 2007) was submitted to provide further evidence that the soil NER is not from failure to extract pyroxsulam or any of its transformation products. The results of the supplementary study are considered acceptable to the PMRA reviewer.

The PMRA reviewer has verified that the half-lives reported in the study report were acceptable, as verified using simple first-order models (y=a*exp(-b*x)). Results of the reviewer's statistical verification as well as Figures of the dissipation are presented in Appendix 1.

The PMRA considers this study as acceptable. It satisfies the guideline requirements for a study of biotransformation of XDE-742 in aerobic soil.

Australian Reviewer Comments. The DEW reviewer has calculated the half lives using simple first order kinetics (SFO) given in Attachment 2. The half lives range from 7 to 27 days for the total duration of the studies. This shows that the XDE-742 half lives calculated in Table 19 are not SFO but are more likely to be first order multi-compartment model (FOMC). DEW has not re-calculated the half lives using a FOMC model to confirm this. There were no other deviations from good scientific practices noted and DEW agrees the study is acceptable.

V. REFERENCES:

1. Turner, B. J., "Determination of Water Solubility for XDE-742", 2004, NAFST806, unpublished report of Dow AgroSciences, LLC.

2. Madsen, S., "Determination of the Surface Tension, Density, and Vapour Pressure of the Pure Active Ingredient XDE-742," NAFST814, 2003, unpublished report of Dow AgroSciences LLC.

3. Sheets, J. J., Gast, R. E., Hanley, T. R., Krieger, M., Mayes, M. A. "Early Stage Registration Assessment of X666742: Phase I Weed Management Sulfonamide for European and Canadian Cereal Markets," DERBI No 79155, unpublished report of Dow AgroSciences LLC, 28

September 2000.

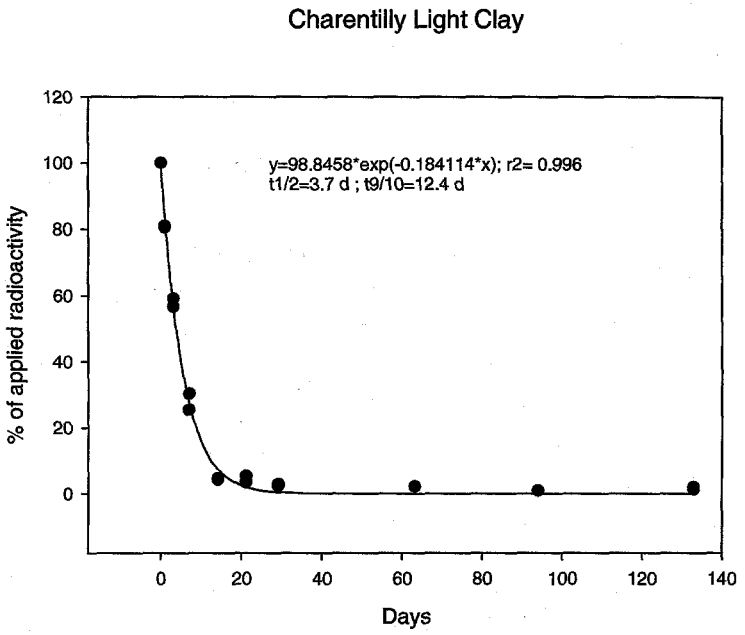
4. Turner, B. J., "Determination of Octanol/Water Partition Coefficient for XDE-742," NAFST807, 2004, unpublished report of Dow AgroSciences LLC.

5. Currie, L. A. "Limits for Qualitative Detection and Quantitative Determination-Application to Radiochemistry", Anal. Chem. 1968, 40, 586-593.

6. Yoder, R.N., K.P. Smith, J.L. Balcer, "Aerobic Degradation of XDE-472 in 4 European Soils Employing Exhaustive Extraction Methods", Study ID 061113, unpublished report of Dow AgroSciences LLC, May 11 2007.

APPENDIX 1. Statistical output from statistical verification by the PMRA reviewer

Charentilly Light Clay



Nonlinear Regression

[Variables]
x = col(1)
y = col(3)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))
[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 98.8458}}
b = if(x50(x,y)-min(x)=0, 1, -ln(.5)/(x50(x,y)-min(x))) "Auto {{previous: 0.184114}}
[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare
[Constraints]
b>0
[Options]

tolerance=0.0001
stepsize=100
iterations=100

R = 0.99803828 Rsqr = 0.99608041 Adj Rsqr = 0.99583543

Standard Error of Estimate = 2.1852

	Coefficient	Std. Error	t	P
a	98.8458	1.5480	63.8539	<0.0001
b	0.1841	0.0067	27.4485	<0.0001

Analysis of Variance:

	DF	SS	MS	F	P
Regression	1	19416.6581	19416.6581	4066.0550	<0.0001
Residual	16	76.4049	4.7753		
Total	17	19493.0630	1146.6508		

PRESS = 98.7423

Durbin-Watson Statistic = 1.1822

Normality Test: K-S Statistic = 0.3461 Significance Level = 0.0198

Constant Variance Test: Passed (P = 0.9149)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

Row	Predicted	Residual	Std. Res.	Stud. Res.	Stud. Del. Res.
1	98.8458	1.1542	0.5282	0.7483	0.7376
3	82.2240	-1.2539	-0.5738	-0.6529	-0.6408
4	82.2240	-1.6270	-0.7445	-0.8472	-0.8394
5	56.8957	-0.1793	-0.0821	-0.0905	-0.0876
6	56.8957	2.3393	1.0705	1.1805	1.1963
7	27.2422	2.9817	1.3645	1.5656	1.6473
8	27.2422	-1.7757	-0.8126	-0.9324	-0.9283
9	7.5080	-2.7505	-1.2587	-1.3166	-1.3500
10	7.5080	-3.2170	-1.4721	-1.5398	-1.6154
11	2.0692	3.3412	1.5290	1.5411	1.6170
12	2.0692	1.3823	0.6325	0.6376	0.6253
13	0.4744	2.4174	1.1062	1.1071	1.1156
14	0.4744	1.9510	0.8928	0.8935	0.8876
15	0.0009	2.2379	1.0241	1.0241	1.0258
17	0.0000	0.9328	0.4269	0.4269	0.4157
18	0.0000	0.9328	0.4269	0.4269	0.4157
19	0.0000	2.0522	0.9391	0.9391	0.9355
20	0.0000	1.3060	0.5976	0.5976	0.5852

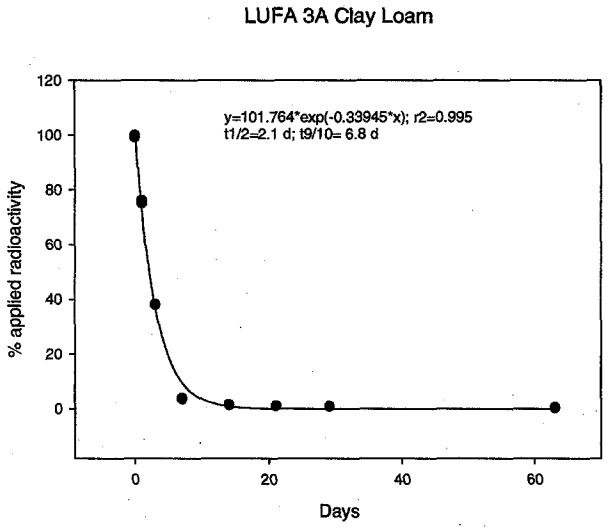
Influence Diagnostics:

Row	Cook'sDist	Leverage	DFFITS
1	0.2820	0.5018	0.7402
3	0.0629	0.2277	-0.3480
4	0.1058	0.2277	-0.4558
5	0.0009	0.1776	-0.0407
6	0.1505	0.1776	0.5559
7	0.3879	0.2404	0.9267
8	0.1376	0.2404	-0.5223
9	0.0816	0.0860	-0.4141
10	0.1116	0.0860	-0.4955
11	0.0189	0.0157	0.2041
12	0.0032	0.0157	0.0789
13	0.0010	0.0016	0.0451
14	0.0007	0.0016	0.0359
15	0.0000	0.0000	0.0002
17	0.0000	0.0000	0.0000
18	0.0000	0.0000	0.0000
19	0.0000	0.0000	0.0000
20	0.0000	0.0000	0.0000

95% Confidence:

Row	Predicted	Regr. 5%	Regr. 95%	Pop. 5%	Pop. 95%
1	98.8458	95.5642	102.1274	93.1687	104.5229
3	82.2240	80.0133	84.4348	77.0910	87.3570
4	82.2240	80.0133	84.4348	77.0910	87.3570
5	56.8957	54.9434	58.8481	51.8686	61.9228
6	56.8957	54.9434	58.8481	51.8686	61.9228
7	27.2422	24.9708	29.5136	22.0827	32.4016
8	27.2422	24.9708	29.5136	22.0827	32.4016
9	7.5080	6.1494	8.8666	2.6804	12.3356
10	7.5080	6.1494	8.8666	2.6804	12.3356
11	2.0692	1.4890	2.6495	-2.5995	6.7379
12	2.0692	1.4890	2.6495	-2.5995	6.7379
13	0.4744	0.2871	0.6617	-4.1619	5.1107
14	0.4744	0.2871	0.6617	-4.1619	5.1107
15	0.0009	0.0001	0.0017	-4.6316	4.6334
17	0.0000	-0.0000	0.0000	-4.6325	4.6325
18	0.0000	-0.0000	0.0000	-4.6325	4.6325
19	0.0000	-0.0000	0.0000	-4.6325	4.6325
20	0.0000	-0.0000	0.0000	-4.6325	4.6325

LUFA 3A



Nonlinear Regression

[Variables]
x = col(1)
y = col(5)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))
[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 101.764}}
b = if(x50(x,y)-min(x)=0, 1, -ln(.5)/(x50(x,y)-min(x))) "Auto {{previous: 0.33945}}
[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare
[Constraints]
b>0
[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.99757796 Rsqr = 0.99516179 Adj Rsqr = 0.99481620

Standard Error of Estimate = 2.7595

	Coefficient	**Std. Error**	**t**	**P**

a	101.7645	1.7727	57.4070	<0.0001
b	0.3395	0.0153	22.1163	<0.0001

Analysis of Variance:

	DF	SS	MS	F	P
Regression	1	21927.2976	21927.2976	2879.6296	<0.0001
Residual	14	106.6047	7.6146		
Total	15	22033.9024	1468.9268		

PRESS = 158.9691

Durbin-Watson Statistic = 1.1774

Normality Test: K-S Statistic = 0.2956 Significance Level = 0.0989

Constant Variance Test: Failed (P = <0.0001)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

Row	Predicted	Residual	Std. Res.	Stud. Res.	Stud. Del. Res.
1	101.7645	-1.7645	-0.6394	-0.8344	-0.8248
2	101.7645	-2.6800	-0.9712	-1.2673	-1.2979
3	72.4728	2.6035	0.9435	1.0433	1.0469
4	72.4728	3.8243	1.3859	1.5325	1.6188
5	36.7563	1.4939	0.5414	0.6398	0.6257
6	36.7563	1.0870	0.3939	0.4655	0.4521
7	9.4547	-5.4872	-1.9885	-2.1158	-2.4721
8	9.4547	-6.0976	-2.2097	-2.3512	-2.9125
9	0.8784	0.6475	0.2347	0.2352	0.2271
10	0.8784	0.4441	0.1609	0.1613	0.1556
11	0.0816	0.9357	0.3391	0.3391	0.3281
12	0.0816	0.9357	0.3391	0.3391	0.3281
13	0.0054	0.9102	0.3298	0.3298	0.3191
14	0.0054	0.8084	0.2930	0.2930	0.2832
15	0.0000	0.3052	0.1106	0.1106	0.1066
16	0.0000	0.5086	0.1843	0.1843	0.1778

Influence Diagnostics:

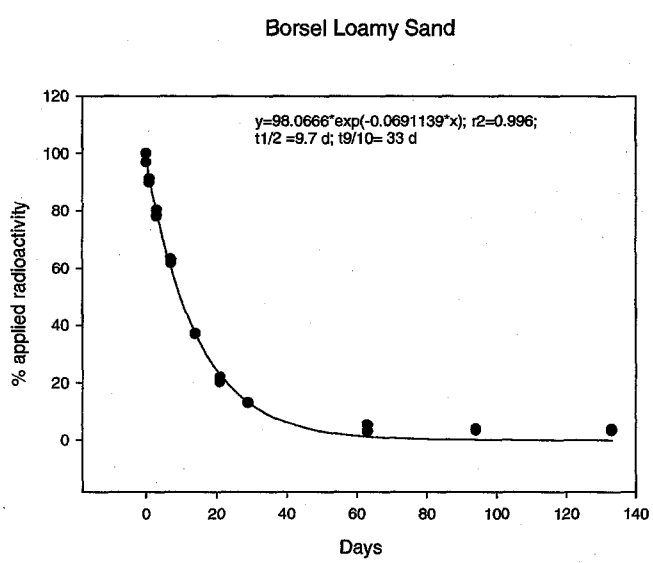
Row	Cook'sDist	Leverage	DFFITS
1	0.2446	0.4127	-0.6914
2	0.5642	0.4127	-1.0880
3	0.1213	0.1823	0.4942
4	0.2617	0.1823	0.7642
5	0.0811	0.2839	0.3940
6	0.0430	0.2839	0.2847
7	0.2958	0.1167	-0.8987
8	0.3653	0.1167	-1.0588
9	0.0001	0.0043	0.0150
10	0.0001	0.0043	0.0103

11	0.0000	0.0001	0.0031
12	0.0000	0.0001	0.0031
13	0.0000	0.0000	0.0003
14	0.0000	0.0000	0.0002
15	0.0000	0.0000	0.0000
16	0.0000	0.0000	0.0000

95% Confidence:

Row	Predicted	Regr. 5%	Regr. 95%	Pop. 5%	Pop. 95%
1	101.7645	97.9624	105.5665	94.7300	108.7989
2	101.7645	97.9624	105.5665	94.7300	108.7989
3	72.4728	69.9461	74.9994	66.0376	78.9080
4	72.4728	69.9461	74.9994	66.0376	78.9080
5	36.7563	33.6028	39.9099	30.0501	43.4626
6	36.7563	33.6028	39.9099	30.0501	43.4626
7	9.4547	7.4327	11.4767	3.2004	15.7090
8	9.4547	7.4327	11.4767	3.2004	15.7090
9	0.8784	0.4886	1.2682	-5.0529	6.8097
10	0.8784	0.4886	1.2682	-5.0529	6.8097
11	0.0816	0.0265	0.1367	-5.8371	6.0003
12	0.0816	0.0265	0.1367	-5.8371	6.0003
13	0.0054	0.0003	0.0105	-5.9131	5.9239
14	0.0054	0.0003	0.0105	-5.9131	5.9239
15	0.0000	-0.0000	0.0000	-5.9185	5.9185
16	0.0000	-0.0000	0.0000	-5.9185	5.9185

Borstel Loamy sand



Nonlinear Regression

[Variables]
x = col(1)
y = col(7)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)
yatxnear0(q,r) = xatymax(q,xnear0(r))
[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 98.0666}}
b = if(x50(x,y)-min(x)=0, 1, -ln(.5)/(x50(x,y)-min(x))) "Auto {{previous: 0.0691138}}
[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare
[Constraints]
b>0
[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.99805159 Rsqr = 0.99610698 Adj Rsqr = 0.99589070

Standard Error of Estimate = 2.3727

	Coefficient	Std. Error	t	P
a	98.0666	1.1253	87.1492	<0.0001
b	0.0691	0.0021	32.9937	<0.0001

Analysis of Variance:

	DF	SS	MS	F	P
Regression	1	25927.5663	25927.5663	4605.6594	<0.0001
Residual	18	101.3310	5.6295		
Total	19	26028.8973	1369.9420		

PRESS = 112.0580

Durbin-Watson Statistic = 0.5612

Normality Test: K-S Statistic = 0.2108 Significance Level = 0.2998

Constant Variance Test: Failed (P = 0.0460)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

Row	Predicted	Residual	Std. Res.	Stud. Res.	Stud. Del. Res.
1	98.0666	1.9334	0.8149	0.9256	0.9217

2	98.0666	-1.1584	-0.4882	-0.5546	-0.5436
3	91.5178	-1.5661	-0.6601	-0.7219	-0.7119
4	91.5178	-0.3101	-0.1307	-0.1429	-0.1390
5	79.7029	0.5870	0.2474	0.2616	0.2547
6	79.7029	-1.5386	-0.6485	-0.6857	-0.6752
7	60.4520	1.4803	0.6239	0.6604	0.6497
8	60.4520	2.8330	1.1940	1.2639	1.2867
9	37.2650	-0.2601	-0.1096	-0.1193	-0.1160
10	37.2650	-0.0669	-0.0282	-0.0307	-0.0298
11	22.9716	-0.9426	-0.3973	-0.4291	-0.4191
12	22.9716	-2.5851	-1.0895	-1.1768	-1.1904
13	13.2149	-0.0748	-0.0315	-0.0332	-0.0322
14	13.2149	-0.2681	-0.1130	-0.1188	-0.1155
15	1.2605	1.8313	0.7718	0.7736	0.7646
16	1.2605	4.0536	1.7084	1.7123	1.8188
17	0.1479	3.8134	1.6072	1.6074	1.6879
18	0.1479	3.4270	1.4444	1.4445	1.4929
19	0.0100	3.3717	1.4210	1.4210	1.4657
20	0.0100	3.9514	1.6654	1.6654	1.7597

Influence Diagnostics:

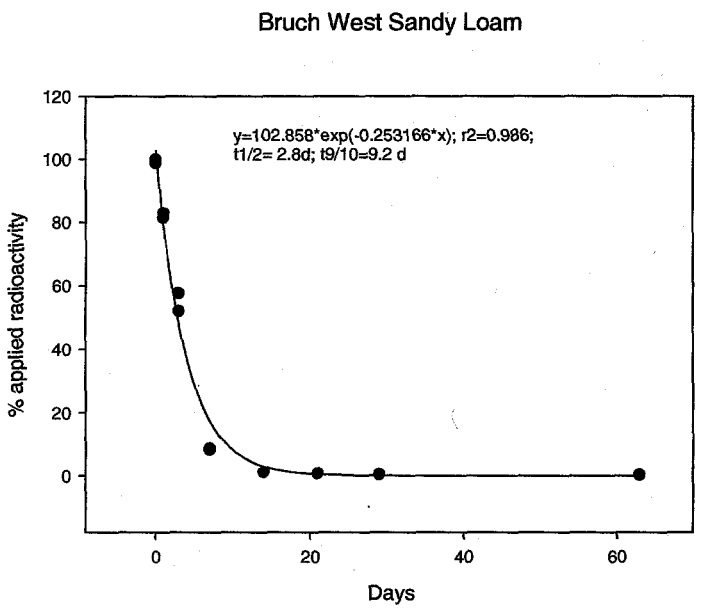
Row	Cook'sDist	Leverage	DFFITS
1	0.1243	0.2249	0.4965
2	0.0446	0.2249	-0.2929
3	0.0511	0.1639	-0.3152
4	0.0020	0.1639	-0.0615
5	0.0040	0.1056	0.0875
6	0.0277	0.1056	-0.2320
7	0.0263	0.1075	0.2255
8	0.0962	0.1075	0.4465
9	0.0013	0.1553	-0.0497
10	0.0001	0.1553	-0.0128
11	0.0153	0.1428	-0.1711
12	0.1154	0.1428	-0.4859
13	0.0001	0.0953	-0.0105
14	0.0007	0.0953	-0.0375
15	0.0014	0.0045	0.0514
16	0.0066	0.0045	0.1222
17	0.0002	0.0001	0.0201
18	0.0001	0.0001	0.0178
19	0.0000	0.0000	0.0017
20	0.0000	0.0000	0.0020

95% Confidence:

Row	Predicted	Regr. 5%	Regr. 95%	Pop. 5%	Pop. 95%
1	98.0666	95.7025	100.4308	92.5497	103.5836
2	98.0666	95.7025	100.4308	92.5497	103.5836
3	91.5178	89.4995	93.5361	86.1399	96.8956
4	91.5178	89.4995	93.5361	86.1399	96.8956
5	79.7029	78.0833	81.3225	74.4616	84.9442

6	79.7029	78.0833	81.3225	74.4616	84.9442
7	60.4520	58.8177	62.0864	55.2062	65.6979
8	60.4520	58.8177	62.0864	55.2062	65.6979
9	37.2650	35.3005	39.2294	31.9071	42.6228
10	37.2650	35.3005	39.2294	31.9071	42.6228
11	22.9716	21.0877	24.8554	17.6427	28.3004
12	22.9716	21.0877	24.8554	17.6427	28.3004
13	13.2149	11.6760	14.7538	7.9980	18.4318
14	13.2149	11.6760	14.7538	7.9980	18.4318
15	1.2605	0.9263	1.5947	-3.7355	6.2564
16	1.2605	0.9263	1.5947	-3.7355	6.2564
17	0.1479	0.0885	0.2073	-4.8372	5.1330
18	0.1479	0.0885	0.2073	-4.8372	5.1330
19	0.0100	0.0043	0.0157	-4.9748	4.9948
20	0.0100	0.0043	0.0157	-4.9748	4.9948

Bruch West Sandy Loam



Nonlinear Regression

[Variables]
x = col(1)
y = col(9)
reciprocal_y = 1/abs(y)
reciprocal_ysquare = 1/y^2
'Automatic Initial Parameter Estimate Functions
xnear0(q) = max(abs(q))-abs(q)

yatxnear0(q,r) = xatymax(q,xnear0(r))
[Parameters]
a = yatxnear0(y,x) "Auto {{previous: 102.858}}
b = if(x50(x,y)-min(x)=0, 1, -ln(.5)/(x50(x,y)-min(x))) "Auto {{previous: 0.253166}}
[Equation]
f = a*exp(-b*x)
fit f to y
"fit f to y with weight reciprocal_y
"fit f to y with weight reciprocal_ysquare
[Constraints]
b>0
[Options]
tolerance=0.0001
stepsize=100
iterations=100

R = 0.99351862 Rsqr = 0.98707924 Adj Rsqr = 0.98615633

Standard Error of Estimate = 4.7174

	Coefficient	Std. Error	t	P
a	102.8585	2.8918	35.5687	<0.0001
b	0.2532	0.0187	13.5254	<0.0001

Analysis of Variance:

	DF	SS	MS	F	P
Regression	1	23801.3882	23801.3882	1069.5278	<0.0001
Residual	14	311.5575	22.2541		
Total	15	24112.9458	1607.5297		

PRESS = 519.1020

Durbin-Watson Statistic = 1.1955

Normality Test: K-S Statistic = 0.2039 Significance Level = 0.4722

Constant Variance Test: Failed (P = 0.0019)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

Row	Predicted	Residual	Std. Res.	Stud. Res.	Stud. Del. Res.
1	102.8585	-2.8585	-0.6059	-0.7669	-0.7551
2	102.8585	-4.0419	-0.8568	-1.0845	-1.0919
3	79.8530	3.1845	0.6750	0.7396	0.7270
4	79.8530	1.6066	0.3406	0.3731	0.3613
5	48.1275	9.5648	2.0275	2.3205	2.8504
6	48.1275	3.9435	0.8359	0.9567	0.9536
7	17.4823	-8.7052	-1.8453	-2.0557	-2.3708
8	17.4823	-9.1983	-1.9498	-2.1722	-2.5707

9	2.9714	-1.6893	-0.3581	-0.3626	-0.3511
10	2.9714	-1.7879	-0.3790	-0.3838	-0.3718
11	0.5050	0.3825	0.0811	0.0812	0.0782
12	0.5050	0.2839	0.0602	0.0602	0.0581
13	0.0666	0.3278	0.0695	0.0695	0.0670
14	0.0666	0.5251	0.1113	0.1113	0.1073
15	0.0000	0.3945	0.0836	0.0836	0.0806
16	0.0000	0.2958	0.0627	0.0627	0.0604

Influence Diagnostics:

Row	Cook'sDist	Leverage	DFFITS
1	0.1770	0.3758	-0.5858
2	0.3540	0.3758	-0.8472
3	0.0548	0.1669	0.3254
4	0.0139	0.1669	0.1617
5	0.8341	0.2365	1.5866
6	0.1418	0.2365	0.5308
7	0.5093	0.1942	-1.1640
8	0.5687	0.1942	-1.2621
9	0.0017	0.0248	-0.0560
10	0.0019	0.0248	-0.0593
11	0.0000	0.0017	0.0032
12	0.0000	0.0017	0.0024
13	0.0000	0.0001	0.0005
14	0.0000	0.0001	0.0008
15	0.0000	0.0000	0.0000
16	0.0000	0.0000	0.0000

95% Confidence:

Row	Predicted	Regr. 5%	Regr. 95%	Pop. 5%	Pop. 95%
1	102.8585	96.6561	109.0608	90.9908	114.7261
2	102.8585	96.6561	109.0608	90.9908	114.7261
3	79.8530	75.7194	83.9866	68.9233	90.7827
4	79.8530	75.7194	83.9866	68.9233	90.7827
5	48.1275	43.2067	53.0483	36.8765	59.3786
6	48.1275	43.2067	53.0483	36.8765	59.3786
7	17.4823	13.0233	21.9413	6.4254	28.5392
8	17.4823	13.0233	21.9413	6.4254	28.5392
9	2.9714	1.3775	4.5652	-7.2713	13.2140
10	2.9714	1.3775	4.5652	-7.2713	13.2140
11	0.5050	0.0900	0.9201	-9.6214	10.6314
12	0.5050	0.0900	0.9201	-9.6214	10.6314
13	0.0666	-0.0101	0.1434	-10.0515	10.1848
14	0.0666	-0.0101	0.1434	-10.0515	10.1848
15	0.0000	-0.0000	0.0000	-10.1179	10.1179
16	0.0000	-0.0000	0.0000	-10.1179	10.1179

APPENDIX 2. DEW calculated half-lives.

Soil	Label	Duration of fit, days	Half life days	r^2
Charentilly Light clay	PY label	29	5.0	0.9103
		133	23.3	0.5828
	TP label	29	5.7	0.8844
		133	26.8	0.566
	Pooled	29	5.3	0.896
		133	24.8	0.5752
LUFA 3A Clay loam	PY label	21	3.0	0.8586
		63	8.7	0.5894
	TP label	21	3.0	0.8797
		63	8.0	0.6751
	Pooled	21	3.0	0.8687
		63	8.3	0.6320
Borstel Loamy Sand	PY label	21	9.7	0.9968
		133	26.4	0.8224
	TP label	29	12.3	0.9812
		133	25.0	0.8046
	Pooled	21	9.8	0.9979
		133	25.7	0.8121
Bruch Sandy Loam	PY label	21	2.8	0.9402
		63	7.4	0.6746
	TP label	29	2.8	0.9368
		63	7.6	0.6408
	Pooled	21	2.8	0.9382
		63	7.5	0.6575

Appendix 3. Summary of supplementary aerobic soil biotransformation study using exhaustive extraction methods (Yoder *et al.* 2007).

Yoder, R.N., K.P. Smith, J.L. Balcer, "Aerobic Degradation of XDE-472 in 4 European Soils Employing Exhaustive Extraction Methods", Study ID 061113, unpublished report of Dow AgroSciences LLC, May 11 2007.

The biotransformation of radiolabeled XDE-742 was studied in one French and three German sils; a Charentilly clay loam (France), a LUFA 3A clay loam, a Borstel sandy loam, and a Bruch West sandy loam. Samples were treated separately with ^{14}C-XDE-742 radiolabeled in the 2,6-position of the pyridine ring (PY) or the 2-position of the triazolopyrimidine ring (TP). XDE-742 was applied at the rate of 0.033 mg a.i./kg soil (equivalent to 25 g a.i./ha). Samples were incubated under aerobic conditions in the dark (20 °C and 40% moisture holding capacity) for up to four months after treatment. The test system consisted of two-chambered biometer flasks; one chamber containing 0.2 N NaOH for the collection of CO_2, and the other contained the treated soil.

Samples were collected for analysis at 0, 1, 4, 7, 14, 29, 42, 63, 82, 100 and 118 days after treatment. One sample of each radiolabel was analyzed at each time point. The soil samples were initially extracted three times with 90:10 acetonitrile: 1.0 N HCl. The acetonitrile extracts were neutralized and XDE-742 residues were analyzed by HPLC after a concentration step. Samples with more than 10% of the applied radioactivity unextracted after the initial extraction procedure were subjected to additional extractions. Samples were sequentially extracted twice with 90:10 methanol:5 N HCl, twice with a borate aqueous buffer (pH ~10) and twice with 90:10 methanol: 2 N NaOH. These extracts were neutralized and combined before concentration. The combined, concentrated extracts were analyzed by HPLC. Average material balance values for the four tested soils were 99-103% of applied radioactivity. The concentration of the parent compound decreased from approximately 95% at 0 DAT to less than 5% of the applied radioactivity at the end of study period in all soil types tested.

Simple first order (SFO) DT_{50} values ranged from 2 to 15 days on the four soils tested in this study. DT_{90} values ranged from 7 to 48 days.

Three metabolites identified by LC/MS in a previous XDE-742 aerobic soil metabolism study were identified by reverse-phase HPLC retention time match with authentic standards. These metabolites were 5-OH-XDE-742, 7-OH-XDE-742 and 6-Cl-7-OH-XDE-742. A fourth metabolite, not observed in the original study, was identified by LC/MS and comparison with an authentic standard of the XDE-742 sulfonamide. Two additional metabolites that reached 5% of applied in the original study, the cyanosulfonamide and the sulfonic acid of XDE-742 were not observed at concentrations above 4% of applied in this study.

At the end of the study period, up to 11% of the applied radioactivity was recovered in the caustic traps. In all but the LUFA 3A clay loam, the TP-labeled traps consistently contained more radioactivity than the PY-labeled traps for the same time point. Conversely higher amounts of radioactivity were extracted from the soil samples treated with PY-labeled XDE-742. XDE-742 sulfonamide contains only the PY radiolabel and its appearance correlates with the higher percent extractable from the PY-labeled samples.

Non-extractable residues (NER) accounted for 30-80% of the applied radioactivity, even after the exhaustive extraction procedures.

The first step in XDE-742 aerobic soil degradation is de-methylation of one of the two methoxy groups on the TP ring to 5-OH- or 7-OH-XDE-742. Each hydroxy metabolite is then further degraded to a variety of other metabolites. The terminal products of XDE-742 aerobic soil degradation are CO_2 and non-extractable residues.