Data Evaluation Report on the aerobic biotransformation of XDE-742 (pyroxsulam) in four European soils employing exhaustive extraction
PMRA Sub. No. 2006-4727; ID 1450772; EPA MRID Number 47202701; APVMA ATS 40362

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	EPA Guideline:	Subdivision N, §162-1 Aerobic Soil Metabolism

Test material:

Common name:	XDE-742 (pyroxsulam)
Chemical name:	
IUPAC	*N*-(5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide
CAS name	N-(5,7-dimethoxy[1,2,4]triazolo[1,5-a]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

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EXECUTIVE SUMMARY:

The biotransformation of radiolabeled XDE-742 was studied in one French and three German soils; a Charentilly clay loam (France), a LUFA 3A clay loam, a Borstel sandy loam, and a Bruch West sandy loam for 118 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. No sterile treatments were used. 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 analyzed 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 analysed 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 2x with 90:10 methanol: 5 N HCl, 2x with a borate aqueous buffer (pH ~ 10) and 2x 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 balances of the four soils ranged from 99.1 to 102.8% of the applied amount. The concentration of the parent compound decreased from a mean of the four soils of 95% (range of 86.2 to 98.7%) of the applied amount at day 0, to below 5% (range 0.2 to 3.9%) of the applied at the end of study period at all test sites. The DT50 and DT90 of XDE-742 in aerobic soil for all soil types ranged from 2.1 to 14.6 days and from 6.8 to 48.4 days, respectively.

Two major and one minor transformation product identified by LC/MS in a previous XDE-742 aerobic soil biotransformation study were identified by reverse-phase HPLC retention time match with authentic standards. 5-OH-XDE-742 was detected at a maximum of 24.4% of applied radioactivity at day 4 in LUFA 3A clay loam, and had declined to less than 1% after 29 days. 6-Cl-7-OH-XDE-742 was detected at a maximum of 11% of the applied radioactivity in Charentilly clay loam on day 7, and had declined to 3.2% by study termination. The transformation product 7-OH-XDE-742 was observed at a maximum concentration of 7.9% of the applied radioactivity on day 14 in Borstel sandy loam, and had declined to 1.4% by study termination. Another 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. XDE-742 sulfonamide reached a maximum of 13.2% of application radioactivity at day 29 in

Charentilly clay loam, and had declined to 8.6% at the end of the study. Two additional transformation products 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 and was assumed to be CO_2. In all but the LUFA 3A clay loam, the TP-labelled traps consistently contained more radioactivity than the PY-labelled traps for the same time point. Conversely, higher amounts of radioactivity were extracted from the soil samples treated with PY-labelled XDE-742. XDE- 742 sulfonamide contains only the PY radiolabel and its appearance correlates with the higher percent extractable from the PY-labelled samples. Non-extractable residues (NER) accounted for 37.9-82.8% 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 triazolopyrimidine (TP) ring system to 5-OH-XDE-742 or 7-OH-XDE-742. The 7-OH transformation product can then undergo chlorination to form 6-Cl-7-OH-XDE-742. Further degradation of the TP ring system occurs to give the cyanosulfonamide, sulfonamide and sulfonic acid transformation products. The terminal transformation products are CO_2 (minor) and bound residues (major).

Results Synopsis:

Soil type	XDE-742 half-life (days)	XDE-742 $t_{9/10}$ (days)
Charentilly	3.7	12.4
LUFA 3A	2.1	6.8
Borstel	14.6	48.4
Bruch West	5.0	16.8

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

Study Acceptability: PMRA, DEW and USEPA: This study is classified acceptable and satisfies the guideline requirement for an aerobic biotransformation study in soil.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with OECD Guideline for the Testing of Chemicals – Aerobic and Anaerobic Transformation in Soil- 307 European Commission Directive 91/414/EEC (as amended by Directive 94/37/EEC), SETAC Part 1 Section 1.

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.

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 (Figure 1, p. 60).

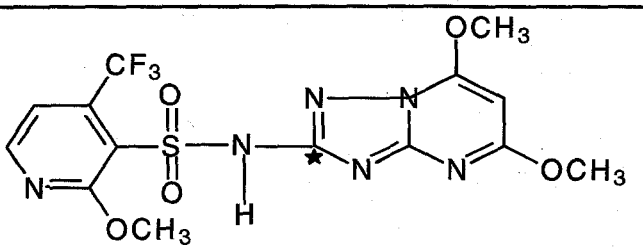
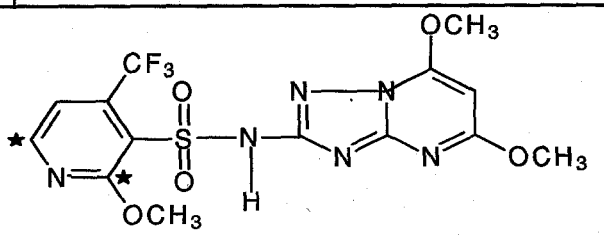
Common Name	TP-XDE-742		
	 * indicates position of radiolabel		
Synonyms	^{14}C-XDE-742-TP, X666742-Het-2-^{14}C		
Inventory#	INV1901	**Description**	Radiolabeled test material
Formula	$C_{14}H_{13}F_3N_6O_5S$	**MW**	434.4 g/mole
Purity (^{14}C)	100% (May 1, 2003)	**Specific Activity**	36.6 mCi/mmole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

Figure 2. XDE-742 PY test material (Figure 1, p. 60).

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	References Number
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)
Vapour pressure/ Volatility	< 10^{-7} Pa <8 x 10^{-10} torr	(2)
pKa	4.67	(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

Table 1: Description of soil collection and storage (p. 82).

Soil Type	LUFA 3A clay loam
Parameter	Description
Geographic Location	Baden-Württenberg, Germany
Site Description	Meadow with apple trees
Pesticide Use History	No pesticide or fertilizer use over last four years
Collection Date	October 18, 2006
Collection Procedures	Spade used to transfer soil to plastic bag
Sampling depth (cm)	0-20 cm
Shipping Date	Not reported.
Shipping Conditions	Handling in accordance with ISO/DIS 10381-6
Storage Conditions at Facility	20°C

Storage Length prior to use	6 weeks
Soil Preparation prior to use	Sieved, 2 mm
Soil Type	Bruch West sandy loam
Parameter	Description
Geographic Location	Reinlan-Pfalz, Germany
Site Description	Sinapis arresis, intercropping
Pesticide Use History	Unknown
Collection Date	October 30, 2006
Collection Procedures	Crop cover removed; 1 m^2 of soil transferred to plastic bag.
Sampling depth (cm)	0-20 cm
Shipping Date	Not reported.
Shipping Conditions	Handling in accordance with ISO/DIS 10381-6
Storage Conditions at Facility	20 °C
Storage Length prior to use	5 weeks
Soil Preparation prior to use	Sieved, 2 mm
Soil Type	Borstel sandy loam
Parameter	Description
Geographic Location	Schmallenberg, Germany
Site Description	Stubble
Pesticide Use History	No chemicals used in current or previous two years
Collection Date	November 5, 2006
Collection Procedures	Sampling was conducted using a driller with 5 cm diameter, several sub-samples were taken and unified to a mixed sample and packed into plastic bags
Sampling depth (cm)	0-60 cm
Shipping Date	Not reported.
Shipping Conditions	Handling in accordance with ISO/DIS 10381-6
Storage Conditions at Facility	20 °C
Storage Length prior to use	1 month
Soil Preparation prior to use	Sieved, 2 mm
Soil Type	Charentilly clay loam
Parameter	Description
Geographic Location	Charentilly, France
Site Description	Oilseed rape plus winter wheat stubble
Pesticide Use History	Trifluralin, lambda cyhalothrin, quinmerac, and metazaclhore (current year); pyraclostrobine, epoxiconazole, mesolufuron, and iodosulfuron (previous year)
Collection Date	November 7, 2006
Collection Procedures	Remove crop cover (5 cm) using a soil corer, collected soil on eight selected areas 30x30 cm, transferred to a plastic bag
Sampling depth (cm)	5-20 cm
Shipping Date	Not reported.
Shipping Conditions	Handling in accordance with ISO/DIS 10381-6

Storage Conditions at Facility	20 °C
Storage Length prior to use	1 month
Soil Preparation prior to use	Sieved, 2 mm

Table 2: Properties of the soils.

Parameter	Results			
Study Designation	M720	M721	M722	M723
Geographic Location	Germany	Germany	Germany	France
Soil Series	LUFA 3A	Bruch West	Borstel	Charentilly
Texture Class	Clay loam	Sandy loam	Sandy loam	Clay loam
International Class [a]				
USDA Texture Class	Sandy clay loam	Loamy Sand	Loamy Sand	Loam
% Sand [a]	59	83	83	45
% Silt [a]	20	8	10	32
% Clay [a]	21	9	7	23
pH [b]	7.5	6.2	5.5	5.6
% Organic Carbon [c]	2.1	0.7	0.8	0.9
Initial Soil Biomass (µg/g) [d]	327.9	57.4	19.9	57.4
Final Soil Biomass(µg/g) [d]	533.2	117.2	90.9	76.1
CEC (meq/100g) [e]	15.1	4.7	5.0	14.2
% Moisture at 0 Bar [f]	60.4	31.2	29.5	59.2
40% MHC	24.2	12.5	11.8	23.7
% Moisture at 1/10 Bar [g]	31.6	8.3	13.9	30.2
% Moisture at 1/3 Bar [g]	20.8	7.4	10.2	23.6
% Moisture at 1 Bar [h]	16.4	6.2	5.7	16.5
% Moisture at 15 Bar [h]	10.9	3.4	2.9	10.5
Bulk Density (disturbed) [i]	1.15	1.36	1.55	1.2

[a] % Texture Analytical Procedure.
[b] pH Analytical Procedure-pH in 0.01 M $CaCl_2$
[c] Organic Carbon (LECO)
[d] Determination of Soil Microbial Biomass
[e] Cation Exchange Capacity
[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 a.i./kg soil	0.033 µg/g
	g a.i./ha	25 g a.i./ha
Number of replicates	Treatments	Duplicates of each soil type at each time point
	Control	No control samples were used
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	Methanol
	Volume of solution	0.1 mL
	Application method	Drop-wise with syringe to soil surface
	Evaporation of solvent	N/A
Test material sorption to walls of apparatus?		N/A
Experimental conditions	Temperature °C	20 ± 2°C
	Moisture content	40% MHC
	Moisture maintenance method	Moisture checked at each time point gravimetrically
	Continuous darkness	Yes
Other details		Soil biomass measured prior to sample initiation and after 100 days incubation.

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: No supplementary study was conducted.

5. Sampling:

Table 4: Sampling details.

Parameters	**Details**
Sampling intervals	0, 1, 4, 7, 14, 29, 42, 63, 82, 100, 118 DAT
Sampling method for soil samples	Soil samples extracted 3X with 90:10 acetonitrile: 1.0 N HCl. Extracts concentrated prior to reverse phase HPLC analysis. Soils subjected to additional, exhaustive extractions in series of 90:10 methanol: 5 N HCl, pH 10 borate buffer, and 90:10 methanol: 2 N NaOH. Additional extracts combined and concentrated via Strata X polymeric reversed phase SPE column before HPLC analysis

Collection of CO_2 and volatile organics		Aspiration of NaOH trap, followed by LSC counting of triplicate aliquots
Sampling interval times	Moisture content	Determined gravimetrically with each sample
	Sterility Check	N/A
	Redox Potential/Other	N/A
Sample storage before analysis		Sample extraction initiated on day of sampling. Organic extracts stored in freezer, aqueous extracts stored in refrigerator prior to HPLC analysis, for less than 90 days.
Other observations		N/A

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.

A series of extractions were conducted to characterize the residues of XDE-742 aerobic soil degradation. The initial extraction solvent was the same solvent used to extract XDE-742 residues in the original study, a 90:10 acetonitrile: 1 N HCl extract. The second extraction procedure utilized a stronger acid extraction and a more polar organic solvent, 90:10 methanol: 5 N HCl. The third extraction procedure was a relatively mild aqueous base extraction, a borate buffer with a pH of approximately 10. Its primary purpose was to change the pH of the soil pellet after the strong acid extraction. The final extraction step was a stronger basic extraction, 90:10 methanol: 2 N NaOH.

Not all samples were subjected to the multi-step extraction process. Sample recoveries were evaluated after the initial extraction procedure. If less than 10% of the applied radioactivity was unextractable with the acetonitrile: 1 N HCl extract, no further extraction took place.

2. **Organic Solvent Extraction:**
Acetonitrile: 1 N HCl Extract
Approximately 75 mL of 90:10 acetonitrile: 1.0 N HCl was added to each soil sample. Samples were placed on a horizontal shaker at low speed for 1 hour and then centrifuged. The extract was decanted into a weighed, labeled jar and 75 mL fresh organic solvent was added to the soil pellet, shaking and centrifuging as before. The extracts were combined and the extraction process was repeated once more with another 75 mL of organic solvent. The combined extract was weighed and triplicate aliquots were assayed for ^{14}C by LSC.

Methanol: 5 N HCl Extract
The second extraction was a variation of the XDE-742 analytical soil method (7). The soil method utilized a 90:10 methanol:1 N HCl extract, however, a stronger acid was selected for this study (5 N HCl) as 1 N HCl had already been used in the first extraction solvent. Approximately 20 mL of 5 N HCl was added to samples previously extracted with acidic acetonitrile. Samples were placed in a sonicator for about 10 minutes. Next, 170 mL of methanol was added and the

samples were placed on a horizontal shaker for 1 hour. Samples were then centrifuged at 2500 rpm for 15 minutes.

Supernatants were decanted into 16-oz jars before the addition of another 20 mL of 5 N HCl to the soil sample. Samples were again sonicated. Methanol (170 mL) was added and the samples were placed on a horizontal shaker for 1 hour. After centrifugation, the supernatant for each sample was combined with the original supernatant for that sample. The weight of each jar plus extract was taken so the volume could be calculated. Triplicate aliquots were assayed by LSC.

Borate Extract
An aqueous borate buffer was used as an extraction solvent for the third extraction step. The buffer was prepared using 0.1 M boric acid and 0.1 N NaOH so the pH was approximately 10. The third extraction step was conducted by adding 100 mL of the borate buffer to the sample previously extracted with acidic methanol. The samples were placed on a horizontal shaker for 1 hour, and then centrifuged at 2500 rpm for 15 minutes. The extracts were decanted into a labeled 8-oz glass jar. Another 100 mL of borate buffer was added to the sample and the extraction procedure was repeated a second time, combining the extracts. The final sample weight was taken and triplicate aliquots were assayed by LSC.

Methanol: 2 N NaOH Extract
The final extraction step employed a stronger base in organic extract. The samples previously extracted with borate buffer were extracted with 90:10 methanol:2 N NaOH. Extraction solvent (100 mL) was added to each sample before shaking on horizontal shaker for 1 hour. The samples were centrifuged at 2500 rpm for 10 minutes and the extracts decanted into a labeled 8-oz glass jar.

The extraction was repeated a second time with another 100 mL of extraction solvent, combining the extracts and taking the final sample weight before removal of triplicate aliquots for LSC assay.

Preparation of Acetonitrile Extract for HPLC Analysis
A detailed account of the neutralization process is reported in Appendix B. Since the acetonitrile: 1 N HCl extract was the same extraction procedure used during the original biotransformation study (5), these extracts were concentrated and analyzed by HPLC separately so a more direct comparison to the original results could be made.

An aliquot of the acetonitrile extract was brought to a pH of approximately 6 (as measured by pH paper) using 2 N NaOH. The extract was centrifuged and the supernatant decanted into a clean centrifuge tube. The extract was concentrated under a stream of nitrogen on a Turbovap with the waterbath temperature set at 30°C.

A precipitate fell out of solution when the pH of the extract was adjusted. This precipitate was rinsed with acetonitrile, shaking briefly to mix. The sample was centrifuged and the acetonitrile

rinse was added to the neutralized extract undergoing concentration. The extract plus rinse was concentrated to approximately 1 mL volume. The concentrated sample was transferred to a 2-mL volumetric flask and brought to volume with acetonitrile and water. Aliquots of the concentrated sample were assayed by LSC and HPLC.

The precipitate was reconstituted with a 50:50 mixture of acetonitrile and 1 N HCl. Triplicate aliquots were counted by LSC.

3. **Preparation of Additional Extracts for HPLC Analysis:** Since the levels of soluble radioactivity were so low in the acidic methanol and the basic extracts, all three extracts were pooled for HPLC analysis.

The pH of the methanol:5 N HCl extract was adjusted with a saturated NaOH solution to approximately 6 (via pH paper). The sample was centrifuged at 2500 rpm for 15 minutes and the supernatant was decanted off, leaving behind a precipitate-soil matrix soluble in the strong acid, but insoluble at a higher pH. Aliquots of the extract were counted by LSC. The extract was then concentrated on a Turbovap under a stream of nitrogen (waterbath set at 40°C).

The pH of the borate extract did not need to be adjusted to prepare the sample for HPLC. Due to the residual acid remaining in the soil after the preceding acidified organic extracts, the first borate extract was actually acidic, even though the initial pH of the borate extract was approximately 10. The pH of the solution after the second extraction step was basic, but the combined extracts had an acidic pH. The borate extract was centrifuged at 2500 rpm for 15 minutes to separate the solids released from the soil by the basic extraction solvent. The supernatant was added to the concentrated, neutralized methanol extract from the previous step.

Changing the pH of the basic methanol extract did not result in the precipitation of additional non-soluble solids. However, the extract was adjusted to a pH of approximately 6 using 5 N HCl prior to concentration on a Turbovap (waterbath set at 40°C). The basic methanol extract was acidified before concentrating so as not to concentrate under basic conditions. The concentrated, neutralized extract was added to the combined borate and first methanol extract. The total combined extract was acidified to a pH of approximately 2 (using pH paper) in preparation of concentration via SPE (solid phase extraction).

A Strata X 33um (500mg/6mL) polymeric reversed phase SPE column was conditioned with 10 mL methanol, followed by 10 mL of water + 0.5% trifluroacetic acid (TFA). The entire combined extract was loaded onto the SPE column. The load was collected and triplicate aliquots were counted by LSC. The column was then rinsed with 5 mL of water + 0.5% TFA and the rinse counted by LSC.

The SPE column was then eluted twice with 5 mL of 90:10 acetonitrile: water, both containing 0.5% TFA. Triplicate aliquots of each eluent were counted by LSC. The first eluent was

concentrated to small volume. Aliquots of the concentrated eluent were counted by LSC and analyzed by HPLC.

4. **Preparation of Soil Pellet and Combustion of Extracted Soil Samples** The extracted soil pellet was allowed to air dry in a hood for at approximately a week prior to combustion analysis to determine the amount of non-extractable residues present.

Extracted, air-dried soil samples were combusted to determine the amount of residues remaining in the soil pellet after the exhaustive extraction procedure. Approximately 0.5-g sub-samples of each extracted soil pellet were weighed in triplicate into glass boats and combusted using a biological oxidizer. The generated $^{14}CO_2$ was then collected in scintillation cocktail and assayed by LSC.

The efficiency of the oxidizer was determined daily by combusting soil blanks and spiking the generated vials with a known volume of a ^{14}C standard (vial spikes). Aliquots of the same standard were then spiked onto soil replicates that were also combusted (soil spikes). The oxidizer efficiency was calculated by dividing the recovered radioactivity from the soil spikes by the radioactivity in the vial spikes. This correction factor was applied to each sample analyzed by combustion on that instrument that day. Acceptable oxidizer recoveries were between 90 and 110%.

5. **Transformation Product Identification Procedures:** Transformation products previously identified in the original XDE-742 aerobic soil biotransformation study (5) were identified by retention time match with authentic standards.

One transformation product (XDE-742 sulfonamide, structure given in Figure 3, page 25 of this DER) not previously observed was identified by LC/MS comparison with an authentic standard. Several PY-labeled high concentration samples were extracted with acetonitrile: 1 N HCl. The extracts of all the ID (transformation product identification) samples were combined and placed on the Turbovap to remove the organic solvent. The extract was then concentrated using the same SPE procedure used to concentrate the combined multi-extraction samples. The concentrated ID sample was submitted for LC/MS analysis.

6. **Radiocarbon Determination Procedures:** Radioactive material in solution was quantified by a liquid scintillation counter. Reference standards obtained from the Packard Instrument Co. were used to verify the performance counter frequently, typically each day samples were analyzed. Scintillation cocktail was to each sample before counting. Samples were generally counted for 5 minutes.

Radioactive material remaining in the soil pellet after extraction was quantified by oxidative combustion as described in Section 3.12.6, Combustion of Extracted Soil Samples.

7. **Chromatographic and Spectroscopic Procedures:** The reverse phase HPLC method was used for sample analysis. A RAM flow-through detector was used to quantify the amount of radioactivity present in each peak. ARC XFlow software (Aim Research, Hockessin, DE) was used to integrate the peaks collected by the RAM. 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 and a UV detector at 254 nm wavelength was used to determine the retention times of non-radiolabeled standards.

Table 5: HPLC Conditions

Time (minutes)	Solvent Ratio	Comment
0.0	90:10 A:B	Initial Conditions
5.0	90:10 A:B	Aqueous Hold
25.0	5:95 A:B	Linear Gradient
26.0	5:95 A:B	Organic Hold
27.0	90:10 A:B	Initial Conditions
32.0	90:10 A:B	Re-equilibration

Column: Column:Zorbax SB-C18
Flow rate: 1mL/min
Solvent A: Water +0.5% TFA
Solvent B: Acetonitrile + 0.5% TFA

Typical Retention Times (in minutes) for Analytical Standards and Transformation Products

Compound	Retention Time (minutes)
XDE-742	19.7
6-Cl-7-OH-XDE-742	18.4
5-OH-XDE-742	17.4
7-OH-XDE-742	17.0
Sulfonamide	16.8
5,7-dihydroxy	16.4
CSF	13.7
PSA	7.7

The pH of sample extracts was adjusted prior to HPLC analysis. Sample pH was modified primarily for two reasons. First, if the samples had been concentrated without changing the pH, the sample would have become increasingly acidic or basic during concentration. Due to concerns about the stability of XDE-742 and its metabolites in extreme pH solutions, the pH of the extracts was adjusted to approximately neutral (6-7) prior to concentration. Second, the extraction solvents removed organic material (humic and fulvic acid) from the soil matrix itself. This material was soluble in acidified organic extract, however, removal of the organic solvent or changing solution pH resulted in precipitation of solid particulate matter.

8. **Definitions of Detection Limits:** Using the method of Currie, the limit of detection can be calculated from the expression:

$$LOD = \frac{2.71 + 4.65\sqrt{dpm_B \times T}}{T}$$

and the limit of quantitation can be calculated:

$$LOQ = \frac{50\left(1 + \sqrt{1 + \frac{dpm_B \times T}{12.5}}\right)}{T}$$

where LOD is the limit of detection (dpm), LOQ is the limit of quantitation (dpm), dpm_B is the typical background (dpm) and T is the counting time (minutes). Samples were normally counted for 5 minutes while the blank was counted for 10 minutes. Typical background levels were 20 dpm. The resulting LOD was 10 dpm above background and LOQ was 40 dpm above background. 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 Quantification

	% of Applied ^{14}C	
Sub-sample Identification	LOD	LOQ
Caustic Trap	<1%	<3%
Soil Extracts	<1%	<3%
Soil Combustion	<1%	<3%

The limit of detection (LOD) was set at 1% of the applied radioactivity for XDE-742 and its transformation products (HPLC analysis). The LOQ (limit of quantitation) was 3X higher, (3% of applied)

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: Aerobic conditions were maintained throughout the study to an oxygen manifold during the incubation period. Samples were kept in the dark at 20°C for up to 4 months after treatment. Gravimetric determination of soil moisture at each time point showed no significant loss of soil moisture during sample incubation. Soil biomass determination at study initiation and later in the study is presented in Table 2.

B. Verification of Extraction Procedures: Samples were initially extracted with 90:10 acetonitrile: 1 N HCl. When less than 90% of the applied radioactivity was extracted with the acidified acetonitrile extract, samples were sequentially extracted with 90:10 methanol:5 N HCl, borate aqueous buffer (pH ~10) and 90:10 methanol:2 N NaOH. In three soils less than 4% of the applied radioactivity was extracted in the final basic methanol extraction step. Less than 6% of the applied radioactivity was extracted from the Charentilly clay loam with the final extraction solvent. These results demonstrate that all extractable radioactivity was removed from all soil types using the exhaustive extraction procedure employed in this study.

C. Verification of Chromatographic Procedures: HPLC column recoveries were determined by directly counting an aliquot of each sample analyzed by HPLC and comparing to the sum of the radioactivity eluted from the column. HPLC recoveries were typically between 90 and 110%. HPLC LOD and LOQ values were defined as described in Table 6.

D. Verification of Method Repeatability: Repeatability of the analytical method was tested by analyzing duplicate aliquots of the same extracts, initially and at a later date. Representative results from the repeatability check were presented and considered acceptable. No change was observed between the sample's initial analysis and the repeat analysis.

E. MATERIAL BALANCE: Material balance results are contained in Table 7 through Table 10. The average mass balance of the four soils ranged from 99.1 to 102.8% of the applied radioactivity in the four soils tested here. Individual sample mass balance ranged from 92.0 to 111.5% of the applied radioactivity. No systematic variation in mass balance was observed in any soil type.

Samples with recoveries less than 90% or greater than 111.5% of the applied radiocarbon were not used to determine degradation rates and are not reported in the listed tables. The kinetics of XDE-742 degradation were well established, even without these few samples with unacceptable recoveries.

Table 7: Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)—LUFA 3A clay loam (Table 6, p. 50).

			Extract				NER	Total
DAT	Label	Trap	ACN 1N HCl	MeOH 5N HCl	pH 10 borate	MeOH 2N NaOH		
0	TP	N/A	91.5	N/A	N/A	N/A	0.5	92
0	PY	N/A	98.8	N/A	N/A	N/A	0.5	99.2
1	TP	0.7	94	N/A	N/A	N/A	7.9	102.5
1	PY	0.5	93.8	N/A	N/A	N/A	6.9	101.2
4	TP	0.3	55.8	12.4	0.7	0.9	35.9	106
4	PY	0.2	58.5	10.7	0.7	0.9	31.8	102.7
7	TP	0.8	28.2	10.9	0.8	1.6	55.1	97.4
7	PY	0.2	69.4	6.6	0.3	0.9	23.4	100.9

14	TP	1.9	10	14.5	0.9	1.8	71.9	100.9
14	PY	1.1	17	12.6	0.9	1.6	65.3	98.6
29	TP	2.8	4.6	12.2	0.8	1.8	73.3	95.6
42	TP	3	3.2	12.5	1.1	1.8	74.8	96.4
42	PY	3	6.3	12.1	1.2	1.5	74.8	98.9
63	TP	3.3	3.2	11.8	0.9	1.2	75.7	96.2
63	PY	4	3.6	23.5	1.1	1.4	76.6	110.2
82	TP	3.9	3.3	15.6	1.1	1.6	78.2	103.7
82	PY	4.7	3.3	14.2	0.9	1.7	75.8	100.5
100	TP	4.1	2.9	13.4	0.9	0.8	78.5	100.7
100	PY	5.1	2.9	17.3	0.9	1	77.5	104.8
118	TP	4.5	2.7	15.3	0.8	1.1	82.8	107.2
118	PY	4.6	7.0	16.4	0.6	1.4	70.7	100.7
							Average	100.8
							Standard Deviation	4.2
							Maximum	110.2
							Minimum	92.0

Table 8: Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)—Bruch West sandy loam (Table 7, p. 51).

			Extract					
DAT	**Label**	**Trap**	**ACN 1N HCl**	**MeOH 5N HCl**	**pH 10 borate**	**MeOH 2N NaOH**	**NER**	**Total**
0	TP	N/A	96.8	N/A	N/A	N/A	0.7	97.5
0	PY	N/A	97.2	N/A	N/A	N/A	0.3	97.5
1	TP	0.7	96.4	N/A	N/A	N/A	2.6	99.7
1	PY	0.5	95.6	N/A	N/A	N/A	2.4	98.4
4	TP	0.8	78.6	10.9	2.2	1.4	13.2	107
4	PY	0.0	81.6	7.7	1.8	1.0	9.4	101.6
7	TP	1.0	70.2	4.3	2.7	1.9	20.5	100.6
7	PY	0.2	68.8	4.3	2.9	2.3	16.2	94.6
14	TP	3.3	42.7	9.6	6.1	4.1	37.2	103
14	PY	0.4	47.8	9.1	8.6	3.2	27.7	96.8
29	TP	5.3	31.5	7.6	7.5	3.7	46.8	102.5
29	PY	1.0	38.1	7.3	6.5	4.1	39.4	96.3
42	TP	6.4	30	7.0	9.2	3.7	43.8	100.1
42	PY	1.3	39	6.3	8.5	3.2	40.6	98.9
63	PY	6.6	29.3	7.0	6.3	3.5	47.4	100.1
63	TP	2.0	35.9	7.1	5.9	3.6	42.8	97.4
82	PY	7.7	26.9	12.0	1.2	4.1	44.2	96.0
82	TP	3.4	33.2	10.7	1.3	4.0	47.5	100.1
100	PY	7.9	24.1	6.6	6.4	3.2	50.7	98.8
100	TP	2.9	32.6	6.0	5.9	3.1	47.9	98.4
118	PY	8.3	23.5	12.5	1.5	3.6	47.5	97.0
118	TP	4.3	30.8	11.4	6.8	3.7	47.8	104.9
							Average	99.4
							Standard Deviation	3.0

Maximum	107.0
Minimum	94.6

Table 9: Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)—Borstel sandy loam (Table 8, p. 52).

DAT	Label	Trap	Extract				NER	Total
			ACN 1N HCl	MeOH 5N HCl	pH 10 borate	MeOH 2N NaOH		
0	TP	N/A	94.0	N/A	N/A	N/A	0.4	94.4
0	PY	N/A	97.6	N/A	N/A	N/A	0.2	97.8
1	TP	0.5	96.0	N/A	N/A	N/A	1.4	98.0
1	PY	0.4	94.1	N/A	N/A	N/A	0.8	95.3
4	TP	0.1	90.9	N/A	N/A	N/A	4.6	95.6
4	PY	0.0	91.8	N/A	N/A	N/A	4.4	96.2
7	TP	0.1	89.7	N/A	N/A	N/A	6.0	95.8
7	PY	0.1	89.7	N/A	N/A	N/A	8.2	98.0
14	TP	1.1	79.3	6.1	2.2	1.8	9.7	100.2
14	PY	0.3	82.2	5.4	3.0	1.6	9.0	101.5
29	TP	3.1	60.4	6.4	2.2	2.8	20.6	95.6
29	PY	0.6	63.2	6.5	4.3	2.8	21.7	99.2
42	TP	4.1	51.2	7.0	6.9	3.1	25.0	97.2
42	PY	0.7	55.5	6.2	6.4	2.9	23.5	95.3
63	PY	1.1	49.8	19.7	5.1	3.5	30.2	109.3
82	TP	7.0	37.6	12.1	1.3	4.0	35.0	97.0
82	PY	1.4	52.3	9.4	1.1	3.9	27.9	96.0
100	TP	7.7	35.5	21.7	6.3	3.8	35.3	110.3
100	PY	1.5	43.7	16.6	5.6	3.6	31.5	102.5
118	TP	8.3	31.1	13.5	6.4	4.0	33.7	97.0
118	PY	2.1	46.3	12.1	6.6	3.7	37.9	108.7
							Average	99.1
							Standard Deviation	4.8
							Maximum	110.3
							Minimum	94.4

Table 10: Radioactive Material Balance (Expressed as Percent of Applied Radiocarbon)—Charentilly clay loam (Table 9, p. 53).

DAT	Label	Trap	Extract				NER	Total
			ACN 1N HCl	MeOH 5N HCl	pH 10 borate	MeOH 2N NaOH		
0	TP	N/A	97.8	N/A	N/A	N/A	1.2	98.9
0	PY	N/A	99.6	N/A	N/A	N/A	0.3	99.9
1	TP	0.4	97.7	N/A	N/A	N/A	2.7	100.8
1	PY	0.4	93.3	N/A	N/A	N/A	2.6	96.2
4	TP	1.0	82.1	13.4	0.5	2.1	11.2	110.3
4	PY	0.0	82.6	11.4	0.6	1.5	11.5	107.7

7	TP	2.6	64.4	6.7	0.3	3.5	21.9	99.4
7	PY	0.2	66.2	7.0	0.4	3.2	23.2	100.2
14	TP	5.3	40.1	11.9	0.6	5.6	43.1	106.5
14	PY	0.6	48.1	11.2	0.6	5.4	35.7	101.6
29	TP	8.6	30.6	12.0	1.3	5.5	42.2	100.1
29	PY	1.4	42.5	11.3	1.1	5.2	39.7	101.2
42	TP	8.5	31.4	11.7	1.1	5.5	43.5	101.7
63	PY	4.3	38.3	22.0	1.3	4.5	40.2	110.7
82	TP	10.3	28.6	13.5	0.8	5.6	44.2	103.0
82	PY	6.3	36.0	12.6	0.9	5.3	38.5	99.6
100	TP	10.5	26.3	22.2	1.6	5.0	45.8	111.5[a]
100	PY	2.3	42.9	18.3	1.7	4.7	36.0	106.0
118	TP	11.4	22.7	15.1	1.0	5.8	49.2	105.1
118	PY	8.6	27.1	13.7	1.0	5.6	49.0	105.1
							Average	102.8
							Standard Deviation	4.0
							Maximum	110.7
							Minimum	96.2

[a] The results of Day 100 (TP label) were not included in the calculations, as explained in the Material Balance Section above.

In the following tables dealing with transformation product concentrations, N/A is not applicable—the PSA and sulfonamide metabolites only contain the PY-label and so were not observed in the TP-labeled samples.

Table 11: Transformation Product Concentrations as Percent of Applied Radioactivity with Time - LUFA 3A Clay Loam (Table 10, p. 54).

DAT	Label	PSA	CSF	Sulfonamide	7-OH	5-OH	6-Cl	Parent
0	TP	N/A	0.0	N/A	0.0	0.0	0.0	96.4
0	PY	0.0	0.0	0.0	0.0	0.0	0.0	97.2
1	TP	N/A	0.0	N/A	2.5	10.7	0.0	91.2
1	PY	0.0	0.0	0.0	0.6	8.8	0.0	75.4
4	TP	N/A	0.0	N/A	0.0	24.4	0.0	24.4
4	PY	0.0	0.0	0.0	0.0	14.1	0.0	18.6
7	TP	N/A	0.0	N/A	0.0	18.9	0.0	4.2
7	PY	0.0	0.0	0.0	0.0	8.2	0.0	51.2
14	TP	N/A	0.0	N/A	0.4	7.2	0.4	2.4
14	PY	0.0	0.1	0.4	1.6	10.7	0.2	2.0
29	TP	N/A	0.0	N/A	0.0	0.6	0.0	0.3
42	TP	N/A	0.0	N/A	0.2	0.5	0.8	0.5
42	PY	0.4	0.0	0.8	0.4	0.7	0.5	1.4
63	TP	N/A	0.0	N/A	0.4	0.6	0.8	1.2
63	PY	0.0	0.0	1.2	0.4	0.5	0.6	0.8
82	TP	N/A	0.0	N/A	0.0	0.2	0.1	0.3
82	PY	0.0	0.0	1.4	0.1	0.6	0.5	0.4

100	TP	N/A	0.0	N/A	0.0	0.0	0.2	0.3
100	PY	0.0	0.0	1.9	0.5	0.4	0.5	0.5
118	TP	N/A	0.0	N/A	0.0	0.3	0.2	0.2
118	PY	0.9	0.0	0.8	0.0	0.3	0.3	0.4

Table 12: Transformation Product Concentrations as Percent of Applied Radioactivity with Time - Bruch West Sandy Loam (Table 11, p. 55).

DAT	Label	PSA	CSF	Sulfonamide	7-OH	5-OH	6-Cl	Parent
0	TP	N/A	0.0	N/A	0.0	0.0	0.0	86.2
0	PY	0.0	0.0	0.0	0.0	0.0	0.0	92.4
1	TP	N/A	0.0	N/A	2.5	0.9	0.0	73.8
1	PY	0.0	0.0	0.0	1.7	3.0	0.0	78.0
4	TP	N/A	0.0	N/A	2.9	0.0	0.9	56.6
4	PY	0.0	0.0	1.4	3.9	2.0	0.4	54.5
7	TP	N/A	0.0	N/A	5.8	1.5	0.8	34.7
7	PY	0.0	0.0	2.5	5.5	2.4	1.8	40.3
14	TP	N/A	0.1	N/A	4.0	0.9	1.5	4.7
14	PY	0.0	0.1	5.1	5.6	0.8	1.8	6.5
29	TP	N/A	0.0	N/A	1.5	0.6	2.8	1.5
29	PY	1.4	0.0	6.0	1.0	1.4	2.3	1.5
42	TP	N/A	0.1	N/A	1.6	0.4	1.3	0.8
42	PY	1.4	0.0	5.0	2.1	0.7	1.3	2.2
63	TP	N/A	0.1	N/A	0.9	0.6	1.9	1.1
63	PY	0	0.2	6.2	2.2	0.5	1.6	1.2
82	TP	N/A	0.0	N/A	1.3	0.6	0.6	0.4
100	TP	N/A	0.0	N/A	1.7	0.5	0.8	0.9
100	PY	2.4	0.2	6.4	1.6	0.8	2.3	1.1
118	TP	0.0	0.1	N/A	0.8	1.2	0.7	1.2
118	PY	3.2	0.0	5.6	0.9	0.2	1.6	1.1

Table 13: Transformation Product Concentrations as Percent of Applied Radioactivity with Time - Borstel West Sandy Loam (Table 12, p. 56).

DAT	Label	PSA	CSF	Sulfonamide	7-OH	5-OH	6-Cl	Parent
0	TP	N/A	0.0	N/A	0.0	0.0	0.0	93.4
0	PY	0.0	0.0	0.0	0.0	0.0	0.0	96.9
1	TP	N/A	0.0	N/A	0.0	0.0	0.0	95.6
1	PY	0.0	0.0	0.0	0.0	0.0	0.0	92.6
4	TP	N/A	0.0	N/A	2.3	0.0	0.8	49.5
4	PY	0.0	0.0	0.0	3.7	0.0	0.4	62.0
7	TP	N/A	0.0	N/A	2.2	0.9	1.0	71.4
7	PY	0.0	0.0	0.0	3.0	0.6	2.2	69.8
14	TP	N/A	0.0	N/A	7.9	0.5	5.4	48.9

14	PY	0.0	0.0	1.0	6.0	1.0	5.1	50.9
29	TP	N/A	0.0	N/A	6.5	0.3	8.7	27.1
29	PY	0.0	0.0	3.1	4.4	1.2	7.8	22.2
42	TP	N/A	0.1	N/A	4.1	1.3	4.6	11.4
42	PY	0.8	0.0	4.3	6.5	0.3	5.2	9.7
63	PY	0.0	0.1	7.7	2.1	0.3	3.8	5.0
82	TP	N/A	0.0	N/A	3.4	1.5	3.9	3.8
82	PY	2.0	0.0	8.5	4.7	1.2	5.8	3.8
100	TP	N/A	0.0	N/A	4.2	0.4	3.4	3.7
100	PY	3.0	0.0	10.5	2.7	0.9	3.3	3.8
118	TP	N/A	0.0	N/A	3.0	0.8	2.5	2.7
118	PY	1.5	0.1	10.6	1.4	1.8	0.8	3.9

Table 14: Transformation Product Concentrations as Percent of Applied Radioactivity with Time - Charentilly Clay Loam (Table 13, p. 57).

DAT	Label	PSA	CSF	Sulfonamide	7-OH	5-OH	6-Cl	Parent
0	TP	N/A	0.0	N/A	0.0	0.0	0.0	97.8
0	PY	0.0	0.0	0.0	0.0	0.0	0.0	98.7
1	TP	N/A	0.0	N/A	3.1	0.0	0.0	94.0
1	PY	0.0	0.0	0.0	3.8	0.7	0.0	87.3
4	TP	N/A	0.0	N/A	4.8	1.0	7.1	55.5
4	PY	0.7	0.0	2.1	4.7	2.6	7.1	34.5
7	TP	N/A	0.0	N/A	3.5	0.5	11.0	36.8
7	PY	0.7	0.2	6.2	2.8	0.6	8.6	22.0
14	TP	N/A	0.0	N/A	2.6	1.2	4.7	6.4
14	PY	2.7	0.0	12.1	2.1	0.5	3.8	4.7
29	TP	N/A	0.0	N/A	1.1	1.1	4.0	1.1
29	PY	0.2	0.0	13.2	0.9	0.9	2.9	2.7
42	TP	N/A	0.0	N/A	1.3	1.0	2.5	2.1
63	PY	0.1	0.7	11.8	1.5	2.2	2.0	2.1
82	TP	N/A	0.6	N/A	2.3	0.7	2.5	1.5
82	PY	0.5	0.0	9.2	0.2	0.2	1.8	1.2
100	TP	N/A	0.1	N/A	1.7	2.2	3.5	1.5
100	PY	3.6	0.0	12.1	2.9	0.4	4.4	2.1
118	TP	N/A	0.0	N/A	1.8	0.3	3.2	0.8
118	PY	0.0	0.0	8.6	1.5	0.4	2.3	1.5

C. **TRANSFORMATION OF PARENT COMPOUND:** The concentration of the parent compound decreased from 96.3% (PY label) of the applied amount at day 0, to 1.2% (TP label) of the applied at the end of the study period (In the following tables dealing with transformation product concentrations, N/A is not applicable—the PSA and sulfonamide metabolites only contain the PY-label and so were not observed in the TP-labeled samples.

Table 11 through Table 14) in the four test sites.

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 (Table 15). The method used for the transformation product degradation determination was the "Top-Down" SFO Model. All of the fits were performed using KinGUI ver 1.1 (Bayer CropScience).

The PMRA reviewer verified the dissipation of XDE-742 with a simple first order model using SigmaPlot, and half-lives are shown in Table 16. 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 0.923 to 0.989 for all soils. The half-lives calculated by the primary reviewer confirm those reported in the study report.

Table 15: SFO Aerobic Soil Degradation Rates of XDE-742 and its Major Aerobic Soil Transformation Products

Soil	DT50 (days)	DT90 (days)	% error χ^2 Passes	r^2	Model Type
LUFA 3A					
XDE-742	2.1	6.8	11	0.97	SFO
5-OH-XDE-742	4.7	15.6	12.7	0.769	SFO
Bruch West					
XDE-742	5	16.8	6.8	0.986	SFO
7-OH-XDE-742	6.4	21.3	16.4	0.882	SFO
sulfonamide	18.6	61.7	N/A	1	Top Down
Borstel					
XDE-742	14.6	48.4	3.9	0.997	SFO
7-OH-XDE-742	33	109	26.7	0.602	SFO
6-Cl-7-OH-XDE-7421[1]	52	173	16.9	0.728	Top Down
Charentilly					
XDE-742	3.7	12.4	7.7	0.981	SFO
6-Cl-7-OH-XDE-7421[1]	56	186	35.6	0.401	Top Down
sulfonamide	183	607	9	0.524	Top Down
XDE-742					
Arithmetic mean	6.4	21.1			
Standard Deviation	5.6	18.7			
Geometric mean	4.9	16.2			
Maximum	14.6	48.4			
Minimum	2.1	6.8			

[1] An aerobic soil degradation study was conducted using 6-Cl-7-OH-XDE-742 as the starting material (6) on the same 4 European soils used in this study. The degradation rates calculated in this study (First order DT50 values ranged from 3 to 16 days) are a much more accurate representation of the degradation rates of the 6-Cl-7-OH transformation product and should be used whenever describing the aerobic soil degradation of the transformation product in aerobic soil.

Table 16 : PMRA-Calculated half-life of XDE-742 in four European Soils

Soil type	Regression equation	R^2	DT50 (Days)	DT90 (Days)
LUFA 3A	y = 99.3771*exp(-0.2630*x)	0.92	2.74	8.86
Bruch West	y = 89.6400*exp(-0.1372*x)	0.99	5.08	16.81
Borstel	y = 91.2391*exp(-0.0476*x)	0.96	13.68	47.49
Charentilly	y = 101.9619*exp(-0.1863*x)	0.98	3.92	12.56

TRANSFORMATION PRODUCTS:
Three major (≥10% of applied radioactivity) and three minor (<10% of applied radioactivity) transformation products were detected.

Major transformation products:

The 5-OH-XDE-742 accounted for 24.4% of the applied radioactivity at 4 DAT in the LUFA 3A clay loam. The 5-OH reached 3% and 2.6% (1 and 4 days after treatment, respectively) in the Bruch West sandy loam and the Charentilly loam, respectively and only accounted for a maximum of 1.8% at study termination in the Borstel loamy sand. 5-OH-XDE-742 was less than or equal to 1.8% of applied radioactivity in all soils at the end of the study.

The 6-Cl-7-OH-XDE-742 reached 11% of applied radioactivity after 7 days in the Charentilly clay loam. It reached 8.7% of applied radioactivity after 29 days in the Borstel sandy loam. Maximum concentrations in LUFA 3A clay loam and Bruch West sandy loam were 0.8% (63DAT) and 2.8% (29 DAT) of applied radioactivity, respectively. At the end of the study, the 6-Cl-7-OH-XDE-742 concentration was less than or equal to 3.2% in all soil types.

XDE-742 sulfonamide was observed at a maximum of 13.2% of applied radioactivity after 29 days in the Charentilly clay loam, and had declined to 8.6% by the end of the study. In Bruch West sandy loam, XDE-742 sulfonamide was a maximum of 6.4% at Day 100, declining to 5.6% of the applied radioactivity after 118 days. It was measured at 10.6% of applied radioactivity at study termination in Borstel sandy loam. In LUFA 3A clay loam, XDE-742 sulfonamide was a maximum of 1.9% of applied radioactivity on Day 100, and was 0.8% of applied radioactivity by study termination.

The 7-OH-XDE-742 reached levels of 5.8% of applied after 7 days in the Bruch West sandy loam and 7.9% of applied radioactivity after 14 days in the Borstel sandy loam. In the Charentilly light clay, the 7-OH-XDE-742 reached 4.8% at DAT 4 whereas the maximum concentration was 2.5% at DAT 1 in the LUFA 3A clay loam. The 7-OH-XDE-742 declined to less than 1.5% of the applied radioactivity at study termination in all tested soils.

The pyridine sulfonic acid (PSA) and cyanosulfonamide (CSF) product were not observed above 5% of the applied radiocarbon at any site. PSA reached a maximum of approximately 4% of applied at 100 DAT while CSF was observed at a maximum of approximately 1% of applied at 63 DAT at Charentilly. Neither product accounted for more than 4% of the applied radiocarbon in any of the other soil types.

NON-EXTRACTABLE AND EXTRACTABLE RESIDUES: Non-extractable residues (NER) accounted for up to 37.9-82.8% of the applied radioactivity, even after the exhaustive extraction procedures.

Non-extractable [^{14}C] residues were 0.5 %, 0.3%, 0.2% and 0.3% of the applied amount at day 0 and increased to 82.8%, 47.8%, 37.9% and 49.2% of the applied for LUFA, Bruch West, Borstel and Charentilly respectively, at study termination.

Significant levels of radioactivity (>10% of the applied radioactivity) were extracted from soil using the more exhaustive extraction methods. However, much of the extractable radioactivity was only soluble at strongly acidic or basic pH values, and precipitated from solution when adjusted to neutral pH values (as necessary for HPLC analysis). This material has been characterized as extractable but insoluble. Insoluble radioactivity was also extracted from soil using the acetonitrile: 1 N HCl extract.

Much of the additional extractable radioactivity was likely due to incorporation of the radiocarbon into soil macromolecules such as humic or fulvic acids. These results are consistent with the general understanding that harsh acidic and basic solvents are destructive to the integrity of the soil organic matter.

This insoluble radioactivity did not contain parent or any of its discreet transformation products. At the initial time points, all extractable radioactivity was soluble, even though the same solid materials precipitated out of solution with the pH adjustment of the extracts.

VOLATILIZATION: In the LUFA 3A clay loam, approximately 5% of the applied radioactivity was recovered in the caustic traps at the end of the study. In the Bruch West sandy loam, 8% and 4% of the applied radioactivity was recovered in the caustic traps for the TP and PY-labeled products, respectively. In the Borstel sandy loam, 8% and 2% of the applied radioactivity was recovered in the caustic traps for the TP and PY-labeled products, respectively. In the Charentilly clay loam, 11% and 9% of the applied radioactivity was recovered in the TP-labelled and PY-labelled caustic traps, respectively. All of the radioactivity recovered in the caustic traps was assumed to be CO_2.

TRANSFORMATION PATHWAY: The first step in XDE-742 aerobic soil degradation is demethylation of one of the two methoxy groups on the triazolopyrimidine (TP) ring system to 5-OH-XDE-742 or 7-OH-XDE-742. The 7-OH transformation product can then undergo chlorination to form 6-Cl-7-OH-XDE-742. Further degradation of the TP ring system occurs to

give the cyanosulfonamide, sulfonamide and sulfonic acid transformation products. The terminal degradation products are CO_2 (minor) and bound residues (major). The proposed degradation pathway is shown in Figure 3.

Figure 3: Proposed Metabolic Pathway for the Test Material in Soil under Aerobic conditions.

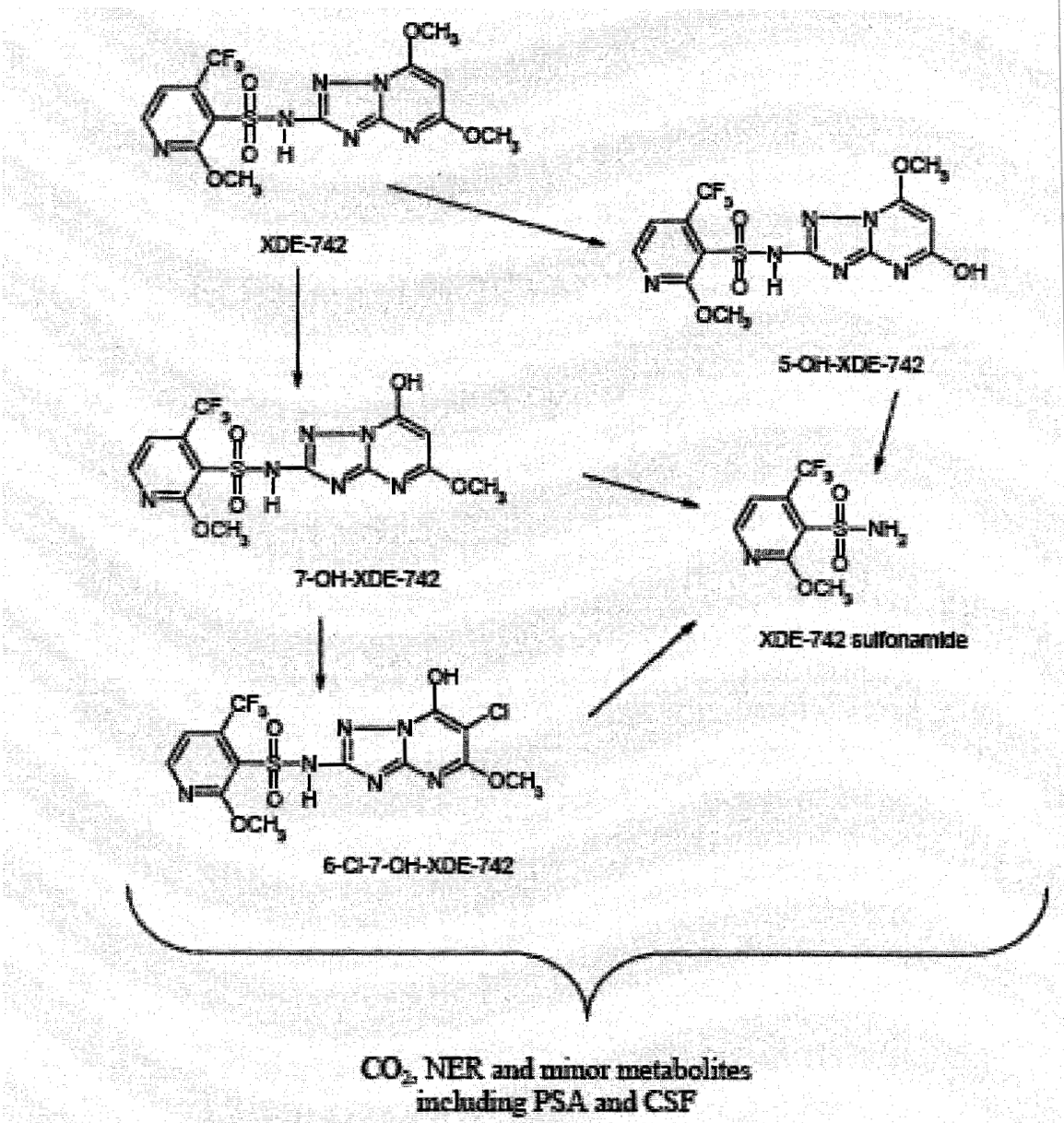
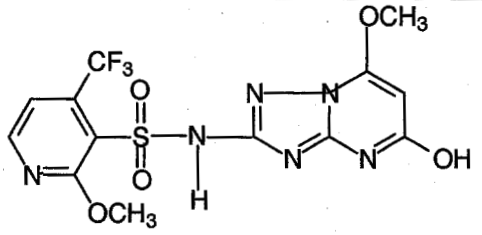


Table 17: Chemical names and CAS numbers for the transformation products of XDE-742.

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

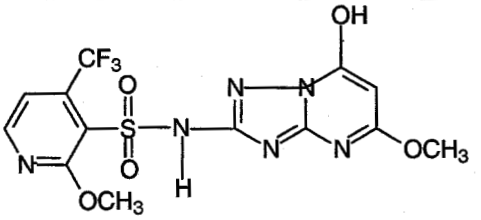
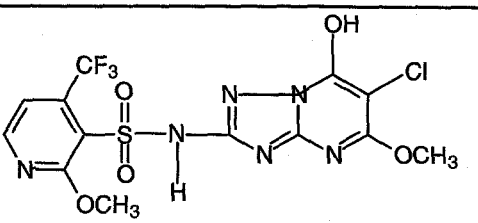
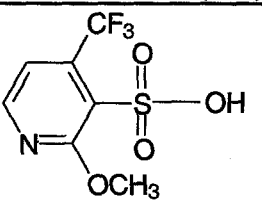
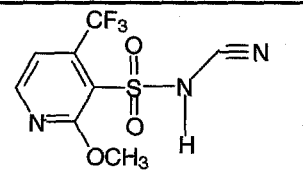
Common Name	7-OH-XDE-742		
			
IUPAC Chemical Name	*N*-(7-hydroxy-5-methoxy[1,2,4]triazolo[1,5-α]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide		
CAS #	N/A	**SMILES String**	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(cc3O)OC)(=O)=O
Formula	$C_{13}H_{11}F_3N_6O_5S$	**MW**	420.3 g/mol

Table 18: Chemical names and CAS numbers for the transformation products of XDE-742.

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

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

D. SUPPLEMENTARY EXPERIMENT-RESULTS: No supplementary study was conducted.

III. STUDY DEFICIENCIES: No deficiencies were noted.

IV. REVIEWER'S COMMENTS: The PMRA reviewer agrees with the conclusions stated in the study report. No significant deviations from good scientific practices were noted by the 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 half-lives calculated by the reviewer confirm those reported in the study report.

The PMRA, DEW and US EPA consider this study as acceptable. It satisfies the guideline requirements for a study of biotransformation of XDE-742 in aerobic soil.

V. REFERENCES:

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

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

3. C. Cathie, "Determination of Dissociation Constant of XR-742 using UV-Visible Spectrophotometry", 04-509-G, unpublished report of Dow AgroSciences LLC2004.

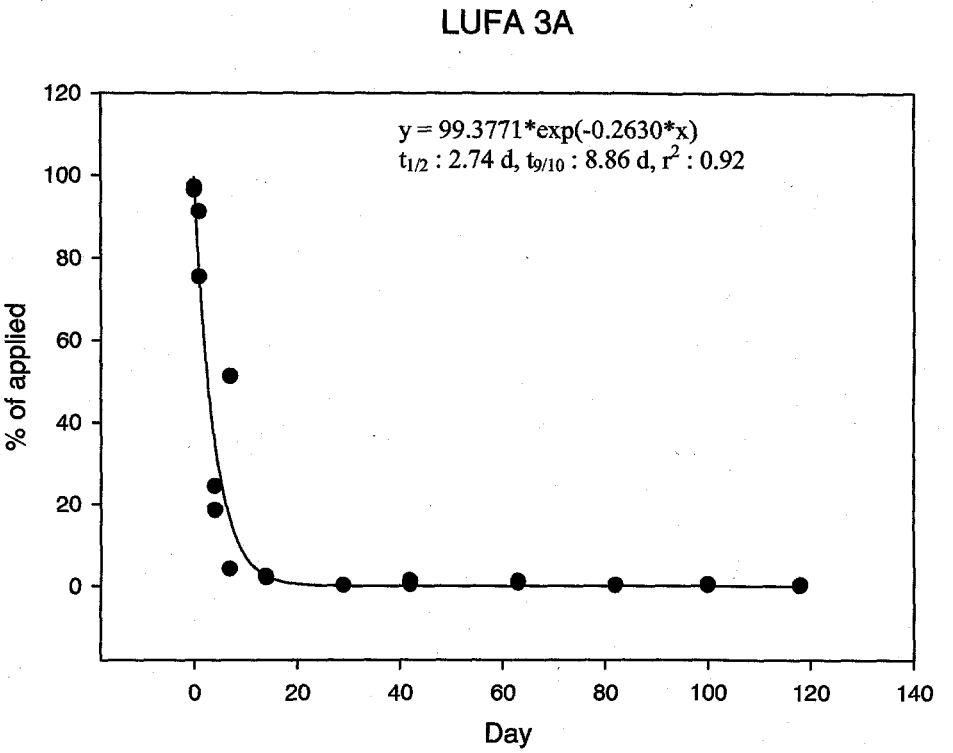
4. Turner, B. J., "Determination of Octanol/Water Partition Coefficient for XDE-742," NAFST807, unpublished report of Dow AgroSciences LLC, 2004.

5. R. N. Yoder, K. P. Smith, J. L. Balcer, S. J. Linder, "Aerobic Soil Degradation of 14CXDE-742 in Four European Soils", 030013, unpublished report of Dow AgroSciences, 2006.

6. R. N. Yoder, K. P. Smith, M. J. Hastings, "Aerobic Soil Degradation Rate of 6-Cl-7-OHXDE-742 in 4 European Soils", 060124, unpublished report of Dow AgroSciences, 2007.

Appendix 1 : Statistical output from statistical verification by the PMRA reviewer

LUFA 3A



Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
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: 99.3771}}
b = if(x50(x,y)-min(x)=0, 1, -ln(.5)/(x50(x,y)-min(x))) "Auto {{previous: 0.262965}}
[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 = 0.96065704 Rsqr = 0.92286194 Adj Rsqr = 0.91880205

Standard Error of Estimate = 10.2446

	Coefficient	Std. Error	t	P
a	99.3771	6.2826	15.8178	<0.0001
b	0.2630	0.0422	6.2347	<0.0001

Analysis of Variance:

	DF	SS	MS	F	P
Regression	1	23856.8971	23856.8971	227.3116	<0.0001
Residual	19	1994.0953	104.9524		
Total	20	25850.9924	1292.5496		

PRESS = 3056.8202

Durbin-Watson Statistic = 2.0828

Normality Test: K-S Statistic = 0.3490 Significance Level = 0.0087

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	99.3771	-2.9771	-0.2906	-0.3679	-0.3594
2	99.3771	-2.1771	-0.2125	-0.2690	-0.2624
3	76.3980	14.8020	1.4449	1.5929	1.6657
4	76.3980	-0.9980	-0.0974	-0.1074	-0.1046
5	34.7112	-10.3112	-1.0065	-1.1654	-1.1772
6	34.7112	-16.1112	-1.5727	-1.8209	-1.9507
7	15.7709	-11.5709	-1.1295	-1.2424	-1.2616
8	15.7709	35.4291	3.4583	3.8041	7.5838
9	2.5028	-0.1028	-0.0100	-0.0101	-0.0099
10	2.5028	-0.5028	-0.0491	-0.0496	-0.0482
11	0.0485	0.2515	0.0246	0.0246	0.0239
12	0.0016	0.4984	0.0487	0.0487	0.0474
13	0.0016	1.3984	0.1365	0.1365	0.1329
14	0.0000	1.2000	0.1171	0.1171	0.1141
15	0.0000	0.8000	0.0781	0.0781	0.0760
16	0.0000	0.3000	0.0293	0.0293	0.0285
17	0.0000	0.4000	0.0390	0.0390	0.0380
18	0.0000	0.3000	0.0293	0.0293	0.0285
19	0.0000	0.5000	0.0488	0.0488	0.0475
20	0.0000	0.2000	0.0195	0.0195	0.0190

21	0.0000	0.4000	0.0390	0.0390	0.0380

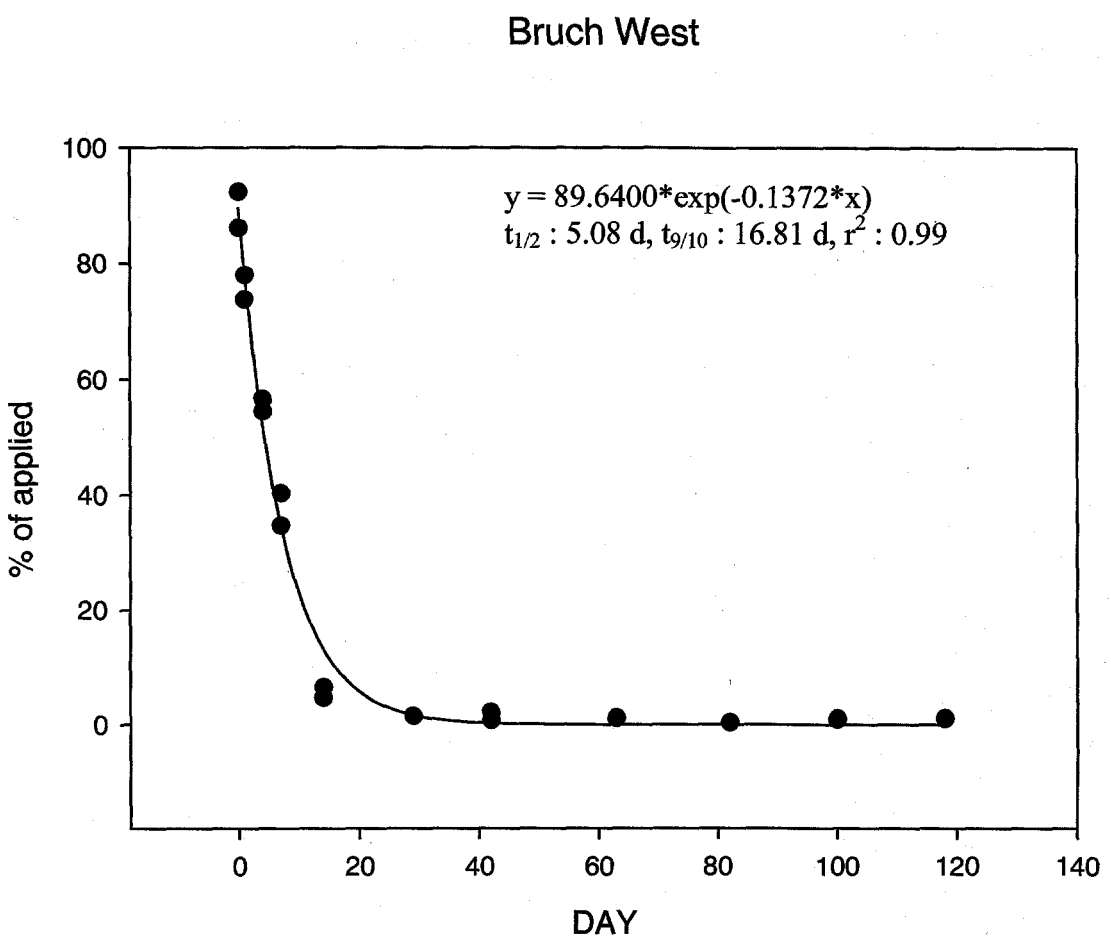
Influence Diagnostics:

Row	Cook'sDist	Leverage	DFFITS
1	0.0408	0.3761	-0.2790
2	0.0218	0.3761	-0.2037
3	0.2734	0.1773	0.7732
4	0.0012	0.1773	-0.0485
5	0.2313	0.2541	-0.6870
6	0.5647	0.2541	-1.1385
7	0.1620	0.1735	-0.5781
8	1.5192	0.1735	3.4750
9	0.0000	0.0190	-0.0014
10	0.0000	0.0190	-0.0067
11	0.0000	0.0000	0.0001
12	0.0000	0.0000	0.0000
13	0.0000	0.0000	0.0000
14	0.0000	0.0000	0.0000
15	0.0000	0.0000	0.0000
16	0.0000	0.0000	0.0000
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
21	0.0000	0.0000	0.0000

95% Confidence:

Row	Predicted	Regr. 5%	Regr. 95%	Pop. 5%	Pop. 95%
1	99.3771	86.2274	112.5267	74.2239	124.5303
2	99.3771	86.2274	112.5267	74.2239	124.5303
3	76.3980	67.3694	85.4266	53.1325	99.6636
4	76.3980	67.3694	85.4266	53.1325	99.6636
5	34.7112	23.9028	45.5196	10.6989	58.7235
6	34.7112	23.9028	45.5196	10.6989	58.7235
7	15.7709	6.8388	24.7031	-7.4573	38.9992
8	15.7709	6.8388	24.7031	-7.4573	38.9992
9	2.5028	-0.4517	5.4573	-19.1420	24.1477
10	2.5028	-0.4517	5.4573	-19.1420	24.1477
11	0.0485	-0.0733	0.1702	-21.3941	21.4911
12	0.0016	-0.0042	0.0074	-21.4407	21.4438
13	0.0016	-0.0042	0.0074	-21.4407	21.4438
14	0.0000	-0.0000	0.0000	-21.4422	21.4423
15	0.0000	-0.0000	0.0000	-21.4422	21.4423
16	0.0000	-0.0000	0.0000	-21.4423	21.4423
17	0.0000	-0.0000	0.0000	-21.4423	21.4423
18	0.0000	-0.0000	0.0000	-21.4423	21.4423
19	0.0000	-0.0000	0.0000	-21.4423	21.4423
20	0.0000	-0.0000	0.0000	-21.4423	21.4423
21	0.0000	-0.0000	0.0000	-21.4423	21.4423

Bruch West



Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
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: 89.64}}
b = if(x50(x,y)-min(x)=0, 1, -ln(.5)/(x50(x,y)-min(x))) "Auto {{previous: 0.137209}}
[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 = 0.99487813 Rsqr = 0.98978250 Adj Rsqr = 0.98924474

Standard Error of Estimate = 3.4909

	Coefficient	Std. Error	t	P
a	89.6400	1.9521	45.9188	<0.0001
b	0.1372	0.0078	17.6350	<0.0001

Analysis of Variance:

	DF	SS	MS	F	P
Regression	1	22429.1568	22429.1568	1840.5550	<0.0001
Residual	19	231.5356	12.1861		
Total	20	22660.6924	1133.0346		

PRESS = 335.3114

Durbin-Watson Statistic = 1.8548

Normality Test: K-S Statistic = 0.2888 Significance Level = 0.0481

Constant Variance Test: Passed (P = 0.1382)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

Row	Predicted	Residual	Std. Res.	Stud. Res.	Stud. Del. Res.
1	89.6400	-3.4400	-0.9854	-1.1887	-1.2026
2	89.6400	2.7600	0.7906	0.9537	0.9513
3	78.1471	-4.3471	-1.2453	-1.3719	-1.4068
4	78.1471	-0.1471	-0.0421	-0.0464	-0.0452
5	51.7780	4.8220	1.3813	1.5035	1.5590
6	51.7780	2.7220	0.7798	0.8487	0.8422
7	34.3066	0.3934	0.1127	0.1266	0.1233
8	34.3066	5.9934	1.7169	1.9286	2.0932
9	13.1296	-8.4296	-2.4148	-2.5991	-3.1514
10	13.1296	-6.6296	-1.8991	-2.0441	-2.2527
11	1.6765	-0.1765	-0.0506	-0.0508	-0.0495
12	1.6765	-0.1765	-0.0506	-0.0508	-0.0495
13	0.2817	0.5183	0.1485	0.1485	0.1446
14	0.2817	1.9183	0.5495	0.5497	0.5393
15	0.0158	1.0842	0.3106	0.3106	0.3031
16	0.0158	1.1842	0.3392	0.3392	0.3312
17	0.0012	0.3988	0.1143	0.1143	0.1112
18	0.0001	0.8999	0.2578	0.2578	0.2514

19	0.0001	1.0999	0.3151	0.3151	0.3075
20	0.0000	1.2000	0.3438	0.3438	0.3356
21	0.0000	1.1000	0.3151	0.3151	0.3075

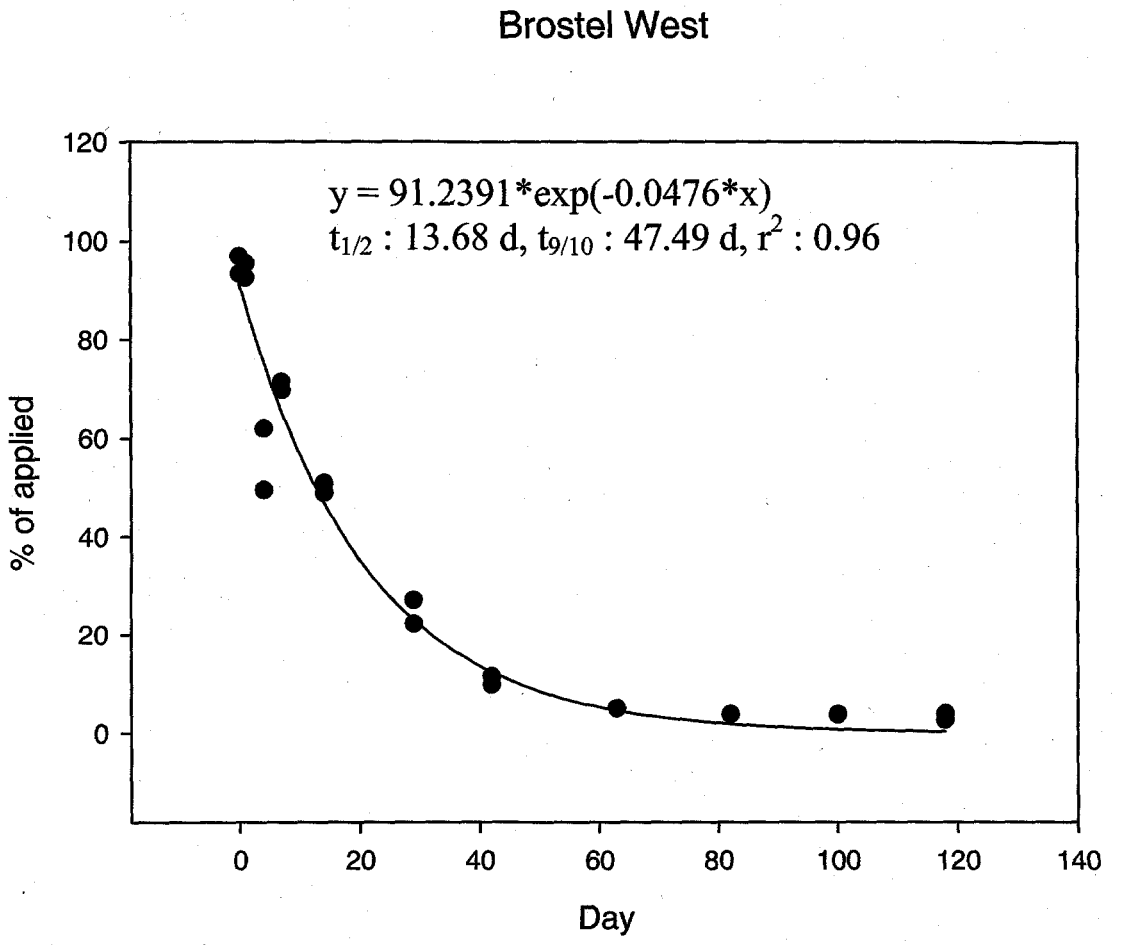
Influence Diagnostics:

Row	Cook'sDist	Leverage	DFFITS
1	0.3215	0.3127	-0.8112
2	0.2069	0.3127	0.6417
3	0.2010	0.1760	-0.6502
4	0.0002	0.1760	-0.0209
5	0.2087	0.1559	0.6699
6	0.0665	0.1559	0.3619
7	0.0021	0.2075	0.0631
8	0.4870	0.2075	1.0711
9	0.5355	0.1368	-1.2548
10	0.3312	0.1368	-0.8970
11	0.0000	0.0104	-0.0051
12	0.0000	0.0104	-0.0051
13	0.0000	0.0006	0.0036
14	0.0001	0.0006	0.0135
15	0.0000	0.0000	0.0006
16	0.0000	0.0000	0.0007
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
21	0.0000	0.0000	0.0000

95% Confidence:

Row	Predicted	Regr. 5%	Regr. 95%	Pop. 5%	Pop. 95%
1	89.6400	85.5541	93.7259	81.2687	98.0113
2	89.6400	85.5541	93.7259	81.2687	98.0113
3	78.1471	75.0816	81.2126	70.2236	86.0706
4	78.1471	75.0816	81.2126	70.2236	86.0706
5	51.7780	48.8933	54.6626	43.9227	59.6332
6	51.7780	48.8933	54.6626	43.9227	59.6332
7	34.3066	30.9782	37.6349	26.2777	42.3354
8	34.3066	30.9782	37.6349	26.2777	42.3354
9	13.1296	10.4268	15.8324	5.3393	20.9200
10	13.1296	10.4268	15.8324	5.3393	20.9200
11	1.6765	0.9321	2.4210	-5.6677	9.0208
12	1.6765	0.9321	2.4210	-5.6677	9.0208
13	0.2817	0.0988	0.4645	-7.0271	7.5904
14	0.2817	0.0988	0.4645	-7.0271	7.5904
15	0.0158	0.0004	0.0312	-7.2907	7.3223
16	0.0158	0.0004	0.0312	-7.2907	7.3223
17	0.0012	-0.0003	0.0026	-7.3053	7.3076
18	0.0001	-0.0001	0.0003	-7.3063	7.3065
19	0.0001	-0.0001	0.0003	-7.3063	7.3065
20	0.0000	-0.0000	0.0000	-7.3064	7.3065
21	0.0000	-0.0000	0.0000	-7.3064	7.3065

Borstel



Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
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: 91.2391}}
b = if(x50(x,y)-min(x)=0, 1, -ln(.5)/(x50(x,y)-min(x))) "Auto {{previous: 0.0476045}}
[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 = 0.97780987 Rsqr = 0.95611215 Adj Rsqr = 0.95380226

Standard Error of Estimate = 7.7459

	Coefficient	Std. Error	t	P
a	91.2391	3.5072	26.0148	<0.0001
b	0.0476	0.0053	9.0482	<0.0001

Analysis of Variance:

	DF	SS	MS	F	P
Regression	1	24834.6561	24834.6561	413.9216	<0.0001
Residual	19	1139.9706	59.9985		
Total	20	25974.6267	1298.7313		

PRESS = 1432.6862

Durbin-Watson Statistic = 1.4136

Normality Test: K-S Statistic = 0.3172 Significance Level = 0.0223

Constant Variance Test: Failed (P = 0.0098)

Power of performed test with alpha = 0.0500: 1.0000

Regression Diagnostics:

Row	Predicted	Residual	Std. Res.	Stud. Res.	Stud. Del. Res.
1	91.2391	2.1609	0.2790	0.3129	0.3053
2	91.2391	5.6609	0.7308	0.8197	0.8123
3	86.9975	8.6025	1.1106	1.2134	1.2296
4	86.9975	5.6025	0.7233	0.7902	0.7821
5	75.4195	-25.9195	-3.3462	-3.5252	-5.8335
6	75.4195	-13.4195	-1.7325	-1.8251	-1.9562
7	65.3823	6.0177	0.7769	0.8156	0.8081
8	65.3823	4.4177	0.5703	0.5987	0.5883
9	46.8533	2.0467	0.2642	0.2851	0.2780
10	46.8533	4.0467	0.5224	0.5636	0.5532
11	22.9416	4.1584	0.5369	0.5869	0.5765
12	22.9416	-0.7416	-0.0957	-0.1047	-0.1019
13	12.3554	-0.9554	-0.1233	-0.1305	-0.1271
14	12.3554	-2.6554	-0.3428	-0.3627	-0.3542
15	4.5467	0.4533	0.0585	0.0596	0.0580
16	1.8403	1.9597	0.2530	0.2543	0.2479
17	1.8403	1.9597	0.2530	0.2543	0.2479
18	0.7812	2.9188	0.3768	0.3773	0.3687
19	0.7812	3.0188	0.3897	0.3903	0.3814
20	0.3316	2.3684	0.3058	0.3059	0.2984

21	0.3316	3.5684	0.4607	0.4608	0.4511

Influence Diagnostics:

Row	Cook'sDist	Leverage	DFFITS
1	0.0126	0.2050	0.1550
2	0.0866	0.2050	0.4125
3	0.1426	0.1623	0.5412
4	0.0605	0.1623	0.3442
5	0.6823	0.0989	-1.9331
6	0.1829	0.0989	-0.6482
7	0.0339	0.0926	0.2581
8	0.0183	0.0926	0.1879
9	0.0067	0.1407	0.1125
10	0.0260	0.1407	0.2239
11	0.0336	0.1633	0.2547
12	0.0011	0.1633	-0.0450
13	0.0010	0.1065	-0.0439
14	0.0078	0.1065	-0.1223
15	0.0001	0.0346	0.0110
16	0.0003	0.0100	0.0249
17	0.0003	0.0100	0.0249
18	0.0002	0.0027	0.0193
19	0.0002	0.0027	0.0200
20	0.0000	0.0007	0.0079
21	0.0001	0.0007	0.0119

95% Confidence:

Row	Predicted	Regr. 5%	Regr. 95%	Pop. 5%	Pop. 95%
1	91.2391	83.8985	98.5798	73.4424	109.0359
2	91.2391	83.8985	98.5798	73.4424	109.0359
3	86.9975	80.4667	93.5282	69.5193	104.4757
4	86.9975	80.4667	93.5282	69.5193	104.4757
5	75.4195	70.3198	80.5192	58.4241	92.4149
6	75.4195	70.3198	80.5192	58.4241	92.4149
7	65.3823	60.4496	70.3151	48.4362	82.3284
8	65.3823	60.4496	70.3151	48.4362	82.3284
9	46.8533	40.7714	52.9351	29.5378	64.1688
10	46.8533	40.7714	52.9351	29.5378	64.1688
11	22.9416	16.3905	29.4927	5.4558	40.4275
12	22.9416	16.3905	29.4927	5.4558	40.4275
13	12.3554	7.0645	17.6463	-4.6984	29.4092
14	12.3554	7.0645	17.6463	-4.6984	29.4092
15	4.5467	1.5313	7.5621	-11.9436	21.0370
16	1.8403	0.2230	3.4575	-14.4525	18.1330
17	1.8403	0.2230	3.4575	-14.4525	18.1330
18	0.7812	-0.0666	1.6289	-15.4533	17.0156
19	0.7812	-0.0666	1.6289	-15.4533	17.0156
20	0.3316	-0.0974	0.7606	-15.8864	16.5496
21	0.3316	-0.0974	0.7606	-15.8864	16.5496

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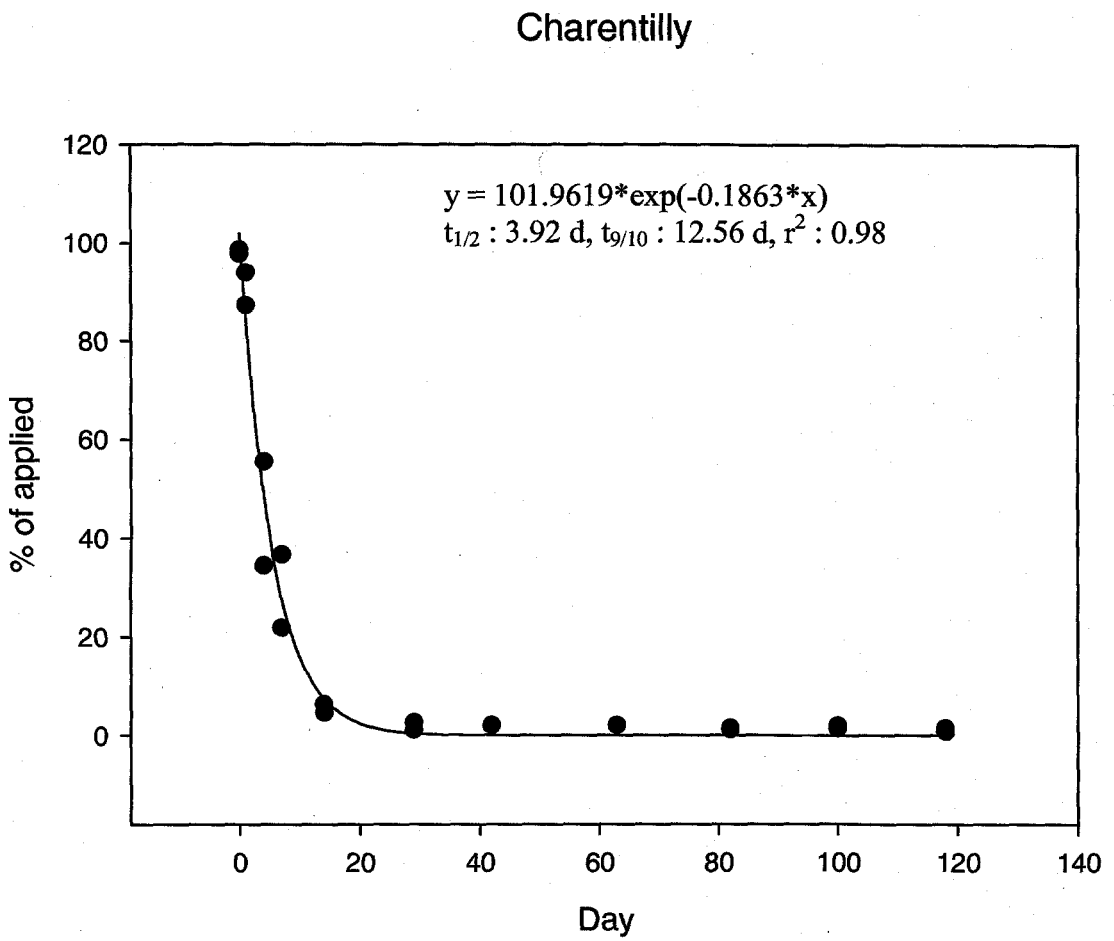

Nonlinear Regression

[Variables]
x = col(1)
y = col(2)
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: 101.962}}
b = if(x50(x,y)-min(x)=0, 1, -ln(.5)/(x50(x,y)-min(x))) "Auto {{previous: 0.186284}}
[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 = 0.99020997 Rsqr = 0.98051579 Adj Rsqr = 0.97943333

Standard Error of Estimate = 5.3663

	Coefficient	Std. Error	t	P
a	101.9619	3.1372	32.5012	<0.0001
b	0.1863	0.0145	12.8445	<0.0001

Analysis of Variance:

	DF	SS	MS	F	P
Regression	1	26085.3925	26085.3925	905.8250	<0.0001
Residual	18	518.3530	28.7974		
Total	19	26603.7455	1400.1971		

PRESS = 809.1031

Durbin-Watson Statistic = 2.8093

Normality Test: K-S Statistic = 0.2492 Significance Level = 0.1416

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	101.9619	-4.1619	-0.7756	-0.9559	-0.9535
2	101.9619	-3.2619	-0.6078	-0.7492	-0.7397
3	84.6322	9.3678	1.7457	1.9199	2.0923
4	84.6322	2.6678	0.4971	0.5468	0.5358
5	48.3982	7.1018	1.3234	1.4803	1.5351
6	48.3982	-13.8982	-2.5899	-2.8970	-3.8535
7	27.6772	9.1228	1.7000	1.9166	2.0877
8	27.6772	-5.6772	-1.0579	-1.1927	-1.2078
9	7.5129	-1.1129	-0.2074	-0.2150	-0.2092
10	7.5129	-2.8129	-0.5242	-0.5435	-0.5326
11	0.4595	0.6405	0.1194	0.1194	0.1161
12	0.4595	2.2405	0.4175	0.4178	0.4080
13	0.0408	2.0592	0.3837	0.3837	0.3745
14	0.0008	2.0992	0.3912	0.3912	0.3818
15	0.0000	1.5000	0.2795	0.2795	0.2722
16	0.0000	1.2000	0.2236	0.2236	0.2176
17	0.0000	1.5000	0.2795	0.2795	0.2722

18	0.0000	2.1000	0.3913	0.3913	0.3819
19	0.0000	0.8000	0.1491	0.1491	0.1450
20	0.0000	1.5000	0.2795	0.2795	0.2722

Influence Diagnostics:

Row	Cook'sDist	Leverage	DFFITS
1	0.2372	0.3418	-0.6871
2	0.1457	0.3418	-0.5330
3	0.3863	0.1733	0.9579
4	0.0313	0.1733	0.2453
5	0.2752	0.2008	0.7694
6	1.0540	0.2008	-1.9313
7	0.4977	0.2132	1.0868
8	0.1928	0.2132	-0.6288
9	0.0017	0.0698	-0.0573
10	0.0111	0.0698	-0.1459
11	0.0000	0.0012	0.0040
12	0.0001	0.0012	0.0141
13	0.0000	0.0000	0.0017
14	0.0000	0.0000	0.0001
15	0.0000	0.0000	0.0000
16	0.0000	0.0000	0.0000
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	101.9619	95.3709	108.5528	88.9024	115.0213
2	101.9619	95.3709	108.5528	88.9024	115.0213
3	84.6322	79.9391	89.3253	72.4202	96.8442
4	84.6322	79.9391	89.3253	72.4202	96.8442
5	48.3982	43.3466	53.4497	36.0440	60.7524
6	48.3982	43.3466	53.4497	36.0440	60.7524
7	27.6772	22.4713	32.8832	15.2591	40.0953
8	27.6772	22.4713	32.8832	15.2591	40.0953
9	7.5129	4.5348	10.4910	-4.1480	19.1738
10	7.5129	4.5348	10.4910	-4.1480	19.1738
11	0.4595	0.0694	0.8496	-10.8215	11.7405
12	0.4595	0.0694	0.8496	-10.8215	11.7405
13	0.0408	-0.0098	0.0914	-11.2335	11.3151
14	0.0008	-0.0007	0.0023	-11.2734	11.2750
15	0.0000	-0.0000	0.0001	-11.2742	11.2742
16	0.0000	-0.0000	0.0001	-11.2742	11.2742
17	0.0000	-0.0000	0.0000	-11.2742	11.2742
18	0.0000	-0.0000	0.0000	-11.2742	11.2742
19	0.0000	-0.0000	0.0000	-11.2742	11.2742
20	0.0000	-0.0000	0.0000	-11.2742	11.2742