Data Evaluation Report on the aerobic biotransformation of pyrasulfotole (AE 0317309) in soil

PMRA Submission Number 2006-2445 EPA MRID Number 46801711

Data Requirement:	PMRA Data Code:	8.2.3.4.1
	EPA DP Barcode:	D328639
	OECD Data Point:	IIA 7.2.3
	EPA Guideline:	162-1

Test material:

Common name:	Pyrasulfotole.
Chemical name:	
IUPAC name:	(5-Hydroxy-1,3-dimethylpyrazol-4-yl)(α,α,α-trifluoro-2-mesyl-*p*-tolyl)methanone. (5-Hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)(2-mesyl-4-trifluoromethylphenyl)methanone.
CAS name:	(5-Hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)[2-methylsulfonyl)-4(trifluoromethyl)phenyl]methanone. Methanone, (5-hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl].
CAS No:	365400-11-9.
Synonyms:	AE 0317309; K-1196; K-1267.
SMILES string:	FC(c1cc(c(cc1)C(=O)c1c(n(nc1C)C)O)S(=O)(=O)C)(F)F (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found as of 6/7/06. Cc1nn(C)c(O)c1C(=O)c2ccc(C(F)(F)F)cc2S(C)(=O)=O. CS(=O)(=O)c1c(ccc(c1)C(F)(F)F)C(=O)c1c(n(nc1C)C)O.

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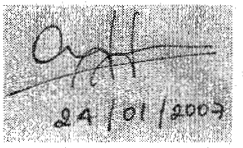
Final Reviewer: Olga Braga **Signature:**
DEH Reviewer **Date:**



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CITATION: Fliege, R. 2005. [Phenyl-UL-^{14}C] and [pyrazole-3-^{14}C]AE 0317309: aerobic soil metabolism in a European soil. Unpublished study performed, sponsored and submitted by Bayer CropScience AG, Monheim, Germany. BCS Study No.: M1251487-8 and Report No.: MEF-05/459. Experimental start date April 14, 2005 and termination date September 22, 2005 (p. 6). Final report issued November 17, 2005.

EXECUTIVE SUMMARY

The biotransformation of [phenyl-U-^{14}C]- and [pyrazole-3-^{14}C]-labeled (5-hydroxy-1,3-dimethylpyrazol-4-yl)(2-mesyl-4-trifluoromethylphenyl)methanone (pyrasulfotole, AE 0317309) was studied in a sandy loam soil (pH 5.9-6.6, organic carbon 1.4%) from Germany for 120 days under aerobic conditions in darkness at 20 ± 1°C and 50% of maximum water holding capacity (MWHC). [^{14}C]Pyrasulfotole was applied at a rate of 0.12-0.13 mg a.i./kg (equivalent to 0.05 kg a.i./ha). This study was conducted in accordance with OECD Guideline for the Testing of Chemicals No. 307, Aerobic and Anaerobic Transformation in Soil (2002), and in compliance with OECD Principles of GLP. The test system consisted of 300-mL Erlenmeyer flasks, each fitted with an air-permeable, solid-phase trap for the collection of CO_2 (soda lime) and volatile organics (polyurethane foam). Duplicate flasks per test substance were taken for analysis after 0, 1, 3, 7, 14, 21, 29, 41, 62, 86 and 120 days of incubation. Soil samples were extracted using an Accelerated Solvent Extraction (ASE) system, which conducted two-phase ["mild" (40°C, 103 bar) and "aggravated" (100°C, 103 bar) conditions], automated, multi-step extractions with acetonitrile:water (2:1, v:v) as the extraction solvent. The subsequent "mild" and "aggravated" extracts were separately concentrated under a stream of nitrogen (45°C) for reverse-phase HPLC analysis. One transformation product, 2-methylsulfonyl-4-trifluoromethylbenzoic acid (AE B197555), was identified via HPLC against reference standard. The identification was confirmed using normal-phase, one-dimensional TLC and LC/MS/MS-ESI against reference standard.

Incubation temperature averaged 19.8 ± <1°C and soil moisture averaged 50.3 ± 1.6 % of MWHC during the 120-day study. No supporting records were provided to establish that aerobicity was maintained throughout the study.

For both labels, overall recovery of material balance averaged 100.5 ± 2.7% (range 93.9-104.9%) of the applied, with no consistent pattern of decline in recoveries for either label. Phenyl-labeled pyrasulfotole decreased from a mean 100.0% of the applied at day 0 to 48.0% at 29 days and was 19.0% at 120 days. Pyrazole-labeled pyrasulfotole reached the observed DT50 somewhat faster decreasing from 98.4% at day 0 to 48.9% at 21 days and was 17.3% at study termination. The reviewer-calculated **linear half-life** for both radiolabels was 48 days (r^2 = 0.9127) and the **nonlinear half-life** was 32.4 days (r^2 = 0.9503). The reviewer-calculated **DT_{50} and DT_{90}** estimates were 23 and 208 days, respectively (r^2 = 0.990). The **observed DT_{50} and DT_{90}** values were 14 – 29 and >120 days, respectively.

No major nonvolatile transformation products were detected for either label.

- 2-Methylsulfonyl-4-trifluoromethylbenzoic acid (AE B197555)

was a minor transformation product in phenyl-label treated soil detected at a maximum 8.9 ± 0.4% of the applied; no other minor products were identified for either label. Unidentified [^{14}C]residues were detected at total means of ≤2.6%. Extractable [^{14}C]residues (both labels)

decreased from means of 98.6-101.4% of the applied at day 0 to 19.0-23.3% at study termination, while nonextractable [^{14}C]residues increased from 2.1-2.7% to 60.1-62.1% at the same respective intervals. Organic matter fractionation of 86-day extracted soil found means of 14.7-17.7%, 22.1-27.3% and 11.6-15.2% of the applied associated with the humin, fulvic acids and humic acids, respectively. At study termination, volatilized $^{14}CO_2$ comprised total means of 16.3-18.0% of the applied, while volatile [^{14}C]organic compounds were ≤0.1% at all intervals.

A transformation pathway was provided by the study author that was consistent with the products detected. Transformation of pyrasulfotole involves hydrolytic cleavage of the phenyl and pyrazole moieties to yield the benzoic acid derivative, 2-methylsulfonyl-4-trifluoromethylbenzoic acid (AE B197555), plus several unidentified minor compounds, with steady formation of bound soil residues and moderate levels of mineralization to CO_2.

In a supplementary experiment, pyrasulfotole and its transformation products remained stable in soil extracts stored frozen up to 92 days.

Results Synopsis:

Test system used: Sandy loam from Germany.

Linear half-life:	47.6 days (r^2 = 0.9127).
Non-linear half-life:	32.4 days (r^2 = 0.9503).
Non-linear, 2-compartment DT_{50}:	23 days (r^2 = 0.990).
Non-linear, 2-compartment DT_{90}:	208 days (r^2 = 0.990).
Observed DT_{50}:	14-29 days.
Observed DT_{90}:	>120 days.

Major transformation products:

CO_2 (maximum 16.3-18.0% of applied).

Minor transformation products:

2-Methylsulfonyl-4-trifluoromethylbenzoic acid (AE B197555, maximum 9.3% of applied).

Study Acceptability: The EPA classifies this study as **supplemental** because it was not established that the German soil used in this study is comparable to soils that would be found in typical use areas for pyrasulfotole in the United States. The PMRA and DEH classify this study as **acceptable**. No significant deviations from good scientific practices were noted.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with OECD Guideline for the Testing of Chemicals No. 307, Aerobic and Anaerobic Transformation in Soil (2002, p. 6). The following significant deviations from the objectives of USEPA Subdivision N Guideline §162-1 were noted:

A US soil was not used, and it was not established that the foreign test soil used in this study was comparable to soils that would be found at intended use sites for pyrasulfotole in the United States. A soil from Germany classified as a sandy loam according to USDA textural classification was used in this study. However, a FAO soil classification was not provided to allow for adequate comparison.

COMPLIANCE: This study was conducted in compliance with [current] OECD Principles of GLP (p. 3). This study met the requirements of USEPA GLP Standards 40 CFR, Part 160; German Chemical Law Principles of GLP (Chemikaliengesetz, 2002); and Japan MAFF - Notification on the GLP Standards for Agricultural Chemicals - JMAFF/11 Nousan No. 6283 (1999, p. 3). Signed and dated Data Confidentiality, GLP and Quality Assurance statements and a Certification of Authenticity were provided (pp. 2-5).

A. MATERIALS:

1. Test Materials [Phenyl-U-^{14}C] and [pyrazole-3-^{14}C]pyrasulfotole (p. 22; Figure 1, p. 57).

Chemical Structure: See DER Attachment 1.

[Phenyl-U-^{14}C]pyrasulfotole

Description:		Technical, solid (p. 22).
Purity:	Radiochemical purity:	>99% (p. 22; Figure 11, p. 67).
	Lot/Batch No.:	SEL/1006.
	Analytical purity:	>99% (HPLC, p. 22).
	Specific activity:	191,400 dpm/µg (86.23 µCi/mg, 3.19 MBq/mg).
	Location of the radiolabel:	Uniformly on phenyl ring.

[Pyrazole-3-^{14}C]pyrasulfotole

Description:		Technical, solid (p. 23).
Purity:	Radiochemical purity:	>99% (p. 23; Figure 12, p. 68).
	Lot/Batch No.:	SEL/1009.
	Analytical purity:	>99% (HPLC, p. 23).
	Specific activity:	330,600 dpm/µg (148.82 µCi/mg, 5.51 MBq/mg).
	Location of the radiolabel:	At 3-C position on pyrazole ring.

Storage conditions of test chemicals: The test substances were dissolved in acetonitrile, then stored in darkness in a freezer (temperature not reported; pp. 22-23).

Physico-chemical properties of pyrasulfotole:

Parameter		Value	Comment
Molecular weight		362.3 g/mol.	
Molecular formula		$C_{14}H_{13}F_3N_2O_4S$	
Water Solubility	In distilled water:	2.3 g/L	At 20°C; Bayer CropScience Report No.: PA03/008. Buffer capacity exceeded at pH 7 and 9.
	Buffered at pH 4:	4.2 g/L	
	Buffered at pH 7:	69.1 g/L	
	Buffered at pH 9:	49.0 g/L	
Vapor Pressure/Volatility		2.7×10^{-7} Pa	At 20°C, extrapolated; Siemens AG Report No.: 20040374.02.
UV Absorption		λ_{max1} = 264 nm/ε = 1.11×10^4 L/(mol*cm) λ_{max2} = 306 nm/ε = 5.93×10^3 L/(mol*cm)	In water; Bayer CropScience Report No.: PA03/023.
Pka		4.2	Bayer CropScience Report No.: PA03/045.
Log K_{ow}	at pH 4:	0.276	At 23°C; Bayer CropScience Study No. PA03/010.
	at pH 7:	-1.362	
	at pH 9:	-1.580	
Stability of compound at room temperature		Stable in solid state. Stable in aqueous solution at pH 5, 7 and 9.	Bayer CropScience Report No.: PA03/076. At 25°C; Bayer CropScience Report No.: 200578.

Data obtained from p. 24; Figure 1, p. 57 of the study report.

2. Soil Characteristics

Table 1: Description of soil collection and storage.

Description		Details
Geographic location	Country:	Germany.
	State:	Northrhine-Westfalia.
	Town:	D-40789 Monheim am Rhein.
	Field:	"Laacher Hof Field Plot - Parzelle 712/718" located at Bayer Field Research Station. Site was an agricultural field of bare, plowed soil at time of soil collection.
Coordinates	Latitude:	N 51° 04.400'
	Longitude:	E 6° 54.598'
Collection date		April 14, 2005.
Pesticide use history at the collection site		2005: Roundup (glyphosate) at 5.0 L/ha. 1999-2004: no pesticide application.
Collection procedures		Five sub-samples collected from field using a spade and combined in a plastic bag (*ca.* 30 kg total soil).
Sampling depth		0- to 20-cm depth (soil horizon A).
Storage conditions		Soil transported to test facility at ambient temperature. At test facility, after sieving and mixing, the soil was stored aerated, in a plastic bag at *ca.* 4°C until use.
Storage length		12 days based on collection date (above) and the date of application on April 26, 2005.
Soil preparation		Large debris (stones, plant material) was removed, then the soil was sieved (2-mm). After sieving, the soil was mixed (method not reported) to yield a homogenous batch.

Data obtained from p. 25; Table 1, p. 49; Appendix 2, p. 90; Appendix 11, p. 99 of the study report.

Table 2: Properties of the soil.

Property		Details
Soil texture		Sandy loam
% Sand (0.05-2.0 mm)		69
% Silt (0.002-0.05 mm)		20
% Clay (<0.002 mm)		11
pH	In water (1:1):	6.5
	In water (saturated paste):	6.6
	In 0.01M $CaCl_2$ (1:1):	6.1
	In 1N KCl (1:1):	5.9
Organic carbon (%)		1.4
Organic matter (%)[1]		2.4
CEC (meq/100g)		9.1
Moisture (%)	At 1/10 bar:	13.3
	At 1/3 bar:	10.4
Maximum water holding capacity (MWHC, %)		45.5
Bulk density, disturbed (g/cm^3)		1.26
Microbial biomass (mg C_{bio}/kg soil)[2]		367
Soil taxonomic classification (USDA)		Sandy, mixed, mesic, typic Cambudolls.
Sol mapping unit		Not reported.

1 As presented in the study report, organic matter (%) = organic carbon (%) x 1.724.
2 At study initiation.
Data obtained from Table 1, p. 49 of the study report.

B. EXPERIMENTAL CONDITIONS:

1. Preliminary experiments: No preliminary experiments were reported.

2. Experimental conditions:

Table 3: Experimental design.

Parameter			Both labels
Duration of the test			120 days.
Soil condition: (Air dried/fresh)			Fresh. The test systems were prepared and acclimatized to study conditions for 4 days prior to treatment.
Soil (g/replicate)			91.21 g wet wt. (80 g dry wt.).
Application rates (mg a.i./kg & equiv. kg a.i./ha)		Nominal	0.13 mg a.i./kg (equivalent to 0.05 kg a.i./ha).[1]
		Actual	0.133 mg a.i./kg for [phenyl-U-^{14}C]-label. 0.122 mg a.i./kg for [pyrazole-3-^{14}C]-label.
Control conditions, if used			Sterile controls were not prepared.
No. of Replications	Controls, if used		Sterile controls were not prepared.
	Treatment		A sufficient number of treated nonsterile soil samples were prepared to allow for duplicate replicates per label at each sampling interval.
Test apparatus	Type/material/volume		300-mL Erlenmeyer flask fitted with an air-permeable, solid-phase, volatiles trap.
	Details of traps for CO_2 and organic volatiles, if any		Polyurethane foam (PUF) plug to trap organic volatiles. Soda lime pellets to trap CO_2 (one 10-g layer for volatilized $^{14}CO_2$, one 4-g layer for atmospheric CO_2). The soda lime pellets contained a carbon dioxide indicator dye to prevent CO_2 saturation. Glass wool (*ca.* 0.2-0.3 g) separated the soda lime layers and PUF plug.
If no traps were used, is the system closed/open?			Volatiles traps were used.
Identity and concentration of co-solvent			Methanol; final concentration 0.19% based on soil weight [1.0 mL of water:methanol (85:15, v:v) test solution in 80 g dry wt. soil].
Test material	Volume of the test solution used/treatment:		1,000 µL
	Application method (eg: mixed/not mixed):		Applied dropwise to soil surface using a microliter pipette, after which soil flask was gently shaken to incorporate test material.
	Is the co-solvent evaporated?		Evaporation of solvent presumed to have occurred during test substance application and incorporation.
Any indication of the test material adsorbing to the walls of the test apparatus?			Not indicated.
Microbial biomass of controls (units)			Sterile controls were not prepared.
Microbial biomass of treated (units)			Treated soil samples were not analyzed for biomass.

Parameter		Both labels
Experimental conditions:	Temperature (°C):	20°C; maintained in a temperature-controlled incubation chamber.
	Continuous darkness (Yes/No):	Yes.
	Moisture content:	50% of maximum water holding capacity; 22.8% soil moisture.
	Moisture maintenance method:	Gravimetric; initial weight of each soil flask maintained with addition of deionized water as needed.
Other details, if any		None.

1 The test application rates of were based on a proposed maximum single seasonal use rate of 50 g a.i./ Assuming a soil incorporation depth of 2.5 cm and bulk density of 1.5 g/cm^3, the 0.12-0.13 mg a.i./kg used in this study was equivalent to the proposed field rate of 50 g a.i./acre (pp. 20-21).
Data obtained from pp. 20-21, 25-29; Table 2, p. 50; Figure 8, p. 64 of the study report.

3. Aerobic conditions: Soil samples were incubated under static conditions in a flask fitted with an air-permeable, solid-phase (polyurethane foam plug, soda lime, glass wool) volatiles trap that allowed for the passive exchange of air (pp. 26, 29). No determinations, such as redox potentials, were made to verify that aerobic conditions were maintained.

4. Supplementary experiments: Microbial biomass in untreated soil. Two additional nonsterile, untreated soil samples were incubated under the same conditions as the treated samples to be used for biomass determinations, with one of the samples treated with the test solution solvent [1,000 µL, water:methanol (85:15, v:v); pp. 25, 27; Table 3, p. 51]. The untreated soil samples were taken for analysis at day 120 of the definitive study.

5. Sampling:

Table 4: Sampling details.

Criteria	Both labels
Sampling intervals (posttreatment)	0, 1, 3, 7, 14, 21, 29, 41, 62, 86 and 120 days.
Sampling method	Duplicate treated samples per label at each interval.
Method of collection of CO_2 and organic volatile compounds	Volatiles traps were collected at each sampling interval.
Sampling intervals/times for:	
Sterility check, if sterile controls are used:	Sterile controls were not prepared.
Moisture content:	Soil moisture adjusted with the addition of 750-1,000 µL of deionized water at 49 and 86 days posttreatment.
Redox potential, other:	None determined.

Criteria	Both labels
Sample storage before analysis	**Soil samples** were extracted the day of collection. **Soil extracts** were analyzed by HPLC by 1-8 days after sample collection. Extracts were stored frozen when not in use. **Extracted soil** (air-dried, milled) was stored frozen until combustion analysis, which was reported as typically occurring within a few weeks after extraction. **Volatiles traps** were stored refrigerated until analysis, which was reported as typically occurring within a few weeks after collection.
Other details, if any	None reported.

Data obtained from pp. 29-31; Table 3, p. 51; Appendices 11-12, pp. 99-101 of the study report.

C. ANALYTICAL METHODS:

Extraction/clean up/concentration methods: Diatomaceous earth (9 g, Bulk Isolute HM-N sorbent) was added to the soil sample, which was then mixed and transferred to a 100-mL extraction cell of an Accelerated Solvent Extraction (ASE) system (Model ASE 300, Dionex; pp. 30-31; Figure 9, p. 65). The test flask was rinsed with acetonitrile (5 mL) and the rinsate added to the soil mixture. Two-phase ("mild" and "aggravated" conditions), automated, multi-step extractions were conducted using acetonitrile:water (4:1, v:v) as the extraction solvent. For "mild" conditions, the soil was extracted over six cycles at 40°C, 103.4 bar cell pressure and 5 min./cycle time, with a final extract pool volume of *ca.* 300 mL. For the subsequent "aggravated" conditions, the extracted soil was further extracted over two cycles at 100°C, *ca.* 103.4 bar cell pressure and 15 min./cycle time, with a final extract pool volume of *ca.* 130 mL. Aliquots (2-3 replicates, volume not specified) of individual extracts were analyzed for total radioactivity using LSC, then respective "mild" extracts and "aggravated" extracts were combined (pp. 31-32).

Prior to HPLC analysis, a sub-sample (20 mL) of each pooled extract was concentrated under a nitrogen stream at 45°C to dryness, with the resulting residues reconstituted in 2 mL of water:acetonitrile (80:20, v:v) via sonication. Aliquots (20 or 50 µL) were analyzed for total radioactivity by LSC; recoveries of sample radioactivity following concentration averaged (both labels/extracts) 99.8 ± 3.2% (DER Attachment 2). The study author reported that comparative TLC analysis of soil extracts prior to and after concentration showed that pyrasulfotole and transformation products remained stable with no artifact formation (p. 31); however, supporting chromatograms were not provided.

Total ^{14}C measurement: Total ^{14}C residues were determined by summing the concentrations of residues measured in the soil extracts, extracted soil and volatile trapping materials (p. 37).

Determination of nonextractable residues: Extracted soil was air-dried, then homogenized to a powder using a soil mill (Retsch; p. 31; Appendix 1, p. 89). Triplicate aliquots (*ca.* 1 g) were analyzed for total radioactivity by LSC following combustion (p. 32).

Organic matter fractionation. Aliquots (25 g) of 86-day extracted soil (both labels) were further extracted for 24 hours via magnetic stirrer with 0.5M sodium hydroxide (NaOH, 50 mL), with the resulting extract separated from soil by centrifugation (speed, interval not reported; p. 31; Figure 30, p. 86). The supernatant was decanted, then the remaining pellet was washed with 0.5M NaOH (20 mL); wash and soil were separated via centrifugation. NaOH supernatants were combined, acidified to pH 1 with 5M hydrochloric acid (conc. HCl), stored overnight at *ca.* 4-4°C, then the resulting precipitate (humic acids) was removed by centrifugation. The supernatant was decanted and the remaining precipitate washed with 5M HCl (10 mL); wash and precipitate were separated via centrifugation. HCl supernatants (fulvic acids) were combined and analyzed for total radioactivity using LSC. The remaining precipitate (humic acids) was dissolved in 0.5M NaOH and analyzed using LSC. [^{14}C]Residues remaining in the extracted soil (humin) were analyzed by LSC following combustion.

Determination of volatile residues: The polyurethane foam plug was extracted with ethyl acetate (50 mL, p. 33). An aliquot (7 mL) of the extract was combined (1:1, v:v) with Quicksafe scintillation cocktail:water (95:5, v:v) and analyzed for total radioactivity by LSC (p. 35).

To recover radioactivity (presumably, $^{14}CO_2$) from the soda lime, 18% (w:w) HCl (6 mL per g soda lime) was applied dropwise to the soda lime with agitation via magnetic stirrer (p. 32; Figure 31, p. 87; Appendix 7, p. 95). Released $^{14}CO_2$ was purged (nitrogen, flow rate not specified) through ice-cooled Carbosorb/Permafluor E$^+$ scintillation cocktail and quantified by LSC.

To confirm the presence of $^{14}CO_2$, the Carbosorb/Permafluor E$^+$ cocktail containing radioactivity from the 86-day soda lime samples was treated with 1M sodium carbonate (100 µL), then glacial acetic acid (110 mL) was applied dropwise as described above (p. 36; Appendix 7, p. 95). Released radioactivity was then purged through 5M NaOH trapping solution, with aliquots subsequently analyzed for total radioactivity by LSC. An aliquot (15 mL) of the NaOH solution was combined with 1M aqueous sodium carbonate (2 mL) and 1M aqueous barium chloride (8 mL). The test solution was mixed via magnetic stirrer for 15 minutes, allowed to stand at room temperature for 15 minutes, then centrifuged to remove the resulting precipitate. Aliquots of the supernatant were analyzed for total radioactivity by LSC.

Derivatization method, if used: None was reported.

Identification and quantification of parent compound: Concentrated extract samples were analyzed by reverse-phase HPLC under the following conditions: Merck Purospher Star RP18-e (4.6 x 250 mm, 5 µm) column, gradient mobile phase combining (A) 1% aqueous formic acid and (B) 1% formic acid in acetonitrile [percent A:B at 0-5 min. 100:0 (v:v), 25 min. 70:30, 35

min. 60:40, 55-65 min. 0:100, 67-75 min. 100:0], injection volume 1.0 mL, flow rate 1.0 mL/minute, UV detector (275 nm), and Ramona Star radioactivity detector equipped with a 370-µL glass solid-phase flow cell (p. 33; Appendix 1, p. 89). Column recoveries of selected chromatogram runs were monitored through the collection and LSC analysis of bulk column eluates, with the average ("n" not specified) recovery reported as 97% (both labels, p. 34); individual column recoveries were not provided.

Parent [^{14}C]pyrasulfotole was identified by co-chromatography with and comparison to the retention time of unlabeled reference standard (pp. 34-35, Figure 10, p. 66; Figures 14-19, pp. 70-75).

To confirm results from HPLC analyses, aliquots (50 µL) of selected extracts were analyzed using one-dimensional TLC on normal-phase plates (silica gel 60 F_{254}, Merck) developed with toluene:ethanol:25% aqueous ammonia (6:5:1, v:v:v; p. 34). Following development, areas of radioactivity were detected using a phosphorimaging system (BAS-2000; Appendix 1, p. 89). Parent [^{14}C]pyrasulfotole was identified by co-chromatography with unlabeled reference standard which was visualized under UV light (254 nm; Figures 20-22, pp. 76-78).

Identification and quantification of transformation products: Transformation products were separated, quantified and identified using HPLC and TLC as described for the parent compound (pp. 33-35, 43; Figure 10, p. 66; Figures 14-22, pp. 70-78).

Identification of transformation product AE B197555 (AE 0317309-benzoic acid) was confirmed in 14-day [phenyl-^{14}C]-label soil extract by LC/MS/MS under the following conditions: Nucleodur C18 Gravity (2 x 125 mm, 3 µm) LC column, gradient mobile phase combining (A) 0.1% aqueous formic acid and (B) 0.1% formic acid in acetonitrile [percent A:B at 0-1 min. 95:5 (v:v), 25-35 min. 5:95], flow rate 0.2 mL/minute, split ratio 35:165, Thermo Finnigan LTQ or TSQ Quantum Ultra AM MS, electrospray ionization (ESI) in positive and negative modes, full-scan m/z range 50-1100, UV detector (wavelength not specified), and radioactivity detector as described above (p. 35; Appendix 1, p. 89). Identification of [^{14}C]AE B197555 in the sample extract was made against reference standard (pp. 35, 43-44; Figure 7, p. 63; Figure 23, p. 79).

Table 5: Reference compounds available for identifying transformation products of pyrasulfotole (AE 0317309).

Applicant codes	**Chemical Name**		**Purity**[1]
AE B197555, RPA 203328, AE 0317309-benzoic acid	IUPAC:	2-Methylsulfonyl-4-trifluoromethylbenzoic acid	99.6%
	CAS:	Benzoic acid, 2-methylsulfonyl-4-(trifluoromethyl)- *(9Cl)*	

1 Purity w/w unless otherwise designated.
Data obtained from p. 24; Figure 1, p. 58 of the study report.

Detection limits (LOD, LOQ) for the parent compound and transformation products: For both labels, LOQs (limit of quantitation) for HPLC and TLC analyses were reported as ≤0.5% and ≤0.6% of the applied, respectively (p. 39; Appendices 9-10, pp. 97-98). For LSC analyses (both labels), LOQs were reported as ≤0.4% of the applied for soil extracts, <0.1% for soil combustions and <0.01% for volatiles solutions (pp. 38-39).

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS: During the 120-day study, incubation temperatures averaged 19.8 ± <1°C and soil moisture averaged 50.3 ± 1.6 % of MWHC (p. 40; Appendix 6, p. 94; DER Attachment 2). No supporting records were provided to establish that aerobicity was maintained throughout the study.

B. MATERIAL BALANCE: Overall recovery (both labels) of radiolabeled material averaged 100.5 ± 2.7% (range 93.9-104.9%, n = 44) of the applied, with no consistent pattern of decline in recoveries for either label (DER Attachment 2, Reviewer's Comment No. 1). For each label, recoveries averaged (n = 22) 101.4 ± 2.2% (range 96.9-104.3%) of the applied in [phenyl-^{14}C]-label treated soil and 99.6 ± 2.8% (range 93.9-104.9%) in [pyrazole-3-^{14}C]-label treated soil.

Table 6. Biotransformation of [phenyl-U-^{14}C]pyrasulfotole (AE 0317309), expressed as percentage of applied radioactivity (n = 1), in German sandy loam soil under aerobic conditions.[1]

Compound	Sampling times (days)										
	0	1	3	7	14	21	29	41	62	86	120
Pyrasulfotole	100.0 ± 0.4	94.0 ± 2.5	84.9 ± 0.8	78.8 ± 1.0	62.9 ± 0.6	57.3 ± 2.4	48.0 ± 2.0	36.9 ± 3.6	29.0 ± 1.3	22.1 ± 1.1	19.0 ± 0.3
AE B197555[2]	1.4 ± 0.0	1.7 ± 0.1	3.3 ± 0.3	5.7 ± 0.1	8.9 ± 0.4	8.8 ± 0.7	8.1 ± 0.4	5.7 ± 0.7	3.4 ± 0.1	3.5 ± 0.1	2.3 ± 0.0
Unidentified [^{14}C][3]	n.d.[4]	n.d.	n.d.	0.5 ± 0.2	1.0 ± 0.1	1.0 ± 0.1	0.8 ± 0.0	n.d., 1.0	1.1, n.d.	1.1 ± 0.2	2.1 ± 0.1
Extractable residues	101.4 ± 0.4	95.6 ± 2.5	88.2 ± 1.0	85.0 ± 0.9	72.7 ± 1.1	67.1 ± 3.0	56.9 ± 2.4	43.0 ± 3.7	33.0 ± 0.7	26.8 ± 1.4	23.3 ± 0.2
Nonextractable residues	2.1 ± 0.6	6.5 ± 0.8	15.1 ± 1.4	16.1 ± 0.7	29.2 ± 1.1	32.7 ± 2.0	42.6 ± 2.1	52.6 ± 4.1	55.0 ± 1.1	57.0 ± 1.3	60.1 ± 1.4
CO_2	---	<0.1	<0.1	0.2 ± 0.0	0.9 ± 0.0	2.3 ± 0.0	3.4[5]	7.0[5]	10.4 ± 0.0	13.4 ± 0.2	16.3 ± 0.0
Volatile organics	---	<0.1, 0.1	<0.1, 0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1	<0.1
Total recovery	103.4 ± 1.0	102.2 ± 1.8	103.3 ± 0.4	101.3 ± 1.6	102.8 ± 0.1	102.0 ± 1.0	102.9 ± 0.3	102.6 ± 0.4	98.3 ± 0.4	97.0 ± 0.1	99.7 ± 1.2

1 Reviewer's Comment No. 1.
2 2-Methylsulfonyl-4-trifluoromethylbenzoic acid (AE 0317309-benzoic acid; Figure 2, p. 58).
3 Summation of up to three minor HPLC components, each ≤1.2% of the applied (Table 6, p. 54).
4 Not detected.
5 Single result of replicate (2); soda lime of replicate (1) not analyzed due to leak in volatiles trap (Table 4, p. 52). Replicate (1) material balance includes volatilized $^{14}CO_2$ from replicate (2).
Data obtained from Table 4, p. 52; Table 6, p. 54; Figure 2, p. 58 of the study report and DER Attachment 2.

Table 7. Biotransformation of [pyrazole-3-^{14}C]pyrasulfotole (AE 0317309), expressed as percentage of applied radioactivity (n = 1), in German sandy loam soil under aerobic conditions.[1]

Compound	Sampling times (days)										
	0	**1**	**3**	**7**	**14**	**21**	**29**	**41**	**62**	**86**	**120**
Pyrasulfotole	98.4 ± 0.6	89.7 ± 3.0	85.7 ± 0.6	75.8 ± 1.3	60.8 ± 0.5	48.9 ± 0.1	40.5 ± 1.0	33.9 ± 0.1	26.0 ± 1.2	22.1 ± 0.2	17.3 ± 1.5
Unidentified [^{14}C][2]	0.4, n.d.[3]	0.4 ± 0.1	0.4 ± 0.0	0.5 ± 0.1	0.7 ± 0.5	1.7 ± 0.2	1.6 ± 0.2	2.6 ± 0.2	1.4 ± 0.1	1.6 ± 0.2	1.8 ± 0.4
Extractable residues	98.6 ± 0.3	90.0 ± 3.0	86.1 ± 0.6	76.2 ± 1.3	61.5 ± 1.0	50.6 ± 0.1	42.0 ± 0.9	36.5 ± 0.3	27.3 ± 1.1	23.6 ± 0.0	19.0 ± 1.8
Nonextractable residues	2.7 ± 0.7	9.7 ± 2.0	14.8 ± 1.3	22.3 ± 1.4	35.2 ± 0.9	44.8 ± 0.3	52.9 ± 1.1	56.4 ± 0.3	56.9 ± 0.8	55.9 ± 0.2	62.1 ± 1.8
CO_2	---	0.1 ± 0.0	0.4 ± 0.1	1.1 ± 0.0	2.7 ± 0.0	4.8 ± 0.0	6.7 ± 0.1	9.5 ± 0.0	12.2 ± 0.2	14.8 ± 0.3	18.0 ± 0.0
Volatile organics	---	<0.1	<0.1	<0.1	<0.1	<0.1, 0.1	<0.1	<0.1	<0.1	0.1, <0.1	<0.1
Total recovery	101.3 ± 0.4	99.9 ± 5.1	101.3 ± 0.8	99.7 ± 0.0	99.4 ± 0.1	100.1 ± 0.4	101.6 ± 0.0	102.5 ± 0.1	96.4 ± 2.1	94.3 ± 0.4	99.1 ± 0.0

1 Reviewer's Comment No. 1.
2 Summation of up to five minor HPLC components, each <1% of the applied (Table 7, p. 55).
3 Not detected.
Data obtained from Table 5, p. 53; Table 7, p. 55 of the study report and DER Attachment 2.

Data Evaluation Report on the aerobic biotransformation of pyrasulfotole (AE 0317309) in soil

PMRA Submission Number 2006-2445 EPA MRID Number 46801711

C. TRANSFORMATION OF PARENT COMPOUND: In [phenyl-U-^{14}C]-pyrasulfotole treated soil, pyrasulfotole decreased from 99.6-100.4% of the applied at day 0 to 45.9-50.0% at 29 days, 27.7-30.3% at 62 days and was 18.6-19.3% at 120 days (DER Attachment 2).

In [pyrazole-3-^{14}C]-pyrasulfotole treated soil, pyrasulfotole decreased from 97.8-99.0% of the applied at day 0 to 48.8-49.0% at 21 days, 24.8-27.1% at 62 days and was 15.8-18.8% at 120 days (DER Attachment 2).

HALF-LIFE/DT50/DT90: Observed DT50 values of [phenyl-U-^{14}C]- and [pyrazole-3-^{14}C]-labeled pyrasulfotole were 21-29 days and 14-21 days, respectively (DER Attachment 2). Based on first order regression analysis (all sampling intervals), reviewer-calculated linear (Excel 2000) half-lives were 47-48 days and nonlinear (SigmaPlot v 8) half-lives were 30-35 days (DER Attachment 2). Reviewer-calculated DT50 and DT90 estimates were 23 and 208 days, respectively (2 compartment non-linear model, SigmaPlot v. 8; $r^2 = 0.990$).

Also using first order regression nonlinear (Model Manager v 1.1) analysis (individual sample data), the study author similarly determined half-lives for [phenyl-U-^{14}C]- and [pyrazole-3-^{14}C]-labeled pyrasulfotole of 34 days ($r^2 = 0.959$) and 30 days ($r^2 = 0.949$), respectively (p. 44; Figures 26-27, pp. 82-83). Using the mean [phenyl-U-^{14}C]- and [pyrazole-3-^{14}C]-pyrasulfotole at each interval, the study author determined a half-life of 32 days ($r^2 = 0.953$; p. 44; Figure 28, p. 84).

Half-lives/DT50/DT90

Compound	Half-life [1] (days)	Regression equation	r^2	DT50 (days)	DT90 (days)
[Phenyl-U-^{14}C]-pyrasulfotole					
Linear/natural log	48.1	y = -0.0144x + 4.4136	0.9266	--	--
Nonlinear/normal	34.5	Y = 92.3*exp(-0.0201*x)	0.959	-	-
Nonlinear/normal		y = 55.5287*exp(-0.0512*x)+41.2865*exp(-0.007*x)	0.992	25	203
Observed DT50/90		--	--	21-29	>120
[Pyrazole-3-^{14}C]-pyrasulfotole					
Linear/natural log	47.1	y = -0.0147x + 4.3571	0.9060	--	--
Nonlinear/normal	30.3	Y = 90.6*exp(-0.0229*x)	0.9492	-	-
Nonlinear/normal		y = 63.5371*exp(-0.0557*x)+34.7417*exp(-0.0055*x)	0.996	22	226
Observed DT50/90		--	--	*ca.* 21	>120
Both labels					
Linear/natural log	47.6	y = -0.01456 + 4.3854	0.9127	--	--
Nonlinear/normal	32.4	Y = 91.4*exp(-0.0214*x)	0.9503	-	-
Nonlinear/normal		y = 58.5412*exp(-0.0538*x)+37.7457*exp(-0.0064*x)	0.990	23	208
Observed DT50/90	14-29	--	--	14-29	>120

1 Determined by the primary reviewer using Excel 2000 (linear) and Sigmaplot v 8.0 (nonlinear) and individual sample data obtained from Appendices 4-5, pp. 92-93 of the study report (DER Attachment 2).

TRANSFORMATION PRODUCTS: No major nonvolatile transformation products were detected for either label. One minor product, 2-methylsulfonyl-4-trifluoromethylbenzoic acid (AE B197555, AE 0317309-benzoic acid), was identified in [phenyl-U-^{14}C]-label treated soil via HPLC, TLC and LC/MS/MS (pp. 43-44; Figure 7, p. 63; Figures 19-20, pp. 75-76; Figure 23, p. 79).

In [phenyl-U-^{14}C]-pyrasulfotole treated soil, AE B197555 was detected at a maximum 9.5% of the applied at 21 days and was 2.2-2.3% at 120 days (Table 6, p. 54; DER Attachment 2). Unidentified [^{14}C]residues, consisting of up to three components, were detected at a maximum total 2.2% at study termination.

In [pyrazole-3-^{14}C]-pyrasulfotole treated soil, unidentified [^{14}C]residues, consisting of up to five components, were detected at a maximum total 2.8% at 41 days and were 1.4-2.1% at study termination (Table 7, p. 55; DER Attachment 2).

NONEXTRACTABLE AND EXTRACTABLE RESIDUES: In [phenyl-U-^{14}C]-pyrasulfotole treated soil, extractable [^{14}C]residues decreased from 101.0-101.7% of the applied at day 0 to 54.5-59.3% at 29 days and were 23.1-23.5% at 120 days (DER Attachment 2). Nonextractable [^{14}C]residues increased from 1.5-2.6% at day 0 to 48.5-56.7% at 41 days and were 58.7-61.5% at 120 days. Organic matter fractionation of 86-day extracted soil found 14.2-15.2%, 26.8-27.8% and 11.4-11.8% of the applied associated with the humin, fulvic acids and humic acids, respectively (Table 8, p. 56).

In [pyrazole-3-^{14}C]-pyrasulfotole treated soil, extractable [^{14}C]residues decreased from 98.2-98.9% at day 0 to 50.5-50.6% at 21 days and were 23.6% at 86 days and were 17.1-20.8% at 120 days (DER Attachment 2). Nonextractable [^{14}C]residues increased from 2.0-3.4% at day 0 to 51.8-53.9% at 29 days and were 60.3-63.9% at 120 days. Organic matter fractionation of 86-day extracted soil found 17.7-17.8%, 22.0-22.3% and 14.4-16.0% of the applied associated with the humin, fulvic acids and humic acids, respectively (Table 8, p. 56).

VOLATILIZATION: At study termination (120 days), volatilized $^{14}CO_2$ comprised 16.2-16.3% and 18.0% of the applied for the [phenyl-U-^{14}C]- and [pyrazole-3-^{14}C]-label treated soils, respectively, while volatile [^{14}C]organic compounds were ≤0.1% (both labels) at all sampling intervals (Tables 4-5, pp. 52-53). Barium chloride precipitation confirmed the presence of $^{14}CO_2$ in 86-day volatiles trap samples (both labels, ≥99.5% of sample radioactivity; p. 36).

TRANSFORMATION PATHWAY: The study author provided a transformation pathway that was consistent with the products detected in this study (p. 45; Figure 29, p. 85). Transformation of pyrasulfotole involves hydrolytic cleavage of the phenyl and pyrazole moieties to yield the benzoic acid derivative, 2-methylsulfonyl-4-trifluoromethylbenzoic acid (AE B197555), plus several unidentified minor compounds, with steady formation of bound soil residues and moderate levels of mineralization to CO_2.

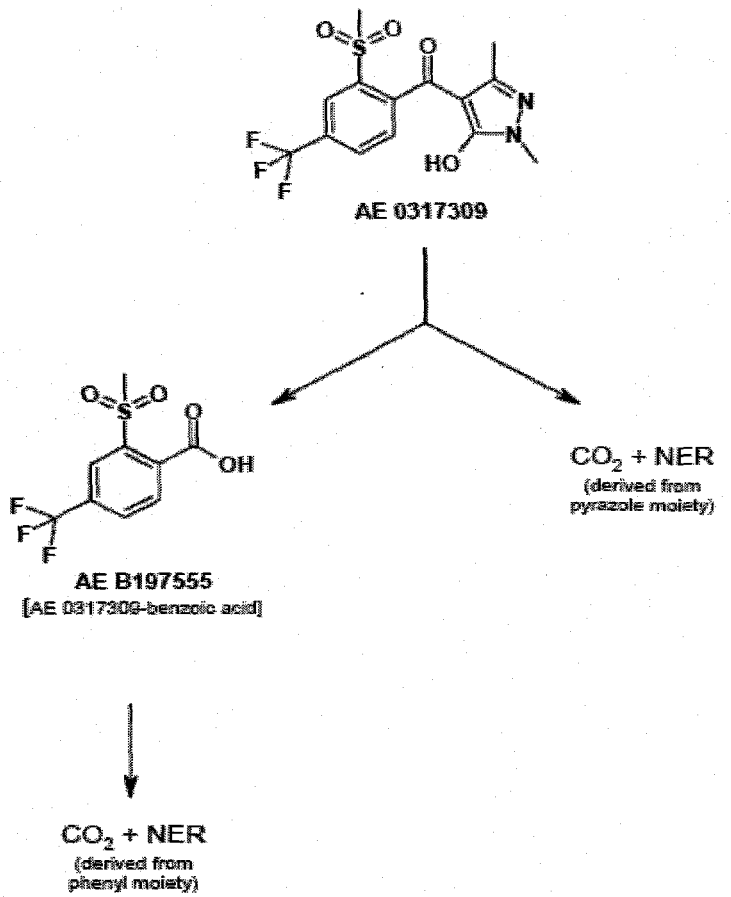


Table 8: Chemical names and CAS numbers for the transformation products of pyrasulfotole.[1]

Applicants Code Name	CAS Number	Chemical Name		Chemical Formula	MW (g/mol)	Smiles String
AE B197555[2], RPA 203328	142994-06-07	IUPAC:	2-Methylsulfonyl-4-trifluoromethylbenzoic acid	$C_9H_7F_3O_4S$	268.2	CS(=O)(=O)c1cc(C(F)(F)F)ccc1C(=O)O
		CAS:	Benzoic acid, 2-(methylsulfonyl)-4-(trifluoromethyl)			

1 Identification confirmed using LC/MS/MS against reference standard (p. 44; Figure 7, p. 63; Figure 23, p. 79).
2 Also referred to as AE 0317309-benzoic acid.
Data obtained from Figure 2, p. 58 of the study report.

D. SUPPLEMENTARY EXPERIMENT-RESULTS: Microbial biomass in untreated soil.
The presence of the water:methanol (85:15, v:v) test solution solvent had no effect on soil

microbial biomass. Microbial biomass was 367 mgC/kg soil in untreated soil at study initiation and was 213 and 202 mgC/kg soil in untreated and test solution solvent treated soil, respectively, at study termination (Table 1, p. 49).

Storage stability. HPLC re-analysis found no significant quantitative differences in the chromatographic profile 14-day soil extracts after 92 days of frozen storage (p. 45; Appendix 8, p. 96).

III. STUDY DEFICIENCIES

No significant deviations from good scientific practices were noted. It was not established that the German soil used in this study was comparable to soils that would be found at intended use sites in the United States. A FAO soil classification was not provided to allow for adequate comparison. Aerobic metabolism studies using soils from the US (North Dakota and North Carolina) were submitted in this data package as MRIDs 46801709 and 46801710.

IV. REVIEWERS' COMMENTS

1. The approach used by the study author underestimate the persistence shown in this study, with up to 19% of the parent still being present at 120 days, having declined very slowly from 29 days after treatment, where 48% was present. Therefore, the reviewers disagree with the study author's interpretation that the parent active ingredient AE 0317309 is not persistent in the tested soil environment.

2. The reviewers agree with the study author's conclusion that transformation products are not persistent in the tested soil environment and that major terminal sinks for pyrasulfotole were AE B197555 (a maximum of 2.3% AR), CO_2 (maximum of 18.0% AR), and non-extractable residues (maximum of 62.1% AR), but adds to the conclusion that residues of pyrasulfotole were found up to 120 days (maximum of 18.9% AR).

3. Mean results and standard deviations presented in this review were determined by the primary reviewer using Microsoft Excel 2000 (9.0.2720) software (DER Attachment 2). Standard deviations were determined using the "biased" or "n" method which determines the standard deviation of the entire sample population. Mean results, standard deviations and summations reported by the study author (Tables 4-7, pp. 52-55) were verified by the primary reviewer and there was consistent agreement (within ± 0.1% of applied) between the study author's reported values and those determined by the primary reviewer (DER Attachment 2).

4. The test application rates of 0.12-0.13 mg a.i./kg used in this study were based on a proposed maximum single seasonal use rate of 50 g a.i./ha (pp. 20-21). Assuming a soil incorporation

depth of 2.5 cm and bulk density of 1.5 g/cm3, the 50 g a.i./acre field rate converts to a test application rate of 0.13 mg a.i./kg.

5. Observed DT50 values for total residues.

Test substance	Parent +nonvolatile [^{14}C]products[1]	Total [^{14}C]residues[2]
[Phenyl-U-^{14}C]-pyrasulfotole	29-41 days	>120 days
[Pyrazole-3-^{14}C]-pyrasulfotole	*ca.* 21 days	>120 days

1 Parent pyrasulfotole plus identified/unidentified [14C]transformation products.
2 All [^{14}C]residues other than volatilized $^{14}CO_2$.
Data obtained from DER Attachment 2.

6. This study was conducted at N51° latitude and on a sandy loam agricultural soil at 20°C. The study conditions are therefore considered comparable to Canadian use conditions and the results will be considered applicable for Canadian registration.

V. REFERENCES

1. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate, Section 162-1, Aerobic Soil Metabolism Studies. Office of Pesticide and Toxic Substances, Washington, DC. EPA 540/9-82-021.

2. U.S. Environmental Protection Agency. 1989. FIFRA Accelerated Reregistration, Phase 3 Technical Guidance. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 540/09-90-078.

3. U.S. Environmental Protection Agency. 1993. Pesticide Registration Rejection Rate Analysis - Environmental Fate. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 738-R-93-010.

Attachment 1: Structures of Parent Compound and Transformation Products

Pyrasulfotole [AE 0317309; K-1196; K-1267]

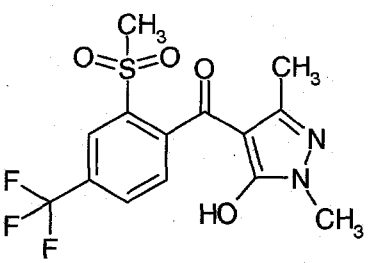
IUPAC Name: (5-Hydroxy-1,3-dimethylpyrazol-4-yl)(α,α,α-trifluoro-2-mesyl-*p*-tolyl)methanone.
(5-Hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)(2-mesyl-4-trifluoromethylphenyl)methanone.

CAS Name: (5-Hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)[2-methylsulfonyl)-4(trifluoromethyl)phenyl]methanone.
Methanone, (5-hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl].

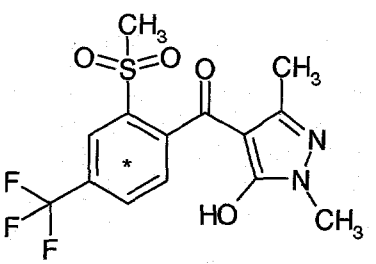
CAS Number: 365400-11-9.

SMILES String: FC(c1cc(c(cc1)C(=O)c1c(n(nc1C)C)O)S(=O)(=O)C)(F)F (ISIS v2.3/Universal SMILES).
No EPI Suite, v3.12 SMILES String found as of 6/7/06.
Cc1nn(C)c(O)c1C(=O)c2ccc(C(F)(F)F)cc2S(C)(=O)=O.
CS(=O)(=O)c1c(ccc(c1)C(F)(F)F)C(=O)c1c(n(nc1C)C)O.

Unlabeled



[Phenyl-U-^{14}C]pyrasulfotole



^{14}C = Position of radiolabel.

Pyrasulfotole [AE 0317309; K-1196; K-1267]

IUPAC Name: (5-Hydroxy-1,3-dimethylpyrazol-4-yl)(α,α,α-trifluoro-2-mesyl-*p*-tolyl)methanone.
(5-Hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)(2-mesyl-4-trifluoromethylphenyl)methanone.

CAS Name: (5-Hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)[2-methylsulfonyl)-4(trifluoromethyl)phenyl]methanone.
Methanone, (5-hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl].

CAS Number: 365400-11-9.

SMILES String: FC(c1cc(c(cc1)C(=O)c1c(n(nc1C)C)O)S(=O)(=O)C)(F)F (ISIS v2.3/Universal SMILES).
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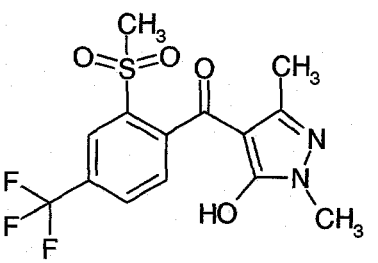
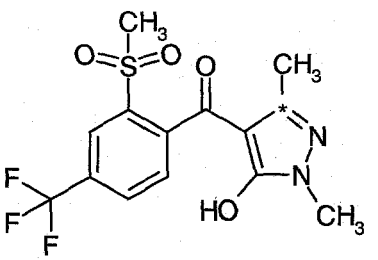
Cc1nn(C)c(O)c1C(=O)c2ccc(C(F)(F)F)cc2S(C)(=O)=O.
CS(=O)(=O)c1c(ccc(c1)C(F)(F)F)C(=O)c1c(n(nc1C)C)O.

Unlabeled



[Pyrazole-3-^{14}C]pyrasulfotole

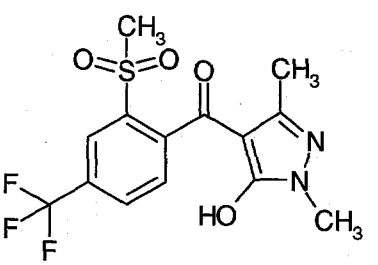


^{14}C = Position of radiolabel.

Identified Compounds

Pyrasulfotole [AE 0317309; K-1196; K-1267]

IUPAC Name:	(5-Hydroxy-1,3-dimethylpyrazol-4-yl)(α,α,α-trifluoro-2-mesyl-*p*-tolyl)methanone. (5-Hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)(2-mesyl-4-trifluoromethylphenyl)methanone.
CAS Name:	(5-Hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)[2-methylsulfonyl)-4(trifluoromethyl)phenyl]methanone. Methanone, (5-hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)[2-(methylsulfonyl)-4-(trifluoromethyl)phenyl].
CAS Number:	365400-11-9.
SMILES String:	FC(c1cc(c(cc1)C(=O)c1c(n(nc1C)C)O)S(=O)(=O)C)(F)F (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found as of 6/7/06. Cc1nn(C)c(O)c1C(=O)c2ccc(C(F)(F)F)cc2S(C)(=O)=O. CS(=O)(=O)c1c(ccc(c1)C(F)(F)F)C(=O)c1c(n(nc1C)C)O.



RPA 203328 [AE B197555-benzoic acid; AE B197555; K-1198; K-1367]

IUPAC Name: 2-Mesyl-4-trifluoromethylbenzoic acid.
CAS Name: Benzoic acid, 2-(methylsulfonyl)-4-(trifluoromethyl)-.
CAS Number: 142994-06-7.
SMILES String: O=C(c1ccc(cc1S(=O)(=O)C)C(F)(F)F)O (ISIS v2.3/Universal SMILES).
No EPI Suite, v3.12 SMILES String found as of 6/7/06.
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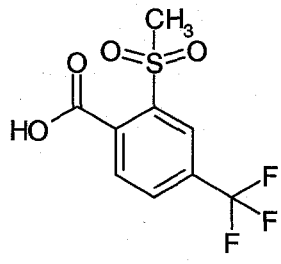
CS(=O)(=O)c1cc(ccc1C(=O)O)C(F)(F)F.



Carbon Dioxide

IUPAC Name: Not reported.
CAS Name: Not reported.
CAS Number: Not reported.

O=C=O

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Nonlinear half-lives (exponential decay/single, 2 parameter)

German sandy loam

[Phenyl-U-^{14}C]-label

Half-life (days)	34.5
R squared	0.9590

[Pyrazole-3-^{14}C]-label

Half-life (days)	30.3
R squared	0.9492

Both labels

Half-life (days)	32.4
R squared	0.9503

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Aerobic metabolism of [^{14}C]pyrasulfotole in a German sandy loam soil.
Confirmation of summations (material balances) and determination of means/standard deviations for applied radioactivity.
[Phenyl-U-^{14}C]-label

	Soil								CO_2			Volatile organics			Material Balance			Study Reported Material Balance		
	Mild	Aggrav	Total extractable			Nonextractable														
Day	% AR	% AR	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.
0	97.2	4.5	101.7			2.6									104.3			104.3		
	97.9	3.1	101.0	101.4	0.4	1.5	2.1	0.6							102.5	103.4	0.9	102.4	103.4	1.0
1	86.3	6.8	93.1			7.3									100.4			100.4		
	91.4	6.7	98.1	95.6	2.5	5.7	6.5	0.8		#DIV/0!	#DIV/0!	0.1	0.1	0.0	103.8	102.1	1.7	103.9	102.2	1.8
3	74.1	13.0	87.1			16.5									103.6			103.6		
	78.1	11.1	89.2	88.2	1.0	13.6	15.1	1.4		#DIV/0!	#DIV/0!	0.1	0.1	0.0	102.8	103.2	0.4	102.9	103.3	0.4
7	68.2	17.7	85.9			16.8			0.2						102.9			102.9		
	71.7	12.4	84.1	85.0	0.9	15.4	16.1	0.7	0.2	0.2	0.0		#DIV/0!	#DIV/0!	99.7	101.3	1.6	99.7	101.3	1.6
14	59.7	14.1	73.8			28.1			0.9						102.8			102.7		
	57.5	14.1	71.6	72.7	1.1	30.2	29.2	1.1	0.9	0.9	0.0		#DIV/0!	#DIV/0!	102.7	102.8	0.1	102.8	102.8	0.0
21	50.9	13.1	64.0			34.7			2.3						101.0			101.0		
	57.2	12.9	70.1	67.1	3.0	30.6	32.7	2.0	2.2	2.3	0.0		#DIV/0!	#DIV/0!	102.9	102.0	0.9	103.0	102.0	1.0
29	47.4	11.9	59.3			40.5			3.4						103.2			103.2		
	40.7	13.8	54.5	56.9	2.4	44.7	42.6	2.1	3.4	3.4	0.0		#DIV/0!	#DIV/0!	102.6	102.9	0.3	102.5	102.9	0.3
41	35.7	11.0	46.7			48.5			7.0						102.2			102.2		
	28.0	11.3	39.3	43.0	3.7	56.7	52.6	4.1	7.0	7.0	0.0		#DIV/0!	#DIV/0!	103.0	102.6	0.4	103.0	102.6	0.4
62	21.0	11.3	32.3			56.1			10.3						98.7			98.6		
	22.4	11.3	33.7	33.0	0.7	53.9	55.0	1.1	10.4	10.4	0.0		#DIV/0!	#DIV/0!	98.0	98.4	0.4	97.9	98.3	0.4
86	15.9	9.5	25.4			58.3			13.5						97.2			97.1		
	18.3	9.8	28.1	26.8	1.4	55.6	57.0	1.3	13.2	13.4	0.2		#DIV/0!	#DIV/0!	96.9	97.1	0.1	96.9	97.0	0.1
120	14.6	8.5	23.1			61.5			16.3						100.9			100.9		
	14.8	8.7	23.5	23.3	0.2	58.7	60.1	1.4	16.2	16.3	0.1		#DIV/0!	#DIV/0!	98.4	99.7	1.2	98.5	99.7	1.2
																101.4	2.2		101.4	2.2

Results from Table 4, p. 52 of the study report.
Means and standard deviations calculated using Microsoft program functions @average(A1:A2) and stdevp(A1:A2).

Both Phe + Pyr labels	
Mean	100.5
std. dev.	2.7
max =	104.9
min =	93.9
n =	44

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Aerobic metabolism of [^{14}C]pyrasulfotole in a German sandy loam soil.
Confirmation of summations (material balances) and determination of means/standard deviations for applied radioactivity.
[Pyrazole-3-^{14}C]-label

	Soil								CO_2			Volatile organics			Material Balance			Study Reported Material Balance		
	Mild	Aggrav	Total extractable			Nonextractable														
Day	% AR	% AR	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.
0	93.4	4.8	98.2			3.4									101.6			101.7		
	95.4	3.5	98.9	98.6	0.3	2.0	2.7	0.7							100.9	101.3	0.4	100.9	101.3	0.4
1	77.7	9.3	87.0			7.7			0.1						94.8			94.8		
	86.3	6.7	93.0	90.0	3.0	11.7	9.7	2.0	0.1	0.1	0.0		#DIV/0!	#DIV/0!	104.8	99.8	5.0	104.9	99.9	5.1
3	75.2	10.3	85.5			16.1			0.3						101.9			102.0		
	77.7	9.0	86.7	86.1	0.6	13.5	14.8	1.3	0.4	0.4	0.1		#DIV/0!	#DIV/0!	100.6	101.3	0.7	100.5	101.3	0.8
7	67.3	10.2	77.5			20.9			1.1						99.5			99.6		
	63.0	11.9	74.9	76.2	1.3	23.6	22.3	1.4	1.1	1.1	0.0		#DIV/0!	#DIV/0!	99.6	99.6	0.0	99.7	99.7	0.1
14	48.0	12.5	60.5			36.1			2.7						99.3			99.3		
	49.9	12.6	62.5	61.5	1.0	34.3	35.2	0.9	2.7	2.7	0.0		#DIV/0!	#DIV/0!	99.5	99.4	0.1	99.5	99.4	0.1
21	39.0	11.5	50.5			44.4			4.8						99.7			99.7		
	38.7	11.9	50.6	50.6	0.1	45.1	44.8	0.3	4.8	4.8	0.0		#DIV/0!	#DIV/0!	100.5	100.1	0.4	100.5	100.1	0.4
29	30.5	10.6	41.1			53.9			6.5						101.5			101.6		
	31.2	11.7	42.9	42.0	0.9	51.8	52.9	1.1	6.8	6.7	0.1	0.1	0.1	0.0	101.5	101.5	0.0	101.6	101.6	0.0
41	27.2	9.6	36.8			56.1			9.5						102.4			102.4		
	25.9	10.3	36.2	36.5	0.3	56.7	56.4	0.3	9.5	9.5	0.0		#DIV/0!	#DIV/0!	102.4	102.4	0.0	102.5	102.5	0.0
62	17.8	10.6	28.4			57.7			12.3						98.4			98.4		
	16.8	9.4	26.2	27.3	1.1	56.1	56.9	0.8	12.0	12.2	0.2		#DIV/0!	#DIV/0!	94.3	96.4	2.1	94.3	96.4	2.1
86	15.4	8.2	23.6			56.1			15.0						94.7			94.7		
	15.1	8.5	23.6	23.6	0.0	55.7	55.9	0.2	14.5	14.8	0.3	0.1	0.1	0.0	93.8	94.3	0.5	93.9	94.3	0.4
120	13.6	7.2	20.8			60.3			18.0						99.1			99.1		
	10.6	6.5	17.1	19.0	1.8	63.9	62.1	1.8	18.0	18.0	0.0		#DIV/0!	#DIV/0!	99.0	99.1	0.0	99.0	99.1	0.0
																99.5	2.8		99.6	2.8

Results from Table 5, p. 53 of the study report.
Means and standard deviations calculated using Microsoft program functions @average(A1:A2) and stdevp(A1:A2).

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Aerobic metabolism of [^{14}C]pyrasulfotole in a German sandy loam soil.
Confirmation/determination of means/std.dev. for pyrasulfotole and its transformation products.

	[Phenyl-U-14C]-label									[Pyrazole-3-14C]-label					
	Pyrasulfotole			AE B197555			Unidentified			Pyrasulfotole			Unidentified		
Day	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.
0	100.4			1.3			0.0			97.8			0.4		
	99.6	100.0	0.4	1.4	1.4	0.0	0.0	0.0	0.0	99.0	98.4	0.6	0.0	0.2	0.2
1	91.5			1.6			0.0			86.6			0.4		
	96.5	94.0	2.5	1.7	1.7	0.1	0.0	0.0	0.0	92.7	89.7	3.0	0.3	0.4	0.1
3	84.1			3.0			0.0			85.0			0.4		
	85.7	84.9	0.8	3.5	3.3	0.3	0.0	0.0	0.0	86.3	85.7	0.6	0.4	0.4	0.0
7	79.8			5.8			0.3			77.0			0.5		
	77.8	78.8	1.0	5.6	5.7	0.1	0.7	0.5	0.2	74.5	75.8	1.3	0.4	0.5	0.1
14	63.4			9.3			1.1			60.3			0.2		
	62.3	62.9	0.6	8.4	8.9	0.4	0.9	1.0	0.1	61.3	60.8	0.5	1.2	0.7	0.5
21	54.9			8.1			1.0			49.0			1.5		
	59.7	57.3	2.4	9.5	8.8	0.7	0.9	1.0	0.1	48.8	48.9	0.1	1.8	1.7	0.2
29	50.0			8.5			0.8			39.5			1.7		
	45.9	48.0	2.0	7.7	8.1	0.4	0.8	0.8	0.0	41.5	40.5	1.0	1.4	1.6	0.2
41	40.4			6.4			0.0			34.0			2.8		
	33.3	36.9	3.6	5.0	5.7	0.7	1.0	0.5	0.5	33.8	33.9	0.1	2.4	2.6	0.2
62	27.7			3.5			1.1			27.1			1.3		
	30.3	29.0	1.3	3.3	3.4	0.1	0.0	0.6	0.6	24.8	26.0	1.2	1.5	1.4	0.1
86	21.0			3.4			0.9			21.9			1.7		
	23.2	22.1	1.1	3.6	3.5	0.1	1.3	1.1	0.2	22.2	22.1	0.2	1.4	1.6	0.2
120	18.6			2.3			2.2			18.8			2.1		
	19.3	19.0	0.3	2.2	2.3	0.0	2.0	2.1	0.1	15.8	17.3	1.5	1.4	1.8	0.4

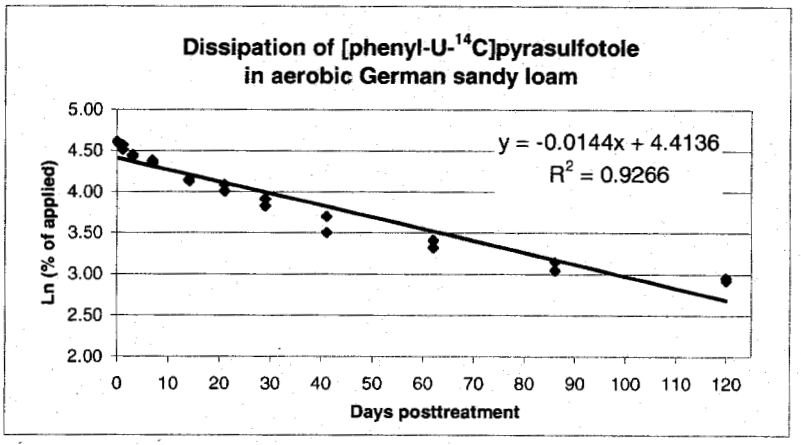
Results from Appendices 4-5, pp. 92-93 of the study report.
Means and standard deviations calculated using Microsoft program functions @average(A1:A2) and stdevp(A1:A2).

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Aerobic metabolism of [^{14}C]pyrasulfotole in a German sandy loam soil.
Half-life determination
[Phenyl-U-^{14}C]-label
Half-life (days) 48.1 (0- to 120-day data)

	Pyrasulfotole	
Days Posttreatment	(% of Applied)	Ln (% applied)
0	100.4	4.609162207
0	99.6	4.601162165
1	91.5	4.516338972
1	96.5	4.569543008
3	84.1	4.432006567
3	85.7	4.450852826
7	79.8	4.379523504
7	77.8	4.354141431
14	63.4	4.149463861
14	62.3	4.131961426
21	54.9	4.005513349
21	59.7	4.08933202
29	50.0	3.912023005
29	45.9	3.826465117
41	40.4	3.698829785
41	33.3	3.505557397
62	27.7	3.321432413
62	30.3	3.411147713
86	21.0	3.044522438
86	23.2	3.144152279
120	18.6	2.923161581
120	19.3	2.960105096

Data obtained from Appendix 4, p. 92 of the study report.



SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.962582265
R Square	0.926564617
Adjusted R Square	0.922892848
Standard Error	0.159423028
Observations	22

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1	6.413608553	6.4136	252.3482778	8.319E-13
Residual	20	0.508314034	0.0254		
Total	21	6.921922587			

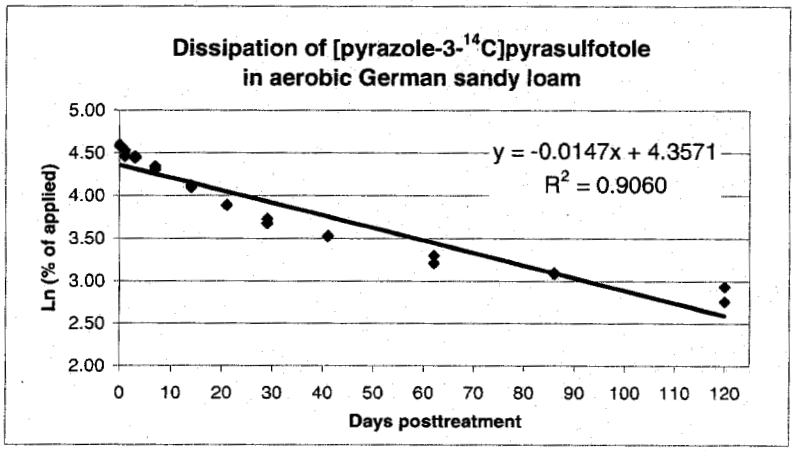
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	4.413631482	0.046448073	95.023	4.9041E-28	4.3167425	4.5105204	4.316742545	4.51052042
X Variable 1	-0.014405592	0.000906841	-15.89	8.31883E-13	-0.016297	-0.012514	-0.01629723	-0.012514

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Aerobic metabolism of [^{14}C]pyrasulfotole in a German sandy loam soil.
Half-life determination
[Pyrazole-3-^{14}C]-label
Half-life (days) 47.1 (0- to 120-day data)

	Pyrasulfotole	
Days Posttreatment	(% of Applied)	Ln (% applied)
0	97.8	4.582924577
0	99.0	4.59511985
1	86.6	4.461299816
1	92.7	4.529368473
3	85.0	4.442651256
3	86.3	4.457829598
7	77.0	4.343805422
7	74.5	4.310799125
14	60.3	4.099332104
14	61.3	4.115779843
21	49.0	3.891820298
21	48.8	3.887730313
29	39.5	3.676300672
29	41.5	3.725693427
41	34.0	3.526360525
41	33.8	3.520460802
62	27.1	3.299533728
62	24.8	3.210843653
86	21.9	3.086486637
86	22.2	3.100092289
120	18.8	2.93385687
120	15.8	2.76000994

Data obtained from Appendix 5, p. 93 of the study report.



SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.951824104
R Square	0.905969125
Adjusted R Square	0.901267581
Standard Error	0.186307097
Observations	22

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1	6.688545881	6.6885	192.6960949	9.957E-12
Residual	20	0.694206687	0.0347		
Total	21	7.382752568			

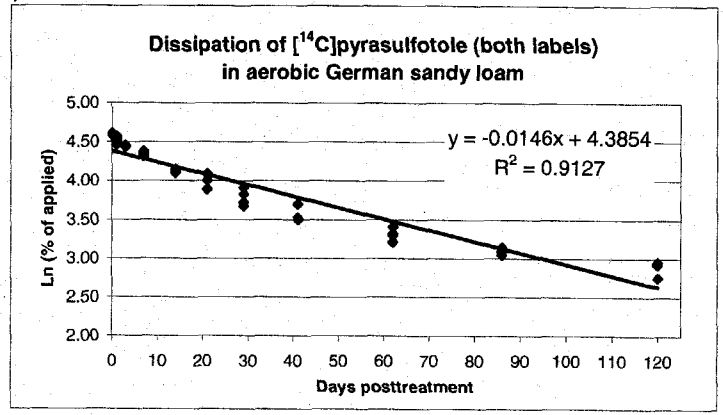
	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*Lower 95.0%*	*Upper 95.0%*
Intercept	4.357101783	0.054280776	80.27	1.42042E-26	4.2438741	4.4703294	4.243874121	4.47032945
X Variable 1	-0.01471112	0.001059764	-13.88	9.95679E-12	-0.016922	-0.0125005	-0.01692175	-0.0125005

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Aerobic metabolism of [^{14}C]pyrasulfotole in a German sandy loam soil.
Half-life determination
[Pyrazole-3-^{14}C]-label
Half-life (days) 47.6 (0- to 120-day data)

Days Post.	Pyrasulfotole Label	(% of Applied)	Ln (% applied)
0	phe	100.4	4.609162207
0	phe	99.6	4.601162165
0	pyr	97.8	4.582924577
0	pyr	99.0	4.59511985
1	phe	91.5	4.516338972
1	phe	96.5	4.569543008
1	pyr	86.6	4.461299816
1	pyr	92.7	4.529368473
3	phe	84.1	4.432006567
3	phe	85.7	4.450852826
3	pyr	85.0	4.442651256
3	pyr	86.3	4.457829598
7	phe	79.8	4.379523504
7	phe	77.8	4.354141431
7	pyr	77.0	4.343805422
7	pyr	74.5	4.310799125
14	phe	63.4	4.149463861
14	phe	62.3	4.131961426
14	pyr	60.3	4.099332104
14	pyr	61.3	4.115779843
21	phe	54.9	4.005513349
21	phe	59.7	4.08933202
21	pyr	49.0	3.891820298
21	pyr	48.8	3.887730313
29	phe	50.0	3.912023005
29	phe	45.9	3.826465117
29	pyr	39.5	3.676300672
29	pyr	41.5	3.725693427
41	phe	40.4	3.698829785
41	phe	33.3	3.505557397
41	pyr	34.0	3.526360525
41	pyr	33.8	3.520460802
62	phe	27.7	3.321432413
62	phe	30.3	3.411147713
62	pyr	27.1	3.299533728
62	pyr	24.8	3.210843653
86	phe	21.0	3.044522438
86	phe	23.2	3.144152279
86	pyr	21.9	3.086486637
86	pyr	22.2	3.100092289
120	phe	18.6	2.923161581
120	phe	19.3	2.960105096
120	pyr	18.8	2.93385687
120	pyr	15.8	2.76000994

Data obtained from Appendices 4-5, pp. 92-93 of the study report.



SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.9553352
R Square	0.9126654
Adjusted R Squar	0.910586
Standard Error	0.1727667
Observations	44

ANOVA

	df	*SS*	*MS*	*F*	*Sig F*
Regression	1	13.100712	13.10071194	438.909098	7.43956E-24
Residual	42	1.2536307	0.029848349		
Total	43	14.354343			

	Coeffs	*Std Error*	*t Stat*	*P-value*	*Low 95%*	*Up 95%*	*Low 95.0%*	*Up 95.0%*
Intercept	4.3853666	0.0355928	123.2094728	2.2095E-55	4.313537489	4.457196	4.313537	4.457196
X Variable 1	-0.014558	0.0006949	-20.9501575	7.4396E-24	-0.01596073	-0.013156	-0.015961	-0.013156

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Aerobic metabolism of [^{14}C]pyrasulfotole in a German sandy loam soil.
Sample concentration recoveries.

Day	[Phenyl-U-^{14}C]-label (A)		[Pyrazole-3-^{14}C]-label (B)	
	"Mild"	"Aggrav."	"Mild"	"Aggrav."
	% Rec	% Rec	% Rec	% Rec
0	104.9		100.6	
	103.2		102.5	
1	95.3	102.5	101.1	97.1
	95.2	96.8	98.2	106.0
3	103.5	99.3	100.5	100.7
	104.7	102.0	101.4	104.1
7	102.7	99.4	104.2	96.2
	102.6	103.4	99.5	98.6
14	101.4	100.4	102.3	96.1
	101.7	97.3	99.7	98.2
21	102.2	98.1	101.8	99.3
	99.4	100.0	102.5	97.5
29	96.0	101.2	105.1	97.0
	100.1	97.9	100.1	97.1
41	96.0	99.7	100.5	95.2
	103.2	100.5	97.1	97.3
62	101.8	95.5	103.6	96.2
	99.8	98.6	102.0	102.1
86	100.8	97.0	101.2	95.7
	97.0	96.0	110.5	97.6
120	99.2	103.3	98.5	92.3
	98.3	100.3	[132.2][1]	90.1
Mean	100.4	99.5	101.6	97.7
std.dev.	3.0	2.3	2.8	3.5
n =	22	20	21	20
Both extracts	**Mean**	100.0	**Mean**	99.7
	std.dev.	2.7	**std.dev.**	3.7
	n =	42	**n =**	41
Both labels/ extracts			**Mean**	99.8
			std.dev.	3.2
			n =	83

[1]Assumed pipetting error; result not included in calculations.
Results from Appendix 13, p. 102 of the study report.
Means and standard deviations calculated using Microsoft program functions @average(A1:A2) and stdevp(A1:A2).

Chemical: Pyrasulfotole (AE 0317309)
PC: 000692
MRID: 46801711
Guideline: 162-1

Aerobic metabolism of [^{14}C]pyrasulfotole in a German sandy loam soil.

Day	Soil moisture[1]			
	[Phenyl-U-^{14}C]-label (A)		[Pyrazole-3-^{14}C]-label (B)	
	g	% MWHC	g	% MWHC
0	19.05	52.3	18.98	52.1
	18.96	52.1	19.02	52.3
1	19.13	52.6	19.00	52.2
	19.21	52.8	19.20	52.7
3	18.36	50.4	18.67	51.3
	18.63	51.2	18.63	51.2
7	18.81	51.7	18.86	51.8
	18.79	51.6	18.78	51.6
14	18.58	51.0	18.80	51.6
	18.80	51.6	18.58	51.0
21	18.32	50.3	18.55	51.0
	18.28	50.2	18.43	50.6
29	18.03	49.5	18.21	50.0
	18.02	49.5	18.24	50.1
41	17.54	48.2	17.42	47.9
	17.92	49.2	17.81	48.9
62	18.18	49.9	18.07	49.6
	17.91	49.2	17.87	49.1
86	17.86	49.1	17.58	48.3
	17.18	47.2	17.21	47.3
120	17.15	47.1	17.29	47.5
	17.87	49.1	17.71	48.7
Both labels	**Mean**		18.31	50.3
	std.dev.		0.59	1.6
	n =		44	44

[1]Treated soil samples only; does not include microbial biomass soil samples.
Results from Appendix 11, pp. 99-100 of the study report.
Means and standard deviations calculated using Microsoft program functions @average(A1:A2) and stdevp(A1:A2).