Final Report

Study Title	[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation
Study Guideline	OECD Guideline 307 (April 2002)
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GLP COMPLIANCE STATEMENT

[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation

The study was performed in accordance with the agreed protocol and with Covance Laboratories Limited Standard Operating Procedures, unless otherwise stated, and the study objectives were achieved.

The study was conducted in compliance with the United Kingdom (GLP Monitoring Authority, Medicines and Healthcare products Regulatory Agency (MHRA)) Good Laboratory Practice Regulations 1999, Statutory Instrument 1999 No. 3106 as amended by the Good Laboratory Practice (Codification Amendments Etc.) Regulations 2004, and the OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring ENV/MC/CHEM(98)17 (Revised 1997, Issued January 1998).

Studies performed in compliance with the GLP regulations and standards referenced above are considered acceptable to the US EPA and Japanese regulatory authorities.

R Graham, BSc (Hons) MRSC
Study Director
Covance Laboratories Ltd

Date

K Nishioka
Sponsor Representative
Sumitomo Chemical Company Limited.

5 October, 2011
Date

Submitter / Applicant

Date

STUDY DIRECTOR AUTHENTICATION AND GLP COMPLIANCE STATEMENT

[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation

I, the undersigned, hereby declare that the work was performed under my supervision and that the findings provide a true and accurate record of the results obtained.

The study was performed in accordance with the agreed protocol and with Covance Laboratories Limited Standard Operating Procedures, unless otherwise stated, and the study objectives were achieved. The study was conducted in compliance with the United Kingdom (GLP Monitoring Authority, Medicines and Healthcare products Regulatory Agency (MHRA)) Good Laboratory Practice Regulations 1999, Statutory Instrument 1999 No. 3106, as amended by the Good Laboratory Practice (Codification Amendments Etc.) Regulations 2004, and the OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring ENV/MC/CHEM(98)17 (Revised in 1997, Issued January 1998).

Studies performed in compliance with the GLP regulations and standards referenced above are considered acceptable to the US EPA and Japanese regulatory authorities.

R Graham BSc (Hons) MRSC
Study Director

Date

QUALITY ASSURANCE STATEMENT

[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation

This study has been reviewed by the GLP Quality Assurance Unit of Covance and the report accurately reflects the raw data. The following inspections were conducted and findings reported to the study director (SD) and associated management.

Critical procedures, which are performed routinely in an operational area, may be audited as part of a "process" inspection programme. This can be in addition to phases scheduled on an individual study basis. Selected process inspections conducted and considered applicable to this study are included below

In addition to the inspection programmes detailed below, a facility inspection programme is also operated. Details of this programme, which covers all areas of the facility annually (at a minimum), are set out in standard operating procedures.

Inspection Dates		Phase	Date Reported to SD and SD Management
From	To		
20 Mar 2009	20 Mar 2009	Protocol Review	20 Mar 2009
24 Apr 2009	24 Apr 2009	Protocol Amendment Review	24 Apr 2009
01 Jun 2009	01 Jun 2009	Dose Preparation	05 Jun 2009
31 Jul 2009	31 Jul 2009	Data Processing	31 Jul 2009
22 Dec 2009	22 Dec 2009	Protocol Amendment Review	22 Dec 2009
07 May 2010	07 May 2010	Protocol Amendment Review	07 May 2010
21 May 2010	21 May 2010	Protocol Amendment Review	12 Aug 2010
01 Oct 2010	01 Oct 2010	Protocol Amendment Review	01 Oct 2010
28 Feb 2011	28 Feb 2011	Protocol Amendment Review	28 Feb 2011
23 May 2011	23 Jun 2011	Draft Report Review	23 Jun 2011
27 Sep 2011	27 Sep 2011	Final Report Review	27 Sep 2011

Process

Inspection Dates		Phase	Date Reported to SD and SD Management
From	To		
29 Apr 2009	29 Apr 2009	Microbial Biomass	30 Apr 2009
30 Apr 2009	30 Apr 2009	Test Article Receipt	30 Apr 2009
12 May 2009	12 May 2009	Water Holding Capacity	12 May 2009
03 Jun 2009	03 Jun 2009	Dose Preparation	03 Jun 2009
04 Jun 2009	04 Jun 2009	Dose Application	04 Jun 2009
24 Jun 2009	24 Jun 2009	High Performance Liquid Chromatography Analysis	24 Jun 2009
24 Jun 2009	24 Jun 2009	Data Collation and Transfer	25 Jun 2009

C Royle
Quality Assurance Unit

Date

REVIEWING SCIENTIST'S STATEMENT

[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation

I, the undersigned, hereby declare that I have reviewed this report in conjunction with the Study Director and that the interpretation and presentation of the data in the report are consistent with the results obtained

C Lewis, BSc, PhD
Scientific Specialist, Environmental Sciences

Date

RESPONSIBLE PERSONNEL

[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation

The following personnel were responsible for key elements of the study:

STUDY MANAGEMENT	**NAME**
Study Director	R Graham
Study Co-ordinator	J Gilbert
OPERATIONAL SUPERVISION	
Study Supervisor	M Jackson (until 23 October 2009) G Crabtree (from 23 October 2009)
In Life Supervisor & Soil Analysis	P Davies
QUALITY ASSURANCE	
Senior Manager, Quality Assurance	L Gillbanks

ARCHIVE STATEMENT

[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation

All primary data (including electronic data), or authenticated copies thereof, will be retained in the Covance Laboratories Limited archives for fifteen years after issue of the Final Report. At this time, the Sponsor will be contacted to determine whether the data should be returned, retained or destroyed on their behalf. Sponsors will be notified of the financial implications of each of these options at that time. One copy of the protocol and Final Report will be held indefinitely in the Covance Laboratories Limited archives.

Selected specimens or samples will be retained for as long as the material permits further evaluation, or up to four weeks after issue of the Final Report (whichever period is the shorter). At finalisation of the report, the Sponsor will be contacted to determine whether specimens or samples should be returned, retained or destroyed on their behalf. Any financial implications of these options will also be communicated at this time. Note that where the Sponsor fails to clarify their requirements within four weeks of our communication, Covance reserve the right to dispose of these materials. Specimens or samples will not be destroyed without prior approval of the Study Director.

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SUMMARY

Method

The route and rate of degradation of S-2167 in aerobic soil were studied at 20 ± 2°C using two radiolabelled forms of the test substance, [benzyl-^{14}C] and [phenoxy-^{14}C]S-2167. The application rate was 0.8 µg/g dry weight equivalent of soil, based on a field application rate of 200 g a.i./ha, and assuming an incorporation depth of 2.5 cm and a soil density of 1.0 g/cm^3.

There were five incubation groups as detailed below:

Incubation group	Radiolabel	Soil	Number of units*
A	[benzyl-^{14}C]	Speyer 5M	20
B	[phenoxy-^{14}C]	Speyer 5M	20
C	[benzyl-^{14}C]	Speyer 2.2	16
D	[benzyl-^{14}C]	SK920191	20
E	[benzyl-^{14}C]	Chelmorton	16

* Excludes control units for biomass determination.

The tests using the Speyer 2.2 and Chelmorton soils were repeated due to low biomass values (< 1% organic carbon) having been observed for these two soils. Fresh batches of soil were obtained for the repeat test. The methods and results for the repeat tests only are reported for these two soils.

Soil properties were as follows:

Soil	pH ($CaCl_2$)	OC %	Sand[1] %	Silt[1] %	Clay[1] %	Classification[1]	WHC %	CEC	Biomass[2]	Soil Taxonomy[3]
Speyer 5M	7.2	1.3	62	28	11	Sandy loam	24.8	15.0	278	Entisol
Speyer 2.2	5.5	2.1	82	12	6	Loamy sand	20.0	10.0	542	Mollisol
SK920191	7.6	3.8	43	27	30	Clay loam	34.2	33.9	779	Inceptisol
Chelmorton	5.9	3.4	25	55	20	Silt loam	38.0	25.0	446	Inceptisol

[1] USDA Particle Size Distribution and Classification
[2] Biomass values determined before soil dispensing (µg C/g soil)
[3] US soil taxonomy,
OC = organic carbon, WHC = water holding capacity at pF 2, CEC = cation exchange capacity (mEq/100g)

Samples of the sieved soil (50 g dry weight equivalent) were dispensed into individual glass vessels through which moistened air was drawn. The units were maintained in the dark at 20 ± 2°C. Soil moisture was adjusted to the water holding capacity value at *ca* pF 2, up to every 11 days. Soils were incubated under experimental conditions for 15 to 28 days prior to test substance application. After application, the air drawn over the surface of the units was passed through a series of liquid traps (ethanediol, paraffin in xylene and sodium hydroxide) to collect evolved radiolabelled material.

[Benzyl-^{14}C]S-2167 (39.8 µg, 536 kBq for incubation groups A and D, 39.5 µg, 220.5 kBq for incubation groups C and E) and [phenoxy-^{14}C]S-2167 (39.9 µg, 565 kBq) was applied dropwise in acetonitrile solution (90 to 100 µL) to the soil surface. An equivalent volume of acetonitrile was applied to the samples used for biomass determination.

Microbial biomass of the soil was determined on soil samples removed from incubation at application and at the end of the incubation period. Samples were removed for analysis from each incubation group, immediately after treatment of [^{14}C]S-2167 and at 7, 14, 30, 59[a] and 120 DAT (days after treatment).

Soil samples were extracted with acetone:water (9:1 v/v, 2 x 100 mL) and acetone (1 x 100 mL). The extracts were combined, quantified by LSC (liquid scintillation counting) and analysed chromatographically. Soils were further extracted with acetone:0.1 M hydrochloric acid (5:1, v/v, 2 x 100 mL) and acetone (1 x 100 mL). The extracts were combined quantified by LSC and analysed chromatographically.

Bound residue fractionation was performed on a 120 DAT representative sample, for each incubation group which had unextracted residues ≥ 10%.

All extracts that contained *ca* 5% or greater of applied radioactivity were analysed by high performance liquid chromatography (HPLC) using co-chromatography with reference standards. Confirmation of identity was by thin layer chromatography (TLC) and co-chromatography with reference standards. The proportions of the two isomers were determined by chiral HPLC analysis of representative extracts.

The percent of applied radioactivity present as test substance was plotted against the incubation time in days. Curves were constructed through appropriate data points using non-linear regression analysis to give lines of best fit. The degradation rate of [^{14}C]S-2167 was determined in each soil using single first order (SFO) kinetics.

Findings

The mean recovery of applied radioactivity for the samples treated with [^{14}C]S-2167, ranged from 94 to 102%. Initially, almost all the radioactivity was extracted (maximum 0.3% unextracted) but recovery in the extracts decreased to 40 to 84% of applied radioactivity at 120 DAT. Between 7 and 33% remained unextracted at 120 DAT.

At 120 DAT, between 4 and 25% applied radioactivity was in the sodium hydroxide traps. The radioactivity in the sodium hydroxide traps for all incubation groups, (except the Speyer 2.2 soil for which only 4% applied radioactivity was detected) was confirmed as carbon dioxide by barium chloride precipitation. There was no detectable radioactivity found in the ethanediol or paraffin in xylene traps.

The distribution of the applied radioactivity in the representative 120 DAT sample bound residue fractionations are shown in the table below.

Soil	Treatment	Percent of applied radioactivity present in		
		Fulvic Acid	Humic Acid	Humin
Speyer 5M	[Benzyl-^{14}C]	10.7	6.2	13.1
Speyer 5M	[Phenoxy-^{14}C]	7.0	5.6	10.0
SK920191	[Benzyl-^{14}C]	8.6	5.6	21.9
Chelmorton	[Benzyl-^{14}C]	7.6	5.6	6.2

[a] 61 DAT for Speyer 2.2 and Chelmorton soils

The mean percent applied radioactivity present as [^{14}C]S-2167, decreased from between 92 and 99% at 0 DAT to between 23 and 64% at 120 DAT. No [^{14}C]S-2354 (S-2200 *S*-isomer) was detected in representative soil extracts.

The metabolite 5-COOH-S-2200 was detected as a major metabolite which was present at ≥ 10% applied radioactivity. 2-COOH-S-2200, DX-CA-S-2200 and MCBX were detected as known metabolites. All other unknown metabolites individually accounted for less than 3% applied radioactivity.

The presence of the known metabolites, excluding 2, 5-dimethylphenol, was confirmed by TLC analysis.

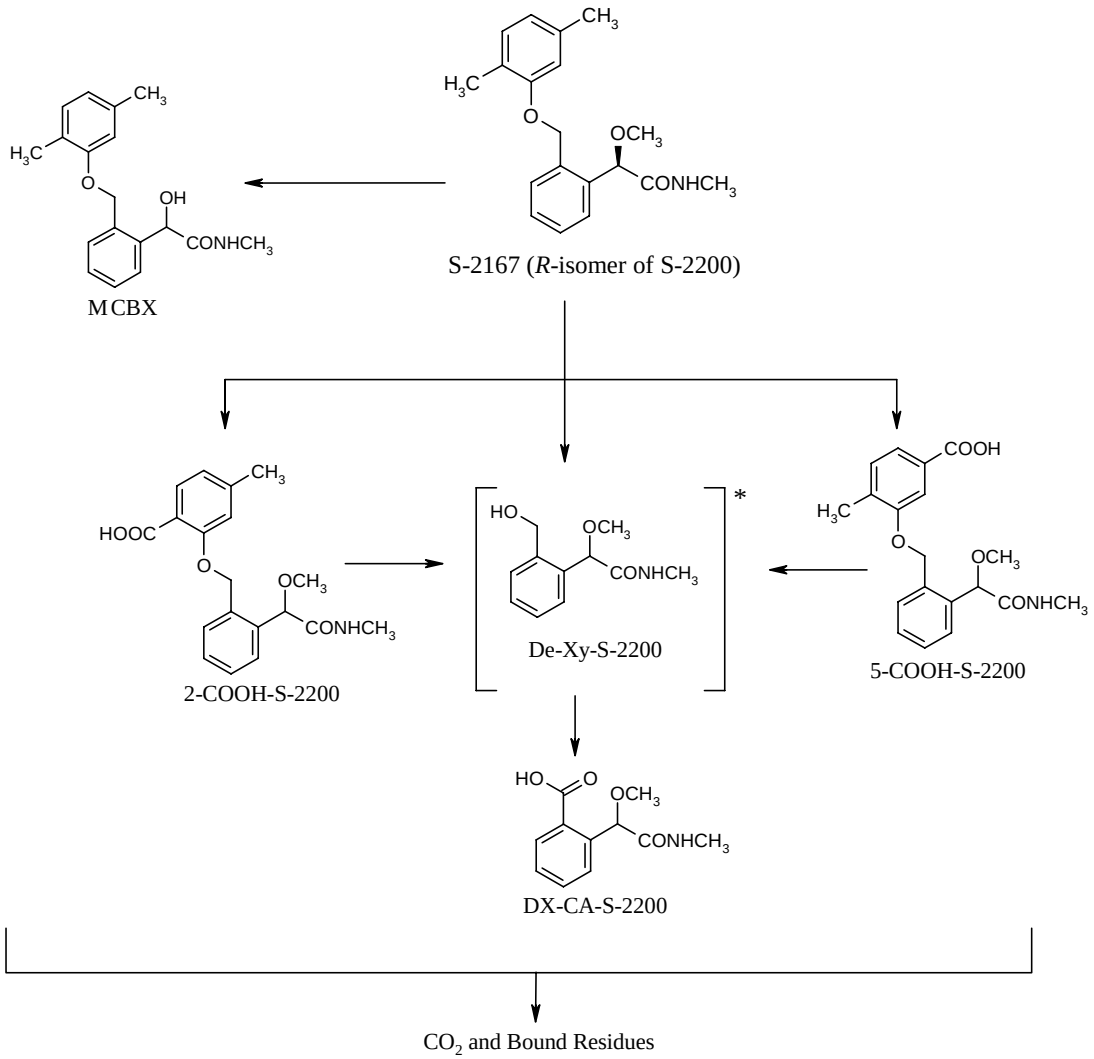
Rate and Route of Degradation
The rates of degradation of [^{14}C]S-2167 in soil are summarised in the table below.

Soil	Treatment	Kinetics	DT-50 (days)	DT-75 (days)	DT-90 (days)	χ^2	R^2
Speyer 5M	[Benzyl-^{14}C]	SFO	53.4	106.7	177.3	4.18	0.9807
Speyer 5M	[Phenoxy-^{14}C]	SFO	84.1	168.2	279.4	3.53	0.9659
Speyer 5M	[Benzyl-^{14}C]/ [Phenoxy-^{14}C]	SFO	66.5	133.1	221.0	2.87	0.9474
Speyer 2.2	[Benzyl-^{14}C]	SFO	227.1	454.2	754.4	4.04	0.8278
SK920191	[Benzyl-^{14}C]	SFO	50.6	101.1	167.9	5.26	0.9697
Chelmorton	[Benzyl-^{14}C]	SFO	102.1	204.2	339.2	8.18	0.8335

Note: DT-75 calculated as twice the DT-50

The proposed metabolic pathway for S-2167 in soil is presented on the following page.

Conclusions
S-2167 was metabolised mainly to carbon dioxide (maximum 25% of applied radioactivity), bound residues and three other metabolites 2-COOH-S-2200, 5-COOH-S-2200 and DX-CA-S-2200. DT-50 and DT-90 values were in the range 51 to 227 days and 168 to 754 days, respectively, for SFO kinetics.

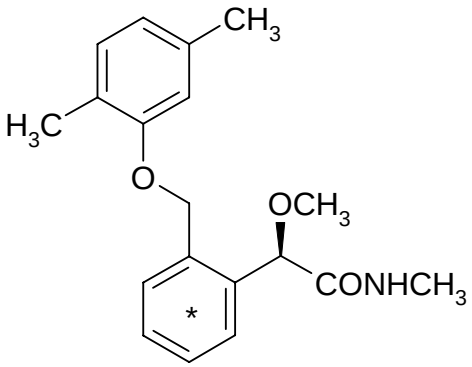


* De-Xy-S-2200 was not confirmed in a second chromatographic system, however it is considered a possible intermediate metabolite

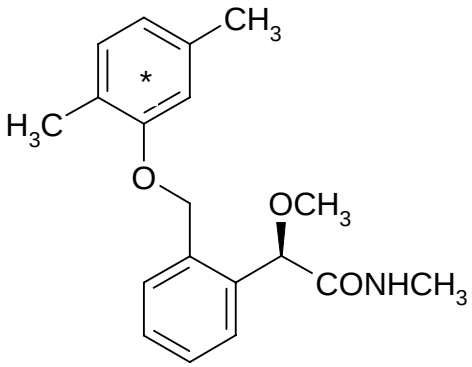
INTRODUCTION

S-2200 is a fungicide undergoing development for use on oilseed rape and wheat. This study investigated the aerobic soil metabolism of the *R*-isomer (S-2167).

The two radiolabelled forms of [^{14}C]S-2167 used in this study had the following structures:



[Benzyl-^{14}C]S-2167



[Phenoxy-^{14}C]S-2167

***** Position of radiolabel.

The study was conducted to comply with the study guideline stated on the front cover of this report.

The tests using the Speyer 2.2 and Chelmorton soils were repeated due to low biomass values (< 1% organic carbon) having been observed for these two soils. Fresh batches of soil were obtained for the repeat test. The methods and results for the repeat tests only are reported for these two soils.

OBJECTIVES

The objectives of the study were:

- to determine the rate of [^{14}C]S-2167 degradation in one soil under aerobic conditions at 20 ± 2°C and determine the quantity and nature of the degradation products formed

- to determine the rate of [^{14}C]S-2167 degradation under aerobic conditions at 20 ± 2°C in three further soils

The study was initiated on 9 March 2009 (date the protocol was signed by the Study Director) and completed on the date the final report was signed by the Study Director. The practical phase of the study was conducted in the Environmental Sciences Department of Covance Laboratories Europe (CLE), Otley Road, Harrogate, North Yorkshire between 3 April 2009 (stock solution preparation) and 1 March 2011 (chromatographic analysis).

PROCEDURES

Protocol Adherence

The study described in this report was carried out according to the agreed protocol and six amendments. There were two protocol deviations, described in Appendix 5.

Test Substance and Reference Standards

Identification

Common Name:	S-2167 (S-2200 *R*-isomer)
Chemical name:	(*R*)-2-[2-(2,5-dimethylphenoxymethyl)phenyl]-2-methoxy-*N*-methylacetamide
Molecular formula:	$C_{19}H_{23}NO_3$
Molecular weight:	313.39
Solubility in water:	25.8 mg/L at 20 ± 0.5°C (GLP)

All information was supplied by the Sponsor

Radiolabelled Test Substances

The two radiolabelled forms of the test substance were supplied by the Sponsor and received at Covance on 19 February 2009. They were stored at < -10°C in the dark. The following information was supplied:

Name	[Benzyl-^{14}C]S-2167
Lot number:	RIS2008-010
Quantity received:	220 MBq
Specific activity:	13.5 MBq/mg
Radiochemical Purity:	99.2%

Name	[Phenoxy-^{14}C]S-2167
Lot number:	RIS2009-002
Quantity received:	200 MBq
Specific activity:	14.2 MBq/mg
Radiochemical Purity:	99.1%

Specification sheets for the test substances are shown in Appendix 2.

Stock solutions were prepared by dissolving the supplied [benzyl-^{14}C]S-2167 and [phenoxy-^{14}C]S-2167 in acetonitrile (75 mL and 70 mL, respectively).

Non-radiolabelled Test Substance

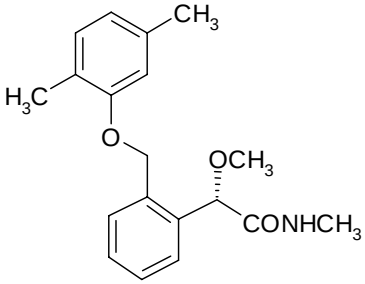
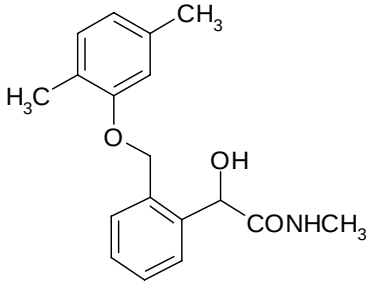
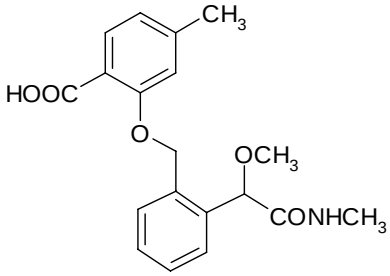
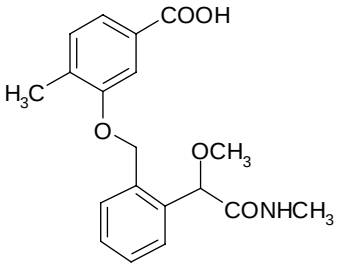
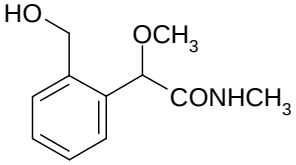
Non-radiolabelled test substance was supplied by the Sponsor and was received at Covance on 2 February 2009. It was stored refrigerated (2 - 8°C) in the dark. The following information was supplied:

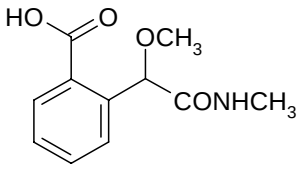
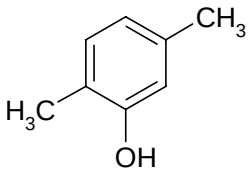
Name	S-2167
Lot number:	060020652
Quantity received:	3 g
Purity:	100%
Expiry date:	9 February 2012

A Certificate of Analysis for the non-radiolabelled test substance was supplied by the Sponsor (Appendix 2).

Reference Standards

Potential degradation product reference standards were supplied by the Sponsor on 23 February 2009 and 2 February 2009 (S-2354). Upon arrival at Covance, the standards were stored refrigerated (2 - 8°C). The 2, 5-dimethylphenol reference standard was obtained commercially by Covance on 7 April 2009 and was stored at room temperature. The following information on the standards was available:

Code	Lot number	Purity	Expiry date	Structure
S-2354	060020653	99.7%	Feb 2012	
MCBX	CTS08015	96.9%	Nov 2011	
2-COOH-S-2200	252-001-60-2	99.8%	Aug 2011	
5-COOH-S-2200	252-001-55-2	99.7%	Aug 2011	
De-Xy-S-2200	CTS08001	99.9%	Aug 2011	

Code	Lot number	Purity	Expiry date	Structure
DX-CA-S-2200	CTS08031	100%	Nov 2011	
2,5-Dimethylphenol	01212TE	99.2%	Not stated	

Certificates of Analysis for the reference standards are presented in Appendix 2 and chromatographic properties of the reference standards are presented in Appendix 3.

Radiochemical Purity

The radiochemical purity of both radiolabelled forms of [^{14}C]S-2167 was assessed by reverse phase HPLC (Method 1, page 24). The radiochemical purity for both radiolabelled forms was < 98% so they were both repurified by HPLC.

A subsample of each [^{14}C]S-2167 stock solution was concentrated to near dryness under nitrogen and reconstituted in acetonitrile:water (1:1, v/v). Each concentrated stock solution was repeatedly injected onto an HPLC (Method 4, page 25) and the eluted fractions collected and quantified by LSC. The fraction containing [^{14}C]S-2167 was analysed for radiochemical purity by HPLC. This fraction was diluted with water and loaded onto a pre-conditioned solid phase extraction cartridge (Bakerbond C18, 1 g). The cartridge was washed with water and [^{14}C]S-2167 eluted in acetonitrile. The resulting eluate was analysed by LSC and HPLC.

This procedure was repeated on a new subsample of the [benzyl-^{14}C]S-2167 stock solution generating a further two fractions from the HPLC step of the repurification. These fractions were further repurified as described above. A total of four repurified [benzyl-^{14}C]S-2167 stock solutions and one [phenoxy-^{14}C]S-2167 were generated.

The radiochemical purity of the repurified [benzyl-^{14}C]S-2167 and [phenoxy-^{14}C]S-2167 stock solutions were each ≥ 98%.

Optical purity was determined on the day of treatment by chiral HPLC and no S-2354 (S-2200 *S*-isomer) was detected in the treatment solutions. Example chromatograms are shown in Appendix 4.

Solvents and Reagents

Reagents and solvents were of Analytical grade (or a suitable alternative) and were obtained principally from VWR International® (formerly Merck, BDH), Rathburn Chemicals Limited, Sigma-Aldrich Chemical Company Limited and Vickers Laboratories Limited.

Irgasafe plus™, obtained from Perkin Elmer® Life and Analytical Sciences, was the liquid scintillant used for general LSC. Ultima-Flo™ M (Lablogic) was the liquid scintillant used in HPLC liquid mixing cells.

Test System

Collection and Storage

The Speyer 5M and Speyer 2.2 soils were supplied by Speyer. The Chelmorton and SK920191 soils were supplied by Land Research Associates. The location of the sites, dates of collection and description of the methods of collection have been included in Appendix 1. The sampling dates, arrival dates at Covance and dispensing date were as follows:

Incubation Group	Soil	Sampling date	Arrival date	Dispensing date
A	Speyer 5M	27 February 2009	9 March 2009	5 May 2009
B	Speyer 5M	27 February 2009	9 March 2009	5 May 2009
C	Speyer 2.2	7 April 2010	20 April 2010	18 May 2010
D	SK920191	3 March 2009	10 March 2009	5 May 2009
E	Chelmorton	14 April 2010	16 April 2010	18 May 2010

On arrival at Covance the soils were given unique codes. The soils were either sieved (2 mm) by the soil supplier or they were sieved (2 mm) at Covance.

Prior to use, the soils were stored in an incubator routinely maintained at 4 ± 2°C, in loosely tied plastic bags in accordance with the ISO international standard ISO 10381-6:1993(E).

Characterisation

The soils were characterised and Certificates of Analysis generated (Appendix 1). Microbial biomass was determined on samples removed from incubation at application and on completion of the incubation period by the fumigation - extraction method.

Soil	Biomass at application		Biomass at completion of incubation period	
	µg C/g soil	% organic carbon	µg C/g soil	% organic carbon
Speyer 5M	171	1.3	170	1.3
Speyer 2.2	838	4.0	194	1.0
SK920191	720	1.9	810	2.1
Chelmorton	941	2.8	353	1.0

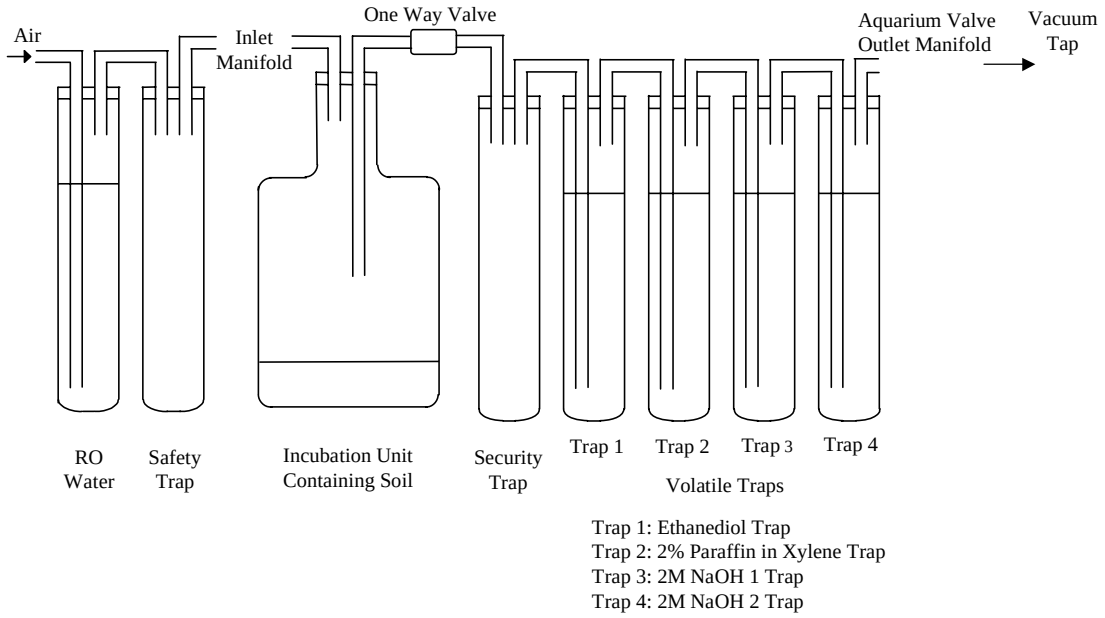
Incubation System

Soil samples (50 g dry weight equivalent) of each of the four soils were weighed into individual incubation flasks and adjusted to the water holding capacity value at pF 2. This moisture level was maintained by weighing each sample up to every eight days (with the exception of two occasions detailed in Appendix 5) and replacing any moisture loss with RO (reverse osmosis) water. Soil units were maintained in the dark, at 20 ± 2°C.

Moistened air at a flow rate of 20 – 60 mL/min was drawn through the units and, after test substance application, through a series of liquid traps. The first trap was empty and acted as a security trap, the second and third contained ethanediol and 2% liquid

paraffin in xylene to trap polar and non-polar volatiles, respectively, and the final two contained 2 M sodium hydroxide solution to trap liberated carbon dioxide.

A schematic diagram of the test system follows:



Soil units were maintained under experimental conditions for 15 to 28 days prior to test substance application. During the pre-incubation phase, the security trap was filled with water to check for airflow through the unit. The water was emptied and trapping reagents were added to the other traps prior to test substance application.

Experimental Procedures

Test Substance Solutions

Speyer 5M and SK920191 Soils

Three of the [benzyl-^{14}C]S-2167 re-purified stock solutions were combined and concentrated to *ca* 10 mL under nitrogen. The concentrated solution was used as the [benzyl-^{14}C]S-2167 treatment solution and was analysed by LSC and HPLC.
The concentration of the solution was 394.75 µg/mL (5.321 MBq/mL). The mean radiochemical purity of [benzyl-^{14}C]S-2167 in the treatment solution was 99.5 % by HPLC prior to test substance application to the Speyer 5M and SK920191 soils.

The [phenoxy-^{14}C]S-2167 re-purified stock solution was used as the [phenoxy-^{14}C]S-2167 treatment solution. The solution was analysed by LSC, HPLC and TLC. The concentration of the solution was 407.184 µg/mL (5.7657 MBq/mL). The mean radiochemical purity of [phenoxy-^{14}C]S-2167 in the treatment solution was 99.2 % by HPLC prior to test substance application to Speyer 5M soil.

Speyer 2.2 and Chelmorton Soils

One of the [benzyl-^{14}C]S-2167 re-purified stock solutions was combined with the remainder of previously described [benzyl-^{14}C]S-2167 treatment solution.
The resulting solution was radio-diluted with a non-radiolabelled stock solution

(2.150 mL of 0.444 mg/mL solution) to give a treatment solution at a specific activity of 5.58 MBq/mg. The solution was analysed by LSC and HPLC. The concentration of the solution was 439.0 µg/mL (2.4498 MBq/mL). The mean radiochemical purity of [benzyl-^{14}C]S-2167 in the treatment solution was 98.4 % by HPLC, prior to test substance application to the Speyer 2.2 and Chelmorton soils.

Test Substance Application

The application rate of 0.8 µg/g soil was based on the field application rate of 200 g ai/ha, an incorporation depth of 2.5 cm and a soil density of 1.0 g/cm^3.

The appropriate volume of test substance treatment solution was dispensed dropwise over the soil surface of the individual soil samples. The solvent was allowed to evaporate and the test substance mixed with the soil. The application was performed according to the following table:

Incubation group	Treatment	No. of units	Volume of treatment solution applied (µL)	Weight of test substance applied (µg)	Radioactivity applied (kBq)
A	[Benzyl-^{14}C]-S-2167	20	100	39.759	535.945
B	[Phenoxy-^{14}C]-S-2167	20	98	39.904	565.041
C	[Benzyl-^{14}C]-S-2167	16	90	39.513	220.483
D	[Benzyl-^{14}C]-S-2167	20	100	39.759	535.945
E	[Benzyl-^{14}C]-S-2167	16	90	39.513	220.483

NA = Not applicable

The concentrations of radioactivity in the [^{14}C]S-2167 treatment solutions were determined by dispensing triplicate aliquots (100 or 98 µL for groups A, B and D, 10 µL for groups C and E), before and after application, into volumetric flasks (50 mL for groups A, B and D, 10 mL for groups C and E) and making up to volume with acetonitrile. Triplicate aliquots (100 µL) of each of these solutions were assayed by LSC. The values obtained were used to calculate the quantity of [^{14}C]S-2167 applied to the units.

In addition to the radiolabelled test units, control units (12 per soil for Speyer 5M and SK920191, 8 per soil for Speyer 2.2 and Chelmorton) were treated with an equivalent volume of acetonitrile. These units were used for determination of microbial biomass at the start and end of the incubation period.

Sampling Intervals

Duplicate units of each soil were removed for analysis immediately after test substance application. Duplicate incubation units and their associated traps were removed for analysis at intervals of 7, 14, 30, 59[a] and 120 DAT. Traps attached to the remaining units were also sampled at 30, 59[a] and 120 DAT. The traps were replenished with fresh reagents before being returned to the incubation system.

Biomass units were removed for analysis at the time of application and at the end of the incubation period.

[a] 61 DAT for Speyer 2.2 and Chelmorton soils

Sample Analysis

Extraction of Soil

Soil samples were extracted twice with acetone:water (9:1 v/v, *ca* 100 mL) by shaking at room temperature (20 minutes) followed by centrifugation to separate the solid and liquid phases. The residue was further extracted with acetone (100 mL), shaking and centrifuging as above and the extracts were combined to form the primary soil extracts.

The residue was extracted twice with acetone:0.1 M hydrochloric acid (5:1, v/v, 100 mL) by shaking at room temperature (20 minutes) followed by centrifugation to separate the solid and liquid phases. The residue was further extracted with acetone (100 mL), shaking and centrifuging as above and the extracts were combined to form the secondary soil extracts.

Separate sub-samples of the primary and secondary extracts were reduced by rotary evaporation to *ca* 1 mL and reconstituted in acetone (5 x 2 mL). The extracts were further concentrated to *ca* 1 mL by evaporation under a stream of nitrogen.

Radioactive concentrations in the extracts, before and after concentration, were determined by LSC. Subsamples of each concentrated extract were analysed chromatographically.

Bound Residue Fractionation

Bound residue fractionation was performed on selected soil samples, following extraction. The method used was based on that recommended by the American Institute Biological Sciences Environmental Chemistry Task Group (AIBS)[a].

A representative 120 DAT soil sample of each soil type, units A12, B11, D11 and E112, were shaken with sodium hydroxide solution (0.5 M, 100 mL, 26.5 hours). The residue (humin fraction) and supernatant were separated by centrifugation (3400 rpm, *ca* 2590 *g*, 30 minutes). The humin fraction was further washed twice with 0.5 M sodium hydroxide solution (25 mL), centrifuged (3400 rpm, *ca* 2590 *g*, 10 minutes) and the washings added to the original supernatant.

The supernatant was acidified to *ca* pH 1 with 5 M hydrochloric acid and the precipitate formed separated by centrifugation (3400 rpm, *ca* 2590 *g*, 10 minutes). The supernatant was decanted and the precipitate was washed twice with 0.1 M hydrochloric acid (*ca* 25 mL), centrifuged (3400 rpm, *ca* 2590 *g*, 10 minutes) and the washings added to the supernatant (fulvic acid fraction). The washed precipitate (humic acid fraction) was reconstituted in 0.5 M sodium hydroxide (*ca* 100 mL).

Radioactivity in the fulvic acid and reconstituted humic acid fractions was determined by LSC. Radioactivity in the humin fraction was determined by combustion followed by LSC.

[a] United States Environmental Protection Agency. 1975. Guidelines for Registering Pesticides in the United States. Federal Register, **40**, *123*, 26802-26928.

Analysis of Extracts

All extracts that contained *ca* 5%, or greater, of applied radioactivity were analysed by HPLC, (Method 2, page 25) using co-chromatography with reference standards. Confirmation of identity was by TLC, (System 2, page 26) and co-chromatography of selected samples with reference standards. The proportions of the *S*-isomer and *R*-isomer were determined in representative samples by chiral HPLC (Method 3, page 25).

Analysis of Trapping Solutions

Radioactivity in the trapping solutions was quantified by LSC.

The nature of the radioactivity trapped in the sodium hydroxide traps for all incubation groups (except Speyer 2.2 soil which had only 4% applied radioactivity evolved as carbon dioxide) was investigated by addition of barium chloride solution. Analyses were performed on the first of two sodium hydroxide traps associated with one replicate from each incubation group, from 120 DAT units A12, B11, D11 and E112.

Each sample tested comprised a sub-sample (4 mL) of the combined sodium hydroxide trap samples collected up to the sampling date. A saturated solution of barium chloride in water (8 mL) was added and mixed with the sample, allowed to stand for at least 1 hour, centrifuged (3000 rpm, *ca* 2000 *g*, 10 minutes) and the radioactivity in the supernatant determined by LSC. Any dissolved $^{14}CO_2$ present would be precipitated as insoluble barium [^{14}C]-carbonate during this process.

Analytical Methods and Measurements

HPLC

The following method was used for determination of radiochemical purity:

Method 1:

Column:	Sumipax ODS A-212 (150 x 6 mm)		
Gradient:	An isocratic system was used consisting of:		
	Solvent A:	Water	
	Solvent B:	Acetonitrile	
	Time (minutes)	% A	% B
	0	45	55
	30	45	55
Flow rate:	1 mL/minute		
Temperature:	22°C		
Detection:	UV absorbance of the eluent was monitored at 254 nm using an Agilent G1314A or G1314B absorbance detector. Radioactivity in the eluent was monitored using a β-ram flow through radioactivity monitor (LabLogic) equipped with a liquid mixing (500 µL) cell using Ultima-Flo™ M (3 mL/min) as liquid scintillant.		

The following method was used for sample analysis:

Method 2:

Column: Sumipax ODS A-212 , 150 x 6 mm, 5 µm

Gradient:
Solvent A: 0.1% Acetic acid in water
Solvent B: Acetonitrile
Solvent C: Methanol

Time (minutes)	% A	% B	% C
0	95	5	0
15	60	40	0
45	0	50	50
50	0	50	50
51	95	5	0
65	95	5	0

Flow rate: 1 mL/minute

Temperature 30°C

Detection: UV absorbance of the eluent was monitored at 254 nm using an Agilent G1314A or G1314B absorbance detector. Radioactivity in the eluent was monitored using a β-ram flow through radioactivity monitor equipped with a liquid mixing cell (500 µL) with Ultima-Flo™ M (3 mL/min) as liquid scintillant.

The following method was used for isomer ratio determinations:

Method 3:

Column: Chiralpak AD-RH , 150 x 4.6 mm, 5 µm

Gradient:
Solvent A: Water
Solvent B: Acetonitrile

Time (minutes)	% A	% B
0	50	50
30	50	50

Flow rate: 0.5 or 1.0 mL/minute

Temperature: 22°C

Detection: UV absorbance of the eluent was monitored at 254 nm using an Agilent G1314A or G1314B absorbance detector. Radioactivity in the eluent was monitored using a β-ram flow through radioactivity monitor equipped with a liquid mixing cell (500 µL) with Ultima-Flo™ M (3 mL/min) as liquid scintillant.

The following method was used for test substance repurification and separation of metabolites De-Xy-S-2200 and DX-CA-S-2200:

Method 4:

Column: Sumipax ODS , 150 x 6 mm, 5 µm

Gradient:
Solvent A: 0.05% Formic acid
Solvent B: Acetonitrile
Solvent C: Methanol

Time (minutes)	% A	% B	%C
0	95	5	0
10	75	25	0
40	0	50	50
45	0	50	50
46	95	5	0
50	95	5	0

Flow rate: 1.0 mL/minute

Temperature: 30°C

Detection: UV absorbance of the eluent was monitored at 254 nm using a Shimadzu SPD-10 or an Agilent G1314A or G1314B absorbance detector. Radioactivity in the eluent was monitored using a β-ram flow through radioactivity monitor equipped with a liquid mixing cell (500 µL) with Ultima-Flo™ M (3 mL/min) as liquid scintillant.

Chromatograms were evaluated using Laura (version 3) software (LabLogic).

TLC

The following 1-D TLC method was used for the determination of radiochemical purity:

TLC System 1

Plates:	Whatman K6F Silica Gel
Solvent:	Chloroform:methanol (50:1 v/v)

The following 2-D TLC method was used for sample extract analysis:

TLC System 2

Plates:	Whatman K6F Silica Gel
Solvent first dimension:	Chloroform:methanol (9:1 v/v)
Solvent second dimension:	Ethyl acetate:toluene:acetic acid (7:5:1 v/v/v)

Extracts were co-chromatographed with appropriate non-radiolabelled standards. Following chromatography, radiolabelled compounds were detected by preparation of a radioluminogram of the TLC plate using a Fuji BAS 1500 Bio-image analyser and non-radiolabelled compounds were visualised by irradiation with UV light at 254 nm. Chromatograms were evaluated from the radioluminograms using the associated software (Tina version 2.09g).

Radioactivity

The radioactivity in samples and traps was determined by measuring the total sample weight and assaying duplicate aliquots by LSC. Weighed portions of these samples were added directly to scintillant (5 mL) prior to LSC quantification.

Following extraction, air-dried soil samples were ground and sub-sampled (*ca* 0.2 g) in triplicate prior to combustion in oxygen using a Harvey Biological Sample Oxidiser, models OX-300 and OX-500. The combusted products were absorbed in Permafluor® E+ and Carbo-Sorb® E (2:1 v/v) and the radioactivity absorbed was determined by LSC. Carbon-14 standards were combusted at the beginning and at regular intervals throughout the day to check the carry-over between samples and to determine the efficiency of the combustion process. Combustion and trapping efficiencies were 99 ± 3% and therefore no correction factors were applied to the reported data.

Radioactivity was measured using a Packard Tricarb model 1900TR or 2900TR liquid scintillation counter with facilities for computing quench corrected disintegrations per minute (dpm).

Efficiency correlation curves were routinely checked by the use of commercially available quenched standards (Perkin Elmer Life and Analytical Sciences) quenched over the range observed in test samples. The limit of detection was taken as 1.5 times the background radioactivity determined by counting samples containing no radioactivity in the same batch as the samples.

Calculations

Determination of Percent of Applied Radioactivity in Samples

Total radioactivity (kBq) applied to incubation unit (1 kBq = 60 x 10^3 dpm)	=	T
Initial sample weight (g)	=	I
Sub-sample weight (g)	=	SS
Total weight of sample for LSC assay (g)	=	A
Weight (g) of aliquots assayed by LSC	=	W
Background corrected radioactivity (dpm) in aliquots assayed by LSC	=	D
Concentration (dpm/g) of radioactivity in sample (C)	=	D/W

The individual estimates of concentration derived from the duplicate or triplicate aliquots were averaged to provide a mean concentration of radioactivity in the sample.

Radioactivity (kBq) in assayed sample (B)	=	C x A / 60,000
Percent of applied radioactivity represented by sample (X)	=	B/T x I/SS x 100%

Determination of Percent of Applied Radioactivity Present as Parent Test Substance and Degradation Products

Percent of applied radioactivity present in sample	=	X
Percent of radioactivity applied to HPLC column or TLC plate evaluated as parent compound or degradation product	=	Y
Percent of applied radioactivity present as parent compound or degradation product	=	X x Y / 100

The limit of detection for HPLC was < *ca* 0.1% of applied radioactivity.

Determination of Concentration

Concentrations of test substances and individual extracted degradation products are based upon 50 g dry weight equivalents of soil and application rates of 39.759, 39.904 or 39.513 µg S-2167 (100% in soil is therefore 0.795, 0.798 or 0.790 µg/g, respectively). Results are expressed as mg equivalents of S-2167 per kg dry weight equivalents of soil.

Determination of DT-50, DT-75 and DT-90

The percent of applied radioactivity present as test substance was plotted against the time after treatment in days. Curves were constructed through appropriate data points using non-linear regression analysis to give lines of best fit. The degradation rates of S-2167 were determined in each soil using single first-order (SFO) kinetics.
The following equation was used:

SFO: $$y = C_o \times e^{-kt}$$

Where y is the percent of test substance at time t days, C_0 is the computed initial concentration and k is the rate constant (slope). The DT-75 was calculated as twice the DT-50 for the SFO model.

All calculations were performed using KinGUI version 1.1 software.

Expression of Results

All tabulated values of percent of applied radioactivity values have been expressed to one decimal place. The tables have been computer generated and data values displayed are rounded values of those held in memory. As a result of the calculation of mean and total values from individual values, data presented in the report will, in some instances, yield a minor variation in the value.

Percent values in the text are expressed as a percent of applied radioactivity. Centrifugal force values (*g*) are approximations only.

Volumes referred to in the text are approximate volumes only. For determination of radioactivity, liquid samples were accurately weighed and accurately weighed aliquots were removed for LSC.

RESULTS

The route and rate of degradation of [benzyl-^{14}C]S-2167 and [phenoxy-^{14}C]S-2167 was studied in one aerobic soil (Speyer 5M) and the rate of degradation of [benzyl-^{14}C]S-2167 was studied in three other aerobic soils (Speyer 2.2, SK920191, Chelmorton), following treatment with radiolabelled test substance.

The tests using the Speyer 2.2 and Chelmorton soils were repeated due to low biomass values (< 1% organic carbon) having been observed for these two soils. Fresh batches of soil were obtained for the repeat test. The methods and results for the repeat tests only are reported for these two soils.

Recovery and Distribution of Applied Radioactivity

The recovery and distribution of the applied radioactivity are shown in Table 1 to Table 5 and in Figure 1 to Figure 5. All percent values described in this results section are mean values unless otherwise stated.

The mean recovery of applied radioactivity for the samples treated with [^{14}C]S-2167, ranged from 94 to 102%. Initially, almost all the radioactivity was extracted (maximum 0.3% unextracted) but recovery in the extracts decreased to 40 to 84% of applied radioactivity at 120 DAT. Between 7 and 33% remained unextracted at 120 DAT.

At 120 DAT, between 4 and 25% applied radioactivity was in the sodium hydroxide traps. The radioactivity in the sodium hydroxide traps for all incubation groups, (except the Speyer 2.2 soil, for which only 4% applied radioactivity was detected as carbon dioxide) was confirmed as carbon dioxide by barium chloride precipitation. There was no detectable radioactivity found in the ethanediol and paraffin in xylene traps.

The distribution of the applied radioactivity in the representative 120 DAT sample bound residue fractionations is shown in the table below:

Soil	Treatment	Percent of applied radioactivity present in		
		Fulvic Acid	Humic Acid	Humin
Speyer 5M	[Benzyl-^{14}C]	10.7	6.2	13.1
Speyer 5M	[Phenoxy-^{14}C]	7.0	5.6	10.0
SK920191	[Benzyl-^{14}C]	8.6	5.6	21.9
Chelmorton	[Benzyl-^{14}C]	7.6	5.6	6.2

Degradation of [^{14}C]S-2167

The percent of applied radioactivity present as [^{14}C]S-2167 and its metabolites are presented in Table 6 to Table 10. The concentrations of [^{14}C]S-2167 and its metabolites are presented in Table 11 to Table 15. Example chromatograms are shown in Figure 6 to Figure 21. The percent of [^{14}C]S-2167 and its metabolites described in this results section are mean values. The rates of degradation and residual errors are illustrated graphically in Figure 22 to Figure 27 and the proposed degradation route is presented in Figure 28.

The percent applied radioactivity present as [^{14}C]S-2167 decreased from between 92 and 99% at 0 DAT to between 23 and 64% at 120 DAT.

The metabolite 5-COOH-S-2200 was detected as a major metabolite which was present at ≥ 5% applied radioactivity in at least two sequential measurements or at ≥ 10% applied radioactivity in all soils. The metabolite 2-COOH-S-2200 accounted for ≥ 5% applied radioactivity in three sequential measurements in SK9020191 soil and ≥ 5% applied radioactivity in Speyer 5M soil at 59 DAT. The metabolite DX-CA-S-2200 was detected at a maximum of 3.3% applied radioactivity in Speyer 2.2 soil.

The metabolite De-Xy-S-2200 was not detected by additional chromatographic analysis (HPLC and TLC) of representative soil extracts.

All other metabolites, including MCBX and unknown metabolites, individually accounted for less than 3% applied radioactivity. A metabolite, tentatively identified as 2,5-dimethylphenol, was detected at very low levels at 120 DAT for the Speyer 5M soil.

No [^{14}C]S-2354 (S-2200 *S*-isomer) was detected in representative soil extracts.

The presence of the known metabolites, excluding 2, 5-dimethylphenol, was confirmed by TLC analysis.

Rate of Degradation

The rates of degradation of [^{14}C]S-2167 in soil are summarised in the table below:

Soil	Treatment	Kinetics	DT-50 (days)	DT-75 (days)	DT-90 (days)	χ^2	R^2
Speyer 5M	[Benzyl-^{14}C]	SFO	53.4	106.7	177.3	4.18	0.9807
Speyer 5M	[Phenoxy-^{14}C]	SFO	84.1	168.2	279.4	3.53	0.9659
Speyer 5M	[Benzyl-^{14}C]/ [Phenoxy-^{14}C]	SFO	66.5	133.1	221.0	2.87	0.9474
Speyer 2.2	[Benzyl-^{14}C]	SFO	227.1	454.2	754.4	4.04	0.8278
SK920191	[Benzyl-^{14}C]	SFO	50.6	101.1	167.9	5.26	0.9697
Chelmorton	[Benzyl-^{14}C]	SFO	102.1	204.2	339.2	8.18	0.8335

Note: DT-75 was calculated as twice the DT-50.

Route of Degradation

S-2167 degraded mainly to 2-COOH-S-2200, 5-COOH-S-2200, DX-CA-S-2200 carbon dioxide and bound residues.

CONCLUSIONS

S-2167 was metabolised mainly to carbon dioxide (maximum 25% of applied radioactivity), bound residues and three other metabolites 2-COOH-S-2200, 5-COOH-S-2200 and DX-CA-S-2200. No isomerisation of S-2167 occurred. DT-50 and DT-90 values were in the range 51 to 227 days and 168 to 754 days, respectively, for SFO kinetics.

TABLES

Table 1
Percent recovery of applied radioactivity from soil Speyer 5M following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	Primary Soil Extract	Secondary Soil Extract	Unextracted from Soil	Total in soil	Ethanediol Trap	Paraffin in Xylene Trap	Sodium Hydroxide Traps	Total Volatiles	Mass Balance
A1	0	100.5	0.7	0.2	101.4	NA	NA	NA	NA	101.4
A2	0	98.5	0.7	0.2	99.4	NA	NA	NA	NA	99.4
Mean		**99.5**	**0.7**	**0.2**	**100.4**	**NA**	**NA**	**NA**	**NA**	**100.4**
A3	7	96.0	3.1	2.7	101.8	ND	ND	0.8	0.8	102.6
A4	7	96.2	2.4	2.4	101.0	ND	ND	0.9	0.9	101.9
Mean		**96.1**	**2.8**	**2.6**	**101.4**	**ND**	**ND**	**0.9**	**0.9**	**102.3**
A5	14	93.3	2.9	3.7	99.9	ND	ND	1.7	1.7	101.6
A6	14	93.0	3.0	3.9	99.9	ND	ND	1.6	1.6	101.5
Mean		**93.2**	**3.0**	**3.8**	**99.9**	**ND**	**ND**	**1.7**	**1.7**	**101.6**
A7	30	82.3	5.3	7.7	95.3	ND	ND	3.9	3.9	99.2
A8	30	84.1	5.0	6.6	95.7	ND	ND	3.5	3.5	99.2
Mean		**83.2**	**5.2**	**7.2**	**95.5**	**ND**	**ND**	**3.7**	**3.7**	**99.2**
A9	59	67.3	2.1	17.9	87.3	ND	ND	12.2	12.2	99.5
A10	59	63.8	2.1	19.1	85.0	ND	ND	5.7	5.7	90.7
Mean		**65.6**	**2.1**	**18.5**	**86.2**	**ND**	**ND**	**9.0**	**9.0**	**95.1**
A11	120	36.6	5.5	29.0	71.1	ND	ND	24.4	24.4	95.5
A12	120	36.0	5.7	29.4	71.1	ND	ND	25.8	25.8	96.9
Mean		**36.3**	**5.6**	**29.2**	**71.1**	**ND**	**ND**	**25.1**	**25.1**	**96.2**

NA = Not Applicable
ND = Not Detected or < 0.1%

Table 2
Percent recovery of applied radioactivity from soil Speyer 5M following application of [phenoxy-^{14}C]S-2167

Unit	Sampling Interval (days)	Primary Soil Extract	Secondary Soil Extract	Unextracted from Soil	Total in soil	Ethanediol Trap	Paraffin in Xylene Trap	Sodium Hydroxide Traps	Total Volatiles	Mass Balance
B1	0	99.9	0.8	0.2	100.9	NA	NA	NA	NA	100.9
B2	0	98.3	0.8	0.2	99.3	NA	NA	NA	NA	99.3
Mean		**99.1**	**0.8**	**0.2**	**100.1**	**NA**	**NA**	**NA**	**NA**	**100.1**
B3	7	92.8	3.2	3.2	99.2	ND	ND	0.7	0.7	99.9
B4	7	95.0	3.1	3.2	101.3	ND	ND	0.5	0.5	101.8
Mean		**93.9**	**3.2**	**3.2**	**100.3**	**ND**	**ND**	**0.6**	**0.6**	**100.9**
B5	14	89.5	2.9	4.3	96.7	ND	ND	1.5	1.5	98.2
B6	14	90.2	3.0	4.5	97.7	ND	ND	1.5	1.5	99.2
Mean		**89.9**	**3.0**	**4.4**	**97.2**	**ND**	**ND**	**1.5**	**1.5**	**98.7**
B7	30	83.5	5.1	6.4	95.0	ND	ND	2.5	2.5	97.5
B8	30	83.3	5.3	7.1	95.7	ND	ND	3.3	3.3	99.0
Mean		**83.4**	**5.2**	**6.8**	**95.4**	**ND**	**ND**	**2.9**	**2.9**	**98.3**
B9	59	67.5	8.7	13.6	89.8	ND	ND	8.3	8.3	98.1
B10	59	74.9	5.3	11.6	91.8	ND	ND	5.1	5.1	96.9
Mean		**71.2**	**7.0**	**12.6**	**90.8**	**ND**	**ND**	**6.7**	**6.7**	**97.5**
B11	120	44.4	6.6	22.1	73.1	ND	ND	21.7	21.7	94.8
B12	120	51.1	7.2	20.4	78.7	ND	ND	17.5	17.5	96.2
Mean		**47.8**	**6.9**	**21.3**	**75.9**	**ND**	**ND**	**19.6**	**19.6**	**95.5**

NA = Not Applicable
ND = Not Detected or < 0.1%

Table 3
Percent recovery of applied radioactivity from Speyer 2.2 soil following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	Primary Soil Extract	Secondary Soil Extract	Unextracted from Soil	Total in soil	Ethanediol Trap	Paraffin in Xylene Trap	Sodium Hydroxide Traps	Total Volatiles	Mass Balance
C101	0	95.9	0.8	0.1	96.8	NA	NA	NA	NA	96.8
C102	0	98.0	0.9	ND	98.9	NA	NA	NA	NA	98.9
Mean		**97.0**	**0.9**	**0.1**	**97.9**	**NA**	**NA**	**NA**	**NA**	**97.9**
C103	7	87.6	3.5	2.1	93.2	ND	ND	1.6	1.6	94.8
C104	7	90.2	3.5	2.0	95.7	ND	ND	1.0	1.0	96.7
Mean		**88.9**	**3.5**	**2.1**	**94.5**	**ND**	**ND**	**1.3**	**1.3**	**95.8**
C105	14	84.7	4.6	3.2	92.5	ND	ND	2.6	2.6	95.1
C106	14	86.4	4.6	2.9	93.9	ND	ND	1.9	1.9	95.8
Mean		**85.6**	**4.6**	**3.1**	**93.2**	**ND**	**ND**	**2.3**	**2.3**	**95.5**
C107	30	84.3	5.7	3.4	93.4	ND	ND	3.1	3.1	96.5
C108	30	84.7	6.1	3.3	94.1	ND	ND	2.5	2.5	96.6
Mean		**84.5**	**5.9**	**3.4**	**93.8**	**ND**	**ND**	**2.8**	**2.8**	**96.6**
C109	61	80.4	8.0	4.2	92.6	ND	ND	2.2	2.2	94.8
C110	61	76.7	9.0	4.7	90.4	ND	ND	2.9	2.9	93.3
Mean		**78.6**	**8.5**	**4.5**	**91.5**	**ND**	**ND**	**2.6**	**2.6**	**94.1**
C111	120	72.7	10.6	6.8	90.1	ND	ND	4.7	4.7	94.8
C112	120	73.2	10.7	6.6	90.5	ND	ND	3.6	3.6	94.1
Mean		**73.0**	**10.7**	**6.7**	**90.3**	**ND**	**ND**	**4.2**	**4.2**	**94.5**

NA = Not Applicable
ND = Not Detected or < 0.1%

Table 4
Percent recovery of applied radioactivity from SK920191 soil following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	Primary Soil Extract	Secondary Soil Extract	Unextracted from Soil	Total in soil	Ethanediol Trap	Paraffin in Xylene Trap	Sodium Hydroxide Traps	Total Volatiles	Mass Balance
D1	0	98.2	1.1	0.2	99.5	NA	NA	NA	NA	99.5
D2	0	98.7	1.3	0.3	100.3	NA	NA	NA	NA	100.3
Mean		**98.5**	**1.2**	**0.3**	**99.9**	**NA**	**NA**	**NA**	**NA**	**99.9**
D3	7	91.1	4.6	4.3	100.0	ND	ND	1.1	1.1	101.1
D4	7	90.7	4.7	4.5	99.9	ND	ND	1.0	1.0	100.9
Mean		**90.9**	**4.7**	**4.4**	**100.0**	**ND**	**ND**	**1.1**	**1.1**	**101.0**
D5	14	85.2	5.4	6.7	97.3	ND	ND	1.5	1.5	98.8
D6	14	87.3	3.5	6.9	97.7	ND	ND	2.0	2.0	99.7
Mean		**86.3**	**4.5**	**6.8**	**97.5**	**ND**	**ND**	**1.8**	**1.8**	**99.3**
D7	30	68.3	8.6	15.4	92.3	ND	ND	6.4	6.4	98.7
D8	30	74.1	9.6	11.2	94.9	ND	ND	3.3	3.3	98.2
Mean		**71.2**	**9.1**	**13.3**	**93.6**	**ND**	**ND**	**4.9**	**4.9**	**98.5**
D9	59	59.7	9.4	20.9	90.0	ND	ND	6.4	6.4	96.4
D10	59	62.0	9.0	19.2	90.2	ND	ND	7.8	7.8	98.0
Mean		**60.9**	**9.2**	**20.1**	**90.1**	**ND**	**ND**	**7.1**	**7.1**	**97.2**
D11	120	28.0	6.3	35.3	69.6	ND	ND	26.2	26.2	95.8
D12	120	37.8	7.8	31.1	76.7	ND	ND	20.1	20.1	96.8
Mean		**32.9**	**7.1**	**33.2**	**73.2**	**ND**	**ND**	**23.2**	**23.2**	**96.3**

NA = Not Applicable
ND = Not Detected or < 0.1%

Table 5
Percent recovery of applied radioactivity from Chelmorton soil following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	Primary Soil Extract	Secondary Soil Extract	Unextracted from Soil	Total in soil	Ethanediol Trap	Paraffin in Xylene Trap	Sodium Hydroxide Traps	Total Volatiles	Mass Balance
E101	0	93.9	1.4	0.2	95.5	NA	NA	NA	NA	95.5
E102	0	92.9	1.4	0.2	94.5	NA	NA	NA	NA	94.5
Mean		**93.4**	**1.4**	**0.2**	**95.0**	**NA**	**NA**	**NA**	**NA**	**95.0**
E103	7	81.3	5.2	6.9	93.4	ND	ND	3.2	3.2	96.6
E104	7	78.5	5.3	6.7	90.5	ND	ND	3.2	3.2	93.7
Mean		**79.9**	**5.3**	**6.8**	**92.0**	**ND**	**ND**	**3.2**	**3.2**	**95.2**
E105	14	72.8	5.7	10.4	88.9	ND	ND	5.8	5.8	94.7
E106	14	72.8	5.7	10.3	88.8	ND	ND	5.6	5.6	94.4
Mean		**72.8**	**5.7**	**10.4**	**88.9**	**ND**	**ND**	**5.7**	**5.7**	**94.6**
E107	30	61.6	7.7	14.9	84.2	ND	ND	9.3	9.3	93.5
E108	30	63.1	8.2	14.0	85.3	ND	ND	9.8	9.8	95.1
Mean		**62.4**	**8.0**	**14.5**	**84.8**	**ND**	**ND**	**9.6**	**9.6**	**94.3**
E109	61	56.8	9.5	16.3	82.6	ND	ND	10.9	10.9	93.5
E110	61	56.6	9.9	16.3	82.8	ND	ND	11.3	11.3	94.1
Mean		**56.7**	**9.7**	**16.3**	**82.7**	**ND**	**ND**	**11.1**	**11.1**	**93.8**
E111	120	48.2	13.1	18.6	79.9	ND	ND	13.8	13.8	93.7
E112	120	46.0	14.1	19.3	79.4	ND	ND	14.9	14.9	94.3
Mean		**47.1**	**13.6**	**19.0**	**79.7**	**ND**	**ND**	**14.4**	**14.4**	**94.0**

NA = Not Applicable
ND = Not Detected or < 0.1%

Table 6
Percent recovery of applied radioactivity present as S-2167 and its metabolites in Speyer 5M soil extracts following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	De-Xy-S-2200 / DX-CA-S-2200 †	Unk A	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
A1	0	99.4	ND	ND	ND	ND	ND	ND	ND	1.1	100.5	ND
A2	0	98.4	ND	ND	ND	ND	ND	ND	ND	0.1	98.5	ND
Mean		**98.9**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**0.6**	**99.5**	**ND**
A3	7	89.2	ND	3.9	2.2	ND	ND	ND	ND	0.7	96.0	ND
A4	7	89.1	ND	3.3	2.0	ND	ND	ND	ND	1.8	96.2	ND
Mean		**89.1**	**ND**	**3.6**	**2.1**	**ND**	**ND**	**ND**	**ND**	**1.3**	**96.1**	**ND**
A5	14	82.0	ND	6.5	3.5	ND	ND	ND	ND	1.3	93.3	ND
A6	14	81.4	ND	6.3	3.2	ND	ND	0.6	ND	1.6	93.0	ND
Mean		**81.7**	**ND**	**6.4**	**3.3**	**ND**	**ND**	**0.3**	**ND**	**1.4**	**93.1**	**ND**
A7*	30	69.6	ND	11.3	4.6	0.5	ND	0.9	ND	0.6	87.6	ND
A8*	30	72.4	ND	10.4	4.8	0.6	ND	0.8	ND	0.1	89.1	ND
Mean		**71.0**	**ND**	**10.9**	**4.7**	**0.6**	**ND**	**0.8**	**ND**	**0.4**	**88.4**	**ND**
A9	59	41.9	ND	16.6	5.7	0.6	0.4	0.7	ND	1.1	67.3	0.3
A10	59	36.9	ND	17.3	5.7	0.4	0.7	0.6	0.4	1.2	63.8	0.6
Mean		**39.4**	**ND**	**16.9**	**5.7**	**0.5**	**0.6**	**0.7**	**0.2**	**1.2**	**65.6**	**0.4**
A11*	120	24.8	ND	11.4	3.6	0.3	0.2	0.4	0.5	0.1	42.1	0.8
A12*	120	24.5	ND	11.7	3.5	0.1	0.3	0.3	0.3	0.1	41.7	0.9
Mean		**24.6**	**ND**	**11.6**	**3.6**	**0.2**	**0.3**	**0.3**	**0.4**	**0.1**	**41.9**	**0.8**

ND = Not Detected or < 0.1%
* Includes acetone:0.1 M HCl (5:1, v/v) extract.
† Only DX-CA-S-2200 was found by further chromatographic analysis of a representative soil extract.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 7
Percent recovery of applied radioactivity present as S-2167 and its metabolites in Speyer 5M soil extracts following application of [phenoxy-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	Unk A	2,5-dimethyl phenol	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
B1	0	99.9	ND	ND	ND	ND	ND	ND	ND	ND	99.9	ND
B2	0	96.4	ND	ND	ND	ND	ND	ND	ND	1.9	98.3	ND
Mean		**98.1**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**1.0**	**99.1**	**ND**
B3	7	86.1	ND	3.8	2.0	ND	ND	ND	ND	1.0	92.8	ND
B4	7	86.8	ND	4.0	2.1	ND	0.4	ND	ND	1.8	95.0	ND
Mean		**86.4**	**ND**	**3.9**	**2.0**	**ND**	**0.2**	**ND**	**ND**	**1.4**	**93.9**	**ND**
B5	14	78.0	ND	6.5	3.7	ND	0.5	ND	ND	0.8	89.5	ND
B6	14	76.8	ND	7.4	3.8	0.3	0.5	ND	ND	1.5	90.2	ND
Mean		**77.4**	**ND**	**6.9**	**3.7**	**0.1**	**0.5**	**ND**	**ND**	**1.1**	**89.9**	**ND**
B7*	30	73.3	ND	8.8	4.8	ND	ND	ND	ND	1.8	88.6	ND
B8*	30	72.4	ND	10.0	5.0	ND	ND	ND	ND	1.3	88.6	ND
Mean		**72.8**	**ND**	**9.4**	**4.9**	**ND**	**ND**	**ND**	**ND**	**1.5**	**88.6**	**ND**
B9*	59	55.0	ND	14.9	5.4	ND	ND	ND	ND	0.1	76.2	0.8
B10*	59	61.8	ND	10.5	5.5	0.5	ND	ND	ND	1.2	80.2	0.8
Mean		**58.4**	**ND**	**12.7**	**5.4**	**0.2**	**ND**	**ND**	**ND**	**0.6**	**78.2**	**0.8**
B11*	120	32.3	ND	12.2	5.1	0.3	0.3	0.1	0.1	0.4	51.0	0.2
B12*	120	38.3	ND	12.8	4.8	0.3	0.5	0.3	ND	0.6	57.7	0.2
Mean		**35.3**	**ND**	**12.5**	**4.9**	**0.3**	**0.4**	**0.2**	**0.1**	**0.5**	**54.4**	**0.2**

ND = Not Detected or < 0.1%
* Includes acetone:0.1 M HCl (5:1, v/v) extract.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 8
Percent recovery of applied radioactivity present as S-2167 and its metabolites in Speyer 2.2 soil extracts following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	De-Xy-S-2200 / DX-CA-S-2200 †	Unk A	Unk B	Unk C	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
C101	0	94.1	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.8	95.9	ND
C102	0	96.3	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.7	98.0	ND
Mean		**95.2**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**1.8**	**97.0**	**ND**
C103	7	81.8	ND	3.5	1.0	ND	ND	0.4	ND	0.3	ND	0.6	87.6	ND
C104	7	84.7	ND	3.1	0.8	ND	ND	ND	ND	ND	ND	1.6	90.2	ND
Mean		**83.2**	**ND**	**3.3**	**0.9**	**ND**	**ND**	**0.2**	**ND**	**0.2**	**ND**	**1.1**	**88.9**	**ND**
C105*	14	80.2	ND	5.5	1.4	ND	0.7	0.4	0.3	ND	0.1	0.6	89.3	0.2
C106*	14	80.4	ND	5.8	1.6	0.3	0.2	0.5	0.6	ND	ND	1.5	91.0	0.1
Mean		**80.3**	**ND**	**5.6**	**1.5**	**0.2**	**0.5**	**0.5**	**0.5**	**ND**	**ND**	**1.0**	**90.2**	**0.1**
C107*	30	80.4	ND	6.0	1.6	ND	0.7	0.3	0.7	ND	ND	0.2	90.0	0.2
C108*	30	79.6	ND	6.3	2.1	ND	0.9	0.3	0.8	ND	ND	0.9	90.8	ND
Mean		**80.0**	**ND**	**6.1**	**1.8**	**ND**	**0.8**	**0.3**	**0.8**	**ND**	**ND**	**0.6**	**90.4**	**0.1**
C109*	61	71.9	ND	5.3	1.8	ND	3.5	0.1	2.7	ND	1.2	1.1	88.4	0.9
C110*	61	67.4	ND	6.1	2.4	0.6	3.4	0.6	2.6	ND	1.0	0.7	85.7	0.9
Mean		**69.6**	**ND**	**5.7**	**2.1**	**0.3**	**3.5**	**0.3**	**2.6**	**ND**	**1.1**	**0.9**	**87.0**	**0.9**
C111*	120	64.5	ND	4.6	2.5	0.5	4.9	0.6	2.8	ND	0.2	1.4	83.3	1.4
C112*	120	63.2	ND	5.1	3.0	0.6	5.1	0.6	2.9	0.2	0.8	0.8	83.9	1.6
Mean		**63.8**	**ND**	**4.9**	**2.8**	**0.6**	**5.0**	**0.6**	**2.8**	**0.1**	**0.5**	**1.1**	**83.6**	**1.5**

ND = Not Detected or < 0.1%
* Includes acetone:0.1 M HCl (5:1, v/v) extract
† DX-CA-S-2200 (maximum 3.3%) and other unknown metabolites were found by further chromatographic analysis of representative soil extracts. De-Xy-S-2200 was not detected.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 9
Percent recovery of applied radioactivity present as S-2167 and its metabolites in SK920191 soil extracts following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	De-Xy-S-2200 / DX-CA-S-2200 †	Unk A	Unk B	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
D1	0	98.2	ND	ND	ND	ND	ND	ND	ND	ND	ND	98.2	ND
D2	0	95.3	ND	ND	ND	ND	ND	ND	ND	ND	3.4	98.7	ND
Mean		**96.7**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**1.7**	**98.5**	**ND**
D3*	7	80.1	ND	9.8	4.1	ND	ND	0.3	ND	ND	1.4	95.7	ND
D4*	7	81.3	ND	9.0	4.5	ND	ND	ND	ND	ND	0.6	95.4	ND
Mean		**80.7**	**ND**	**9.4**	**4.3**	**ND**	**ND**	**0.2**	**ND**	**ND**	**1.0**	**95.5**	**ND**
D5*	14	70.2	ND	12.7	6.6	0.2	ND	0.3	ND	ND	0.6	90.6	ND
D6*	14	71.0	ND	12.8	5.8	ND	ND	ND	ND	ND	1.2	90.8	ND
Mean		**70.6**	**ND**	**12.7**	**6.2**	**0.1**	**ND**	**0.2**	**ND**	**ND**	**0.9**	**90.7**	**ND**
D7*	30	53.2	ND	16.2	6.6	0.3	ND	0.4	ND	ND	0.3	76.9	ND
D8*	30	59.0	ND	15.6	7.8	0.5	0.3	ND	ND	ND	0.6	83.7	ND
Mean		**56.1**	**ND**	**15.9**	**7.2**	**0.4**	**0.1**	**0.2**	**ND**	**ND**	**0.4**	**80.3**	**ND**
D9*	59	39.4	ND	15.8	7.9	ND	ND	ND	ND	ND	6.0	69.1	ND
D10*	59	42.9	ND	18.0	9.2	ND	ND	ND	ND	ND	0.9	71.0	ND
Mean		**41.2**	**ND**	**16.9**	**8.6**	**ND**	**ND**	**ND**	**ND**	**ND**	**3.4**	**70.0**	**ND**
D11*	120	20.3	ND	10.4	2.2	0.2	ND	0.1	0.1	0.1	0.3	34.3	0.7
D12*	120	24.6	ND	12.6	4.5	0.2	ND	0.1	ND	0.2	0.1	45.6	3.2
Mean		**22.5**	**ND**	**11.5**	**3.3**	**0.2**	**ND**	**0.1**	**ND**	**0.1**	**0.2**	**39.9**	**1.9**

ND = Not Detected or < 0.1%
* Includes acetone:0.1 M HCl (5:1, v/v) extract.
† De-Xy-S-2200 and DX-CA-S-2200 not detected by further chromatographic analysis of a representative soil extract due to low levels of radioactivity.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 10
Percent recovery of applied radioactivity present as S-2167 and its metabolites in Chelmorton soil extracts following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	De-Xy-S-2200 / DX-CA-S-2200 †	Unk A	Unk B	Unk C	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
E101	0	92.7	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.2	93.9	ND
E102	0	91.4	ND	ND	ND	ND	ND	ND	ND	ND	ND	1.5	92.9	ND
Mean		**92.1**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**1.3**	**93.4**	**ND**
E103*	7	77.2	ND	4.6	3.3	ND	0.2	0.3	ND	ND	ND	0.8	86.5	0.1
E104*	7	75.1	ND	4.9	3.0	ND	0.2	0.4	ND	ND	ND	0.2	83.8	ND
Mean		**76.1**	**ND**	**4.8**	**3.2**	**ND**	**0.2**	**0.4**	**ND**	**ND**	**ND**	**0.5**	**85.1**	**0.1**
E105*	14	68.3	ND	5.3	3.0	0.3	0.1	0.7	0.1	0.4	0.1	0.1	78.5	0.1
E106*	14	67.5	ND	5.4	3.3	0.4	0.2	0.6	0.1	ND	ND	1.1	78.5	ND
Mean		**67.9**	**ND**	**5.3**	**3.1**	**0.4**	**0.1**	**0.7**	**0.1**	**0.2**	**ND**	**0.6**	**78.5**	**ND**
E107*	30	58.6	ND	6.0	3.4	ND	0.3	ND	ND	ND	ND	1.0	69.3	ND
E108*	30	59.8	ND	6.5	3.8	ND	0.3	ND	ND	ND	ND	0.9	71.3	ND
Mean		**59.2**	**ND**	**6.3**	**3.6**	**ND**	**0.3**	**ND**	**ND**	**ND**	**ND**	**0.9**	**70.3**	**ND**
E109*	61	50.2	ND	6.6	4.7	0.8	2.3	0.8	0.2	0.6	ND	0.1	66.3	0.1
E110*	61	50.4	ND	7.4	4.5	0.4	2.2	0.8	0.2	0.3	ND	0.4	66.5	0.1
Mean		**50.3**	**ND**	**7.0**	**4.6**	**0.6**	**2.2**	**0.8**	**0.2**	**0.4**	**ND**	**0.2**	**66.4**	**0.1**
E111*	120	43.8	ND	6.8	4.6	0.6	3.0	0.7	0.2	0.7	ND	0.9	61.3	0.1
E112*	120	42.4	ND	7.8	4.9	0.2	3.1	0.7	0.1	0.5	0.1	0.1	60.1	0.1
Mean		**43.1**	**ND**	**7.3**	**4.8**	**0.4**	**3.1**	**0.7**	**0.1**	**0.6**	**0.1**	**0.5**	**60.7**	**0.1**

ND = Not Detected or < 0.1%
* Includes acetone:0.1 M HCl (5:1, v/v) extract.
† Only DX-CA-S-2200 was found by further chromatographic analysis of representative soil extracts.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 11
Concentration (mg a.i. eq./kg soil) of S-2167 and its metabolites in Speyer 5M soil extracts following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	De-Xy-S-2200 / DX-CA-S-2200 †	Unk A	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
A1	0	0.790	ND	ND	ND	ND	ND	ND	ND	0.009	0.799	ND
A2	0	0.782	ND	ND	ND	ND	ND	ND	ND	0.001	0.783	ND
Mean		**0.786**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**0.005**	**0.791**	**ND**
A3	7	0.709	ND	0.031	0.017	ND	ND	ND	ND	0.006	0.763	ND
A4	7	0.708	ND	0.026	0.016	ND	ND	ND	ND	0.015	0.765	ND
Mean		**0.709**	**ND**	**0.029**	**0.017**	**ND**	**ND**	**ND**	**ND**	**0.010**	**0.764**	**ND**
A5	14	0.652	ND	0.052	0.028	ND	ND	ND	ND	0.010	0.742	ND
A6	14	0.647	ND	0.050	0.025	ND	ND	0.004	ND	0.013	0.739	ND
Mean		**0.650**	**ND**	**0.051**	**0.026**	**ND**	**ND**	**0.002**	**ND**	**0.011**	**0.741**	**ND**
A7*	30	0.554	ND	0.090	0.037	0.004	ND	0.007	ND	0.005	0.696	ND
A8*	30	0.575	ND	0.083	0.038	0.004	ND	0.006	ND	0.001	0.708	ND
Mean		**0.564**	**ND**	**0.086**	**0.038**	**0.004**	**ND**	**0.006**	**ND**	**0.003**	**0.702**	**ND**
A9	59	0.333	ND	0.132	0.045	0.005	0.003	0.006	ND	0.009	0.535	0.003
A10	59	0.293	ND	0.137	0.045	0.003	0.005	0.005	0.003	0.010	0.507	0.004
Mean		**0.313**	**ND**	**0.135**	**0.045**	**0.004**	**0.004**	**0.005**	**0.002**	**0.009**	**0.521**	**0.004**
A11*	120	0.197	ND	0.091	0.029	0.002	0.002	0.003	0.004	0.001	0.335	0.006
A12*	120	0.195	ND	0.093	0.028	0.001	0.002	0.002	0.002	0.001	0.332	0.007
Mean		**0.196**	**ND**	**0.092**	**0.028**	**0.001**	**0.002**	**0.002**	**0.003**	**0.001**	**0.333**	**0.007**

ND = Not detected or < 0.001 mg/kg
* Includes acetone:0.1 M HCl (5:1, v/v) extract.
† Only DX-CA-S-2200 was found by further chromatographic analysis of a representative soil extract.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 12
Concentration (mg a.i. eq./kg soil) of S-2167 and its metabolites in Speyer 5M soil extracts following application of [phenoxy-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	Unk A	2,5-dimethyl phenol	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
B1	0	0.797	ND	ND	ND	ND	ND	ND	ND	0.000	0.797	ND
B2	0	0.769	ND	ND	ND	ND	ND	ND	ND	0.015	0.784	ND
Mean		**0.783**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**0.008**	**0.791**	**ND**
B3	7	0.687	ND	0.030	0.016	ND	ND	ND	ND	0.008	0.741	ND
B4	7	0.692	ND	0.032	0.016	ND	0.003	ND	ND	0.014	0.758	ND
Mean		**0.690**	**ND**	**0.031**	**0.016**	**ND**	**0.002**	**ND**	**ND**	**0.011**	**0.749**	**ND**
B5	14	0.622	ND	0.051	0.030	ND	0.004	ND	ND	0.006	0.714	ND
B6	14	0.613	ND	0.059	0.030	0.002	0.004	ND	ND	0.012	0.720	ND
Mean		**0.617**	**ND**	**0.055**	**0.030**	**0.001**	**0.004**	**ND**	**ND**	**0.009**	**0.717**	**ND**
B7*	30	0.585	ND	0.070	0.038	ND	ND	ND	ND	0.014	0.707	ND
B8*	30	0.578	ND	0.079	0.040	ND	ND	ND	ND	0.010	0.707	ND
Mean		**0.581**	**ND**	**0.075**	**0.039**	**ND**	**ND**	**ND**	**ND**	**0.012**	**0.707**	**ND**
B9*	59	0.439	ND	0.119	0.043	ND	ND	ND	ND	0.001	0.608	0.006
B10*	59	0.493	ND	0.084	0.044	0.004	ND	ND	ND	0.009	0.640	0.006
Mean		**0.466**	**ND**	**0.101**	**0.043**	**0.002**	**ND**	**ND**	**ND**	**0.005**	**0.624**	**0.006**
B11*	120	0.258	ND	0.098	0.040	0.002	0.002	0.001	0.001	0.003	0.407	0.002
B12*	120	0.305	ND	0.102	0.038	0.002	0.004	0.002	ND	0.004	0.460	0.002
Mean		**0.282**	**ND**	**0.100**	**0.039**	**0.002**	**0.003**	**0.001**	**ND**	**0.004**	**0.434**	**0.002**

ND = Not detected or < 0.001 mg/kg
* Includes acetone:0.1 M HCl (5:1, v/v) extract.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 13
Concentration (mg a.i. eq./kg soil) of S-2167 and its metabolites in Speyer 2.2 soil extracts following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	De-Xy-S-2200 / DX-CA-S-2200 †	Unk A	Unk B	Unk C	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
C101	0	0.744	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.014	0.758	ND
C102	0	0.761	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.014	0.774	ND
Mean		**0.752**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**0.014**	**0.766**	**ND**
C103	7	0.646	ND	0.027	0.008	ND	ND	0.003	ND	0.003	ND	0.005	0.692	ND
C104	7	0.670	ND	0.024	0.007	ND	ND	ND	ND	ND	ND	0.012	0.713	ND
Mean		**0.658**	**ND**	**0.026**	**0.007**	**ND**	**ND**	**0.002**	**ND**	**0.001**	**ND**	**0.009**	**0.702**	**ND**
C105*	14	0.633	ND	0.043	0.011	ND	0.006	0.003	0.003	ND	ND	0.005	0.706	0.001
C106*	14	0.635	ND	0.046	0.013	0.002	0.002	0.004	0.005	ND	ND	0.012	0.719	0.001
Mean		**0.634**	**ND**	**0.044**	**0.012**	**0.001**	**0.004**	**0.004**	**0.004**	**ND**	**ND**	**0.008**	**0.712**	**0.001**
C107*	30	0.635	ND	0.047	0.012	ND	0.006	0.002	0.006	ND	ND	0.002	0.711	0.002
C108*	30	0.629	ND	0.050	0.016	ND	0.007	0.002	0.006	ND	ND	0.007	0.717	ND
Mean		**0.632**	**ND**	**0.048**	**0.014**	**ND**	**0.006**	**0.002**	**0.006**	**ND**	**ND**	**0.005**	**0.714**	**0.001**
C109*	61	0.568	ND	0.042	0.014	ND	0.028	ND	0.021	ND	0.009	0.008	0.698	0.007
C110*	61	0.532	ND	0.049	0.019	0.005	0.027	0.005	0.020	ND	0.008	0.005	0.677	0.007
Mean		**0.550**	**ND**	**0.045**	**0.017**	**0.002**	**0.027**	**0.003**	**0.021**	**ND**	**0.009**	**0.007**	**0.688**	**0.007**
C111*	120	0.510	ND	0.036	0.020	0.004	0.039	0.005	0.022	ND	0.002	0.011	0.658	0.011
C112*	120	0.499	ND	0.040	0.024	0.005	0.040	0.004	0.023	0.002	0.007	0.006	0.663	0.013
Mean		**0.504**	**ND**	**0.038**	**0.022**	**0.004**	**0.039**	**0.004**	**0.022**	**0.001**	**0.004**	**0.009**	**0.660**	**0.012**

ND = Not detected or < 0.001 mg/kg
* Includes acetone:0.1 M HCl (5:1, v/v) extract
† Only DX-CA-S-2200 was found by further chromatographic analysis of representative soil extracts.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 14
Concentration (mg a.i. eq./kg soil) of S-2167 and its metabolites in SK920191 soil extracts following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	De-Xy-S-2200 / DX-CA-S-2200 †	Unk A	Unk B	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
D1	0	0.780	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.781	ND
D2	0	0.758	ND	ND	ND	ND	ND	ND	ND	ND	0.027	0.785	ND
Mean		**0.769**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**0.014**	**0.783**	**ND**
D3*	7	0.637	ND	0.078	0.033	ND	ND	0.003	ND	ND	0.011	0.761	ND
D4*	7	0.647	ND	0.071	0.036	ND	ND	ND	ND	ND	0.005	0.758	ND
Mean		**0.642**	**ND**	**0.075**	**0.034**	**ND**	**ND**	**0.001**	**ND**	**ND**	**0.008**	**0.760**	**ND**
D5*	14	0.558	ND	0.101	0.052	0.002	ND	0.003	ND	ND	0.005	0.720	ND
D6*	14	0.565	ND	0.102	0.046	ND	ND	ND	ND	ND	0.009	0.722	ND
Mean		**0.561**	**ND**	**0.101**	**0.049**	**0.001**	**ND**	**0.001**	**ND**	**ND**	**0.007**	**0.721**	**ND**
D7*	30	0.423	ND	0.128	0.052	0.002	ND	0.003	ND	ND	0.002	0.611	ND
D8*	30	0.469	ND	0.124	0.062	0.004	0.002	ND	ND	ND	0.005	0.665	ND
Mean		**0.446**	**ND**	**0.126**	**0.057**	**0.003**	**0.001**	**0.002**	**ND**	**ND**	**0.004**	**0.638**	**ND**
D9*	59	0.313	ND	0.125	0.063	ND	ND	ND	ND	ND	0.047	0.549	ND
D10*	59	0.341	ND	0.143	0.073	ND	ND	ND	ND	ND	0.007	0.564	ND
Mean		**0.327**	**ND**	**0.134**	**0.068**	**ND**	**ND**	**ND**	**ND**	**ND**	**0.027**	**0.557**	**ND**
D11*	120	0.161	ND	0.083	0.017	0.002	ND	0.001	ND	ND	0.002	0.273	0.005
D12*	120	0.196	ND	0.100	0.036	0.002	ND	0.001	ND	0.002	0.001	0.363	0.025
Mean		**0.179**	**ND**	**0.092**	**0.027**	**0.002**	**ND**	**0.001**	**ND**	**0.001**	**0.002**	**0.318**	**0.015**

ND = Not detected or < 0.001 mg/kg
* Includes acetone:0.1 M HCl (5:1, v/v) extract.
† De-Xy-S-2200 and DX-CA-S-2200 not detected by further chromatographic analysis of a representative soil extract due to low levels of radioactivity.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

Table 15
Concentration (mg a.i. eq./kg soil) of S-2167 and its metabolites in Chelmorton soil extracts following application of [benzyl-^{14}C]S-2167

Unit	Sampling Interval (days)	S-2167	S-2354 ‡	5-COOH-S-2200	2-COOH-S-2200	MCBX	De-Xy-S-2200 / DX-CA-S-2200 †	Unk A	Unk B	Unk C	Total Minor Unknowns	Unresolved Background	Total	Largest Other Unknown
E101	0	0.733	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.009	0.742	ND
E102	0	0.722	ND	ND	ND	ND	ND	ND	ND	ND	ND	0.012	0.734	ND
Mean		**0.728**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**ND**	**0.010**	**0.738**	**ND**
E103*	7	0.610	ND	0.036	0.026	ND	0.002	0.003	ND	ND	ND	0.006	0.684	0.001
E104*	7	0.593	ND	0.039	0.024	ND	0.001	0.003	ND	ND	ND	0.002	0.662	ND
Mean		**0.601**	**ND**	**0.038**	**0.025**	**ND**	**0.001**	**0.003**	**ND**	**ND**	**ND**	**0.004**	**0.673**	**ND**
E105*	14	0.540	ND	0.042	0.024	0.003	0.001	0.005	0.001	0.003	ND	0.001	0.620	ND
E106*	14	0.533	ND	0.043	0.026	0.003	0.001	0.005	0.001	ND	ND	0.008	0.620	ND
Mean		**0.537**	**ND**	**0.042**	**0.025**	**0.003**	**0.001**	**0.005**	**0.001**	**0.002**	**ND**	**0.005**	**0.620**	**ND**
E107*	30	0.463	ND	0.047	0.027	ND	0.003	ND	ND	ND	ND	0.008	0.548	ND
E108*	30	0.473	ND	0.052	0.030	ND	0.002	ND	ND	ND	ND	0.007	0.563	ND
Mean		**0.468**	**ND**	**0.049**	**0.028**	**ND**	**0.002**	**ND**	**ND**	**ND**	**ND**	**0.007**	**0.556**	**ND**
E109*	61	0.397	ND	0.052	0.037	0.006	0.018	0.006	0.001	0.004	ND	0.001	0.524	0.001
E110*	61	0.399	ND	0.058	0.035	0.003	0.017	0.006	0.001	0.002	ND	0.003	0.526	0.001
Mean		**0.398**	**ND**	**0.055**	**0.036**	**0.005**	**0.017**	**0.006**	**0.001**	**0.003**	**ND**	**0.002**	**0.525**	**0.001**
E111*	120	0.346	ND	0.054	0.036	0.005	0.024	0.005	0.001	0.005	ND	0.007	0.484	0.001
E112*	120	0.335	ND	0.062	0.039	0.002	0.025	0.005	0.001	0.004	0.001	0.001	0.475	0.001
Mean		**0.341**	**ND**	**0.058**	**0.038**	**0.003**	**0.024**	**0.005**	**0.001**	**0.004**	**ND**	**0.004**	**0.480**	**0.001**

ND = Not detected or < 0.001 mg/kg
* Includes acetone:0.1 M HCl (5:1, v/v) extract.
† Only DX-CA-S-2200 was found by further chromatographic analysis of representative soil extracts.
‡ No isomerisation of S-2167 occurred based on a representative soil extract.

FIGURES

Figure 1
Distribution of applied radioactivity for Speyer 5M soil treated with [benzyl-^{14}C]S-2167

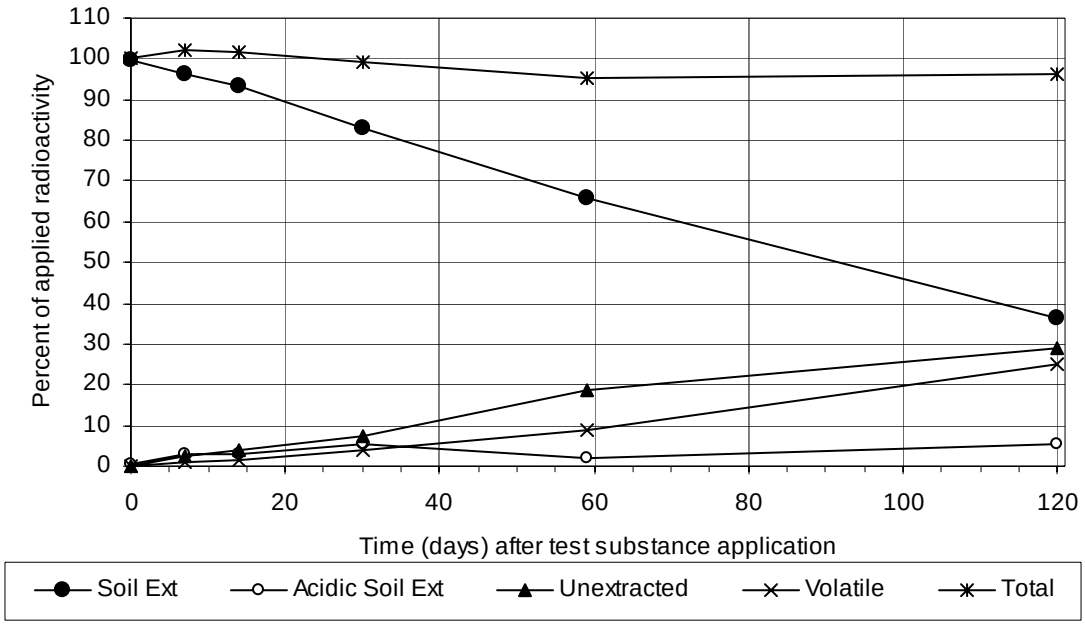


Figure 2
Distribution of applied radioactivity for Speyer 5M soil treated with [phenoxy-^{14}C]S-2167

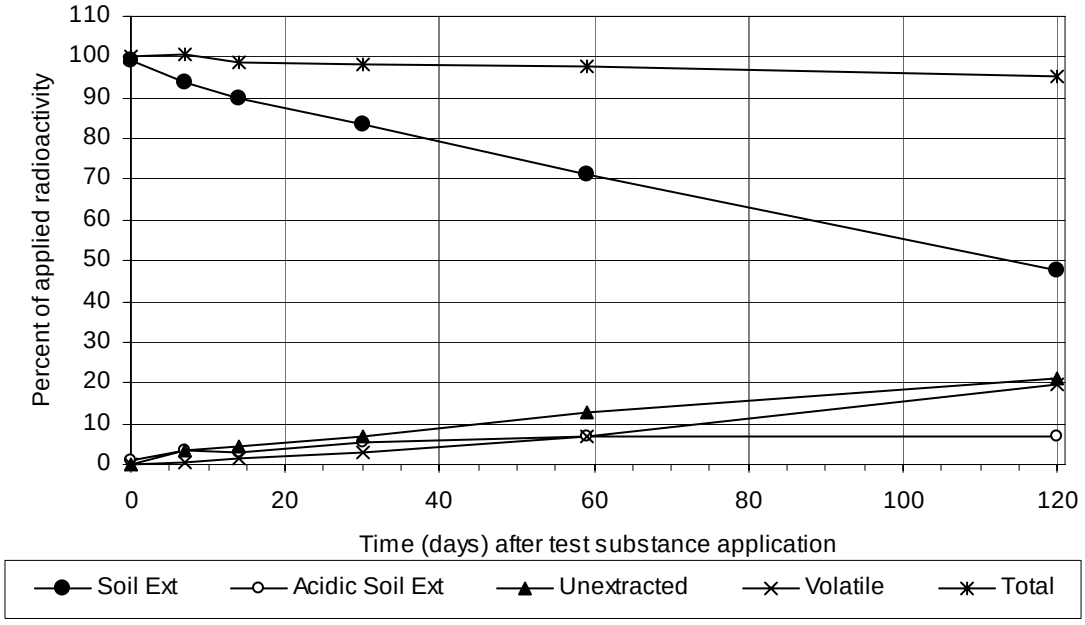


Figure 3
Distribution of applied radioactivity for Speyer 2.2 soil treated with [benzyl-^{14}C]S-2167

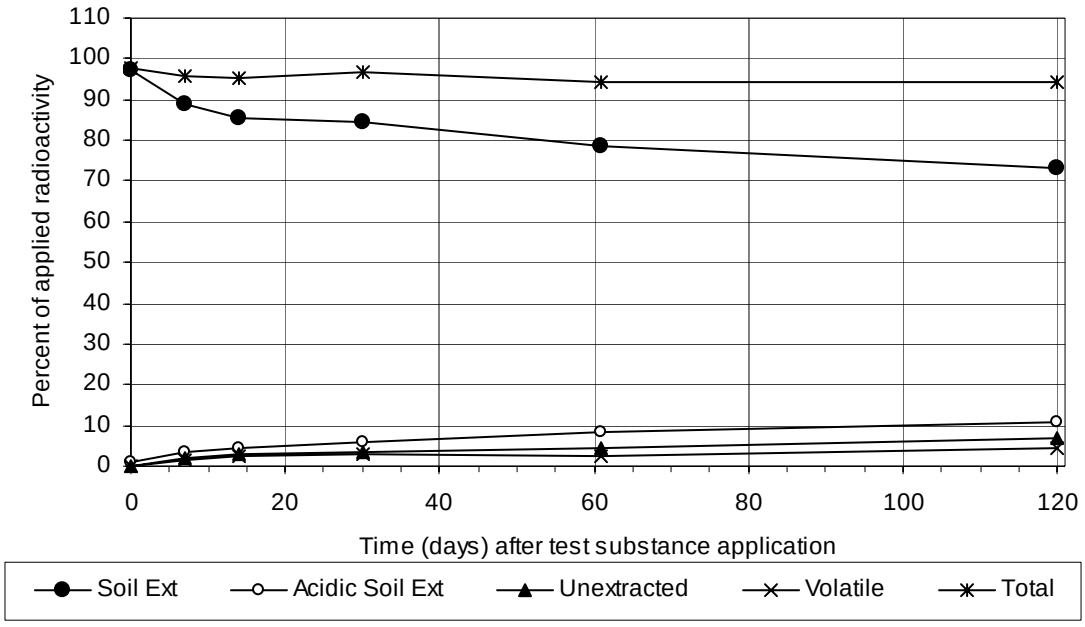


Figure 4
Distribution of applied radioactivity for SK920191 soil treated with [benzyl-^{14}C]S-2167

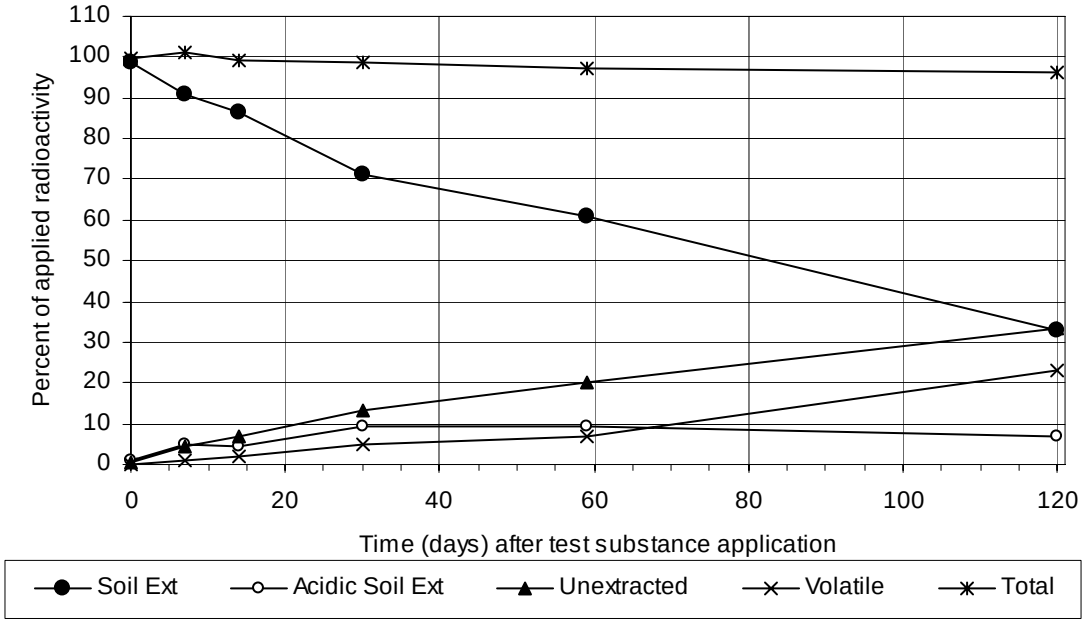


Figure 5
Distribution of applied radioactivity for Chelmorton soil treated with [benzyl-^{14}C]S-2167

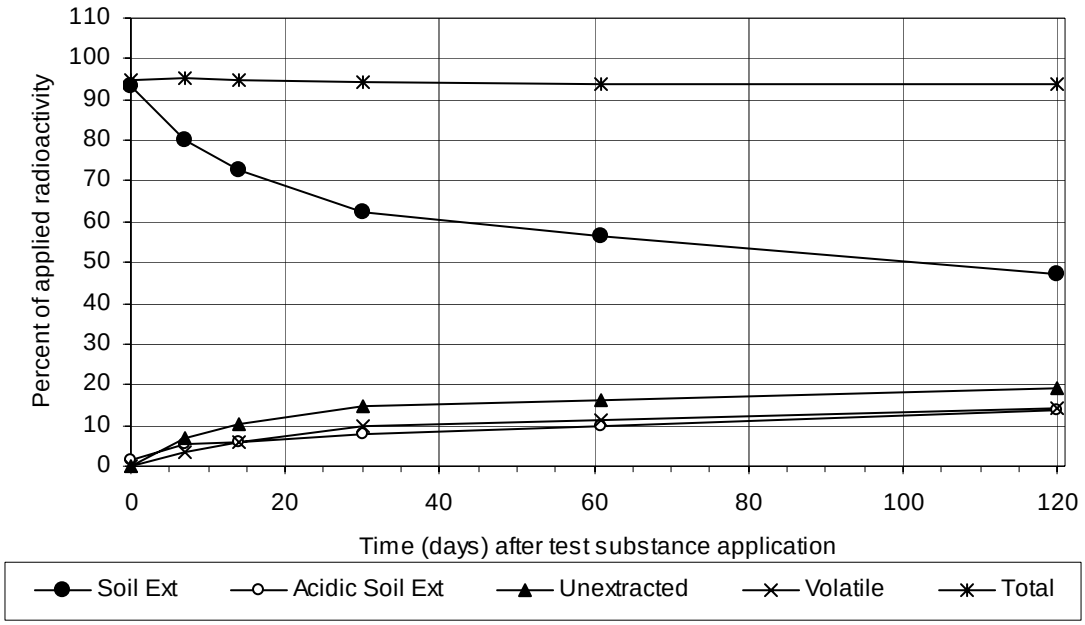
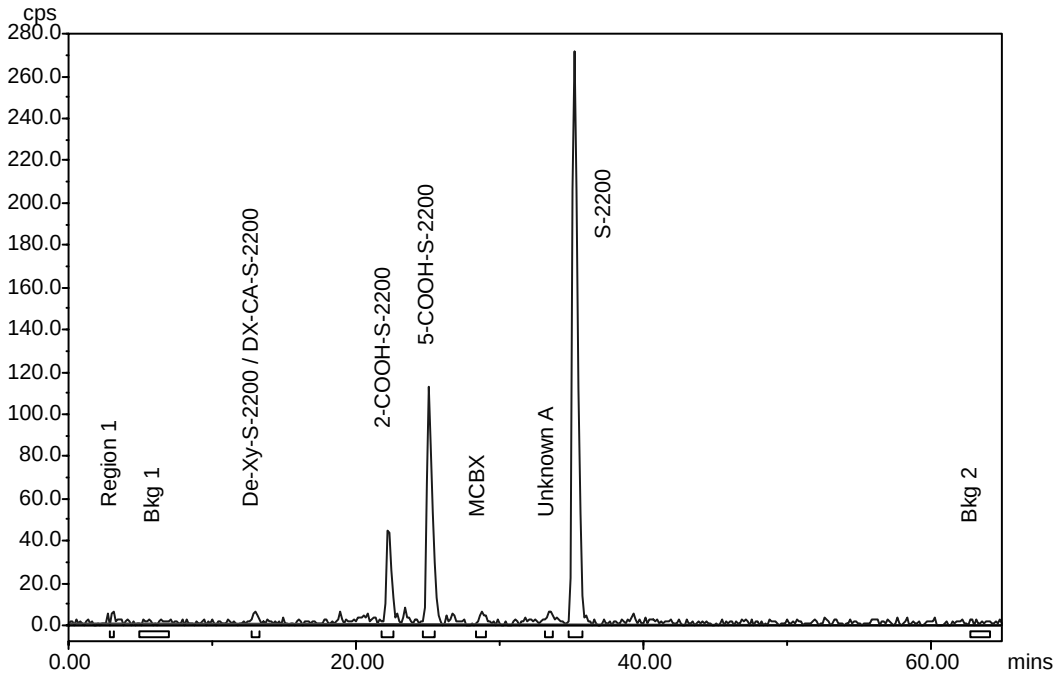


Figure 6
HPLC chromatogram of a primary soil extract from Speyer 5M soil 59 days after treatment with [benzyl-^{14}C]S-2167 (Method 2)

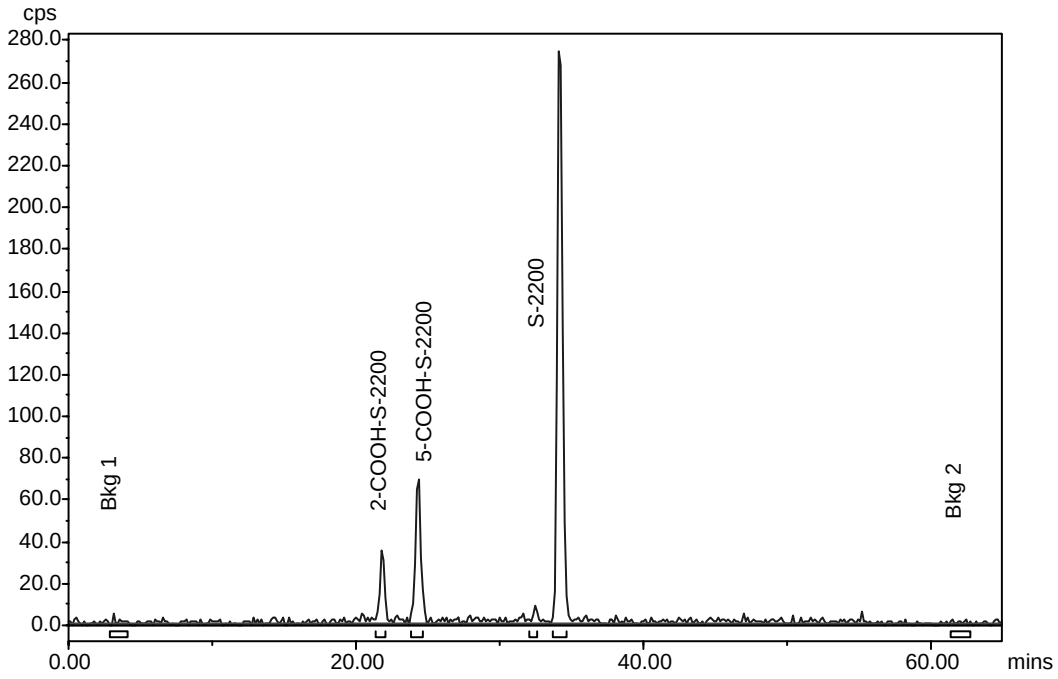


Chromatogram: 4CHR057-1
Sample: A9

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)	%TRR (%)
Region 1	2.87	3.17	3.03	7.0	42.6	0.49	0.33
Bkg 1	4.95	7.02	6.02				
De-Xy-S-2200/ DX-CA-S-2200	12.72	13.25	12.93	7.0	54.8	0.63	0.42
2-COOH-S-2200	21.85	22.65	22.13	45.0	731.0	8.39	5.65
5-COOH-S-2200	24.67	25.57	25.03	113.0	2147.5	24.65	16.59
MCBX	28.45	29.08	28.63	7.0	75.5	0.87	0.58
Unknown A	33.17	33.70	33.40	7.0	90.6	1.04	0.70
S-2200	34.77	35.73	35.07	272.0	5425.3	62.27	41.91
Bkg 2	62.80	64.17	62.97				
7 Peaks					8567.3	98.33	66.18

Total Area:	8712.6 Counts
Average Background:	0.5 cps
Unallocated Area:	145.2 Counts

Figure 7
HPLC chromatogram of a primary soil extract from Speyer 5M soil 59 days after treatment with [phenoxy-^{14}C]S-2167 (Method 2)

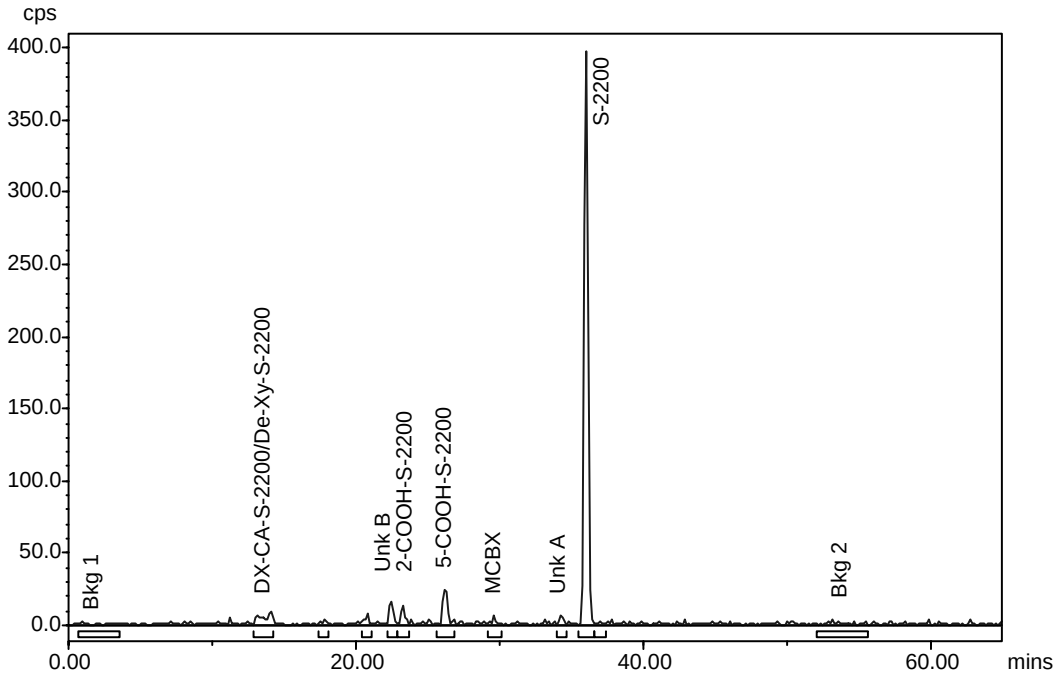


Chromatogram: 6CHR058-2
Sample: B9

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)	%TRR (%)
Bkg 1	2.82	4.12	3.02				
2-COOH-S-2200	21.33	22.10	21.70	36.0	495.2	6.82	4.60
5-COOH-S-2200	23.82	24.72	24.23	70.0	1300.4	17.91	12.09
	32.15	32.63	32.33	9.0	84.1	1.16	0.78
S-2200	33.70	34.68	34.05	275.0	5376.0	74.04	49.98
Bkg 2	61.38	62.75	61.87				
4 Peaks					7255.7	99.93	67.45

Total Area:	7261.1 Counts
Average Background:	0.6 cps
Unallocated Area:	5.4 Counts

Figure 8
HPLC chromatogram of a primary soil extract from Speyer 2.2 soil 61 days after treatment with [benzyl-^{14}C]S-2167 (Method 2)

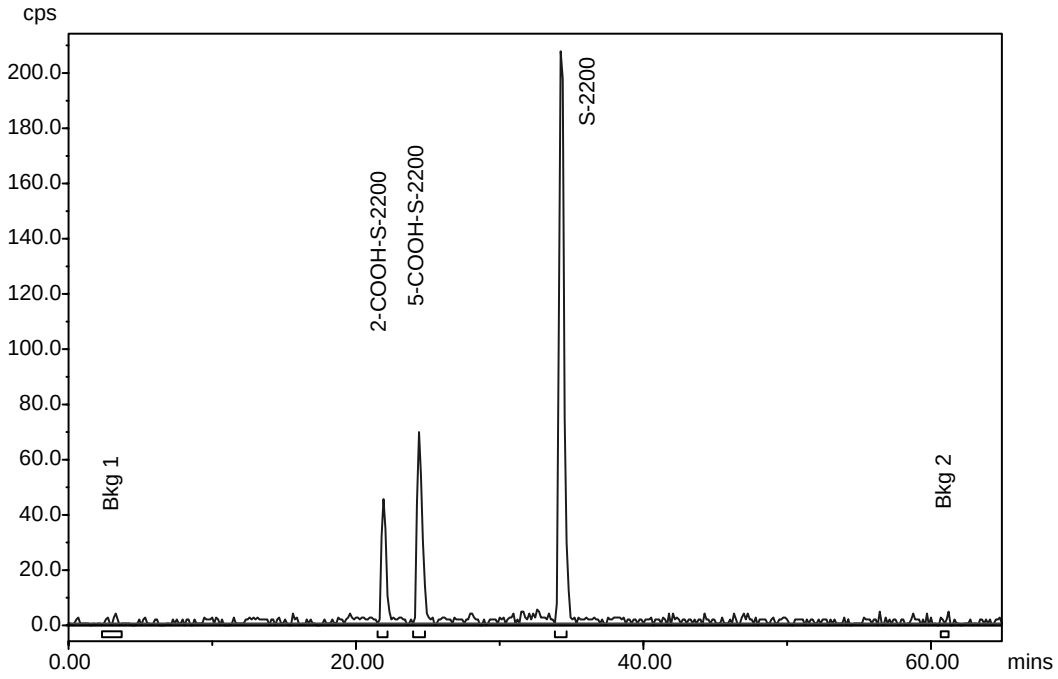


Chromatogram: 6CHR108 r2
Sample: C110

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)	%TRR (%)
Bkg 1	0.63	3.62	0.87				
DX-CA-S-2200/De-Xy-S-2200	12.88	14.32	13.98	9.0	203.1	3.33	2.56
	17.42	18.13	17.67	4.0	30.5	0.50	0.38
	20.45	21.18	20.75	8.0	51.8	0.85	0.65
Unk B	22.15	22.88	22.40	16.0	173.6	2.85	2.19
2-COOH-S-2200	22.95	23.73	23.13	14.0	139.5	2.29	1.76
5-COOH-S-2200	25.70	26.85	26.12	24.0	355.7	5.84	4.48
MCBX	29.23	30.17	29.48	7.0	39.5	0.65	0.50
Unk A	33.98	34.63	34.20	7.0	47.9	0.79	0.60
S-2200	35.47	36.55	35.93	398.0	4991.2	81.95	62.86
	36.60	37.40	36.95	3.0	14.3	0.23	0.18
Bkg 2	52.10	55.73	53.03				
10 Peaks					6047.3	99.29	76.16

Total Area: 6090.4 Counts
Average Background: 0.4 cps
Unallocated Area: 43.2 Counts

Figure 9
HPLC chromatogram of a primary soil extract from SK920191 soil 59 days after treatment with [benzyl-^{14}C]S-2167 (Method 2)

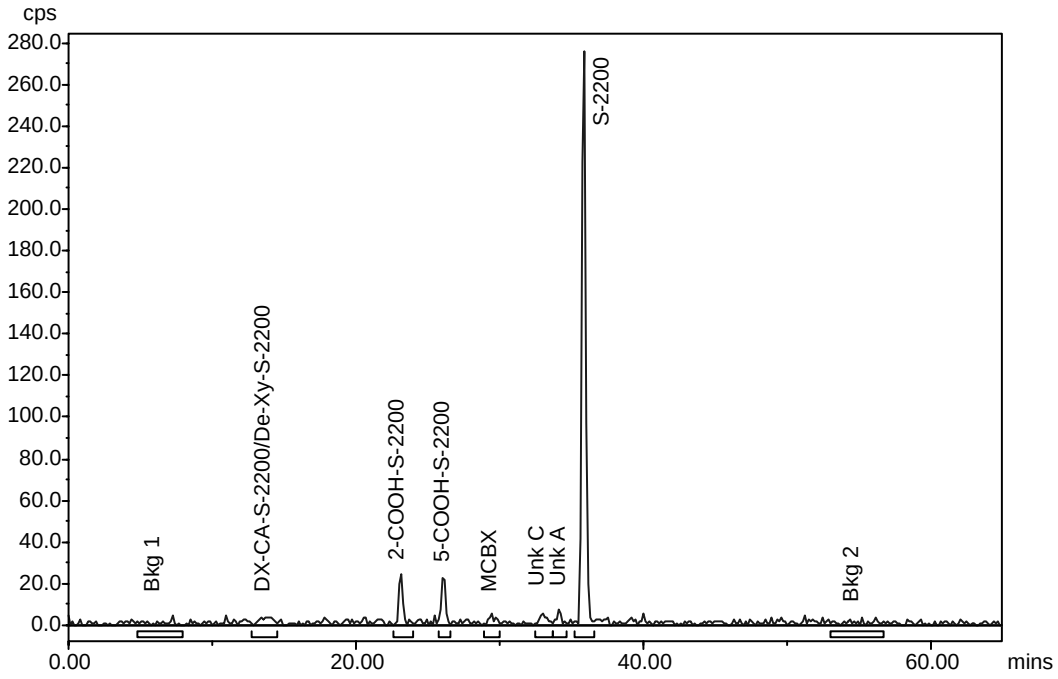


Chromatogram: 6CHR60-2
Sample: D10

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)	%TRR (%)
Bkg 1	2.33	3.77	3.20				
2-COOH-S-2200	21.55	22.22	21.82	46.0	657.6	11.70	7.26
5-COOH-S-2200	23.98	24.82	24.32	70.0	1185.5	21.10	13.08
S-2200	33.92	34.75	34.18	208.0	3693.8	65.75	40.77
Bkg 2	60.75	61.33	61.20				
3 Peaks					5536.9	98.56	61.11

Total Area: 5618.0 Counts
Average Background: 0.5 cps
Unallocated Area: 81.1 Counts

Figure 10
HPLC chromatogram of a primary soil extract from Chelmorton soil 61 days after treatment with [benzyl-^{14}C]S-2167 (Method 2)

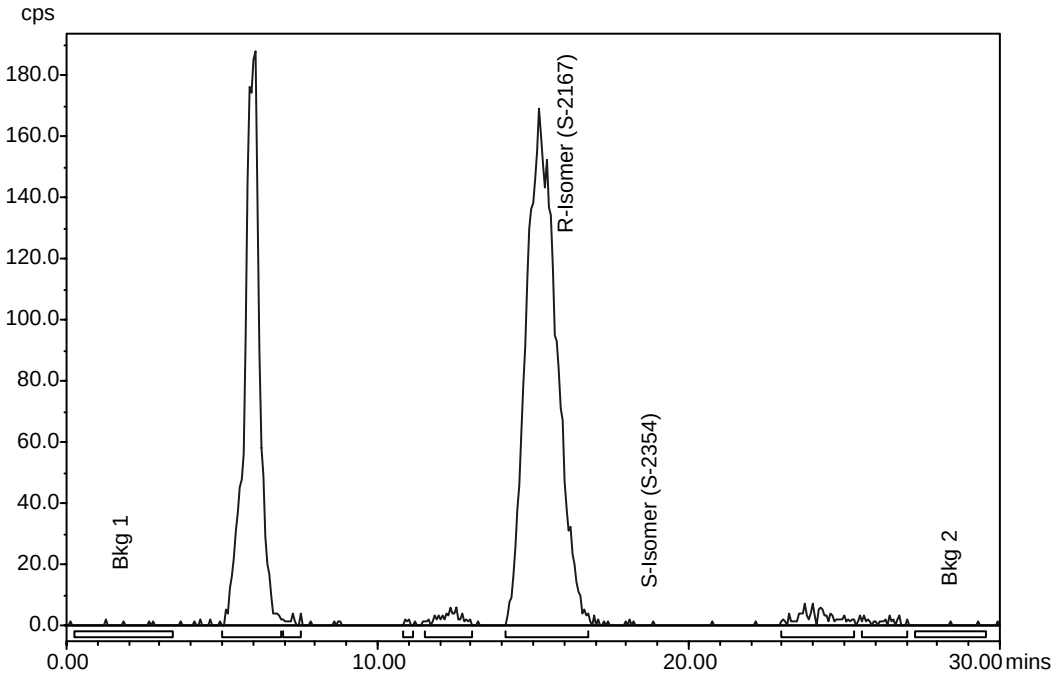


Chromatogram: 6CHR109 r1
Sample: E109

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)	%TRR (%)
Bkg 1	4.80	8.02	7.12				
DX-CA-S-2200/De-Xy-S-2200	12.73	14.52	13.67	4.0	93.7	2.23	1.27
2-COOH-S-2200	22.65	23.93	23.03	25.0	261.3	6.21	3.53
5-COOH-S-2200	25.77	26.57	25.97	23.0	300.9	7.15	4.06
MCBX	28.95	30.03	29.37	6.0	54.0	1.28	0.73
Unk C	32.57	33.72	32.92	6.0	40.6	0.97	0.55
Unk A	33.72	34.63	34.08	8.0	48.8	1.16	0.66
S-2200	35.25	36.55	35.75	276.0	3398.4	80.81	45.90
Bkg 2	53.03	56.72	55.58				
7 Peaks					4197.7	99.82	56.70

Total Area: 4205.5 Counts
Average Background: 0.4 cps
Unallocated Area: 7.5 Counts

Figure 11
Chiral HPLC chromatogram of a primary soil extract from Speyer 5M soil 120 days after treatment with [benzyl-^{14}C]S-2167 (Method 3)

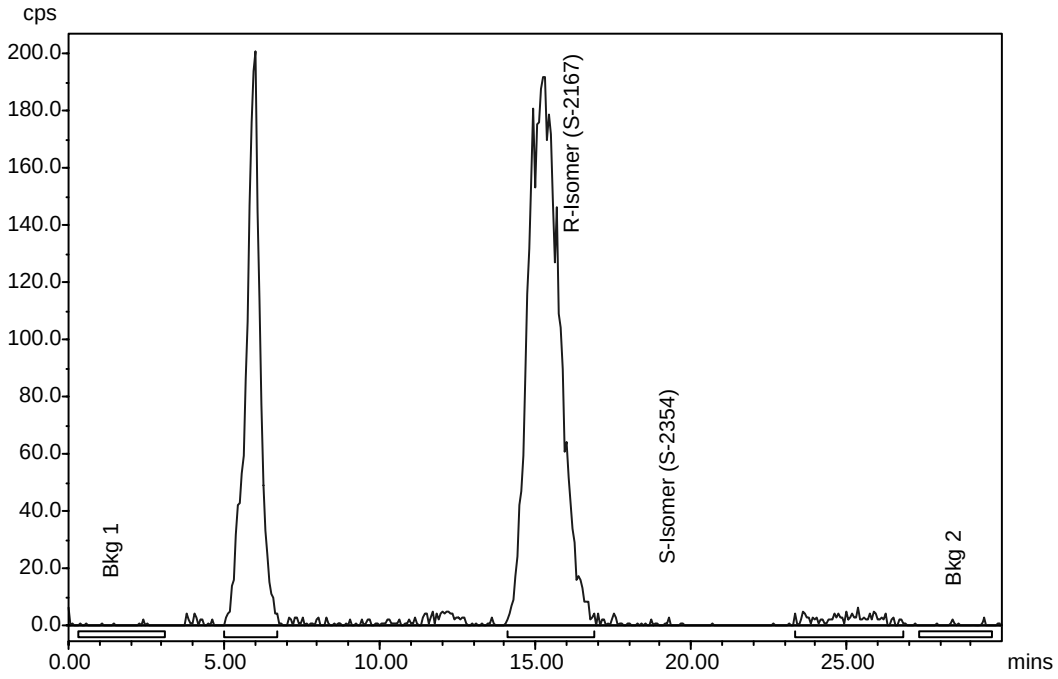


Chromatogram: 5CHR075-2
Sample: A11 ext 4

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	0.28	3.43	1.22			
	5.02	6.90	6.00	188.0	5537.1	34.60
	6.98	7.50	7.33	4.0	14.2	0.09
	10.82	11.12	10.90	2.0	4.6	0.03
	11.53	13.05	12.40	6.0	111.8	0.70
R-Isomer (S-2167)	14.12	16.77	15.13	169.0	10114.2	63.19
	22.97	25.33	23.82	7.0	164.8	1.03
	25.55	27.03	26.15	3.0	31.1	0.19
Bkg 2	27.25	29.58	28.82			
7 Peaks					15977.7	99.83

Total Area	16004.9 Counts
Average Background	0.0 cps
Unallocated Area	27.1 Counts

Figure 12
Chiral HPLC chromatogram of a primary soil extract from Speyer 5M soil 120 days after treatment with [phenoxy-^{14}C]S-2167 (Method 3)

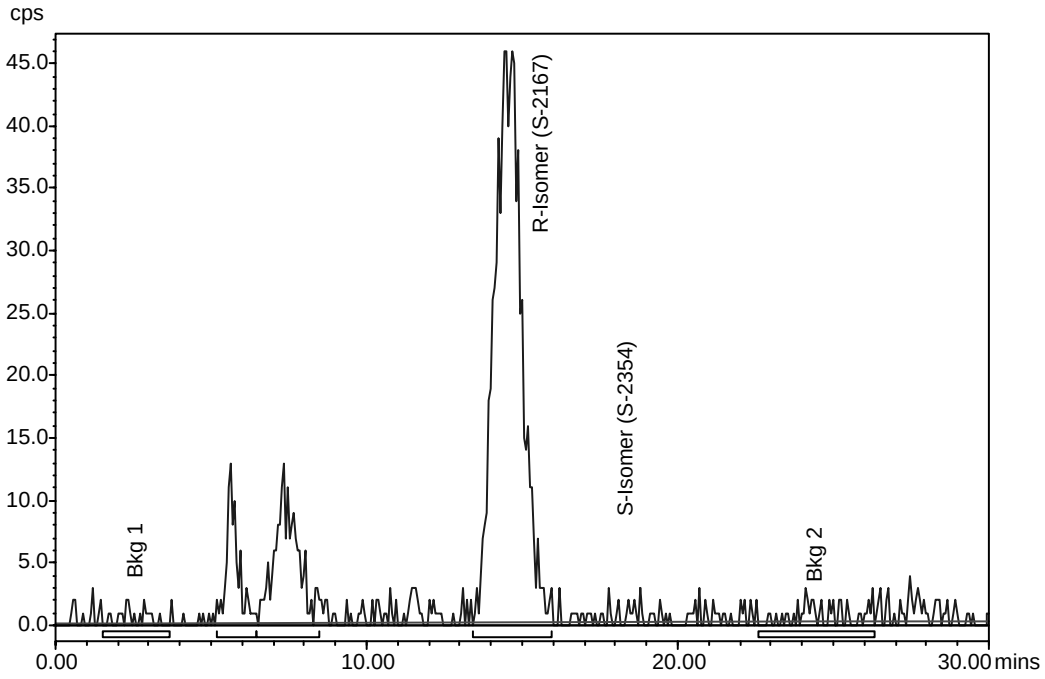


Chromatogram: 5CHR075-3
Sample: B11 Ext 4

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	0.32	3.12	2.38			
	5.00	6.73	5.93	201.0	5555.5	30.50
R-Isomer (S-2167)	14.08	16.90	15.23	192.0	12087.2	66.36
	23.35	26.80	25.32	6.0	248.0	1.36
Bkg 2	27.35	29.65	29.35			
3 Peaks					17890.7	98.23

Total Area	18213.9 Counts
Average Background	0.1 cps
Unallocated Area	323.2 Counts

Figure 13
Chiral HPLC chromatogram of a primary soil extract from Speyer 2.2 soil 120 days after treatment with [benzyl-^{14}C]S-2167 (Method 3)

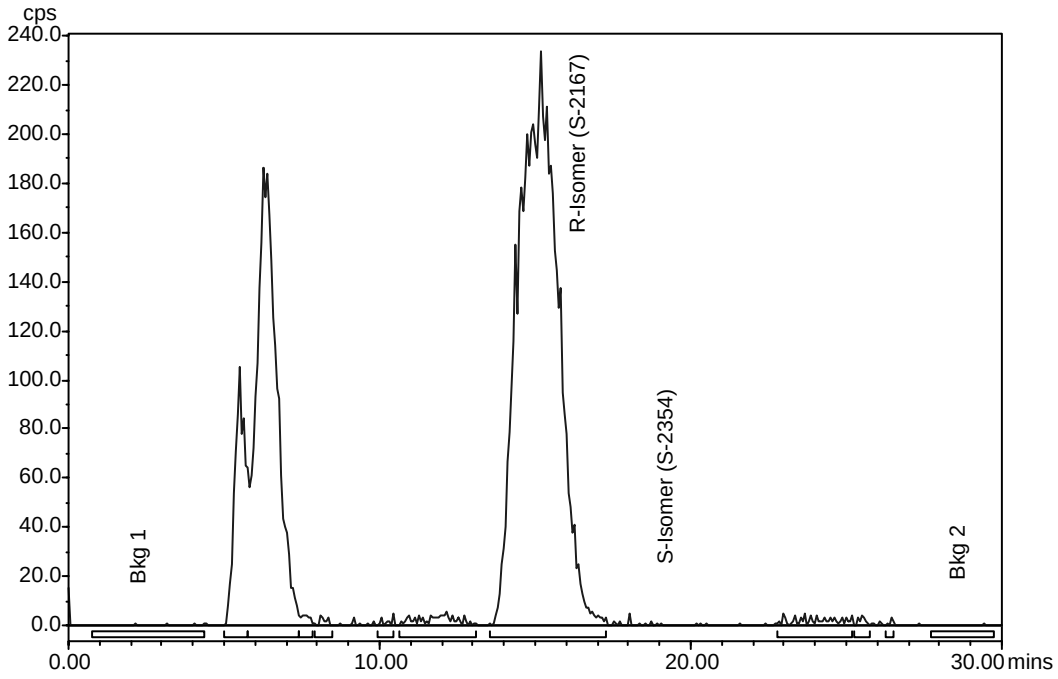


Chromatogram: 4CHR113R1
Sample: C111 Ext 3

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	1.50	3.68	2.50			
	5.18	6.43	5.60	13.0	162.2	5.82
	6.45	8.47	7.30	13.0	345.4	12.39
R-Isomer (S-2167)	13.40	15.97	14.50	46.0	2249.9	80.72
Bkg 2	22.62	26.33	25.13			
3 Peaks					2757.5	98.93

Total Area: 2787.2 Counts
Average Background: 0.3 cps
Unallocated Area: 29.7 Counts

Figure 14
Chiral HPLC chromatogram of a primary soil extract from SK920191 soil 120 days after treatment with [benzyl-^{14}C]S-2167 (Method 3)

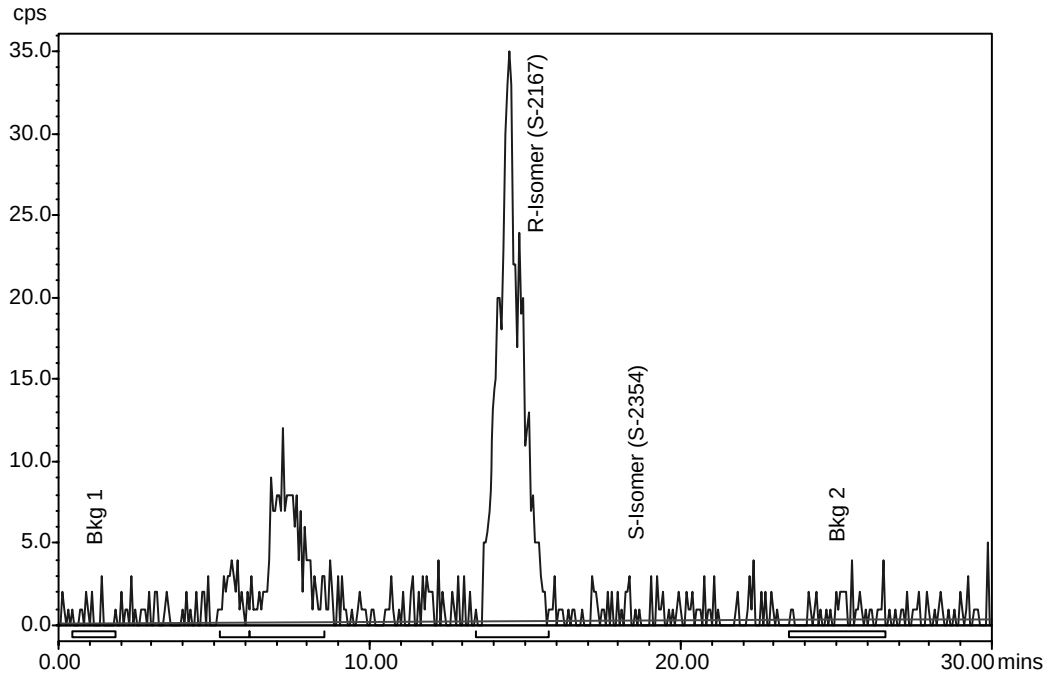


Chromatogram: 5CHR075-4
Sample: D12 ext 4

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	0.78	4.38	3.22			
	5.00	5.77	5.48	105.0	2200.0	7.63
	5.78	7.43	6.25	186.0	7590.9	26.31
	7.43	7.85	7.53	4.0	38.5	0.13
	7.93	8.47	8.08	4.0	20.4	0.07
	9.93	10.47	10.38	5.0	15.4	0.05
	10.62	13.08	12.10	6.0	167.4	0.58
R-Isomer (S-2167)	13.55	17.30	15.17	234.0	18558.5	64.33
	22.80	25.17	23.27	5.0	127.5	0.44
	25.28	25.73	25.43	4.0	23.7	0.08
	26.27	26.55	26.38	3.0	7.8	0.03
Bkg 2	27.70	29.75	29.38			
10 Peaks					28750.0	99.66

Total Area	28847.3 Counts
Average Background	0.0 cps
Unallocated Area	97.2 Counts

Figure 15
Chiral HPLC chromatogram of a primary soil extract from Chelmorton soil 120 days after treatment with [benzyl-^{14}C]S-2167 (Method 3)

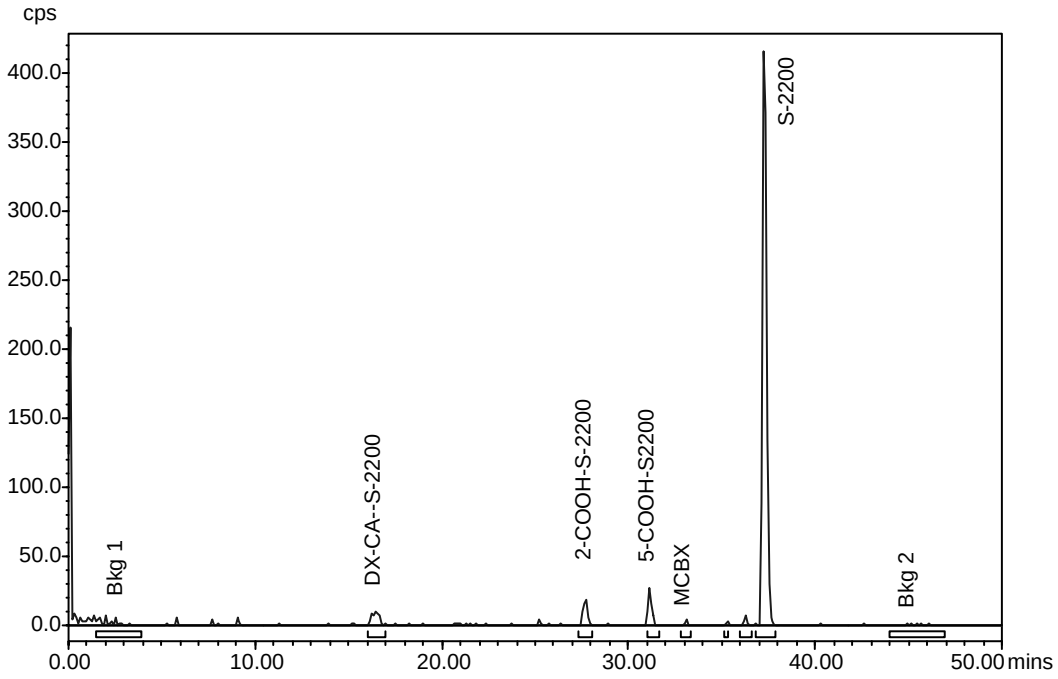


Chromatogram: 4CHR113R2
Sample: E112 Ext 3

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	0.43	1.85	1.37			
	5.22	6.15	5.63	4.0	54.2	2.96
	6.15	8.55	7.17	12.0	380.7	20.82
R-Isomer (S-2167)	13.40	15.77	14.43	35.0	1350.7	73.87
Bkg 2	23.45	26.58	25.97			
3 Peaks					1785.6	97.65

Total Area: 1828.5 Counts
Average Background: 0.2 cps
Unallocated Area: 42.9 Counts

Figure 16
Example HPLC chromatogram of a primary soil extract from Speyer 2.2 soil 61 days after treatment with [benzyl-^{14}C]S-2167 (Method 4)



Chromatogram: 5CHR113r6
Sample: C110 Ext 3

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	1.45	3.93	1.92			
DX-CA--S-2200	16.02	16.97	16.32	10.0	142.2	2.68
2-COOH-S-2200	27.32	28.07	27.67	18.0	188.7	3.55
5-COOH-S2200	30.98	31.65	31.00	27.0	211.3	3.97
MCBX	32.77	33.32	33.00	4.0	5.4	0.10
	35.10	35.38	35.25	3.0	3.4	0.06
	35.97	36.65	36.18	7.0	27.4	0.51
S-2200	36.77	37.83	37.18	416.0	4492.7	84.51
Bkg 2	44.00	46.95	45.03			
7 Peaks					5071.1	95.39

Total Area:	5316.2 Counts
Average Background:	0.2 cps
Unallocated Area:	245.1 Counts

Figure 17
Example TLC radioluminogram of a primary soil extract from Speyer 5M soil 59 days after treatment with [benzyl-^{14}C]S-2167 (System 2)

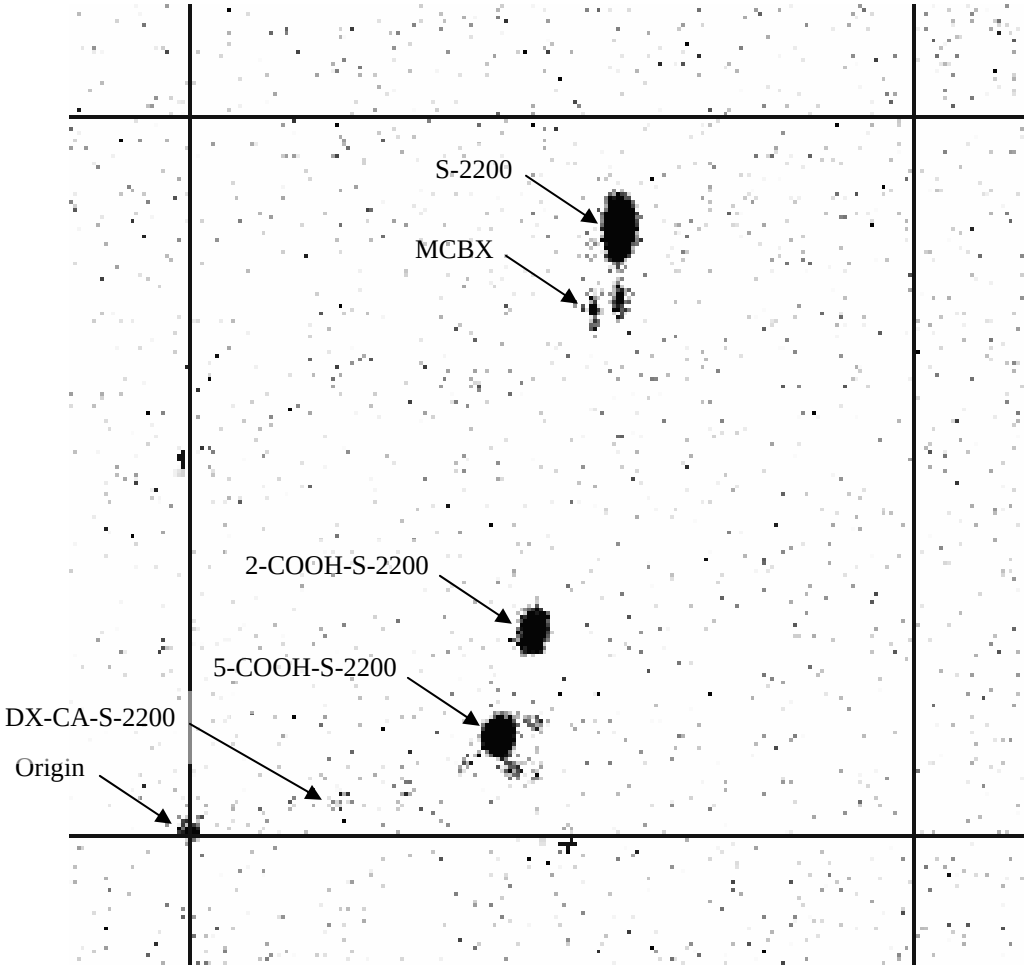


Plate 11

Figure 18
Example TLC chromatogram of a primary soil extract from Speyer 5M soil 59 days after treatment with [phenoxy-^{14}C]S-2167 (System 2)

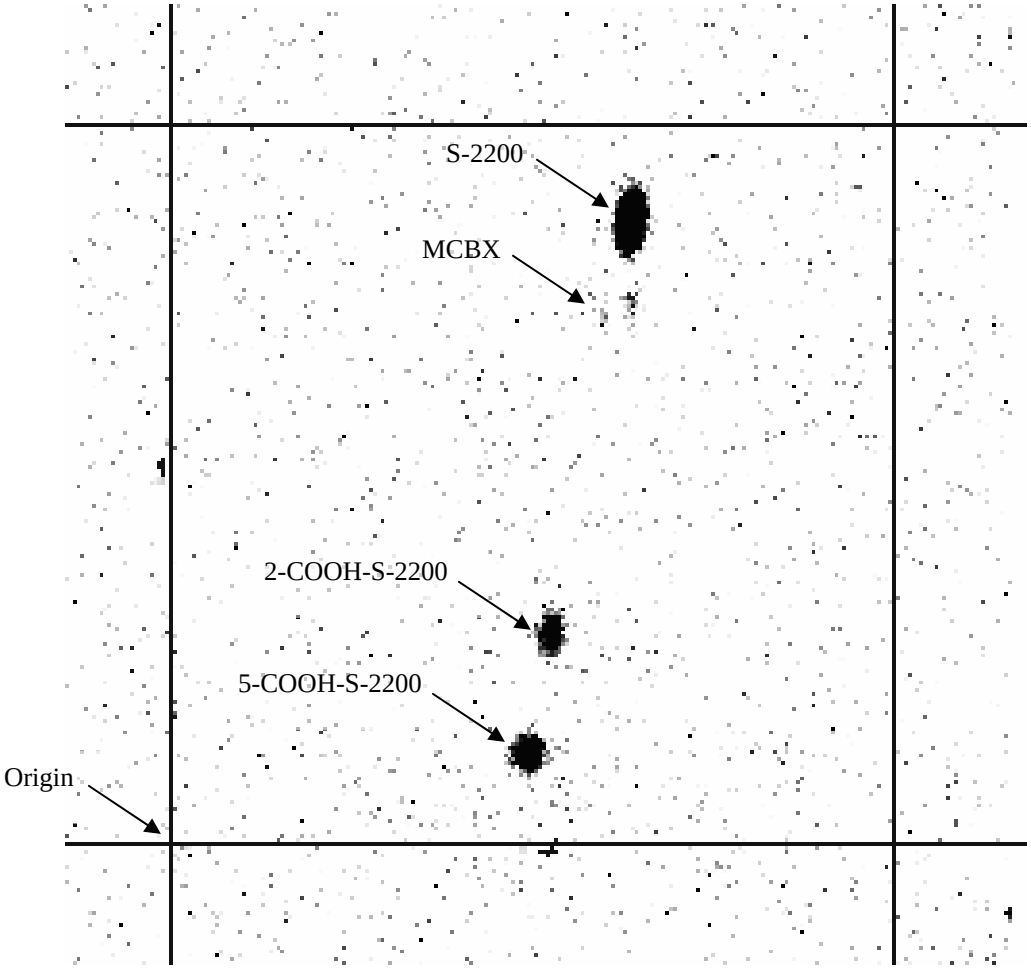


Plate 12

Figure 19
Example TLC chromatogram of a primary soil extract from Speyer 2.2 soil 120 days after treatment with [benzyl-^{14}C]S-2167 (System 2)

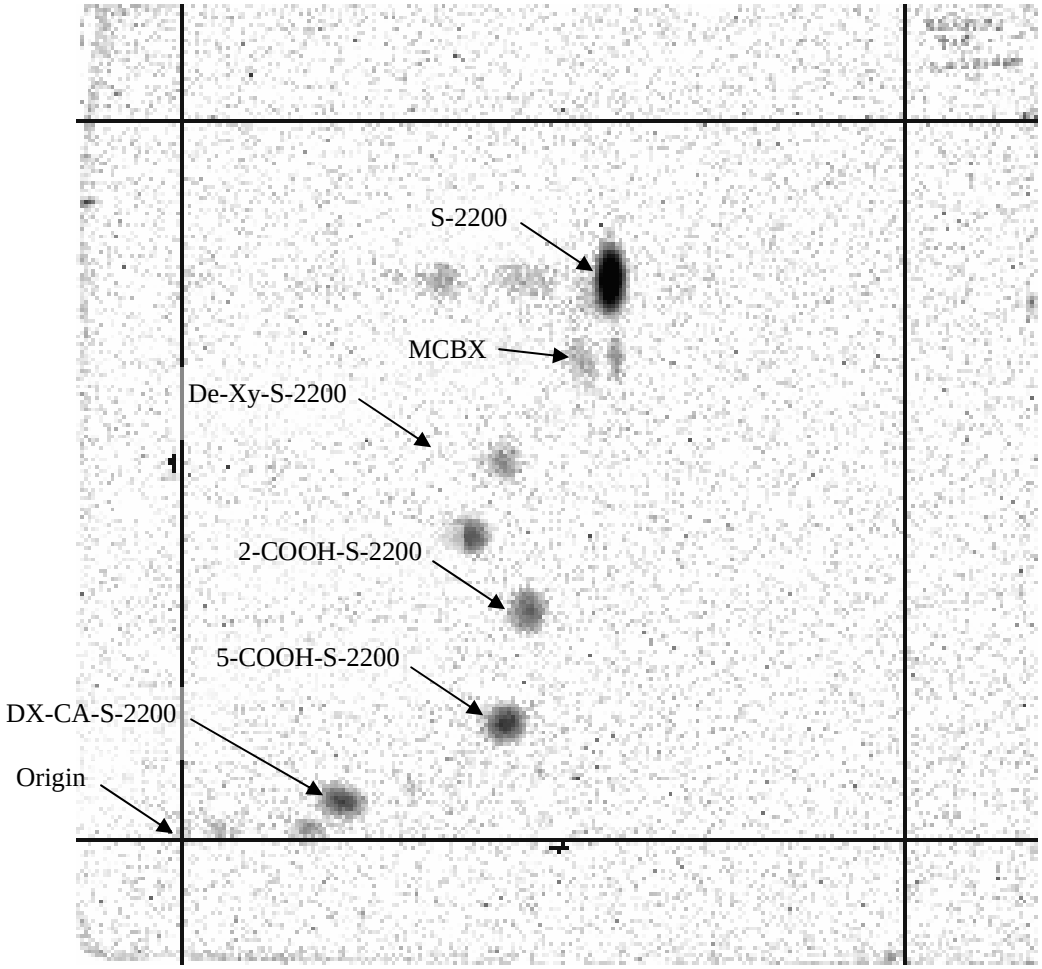


Plate 16

Figure 20
Example TLC chromatogram of a primary soil extract from SK920191 soil 59 days after treatment with [benzyl-^{14}C]S-2167 (System 2)

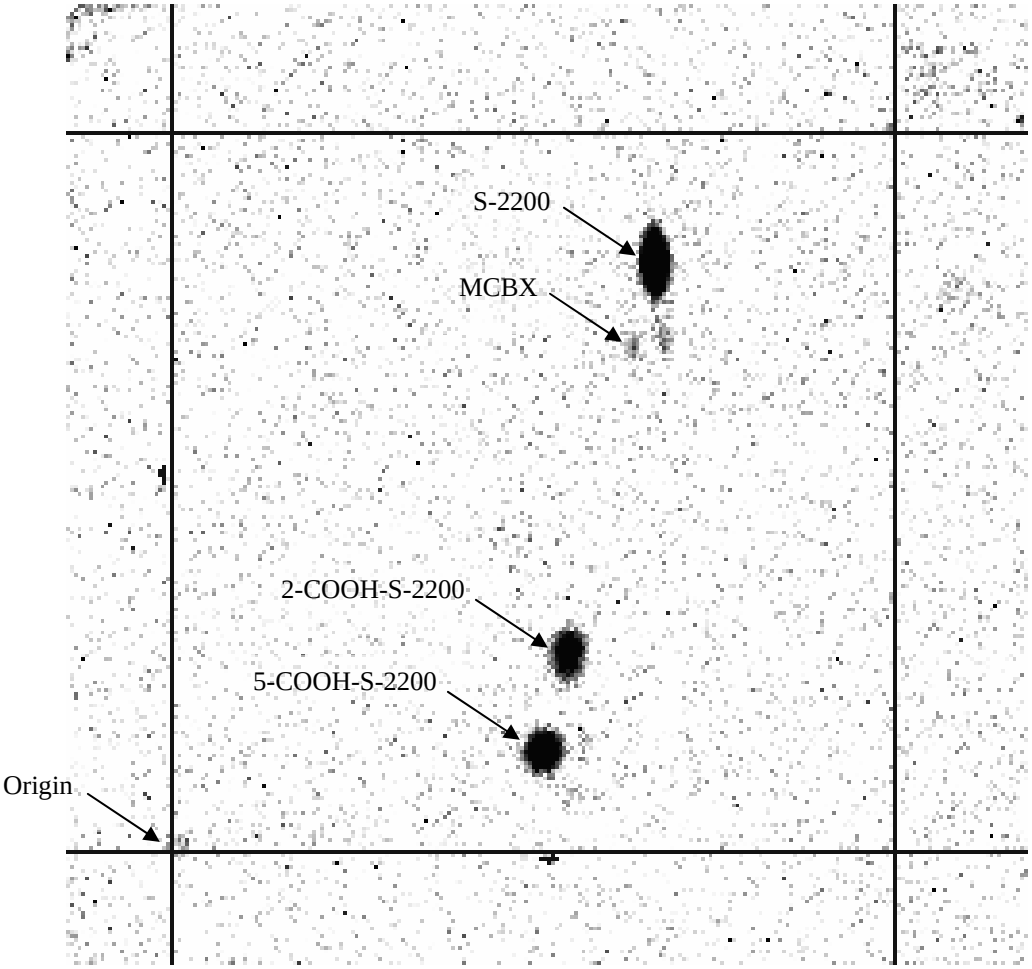


Plate 14

Figure 21
Example TLC chromatogram of a primary soil extract from Chelmorton soil 120 days after treatment with [benzyl-^{14}C]S-2167 (System 2)

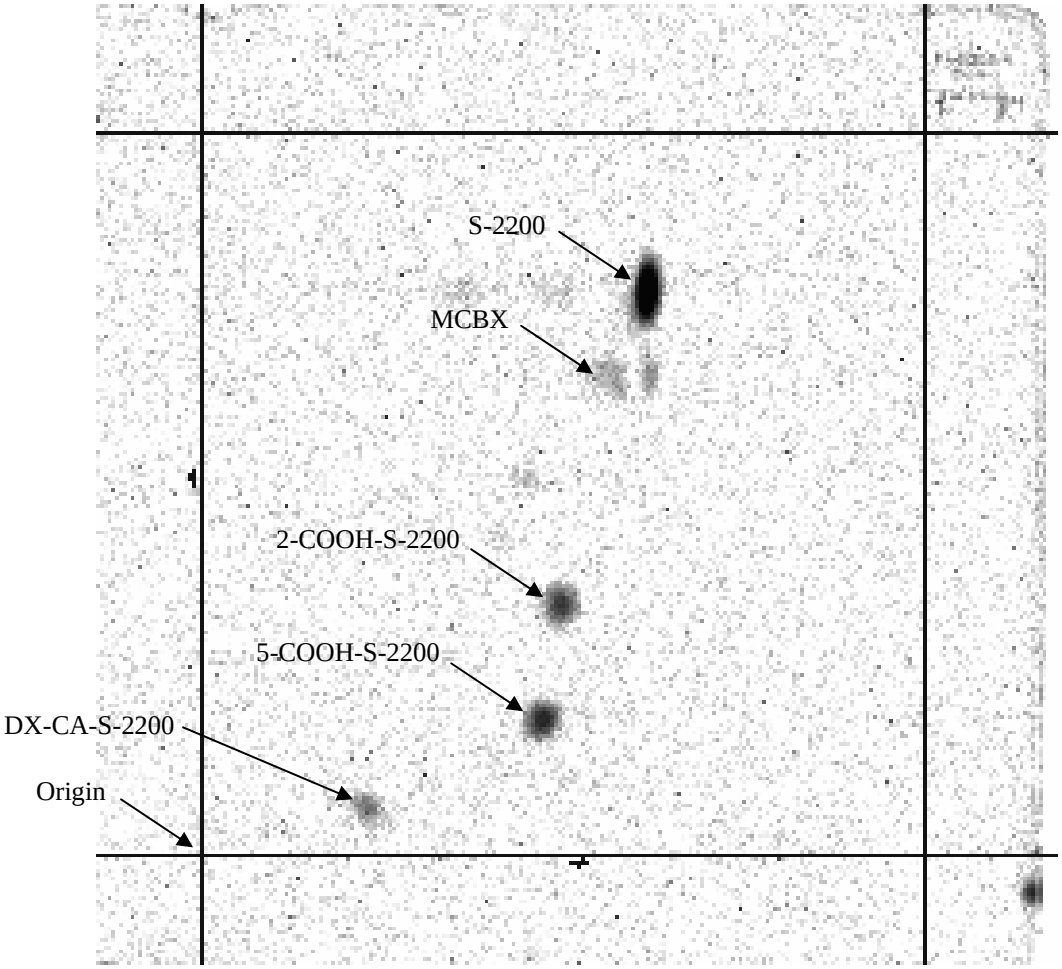
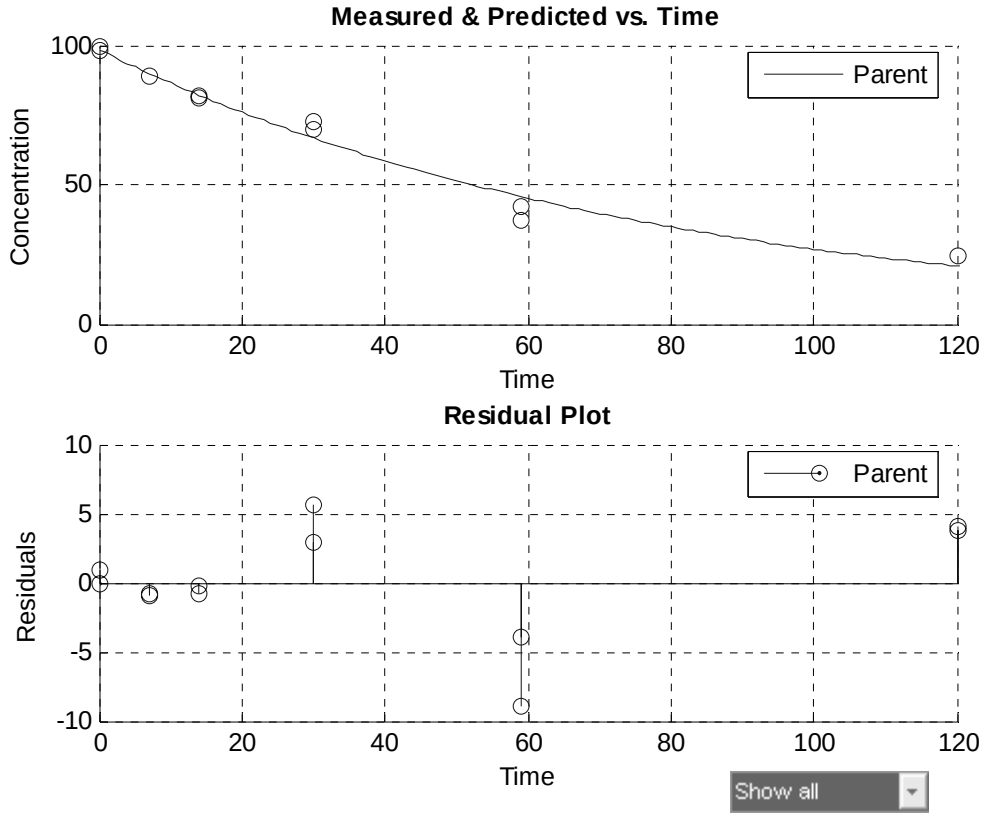


Plate 17

Figure 22
Rate of degradation of [benzyl-^{14}C]S-2167 in Speyer 5M soil (SFO kinetics)



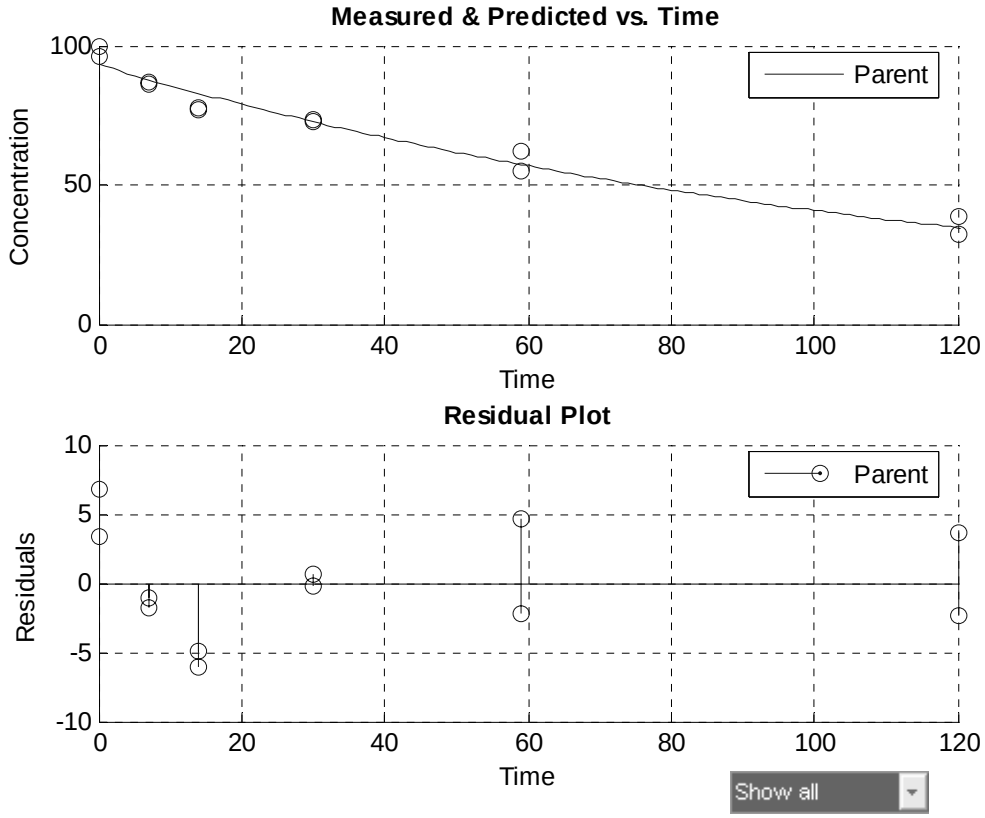
Note: x axis = days, y axis = % applied radioactivity

Chi^2 error = 4.18

k = 0.0130 day^{-1}	SD = 8.2 x 10^{-4}	Prob > t = 1.0 x 10^{-8}
M(0) = 98.53 %	SD = 1.9929	
DT-50 = 53.4 days	DT-75 = 106.7 days*	DT-90 = 177.3 days

* Not given by programme but calculated as twice the DT-50 value

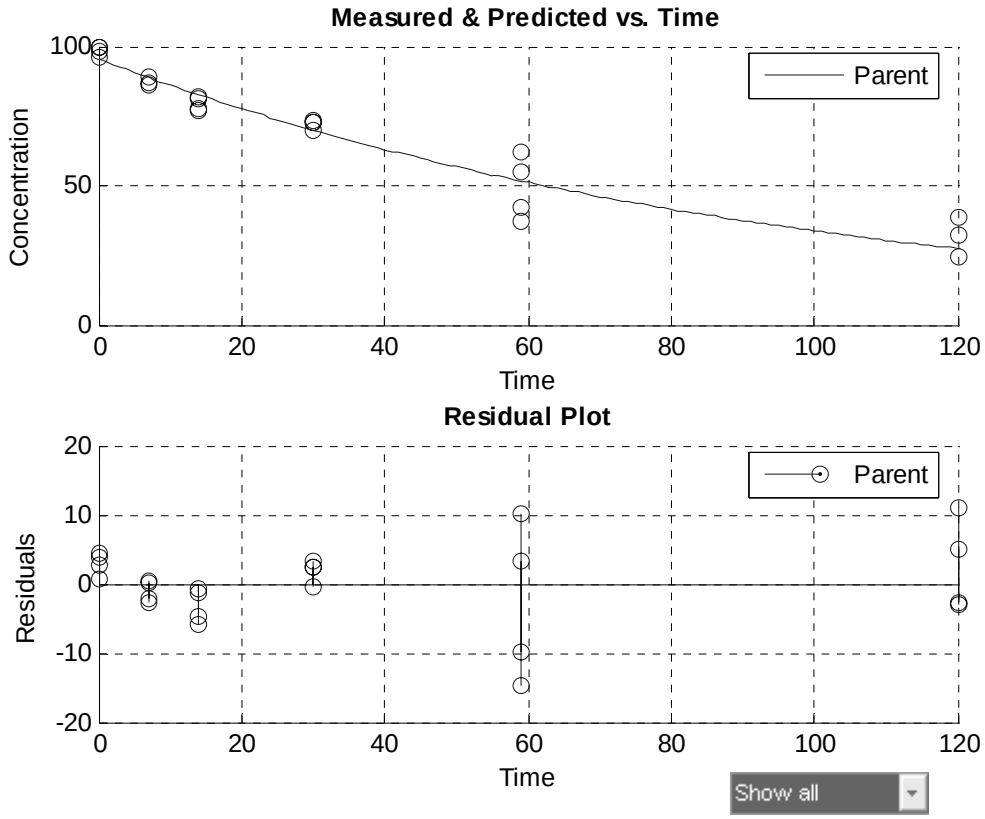
Figure 23
Rate of degradation of [phenoxy-^{14}C]S-2167 in Speyer 5M soil (SFO kinetics)



Note: x axis = days, y axis = % applied radioactivity

Chi^2 error = 3.53
k = 0.0082 day^{-1} SD = 6.1 x 10^{-4} Prob > t = 5.0 x 10^{-8}
M(0) = 93.05% SD = 1.8606
DT-50 = 84.1 days DT-75 = 168.2 days* DT-90 = 279.4 days
* Not given by programme but calculated as twice the DT-50 value

Figure 24
Rate of degradation of [benzyl-^{14}C]S-2167 and [phenoxy-^{14}C]S-2167 in Speyer 5M soil (SFO kinetics)



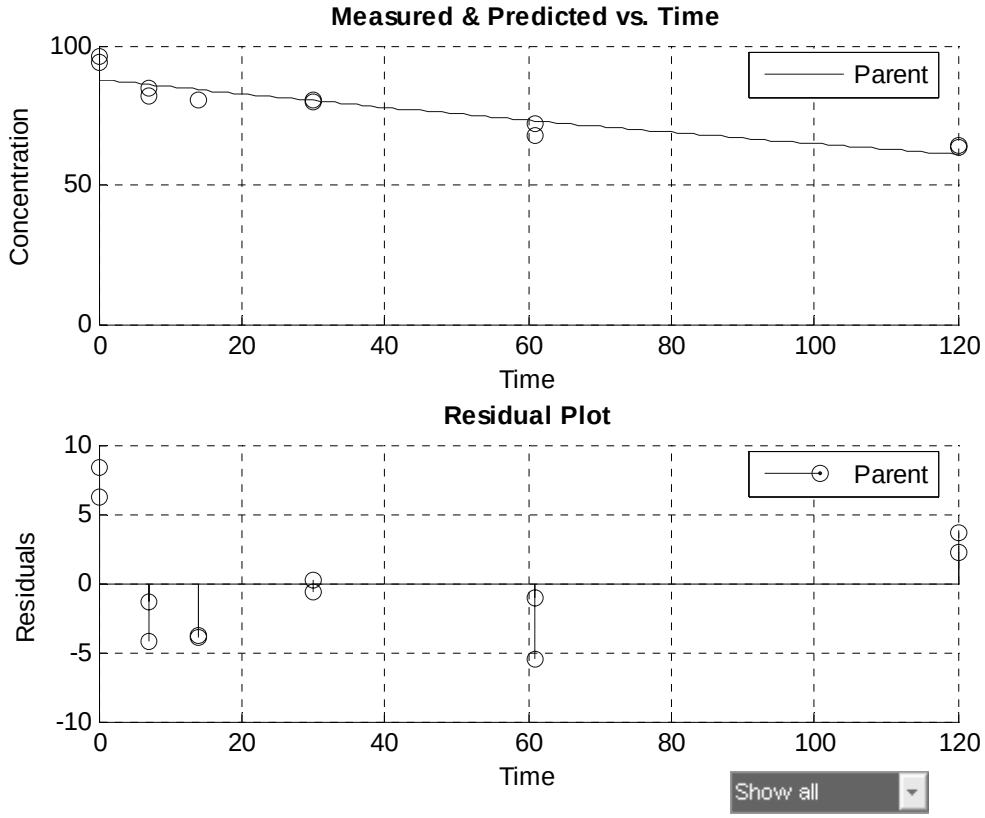
Note: x axis = days, y axis = % applied radioactivity

Chi^2 error = 2.87

k = 0.0104 day^{-1}	SD = 6.9 x 10^{-4}	Prob > t = 2.4 x 10^{-13}
M(0) = 95.59%	SD = 1.8950	
DT-50 = 66.5 days	DT-75 = 133.1days*	DT-90 = 221.0 days

* Not given by programme but calculated as twice the DT-50 value

Figure 25
Rate of degradation of [benzyl-^{14}C]S-2167 in Speyer 2.2 soil (SFO kinetics)



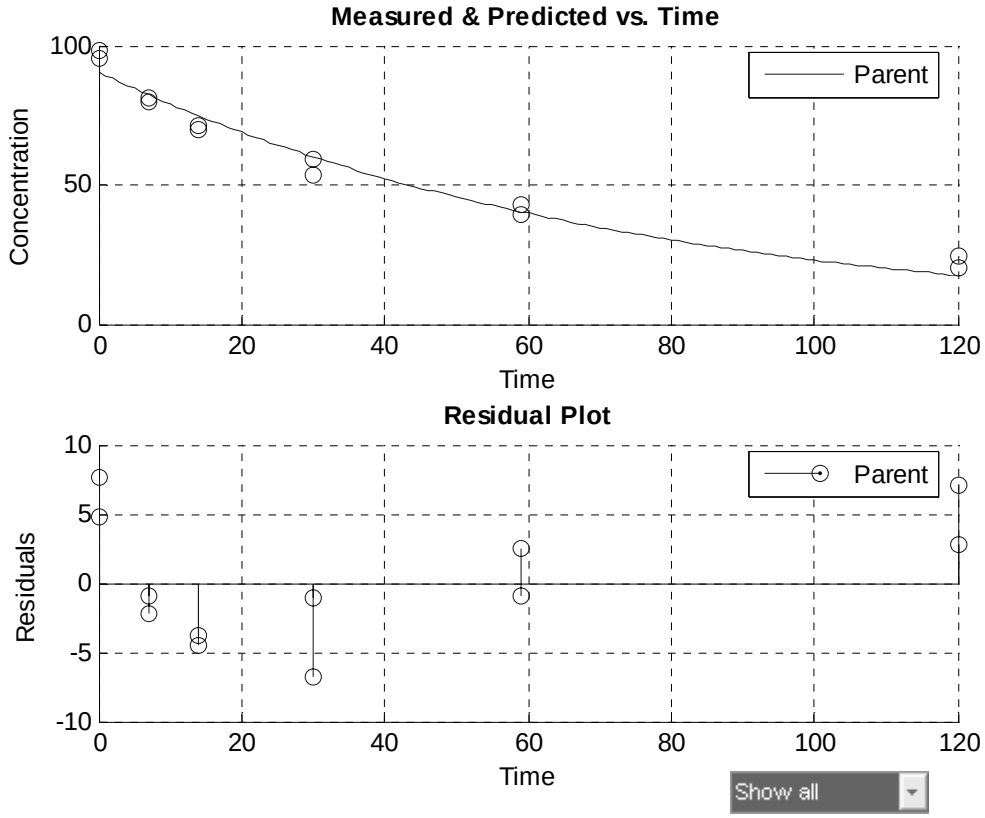
Note: x axis = days, y axis = % applied radioactivity

Chi^2 error = 4.04

k = 0.0031 day^{-1}	SD = 4.7 x 10^{-4}	Prob > t = 3.4 x 10^{-5}
M(0) = 87.88%	SD = 1.9057	
DT-50 = 227.1 days	DT-75 = 454.2 days*	DT-90 = 754.4 days

* Not given by programme but calculated as twice the DT-50 value

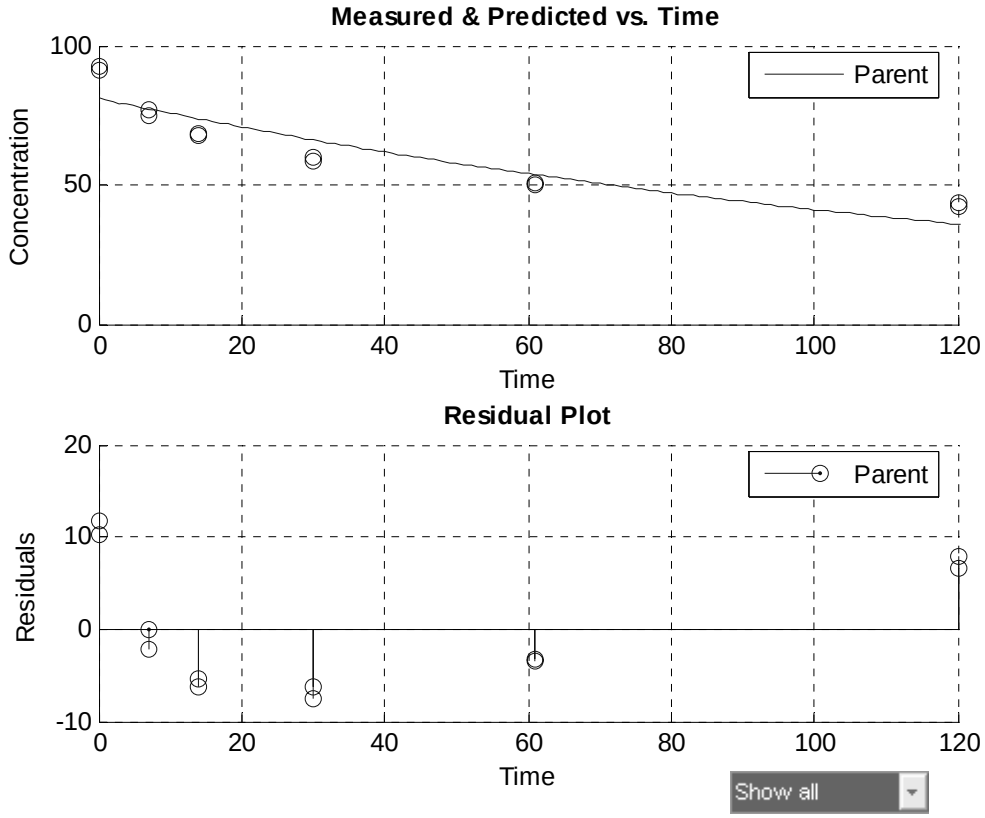
Figure 26
Rate of degradation of [benzyl-^{14}C]S-2167 in SK920191 soil (SFO kinetics)



Note: x axis = days, y axis = % applied radioactivity

Chi^2 error = 5.26
k = 0.0137 day^{-1} SD = 0.0011 Prob > t = 1.1 x 10^{-7}
M(0) = 90.58% SD = 2.3819
DT-50 = 50.6 days DT-75 = 101.1 days* DT-90 = 167.9 days
* Not given by programme but calculated as twice the DT-50 value

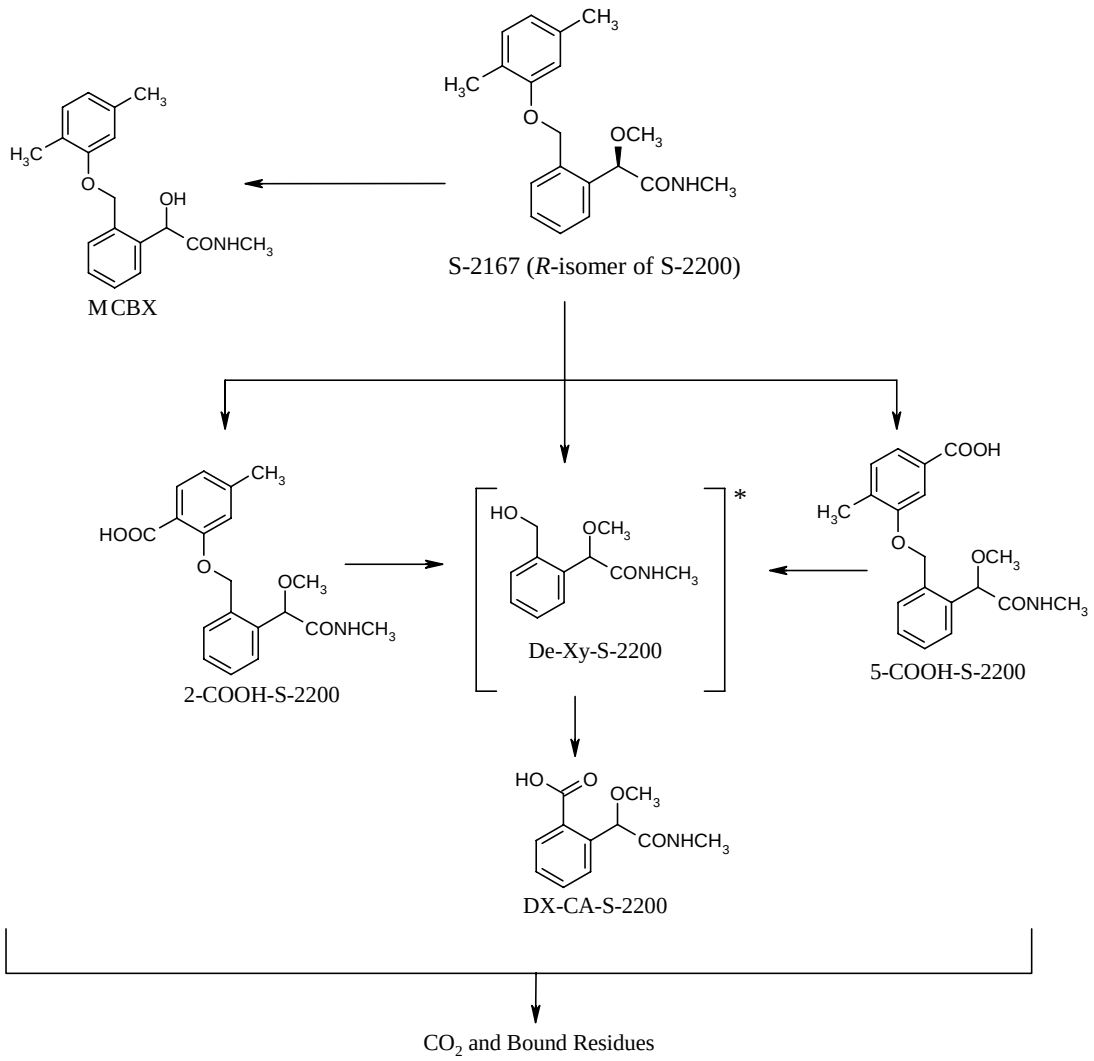
Figure 27
Rate of degradation of [benzyl-^{14}C]S-2167 in Chelmorton soil (SFO kinetics)



Note: x axis = days, y axis = % applied radioactivity

Chi^2 error = 8.18
k = 0.0068 day^{-1} SD = 0.0011 Prob > t = 5.6 x 10^{-5}
M(0) = 81.06% SD = 3.2428
DT-50 = 102.1 days DT-75 = 204.2 days* DT-90 = 339.2 days
* Not given by programme but calculated as twice the DT-50 value

Figure 28
Proposed metabolic pathway for S-2167 in soil



* De-Xy-S-2200 was not confirmed in a second chromatographic system, however it is considered a possible intermediate metabolite

APPENDICES

Appendix 1
Soil Characterisation

Certificate of Analysis for Speyer 5M Soil

TEST SYSTEM CERTIFICATE OF ANALYSIS

Test system code	CS17/09		
Test system name	Speyer 5M		
Supplied by	Speyer		
Sampling location	"In der Speyerer Hohl", Nr. 977, Mechtersheim, Rheinland-Pflaz, Germany		
Date of field sampling	27 February 2009	Depth of sampling	*ca* 20cm
Date of arrival at Covance	09 March 2009		
Pesticide history	No pesticides applied in the last 5 years.		
Land use	Meadow		
Method of soil collection	In accordance with ISO 10381-6.		
Soil order (FAO soil classification)	Entisol		
Handling	The 2 mm sieved soil was given a unique code and thoroughly mixed with the minimum of air drying. Prior to use the soil was stored in the dark, in an incubator routinely maintained at 4 ± 2°C, in loosely tied plastic bags in accordance with ISO 10381-6.		

UK & BBA Particle Size Distribution (PSD) *		pH in H_2O (Commenced: 14/4/09)	8.2
Sand % (2000 – 63 µm)	55		
Silt % (63 – 2 µm)	34	pH in 1M KCl	7.6
Clay % (< 2 µm)	11	(Commenced: 14/4/09)	
USDA Particle Size Distribution *		pH in 0.01M $CaCl_2$ *	7.2
Sand % (2000 – 50 µm)	62	(Commenced: 27/2/09)	
Silt % (50 – 2 µm)	28		
Clay % (< 2 µm)	11	Organic Carbon (OC) % *	1.3
		Organic Matter % *	2.2
ISSS Particle Size Distribution *		(Commenced: 27/2/09)	
Sand % (2000 – 20 µm)	75		
Silt % (20 – 2 µm)	15	Cation Exchange Capacity (CEC)	
Clay % (< 2 µm)	11	meq/100g *	15
		mmol/Kg	150
UK Textural Class	Sandy loam	(Commenced: 27/2/09)	
BBA Textural Class	mittel lehmiger Sand		
USDA Textural Class	Sandy loam	Microbial Biomass µg C/g	277.5
ISSS Textural Class	Sandy loam	(Commenced: 25/3/09)	
Water Holding Capacity at pF 0 MWHC (0.001 bar) %	36.6	Microbial Biomass as a % of OC (Commenced: 27/2/09)	2.1
Water Holding Capacity at pF 2.0 (0.1 bar) %	24.8	Disturbed Bulk Density g/cm^3	1.3
Water Holding Capacity at pF 2.5 (0.33 bar) %	14.5		

Methods used: PSD (hydrometer); pH H_20 and KCl(ISO 10390, 1:5 ratio soil to solution); Microbial Biomass (fumigation-extraction); MWHC (capillary foam saturation); pF2 & 2.5 (pressure plate)

The analytical procedures undertaken at Covance Laboratories Ltd., Harrogate were performed in accord with the current national UK GLP Regulations and the current OECD Principles of GLP.
All data is retained in the GLP archive of Covance Laboratories Ltd., Harrogate.

* Analysis performed by Speyer (Analysis Data Sheet for Standard Soils According to GLP dated 4/3/09). No claim is being made for the compliance status of this work.

Compiled by: 16 Apr 09

Approved by: 16 Apr 09

Quality Assurance: D. Arpe 14 May 2009

Note: The above analyses were not performed under this study. The analyses performed at Covance were performed as non-study specific.

Certificate of Analysis for Speyer 2.2 Soil

TEST SYSTEM CERTIFICATE OF ANALYSIS

Test system code	CS12/10
Test system name	Speyer 2.2
Supplied by	Speyer
Sampling location	"Großer Striet", Nr.585, Hanhofen, Rheinland-Pfalz, Germany
Date of field sampling	07 April 2010 Depth of sampling *ca* 20cm
Date of arrival at Covance	20 April 2010
Pesticide history	No pesticides applied in the last 5 years.
Land use	Meadow
Method of soil collection	In accordance with ISO 10381-6.
Soil order (FAO soil classification)	Mollisol
Handling	The 2 mm sieved soil was given a unique code and thoroughly mixed with the minimum of air drying. Prior to use the soil was stored in the dark, in an incubator routinely maintained at 4 ± 2°C, in loosely tied plastic bags in accordance with ISO 10381-6.

UK & BBA Particle Size Distribution (PSD) *		pH in 0.01M $CaCl_2$ *	5.5
Sand % (2000 – 63 µm)	80.7		
Silt % (63 – 2 µm)	12.8		
Clay % (< 2 µm)	6.4	Organic Carbon (OC) % *	2.1
		Organic Matter % *	3.6
USDA Particle Size Distribution *			
Sand % (2000 – 50 µm)	82.0	Cation Exchange Capacity (CEC) *	
Silt % (50 – 2 µm)	11.6	meq/100g	10.0
Clay % (< 2 µm)	6.4	mmol/Kg	100.0
ISSS Particle Size Distribution *		Microbial Biomass µg C/g (Commenced: 21 Apr 10)	541.5
Sand % (2000 – 20 µm)	86.5		
Silt % (20 – 2 µm)	7.0		
Clay % (< 2 µm)	6.4	Microbial Biomass as a % of OC (Commenced: 21 Apr 10)	2.6
UK Textural Class	Loamy sand	Disturbed Bulk Density g/cm³	1.2
BBA Textural Class	schwach lehmiger Sand		
USDA Textural Class	Loamy sand	pH in H_2O (Commenced: 23 Apr 10)	6.0
ISSS Textural Class	Loamy sand		
Water Holding Capacity at pF 0* MWHC (0.001 bar) %	46.5	pH in KCl (Commenced: 23 Apr 10)	5.1
Water Holding Capacity at pF 2.0 (0.1 bar) %	20.0		
Water Holding Capacity at pF 2.5 (0.33 bar) %	13.6		

Methods used: pH H_2O, KCl (ISO 10390, 1:5 ratio soil to solution); Microbial Biomass (fumigation-extraction); pF2 & 2.5 (pressure plate)

The analytical procedures * undertaken at Covance Laboratories Ltd., Harrogate were performed in accord with the current national UK GLP Regulations and the current OECD Principles of GLP.
All data is retained in the GLP archive of Covance Laboratories Ltd., Harrogate.
* Analysis performed by Speyer (Analysis Data Sheet for Standard Soils According to GLP dated 15/April/10). No claim is being made for the compliance status of this work.

Compiled by: 13 Aug 10

Approved by: 15 Sept 10

Quality Assurance: 8 Oct 10

Note: The above analyses were not performed under this study. The analyses performed at Covance were performed as non-study specific.

Certificate of Analysis for SK920191 Soil

TEST SYSTEM CERTIFICATE OF ANALYSIS

Test system code	CS14/09		
Test system name	SK920191		
Supplied by	Land Research Associates		
Sampling location	South Witham Quarry, South Witham, Lincolnshire		
Date of field sampling	03 March 2009	Depth of sampling	5-20cm
Date of arrival at Covance	10 March 2009		
Grid reference (Coordinates)	SK920191 (52° 45' 44.4"N, 0° 38' 11.3"W)		
Pesticide history	No pesticides applied in the last 5 years.		
Land use	Undisturbed arable land		
Method of soil collection	Spade		
Soil order (FAO soil classification)	Inceptisol		
Handling	The 2 mm sieved soil was given a unique code and thoroughly mixed with the minimum of air drying. Prior to use the soil was stored in the dark, in an incubator routinely maintained at 4 ± 2°C, in loosely tied plastic bags in accordance with ISO 10381-6.		

UK & BBA Particle Size Distribution (PSD)		pH in H_2O (Commenced: 25/3/09)	7.9
Sand % (2000 – 63 µm)	42		
Silt % (63 – 2 µm)	28	pH in 1M KCl (Commenced: 25/3/09)	7.7
Clay % (< 2 µm)	30		
USDA Particle Size Distribution		pH in 0.01M $CaCl_2$ (Commenced: 25/3/09)	7.6
Sand % (2000 – 50 µm)	43		
Silt % (50 – 2 µm)	27		
Clay % (< 2 µm)	30	Organic Carbon (OC) %	3.8
		Organic Matter %	6.6
ISSS Particle Size Distribution		(Commenced: 23/3/09)	
Sand % (2000 – 20 µm)	54		
Silt % (20 – 2 µm)	16	Cation Exchange Capacity (CEC)	
Clay % (< 2 µm)	30	meq/100g	33.9
		mmol/Kg	339.2
UK Textural Class	Clay loam	(Commenced: 24/3/09)	
BBA Textural Class	sandiger toniger Lehm		
USDA Textural Class	Clay loam	Microbial Biomass µg C/g	778.9
ISSS Textural Class	Light clay	(Commenced: 25/3/09)	
Water Holding Capacity at pF 0 MWHC (0.001 bar) %	65.7	Microbial Biomass as a % of OC (Commenced: 23/3/09)	2.1
Water Holding Capacity at pF 2.0 (0.1 bar) %	34.2	Disturbed Bulk Density g/cm^3	1.1
		Microbial Biomass µg C/g	773.9
Water Holding Capacity at pF 2.5 (0.33 bar) %	26.9	(Commenced: 27/5/09)	
		Microbial Biomass as a % of OC	2.0
		(Commenced: 23/3/09)	

Methods used: PSD (hydrometer); pH (ISO 10390, 1:5 ratio soil to solution); Organic Carbon & Organic Matter (Walkley-Black rapid titration); CEC (buffered $BaCl_2$); Microbial Biomass (fumigation-extraction); Nitrogen (Kjeldahl digestion & spectrophotometer); MWHC (capillary foam saturation); pF2 & 2.5 (pressure plate)

The analytical procedures undertaken at Covance Laboratories Ltd., Harrogate were performed in accord with the current national UK GLP Regulations and the current OECD Principles of GLP.
All data is retained in the GLP archive of Covance Laboratories Ltd., Harrogate.

Compiled by: 9 June 09

Approved by: 18 July 09

Quality Assurance: 09 October 2009

Note: The above analyses were not performed under this study. The analyses performed at Covance were performed as non-study specific.

Certificate of Analysis for Chelmorton Soil

TEST SYSTEM CERTIFICATE OF ANALYSIS

Test system code	CS11/10
Test system name	Chelmorton
Supplied by	Land Research Associates
Sampling location	Farditch Farm, Chelmorton, Derbyshire
Date of field sampling	14 April 2010 Depth of sampling Topsoil 10-20cm
Date of arrival at Covance	16 April 2010
Grid reference (Coordinates)	SK104691 (53° 13' 8.6"N, 1° 50' 39.4"W)
Pesticide history	No pesticide use
Land use	Permanent grassland
Method of soil collection	Spade, in accordance with ISO10381-6
Soil taxonomy (USDA soil classification)	Inceptisol
Handling	The 2 mm sieved soil was given a unique code and thoroughly mixed. Prior to use the soil was st the dark, in an incubator routinely maintained at 4 ± 2°C, in loosely tied plastic bags in accordan ISO 10381-6.

UK & BBA Particle Size Distribution (PSD)		pH in H_2O (Commenced: 23 Apr 10)	6.6
Sand % (2000 – 63 µm)	21		
Silt % (63 – 2 µm)	59	pH in 1M KCl (Commenced: 23 Apr 10)	5.7
Clay % (< 2 µm)	20		
USDA Particle Size Distribution		pH in 0.01M $CaCl_2$ (Commenced: 23 Apr 10)	5.9
Sand % (2000 – 50 µm)	25		
Silt % (50 – 2 µm)	55	Organic Carbon (OC) %	3.4
Clay % (< 2 µm)	20	Organic Matter % (Commenced: 19 Apr 10)	5.9
ISSS Particle Size Distribution			
Sand % (2000 – 20 µm)	52		
Silt % (20 – 2 µm)	28	Cation Exchange Capacity (CEC)	
Clay % (< 2 µm)	20	meq/100g	25.0
		mmol/Kg	249.6
UK Textural Class	Clay loam	(Commenced: 27 Apr 10)	
BBA Textural Class	schluffiger Lehm		
USDA Textural Class	Silt loam	Microbial Biomass µg C/g (Commenced: 20 Apr 10)	446.0
ISSS Textural Class	Clay loam		
Water Holding Capacity at pF 0 MWHC (0.001 bar) %	71.0	Microbial Biomass as a % of OC (Commenced: 19 Apr 10)	1.3
Water Holding Capacity at pF 2.0 (0.1 bar) %	38.0	Disturbed Bulk Density g/cm^3	0.9
Water Holding Capacity at pF 2.5 (0.33 bar) %	28.6		

Methods used: PSD (hydrometer); pH (ISO 10390, 1:5 ratio soil to solution); Organic Carbon & Organic Matter (Walkley-Black rapid titration); CEC (buffered B Microbial Biomass (fumigation-extraction); MWHC (capillary foam saturation); pF2 & 2.5 (pressure plate)

The analytical procedures undertaken at Covance Laboratories Ltd., Harrogate were performed in accord with the current national UK GLP Regulations and the current OECD Principles of GLP.
All data is retained in the GLP archive of Covance Laboratories Ltd., Harrogate.

Compiled by: 12 Aug 10 Approved by: 1 Sept 10 Quality Assurance: 30 Aug 10

Note: The above analyses were not performed under this study. The analyses performed at Covance were performed as non-study specific.

Appendix 2
Certificates of Analysis and Specification Sheets

Specification Sheet for [Benzyl-^{14}C]S-2167

Sumitomo Chemical Co.,Ltd.
Environmental Health Science
Laboratory (Takarazuka)

SPECIFICATIONS

Name of Compound（化合物名）：[benzyl-^{14}C]S-2167

Chemical Formula（化学式）：$C_{19}H_{23}NO_3$　(MW 313.39, non-radiolabeled)

Lot No.（ロット番号）：RIS2008-010

RI No.（RI 番号）：C-2008-021T

Total Activity（総放射能量）：1.26 GBq

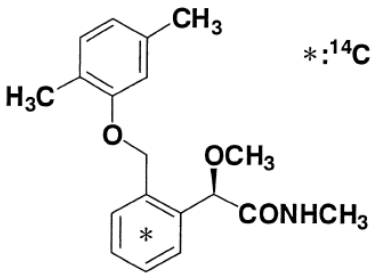
Weight（重量）：93.5 mg

Specific Activity（比放射能）：4.22 GBq/mmol

Physical Form（物理的様態）：solution (acetonitrile, 100 ml)
[concentration（濃度）：12.6 MBq/ml]

Purity（純度）：radiochemical（放射化学的）99.2%
chemical（化学的）98.0%（UV 254 nm）
optical（光学的）100%（UV 275 nm）

Structure（構造式）



Senior Research Associate：Motohiro Kurosawa　Date：Nov. 19, 2008
Motohiro Kurosawa, M.Sc.

Specification Sheet for [Phenoxy-^{14}C]S-2167

Sumitomo Chemical Co.,Ltd.
Environmental Health Science
Laboratory (Takarazuka)

SPECIFICATIONS

Name of Compound（化合物名）：[phenoxy-^{14}C]S-2167

Chemical Formula（化学式）：$C_{19}H_{23}NO_3$　(MW 313.39, non-radiolabeled)

Lot No.（ロット番号）：RIS2009-002

RI No.（RI 番号）：C-2009-008T

Total Activity（総放射能量）：1.15 GBq

Weight（重量）：81.2 mg

Specific Activity（比放射能）：4.44 GBq/mmol

Physical Form（物理的様態）：solution (acetonitrile, 100 ml)

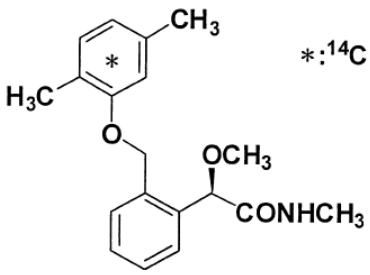
[concentration（濃度）：11.5 MBq/ml]

Purity（純度）：radiochemical（放射化学的）99.1%

chemical（化学的）98.3%（UV 254 nm）

optical（光学的）100%（UV 275 nm）

Structure（構造式）



Senior Research Associate：Motohiro Kurosawa　Date：JAN 15, 2009

Motohiro Kurosawa, M.Sc.

Certificate of Analysis for Non-radiolabelled S-2167 Analytical Standard

Sumika Technoservice Corporation.
2-1, Takatsukasa 4-Chome, Takarazuka, Hyogo 665-0051, Japan
TEL +81-797-74-2101
FAX +81-797-74-2715

CERTIFICATE OF ANALYSIS

Name of Substance : S-2200 *R*-isomer Analytical Standard
Lot No. : 060020652
Analysis Date : December 26, 2008
Storage Condition : Refrigeration (0-10℃)

Content (Purity) : 100 %

Purity analysis (Sumika Technoservice Corporation. Study No. 08077PUR), which was conducted in accordance with the following Good Laboratory Practice Standards:

* Good Laboratory Practice (GLP) for Agricultural Chemicals, Japanese Ministry of Agriculture, Forestry and Fisheries, Annex to 11-Nousan-No.6283
* EPA FIFRA Good Laboratory Practice Standards, Title 40 of U.S. Code of Federal Regulations Part 160

Study Director Satoru Nagasawa Date: 9 February 2009
Satoru Nagasawa
Sumika Technoservice Corporation.

Certificate of Analysis for Non-radiolabelled S-2354 (S-2200 *S*-isomer) Analytical Standard

Sumika Technoservice Corporation.
2-1, Takatsukasa 4-Chome, Takarazuka, Hyogo 665-0051, Japan
TEL +81-797-74-2101
FAX +81-797-74-2715

CERTIFICATE OF ANALYSIS

Name of Substance : S-2200 *S*-isomer Analytical Standard
Lot No. : 060020653
Analysis Date : December 26, 2008
Storage Condition : Refrigeration (0-10℃)

Content (Purity) : 99.7 %

Purity analysis (Sumika Technoservice Corporation. Study No. 08078PUR), which was conducted in accordance with the following Good Laboratory Practice Standards:

* Good Laboratory Practice (GLP) for Agricultural Chemicals, Japanese Ministry of Agriculture, Forestry and Fisheries, Annex to 11-Nousan-No.6283
* EPA FIFRA Good Laboratory Practice Standards, Title 40 of U.S. Code of Federal Regulations Part 160

Study Director Satoru Nagasawa Date: 9 February 2009
Satoru Nagasawa
Sumika Technoservice Corporation.

Certificate of Analysis for 5-COOH-S-2200 Reference Standard

Sumitomo Chemical Co., Ltd.
Environmental Health Science Laboratory
2-1, Takatsukasa 4-Chome, Takarazuka,
Hyogo 665-8555, Japan
TEL 81-797-74-2099
FAX 81-797-74-2087

CERTIFICATE OF QUALITY
REFERENCE STANDARDS

Chemical: 5-COOH-S-2200

Lot No.: 252-001-55-2

Maintenance No.: MA080005
(SCC-GLPNo.)

Purity: 99.7%

Analysis Date: September 9, 2008

Expiration Date: August 31, 2011

Storage Condition: in refrigerator

Hiroshi Komori Date: October 20, 2008

Hiroshi Komori
Environmental Health Science Laboratory
Sumitomo Chemical Co., Ltd.

Certificate of Analysis for 2-COOH-S-2200 Reference Standard

Sumitomo Chemical Co., Ltd.
Environmental Health Science Laboratory
2-1, Takatsukasa 4-Chome, Takarazuka,
Hyogo 665-8555, Japan
TEL 81-797-74-2099
FAX 81-797-74-2087

CERTIFICATE OF QUALITY
REFERENCE STANDARDS

Chemical: 2-COOH-S-2200

Lot No.: 252-001-60-2

Maintenance No.: MA080004
(SCC-GLPNo.)

Purity: 99.8%

Analysis Date: September 9, 2008

Expiration Date: August 31, 2011

Storage Condition: in refrigerator

Hiroshi Komori Date: October 20, 2008

Hiroshi Komori
Environmental Health Science Laboratory
Sumitomo Chemical Co., Ltd.

Certificate of Analysis for De-Xy-S-2200 Reference Standard

Sumitomo Chemical Co., Ltd.
Environmental Health Science Laboratory
2-1, Takatsukasa 4-Chome, Takarazuka,
Hyogo 665-8555, Japan
TEL 81-797-74-2099
FAX 81-797-74-2087

CERTIFICATE OF QUALITY
REFERENCE STANDARDS

Chemical: De-Xy-S-2200

Lot No.: CTS08001

Maintenance No.: MA080003
(SCC-GLPNo.)

Purity: 99.9%

Analysis Date: September 8, 2008

Expiration Date: August 31, 2011

Storage Condition: in refrigerator

Hiroshi Komori Date: October 20, 2008

Hiroshi Komori
Environmental Health Science Laboratory
Sumitomo Chemical Co., Ltd.

Certificate of Analysis for DX-CA-S-2200 Reference Standard

Sumitomo Chemical Co., Ltd.
Environmental Health Science Laboratory
2-1,Takatsukasa 4-Chome, Takarazuka,
Hyogo 665-8555, Japan
TEL 81-797-74-2099
FAX 81-797-74-2087

CERTIFICATE OF QUALITY
REFERENCE STANDARDS

Chemical: DX-CA-S-2200

Lot No.: CTS08031

Maintenance No.: MA080016
(SCC-GLPNo.)

Purity: 100%

Analysis Date: December 12, 2008

Expiration Date: November 30, 2011

Storage Condition: in refrigerator

Hiroshi Komori Date: January 30, 2009

Hiroshi Komori
Environmental Health Science Laboratory
Sumitomo Chemical Co., Ltd.

Certificate of Analysis for MCBX Reference Standard

Sumitomo Chemical Co., Ltd.
Environmental Health Science Laboratory
2-1, Takatsukasa 4-Chome, Takarazuka,
Hyogo 665-8555, Japan
TEL 81-797-74-2099
FAX 81-797-74-2087

CERTIFICATE OF QUALITY
REFERENCE STANDARDS

Chemical: MCBX

Lot No.: CTS08015

Maintenance No.: MA080006
(SCC-GLPNo.)

Purity: 96.9%

Analysis Date: December 19, 2008

Expiration Date: November 30, 2011

Storage Condition: in refrigerator

Hiroshi Komori Date: January 30, 2009

Hiroshi Komori
Environmental Health Science Laboratory
Sumitomo Chemical Co., Ltd.

Certificate of Analysis for 2,5-Dimethylphenol Reference Standard

SIGMA-ALDRICH

sigma-aldrich.com

Certificate of Analysis

Product Name	2,5-Dimethylphenol, ≥99%
Product Number	D174602
Product Brand	Aldrich
CAS Number	95-87-4
Molecular Formula	$(CH_3)_2C_6H_3OH$
Molecular Weight	122.16

TEST	SPECIFICATION	LOT 01212TE RESULTS
APPEARANCE	WHITE TO OFF-WHITE NEEDLES, FIBERS, CRYSTALS	OFF-WHITE CRYSTALLINE SOLID
INFRARED SPECTRUM	CONFORMS TO STRUCTURE AND STANDARD AS	CONFORMS TO STRUCTURE.
GAS LIQUID CHROMATOGRAPHY	99.0% (MINIMUM)	99.2%
QUALITY CONTROL ACCEPTANCE DATE		DECEMBER 2006

Barbara Rajzer, Supervisor
Quality Control
Milwaukee, Wisconsin USA

Appendix 3
Chromatography of Reference Standards

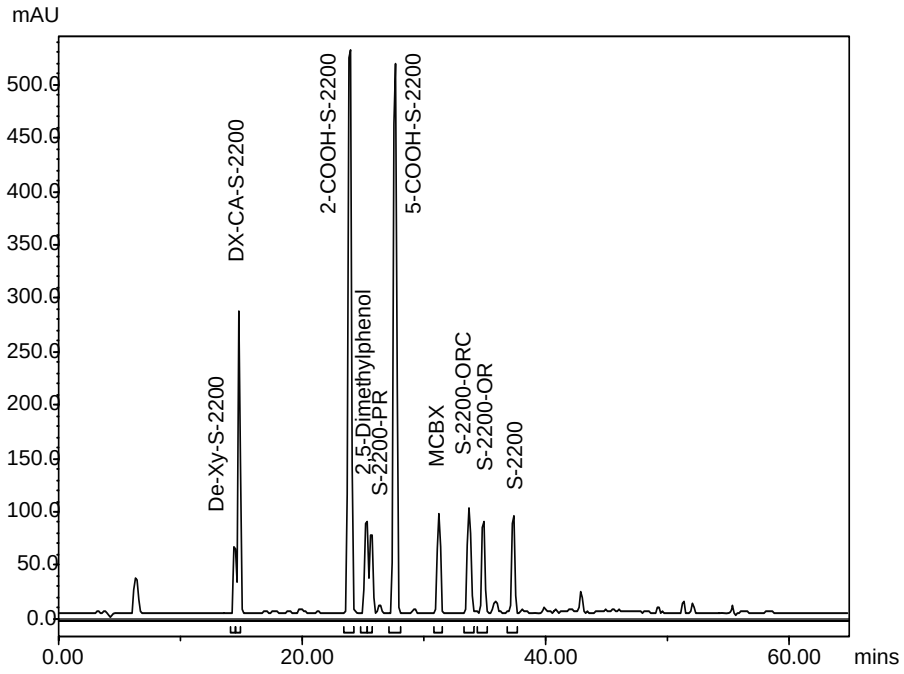
Retention Times of S-2167 and Reference Standards by HPLC

Reference Standard	Retention time by UV detection (min)			
	Method 1	Method 2	Method 3	Method 4
De-Xy-S-2200	-	14.3	-	15.7
DX-CA-S-2200	-	14.7	-	16.3
2-COOH-S-2200	-	23.8	-	27.3
2,5-dimethylphenol	-	25.2	-	-
5-COOH-S-2200	-	27.5	-	30.7
MCBX	-	31.2	-	32.7
S-2200	16.5	37.3	-	36.9
S-2167	-	-	12.7	-
S-2354	-	-	16.8	-

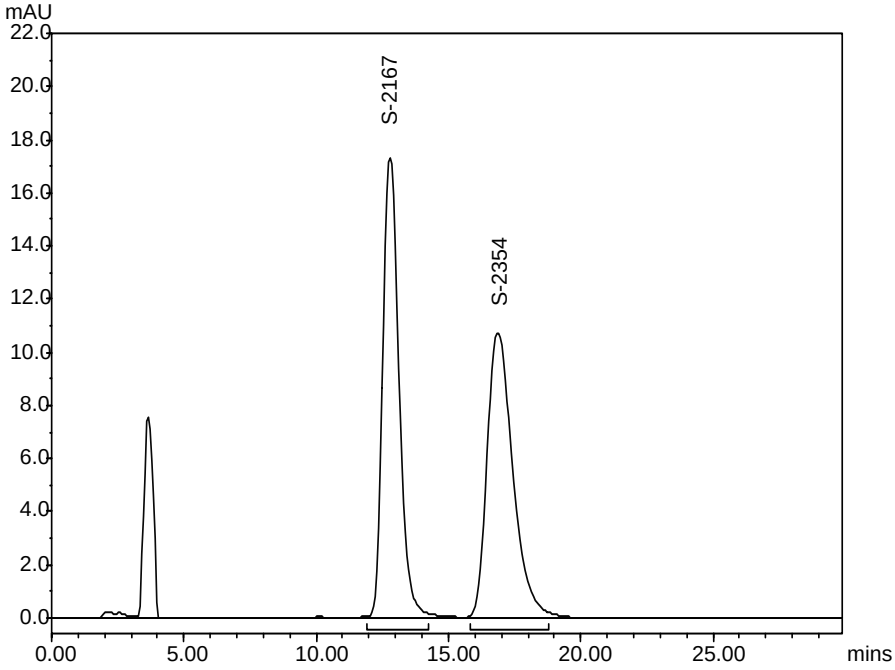
Results from 4CHR001 run 1, 1CHR015 run 1, 3CHR035-2, 6std11

Solvent system and chromatographic conditions are described on pages 24 to 25. The retention time of the UV peak was *ca* 0.1 min (data from chromatogram 4CHR038-1) before the retention time of the corresponding ^{14}C peak due to the positioning of the detectors.

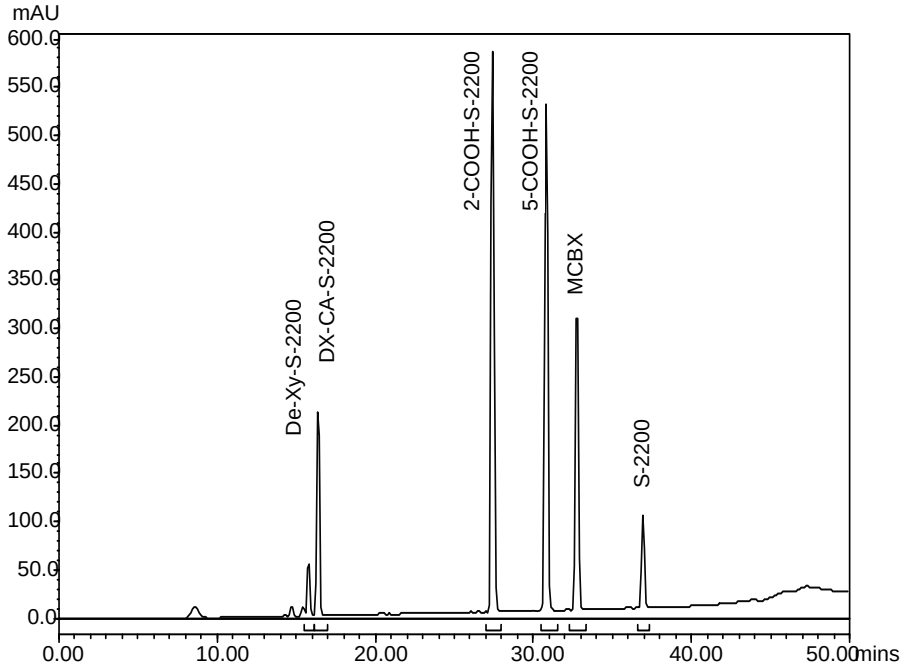
1CHR015 run 1 -(UV) (Method 2):



3CHR035 run 2 -(UV) (Method 3):



6std11 -(UV) (Method 4):



R_f Values for S-2200 and Reference Standards by TLC

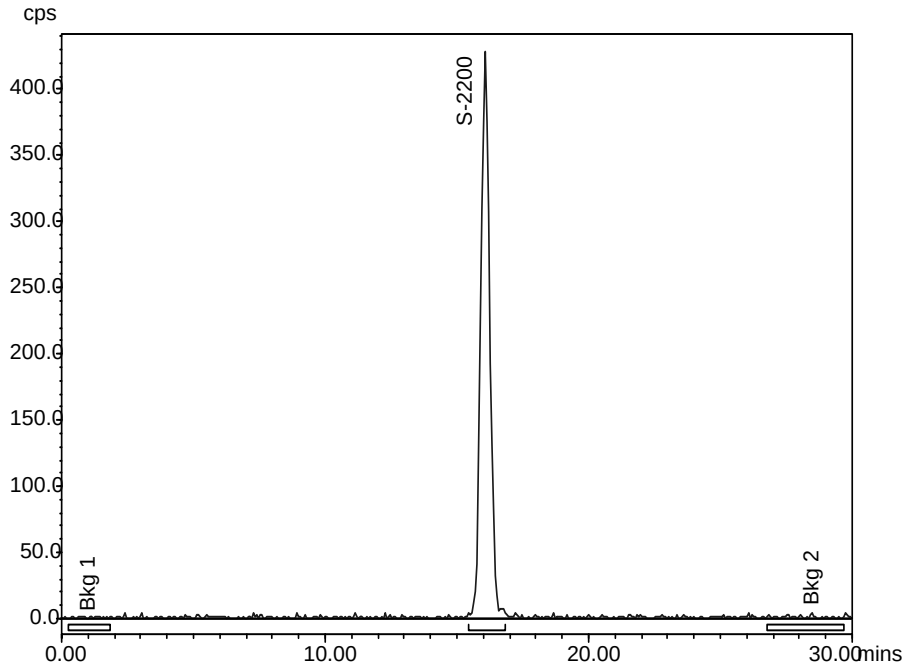
Reference Standard	R_f value		
	TLC System 1	TLC System 2	
		x-axis	y-axis
De-Xy-S-2200	-	0.38	0.62
DX-CA-S-2200	-	0.25	0.10
2-COOH-S-2200	-	0.44	0.47
2,5-dimethylphenol	-	0.69	0.74
5-COOH-S-2200	-	0.45	0.25
MCBX	-	0.50	0.77
S-2200	0.56	0.55	0.86

Results from Plate 1 and Plate 7

Solvent system and chromatographic conditions are described on page 26.
The R_f values for S-2200 and other reference compounds varied slightly depending on the chromatographic conditions and the amount of material chromatographed, however the relative position of these compounds was found to be consistent.

Appendix 4
Radiochemical Purity of S-2167

Pre-application Radiochemical Purity by HPLC for [Benzyl-^{14}C]S-2167

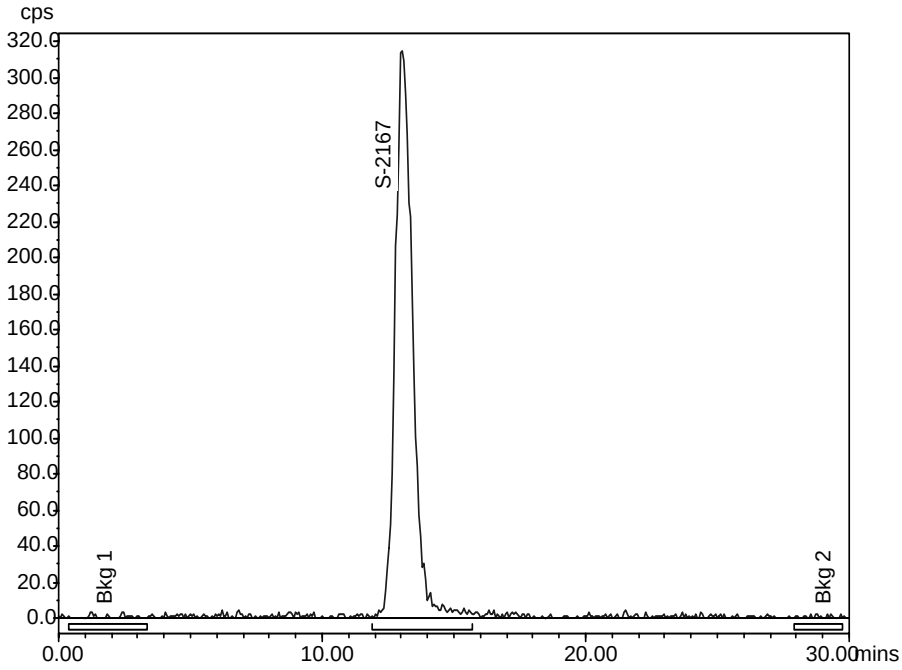


Chromatogram: 4CHR033-4
Sample: F5RCP1

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	0.28	1.83	0.98			
S-2200	15.45	16.87	16.03	429.0	9165.9	99.87
Bkg 2	26.78	29.68	28.45			
1 Peak					9165.9	99.87

Total Area:	9178.1 Counts
Average Background:	0.4 cps
Unallocated Area:	12.2 Counts

Pre-application Isomer Ratio by HPLC for [Benzyl-^{14}C]S-2167

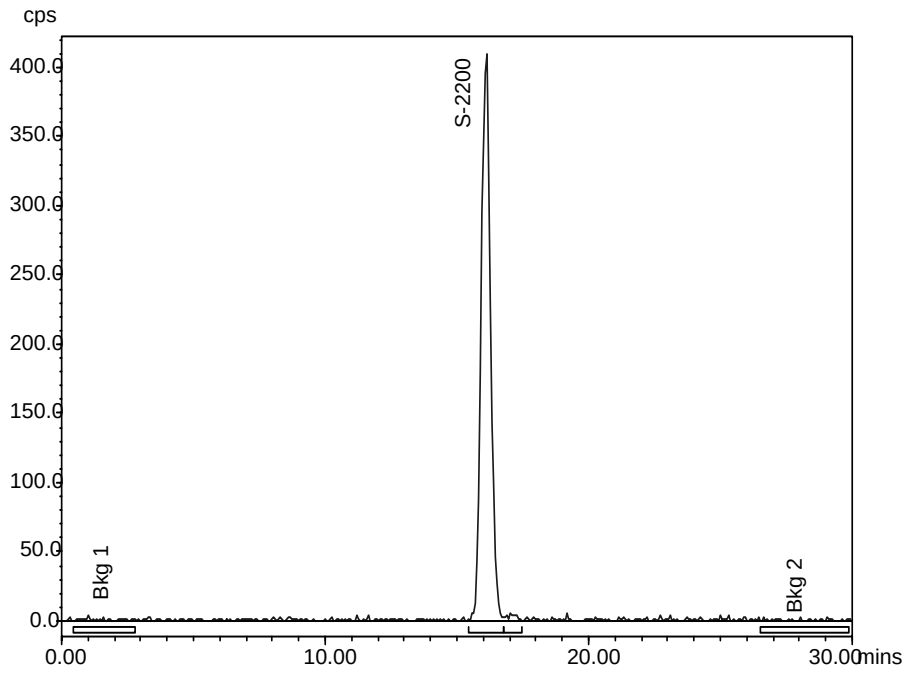


Chromatogram: 3CHR035-5
Sample: F5RCP1

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	0.38	3.37	1.77			
S-2167	11.92	15.68	12.98	315.0	13038.5	98.31
Bkg 2	27.88	29.77	29.05			
1 Peak					13038.5	98.31

Total Area:	13263.3 Counts
Average Background:	0.2 cps
Unallocated Area:	224.8 Counts

Pre-application Radiochemical Purity by HPLC for [Phenoxy-^{14}C]S-2167

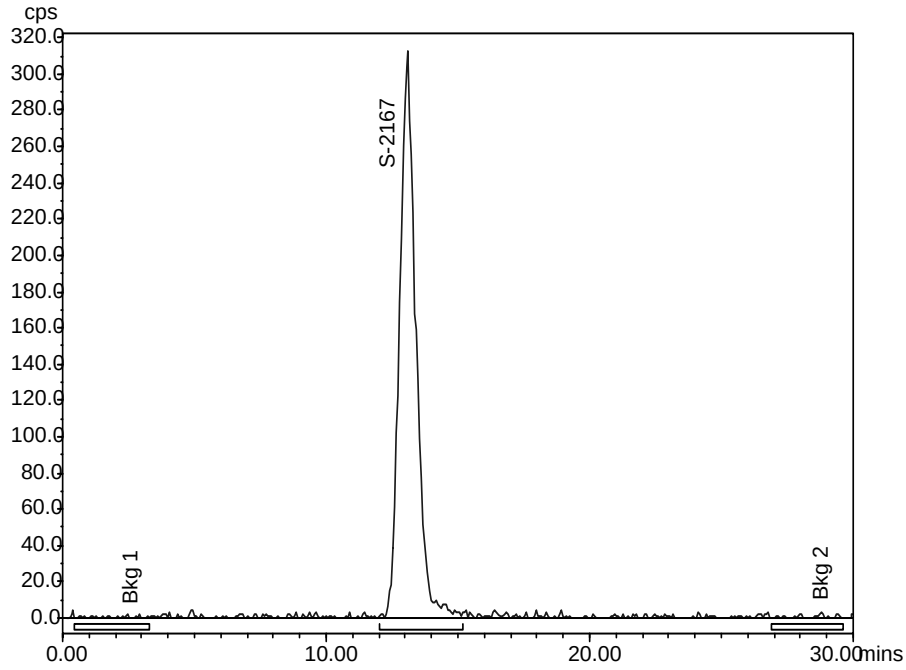


Chromatogram: 4CHR033-2
Sample: F6RCP1

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	0.43	2.80	0.95			
S-2200	15.43	16.75	16.07	410.0	9038.6	98.89
	16.75	17.47	16.98	6.0	59.4	0.65
Bkg 2	26.55	29.88	27.82			
2 Peaks					9098.0	99.54

Total Area: 9140.0 Counts
Average Background: 0.3 cps
Unallocated Area: 42.0 Counts

Pre-application Isomer Ratio by HPLC for [Phenoxy-^{14}C]S-2167



Chromatogram: 3CHR035-3
Sample: F6RCP1

Name (C-14)	Start (mins)	End (mins)	Retention (mins)	Height (cps)	Area (Counts)	%Total (%)
Bkg 1	0.47	3.32	2.62			
S-2167	12.00	15.17	13.03	313.0	12101.0	98.88
Bkg 2	26.88	29.62	28.77			
1 Peak					12101.0	98.88

Total Area:	12237.7 Counts
Average Background:	0.2 cps
Unallocated Area:	136.7 Counts

Appendix 5
Deviations from Protocol

In the protocol, it stated that the soil samples would be incubated at 20 ± 2°C, however on two occasions the temperature was measured as 23 and 17°C. On each occasion the temperature was out of specification for less than 3 hours.

In the protocol it stated that the soil units would be weighed up to every eight days to check the moisture content. However, on one occasion the period between sample weighings was nine days and on a second it was eleven days. No notable loss of moisture was observed.

The Study Director does not anticipate that these deviations have affected the integrity of the study.

ANNEX

This annex consists of 30 pages, including this one and includes:

Protocol (11 pages)

Protocol Amendment 1 (3 pages)

Protocol Amendment 2 (3 pages)

Protocol Amendment 3 (3 pages)

Protocol Amendment 4 (3 pages)

Protocol Amendment 5 (3 pages)

Protocol Amendment 6 (3 pages)

Definitive Protocol

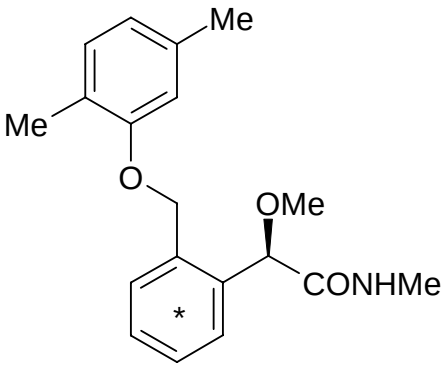
Study Title	[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation
Study Guideline	OECD Guideline 307 (April 2002)
Study Director	R Graham
Sponsor	Sumitomo Chemical Company Limited 27-1 Shinkawa 2-Chome Chuo-ku Tokyo 104-8260 JAPAN
Study Monitor	T Yano
Test Facility	Covance Laboratories Limited Otley Road Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Sponsor ID Number	1002463
Covance Study Number	8200203
Page Number	1 of 11

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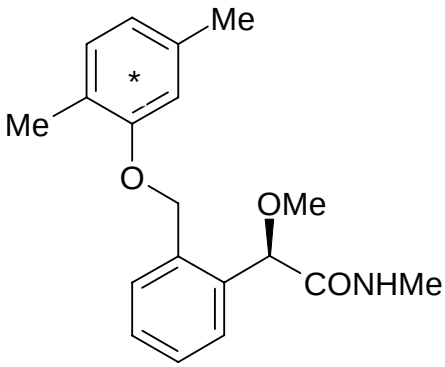
INTRODUCTION

S-2200 is a fungicide undergoing development for use on oilseed rape and wheat. This study will investigate the aerobic soil metabolism of the *R*-isomer (S-2167).

The two radiolabelled forms of [^{14}C]S-2167 to be used in this study have the following structures:



[Benzyl-^{14}C]S-2167



[Phenoxy-^{14}C]S-2167

***** Position of radiolabel.

The study will be conducted to comply with the data requirements and study guidelines stated on the front cover of the protocol.

OBJECTIVES

The objectives of the study are:

- to determine the rate of [^{14}C]S-2167 degradation in one soil under aerobic conditions at 20 ± 2°C and determine the quantity and nature of the degradation products formed
- to determine the rate of [^{14}C]S-2167 degradation under aerobic conditions at 20 ± 2°C in three further soils

TEST SUBSTANCE

[^{14}C]S-2167 in two radiolabelled forms will be supplied by the Sponsor at a radiochemical purity of not less than 98%. The radiochemical purity and the stability of the test substance in the dosing solvent will be checked at Covance prior to use in this study using two chromatographic systems supplied by the Sponsor or developed at Covance. If the radiochemical purity of either radiolabel is below 98%, the test substance may be purified by a suitable procedure subject to a separate agreement with the Sponsor.

Non-radiolabelled test substance and any potential degradation products will be provided by the Sponsor along with their analytical specifications.

All precautions required in the handling, storage and disposal of the test substance will be outlined by the Sponsor. Unless otherwise advised, [^{14}C]S-2167 will be stored frozen (<-10^{o}C) in the dark, non-radiolabelled test substance and potential degradation products will be stored refrigerated (1 to 10^{o}C) in the dark.

Any unused radiolabelled test substance will be retained by Covance until the end of the series of experiments to be performed on the compound. At the end of this period it will either be returned to the Sponsor or disposed of by Covance.

Non-radiolabelled test substance and reference standards will normally be disposed of when the expiry date has been exceeded, unless the Sponsor requests retention.

TEST SYSTEM

Supply
A sandy loam or silt loam soil (organic carbon 0.5 to 2.5%, pH in 0.01 M $CaCl_2$ of 5.5 to 8.0) and three other soils obtained by Covance will be used. Choice of soils will be to comply with the known data requirements and study guidelines stated on the front cover of the protocol. The additional three soils selected will cover a range of relevant soils and vary in their organic carbon content, pH, clay content and microbial biomass. The soils will be freshly collected from the field (from the A horizon or top 20 cm layer). Each soil will have a unique code.

Preparation and Characterisation
Prior to use, test soils will have been thoroughly mixed and passed through a 2 mm mesh sieve, with the minimum of air drying. Soils will have an audited Certificate of Analysis, detailing at a minimum, the following characterisation:

- pH (H_2O)
- pH ($CaCl_2$)
- pH (KCl)
- organic carbon content
- organic matter content
- particle size distribution (USDA and UK/BBA)
- textural class (USDA, UK and BBA)
- cation exchange capacity
- disturbed bulk density
- moisture holding capacity at pF 0 (maximum water holding capacity, MWHC), pF 2.0 (10 kPa) and pF 2.5 (33 kPa)
- microbial biomass (by fumigation-extraction)

Microbial biomass will be determined on completion of the incubation period (by fumigation-extraction) and at application if organic solvents are to be used in the treatment solution. If the incubations exceed *ca* 120 days then microbial biomass will also be determined during the incubation phase.

If the soil is obtained from Speyer, Germany, the Speyer characterisation results will be used.

Storage

Prior to use, soils will be stored in the dark, in an incubator routinely maintained at 4 ± 2°C, in loosely tied plastic bags, in accordance with the ISO international standard ISO 10381-6. Test soils will be dispensed and dosed within three months of collection. If used after this time, further analysis may be required.

Incubation Unit Preparation

There will be five incubation groups as detailed below:

Incubation group	Radiolabel	Soil type	Study type	Number of Units*
A	[benzyl-^{14}C]S-2167	soil type 1	Route and rate of degradation	20
B	[phenoxy-^{14}C]S-2167	soil type 1	Route and rate of degradation	20
C	[benzyl-^{14}C]S-2167	soil type 2	Rate of degradation	20
D	[benzyl-^{14}C]S-2167	soil type 3	Rate of degradation	20
E	[benzyl-^{14}C]S-2167	soil type 4	Rate of degradation	20

*Includes spare treated units but excludes biomass units (see below)

Soil samples (50 g dry weight equivalent) will be weighed into individual glass vessels, through which moistened air will be drawn, before being passed through a series of traps. The first trap will be empty and will act as a security trap, the second and third will contain ethanediol and 2% liquid paraffin in xylene to trap polar and non-polar volatiles respectively. The final two will contain 2 M sodium hydroxide solution to trap liberated carbon dioxide. Effluent air from the units will be drawn through the traps.

A sufficient number of soil samples will be dispensed to allow duplicate analyses at each sampling interval plus eight spares per incubation group.

Control soil samples (50 g dry weight equivalent) to be used for biomass determination will also be weighed into individual glass vessels, through which moistened air will be drawn, but will not be connected to a series of traps. Twelve samples per soil type will be dispensed to allow determination of biomass to be conducted at application and at the end of the test. If in any incubation group the incubation period exceeds *ca* 120 days then there will be an additional biomass determination at this time. The control soil samples will be dispensed at the same time as the test units.

Soil units will be maintained under experimental conditions (moisture adjusted to a water holding capacity (WHC) of pF 2.0 and incubation in the dark at a temperature of 20 ± 2^{o}C) for at least two weeks prior to test substance application. Any seeds that

germinate will be removed as far as is practical immediately prior to test substance application.

EXPERIMENTAL PROCEDURES

Test Substance Application

[^{14}C]S-2167 (equivalent to 200 g ai/ha) will be added to soil in organic solvent. The application rate of 200 g/ha is equivalent to 0.8 µg/g soil if a soil density of 1 g/cm^3 and an incorporation depth of 2.5 cm are assumed. The homogeneity of the application solution will be checked before and after use.

Control units will be treated with an equivalent volume of organic solvent.

Each incubation unit will be labelled with the study number and a unique sample code.

The radiochemical and optical purities of [^{14}C]S-2167 will be determined in the application solution. This will be performed both before and after application unless the purities before application are determined on the same day as the application.

Aliquots of the treatment solution will be applied on one occasion, to a sufficient number of soil samples to enable duplicate analyses at each sampling interval. A further eight units per incubation group will be set up as spare samples which will only be analysed in the event of the loss of any other sample. Alternatively, the units will be used to extend the duration of the test by protocol amendment.

The test substance will be dispensed dropwise on the surface of the soil. The solvent will be allowed to evaporate before initiation of the incubation. The treated soil will be mixed thoroughly.

Soil Incubation

The water content of all soil units will be adjusted to pF 2.0 on the day of treatment (after treatment, where applicable). Units will be weighed up to every eight days and any moisture loss will be replaced with reverse osmosis (RO) water. Samples will be incubated in the dark at a temperature of 20 ± 2^{o}C.

Sampling Intervals

At intervals of 0 hours (immediately after treatment) and at 7 ± 1, 14 ± 1, 30 ± 2, 60 ± 2 and 120 ± 2 days after application, duplicate units treated with radiolabelled test substance will be removed for analysis. A decision will be made whether further sampling is required after the results of the 120-day sampling interval become available.

The radioactivity in the trapping reagents will be quantified by liquid scintillation counting (LSC). The traps will be analysed when the units to which they are attached are removed for analysis.

Sample Analysis
The total sample for each soil incubate will be extracted based upon methods supplied by the Sponsor or developed at Covance. Extracts containing ≥ 5% of applied radioactivity will be concentrated and analysed by high performance liquid chromatography (HPLC). The optical purity of [^{14}C]S-2167 will be determined in representative extracts.

The HPLC method used for analysis will be based on the method supplied by the Sponsor. The identity of parent compound and degradation products will be confirmed in selected samples by thin layer chromatography (TLC). If authentic standards are not available, the structure of metabolites may be elucidated by mass spectrometry, subject to a separate agreement with the Sponsor and will be covered by a protocol amendment.

Chromatographic data will be collected and processed by Laura (HPLC) or Tina (TLC) software. The versions used will be documented in the final report.

If ≥ 5% of applied radioactivity is recovered in sodium hydroxide traps, confirmation of $^{14}CO_2$ in selected samples will be performed by barium carbonate precipitation. If ≥ 5% of applied radioactivity is recovered in traps designed to collect organic volatiles, the nature of the trapped material may be investigated using chromatographic techniques or mass spectrometry (this would be the subject of a separate agreement with the Sponsor).

Samples and extracts will be stored frozen when not in use. This is an appropriate method for minimising decomposition of metabolites. An extract from the route of degradation soil that contains metabolites will be analysed before and after a frozen storage period of two months to assess storage stability of extracts. Efforts will be made to analyse all extracts as soon as possible after preparation and periods of frozen storage of more than a few days prior to analysis will be avoided wherever possible.

If unextracted residues are present at ≥10% of applied radioactivity, the Sponsor will be consulted about bound residue analysis.

Determination of Radioactivity
Weights of all samples will be measured where appropriate. Triplicate portions of each soil sample, post-extraction, will be combusted in oxygen using a Packard or Harvey Oxidiser. The combusted products will be absorbed in Permafluor®E$^+$: Carbosorb®E (2:1 v/v) (Perkin Elmer Life Sciences) or suitable alternative and the radioactivity determined by LSC using a Packard Tricarb liquid scintillation counter.

Duplicate portions of extracts of soil and trap contents will be added directly to scintillant and the radioactive content determined by LSC using a Packard Tricarb liquid scintillation counter.

Method development Test
Ten incubation units (two per incubation group to be used in the definitive test) will be incubated for up to 14 days. Five of the incubated samples will be analysed by the proposed method to determine the approximate degradation rate and refine experimental conditions. The other five samples will be kept as spares and analysed if

necessary. Zero time samples will also be prepared to check extractability and for any degradation during work-up.

DATA PRESENTATION AND ANALYSIS

Individual and mean data will be tabulated and presented in graphical form as appropriate. The following parameters will be reported, but not necessarily limited to:

- an overall mass balance for the applied radioactivity in each soil sample
- the half life (in case of pseudo first order kinetics) and or the times for 50% (DT-50), 75% (DT-75) and 90% (DT-90) disappearance of [^{14}C]S-2167. Kinetics will be based on FOCUS recommendations
- the amounts of test substance, transformation products, volatile substances (in % only) and non-extractable as % of applied initial amount and as mg/kg soil (based on the soil dry weight) for each sampling interval
- identification of degradation products if possible
- if possible from the data, the times for 50% (DT-50), 75% (DT-75) and 90% (DT-90) disappearance of any metabolites of [^{14}C]S-2167 that are present at ≥5% of applied radioactivity at two consecutive timepoints
- a diagram of the proposed transformation route(s) will be prepared if possible

RECORDS TO BE MAINTAINED

Study records maintained will include, but will not necessarily be limited to, the protocol (and any amendments); notes to file; study-related correspondence and all laboratory raw data generated.

GLP COMPLIANCE

Protocol Adherence
Covance undertake to adopt all reasonable measures to record data in accordance with the protocol. Under practical working conditions, however, some minor variations may occur due to circumstances beyond the control of Covance. All such variations will be documented in the study records, together with the reason for their occurrence, where appropriate, and detailed in the final report. If planned alterations in protocol specifications occur, a protocol amendment will be issued for authorisation by the study Sponsor.

The study will be conducted in accordance with Covance Standard Operating Procedures and the following national and international Codes of Good Laboratory Practice:

- The United Kingdom (GLP Monitoring Authority, Medicines and Healthcare products Regulatory Agency (MHRA)) Good Laboratory Practice Regulations

1999, Statutory Instrument 1999 No. 3106, as amended by the Good Laboratory Practice (Codification Amendments Etc.) Regulations 2004

- The OECD Principles of Good Laboratory Practice (1998) ENV/MC/CHEM(98)17 (Revised in 1997, Issued January 1998)

Studies performed in compliance with the GLP regulation and standard referenced above will be fully acceptable to the US EPA and Japanese regulatory authorities.

Protocol Amendments
If planned alterations in protocol specifications occur, a protocol amendment will be issued for authorisation by the Sponsor.

Quality Assurance Evaluation
The study described in this protocol will be subject to Quality Assurance Evaluation. The form of this inspection will be described in the QA Standard Operating Procedures.

Inspection by Regulatory Authorities
In the event of any inspection of Covance by an outside authority during the course of the study, the Sponsor will be consulted before the inspectors are permitted access to any of the study records (unless required by law or regulation).

REPORTING

Following completion of the experimental phase and internal scientific review, a draft report will be issued to the Sponsor for comments and submitted to Covance Quality Assurance Unit (QAU) for audit. A single set of Sponsor comments should be supplied for inclusion into a final document within three months of receipt of the draft document.

Once the Sponsor comments and QA findings have been incorporated a revised draft report may be issued to the Sponsor. If subsequently, further revised versions of the draft report are issued at the request of the Sponsor, this may result in additional cost to the Sponsor.

The final report will be issued following QA audit of the complete draft report and approval of the revised draft report by the Sponsor.

In accordance with requirements of the UK Medicines and Healthcare Products Regulatory Agency GLP Monitoring Authority, if no Sponsor comments are received within six months of issue, the report will be finalised. Any further changes after this time will be addressed as an amended final report, which may result in additional costs.

SAMPLE STORAGE

The following samples will be retained until at least issue of the Final Report:

- Traps from the terminal timepoint that contain detectable radioactivity (stored at room temperature)
- All other traps that contain ≥1% of applied radioactivity (stored at room temperature)
- Unused sub-samples (if any)
- Work-up phases containing ≥1% of applied radioactivity
- Post-extraction solids
- Spare samples (if any)
- Extracts used for chromatography
- Isolated metabolites (if any)

All other samples may be discarded as the study proceeds.

The following samples will be retained after the issue of the Final Report:

- Unused sub-samples (if any)
- Post-extraction solids
- Spare samples (if any)
- Extracts used for chromatography
- Isolated metabolites (if any)

All other samples may be discarded after the Final Report is issued.

All samples will be stored at <-10°C unless otherwise stated.

ARCHIVE STATEMENT

All primary data (including electronic data), or authenticated copies thereof, will be retained in the Covance Laboratories Limited archives for fifteen years after issue of the Final Report. At this time, the Sponsor will be contacted to determine whether the data should be returned, retained or destroyed on their behalf. Sponsors will be notified of the financial implications of each of these options at that time. One copy of the protocol and Final Report will be held indefinitely in the Covance Laboratories Limited archives.

Selected specimens or samples[a] will be retained for as long as the material permits further evaluation, or up to four weeks after issue of the Final Report (whichever period is the shorter). At finalisation of the report, the Sponsor will be contacted to determine whether specimens or samples should be returned, retained or destroyed on their behalf. Any financial implications of these options will also be communicated at this time. Note that where the Sponsor fails to clarify their requirements within four weeks of our communication, Covance reserve the right to dispose of these materials. Specimens or samples will not be destroyed without prior approval of the Study Director.

[a] See Sample Storage section

PROPOSED TIMELINES

Experimental start:	March 2009
Experimental completion:	October 2009
Draft report:	December 2009

RESPONSIBLE PERSONNEL

STUDY MANAGEMENT	**NAME**
Study Director[1]	R Graham
Study Co-ordinator[2]	J Gilbert
OPERATIONAL SUPERVISION[2]	
Study Supervisor	To be confirmed
In Life Supervisor & Test System Analysis	P Davies
Sterility Confirmation	M Ballantyne
QUALITY ASSURANCE[2]	
Director, Quality Systems	C Clare

[1] = Any change documented by protocol amendment
[2] = Any change documented in study records

Distribution:
Personnel above, Resource Management, Resource Estimation

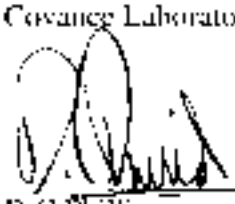
APPROVAL

T Yano
Study Monitor
Sumitomo Chemical Company Limited

Date

R Grattan
Study Director
Covance Laboratories Limited

Date



D C Phillips
Associate Director, Environmental Sciences
Covance Laboratories Limited

06 March 2009
Date

Protocol Amendment

Study Title	[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation
Study Guideline	OECD Guideline 307 (April 2002)
Study Director	R Graham
Sponsor	Sumitomo Chemical Company Limited 27-1 Shinkawa 2-Chome Chuo-ku Tokyo 104-8260 JAPAN
Study Monitor	T Yano
Test Facility	Covance Laboratories Limited Otley Road Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Sponsor ID Number	1002463
Covance Study Number	8200203
Test Facility	Covance Laboratories Limited Otley Road, Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Amendment Number	1
Page Number	1 of 3

TEST SUBSTANCE

Delete
If the radiochemical purity of either radiolabel is below 98%, the test substance may be purified by a suitable procedure subject to a separate agreement with the Sponsor.

Insert
The two radiolabelled forms of the test substance will be purified by a suitable procedure.

Reason
The radiochemical purity of the two radiolabelled forms of the test substance is below 98%.

EXPERIMENTAL PROCEDURES

Sampling Intervals

Delete
The traps will be analysed when the units to which they are attached are removed for analysis.

Insert
The traps will be analysed when the units to which they are attached are removed for analysis, or will be analysed and replenished with fresh reagents after every *ca* 30 to 40 days, whichever comes sooner.

Method Development

Insert
The method development test will not be reported.

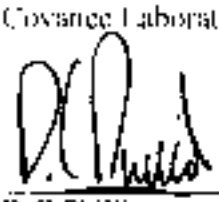
APPROVAL

T Yano
Study Monitor
Sumitomo Chemical Company Limited

Date

R Graham
Study Director
Covance Laboratories Limited

Date



D C Phillips
Associate Director, Environmental Sciences
Covance Laboratories Limited

17 April 2009
Date

Protocol Amendment

Study Title	[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation
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Sponsor	Sumitomo Chemical Company Limited 27-1 Shinkawa 2-Chome Chuo-ku Tokyo 104-8260 JAPAN
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Test Facility	Covance Laboratories Limited Otley Road Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Sponsor ID Number	1002463
Covance Study Number	8200203
Test Facility	Covance Laboratories Limited Otley Road, Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Amendment Number	2
Page Number	1 of 3

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EXPERIMENTAL PROCEDURES

Sample Analysis

Delete

If unextracted residues are present at ≥10% of applied radioactivity, the Sponsor will be consulted about bound residue analysis.

Insert

Bound residue analysis will be performed on a representative sample from each soil type and radiolabelled treatment in which unextracted residues are present at ≥10% of applied radioactivity.

Reason

Unextracted residues are present at ≥10% of applied radioactivity.

PROPOSED TIMELINES

Delete

Experimental completion:	October 2009
Draft report:	December 2009

Insert

Experimental completion:	January 2010
Draft report:	February 2010

Reason

The proposed timelines have been changed due additional analysis.

APPROVAL

T Yano
Study Monitor
Sumitomo Chemical Company Limited

Date

R Graham
Study Director
Covance Laboratories Limited

Date

D C Phillips
Associate Director, Environmental Sciences
Covance Laboratories Limited

14 Dec 2009
Date

Protocol Amendment 3

Study Title	[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation
Study Guideline	OECD Guideline 307 (April 2002)
Study Director	R Graham
Sponsor	Sumitomo Chemical Company Limited 27-1 Shinkawa 2-Chome Chuo-ku Tokyo 104-8260 JAPAN
Study Monitor	K Nishioka
Test Facility	Covance Laboratories Limited Otley Road Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Sponsor ID Number	1002463
Covance Study Number	8200203
Test Facility	Covance Laboratories Limited Otley Road, Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
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REASON FOR THIS AMENDMENT

This protocol amendment has been issued to document a change in Study Monitor at Sumitomo Chemical Co., Ltd.

Effective from the 1st April 2010, the role of Study Monitor for this study has transferred from Dr T Yano to Dr K Nishioka.

APPROVAL

K Nishioka
Study Monitor
Sumitomo Chemical Company Limited

Date

R Graham
Study Director
Covance Laboratories Limited

Date

D C Phillips
Associate Director, Environmental Sciences
Covance Laboratories Limited

Date

Protocol Amendment 4

Study Title	[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation
Study Guideline	OECD Guideline 307 (April 2002)
Study Director	R Graham
Sponsor	Sumitomo Chemical Company Limited 27-1 Shinkawa 2-Chome Chuo-ku Tokyo 104-8260 JAPAN
Study Monitor	K Nishioka
Test Facility	Covance Laboratories Limited Otley Road Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Sponsor ID Number	1002463
Covance Study Number	8200203
Test Facility	Covance Laboratories Limited Otley Road, Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
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REASON FOR THIS AMENDMENT

This protocol amendment has been issued to document procedures to be repeated for Soil types 3 and 5 (incubation groups C and E in the protocol). The main test will be repeated on fresh batches of these two soil types following the procedures documented in the protocol and amendments 1 to 3, with the exception of the following points:

Four spare samples will be prepared for each incubation group in place of eight spare samples in the original protocol.

Eight samples per soil type will be dispensed to allow determination of biomass to be conducted at application and at the end of the test.

These procedures will be repeated due to low biomass values potentially having affected the viability of the original batches of soil.

APPROVAL

K. Nishioka

25 May 2010

K Nishioka
Study Monitor
Sumitomo Chemical Company Limited

Date

R Graham
Study Director
Covance Laboratories Limited

Date

D C Phillips
Associate Director, Environmental Sciences
Covance Laboratories Limited

18TH May 2010

Date

Protocol Amendment 5

Study Title	[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation
Study Guideline	OECD Guideline 307 (April 2002)
Study Director	R Graham
Sponsor	Sumitomo Chemical Company Limited 27-1 Shinkawa 2-Chome Chuo-ku Tokyo 104-8260 JAPAN
Study Monitor	K Nishioka
Test Facility	Covance Laboratories Limited Otley Road Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Sponsor ID Number	1002463
Covance Study Number	8200203
Test Facility	Covance Laboratories Limited Otley Road, Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
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PROPOSED TIMELINES

Delete
Experimental completion: January 2010

Draft report: February 2010

Insert
Experimental completion: October 2010

Revised draft report: December 2010

Reason
The proposed timelines have been changed due to the additional work described in protocol amendment 4.

APPROVAL

K Nishioka
Study Monitor
Sumitomo Chemical Company Limited

4 October 2010
Date

R Graham
Study Director
Covance Laboratories Limited

Date

D C Phillips
Associate Director, Environmental Sciences
Covance Laboratories Limited

01 October 2010
Date

Protocol Amendment 6

Study Title	[^{14}C]S-2167 (S-2200 *R*-isomer): Aerobic Soil Metabolism and Degradation
Study Guideline	OECD Guideline 307 (April 2002)
Study Director	R Graham
Sponsor	Sumitomo Chemical Company Limited 27-1 Shinkawa 2-Chome Chuo-ku Tokyo 104-8260 JAPAN
Study Monitor	K Nishioka
Test Facility	Covance Laboratories Limited Otley Road Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
Sponsor ID Number	1002463
Covance Study Number	8200203
Test Facility	Covance Laboratories Limited Otley Road, Harrogate North Yorkshire HG3 1PY UNITED KINGDOM
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EXPERIMENTAL PROCEDURES

Sample Analysis

Insert

The DX-CA-S-2200 peak will be isolated from extracts of representative soil samples by HPLC with fraction collection. The isolated samples will be analysed by TLC.

Reason

This isolation and analysis will be performed to investigate whether the DX-CA-S-2200 peak is made up of just one or more than one component.

DATA PRESENTATION AND ANALYSIS

Delete

Kinetics will be based on FOCUS recommendations

Insert

Kinetics will be based on Single First Order kinetics only.

Reason

This change has been made at the request of the Sponsor.

PROPOSED TIMELINES

Delete

Experimental completion: October 2010

Insert

Experimental completion: March 2011

Reason

The proposed experimental completion timeline has been changed due to the additional work described above.

APPROVAL

K Nishioka
Study Monitor
Sumitomo Chemical Company Limited

21 February 2011
Date

R Graham
Study Director
Covance Laboratories Limited

Date

D C Phillips
Associate Director, Environmental Sciences
Covance Laboratories Limited

17 Feb 2011
Date