Data Evaluation Report on the adsorption-desorption of XDE-742 (pyroxsulam) transformation products in soil

PMRA Submission Number 2006-4727; EPA MRID Number 46908333; APVMA ATS 40362

Data Requirement:	PMRA DATA CODE:	8.2.4.2b
	EPA DP Barcode:	332118
	OECD Data Point:	IIA 7.4.1, IIA 7.4.2
	EPA Guideline:	Subdivision N, § 163-1 Leaching and Adsorption/Desorption

Test material:	5-OH-XDE-742
IUPAC	*N*-(5-hydroxy-7-methoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide
SMILES string	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(cc3OC)O)(=O)=O
Test material:	7-OH-XDE-742
IUPAC	*N*-(7-hydroxy-5-methoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide
SMILES string	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(cc3O)OC)(=O)=O
Test material:	6-Cl-7-OH-XDE-742
IUPAC	*N*-(6-chloro-7-hydroxy-5-methoxy[1,2,4]triazolo[1,5-*a*]pyrimidin-2-yl)- 2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide
SMILES string	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(c(c3O)Cl)OC)(=O)=O
Test material:	5,7-di-OH-XDE-742
IUPAC	N-(5,7-dihydroxy[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide
SMILES string	c1(c(ccnc1OC)C(F)(F)F)S(Nc2nn3c(n2)nc(cc3O)O)(=O)=O
Test material:	XDE-742 Cyanosulfonamide
IUPAC	N-cyano-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide
SMILES string	c1(c(ccnc1OC)C(F)(F)F)S(NC#N)(=O)=O
Test material:	XDE-742 Sulfonic Acid
IUPAC	2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonic acid
SMILES string	c1(c(ccnc1OC)C(F)(F)F)S(O)(=O)=O

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CITATION: Smith, J.K., 2006, Soil Batch Equilibrium Adsorption of 14C-XDE-742 Metabolites, Dow AgroSciences LLC, 9330 Zionsville Road, Indianapolis, IN 46268, 050019, M. D. Culy, 8 Feb 2006.

EXECUTIVE SUMMARY:

The adsorption characteristics of radiolabeled XDE-742 transformation products 5-OH-XDE-742, 7-OH-XDE-742, 5,7di-OH-XDE-742, 6-Cl-7-OH-XDE-742, XDE-742 sulfonic acid, and XDE-742 cyanosulfonamide were studied in four soil types: a Charentilly loam (pH 6.3, 1.0% organic carbon) from France, a Speyer LUFA 3A sandy loam (pH 7.8, 2.5% organic carbon) from Germany, a Borstel loamy sand (pH 5.7, 1.3% organic carbon) from Germany, and a Bruch West sandy loam (pH 7.9, 2.5% organic carbon) from Germany. Soil samples were sterilized by gamma radiation prior to treatment with test material. Samples were sterilized to eliminate microbial degradation during the sorption tests.

The experiment was conducted in partial fulfillment with the OECD 106, FIFRA 163-1, SETAC Part 1 Section 4, and OPPTS 835.1220 guidelines, and to meet the GLP standards U.S. EPA FIFRA 40 CFR part 160. To determine the soil: solution ratio, a preliminary study (Tier 1) was conducted. The adsorption phase of the study was carried out by equilibrating sterile soil with each transformation product in solution at nominal concentrations of 0.01 µg/mL solution in the dark at 25 °C. The equilibrating solution used was 0.01 M $CaCl_2$, with soil: solution ratios of 1:2, 1:5 and 1:10. Samples were equilibrated for 2, 4, 8, 24 and 48 hours. Based on the results of the preliminary testing, a soil: solution ratio of 1:2 was selected for the subsequent experiments.

The objectives of the definitive test were to determine the K_d and K_{oc} of the six transformation products in the four soils. The adsorption phase of the study was carried out by equilibrating sterile soil with each transformation product in solution at nominal concentrations of 0.01 µg/mL solution in the dark at 25°C. The equilibrating solution used was 0.01 M $CaCl_2$, with a soil: solution ratio of 1:2. Samples were equilibrated for 2, 4, 8, 24 and 48 hours, except for the 5,7-dihydroxy-XDE-742.

Soil and aqueous phases were separated by centrifugation after the desorption step. Selected soil samples were extracted twice with 90:10 (v:v) acetonitrile: 0.1 N HCl, centrifuged, and the extracts decanted and combined. The aqueous solution and organic extracts were assayed by LSC. ^{14}C-residue remaining in the soil after extraction was determined by oxidative combustion. For the definitive adsorption study using these transformation products, the average adsorption K_d value for four soils and the corresponding average K_{oc} values were calculated.

Representative samples of each type were analyzed by HPLC to determine stability of the test

materials over the course of the study. The % purity for 5-OH-XDE-742, 6-Cl-7-OH-XDE-742, XDE-742 sulfonic acid and XDE-742 cyanosulfonamide metabolite samples did not change over the course of the study, proving their stability through the adsorption and extraction phases. 7OH-XDE-742 did show degradation over the course of the study. Also, 5,7-di-OH-XDE-742 had a low purity at the beginning of the experiment. All calculations were made on the assumption that 100% of the extractable ^{14}C-material was the starting test material and would therefore present the worst case scenario for the adsorption calculations.

The average mass balance for 6-Cl-7-OH-XDE-742 in all four soils at the end of the adsorption phase was 100.5 ± 1.6% of the applied. The average mass balance in all four soils at the end of the adsorption phase was 99.6 ± 4.8% of the applied for 5-OH-XDE-742. The average mass balance in all four soils at the end of the adsorption phase was 101.4 ± 0.8% of the applied for 7OH-XDE-742. The average mass balance in all four soils at the end of the adsorption phase was 101.7 ± 3.1% of the applied for 5,7-di-OH-XDE-742. The average mass balance in all four soils at the end of the adsorption phase was 101.9 ± 2.8% of the applied for XDE-742 cyanosulfonamide. The average mass balance in all four soils at the end of the adsorption phase was 107.2 ± 1.9% of the applied for XDE-742 sulfonic acid.

After 48 hours of equilibration, an average of 81.3%, 83.4%, 66.1% and 85.5% of the applied 6-Cl-7-OH-XDE-742 was recovered in the adsorption solution for the Charentilly loam, the Speyer LUFA 3A sandy loam, the Borstel loamy sand and the Bruch West sandy loam, respectively. An average of 92.9%, 96.5%, 86.2% and 97.4% of the applied 5-OH-XDE-742 was recovered in the adsorption solution for the Charentilly loam, the Speyer LUFA 3A sandy loam, the Borstel loamy sand and the Bruch West sandy loam, respectively. An average of 70.1%, 71.2%, 59.3% and 80.4% of the applied 7-OH-XDE-742 was recovered in the adsorption solution for the Charentilly loam, the Speyer LUFA 3A sandy loam, the Borstel loamy sand and the Bruch West sandy loam, respectively. An average of 26.7%, 60.0%, 25.4% and 59.3% of the applied 5,7-di-OH-XDE-742 was recovered in the adsorption solution for the Charentilly loam, the Speyer LUFA 3A sandy loam, the Borstel loamy sand and the Bruch West sandy loam, respectively. An average of 97.9%, 100.4%, 97.8% and 100.5% of the applied XDE-742 cyanosulfonamide was recovered in the adsorption solution for the Charentilly loam, the Speyer LUFA 3A sandy loam, the Borstel loamy sand and the Bruch West sandy loam, respectively. An average of 102.8%, 102.4%, 100.7% and 101.7% of the applied XDE-742 sulfonic acid was recovered in the adsorption solution for the Charentilly loam, the Speyer LUFA 3A sandy loam, the Borstel loamy sand and the Bruch West sandy loam, respectively.

The average 6-Cl-7-OH-XDE-742 adsorption K_d value was 0.571 mL/g; the average K_{oc} value was 40 mL/g (very high mobility). The average 5-OH-XDE-742 adsorption K_d value was 0.151 mL/g; the average Koc value was 11 mL/g (very high mobility). The average 7-OH-XDE-742 adsorption Kd value was 0.903 mL/g; the average K_{oc} value was 62 mL/g (high mobility). The average 5,7-di-OH-XDE-742 adsorption K_d value was 3.556 mL/g; the average K_{oc} value was 280 mL/g (moderate mobility). The average XDE-742 cyanosulfonamide adsorption K_d value was 0.073 mL/g; the average K_{oc} value was 7 mL/g (very high mobility). The average XDE-742 sulfonic acid adsorption K_d and K_{oc} values were <LOD (very high mobility).

Based on the average adsorption coefficients ($K_{OC\text{-}ads}$ values) for the four soils used in this study the XDE-742 transformation products are expected to exhibit moderate to very high mobility in mineral soils according to the classification criteria of McCall et al. (1981) and moderate to high mobility according to the classification scheme of the FAO (2000). This study is scientifically sound and satisfies the conditional DACO requirements for an adsorption study with transformation products of the active ingredient (DACO 8.2.4.2).

Results Synopsis:

Soil type:	Charentilly Loam	Speyer LUFA 3A Sandy Loam	Borstel Loamy Sand	Bruch West Sandy Loam
		6-Cl-7-OH-XDE-742		
Amount adsorbed [a]:				
Adsorption Kd (mL/g):	0.473	0.404	1.057	0.350
Adsorption Koc (mL/g):	47	16	81	14
Average $K_{OC\text{-}ads}$ (± S.D.) (mL/g)	40 (30)			
Mobility Classification*	Very high			
		5-OH-XDE-742		
Amount adsorbed [a]:				
Adsorption Kd (mL/g):	0.156	0.073	0.322	0.053
Adsorption Koc (mL/g):	16	3	22	2
Average $K_{OC\text{-}ads}$ (± S.D.) (mL/g)	11 (8)			
Mobility Classification*	Very high			
		7-OH-XDE-742		
Amount adsorbed [a]:				
Adsorption Kd (mL/g):	0.877	0.823	1.408	0.502
Adsorption Koc (mL/g):	88	33	108	20
Average $K_{OC\text{-}ads}$ (± S.D.) (mL/g)	62 (39)			
Mobility Classification*	High			
		5,7-di-OH-XDE-742		
Amount adsorbed [a]:				
Adsorption Kd (mL/g):	5.572	1.333	5.923	1.396
Adsorption Koc (mL/g):	557	53	456	56
Average $K_{OC\text{-}ads}$ (± S.D.) (mL/g)	280 (255)			
Mobility Classification*	Moderate			
		XDE-742 cyanosulfonamide		

Amount adsorbed [a]:				
Adsorption Kd (mL/g):	0.098	<LOD[b]	0.046	<LOD[b]
Adsorption Koc (mL/g):	10	<LOD	4	<LOD
Average $K_{OC\text{-}ads}$ (± S.D.) (mL/g)	7 (4)			
Mobility Classification*	Very high			
XDE-742 sulfonic acid				
Amount adsorbed [a]:				
Adsorption Kd (mL/g):	<LOD[c]	<LOD[c]	<LOD[c]	<LOD[c]
Adsorption Koc (mL/g):	<LOD	<LOD	<LOD	<LOD
Average $K_{OC\text{-}ads}$ (± S.D.) (mL/g)	<LOD (no measurable adsorption)			
Mobility Classification*	Very high			

[a] Expressed as percent of the applied radioactivity

[b] LOD = 0.354% of applied ^{14}C or 0.38 ng

[c] LOD = 0.463% of applied ^{14}C or 0.45 ng

Study Acceptability:

PMRA: This study is classified acceptable and satisfies the conditional DACO requirements for an adsorption study with transformation products of the active ingredient in soil.

USEPA: This study is classified supplemental, as it is conducted with transformation products at only one concentration. The results of this study complement the batch equilibrium study of the active ingredient.

DEW: This study is classified as acceptable.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted to fulfill U.S. Environmental Protection Agency (EPA) requirements for aerobic soil metabolism as outlined in the EPA Pesticide Registration Guidelines, Subdivision N, §163-1, Leaching and Adsorption/Desorption. There were no deviations reported from the guidelines.

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

A. MATERIALS:

1. Test Material

Common Name:	5-OH-XDE-742
Synonyms:	INV1983
Specific Activity:	49.3 mCi/mmole
GLP:	Yes (4/5/2005)
Expiration Date:	4/5/2008
Purity (14C):	99.3% (FA&PC 054-004)

Common Name:	7-OH-XDE-742
Synonyms:	INV1982
Specific Activity:	49.3 mCi/mmol
GLP:	Yes (4/5/2005)
Expiration Date:	4/5/2008
Purity (14C):	97.6% (FA&PC 054-005)

Common Name:	6-Cl-7-OH-XDE-742
Synonyms:	INV1989
Specific Activity:	44.0 mCi/mmole
GLP:	Yes (4/5/2005)
Expiration Date:	4/8/2008
Purity (14C):	99.2% (FA&PC 054-008)

Common Name:	5,7-di-OH-XDE-742
Synonyms:	INV2003
Molecular Weight:	406.3 g/mol
Specific Activity:	52.4 mCi/mmole
GLP:	Yes (6/2/2005)
Expiration Date:	6/2/2008
Purity (14C):	72.1% (FA&PC 054-014)

Common Name:	XDE-742 Cyanosulfonamide
Synonyms:	INV1987
Specific Activity:	35.5 mCi/mmol
GLP:	Yes (4/5/2005)
Expiration Date:	4/5/2008
Purity (14C):	98.3% (FA&PC 054-007)

* Denotes position of radiolabel

Physico-chemical properties of XDE-742 transformation products not available

2. Soil Characteristics

Table 1: Description of soil collection and storage.

Charentilly Loam	
Geographic location	Charentilly France
Site description	Loire Valley
Pesticide use history	Glyposate last 2 years
Collection date	26 March 02
Collection procedures	Per SOP
Sampling depth (cm)	Per SOP
Shipping date	26 March 02
Shipping conditions	Ambient
Storage conditions at facility	Refrigerated
Soil preparation prior to use	Sieved, 2 mm, gamma sterilized

Speyer LUFA 3A Sandy Loam	
Geographic location	Baden-Wurtemberg, Germany
Site description	Meadow
Pesticide use history	None
Collection date	25 February 2003
Collection procedures	Spade, plastic box
Sampling depth (cm)	20 cm
Shipping date	13 March 2003
Shipping conditions	Ambient
Storage conditions at Facility	Refrigerated
Soil preparation prior to use	Sieved, 2 mm, gamma sterilized
Borstel Loamy Sand	
Geographic location	Description
Site description	Borstel, Germany
Pesticide use history	Field
Collection date	2000-herbicide used
Collection procedures	6 Mar 2003
Sampling depth (cm)	Per SOP
Shipping date	0-25 cm
Shipping conditions	8 April 2003
Storage conditions at Facility	Ambient
Soil preparation prior to use	Refrigerated
Soil Preparation prior to use	Sieved, 2 mm, gamma sterilized

Bruch West Sandy Loam	
Geographic location	Description
Site description	Bruch West, Germany
Pesticide use history	Field
Collection date	None since 1997
Collection procedures	2 Feb 2003
Sampling depth (cm)	Per SOP
Shipping date	0-25 cm
Shipping conditions	8 April 2003
Storage conditions at Facility	Ambient
Soil preparation prior to use	Refrigerated
Geographic location	Sieved, 2 mm, gamma sterilized

Following sampling, the soil was handled at all times in accordance with ISO/DIS 10381-6. The soils were sieved through a 2-mm mesh screen before using. Agvise Laboratories, Inc. characterized the soils. Soil moisture contents (based on the dry soil weight) were determined using a Denver IR Moisture Analyzer.

Table 2: Properties of the soils.

Property	**M630**	**M642**	**M661**	**M662**
Common Name	Charentilly	Speyer LUFA 3A	Borstel	Bruch West
USDA Textural Class	Loam	Sandy Loam	Loamy Sand	Sandy Loam
% sand	26	55	82	65
% silt	48	28	14	23
% clay	26	17	4	12
International Textural Class	Light Clay	Clay Loam	Loamy Sand	Sandy Loam
% sand	42	63	89	76
% silt	32	20	7	12
% clay	26	17	4	12
ADAS Textural Class	Clay Loam	Sandy Loam	Loamy Sand	Sandy Loam
% sand	24	51	82	62
% silt	50	32	14	26
% clay	26	17	4	12
German BBA Textural Class	Sandy Clay Loam	Sandy Loam	Silty Sand	Loamy Sand
% sand	24	47	82	62
% silt	50	36	14	26

Property	M630	M642	M661	M662
% clay	26	17	4	12
pH [a]	6.3	7.8	5.7	7.9
Organic Matter (%)	1.9	3.4	1.9	2.3
Organic Carbon (%) [b]	1.0	2.5	1.3	2.5
CEC (meq/100 g)	13.3	14.5	6.7	9.9
Moisture at 1/3 atm (%)	21.7	22.0	8.9	12.6
Bulk Density (g/cm^3)	1.08	1.15	1.40	1.29
Biomass [c]	54.7	512.5	55.7	144.6

[a] 1:1 soil:water ratio
[b] LECO
[c] µg/g dry weight soil

C. STUDY DESIGN:

1. **Preliminary study:** The preliminary study was conducted to evaluate the approximate soil/solution ratios and equilibration time required for the two soil matrices (high organic matter (Speyer LUFA 3A), and the other soil low organic matter and high clay content (Charentilly)).

Duplicates of the two soil types were prepared for each time point at three soil:solution ratios. Weights of soils were 5 g, 5 g, and 2 g target dry soil weight for soil:solution ratios 1:2, 1:5, and 1:10, respectively. The soils were then sterilized (gamma irradiation) before dosing. The dosing solution was analyzed in triplicate by LSC both before and after dosing to determine concentration and homogeneity of the solution. An aliquot of the dosing solution was analyzed by HPLC to determine radiopurity. In addition, the pH of an aliquot of the dosing solution in 0.01 M $CaCl_2$ was measured. Duplicate controls containing test substance but no soil in 0.01 M $CaCl_2$ solution were included. Duplicate blanks for each soil type containing soil and 0.01 M $CaCl_2$ solution (soil:solution ratio of 1:2 only) but no test substance, were also included. The test, blank, and control samples were equilibrated in a darkened incubator on a reciprocating shaker. The incubator was set at 25 °C. At defined time intervals (approximately 2, 4, 8, 24, and 48 hours after initiation) duplicate test and blank samples were removed from the shaker. The soil and solution phases in the test samples were separated by centrifugation and then decanted. The volume of the adsorption supernatant was measured (by weight) and triplicate aliquots of the supernatant were analyzed by LSC. Blank samples were removed for LSC analysis, and the samples immediately returned to the shaker. HPLC was conducted on 1:2 soil:solution supernatant at 2, 8, 24 or 48 hours. Extractions were performed on select soils and extracts were analyzed by LSC and HPLC. The radioactivity remaining on the soil pellet was determined by combustion to provide ^{14}C-mass balance. The control samples were only analyzed by LSC at the 24-hour time interval.

2. Definitive study experimental conditions:

Table 3: Study design for the adsorption phase.

Parameter		**Description**
Condition of soil (air dried/fresh)		Fresh; Soils sterilized prior to dosing
Have these soils been used for other laboratory studies? (specify which)		Yes. Aerobic Soil Metabolism (1) and Adsorption Desorption (2) of XDE-742
Soil (g/replicate)		5 g DWB
Equilibration solution used		9 mL of 0.01 M $CaCl_2$
Control used (with salt solution only) (Yes/No)		No
Test Material Concentrations	Nominal concentration (µg a.i./mL solution)	0.01µg/mL equilibrium test
	Measured concentration (µg a.i./mL solution)	0.009 – 0.019 µg/mL equilibrium test
Identity and concentration of co-solvent:		**5-OH-XDE-742:** 64 µL of ACN:MeOH in 200 mL 0.01 M $CaCl_2$ **XDE-742 cyanosulfonamide:** 47 µL of ACN:MeOH in 200 mL 0.01 M $CaCl_2$ **5,7-di-OH-XDE-742:** 65 µL of MeOH in 200 mL 0.01 M $CaCl_2$ **7-OH-XDE-742:** 40 µL of ACN in 200 mL 0.01 M $CaCl_2$ **6-Cl-7-OH-XDE-742:** 62 µL of ACN:MeOH in 200mL 0.01 M $CaCl_2$ **XDE-742-sulfonic acid:** 33 µL of ACN in 200 mL 0.01 M $CaCl_2$
Soil: solution ratio		1:2 equilibrium test
Initial pH of the equilibration solution		N/A
No. of replication	Controls	N/A
	Treatments	Duplicates per sample type
Equilibration	Time	2, 4, 8, 24 and 48 hours
	Temperature (°C)	25 °C
	Darkness (Yes/No)	Yes
	Shaking method	Horizontal shaker at high speed
	Shaking time	2, 4, 8, 24 and 48 hours
Method of separation of supernatant		Centrifugation
Centrifugation	Speed (rpm)	3500 rpm

Parameter		**Description**
	Duration (min)	30 minutes
	Method of separation of soil and solution	Decant

3. Description of analytical procedures: The soil pellets were extracted for purposes of ^{14}C mass balance and stability verification (as necessary).

Extraction

Soil pellets were extracted with 3 x 5 mL of the extraction solvent (90:10 v:v, acetonitrile:0.1N HCl). After addition of the extraction solvent, the tubes were capped and the soil pellets resuspended by shaking and vortexing. The samples were then placed on a shaker for 20 minutes at high speed. The samples were removed and the phases separated by centrifugation. The extracts were then decanted into 25-mL volumetric flasks. The process was repeated an additional two times and the extracts were combined. The final volume was adjusted to 25 mL using acetonitrile and transferred to a labeled vial. Triplicate 1-mL aliquots of each extract were analyzed by LSC for recovery calculations. Soils were allowed to air dry for combustion analysis. Radioactivity measurements were made using an LSC. ^{14}C-quench curves were generated for each instrument once every 6 months. The quench curve was used to resolve sample efficiency and convert raw counts per minute (cpm) to disintegrations per minute (dpm).

Aliquots of soil (approximately 0.5 g sub-samples) were combusted in triplicate to determine ^{14}C mass balance. All combustion were performed using a Harvey Biological Oxidizer OX-500 using a scintillation cocktail (R.J. Harvey Carbon-14 Counting Cocktail) as a trapping agent and scintillation. The trapped ^{14}C activity was measured by LSC analysis.

The oxidizer efficiency was determined by combusting known levels of ^{14}C standard on cellulose and determining the amount of ^{14}C activity recovered vs. the amount applied. The efficiency of the oxidizer was checked both before and after combustion of a sample set. Acceptable recoveries of 80 to 110 % were observed for all combustion sets.

HPLC was used as the primary analytical method. The following HPLC parameters were used to verify the radiopurity of the test substance, analyze dosing solutions, adsorption and desorption supernatants, and soil extracts. The HPLC system was equipped with a Zorbax 300 SB-C18 (4.6 x 250 mm, 5 micron packing) with an appropriate guard column. HPLC conditions consisted of the gradient using water with 1% acetic acid and acetonitrile with 1% acetic acid as mobile phase. The gradient conditions are summarized below:

Reverse Phase HPLC

Time (minutes)	Solvent Ratio	Comment
0	95:5 A:B	Initial conditions

5	95:5 A:B	Aqueous hold
20	5:95 A:B	End steep linear gradient
24.2	5:95 A:B	Organic hold

Column: Zorbax 300 SB-C18 4.6 x 250 mm
Flow rate: 1 mL/min
UV detector at 254 nm
Solvent A: Water with 1.0% acetic acid
Solvent B: Acetonitrile with 1.0% acetic acid

The flow rate was 1 mL/minute and the UV detector wavelength was 254 nm. Typically 1800 μL of sample was injected with 100 μL reference standards. Fraction collection began after 5 minutes (to account for HPLC void volume) and ended at 24.2 minutes for a total collection time of 19.2 minutes. Fractions of 0.1 mL were collected into two 96-well plates with 0.150 mL scintillation cocktail in each well.

Using the method of Currie (3), the limit of detection can be calculated from the expression:

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

and the limit of quantitation can be calculated from the expression:

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

where LOD is the limit of detection (dpm), LOQ is the limit of quantitation (dpm), dpmB is the typical background (dpm) and T is the counting time (minutes). Samples were typically counted for 5 minutes while the blank was typically counted for 10 minutes. Typical background levels were 20 dpm. The resulting LOD was 10 dpm above background and LOQ was 40 dpm above background. The quantitation limit of ^{14}C for the subsamples (e.g., organic extracts, combustions) and HPLC analyses were <8.5% of applied radiocarbon for each process. Limits of quantitation and detection for each subsample as a percentage of the applied radiocarbon are given below.

Sub-sample Identification	% of Applied ^{14}C	
	LOD	LOQ
7-OH-XDE-742	0.385	1.564
6-Cl-7-OH-XDE-742	0.466	1.894
XDE-742 Sulfonic Acid	0.463	1.881
5-OH-XDE-742	0.264	1.074
XDE-742 Cyanosulfonamide	0.354	1.438
5,7-di-OH-XDE-742	0.327	1.328

II. RESULTS AND DISCUSSION

A. **TEST CONDITIONS:** Aqueous and organic samples were stored refrigerated when not in use. All solutions were assayed for radioactivity by LSC the day they were generated. HPLC analyses were generally conducted within a week after generation. The % purity for 5-OH-XDE-742, 6-Cl-7-OH-XDE-742, XDE-742 sulfonic acid and XDE-742 cyanosulfonamide metabolite samples did not change over the course of the study, proving their stability through the adsorption and extraction phases. 7-OH-XDE-742 did show degradation over the course of the study. Also, 5,7-di-OH-XDE-742 had a low purity at the beginning of the experiment. All calculations were made on the assumption that 100% of the extractable ^{14}C-material was the starting test material and would therefore present the worst case scenario for the adsorption calculations.

B. **MASS BALANCE:** Mass balance was calculated for each definitive sample as the sum of the radioactivity recovered from the adsorption supernatant, the desorption supernatant (if applicable), the organic extract, and combustion of the extracted soil pellet.

Table 4: Recovery of XDE-742 metabolites expressed as percentage of applied radioactivity, in soil after adsorption.

Phase	Charentilly	Speyer LUFA 3A	Borstel	Bruch West
6-Cl-7-OH-XDE-742				
Rep 1				
Adsorption [a]	80.5	83.6	63.8	84.2
Extract [b]	13.4	9.2	33.4	9.5
Pellet [c]	6.5	7.7	5.4	5.1
Total [d]	100.4	100.5	102.6	98.9
Rep 2				
Adsorption	82.1	83.3	68.3	86.8
Extract	12.6	10.2	27.3	5.8
Pellet	6.7	8.3	4.7	5.2
Total	101.4	101.8	100.3	97.8
5-OH-XDE-742				
Rep 1				
Adsorption	95.3	96.2	86.2	96.8
Extract	0.0	0.8	12.9	0.3
Pellet	3.2	5.2	1.6	2.8
Total	98.5	102.2	100.7	100.0
Rep 2				
Adsorption	90.4	96.7	ND	98.0
Extract	9.8	0.2	ND	0.8
Pellet	4.1	3.8	ND	3.1

Phase	Charentilly	Speyer LUFA 3A	Borstel	Bruch West
Total	104.4	100.7	ND	101.9
7-OH-XDE-742				
Rep 1				
Adsorption [a]	69.4	71.2	58.5	79.9
Extract [b]	8.5	4.4	18.3	4.7
Pellet [c]	24.3	25.5	25.6	17.1
Total [d]	102.1	101.0	102.4	101.7
Rep 2				
Adsorption	70.7	71.3	60.1	80.9
Extract	6.4	6.4	18.0	5.0
Pellet	24.4	23.5	21.6	15.4
Total	101.6	101.2	99.8	101.9
5,7-di-OH-XDE-742				
Rep 1				
Adsorption	24.7	59.8	25.4	62.0
Extract	3.0	0.0	10.0	0.0
Pellet	73.1	46.1	62.0	39.9
Total	100.8	105.8	97.3	101.9
Rep 2				
Adsorption	28.7	60.2	ND	56.5
Extract	1.1	0.0	ND	0.0
Pellet	69.7	45.6	ND	44.4
Total	99.5	105.8	ND	100.9
XDE-742 Sulfonic acid				
Rep 1				
Adsorption [a]	103.0	102.2	100.9	100.9
Extract [b]	0.0	0.0	0.0	0.0
Pellet [c]	3.0	2.9	7.9	8.2
Total [d]	106.0	105.1	108.0	109.2
Rep 2				
Adsorption	102.6	102.5	100.5	102.4
Extract	0.0	0.0	0.0	0.0
Pellet	2.5	3.5	7.1	7.5
Total	105.1	106.1	107.6	109.8
XDE-742 Cyanosulfonamide				
Rep 1				
Adsorption	95.4	100.6	ND	99.8
Extract	0.0	0.0	ND	0.0
Pellet	4.2	5.0	ND	0.8
Total	99.5	105.6	ND	100.6

Phase	Charentilly	Speyer LUFA 3A	Borstel	Bruch West
Rep 2				
Adsorption	100.4	100.2	97.8	101.1
Extract	0.0	0.0	2.3	0.0
Pellet	4.6	3.9	1.0	0.9
Total	105.0	104.1	101.0	102.0

[a] Percent of applied radioactivity recovered in adsorption solution
[b] Percent of applied radioactivity extracted from the soil pellet, post adsorption phase
[c] Percent of applied radioactivity remaining in soil pellet after extraction, determined by oxidative combustion
[d] Total amount of radioactivity recovered from all phases
ND Not determined

Table 5: Concentration of XDE-742 transformation products in the solid and liquid phases at the end of adsorption equilibration period.

Compound	Rep	**Charentilly Loam**			**Speyer LUFA 3A sandy loam**		
		on soil (mg/Kg) [a]	in solution (mg/L) [b]	% [c] adsorbed	on soil (mg/Kg) [a]	in solution (mg/L) [b]	% [c] adsorbed
5-OH-XDE-742	1	0.00135	0.0136	0.0	0.00109	0.0138	0.8
	2	0.00276	0.0129	9.8	0.00093	0.0138	0.2
7-OH-XDE-742	1	0.00617	0.0068	8.5	0.00577	0.0070	4.4
	2	0.00591	0.0069	6.4	0.00575	0.0070	6.4
6-Cl-7-OH-XDE-742	1	0.00394	0.0079	13.4	0.00329	0.0082	9.2
	2	0.00362	0.0081	12.6	0.00334	0.0082	10.2
5,7-di-OH-XDE-742	1	0.01585	0.0026	3.0	0.00839	0.0062	0.0
	2	0.01502	0.0030	1.1	0.00832	0.0063	0.0
XDE-742 Cyanosulfonamide	1	0.00100	0.0102	0.0	<LOD	0.0108	0.0
	2	<LOD	0.0107	0.0	<LOD	0.0107	0.0
XDE-742 Sulfonic acid	1	<LOD	0.0098	0.0	<LOD	0.0097	0.0
	2	<LOD	0.0098	0.0	<LOD	0.0098	0.0
Compound	Rep	**Borstel Loamy Sand**			**Bruch West Sandy Loam**		
		on soil (mg/Kg) [a]	in solution (mg/L) [b]	% [c] adsorbed	on soil (mg/Kg) [a]	in solution (mg/L) [b]	% [c] adsorbed
5-OH-XDE-742	1	NA	NA	NA	0.00091	0.0138	0.3
	2	0.00397	0.0123	12.9	0.00056	0.0140	0.8
7-OH-XDE-742	1	0.00837	0.0057	18.3	0.00406	0.0079	4.7
	2	0.00804	0.0059	18.0	0.00386	0.0079	5.0
6-Cl-7-OH-XDE-742	1	0.00730	0.0063	33.4	0.00320	0.0083	9.5
	2	0.00639	0.0067	27.3	0.00268	0.0085	5.8
5,7-di-OH-XDE-	1	0.01570	0.0027	10.0	0.00802	0.0065	0.0

742	2	NA	NA	NA	0.00918	0.0059	0.0
XDE-742 Cyanosulfonamide	1	NA	NA	NA	<LOD	0.0107	0.0
	2	0.00048	0.0105	2.3	<LOD	0.0108	0.0
XDE-742 Sulfonic acid	1	<LOD	0.0096	0.0	<LOD	0.0096	0.0
	2	<LOD	0.0096	0.0	<LOD	0.0097	0.0

[a] Concentration of test material present in organic extract
[b] Concentration of test material in adsorption solution
[c] Percent of applied radioactivity present in the organic extract
NA Not applicable

Table 6: Adsorption Constants of XDE-742 transformation products in the soils.

Soil	Adsorption		
	% OC	K_d [a] mL/g	K_{oc} [a] mL/g
5-OH-XDE-742			
Charentilly	1.0	0.156	16
Speyer LUFA 3A	2.5	0.073	3
Borstel	1.3	0.322	22
Bruch West	2.5	0.053	2
Average		0.151	11
SD		0.062	8
7-OH-XDE-742			
Charentilly	1.0	0.877	88
Speyer LUFA 3A	2.5	0.823	33
Borstel	1.3	1.408	108
Bruch West	2.5	0.502	20
Average		0.903	62
SD		0.349	39
5,7-di-OH-XDE-742			
Charentilly	1.0	5.572	557
Speyer LUFA 3A	2.5	1.333	53
Borstel	1.3	5.923	456
Bruch West	2.5	1.396	56
Average		3.556	280
SD		2.339	255
6-Cl-7-OH-XDE-742			
Charentilly	1.0	0.473	47
Speyer LUFA 3A	2.5	0.404	16

Borstel	1.3	1.057	81
Bruch West	2.5	0.350	14
Average		0.571	40
SD		0.310	30
XDE-742 Cyanosulfonamide			
Charentilly	1.0	0.098	10
Speyer LUFA 3A	2.5	<LOD	<LOD
Borstel	1.3	0.073	4
Bruch West	2.5	<LOD	<LOD
Average		0.073	7
SD		0.029	4
XDE-742 Sulfonic Acid			
Charentilly	1.0	<LOD	<LOD
Speyer LUFA 3A	2.5	<LOD	<LOD
Borstel	1.3	<LOD	<LOD
Bruch West	2.5	<LOD	<LOD
Average		NA	NA
SD		NA	NA

[a] K_d and K_{oc} values reported as averages

C. ADSORPTION: The average 6-Cl-7-OH-XDE-742 adsorption K_d value was 0.571 mL/g; the average K_{oc} value was 40 mL/g. The average 5-OH-XDE-742 adsorption K_d value was 0.151 mL/g; the average Koc value was 11 mL/g. The average 7-OH-XDE-742 adsorption Kd value was 0.903 mL/g; the average K_{oc} value was 62 mL/g. The average 5,7-di-OH-XDE-742 adsorption K_d value was 3.556 mL/g; the average K_{oc} value was 280 mL/g. The average XDE-742 cyanosulfonamide adsorption K_d value was 0.073 mL/g; the average K_{oc} value was 7 mL/g. The average XDE-742 sulfonic acid adsorption K_d and K_{oc} values were <LOD.

D. DESORPTION: No desorption cycles were conducted.

III. STUDY DEFICIENCIES:

1. The study authors reported that 7-OH-XDE-742 degraded over the course of the study, and that 5,7-di-OH-XDE-742 had a low purity at the beginning of the experiment. However, mass balances at the end of the study were acceptable for both compounds, indicating that radioactivity was not

lost from the system as CO_2, or volatile organics. Therefore the PMRA accepts the study author's rationale that because all calculations were made on the assumption that 100% of the extractable ^{14}C-material was the starting test material, this would represent the worst case scenario for the adsorption calculations.

2. Adsorption studies should be equilibrated at a minimum of 4 concentrations to produce adsorption isotherms.

IV. REVIEWERS COMMENTS:

PMRA Comments:

The PMRA normally requires adsorption studies to be conducted with a minimum of four to five test concentrations to produce an adsorption isotherm. However, the PMRA feels that the single adsorption coefficients adequately demonstrate the high mobility potential for these transformation products in representative agricultural soils. The EAD reviewer verified the study author's $K_{d\text{-}ads}$ and $K_{OC\text{-}ads}$ values and agrees with the values presented by the author.

PMRA Conclusion:

Based on the average adsorption coefficients ($K_{OC\text{-}ads}$ values) for the four soils used in this study the XDE-742 transformation products are expected to exhibit moderate to very high mobility in mineral soils according to the classification criteria of McCall et al. (1981). This study is scientifically sound and satisfies the conditional DACO requirements for an adsorption study with transformation products of the active ingredient (DACO 8.2.4.2).

Australian Reviewer's Comments: The Australian reviewer agrees with the above and notes that the studies were performed using sterile soils. While this is not included in the US EPA 835.1220 Guideline, the use of sterile soil is not excluded either (835.1220 is not for compunds which are unstable in the time scale of the test). However, given the short half lives of some of these metabolites, in particular the 5,7-di-OH-XDE-742 (half life <0.4 days, see report on aerobic transformation of di-OH XDE 742), the use of gamma-ray sterilized soils is acceptable.

V. REFERENCES:

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