Data Evaluation Report on the Leaching of Orthosulfamuron in Aged Soil Columns

PMRA Submission Number {.....} EPA MRID Number 46219018

Data Requirement: PMRA Data Code:
EPA DP Barcode: D304186
OECD Data Point:
EPA Guideline: 163-1

Test material:
Common name: Orthosulfamuron.
Chemical name
IUPAC: 1-(4,6-Dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea.
CAS name: 2-[[[[[(4,6-Dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]amino]-N,N-dimethylbenzamide.
CAS No: 213464-77-8
Synonyms: IR5878.
SMILES String: CN(C(=O)c1ccccc1NS(=O)(=O)NC(=O)Nc1nc(cc(n1)OC)OC)C.

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Company Code:
Active Code:
Use Site Category:
EPA PC Code: 108209

CITATION: Scacchi, A. and G. Pizzingrilli. 2003. Aged Residue Column Leaching of ^{14}C-IR5878 in an American Soil. Unpublished study performed by Isagro Ricerca Srl, Novara, Italy; sponsored and submitted by Isagro SpA, Milano, Italy. Study Number: MEF.02.17. Experiment initiation July 08, 2002 and completion November 04, 2002. Final report issued February 18, 2003. 194 pp.

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CITATION: Scacchi, A. and G. Pizzingrilli. 2003. Aged residue column leaching of ^{14}C-IR5878 in an American soil. Unpublished study performed by Isagro Ricerca Srl, Novara, Italy; sponsored and submitted by Isagro SpA, Milano, Italy. Study Number: MEF.02.17. Experiment initiation July 08, 2002 and completion November 04, 2002 (p. 16). Final report issued February 18, 2003.

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Data Evaluation Report on the Leaching of Orthosulfamuron in Aged Soil Columns

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EXECUTIVE SUMMARY:

Leaching - Aged Column

The column leaching of aged [^{14}C-5-pyrimidinyl]-labeled 1-(4,6-dimethyoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea (orthosulfamuron; IR5878; radiochemical purity >98%; specific activity 4.152 MBq/mg, 112.217 µCi/mg, 249121 dpm/µg; Lot # 180) and [^{14}C-U-phenyl]-labeled orthosulfamuron (radiochemical purity >98%; specific activity 5.7 MBq/mg, 154.058 µCi/mg, 342008 dpm/µg; Lot # 183) was investigated in a soil:water system (Arkansas loam soil, pH 6.2, organic matter 1.5%; Arkansas well water, pH 7.8) in order to reproduce a rice paddy condition. The surface of pre-equilibrated test soil samples, contained in glass cylinders (4.50-cm i.d), was treated with [^{14}C-5-pyrimidinyl]- or [^{14}C-U-phenyl]-labeled orthosulfamuron at 11.99 µg and 11.83 µg, respectively, corresponding to a treatment rate of 75 g/ha, assuming a surface area of 15.90 cm^2. The samples were incubated in the dark for 34 days or 55 days at 20 ± 2°C. The glass cylinders were evacuated by pumping pre-moistened carbon dioxide-free air through each cylinder. Evolved $^{14}CO_2$ was trapped using glass drechsels containing 2N KOH solution. Following the 55-day aging period, the soils were incubated to 69 days to ensure that degradation of [^{14}C-5-pyrimidinyl]- and [^{14}C-U-phenyl]orthosulfamuron was greater than 50%. Following the 69-day aging period, the treated soils were transferred to the top of five glass columns (450-mm length, 50-mm i.d.) that were filled to a height of 30 cm with air-dried, untreated soil; the final column heights were not reported. Two aged soils for each label were added to the top of two columns (two columns per label), and a blank soil sample was added to the fifth column. The water layers (*ca.* 90 mL) removed from each sample following aging were then added to the top of each column. The columns were continuously leached under saturated conditions with 997 mL (equivalent to 508 mm of rainfall) of 0.01M $CaCl_2$ solution in the dark for 9 days (temperature not reported), resulting in *ca.* 6 pore volumes of leachate. The elution flow rate was 4.6 mL/hour and the infiltration rate was 0.23 cm/hour. A constant head (*ca.* 3 cm) was maintained (method not specified) on the top of each column. Leachate volumes were collected (method not specified), and duplicate aliquots were analyzed for total radioactivity using LSC.

At the end of the 9-day leaching period, leachate volumes were collected, and duplicate aliquots were analyzed for total radioactivity using LSC. For the pyrimidinyl label columns, aliquots of the leachates were acidified to pH 3 with 4N HCl and extracted three times with ethyl acetate. The extracts were pooled, evaporated under vacuum, and redissolved in a CH_3CN-33 mM $NaHCO_3$ mixture (7:3, v:v). For the phenyl label columns, aliquots of the leachates were concentrated and aliquots were analyzed by TLC. The soils were extruded from each column by gentle nitrogen pressure and then separated into one segment (A-1) containing the aged soil layer, 2-3 cm in thickness, and five equal segments (A through E), each *ca.* 6 cm in thickness. Each soil segment was extracted once with a CH_3CN-33 mM $NaHCO_3$ mixture (7:3, v:v) and once with a CH_3CN-33 mM $NaHCO_3$ mixture (1:1, v:v). Soil segments A-1 and A of the pyrimidinyl label columns were extracted a third time with a CH_3CN-33 mM $NaHCO_3$ mixture (1:1, v:v) after sonication. Following each extraction, the samples were centrifuged. Then, the supernatants were removed and brought to volume, and duplicate aliquots were analyzed for total radioactivity using LSC. The remaining soils from all label columns were air-dried and analyzed for total radioactivity using LSC following combustion. To isolate and quantify [^{14}C]residues from the soil column

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segments, aliquots of the soil extracts were pooled, concentrated under vacuum, and analyzed by one-dimensional TLC analysis. Mass balances were determined by summing the radioactivity recovered from the column leachates, soil extracts, combusted residues, and KOH traps.

[^{14}C-5-Pyrimidinyl]orthosulfamuron treatment: Following aging, material balances for the loam soil were 103.20% and 96.33% of the applied for Sample 7 (aged 34 days) and Sample 9 (aged 55 days), respectively. In Sample 7, 43.94%, 49.45%, and 9.63% of the applied was recovered from the water layer, extracted residues, and non-extracted residues, respectively; $^{14}CO_2$ was 0.18% of the applied. In Sample 9, 35.86%, 50.35%, and 9.83% of the applied was recovered from the water layer, extracted residues, and non-extracted residues, respectively; $^{14}CO_2$ was 0.29% of the applied.

Six compounds were identified in the water layers and soil extracts. In Sample 7 (aged 34 days), [^{14}C]orthosulfamuron comprised 36.97% and 22.01% of the applied in the water layers and extracted residues, respectively, and was 58.98% of the applied in the whole system. In Sample 9 (aged 55 days), [^{14}C]orthosulfamuron comprised 28.79% and 14.41% of the applied in the water layer and extracted residues, respectively, and was 43.20% in the whole system. The major transformation product S12 (DOP-urea; N-(4,6-dimethoxypyrimidin-2-yl)urea) was 28.80% and 35.94% of the applied in Samples 7 and 9, respectively. Transformation product S9 (O-desmethyl IR 5878; 1-(4-methoxy-6-hydroxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenyl-sulfamoyl]urea) was 2.58% and 4.46% of the applied in Samples 7 and 9, respectively. Transformation products S11, S13 (DOP amine; 2-amino-4,6-dimethoxypyrimidine), and S15 were not detected above 3% of the applied in either sample.

Following leaching, a mean of 89.86% of the applied was recovered in the soil segments of the two columns. Mean recoveries for each soil segment were 46.41%, 34.26%, 6.98%, 1.99%, and 0.24% of the applied for the A-1 (aged soil layer), A, B, C, and D segments, respectively. For the two columns, total extracted [^{14}C]residues averaged 79.46% of the applied, non-extracted residues averaged 10.41%, and $^{14}CO_2$ averaged 0.66% of the applied; an average 4.55% of the applied was recovered in the leachate samples. The mean mass balance for the two soil columns was 95.06%.

Based on TLC analyses of leachate samples from both columns, [^{14}C]orthosulfamuron and transformation product S12 did not leach. Transformation products S9 and S11 did leach, accounting for 4.07-4.57% and 0.21-0.24% of the applied, respectively. Transformation products found in the leachate samples were equivalent for the two columns.

In soil segment extracts for both columns, [^{14}C]orthosulfamuron averaged 23.11% of the applied, of which 7.27%, 9.27%, 4.81%, and 1.76% of the applied was recovered in soil segments A-1, A, B, and C, respectively. Transformation products S9 and S12 were found in soil segments A-1, A, B, and C and averaged 1.05% and 51.68% of the applied, respectively. Transformation products S11, S13, and S15 averaged 0.26%, 2.46%, and 0.69% of the applied, respectively. Transformation products found in the soil segment extracts of each column were equivalent.

[^{14}C-U-Phenyl]orthosulfamuron treatment: Following aging, material balances for the loam soil were 107.08% and 104.21% of the applied for Sample 8 (aged 34 days) and Sample 10 (aged 55 days), respectively. In Sample 8, 64.32%, 34.46%, and 8.16% of the applied was recovered from

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the water layer, extracted residues, and non-extracted residues, respectively; $^{14}CO_2$ was 0.14% of the applied. In Sample 10, 64.83%, 28.52%, and 10.58% of the applied was recovered from the water layer, extracted residues, and non-extracted residues, respectively; $^{14}CO_2$ was 0.28% of the applied.

Six compounds were identified in the water layers and soil extracts. In Sample 8 (aged 34 days), [^{14}C]orthosulfamuron accounted for 41.72% and 28.14% of the applied in the water layers and extracted residues, respectively, and was 69.86% in the whole system.. In Sample 10 (aged 55 days), [^{14}C]orthosulfamuron accounted for 34.70% and 20.52% of the applied in the water layer and extracted residues, respectively, and was 55.22% in the whole system. The major transformation product S1 (DBS-acid; 2-sulfoamino-N,N-dimethylbenzamide) was 16.03% and 24.73% of the applied in Samples 8 and 10, respectively. Transformation product S9 was 2.84% and 5.18% of the applied in Samples 8 and 10, respectively. Transformation product S2 (DBS-amide; 2-sulfamoylamino-N,N-dimethylbenxamide) was 7.21% and 6.22% of the applied in Samples 8 and 10, respectively. Transformation products S4 and S5 were not detected above 3% of the applied in either sample.

Following leaching, a mean of 35.89% of the applied radioactivity was recovered in the soil segments of both columns. Mean recoveries for each soil segment were 11.76%, 10.31%, 7.25%, 4.00%, 2.06%, and 0.53% of the applied for the A-1 (aged soil layer), A, B, C, D, and E segments, respectively. For the two columns, total extracted [^{14}C]residues averaged 27.83% of the applied, non-extracted residues averaged 8.06%, and $^{14}CO_2$ averaged 0.48% of the applied; an average 62.50% of the applied was recovered in the leachate samples. The mean mass balance for the two soil columns was 98.87%.

Based on TLC analyses of leachate samples from both columns, [^{14}C]orthosulfamuron did not leach, whereas several transformation products did leach. The major transformation product, S1, accounted for 44.26-50.56% of the applied radioactivity. Minor transformation products S9, S2, and S5 accounted for 3.59-3.76%, 7.32-8.01%, and 1.33-2.47% of the applied, respectively. Minor transformation product S4 was found in leachate from one column, comprising 3.71% of the applied. Transformation products found in leachate samples from the two soil columns were equivalent.

In soil segment extracts for both columns, [^{14}C]orthosulfamuron averaged 24.24% of the applied, of which 4.98%, 7.94%, 6.07%, 3.47%, and 1.78% of the applied was recovered in soil segments A-1, A, B, C, and D, respectively. Transformation products S9 and S1 were found in soil segments A-1, A, B, C, and D, and averaged 0.91% and 1.50% of the applied, respectively. Transformation products S2, S4, and S5 averaged 0.21%, 0.17%, and 0.31% of the applied, respectively. Transformation products found in soil segment extracts of the two soil columns were equivalent.

Results Synopsis:

Recoveries of Orthosulfamuron and Degradates (% of applied) per Column Segment at Study Termination (mean, n=2).						
Phenyl label						
Compound	**Segment A-1 (2-3 cm)**	**Segment A (*ca.* 6 cm)**	**Segment B (*ca.* 6 cm)**	**Segment C (*ca.* 6 cm)**	**Segment D (*ca.* 6 cm)**	**Segment E (*ca.* 6 cm)**
Orthosulfamuron	4.98	7.94	6.07	3.47	1.78	Not detected
DBS-acid	0.23	0.51	0.33	0.29	0.15	Not detected
DBS-amide	Not detected	0.11	Not detected	0.06	0.04	Not detected
DB amine	0.08	Not detected	0.09	Not detected	Not detected	Not detected
Unresolved compounds	0.26	0.05	Not detected	Not detected	Not detected	Not detected
O-desmethyl orthosulfamuron	0.27	0.20	0.15	0.20	0.09	Not detected
Pyrimidinyl label						
Orthosulfamuron	7.27	9.27	4.81	1.76	Not detected	Not detected
O-desmethyl orthosulfamuron	0.39	0.35	0.21	0.10	Not detected	Not detected
Unresolved compounds	0.20	0.06	Not detected	Not detected	Not detected	Not detected
DOP urea	29.66	20.83	1.06	0.13	Not detected	Not detected
DOP amine	1.36	1.10	Not detected	Not detected	Not detected	Not detected
O-desmethyl DOP urea	0.34	0.35	Not detected	Not detected	Not detected	Not detected

Study Acceptability: This study is classified as **acceptable** and satisfies Subdivision N Guideline §163-1 data requirements for a mobility study using aged soil.

I. MATERIALS AND METHODS:

GUIDELINE FOLLOWED: This study was conducted according to the USEPA Pesticide Assessment Guidelines, Subdivision N, §163-1 and §162-4 (p. 15). No significant deviations from USEPA Subdivision N Guideline §163-1 were noted.

COMPLIANCE: The study was conducted according to the OECD Principles of Good Laboratory Practice as defined by the Republic of Italy (pp. 3, 4; Appendix 11, pp. 191-194). Data Confidentiality, GLP, Compliance, Quality Assurance, and Declaration statements were provided (pp. 2-6; Appendix 11, pp. 191-194).

A. MATERIALS:

The mobility of [^{14}C-5-pyrimidinyl]-labeled 1-(4,6-dimethyoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea (orthosulfamuron; IR5878; radiochemical purity >98%; specific activity 4.152 MBq/mg, 112.217 µCi/mg, 249121 dpm/µg; Lot # 180) and [^{14}C-U-phenyl]-labeled orthosulfamuron (radiochemical purity >98%; specific activity 5.7 MBq/mg, 154.058 µCi/mg, 342008 dpm/µg; Lot # 183) was investigated in a loam soil:water system in order to reproduce a rice paddy condition (pp. 13, 15, 18).

Table 1: Characteristics of the test soil.

Property	Loam
Source	Shoffner Farm Research, Inc, Newport, Arkansas
Taxonomic class	Not reported
Horizon/depth	20 cm
Soil texture	Loam
% sand	51
% silt	38
% clay	11
pH water 0.01M $CaCl_2$	 6.9 6.2
Organic carbon (%)[1]	0.87
Organic matter (%)	1.5
CEC (meq/100 g)	7.5
Bulk density (g/cm^3)	1.24
Moisture at 0.33 bar (%)	21.1

Property		Loam
Maximum water holding capacity (%)		30.5
Microbial biomass C (mg C/100 g dry weight)	Initial	121.97
	Final	189.84

Data were obtained from p. 19; Table 1, p. 47; and Appendix 3, pp. 135-137 of the study report.
[1] Calculated as follows: organic carbon = organic matter ÷ 1.72.

Table 2: Characteristics of the test water.

Property	Water
Source	Well; Shoffner Farm Research, Inc, Newport, Arkansas
pH (0.01M $CaCl_2$)	7.8
Harness (mg equivalent $CaCO_3$/L)	224
Conductivity (mmhos/cm)	0.52
Calcium (mg/L)	69
Total Nitrogen (mg/L)	0.7
Total Phosphorus (mg/L)	0.1

Data were obtained from p. 19 and Table 1, p. 47 of the study report.

B. EXPERIMENTAL CONDITIONS (Aging Phase):

Prior to study initiation, radiolabeled test materials were stored at <-10°C and the soil and water samples were stored at 2-7°C (p. 19). The test soils were sieved (2 mm) and the water was filtered. For soil biomass determination, eight soil-water systems were prepared by adding aliquots of the test soil to glass cylinders (4.50-cm i.d.; 15.90 cm^2 area) to a depth of 2.5 cm (pp. 19, 21-22). Aliquots (*ca.* 105 mL) of water were added to each vessel to a depth of 6 cm above the test soil. The test cylinders were closed with permeable stoppers and incubated in the dark at 20 ± 2°C. Soil microbial biomass determinations were made prior to and following the aging period.

Ten soil-water samples (Blanks 1 and 6, Samples 2-5, 7-10) were prepared by adding ten aliquots of the test soil to individual glass cylinders (4.50-cm i.d.; 15.90 cm^2 area) to a depth of 2.5 cm (pp. 21-22). Aliquots (*ca.* 105 mL) of water were added to each vessel to a depth of 6 cm above the test soil. The water level of each vessel was maintained throughout the study by adding distilled water as necessary. Duplicate control samples were prepared to determine physico-chemical parameters. The samples were aerated and shaken in the dark at 20°C until equilibrium was established. The surface of four soil samples (Samples 2, 3, 7, and 9) was treated with a 0.49-mL aliquot of a 25 µg/mL solution containing 11.99 µg of [^{14}C-5-pyrimidinyl]orthosulfamuron, dissolved in acetonitrile (pp. 22-23). The surface of an additional four soil samples (Samples 4, 5, 8, and 10) was treated with a 0.83-mL aliquot of a 12 µg/mL solution containing 11.83 µg. of [^{14}C-U-phenyl]orthosulfamuron, dissolved in acetonitrile. Both applications corresponded to a treatment rate of 75 g/ha, assuming a surface area of 15.90 cm^2 (pp. 13, 22-23). The sample

vessels were closed with glass stoppers equipped with inlet and outlet openings, and the samples were incubated in the dark at 20 ± 2°C. Pre-moistened CO_2-free air was passed over the soil surfaces (air flow rate not reported) of the samples. Evolved CO_2 for all samples, except the blank and control samples, was trapped using glass drechsels containing 2N KOH solution. During equilibrium and aging, oxygen concentrations, redox potentials, and pH levels were measured and recorded (p. 13; Appendix 5, pp. 141-142).

C. ANALYTICAL METHODS (Aging Phase):

Samples were removed after 34 days (Samples 7 and 8) and 55 days (Samples 9 and 10) of aging (p. 24; Scheme 1, p. 43). The water layers were removed by pipette and brought to 100 mL with CH_3CN-33 mM $NaHCO_3$ mixture (7:3, v:v). Duplicate 0.5-mL aliquots of the water layers were analyzed for total radioactivity using LSC (pp. 24, 28). For Samples 7, 8, 9, and 10, the KOH trapping solutions were brought to 100 mL and duplicate 1.0 mL aliquots were analyzed using LSC (pp. 25, 28). The soil samples were extracted by shaking for 1 hour at 300 strokes/minute with CH_3CN-33 mM $NaHCO_3$ mixture (7:3, v:v) and CH_3CN-33 mM $NaHCO_3$ mixture (1:1, v:v; pp. 24-25). Sample 9 (soil treated with [^{14}C-5-pyrimidinyl]orthosulfamuron and incubated for 55 days) was extracted a third time with 250 mL of a CH_3CN-33 mM $NaHCO_3$ mixture (1:1, v:v) after sonication at 40°C for 50 minutes. Following each extraction, the samples were centrifuged for 20 minutes, and the supernatants were removed and brought to 250 mL with acetonitrile. Duplicate 1-mL aliquots of the soil extracts were analyzed for total radioactivity using LSC (pp. 25, 28). The remaining soil from Samples 7, 8, 9, and 10 was air-dried, and a minimum of three *ca.* 0.5-2.5 g aliquots were combusted and aliquots were analyzed for total radioactivity using LSC following combustion; combustion efficiency was >94% (pp. 25, 28; Appendix 7, Table V, p. 155, Table XIV, p. 164). For soil segment extracts, limits of detection for LSC analysis were 0.003-0.004% and 0.003% for [^{14}C-5-pyrimidinyl]- and [^{14}C-U-phenyl]orthosulfamuron-treated samples, respectively (Appendix 7, Tables X-XIII, pp. 160-163). For combusted samples, limits of detection for LSC analysis were 0.007-0.008% and 0.006-0.007% for [^{14}C-5-pyrimidinyl]- and [^{14}C-U-phenyl]orthosulfamuron-treated samples, respectively (Appendix 7, Tables XV-XVIII, pp. 165-168). Mass balances were determined by summing the radioactivity recovered from the soil extracts, combusted residues, and KOH traps (p. 25).

To isolate and quantify [^{14}C]residues, 25-mL aliquots of the water layers and 50-mL aliquots of the pooled soil extracts were concentrated to 1 mL, and analyzed by one-dimensional TLC (p. 26). TLC analysis was performed within 25 days of sample collection using two stationary phases (pp. 29-30). Normal-phase TLC was performed using silica gel coated 60 F_{254} plates (250-µm thickness) developed in chloroform:methanol:8N ammonium hydroxide (75:22:3, v:v:v; Solvent System 1). Reversed-phase TLC was performed using RP-18 F_{254} plates (250-µm thickness) developed in acetonitrile:water (92:8, v:v; Solvent System 2). All samples were co-chromatographed with the following reference standards (pp. 27-29; 40; Appendix 8, Table XX, p. 171; Appendix 9, pp. 185-188):

S1 [DBS-acid; 2-sulfoamino-N,N-dimethylbenzamide; radiochemical purity >98%; R_f 0.15 (SS1), R_f 0.67 (SS2)];

S2 [DBS-amide; 2-sulfamoylamino-N,N-dimethylbenxamide; radiochemical purity >99%; R_f 0.46 (SS1), R_f 0.83 (SS2)];

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S3 [IR5878; orthosulfamuron; 1-(4,6-dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)-henylsulfamoyl]urea; R_f 0.35 (SS1), R_f 0.68 (SS2)];

S4 [R_f 0.77 (SS1), R_f 0.50 (SS2)];

S5 [R_f 0 (SS1)];

S9 [O-desmethyl IR 5878; 1-(4-methoxy-6-hydroxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)-phenylsulfamoyl]urea; R_f 0.25 (SS1), R_f 0.65 (SS2)];

S11 [R_f 0.01 (SS1)];

S12 [DOP-urea; N-(4,6-dimethoxypyrimidin-2-yl)urea; radiochemical purity >99%; R_f 0.71 (SS1), R_f 0.55 (SS2)];

S13 [DOP amine; 2-amino-4,6-dimethoxypyrimidine; radiochemical purity >99%; R_f 0.81 (SS1), R_f 0.61 (SS2)]; and

S15 [R_f 0.08 (SS1)].

Following development, areas of radioactivity were detected and quantified using a Fuji BAS 1500 Bio-Imaging Analyzer, with two-dimensional images generated using a Fuji BAS 1500 Autoradiographic Imaging System (p. 30). For aged samples, limits of detection for TLC analysis were 0.27% and 0.21% for [^{14}C-5-pyrimidinyl]orthosulfamuron soil extracts and water layers, respectively, and were 0.20% and 0.16% for [^{14}C-U-phenyl]orthosulfamuron soil extracts and water layers, respectively (p. 31).

Following the 55-day aging period, Samples 2-5 were further incubated to 69 days to ensure that degradation of [^{14}C-5-pyrimidinyl]- and [^{14}C-U-phenyl]orthosulfamuron was greater than 50% (pp. 13, 34; Tables 2-3, pp. 48-49). Following the 69-day aging period, the KOH trapping solutions for Samples 2, 3, 4, and 5 were brought to 100 mL and duplicate 1.0-mL aliquots were analyzed using LSC (pp. 27-28).

D. EXPERIMENTAL CONDITIONS (Leaching Phase):

The soil column leaching study was conducted by packing five glass columns (450-mm length; 50-mm i.d.) with air-dried, untreated soil using vibration (30 cm; p. 23; Appendix 4, p. 139). Prior to packing, the column outlets were plugged with quartz wool and the conical parts filled with sea sand. The soil surfaces were covered with glass fibre filters and the soils were saturated by adding 0.01M $CaCl_2$ solution dropwise to each column (pp. 23-24). Then, the glass fibre filters were removed and the 69-day aged test soils (Blank 1 and Samples 2-5) were transferred to the top of the saturated soil columns. The soils were pressed down with slight pressure and new glass fibre filters were added to the top of each column. The columns were then wrapped with aluminum foil to protect from light and the water layers (*ca.* 90 mL) removed from each sample following aging were added to each column. The columns were then leached with an additional 997 mL of 0.01M $CaCl_2$ solution (equivalent to 508 mm of rain), maintaining a constant head of *ca.* 3 cm (method

not specified) at a flow rate of *ca.* 4.6 mL/hour and an infiltration rate of *ca.* 0.23 cm/hour for 9 days (using Darcy's law "infiltration rate = flow rate ÷ A" where "A" = 19.63 cm^2; p. 24).

E. ANALYTICAL METHODS (Leaching Phase):

Following leaching, leachate volumes of 1056, 1062, 1070, and 1082 mL were collected from Columns 2, 3, 4, and 5, respectively, and duplicate 5 mL aliquots were analyzed for total radioactivity using LSC (pp. 26, 28; Scheme 2, p. 44). For Columns 2 and 3 (pyrimidinyl label), 100-mL aliquots of the leachates were acidified to pH 3 with 4N HCl and extracted with ethyl acetate (3 H 50 mL). The extracts were pooled, evaporated under vacuum, and redissolved in 0.3 mL of a CH_3CN-33 mM $NaHCO_3$ mixture (7:3, v:v). For Columns 4 and 5 (phenyl label), 75-mL aliquots of the leachates were concentrated to 1 mL and aliquots were analyzed by one-dimensional TLC analysis as previously described. For Samples 2, 3, 4, and 5, the KOH trapping solutions were brought to 100 mL and duplicate 1-mL aliquots were analyzed using LSC (pp. 27-28). Following leaching, the soils were extruded from each column by gentle nitrogen pressure and then separated into one segment (A-1), 2-3 cm in thickness, containing the aged soil layer, and five equal segments (A, B, C, D, and E), each *ca.* 6 cm in thickness (p. 24). Each soil segment was extracted by shaking for 1 hour at 300 strokes/minute with 250 mL each of a CH_3CN-33 mM $NaHCO_3$ mixture (7:3, v:v) and CH_3CN-33 mM $NaHCO_3$ mixture (1:1, v:v; p. 26). Soil segments A-1 and A of Columns 2 and 3 (pyrimidinyl label) were extracted a third time with 250 mL of a CH_3CN-33 mM $NaHCO_3$ mixture (1:1, v:v) after sonication at 40°C for 50 minutes. Following each extraction, the samples were centrifuged for 20 minutes and the supernatants were removed and brought to 250 mL with the appropriate solvent. Duplicate 1-mL aliquots of the soil extracts were analyzed for total radioactivity using LSC (pp. 27-28). The remaining soil from Columns 2, 3, 4, and 5 (both labels) was air-dried, and a minimum of three *ca.* 1-g aliquots were combusted and aliquots were analyzed for total radioactivity using LSC following combustion. To isolate and quantify [^{14}C]residues from the soil column segments, 100-mL aliquots of the soil extracts were pooled, concentrated under vacuum to 1 mL, and analyzed by TLC as previously described (pp. 26-29). For leachates, limits of detection for TLC analysis were 0.11% and 0.56% for [^{14}C-5-pyrimidinyl]- and [^{14}C-U-phenyl]orthosulfamuron treated samples, respectively. For soil segments, limits of detection for TLC analysis were 0.13% and 0.10% for [^{14}C-5-pyrimidinyl]- and [^{14}C-U-phenyl]orthosulfamuron treated samples, respectively (p. 31). Mass balances were determined by summing the radioactivity recovered from the column leachates, soil extracts, combusted residues, and KOH traps (p. 27).

II. RESULTS AND DISCUSSION:

[^{14}C-5-Pyrimidinyl]orthosulfamuron treatment following aging: Material balances for the loam soil were 103.20% and 96.33% of the applied for Sample 7 (aged 34 days) and Sample 9 (aged 55 days; p. 33; Table 2, p. 48; Appendix 7, Table IIIa, p. 153; Table IVa, p. 154; Table VIa, p. 156; Table VIIa, p. 157). For Sample 7 (aged 34 days), a total of 43.94%, 49.45%, and 9.63% of the applied was recovered from the water layer, extracted residues, and non-extracted residues, respectively; $^{14}CO_2$ was 0.18% of the applied. For Sample 9 (aged 55 days), 35.86%, 50.35%, and 9.83% of the applied was recovered from the water layer, extracted residues, and non-extracted residues, respectively; $^{14}CO_2$ was 0.29% of the applied.

Based on TLC analysis, 4 to 6 compounds were identified in the water layers and soil extracts of the aged samples (p. 33; Figures 6-7, pp. 66-67). For Sample 7 (aged 34 days), [^{14}C]orthosulfamuron (S3; IR5878; 1-(4,6-dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea) accounted for 36.97% and 22.01% of the applied in the water layers and extracted residues, respectively, and was 58.98% in the whole system (p. 33; Table 7, p. 53; Appendix 8, Table XXIb, p. 172). For Sample 9 (aged 55 days), [^{14}C]orthosulfamuron accounted for 28.79% and 14.41% of the applied in the water layer and extracted residues, respectively, and was 43.20% in the whole system. The major transformation product S12 (DOP-urea; N-(4,6-dimethoxypyrimidin-2-yl)urea) was 28.80% and 35.94% of the applied in Samples 7 and 9, respectively. Transformation product S9 (O-desmethyl IR 5878; 1-(4-methoxy-6-hydroxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea) comprised 2.58% and 4.46% of the applied in Samples 7 and 9, respectively. Transformation products S11, S13 (DOP amine; 2-amino-4,6-dimethoxypyrimidine), and S15 were not detected above 3% of the applied in either sample.

[^{14}C-U-Phenyl]orthosulfamuron treatment following aging: Material balances for the loam soil were 107.08% and 104.21% of the applied for Sample 8 (aged 34 days) and Sample 10 (aged 55 days; p. 33; Table 3, p. 49; Appendix 7, Table IIIb, p. 153, Table IVb, p. 154, Table VIb, p. 156, Table VIIb, p. 157). For Sample 8 (aged 34 days), a total of 64.32%, 34.46%, and 8.16% of the applied radioactivity was recovered from the water layer, extracted residues, and non-extracted residues; $^{14}CO_2$ was 0.14% of the applied. For Sample 10 (aged 55 days), 64.83%, 28.52%, and 10.58% of the applied was recovered from the water layer, extracted residues, and non-extracted residues, respectively; $^{14}CO_2$ was 0.28% of the applied.

Based on TLC analysis, 4 to 6 compounds were identified in the water layers and soil extracts of the aged samples (p. 33; Figures 8-9, pp. 68-69). For Sample 8 (aged 34 days), [^{14}C]orthosulfamuron accounted for 41.72% and 28.14% of the applied in the water layers and extracted residues, respectively, and was of 69.86% of the applied in the whole system (Table 8, p. 53; Appendix 8, Table XXIIb, p. 173). For Sample 10 (aged 55 days), [^{14}C]orthosulfamuron accounted for 34.70% and 20.52% of the applied in the water layer and extracted residues, respectively, and was 55.22% in the whole system. The major transformation product S1 (DBS-acid; 2-sulfoamino-N,N-dimethylbenzamide) accounted for a total of 16.03% and 24.73% of the applied in Samples 8 and 10, respectively, after 34 and 55 days of aging. Transformation product S9 comprised 2.84% and 5.18% of the applied in Samples 8 and 10, respectively. Transformation product S2 (DBS-amide; 2-sulfamoylamino-N,N-dimethylbenxamide) was 7.21% and 6.22% of the applied in Samples 8 and 10, respectively. Transformation products S4 and S5 were not detected above 3% of the applied in either sample.

[^{14}C-5-Pyrimidinyl]orthosulfamuron treatment following leaching: A mean of 89.86% of the applied radioactivity was recovered in the soil segments of both columns (pp. 35-36; Table 4, p. 50). Mean recoveries for each soil segment were 46.41% of the applied for the A-1 segment (aged soil layer), 34.26% in the A segment, 6.98% in the B segment, 1.99% in the C segment, and 0.24% in the D segment. Total extracted [^{14}C]residues averaged 79.46% of the applied, and non-extracted residues averaged 10.41% of the applied (p. 35; Table 2, p. 48; Table 4, p. 50). $^{14}CO_2$ averaged 0.66% of the applied (Appendix 7, Table XIXa, p. 169). In the leachate samples, an average of 4.55% of the applied was recovered (p. 34; Table 6, p. 52; Appendix 7, Table VIIa, p. 158). The mean mass balance for the two columns was 95.06%.

Based on TLC analyses of leachate samples from both columns, [^{14}C]orthosulfamuron (S3) and the transformation product S12 did not leach (p. 34; Table 9, p. 54; Figure 1, p. 61; Figures 10-11, pp. 70-71; Figure 23, p. 83; Appendix 8, Table XXIIIb, p. 174). Transformation products S9 and S11 comprised 4.07-4.57% and 0.21-0.24% of the applied, respectively. Transformation products found in the leachate samples from both columns were equivalent (p. 36; Figure 27, p. 87; Figures 29-30, pp. 89-90).

In soil segment extracts from both columns, [^{14}C]orthosulfamuron averaged 23.11% of the applied, of which 7.27%, 9.27%, 4.81%, and 1.76% of the applied was recovered in soil segments A-1, A, B, and C, respectively (p. 35; Table 11, p. 56; Figure 3, p. 63; Figures 14-17, pp. 74-77; Appendix 8, Table XXVII, p. 178). Transformation products S9 and S12 were found in soil segments A-1, A, B, and C and averaged 1.05% and 51.68% of the applied, respectively (Figure 5, p. 65). Transformation products S11, S13, and S15 averaged 0.26%, 2.46%, and 0.69% of the applied, respectively. Transformation products found in soil segment extracts of both columns were equivalent (p. 37; Figure 37, p. 97; Figures 39-44, pp. 99-104).

[^{14}C-U-Phenyl]orthosulfamuron treatment following leaching: A mean of 35.89% of the applied radioactivity was recovered in soil segments of both columns (pp. 35-36; Table 5, p. 51). Mean recoveries for each soil segment were 11.76% of the applied for the A-1 segment (aged soil layer), 10.31% in the A segment, 7.25% in the B segment, 4.00% in the C segment, 2.06% in the D segment, and 0.53% in the E segment. Total extracted [^{14}C]residues averaged 27.83% of the applied, and non-extracted residues averaged 8.06% of the applied (Table 3, p. 49; Table 5, p. 51). $^{14}CO_2$ averaged 0.48% of the applied (Appendix 7, Table XIXb, p. 169). In the leachate samples, an average of 62.50% of the applied was recovered (p. 34; Table 6, p. 52; Appendix 7, Table VIIIb, p. 158). The mean mass balance for the two columns was 98.87%.

Based on TLC analyses of leachate samples from both columns, [^{14}C]orthosulfamuron (S3) did not leach (p. 34; Table 10, p. 55; Figure 2, p. 62; Figure 4, p. 64; Figures 12-13, pp. 72-73; Figure 24, p. 84; Appendix 8, Table XXIVb, p. 175). The major transformation product, S1, comprised 44.26-50.56% of the applied. Minor transformation products S9, S2, and S5 comprised 3.59-3.76%, 7.32-8.01%, and 1.33-2.47% of the applied, respectively. The minor transformation product S4 was found in leachate from one column, and was 3.71% of the applied. Transformation products found in leachate samples from both columns were equivalent (p. 36; Figure 28, p. 88; Figures 31-36, pp. 91-96).

In soil segment extracts from both columns, S3 averaged 24.24% of the applied, of which 4.98%, 7.94%, 6.07%, 3.47%, and 1.78% of the applied was recovered in soil segments A-1, A, B, C, and D, respectively (p. 35; Table 12, p. 57; Figure 4, p. 64; Figures 18-22, pp. 78-82; Appendix 8, Table XXXI, p. 182). Transformation products S9 and S1 were found in soil segments A-1, A, B, C, and D and averaged 0.91% and 1.50% of the applied, respectively. Transformation products S2, S4, and S5 averaged 0.21%, 0.17%, and 0.31% of the applied, respectively. Transformation products found in soil segment extracts of both columns were equivalent (p. 37; Figure 38, p. 98; Figures 45-50, pp. 105-110).

Table 3. Recoveries of Orthosulfamuron and Degradates (% of applied) per Column Segment at Study Termination (mean, n=2).

Phenyl label						
Compound	**Segment A-1 (2-3 cm)**	**Segment A (*ca.* 6 cm)**	**Segment B (*ca.* 6 cm)**	**Segment C (*ca.* 6 cm)**	**Segment D (*ca.* 6 cm)**	**Segment E (*ca.* 6 cm)**
Orthosulfamuron	4.98	7.94	6.07	3.47	1.78	Not detected
DBS-acid	0.23	0.51	0.33	0.29	0.15	Not detected
DBS-amide	Not detected	0.11	Not detected	0.06	0.04	Not detected
DB amine	0.08	Not detected	0.09	Not detected	Not detected	Not detected
Unresolved compounds	0.26	0.05	Not detected	Not detected	Not detected	Not detected
O-desmethyl orthosulfamuron	0.27	0.20	0.15	0.20	0.09	Not detected
Pyrimidinyl label						
Orthosulfamuron	7.27	9.27	4.81	1.76	Not detected	Not detected
O-desmethyl orthosulfamuron	0.39	0.35	0.21	0.10	Not detected	Not detected
Unresolved compounds	0.20	0.06	Not detected	Not detected	Not detected	Not detected
DOP urea	29.66	20.83	1.06	0.13	Not detected	Not detected
DOP amine	1.36	1.10	Not detected	Not detected	Not detected	Not detected
O-desmethyl DOP urea	0.34	0.35	Not detected	Not detected	Not detected	Not detected

III. REVIEWER'S COMMENTS:

1. The incubation temperature during the leaching portion of the experiment was not reported. The temperature during leaching of the soil columns should be maintained at a temperature within the range of normal environmental parameters (18-30°C).

2. The method used to maintain a constant head during leaching of the soil columns was not reported. Column leachates were *ca.* six pore volumes (p. 26).

3. The actual test concentrations of the [^{14}C-5-pyrimidinyl]-labeled and [^{14}C-U-phenyl]-labeled orthosulfamuron test solutions were confirmed by LSC analysis to be 24.47 µg/mL (0.102 MBq/mL) and 14.26 µg/mL (0.081 MBq/mL), respectively (pp. 23, 32; Appendix 7, Tables I-II, pp. 151-152). The actual doses of the [^{14}C-5-pyrimidinyl]-labeled and [^{14}C-U-phenyl]-labeled orthosulfamuron treatment solutions were 11.99 µg/sample (75.41 g a.i./ha) and 11.83

µg/sample (74.40 g a.i./ha), respectively. In addition, the maximum recommended field application rate of orthosulfamuron was not reported. Subdivision N guidelines state that if possible, one concentration should be roughly equivalent to the maximum proposed or registered field application rate of the parent compound.

4. Following the aging and leaching phases, the extracts were stored at 4-6°C when not in use (pp. 25, 27). TLC analysis was performed within 25 days from the collection and extraction of samples (p. 29). Storage stability data were not provided.

5. The reference substance S9 (O-desmethyl IR 5878; 1-(4-methoxy-6-hydroxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea) used in the study was isolated from urine samples of rats used in the study MEF.01.13, "Profiling of radiolabeled metabolites of [^{14}C-U-Phenyl]IR5878 in urine and feces of rats following single and repeated oral administrations" (p. 20).

6. An experimental protocol was included in Appendix 1 of the study report (pp. 113-126). Figures depicting the apparatus used during the aging period and the soil columns were included in Appendix 10 of the study report (pp. 189-190).

7. Information on the collection site for the loam soil used in the study was reported as follows:

Property	**Loam**
GPS Coordinates	N 35° 28', W 91° 13'
Farm	Shoffner
Previous Crop	Soybeans
Present Crop	Cotton
Pesticide	Roundup Ultra Max Karate Z Pix Plus
Manuring	None

Data were obtained from Appendix 3, p. 135 of the study report.

Attachment 1: Structures of Parent and Transformation Products

Orthosulfamuron [IR5878; S3]

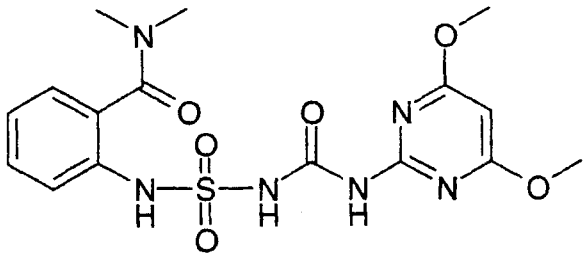
IUPAC name: 1-(4,6-Dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea.

CAS name: 2-[[[[[(4,6-Dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]amino]-N,N-dimethylbenzamide.

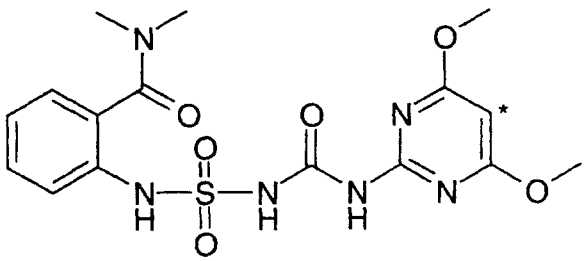
CAS No: 213464-77-8.

SMILES String: CN(C(=O)c1ccccc1NS(=O)(=O)NC(=O)Nc1nc(cc(n1)OC)OC)C.

Unlabeled



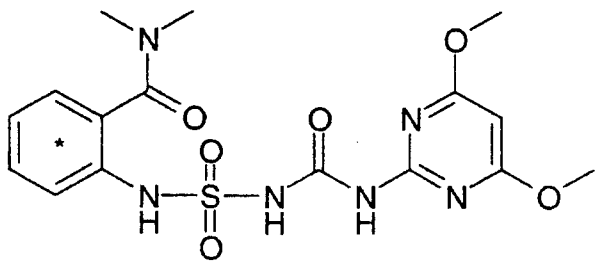
[Pyrimidinyl-5-^{14}C]IR5878



* Position of radiolabel.

17

Phenyl-U-^{14}C]IR5878



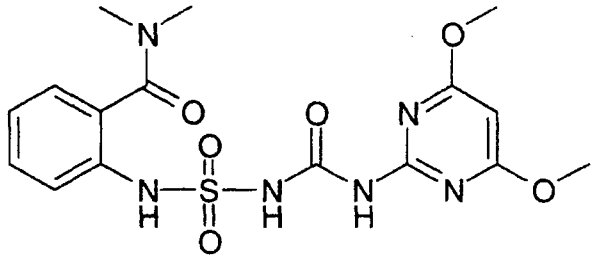
* Position of radiolabel

18

Identified Compounds

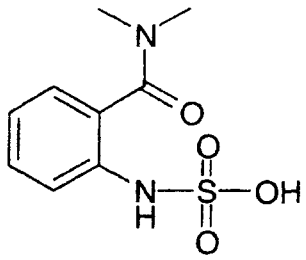
Orthosulfamuron [IR5878; S3]

IUPAC name: 1-(4,6-Dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea.
CAS name: 2-[[[[[(4,6-Dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]amino]-N,N-dimethylbenzamide.
CAS No: 213464-77-8.
SMILES String: CN(C(=O)c1ccccc1NS(=O)(=O)NC(=O)Nc1nc(cc(n1)OC)OC)C.



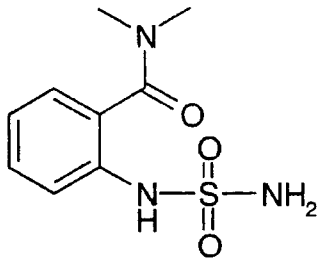
S1 [DBS-acid]

IUPAC name: 2-Sulfoamino-N,N-dimethylbenzamide.
CAS name: Not reported.
CAS No: Not reported.



S2 [DBS-amide]

IUPAC name: 2-Sulfamoylamino-N,N-dimethylbenzamide.
CAS name: Not reported.
CAS No: Not reported.



S4

IUPAC name: Not reported.
CAS name: Not reported.
CAS No: Not reported.

Structure not provided.

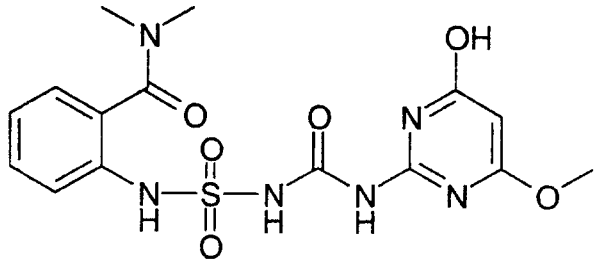
S5

IUPAC name: Not reported.
CAS name: Not reported.
CAS No: Not reported.

Structure not provided.

S9 [O-desmethyl IR 5878]

IUPAC name: 1-(4-Methoxy-6-hydroxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea.
CAS name: Not reported.
CAS No: Not reported.



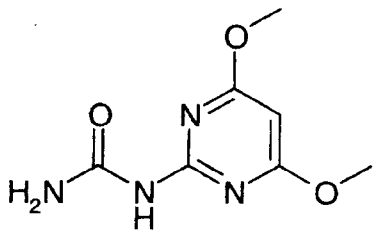
S11

IUPAC name: Not reported.
CAS name: Not reported.
CAS No: Not reported.

Structure not provided.

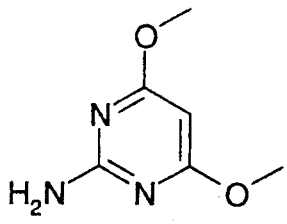
S12 [DOP-urea]

IUPAC name: N-(4,6-Dimethoxypyrimidin-2-yl)urea.
CAS name: Not reported.
CAS No: Not reported.



S13 [DOP amine]

IUPAC name: 2-Amino-4,6-dimethoxypyrimidine.
CAS name: Not reported.
CAS No: Not reported.



S15

IUPAC name: Not reported.
CAS name: Not reported.
CAS No: Not reported.

Structure not provided.