Data Evaluation Report on the Hydrolysis of Orthosulfamuron (IR5878)

PMRA Submission Number {.....} EPA MRID Number 46219015

Data Requirement: PMRA Data Code:
EPA DP Barcode: D304186
OECD Data Point:
EPA Guideline: 161-1

Test material:

Common name:	Orthosulfamuron.
Chemical name:	
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.
Synonyms:	o-Sulfamuron, IR5878.
Smiles string:	CN(C(=O)c1ccccc1NS(=O)(=O)NC(=O)Nc1nc(cc(n1)OC)OC)C (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found as of 7/6/06.

Primary Reviewer: Leanne Ganser
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Company Code:
Active Code:
Use Site Category:
EPA PC Code: 108209

CITATION: Castoldi, F. and G. Pizzingrilli. 2000. Hydrolysis of [^{14}C-U-phenyl] IR5878 in Buffered Solutions at pH 4, 7 and 9. Unpublished study performed by ISAGRO RICERCA Srl, Novara, Italy and sponsored by ISAGRO SpA, Milano, Italy. Study No.: ABT.99.13. Experiment started November 9, 1999 and completed June 14, 2000. Final reported issued July 3, 2000. 120 pp.

Data Evaluation Report on the hydrolysis of o-sulfamuron (IR5878)

PMRA Submission Number {.....} EPA MRID Number 46219015

Data Requirement: PMRA Data Code:
EPA DP Barcode: D319377
OECD Data Point:
EPA Guideline: 161-1

Test material:

Common name:	O-Sulfamuron.
Chemical name:	
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.
Synonyms:	Orthosulfamuron, IR5878.
Smiles string:	CN(C(=O)c1ccccc1NS(=O)(=O)NC(=O)Nc1nc(cc(n1)OC)OC)C (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found as of 7/6/06.

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CITATION: Castoldi, F.C. and G. Pizzingrilli. 2000. Hydrolysis of [^{14}C-U-phenyl] IR5878 in buffered solutions at pH 4, 7 and 9. Unpublished study performed by ISAGRO RICERCA Srl, Novara, Italy and sponsored by ISAGRO SpA, Milano, Italy. Study No.: ABT.99.13. Experiment started November 9, 1999 and completed June 14, 2000 (p. 12). Final reported issued July 3, 2000.

EXECUTIVE SUMMARY

The hydrolysis of [phenyl-U-^{14}C]-labeled 1-(4,6-dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea (orthosulfamuron, radiochemical purity >97%), at 1 µg a.i./mL, was studied in sterile aqueous buffered pH 4 (0.01M acetate), pH 7 (0.01M citrate), or pH 9 (0.01M borate) solutions that were incubated in the dark in four experiments: The definitive experiment was conducted at 25°C with pH 7 or pH 9 solutions for up to 176 days. Two other experiments were conducted at 50°C, one preliminary experiment with pH 4, pH 7, or pH 9 solutions for 5 days, and two supplemental experiments with pH 7 or pH 9 solutions at either 1 µg a.i./mL or higher concentrations for up to 29 days. Sampling times of the experiments are as follows:

Definitive experiment
25°C/pH 7: 0, 3, 8, 21, 28 and 37 days.
25°C/pH 9: 0, 8, 21, 37, 113 and 176 days.

Preliminary experiment
50°C/pH 4: 0, 1, and 3 hours and 1, 2, and 5 days.
50°C/pH 7: 0, 1, and 3 hours and 1, 2, and 5 days.
50°C/pH 9: 0, 1, and 3 hours and 1, 2, and 5 days.

Supplementary experiments
50°C/pH 7: 0, 17, 24, 41, 45, 48, 65, 72, 89, 95, and 166 hours.
50°C/pH 9: 0, 3, 6, 8, 10, 13, 14, 17, 20, and 29 days.

The study was conducted in accordance with Council Directive 91/414/EEC Part A of Annex II, Section 2 as amended by Commission Directive 94/37/EC, Annex I, Section 2 and in compliance with OECD Principles of GLP. The test system consisted of sealed glass tubes (10 mL volume) containing treated buffer solution (1.5-4 mL/tube). Volatiles were not trapped. Single samples were collected for analysis at each sampling. The buffer solutions were analyzed directly by TLC without extraction or concentration. Orthosulfamuron and its transformation products were identified by cochromatography with reference standards. Identifications were confirmed using HPLC and LC/MS.

The temperature and pH of the buffer solutions was reportedly maintained throughout the study; no supporting data were provided. The sterility of the test solutions was not determined.

In the experiment conducted at 25°C, overall recoveries of [^{14}C]residues averaged 100.20 ± 0.95% of the applied (range 99.05-101.18%) from the pH 7 buffer solution and 99.34 ± 1.40% (range 98.01-101.97%) from the pH 9 buffer solution. Three transformation products were identified: 2-sulfoamino-N,N-dimethylbenzamide (H1), 2-sulfamoylamino-N,N-dimethylbenzamide (H2), and 2-amino-N,N-dimethylbenzamide (H4). There was no loss of material over time.

In the pH 7 buffer at 25°C, [^{14}C]orthosulfamuron decreased from 96.99% of the applied at day 0 to 76.14% at 8 days posttreatment and 32.91% at 37 days, dissipating with a half-life of 24.4 days.

The only major transformation product was H1, which was a maximum 58.36% of the applied at 37 days post-treatment (study termination). The minor transformation products, H2 and H4, were detected at maximum concentrations of 6.50% and 2.22% of the applied, respectively. Volatiles were not collected.

In the pH 9 buffer at 25°C, [^{14}C]orthosulfamuron decreased from 96.57% of the applied at day 0 to 56.19% at 176 days, dissipating with a half-life of 228 days. Two major transformation products, H1 and H4, were isolated. H1was a maximum 22.78% of the applied and H4 was a maximum 13.02%, both at 176 days post-treatment (study termination). The only minor transformation product was H2, which was a maximum 8.73% of the applied at 113 days posttreatment. Volatiles were not collected.

In the 50°C experiments (combined data for pH 7 buffers and for pH 9 buffers), orthosulfamuron dissipated with a half-life of 0.5 hours in the pH 4 buffer, 1.5 days in the pH 7 buffer, and 8 days in pH 9 buffer. In the pH 4 solution, H1 was a maximum of 90.44% of the applied (1 day post-treatment) and declined to 86.34% at study termination (5 days); H2 was 8.54% (3 hours) and declined to 1.16%; and H4 was 12.50% (5 days). In the pH 7 solution, H1 was a maximum of 80.94% of the applied (166 hours post-treatment, study termination); H2 was 6.67% (48 hours) and declined to 2.32%; and H4 was 13.62% (166 hours). In the pH 9 solution, H1 was a maximum of 41.22% of the applied (29 days post-treatment, study termination); H2 was 17.00% (6 days) and declined to 2.62%; and H4 was 49.32% (29 days).

The study authors provided a transformation pathway for orthosulfamuron. Orthosulfamuron hydrolyzes primarily into 2-sulfoamino-N,N-dimethylbenzamide (H1) and, to a lesser extent, into 2-sulfamoylamino-N,N-dimethylbenzamide (H2) and 2-amino-N,N-dimethylbenzamide (H4). H1 and H2 both hydrolyze to H4.

RESULTS SYNOPSIS:

pH	Temperature (°C)	Half-life	Transformation products	
			Major	Minor
7	25	24.4 days	H1	H2, H4
9	25	228 days	H1, H4	H2
4	50	0.02 days	H1, H4	H2
7	50	1.5 days	H1, H4	H2
9	50	8.0 days	H1, H2, H4	None.

Study Acceptability: This study is classified as **supplemental**, as the sterility of the test solutions was not confirmed. Furthermore, only pH 7 and pH 9 buffers were studied at 25°C.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with Council Directive 91/414/EEC Part A of Annex II, Section 2 as amended by Commission Directive 94/37/EC, Annex I, Section 2 (p. 1). One significant deviation from the objectives of Subdivision N guidelines was noted:

The sterility of the test solutions was not confirmed.

Hydrolysis in pH 5 (or pH 4) buffer at 25°C was not studied.

COMPLIANCE: This study was conducted in compliance with OECD Principles of GLP (p. 3). Signed and dated Data Confidentiality, GLP, Quality Assurance, and Declaration and Signatures statements were provided (pp. 2-3, 5-6).

A. MATERIALS:

1. Test Material [^{14}C-U-Phenyl]Orthosulfamuron (p. 13).

Chemical Structure: See DER Attachment 1.

Description: Technical grade; solid (p. 13).

Purity: Radiochemical purity: >97% (pp. 13, 23 and Appendix 5, pp. 114-117).
Lot No.: 182.
Analytical purity: not reported.
Specific activity: 5.700 MBq/mg (342008 dpm/µg, 154.058 µCi/mg).
Location of the radiolabel: Labeled uniformly on the phenyl ring.

Storage conditions of test chemicals: The test substance was stored at -20°C (p. 14). The reference compound was stored at room temperature.

Physico-chemical properties of orthosulfamuron.

Parameter	Value	Comment
Molecular weight	424.44 g/mole	
Molecular formula	$C_{16}H_{20}N_6O_6S$	
Water Solubility	Not reported.	
Vapor Pressure/Volatility	Not reported.	
UV Absorption	Not reported.	
Pka	Not reported.	
K_{ow}/log K_{ow}	Not reported.	
Stability of compound at room temperature, if provided	Not reported.	

Data obtained from p. 13 of the study report.

2. Buffer Solution: Buffer solutions were bubbled with nitrogen gas to remove oxygen (p. 16). Buffer solutions were prepared with CO_2 free distilled water as follows:

Table 1: Description of buffer solutions.

pH	Type and molarity of buffer	Composition
4	0.01M Acetate	0.1476 g of sodium acetate was dissolved in 500 mL of water. The pH was adjusted to 4.0 with 4.69 mL of 1.75N acetic acid.
7	0.01M Citrate	1.921 g of citric acid was dissolved in 250 mL of water. The pH was adjusted to 7.0 with 285 mL of 0.1N sodium hydroxide.
9	0.01M Borate	0.620 g of boric acid and 0.746 g of potassium chloride were dissolved in 500 mL of water. The pH was adjusted to 9.0 with 43 mL of 0.1N sodium hydroxide.

Data obtained from p. 16 of the study report.

B. EXPERIMENTAL CONDITIONS

1. Preliminary Study: A preliminary study was performed with *ca.* 1 µg/mL orthosulfamuron at 50°C in the dark at pH 4, 7 and 9 (p. 17). The buffer solutions were analyzed by TLC and HPLC at 0, 1 and 3 hours and at 1, 2 and 5 days.

2. Experimental conditions

Table 2: Experimental parameters.

Parameters		pH 7	pH 9
Duration of study		37 days.	176 days.
Test concentrations Nominal: Measured:		1 µg/mL. 1.086 µg/mL.	 1.079 µg/mL.
No. of replications		Single samples were collected at each interval.	
Preparation of test medium	Volume used/treatment	0.19 mL of stock solution was added to 18.81 mL of buffer solution and 1.5 -4 mL aliquots of the bulk solution were dispensed into glass tubes.	
	Method of sterilization	Glassware and materials necessary for the study were sterilized by autoclaving (20 minutes, 121°C). Buffer solutions were sterilized (method not reported).	
	Co-solvent	1% acetonitrile.	
Test apparatus (type/material/volume)		Glass tubes (10 mL) containing treated buffer solution (1.5 - 4 mL) were sealed with glass plugs.	
Details of traps for volatile, if any		Volatile traps were not used.	
If no traps were used, is the test system closed/open?		Closed.	
Is there any indication of the test material adsorbing to the walls of the test apparatus?		None.	
Experimental conditions Temperature (°C): Lighting: pH ranges:		 25°C. Dark. 7.0, 9.0 (ranges not reported).	
Other details, if any		None.	

Data were obtained from pp. 16-18 and 23 of the study report.

3. Supplementary Experiments: Based on the results of the preliminary experiment, the hydrolysis study with *ca.* 1 µg/mL orthosulfamuron at 50°C was repeated in a primary supplementary experiment using only the pH 7 and 9 buffers (p. 18). The samples were incubated as described, and samples were collected for analysis after 0, 17, 24, 41, 45, 48, 65, 72, 89, 95 and 166 hours (6.92 days) for pH 7 buffer solution and after 0, 3, 6, 8, 10, 13, 14, 17, 20, 29 days for pH 9 buffer solution.

A secondary supplementary experiment was performed with higher concentrations of unlabeled orthosulfamuron for identification of hydrolysis compounds (p. 18). Unlabeled orthosulfamuron was dissolved in acetonitrile (100 mg/500 µL) and added to 50 mL of pH 9 buffer solution. The solution (ULpH9) was incubated for 8 days at 50°C in the dark. A second solution (ULpH4) of unlabeled orthosulfamuron dissolved in acetonitrile (150 mg/500 µL) and added to 50 mL of pH 4 buffer solution was incubated for 1 day at 50°C in the dark. ULpH4 was extracted twice with dichloromethane and twice with ethyl acetate (aqueous sample:organic solvent, 1:2, v:v). The aqueous phase (ULpH4A) was made up to pH 9 with 0.1N NaOH. The solutions were analyzed by LC-MS and MS (pp. 19, 21-22).

4. Sampling:

Table 3: Sampling details.

Criteria	pH 7	pH 9
Sampling intervals	0, 3, 8, 21, 28 and 37 days.	0, 8, 21, 37, 113 and 176 days.
Sampling method	Single tube of each treatment was collected at each interval.	
Method of collection of CO_2 and organic volatile compounds	Volatiles were not collected.	
Sampling intervals/times for: pH measurement: Sterility check:	During incubation period for samples prepared with unlabeled test substance at the experimental concentration in each buffered solution. None reported.	
Sample storage before analysis	Not reported.	
Other observation, if any:	None.	

Data were obtained from p. 18 of the study report.

C. ANALYTICAL METHODS

Extraction/clean up/concentration methods: Samples were analyzed directly without extraction or concentration by LSC, TLC and HPLC (p. 19).

Volatile residue determination: Volatiles were not trapped.

Total ^{14}C measurement: Aliquots (2 x 100 µL) of each sample were analyzed for total [^{14}C] residues using LSC (pp. 19 and 107).

Derivatization method, if used: A derivatization method was not employed.

Identification and quantification of parent compound: Aliquots (8-10 µL) of the samples were analyzed for orthosulfamuron using TLC on silica gel 60 F_{254} plates developed with two solvent systems (A) acetonitrile:water (90:10, v:v) and (B) n-hexane:chloroform:methanol (50:40:10, v:v:v; p. 20). Samples were also analyzed on RP-18 $F_{254}S$ plates developed with acetonitrile: water (70:30, v:v). Radioactive zones were detected with Fuji BAS 1500 bio-imaging analyzer using imaging plates coated with photostimulable phosphor $BaFBr:Eu^{2+}$. [^{14}C]Orthosulfamuron was identified by cochromatography with ^{14}C-reference standards (p. 19 and Figure 31, p. 71).

The TLC results were confirmed with HPLC under the following conditions (pp. 20-21): Supelcosil LC-18 (250 x 4.6 mm, 5 µm) column, gradient mobile phase consisting of (A) 4mM KH_2PO_4 (pH 5) and (B) acetonitrile [percent A:B (v:v), 0-20 minutes, 80:20 to 10:90; 20-25 minutes, 10:90; 25-27 minutes, 10:90 to 80:20]; flow rate 0.8 mL/minute; 20 µL aliquots; with RAMONA-2000 radiodetector. A second method used a mobile phase of (A) 1 mM CH_3COONH_4 (pH 4.5) and (B) acetonitrile. [^{14}C]Orthosulfamuron was identified by cochromatography with ^{14}C-reference standards, [^{14}C]orthosulfamuron and [^{14}C-U-phenyl] DB amine (H4; radiochemical purity >96%), and by comparison to an unlabeled reference standard of orthosulfamuron (purity 98.72%; pp. 13, 19, Figure 29, p. 69, Figure 32, p. 72 and Appendix III, p. 118).

Identification and quantification of transformation products: Transformation products were identified and quantified using TLC and HPLC as for the parent compound (pp. 19, 21-22).

Detection limits (LOD, LOQ) for the parent compound: For LSC, the limit of determination was set as twice background (p. 19). The limit of detection and the limit of quantification were not reported for TLC and HPLC.

Detection limits (LOD, LOQ) for the transformation products: The limits of detection and quantification were the same as for the parent compound (p. 19).

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS: During the study, the temperature of the buffer solutions was 25°C and the buffer solutions were maintained at pH 7 and 9 (no supporting records provided). The sterility of the test solutions was not reported.

B. MASS BALANCE: Overall recoveries of [^{14}C]residues of the applied averaged 100.21 ± 0.95% (range 99.05-101.18%) from the pH 7 buffer solution and 99.34 ± 1.41% (range 98.01-101.97%) from the pH 9 buffer solution (Table 1, p. 35). There was no pattern of loss of material over time from any of the buffer solutions.

Table 4a: Hydrolysis of Orthosulfamuron, expressed as percentage of the applied radioactivity (n = 1), at pH 7.

Compound	Sampling times (days)					
	0	3	8	21	28	37
Orthosulfamuron (H3)	96.99	88.07	76.14	53.89	44.87	32.91
2-sulfoamino-N,N-dimethylbenzamide (H1)	2.18	9.67	18.84	39.79	48.95	58.36
2-sulfamoylamino-N,N-dimethylbenzamide (H2)	ND	1.77	4.05	4.94	4.17	6.50
2-amino-N,N-dimethylbenzamide (H4)	0.83	0.49	0.97	1.38	2.02	2.22
CO_2	Volatiles were not collected.					
Volatile organics	Volatiles were not collected.					
Total Recovery	99.05	100.17	100.57	99.12	101.14	101.18

Data obtained from Table 1, p. 35, Table 3, p. 37 and Appendix 3, Table XIII, p. 111 of the study report.
ND = Not detected.

Table 4b: Hydrolysis of Orthosulfamuron, expressed as percentage of the applied radioactivity (n = 1), at pH 9.

Compound	Sampling times (days)					
	0	8	21	37	113	176
Orthosulfamuron (H3)	96.57	92.95	89.25	85.64	67.64	56.19
2-sulfoamino-N,N-dimethylbenzamide (H1)	2.67	5.08	5.73	7.34	17.06	22.78
2-sulfamoylamino-N,N-dimethylbenzamide (H2)	ND	1.39	3.84	5.25	8.73	8.01
2-amino-N,N-dimethylbenzamide (H4)	0.76	0.58	1.18	1.77	6.57	13.02
CO_2	Volatiles were not collected.					
Volatile organics	Volatiles were not collected.					
Total Recovery	98.01	101.97	98.45	99.59	99.31	98.69

Data obtained from Table 1, p. 35, Table 4, p. 38 and Appendix 3, Table XIV, p. 112 of the study report.
ND = Not detected.

C. TRANSFORMATION OF PARENT COMPOUND: The concentration of [^{14}C]orthosulfamuron decreased steadily in the pH 7 buffer solution, decreasing from 96.99% of the applied at day 0 to 76.14% at day 8 and was 32.91% at study termination (day 37; Table 3, p. 37 and Appendix 3, Table XIII, p. 111). [^{14}C]Orthosulfamuron was slowly hydrolyzed in pH 9, decreasing from 96.57% of the applied at day 0 to 56.19% at study termination (day 176; Table 4, p. 38 and Appendix 3, Table XIV, p. 112).

HALF-LIVES/DT_{50}/DT_{90}: Based on first order linear regression analysis (Excel 2003), orthosulfamuron at 25°C dissipated from the buffer solutions of pH 7 and pH 9 with a calculated half-life of 24.4 days and 228 days, respectively (DER Attachment 2). The observed DT_{50} was 21-28 days in pH 7 and <176 days in pH 9 (Tables 3-4, pp. 37-38).

Table 5: Half-lives/DT_{50}/DT_{90} at 25°C.

pH	First order linear			DT_{50}	DT_{90}
	Half-life (days)	Regression equation	r^2		
7	24.4	y = -0.0284x + 4.5711	0.9979	21-28 days	--
9	228	y = -0.0030x + 4.5610	0.9993	<176 days	--

Calculated using data obtained from Tables 3-4, pp. 37-38 and Appendix 3, Tables XIII-XIV, pp. 111-112 in the study report (DER Attachment 2).

TRANSFORMATION PRODUCTS: At 25°C, two major transformation products were identified. At pH 7, 2-sulfoamino-N,N-dimethylbenzamide (H1) was a maximum concentration of 58.36% of the applied at study termination (day 37; Table 3, p. 37). At pH 9, H1 was a maximum concentration of 22.78% of the applied at study termination (day 176; Table 4, p. 38). At pH 7, 2-amino-N,N-dimethylbenzamide (H4) only reached a maximum of 2.22% of the applied at study termination (day 37). However, in pH 9, H4 was 13.02% of the applied at study termination (day 176). The minor transformation product 2-sulfamoylamino-N,N-dimethylbenzamide (H2) was

detected at maximum concentrations of 6.50% (day 37) and 8.73% (113 days) in pH 7, and pH 9, respectively.

Table 6: Chemical names and CAS numbers for the transformation products of orthosulfamuron.

Applicants Code Name	CAS Number	Chemical Name	Chemical Formula	MW (g/mol)	Smiles String
H1	NR	2-Sulfoamino-N,N-dimethylbenzamide	NR	NR	NR
H2	NR	2-Sulfamoylamino-N,N-dimethylbenzamide	NR	NR	NR
H4	NR	2-Amino-N,N-dimethylbenzamide	NR	NR	NR

Data obtained from pp. 27-28 of study report.
NR = Not reported.

VOLATILIZATION: Volatiles were not collected.

TRANSFORMATION PATHWAY: The study authors provided a transformation pathway for orthosulfamuron (pp. 29, 31). Orthosulfamuron hydrolyzes primarily into 2-sulfoamino-N,N-dimethylbenzamide (H1), with 2-sulfamoylamino-N,N-dimethylbenzamide (H2) and 2-amino-N,N-dimethylbenzamide (H4) formed in lesser amounts. H1 and H2 both hydrolyze to H4.

D. PRELIMINARY EXPERIMENT RESULTS: [^{14}C]Orthosulfamuron was rapidly hydrolyzed at 50°C in pH 4 buffer solution, decreasing from 94.02% of the applied at 0 hours to 19.00% at 1 hour and was last detected at 0.77% at 3 hours (Table 2, p. 36). [^{14}C]Orthosulfamuron was hydrolyzed more slowly in pH 7 and 9 buffer solutions. In pH 7 buffer solution, orthosulfamuron decreased from 97.34% of applied at 0 hours to 65.27% at 24 hours and was 44.74% at 48 hours (Table 3, p. 37). In pH 9 buffer solution, orthosulfamuron decreased from 97.14% of applied at 0 hours to 71.54% at 5 days (Table 4, p. 38).

Two major transformation products, 2-sulfoamino-N,N-dimethylbenzamide (H1) and 2-amino-N,N-dimethylbenzamide (H4), accounted for up to 90.44% and 12.50% of applied radioactivity, respectively, in pH 4, 7 and 9. The minor transformation product, 2-sulfamoylamino-N,N-dimethylbenzamide (H2), accounted for up to 9.79% of applied radioactivity in pH 4, 7 and 9.

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Table 7a: Hydrolysis of orthosulfamuron, expressed as percentage of the applied radioactivity (n = 1), at pH 4 and 50°C.

Compound	Sampling times (days)					
	0	0.04	0.13	1	2	5
Orthosulfamuron	94.02	19.00	0.77	ND	ND	ND
H1 (DBS acid)	5.29	70.96	89.56	90.44	88.14	86.34
H2 (DBS amide)	ND	8.40	8.54	5.46	3.84	1.16
H4 (DB amine)	0.69	1.64	1.13	4.10	8.02	12.50
CO_2	Volatiles were not collected.					
Volatile organics	Volatiles were not collected.					
Total Recovery	100.16	100.43	102.87	103.60	103.00	103.15

Data obtained from Tables 1-2, pp. 35-36 of the study report.
ND = Not detected.

Table 7b: Hydrolysis of orthosulfamuron, expressed as percentage of the applied radioactivity (n = 1), at pH 7 and 50°C.

Compound	Sampling times (days)					
	0	0.04	0.13	1	2	5
Orthosulfamuron	97.34	94.45	93.81	65.27	44.74	17.82
H1 (DBS acid)	1.85	3.92	4.32	26.77	43.79	65.97
H2 (DBS amide)	ND	0.78	0.72	6.23	7.54	5.28
H4 (DB amine)	0.80	0.85	1.15	1.73	3.93	10.94
CO_2	Volatiles were not collected.					
Volatile organics	Volatiles were not collected.					
Total Recovery	100.51	100.55	102.13	99.90	101.11	102.24

Data obtained from Table 1, p. 35, Table 3, p. 37 of the study report.
ND = Not detected.

Table 7c: Hydrolysis of orthosulfamuron, expressed as percentage of the applied radioactivity (n = 1), at pH 9 and 50°C.

Compound	Sampling times (days)					
	0	0.04	0.13	1	2	5
Orthosulfamuron	97.14	95.35	94.94	85.00	82.28	71.54
H1 (DBS acid)	1.89	2.99	2.81	7.00	7.51	12.37
H2 (DBS amide)	ND	0.70	0.91	6.41	7.97	9.79
H4 (DB amine)	0.96	0.96	1.34	1.60	2.24	6.30
CO_2	Volatiles were not collected.					
Volatile organics	Volatiles were not collected.					
Total Recovery	99.64	99.41	99.76	99.91	101.08	100.72

Data obtained from Table 1, p. 35, Table 4, p. 38 of the study report.
ND = Not detected.

Half-lives/DT_{50}/DT_{90} from the preliminary experiment at 50°C.

pH	First order linear			DT_{50}	DT_{90}
	Half-life (days)	Regression equation	r^2		
4	0.02 (0.43 hours)	y = -38.465x + 4.5501	1.0000	--	--
7	2.03	y = -0.3411x + 4.5523	0.9960	--	--
9	11.7	y = -0.0592x + 4.5489	0.9438	--	--

Data obtained from p. 29 and Tables 2-4, pp. 36-38 in the study report (DER Attachment 2).

E. SUPPLEMENTARY EXPERIMENT-RESULTS: The overall recoveries of [^{14}C] residues from the primary supplementary experiment with *ca.* 1 µg a.i./mL at 50°C averaged 97.65 ± 2.76% of the applied (range 93.23-101.77%) in pH 7 buffer solutions and 102.15 ± 2.33% of the applied (range 98.69-105.94%) in pH 9 buffer solutions (Table 1, p. 35). In the pH 7 buffer, [^{14}C]orthosulfamuron decreased from 97.02% of the applied at day 0 to 61.25% at day 1 to 23.44% at day 3 and was 3.12% at *ca.* day 7 (Table 3, p. 37). In the pH 9 buffer, orthosulfamuron decreased from 97.01% of the applied at day 0 to 54.95% at day 6 to 23.39% at day 17 and was 6.85% at day 29 (Table 4, p. 38).

All three transformation product analytes reached major quantities: 2-sulfoamino-N,N-dimethylbenzamide (H1) was a maximum of 80.94% of the applied in pH 7 (*ca.* 7 days) and 41.22% in pH 9 (29 days), both occurring at study termination; 2-amino-N,N-dimethylbenzamide (H4) was a maximum of 13.62% of the applied in pH 7 and 49.32% in pH 9, both occurring at study termination; 2-sulfamoylamino-N,N-dimethylbenzamide (H2) was a maximum of 6.44% of the applied (*ca.* 2 days) and 17.00% (6 days) in pH 7 and pH 9, respectively.

Half-lives were calculated for orthosulfamuron at 50°C in the pH 7 and 9 solutions by combining data for each pH from the preliminary and supplementary experiments. At 50°C, based on first order linear regression analysis (Excel 2003), orthosulfamuron dissipated with a linear half-life of 1.48 days in the pH 7 buffer and 7.96 days in pH 9 buffer (DER Attachment 2).

Half-lives/DT_{50}/DT_{90} combining the preliminary and supplementary experiments at 50°C.

pH	First order linear			DT_{50}	DT_{90}
	Half-life (days)	Regression equation	r^2		
7	1.48	y = -0.0196x + 4.5913	0.9540	--	--
9	7.96	y = -0.0868x + 4.5929	0.9929	--	--

Data obtained from p. 29 and Tables 3-4, pp. 37-38 in the study report (DER Attachment 2).

In the secondary supplementary experiment performed with high concentrations of unlabeled orthosulfamuron, analysis by MS of the aqueous phase (ULpH4A) after incubation identified compound H1 as 2-sulfoamino-N, N-dimethylbenzamide (p. 27 and Figures 37-38, pp. 77-78). Analysis by LC-MS of unlabeled orthosulfamuron incubated in pH 9 buffer solution (ULpH9) identified compounds H2 and H4 as 2-sulfamoylamino-N, N-dimethylbenzamide and 2-amino-N,N-dimethylbenzamide, respectively (p. 28 and Figures 39-43, pp. 79-83).

III. STUDY DEFICIENCIES

1. The sterility of the test solutions was not confirmed. Sterility should be assured to confirm degradation by hydrolysis.

2. No experiment was conducted in pH 5 buffer at 25°C.

IV. REVIEWER'S COMMENTS

1. The results from the preliminary and primary supplementary experiments with *ca.* 1 µg a.i./mL at 50°C were combined for each of the pH 7 and pH 9 conditions in order to generate more statistically powerful half-lives (DER Attachment 2). Combination of results was appropriate because both experiments were conducted under the same conditions with *ca.* 1 µg/mL orthosulfamuron in pH 7 or pH 9 buffered solutions at 50°C in the dark.

2. No data were provided to support the reported temperatures and pH.

3. The limits of detection and quantification were not reported for TLC and HPLC.

V. REFERENCES

1. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate, Section 161-1. Hydrolysis studies. Office of Pesticide and Toxic Substances, Washington, DC. EPA 540/9-82-021.

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

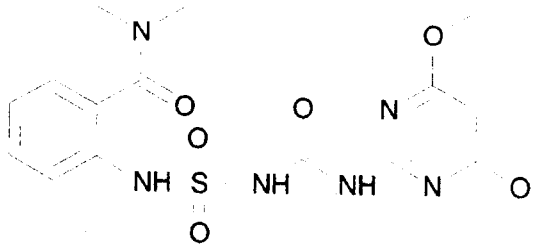
3. U.S. Environmental Protection Agency. 1993. Pesticide Registration Rejection Rate Analysis - Environmental Fate. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 738-R-93-010.

Attachment 1: Structure of Parent Compound and Transformation Products

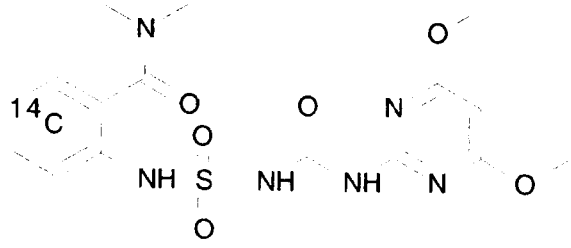
Orthosulfamuron [IR5878; S3; H3]

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 Number:	213464-77-8.
SMILES String:	CN(C(=O)c1ccccc1NS(=O)(=O)NC(=O)Nc1nc(cc(n1)OC)OC)C (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found 11/21/05.

Unlabeled



[Phenyl-U-^{14}C]IR5878

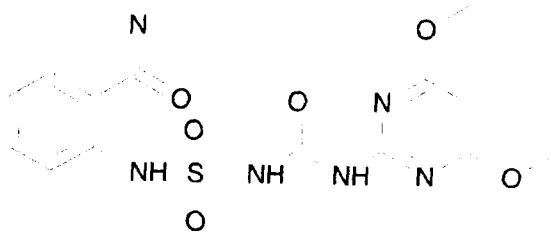


^{14}C = Location of the radiolabel.

Identified Compounds

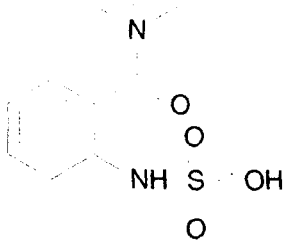
Orthosulfamuron [IR5878; S3; H3]

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 Number:	213464-77-8.
SMILES String:	CN(C(=O)c1ccccc1NS(=O)(=O)NC(=O)Nc1nc(cc(n1)OC)OC)C (ISIS v2.3/Universal SMILES). No EPI Suite, v3.12 SMILES String found 11/21/05.



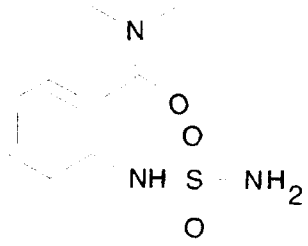
DBS acid [IR7863; S1; H1]

IUPAC Name: (2-Dimethylcarbamoylphenyl)sulfamic acid.
CAS Name: Sodium (2-dimethylcarbamoylphenyl)sulfamate.
CAS Number: Not reported.



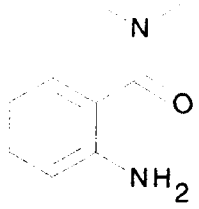
DBS amide [S2; H2]

IUPAC Name: 2-[(Aminosulfonyl)amino]-N,N-dimethylbenzamide.
CAS Name: Not reported.
CAS Number: Not reported.



DB amine [S4; H4]

IUPAC Name: 2-Amino-N,N-dimethylbenzamide.
CAS Name: Not reported.
CAS Number: Not reported.



Attachment 2: Excel Spreadsheets

Chemical: Orthosulfamuron
MRID: 46219015
PC Code: 108209
Guideline: 161-1

Recovery of Radioactivity after Incubation at 25°C

pH 7

Days post-treatment	% applied radioactivity Total
0	99.05
3	100.17
8	100.57
21	99.12
28	101.14
31	101.18
Average	100.21
SD	0.95

Data obtained from Table 1, p. 35 of the study report.

pH 9

Days post-treatment	% applied radioactivity Total
0	98.01
8	101.97
21	98.45
37	99.59
113	99.31
176	98.69
Average	99.34
SD	1.41

Data obtained from Table 1, p. 35 of the study report.

Recovery of Radioactivity after Incubation at 50°C

pH 7

Hours post-treatment	% applied radioactivity Total
0	98.08
17	95.79
24	101.77
41	93.23
45	95.57
48	97.29
65	95.28
72	97.26
89	100.91
95	101.54
166	97.38
Average	97.65
SD	2.76

Data obtained from Table 1, p. 35 of the study report.

pH 9

Days post-treatment	% applied radioactivity Total
0	101.08
3	104.02
6	105.94
8	98.69
10	105.56
13	101.95
14	101.14
17	100.24
20	101.99
29	100.91
Average	102.15
SD	2.33

Data obtained from Table 1, p. 35 of the study report.

Chemical: Orthosulfamuron
MRID: 46219015
PC Code: 108209
Guideline: 161-1
25°C
pH 7

Days post-treatment	Orthosulfamuron	
	% of applied	ln (% of applied)
0	96.99	4.5746
3	88.07	4.4781
8	76.14	4.3326
21	53.89	3.9869
28	44.87	3.8038
37	32.91	3.4938

Data obtained from Table 3, p. 37 of the study report.

Half-life (days)
24.4

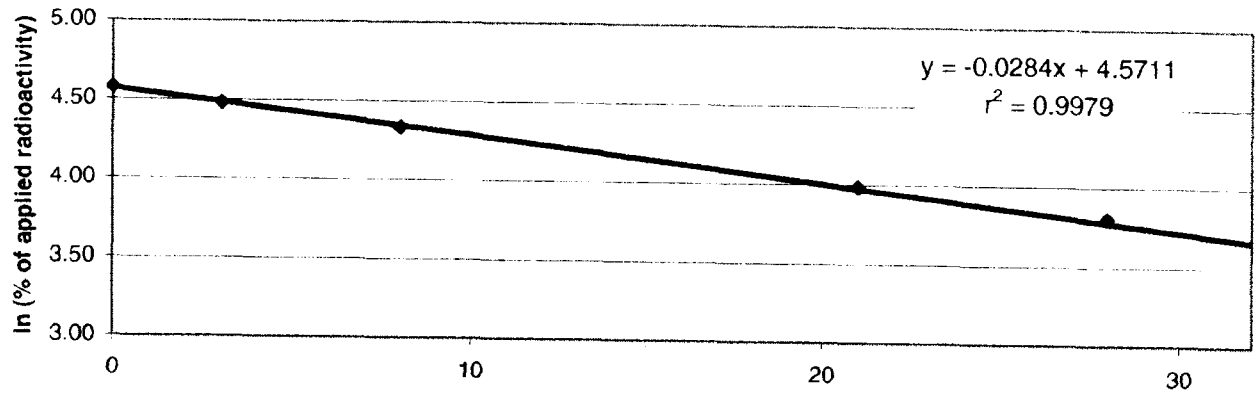
pH 9

Days post-treatment	Orthosulfamuron	
	% of applied	ln (% of applied)
0	96.57	4.5703
8	92.95	4.5321
21	89.25	4.4914
37	85.64	4.4502
113	67.64	4.2142
176	56.19	4.0287

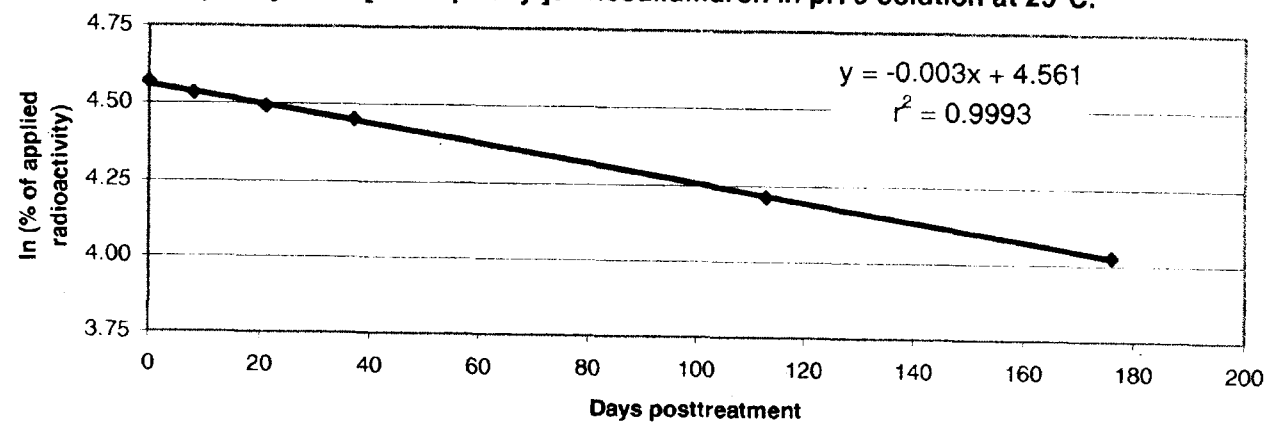
Data obtained from Table 4, p. 38 of the study report.

Half-life (days)
228

Hydrolysis of [^{14}C-U-phenyl]orthosulfamuron in pH 7 solution at 25°C.



Hydrolysis of [^{14}C-U-phenyl]orthosulfamuron in pH 9 solution at 25°C.



Chemical: Orthosulfamuron
MRID: 46219015
PC Code: 108209
Guideline: 161-1
50°C, preliminary

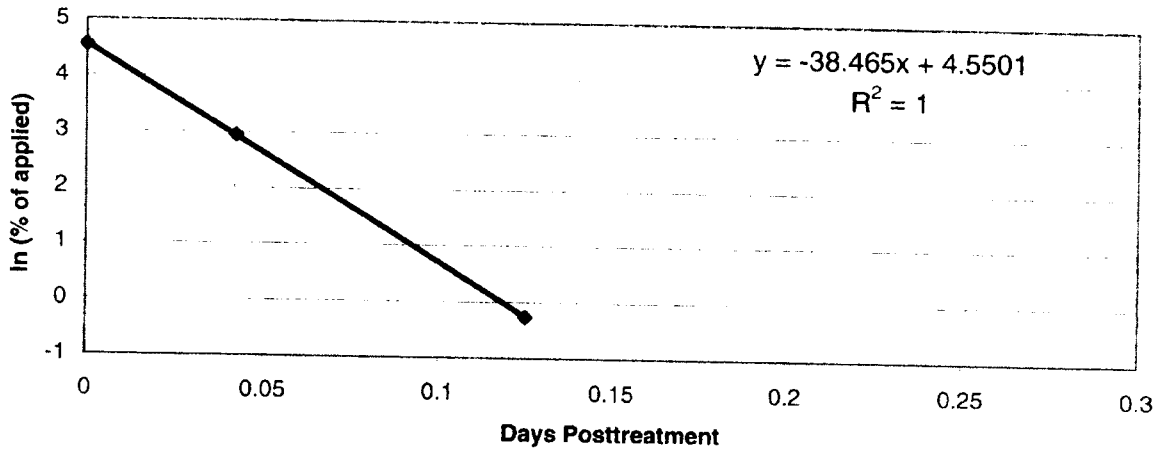
Half-life (days) **0.02**

pH 4

Days post-treatment	Orthosulfamuron	
	% of applied	ln (% of applied)
0	94.02	4.5435
0.042	19.00	2.9444
0.13	0.77	-0.2614

Data obtained from Table 2, p. 36 of the study report.

Hydrolysis of orthosulfamuron in pH 4 buffer solution at 50°C.



Chemical: Orthosulfamuron
MRID: 46219015
PC Code: 108209
Guideline: 161-1
50°C, preliminary & supplemental

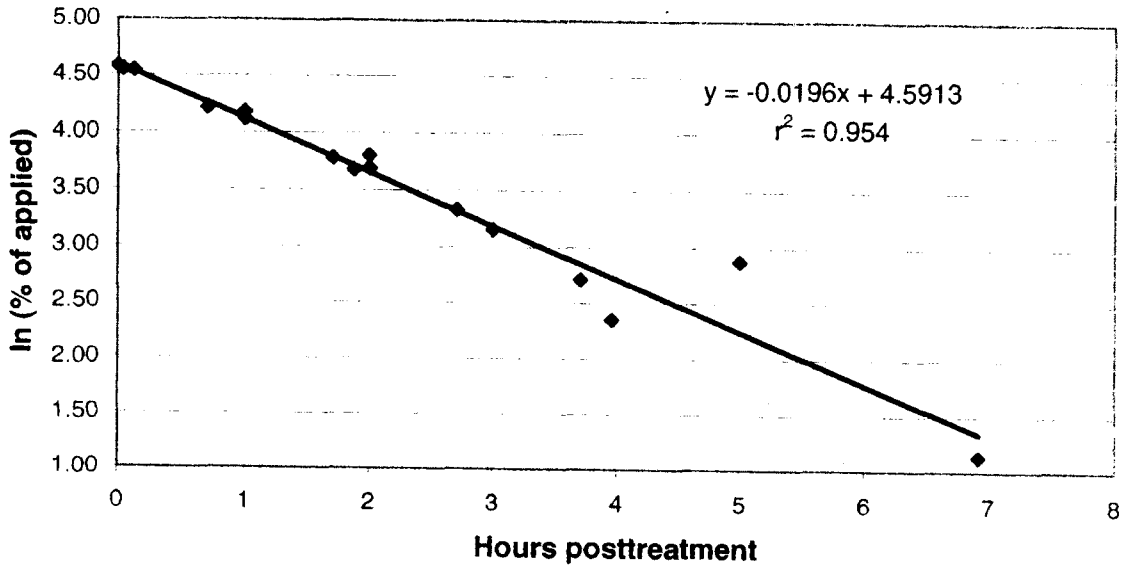
Half-life (days) **1.48**

pH 7

Days post-treatment	Orthosulfamuron % of applied	ln (% of applied)
0	97.34	4.5782
0	97.02	4.5749
0.042	94.45	4.5481
0.13	93.81	4.5413
0.71	67.74	4.2157
1	65.27	4.1785
1	61.25	4.1150
1.7	43.80	3.7796
1.9	39.47	3.6755
2	44.74	3.8009
2	40.04	3.6899
2.7	27.98	3.3315
3	23.44	3.1544
3.7	15.04	2.7107
4.0	10.53	2.3542
5	17.82	2.8803
6.9	3.12	1.1378

Data obtained from Table 3, p. 37 of the study report.

Hydrolysis of orthosulfamuron at 50°C in pH 7 buffer.



Chemical: Orthosulfamuron
MRID: 46219015
PC Code: 108209
Guideline: 161-1
50°C, preliminary & supplemental

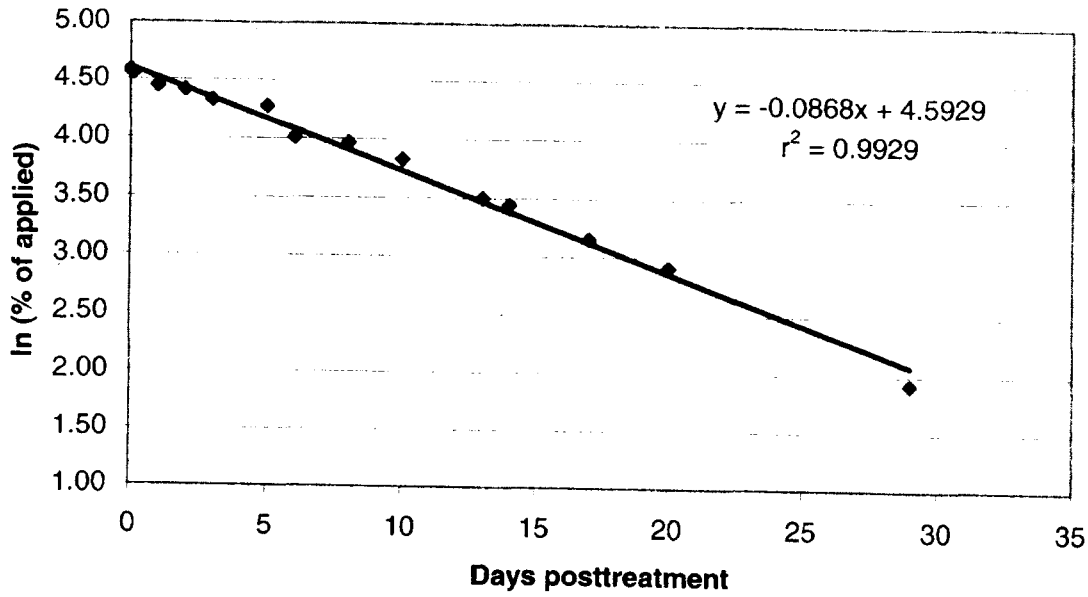
Half-life (days) **7.96**

pH 9

Days post-treatment	Orthosulfamuron	
	% of applied	ln (% of applied)
0	97.14	4.5762
0	97.01	4.5748
0.042	95.35	4.5576
0.13	94.94	4.5532
1	85.00	4.4427
2	82.28	4.4101
3	75.38	4.3225
5	71.54	4.2703
6	54.95	4.0064
8	52.68	3.9642
10	45.96	3.8278
13	33.13	3.5004
14	31.41	3.4471
17	23.39	3.1523
20	18.41	2.9129
29	6.85	1.9242

Data obtained from Table 4, p. 38 of the study report.

Hydrolysis of orthosulfamuron at 50°C in pH 9 buffer.



Attachment 3: Transformation Pathway Presented by Registrant

DER for MRID # 46219015

Page 28 is not included in this copy.

Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

✓ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

_____ Internal deliberative information.

_____ Attorney-Client work product.

_____ Claimed Confidential by submitter upon submission to the Agency.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
