Data Evaluation Report on the Hydrolysis of Orthosulfamuron

PMRA Submission Number {.....} EPA MRID Number 46578970

Data Requirement: PMRA Data Code:
EPA DP Barcode: D320283
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 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 11/21/05.

Primary Reviewer: Joan Gaidos
Cambridge Environmental
Signature:
Date: 12/1/05

Secondary Reviewer: Kathleen Ferguson
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Date: 7/19/06

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

CITATION: Faltynski, K.H. 2005. Determination of Aquatic Dissolution Rate of IR5878GR and pH 5 Hydrolysis Rate of IR5878 Standard. Unpublished study performed by EN-CAS Analytical Laboratories, Winston-Salem, NC; and sponsored and submitted by Isagro, USA, Morrisville, NC. EN-CAS Study ID #: 04-0041. Experimental phase (hydrolysis experiment) initiated and completed on January 12, 2005. Final report issued March 17, 2005. 67 pp.

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EXECUTIVE SUMMARY

The hydrolysis of unlabeled 1-(4,6-dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)phenylsulfamoyl]urea (orthosulfamuron; IR5878; purity 99.43%), at 20 mg a.i./L, was studied in an aqueous pH 5 (phthalate) buffered solution in the dark at 25°C for 24 hours. The experiment was conducted in accordance with the USEPA Subdivision N §161-1 guidelines, and in compliance with USEPA GLP standards. Vials of treated buffer solution (10 mL) were sealed and the headspace air replaced with nitrogen gas, then incubated in the dark in a water bath. Volatiles were not collected. Single vials were collected at 0, 1, 3, and 8 hours posttreatment, and duplicate vials were collected at 24 hours posttreatment. The test solutions were immediately adjusted to pH 9. Samples were frozen for *ca.* 1 day, then all samples were analyzed using HPLC. Orthosulfamuron was identified by comparison to the retention time of a reference standard. Transformation products were not addressed.

The test conditions were reportedly maintained throughout the experiment; however, no supporting data were provided.

A material balance could not be determined.

Orthosulfamuron decreased from 87% of the applied at time 0 to 51% at 8 hours posttreatment and 18% at 24 hours (study termination). Based on first-order linear regression analysis (Excel 2000), the half-life in the pH 5 buffer solution was **10.6 hours**. Transformation products were not addressed.

A transformation pathway was not proposed and could not be determined from the data provided.

In a supplementary experiment, formulated orthosulfamuron 0.5 GR (IR5878GR; 0.49% a.i. granular), at 1 g/L, was placed in pH 7 (phosphate) and pH 9 (borate) buffer solutions and shaken for 24 hours at ambient lab temperature. After 24 hours, the buffer solution contained 108-118% of the initial orthosulfamuron and the dried used pellets contained 0%.

RESULTS SYNOPSIS:

	Half-life	Transformation products
pH 5	10.6 hours	Not determined

Study Acceptability: This study is classified as **supplemental**. The study is scientifically valid. The test solution was analyzed only for orthosulfamuron, so the material balance was incomplete and transformation products were not characterized. In addition, the study was conducted only at pH 5.

Physico-chemical properties of orthosulfamuron:

Parameter	Value	Comment
Molecular weight (g/mol)	424.44 g/mol	
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 Appendix II, p. 51 of the study report.

2. Buffer Solution:

Table 1: Description of buffer solutions.

pH	Type and molarity of buffer	Composition
5	Phthalate (0.0726M)	Not reported.[1]
7	Not tested in this experiment	
9	Not tested in this experiment	

Data obtained from pp. 9-11 of the study report.
1 The study author reported that all buffers were prepared according to p. 10 of OPPTS 835.2130.

B. EXPERIMENTAL CONDITIONS

1. Preliminary Study: In order to determine sampling intervals for the definitive hydrolysis experiment, orthosulfamuron was dissolved in 0.0726M pH 5 buffer (phthalate) at 20 mg a.i./L and incubated in the dark in a water bath at 25°C for 24 hours (p. 10). Aliquots of the test solution were analyzed immediately after preparation and at 24 hours posttreatment (Table 1, p. 16). Samples were analyzed using HPLC as described for the definitive study. Orthosulfamuron was measured at 93% of the nominal applied at time 0 and 18% at 24 hours (Table 1, p. 16).

2. Experimental conditions

Table 2: Experimental parameters.

Parameters		Details
Duration of study		24 hours
Test concentrations (mg a.i./L) Nominal: Measured:		 20 17.47
No. of replications		One sample was collected at each sampling interval (duplicate samples were collected at the final sampling interval).
Preparation of test medium	Volume used/treatment	10 mL
	Method of sterilization	Not reported.
	Co-solvent	Acetonitrile, 2% (2 mL in 100 mL buffer).
Test apparatus (type/material/volume)		According to the study protocol, five vials, each containing 10 mL of treated buffer solution, were capped with septa. The air in the headspace was replaced with nitrogen gas, and the samples were incubated in the dark in a water bath at 25°C.
Details of traps for volatile, if any		Volatiles were not collected.
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?		Could not be determined.
Experimental conditions Temperature (°C): Lighting: pH ranges:		 25 Dark pH 5
Other details, if any		None.

Data obtained from pp. 8, 10-11; Table 2, p. 17; and Appendix I, p. 39 of the study report.

3. Supplementary Experiments: Formulated orthosulfamuron 0.5 GR (IR5878GR; 0.49% a.i. granular), at 1 g/L, was placed in pH 7 (phosphate) and pH 9 (borate) buffer solutions and shaken for 24 hours at ambient lab temperature (not specified; pp. 9-11). After 24 hours, the solution and pellets were separated by filtering (Whatman #2). The solution was filtered through a Teflon filter (0.45-µm) and analyzed using HPLC as described. The pellets were dried overnight (100°C). A pellet taken directly from the formulation bottle was also dried as a control. The dried pellets plus a fresh (undried) pellet were extracted by sonication with 50 mL acetonitrile:0.033M sodium bicarbonate solution (70:30, v:v), and the extracts were analyzed by HPLC.

4. Sampling:

Table 3: Sampling details.

Criteria	Details
Sampling intervals	0, 1, 3, 8, and 24 hours.
Sampling method	Based on the protocol, entire vials were collected at each sampling interval.
Sampling methods for the volatile compounds	Volatiles were not collected.
Sampling intervals/times for: pH measurement: Sterility check:	 Not reported. Not reported.
Sample storage before analysis	Samples were raised to pH 9, then stored frozen for *ca.* 1 day after collection. All samples were extracted on the same date and analyzed 1 day later.
Other observation, if any:	None.

Data obtained from pp. 10-11; Table 2, p.17; and Appendix I, p. 39 of the study report.

C. ANALYTICAL METHODS:

Extraction/clean up/concentration methods, if used: Immediately after collection, the samples (10 mL) were adjusted to pH >9 using 0.5 mL of 1.0M NaOH:0.033M $NaHCO_3$ (1:1, v:v), then frozen (Appendix I, p. 39).

Volatile residue determination: Volatile compounds were not measured.

Total ^{14}C measurement: The test material was not radiolabeled.

Derivatization method, if used: No derivatization was used.

Identification and quantification of parent compound: Orthosulfamuron was quantified by HPLC under the following conditions: Shimadzu C18 reverse-phase column (5µm, 250 x 4 mm), gradient mobile phase consisting of Solvent A: 0.004M KH_2PO_4 in H_2O, and Solvent B: acetonitrile [A:B (v:v): 1 minute 75:25; 10 minutes 20:80; 1 minute 20:80; 10 minutes 75:25], flow rate 1 mL/minute, with UV detection (265 nm; p. 11; Appendix I, pp. 39-40; Appendix II, p. 53). Orthosulfamuron was identified by comparison to the retention time of the reference standard (Rt *ca.* 11.0 minutes).

Identification and quantification of transformation products: Transformation products were not analyzed.

Detection limits (LOD, LOQ) for the parent compound: LODs and LOQs were not reported.

Detection limits (LOD, LOQ) for the transformation products: LODs and LOQs were not reported.

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS: The study author stated that there were no deviations from the protocol (p. 15). However, no data were provided to demonstrate that the pH, temperature and other experimental conditions remained stable during the study.

B. MASS BALANCE: A mass balance could not be determined.

Table 4: Hydrolysis of orthosulfamuron, expressed as percentage of the applied radioactivity, at pH 5.

Compound	Sampling times (hours)				
	0	1	3	8	24
Orthosulfamuron	87	80	71	51	18 ± 0
Transformation products	Transformation products were not addressed.				
CO_2	Not reported.				
Volatile organics	Not reported.				
Total Recovery	Not reported.				

Data obtained from Table 2, p. 17 of the study report. With the exception of 24 hours, only a single sample was collected at each sampling interval.

C. TRANSFORMATION OF PARENT COMPOUND: Orthosulfamuron decreased from 87% of the applied at time 0 to 51% at 8 hours posttreatment and 18% at 24 hours (study termination; Table 2, p. 17).

HALF-LIVES/DT_{50}/DT_{90}: Based on first-order linear regression analysis (Excel 2000), orthosulfamuron degraded with a half-life of 10.6 hours at pH 5 (DER Attachment 2; Table 2, p. 17). The observed DT_{50} was *ca.* 8 hours.

Half-lives/ DT_{50}/DT_{90}

pH	First order linear			Observed DT_{50}	DT_{90}
	Half-life	Regression equation	r^2		
5	10.6 hours	y = -0.0653x + 4.4568	0.9999	*ca.* 8 hours	ND

Half-life calculated using data obtained from Table 2, p. 17 of the study report (DER Attachment 2).

TRANSFORMATION PRODUCTS: Transformation products were not addressed.

Table 5: Chemical names and CAS numbers for the transformation products of orthosulfamuron.

Applicants Code Name	CAS Number	Chemical Name	Chemical Formula	Molecular Weight (g/mol)	Smiles String
Transformation products were not addressed.					

VOLATILIZATION: Volatilization was not measured.

TRANSFORMATION PATHWAY: A transformation pathway was not provided. A transformation pathway could not be developed because only the concentrations of orthosulfamuron were reported; transformation products were not addressed.

D. SUPPLEMENTARY EXPERIMENT-RESULTS: After 24 hours of shaking granular orthosulfamuron in pH 7 or 9 buffer solution, the buffer solution contained 108-118% of the applied orthosulfamuron and the used pellets contained 0% (p. 14; Tables 1-2, pp. 16-17). In the controls, the undissolved dried granule contained 57% of the initial concentration and the "fresh" granule contained 120%.

III. STUDY DEFICIENCIES

1. The solutions were analyzed only for orthosulfamuron. Transformation products and volatilization were not addressed, and a material balance could not be determined.

2. The study was conducted only at pH 5. Subdivision N guidelines require the test material to be analyzed in pH 5, 7 and 9 solutions. The study author reported that rapid hydrolysis was unlikely to occur under neutral or basic conditions based on the results of experiments performed at elevated temperature (p. 10). The elevated temperature experiments were not cited and were not included in this data package.

3. The sterility of the test solutions was not confirmed. However, since the duration of the study was only 24 hours and the half-life is <10 hours, it is unlikely that microbial degradation had a significant impact on the study results.

IV. REVIEWER'S COMMENTS

1. The study was poorly organized, so it was difficult to determine which statements related to the preliminary non-GLP experiments, to the dissolution experiments, and to the definitive hydrolysis study. For example, it was reported that any samples that contained solids were filtered through a Teflon membrane (0.45 µm) prior to analysis (p. 11). It seems likely that this refers to the experiments using the granular formulation rather than the definitive study using the analytical grade. However, since the water solubility of orthosulfamuron was not reported, it is not certain that all of the applied orthosulfamuron was in solution.

2. The study author indicated that the quenching and freezing of samples may have contributed to the lower recovery of material at time 0 in the definitive experiment (87% of the applied) in which the samples were frozen. In the preliminary hydrolysis experiment in which the samples were immediately injected into the HPLC system for analysis study, recovery at time

0 was 93% of the applied (p. 14).

3. The study author reported a half-life of 8.34 hours based on linear regression analysis (pp. 11, 14; Figure 15, p. 32). However, the regression equation reported by the study author is identical to that generated by the reviewer and should have resulted in the same final value. The reviewer could not determine how the study author arrived at 8.34 hours.

4. No data were provided to show that the pH, temperature, and other experimental conditions were maintained throughout the 24-hour incubation.

5. The study author identified IR5878GR as a granular herbicide for rice (Appendix I, p. 36).

V. REFERNCES

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: Structures of Parent Compound 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 Number:	213464-77-8.
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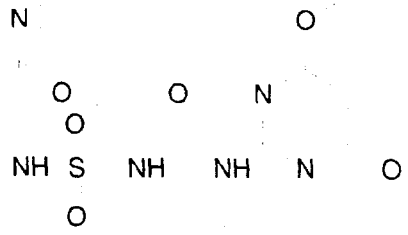

Identified Compounds

Orthosulfamuron [IR5878; S3]

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CAS Name:	2-[[[[[(4,6-Dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]amino]-N,N-dimethylbenzamide.
CAS Number:	213464-77-8.
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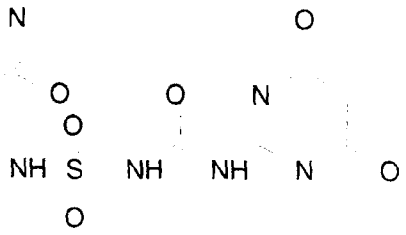


Attachment 2: Excel Spreadsheets

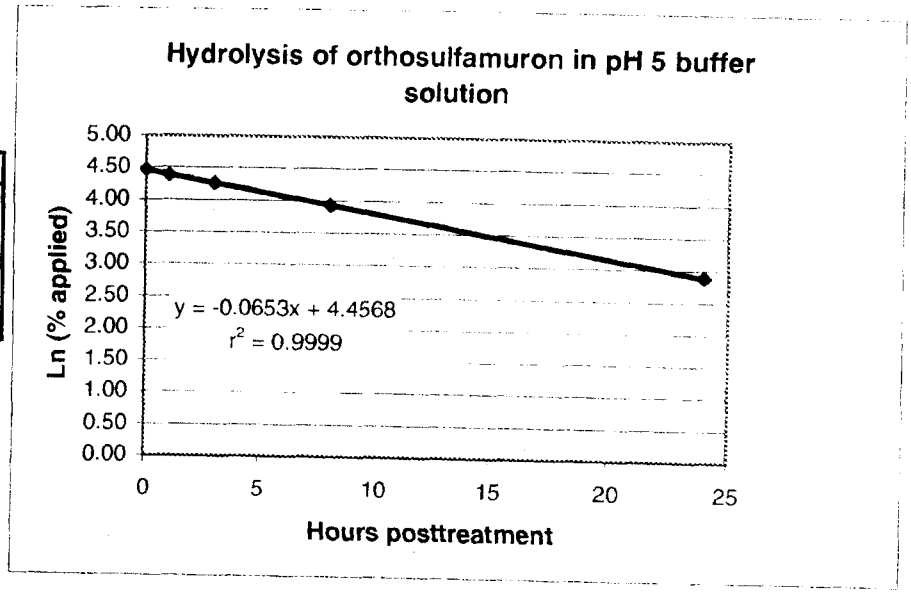
Chemical: **Orthosulfamuron**
PC Code: **108209**
MRID: **46578970**
Guideline **161-1**

Half life (hours): **10.61**

pH 5

Hours	% applied	Ln (% applied)
0	87	4.4659
1	80	4.3820
3	71	4.2627
8	51	3.9318
24	18	2.8904

Data obtained from Table 2, p. 17 of the study report.



SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.999945101
R Square	0.999890204
Adjusted R	0.999853606
Standard Ei	0.007810965
Observatior	5

ANOVA

	df	*SS*	*MS*	*F*	*Significance F*
Regression	1	1.666852144	1.666852144	27320.44336	4.88295E-07
Residual	3	0.000183034	6.10112E-05		
Total	4	1.667035178			

	Coefficients	*Standard Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*ower 95.0%*	*Jpper 95.0%*
Intercept	4.456785285	0.004505044	989.2877817	2.27772E-09	4.442448223	4.471122	4.442448	4.471122
X Variable :	-0.065308733	0.000395119	-165.2889693	4.88295E-07	-0.066566177	-0.064051	-0.066566	-0.064051

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