Data Evaluation Record on the hydrolysis of oryzalin

PMRA Submission Number {.....} EPA MRID Number 41378401

Data Requirement:	PMRA Data Code:	
	EPA DP Barcode:	378627
	OECD Data Point:	
	EPA Guideline:	835.2120

Test material:

Common name:	Oryzalin.
Chemical name:	
IUPAC name:	3,5-Dinitro-4-(dipropylamino)benzenesulfonamide. 3,5-Dinitro-N^4,N^4-dipropylsulfanilamide.
CAS name:	4-(Dipropylamino)-3,5-dinitrobenzenesulfonamide.
CAS No.:	19044-88-3.
Synonyms:	OR-1; EL-119.
Smiles string:	CCCN(CCC)c1c(cc(cc1N(=O)=O)S(N)(=O)=O)N(=O)=O (EpiSuite version 4.0).

Primary Reviewer: Kindra Bozicevich
Cambridge Environmental
Signature:
Date: 10/25/10

Secondary Reviewer: Kathleen Ferguson
Cambridge Environmental
Signature:
Date: 10/25/10

QC/QA Manager: Joan Gaidos
Cambridge Environmental
Signature:
Date: 10/25/10

Final Reviewer: Chuck Peck
EPA
Signature:
Date: 19 MAY 2011

Final Reviewer: Cheryl Sutton, Ph.D.
EPA
Signature:
Date: 5/19/11

Company Code:
Active Code:
Use Site Category:
EPA PC Code: 104201

CITATION: Saxena, A.M. 1990. Hydrolysis of oryzalin in buffered aqueous solutions. Unpublished study performed by Hazelton Laboratories America, Inc., Madison, Wisconsin; submitted and sponsored by DowElanco (now Dow AgroChemicals), Greenfield, Indiana. Laboratory Study ID: HLA 6313-100. Experimental started November 8, 1989 and terminated December 11, 1989 (p. 5). Study completion date January 29, 1990.

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EXECUTIVE SUMMARY

The hydrolysis of nonradiolabeled 3,5-dinitro-N^4,N^4-dipropylsulfanilamide (oryzalin; purity 98.3%), at 1.23 µg a.i./L, was studied in the dark in sterile aqueous buffered pH 5 (0.01M acetate), pH 7 (0.01M phosphate), and pH 9 (0.01M borate) solutions at 24-26°C for up to 33 days. The experiment was conducted in accordance with USEPA Pesticide Assessment Guidelines, Subdivision N §161-1, and in compliance with USEPA FIFRA GLP standards (40 CFR Part 160). The test system consisted of amber glass vials containing treated buffer solution (*ca*. 2 mL) that were sealed with crimp-top caps lined with Teflon-coated rubber septa. Volatiles were not addressed. The vials were maintained in the dark in a temperature-controlled room. Duplicate samples were collected from each buffer at 0, 2, 5, 12, 19, 26, and 33 days posttreatment. The buffer solutions were analyzed by HPLC with UV detection (290 nm). Oryzalin was identified by comparison to the retention time of a reference standard, and quantified by comparison to a standard curve. Degradation components were not detected.

The temperature was reportedly maintained at 24-26°C; supporting data were not provided. The pH ranges of the buffer solutions throughout the study were 5.00-5.03, 7.04-7.07, and 8.97-9.01. The sterility of the buffer solutions was not verified.

Oryzalin was stable in the pH 5 and 7 buffer solutions with individual sample concentrations ranging from 96.6% to 109.0% (mean 103.1 ± 3.5%) of the applied at pH 5 and from 99.1% to 107.1% (mean 104.7 ± 2.7%) at pH 7. HPLC chromatograms from 33 days posttreatment showed only peaks associated with the solvent front and oryzalin. As such, transformation products and volatile compounds were not evaluated.

Oryzalin was relatively stable in the pH 9 buffer, but data showed temporal variability, with individual sample concentrations ranging from 97.9% to 102.9% of the applied through 26 days posttreatment and 92.9-93.7% at 33 days (mean 0-33 days = 99.4 ± 2.9%). The HPLC chromatogram from 33 days posttreatment showed only peaks associated with the solvent front and oryzalin. As such, transformation products and volatile compounds were not evaluated.

Based on the study results, oryzalin should be considered stable to hydrolysis in sterile aqueous solutions at pH 5-9.

RESULTS SYNOPSIS:

pH	Half-life (days)	Transformation products	
		Major	Minor (identified)
5	Stable.	None.	None.
7	Stable.	None.	None.
9	Stable.[1]	None.	None.

1 Oryzalin was stable in the pH 9 buffer through 26 days posttreatment. A decrease in oryzalin concentrations at 33 days is not believed to be the result of hydrolysis.

Study Acceptability: This study is classified as **acceptable**. No significant deviations from good scientific practices were noted. Although samples were analyzed only for oryzalin and the sterility of the buffer systems was not verified, the parent compound did not hydrolyze.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with USEPA Pesticide Assessment Guidelines, Subdivision N §161-1 (p. 10).

COMPLIANCE: This study was conducted in compliance with USEPA FIFRA GLP standards (40 CFR Part 160, 1989; p. 3). Signed and dated Data Confidentiality, GLP, and Quality Assurance statements were provided (pp. 2-4). A certification of authenticity is included in the Quality Assurance statement (p. 4).

A. MATERIALS:

1. Test Materials Oryzalin (p. 10; Figure 1, p. 28).

Chemical Structure: See DER Attachment 1.
Description: Not reported.
Purity: Radiochemical purity: Not applicable.
HLA ID No. 6016-STDS-89-0019 (p. 10).
Analytical purity: 98.3%.
Specific activity: Not applicable.
Location of the radiolabel: Not applicable.

Storage conditions of test chemicals: The test substance was stored at 25°C.

Physico-chemical properties of oryzalin:

Parameter	Value	Comment
Molecular weight	Not reported.	
Chemical formula	$C_{12}H_{18}N_4O_6S$	
Water Solubility	2.6 ± 0.1 ppm	
Vapor Pressure	Not reported.	
UV Absorption	Not reported.	
pKa	Not reported.	
K_{ow}	Not reported.	
Stability of compound at room temperature, if provided	Stable for up to 36 months.	Stored in glass at 25°C.

Data obtained from p. 10 in the study report.

2. Buffer Solution: Buffer solutions were prepared with purified water as follows:

Table 1: Description of buffer solutions.

pH	Type and molarity of buffer	Composition
5	0.01M Acetate	Sodium acetate in water was adjusted to pH 5 with glacial acetic acid.
7	0.01M Phosphate	Sodium phosphate in water was adjusted to pH 7 with 1% sodium hydroxide.
9	0.01M Borate	Sodium borate in water was adjusted to pH 9 with boric acid.

Data obtained from p. 11 of the study report.

B. EXPERIMENTAL CONDITIONS

1. Preliminary Study: The HPLC analytical method was validated by comparing recoveries of oryzalin from buffered and standard solutions treated at 0.25, 1.0, and 2.0 µg/mL (p. 14). Recoveries at 0.25 µg/mL were low, and the lowest target concentration used in the definitive experiment was increased to 0.50 µg/mL (p. 16, Table XI, p. 27).

2. Experimental conditions

Table 2: Experimental parameters

Parameters		Details
Duration of study		33 days.
Test concentrations	Nominal:	Not reported.
	Measured:	1.23 µg a.i./L
No. of replications		Duplicate samples were collected from each buffer at each sampling interval.
Preparation of test medium	Volume used/treatment	The test substance in acetonitrile (60 µL) was transferred to mixing flasks and the acetonitrile was evaporated. 25 mL of buffer solution was added to the flask, the flask was vortexed (1 minute), then the solution was brought to a 50-mL volume and again vortexed (0.5 minutes). Aliquots of the treated buffer solutions were transferred to individual test vials.
	Method of sterilization	Buffer solutions were sterilized by vacuum filtration (0.45 µm). All equipment used was sterilized via autoclaving at 270°C for 15 minutes.
	Co-solvent	None. The acetonitrile solvent was evaporated before the buffer solution was transferred to the mixing flask.
Test apparatus (type/material/volume)		The test system consisted of amber glass vials that were filled to capacity (no headspace) with aliquots (*ca*. 2 mL) of the treated buffer solutions. The vials were sealed with crimp-top caps lined with Teflon-coated rubber septa, and stored in a dark, temperature-controlled room.
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.

Parameters		Details
Experimental conditions	Temperature (°C):	24-26°C.
	Lighting:	Dark.
	pH ranges:	pH 5: 5.00-5.03. pH 7: 7.04-7.07. pH 9: 8.97-9.01.
Other details, if any		None.

Data were obtained from pp. 11-12 and Table 1, p. 17, of the study report.

3. Supplementary Experiments: Because the measured concentration of oryzalin in the pH 5 samples was consistently low when compared with the nominal application rate, additional pH 5 buffer solutions were prepared as described (p. 13). After aliquots of the treated solution were transferred to individual vials to mimic the definitive experiment, the buffer solution remaining in the mixing flask was vortexed (duration not specified; p. 16).

4. Sampling:

Table 3: Sampling details.

Criteria		Details
Sampling intervals		0[1], 2, 5, 12, 19, 26, and 33 days.
Sampling method		Duplicate vials of each buffer solution were collected at each sampling interval.
Method of collection of CO_2 and organic volatile compounds		Volatiles were not collected.
Sampling intervals/times for:	pH measurement:	0, 19, and 33 days.
	Sterility check:	Not determined.
Sample storage before analysis		All samples analyzed on the day of sampling. Reserve samples were stored at *ca*. 25°C.
Other observation, if any:		None.

Data were obtained from pp. 12-13 of the study report.
1 Time zero samples were collected *ca.* 1 hour after fortification.

C. ANALYTICAL METHODS

Extraction/clean up/concentration methods: The samples were analyzed as collected, without manipulation or modification.

Volatile residue determination: Volatiles were not trapped.

Total ^{14}C measurement: The test material was not radiolabeled. Quantitative data were provided only for oryzalin (Tables VIII-X, pp. 24-26).

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

Identification and quantification of parent compound: Aliquots (100 µL) of the buffer solutions were analyzed for oryzalin using HPLC under the following conditions: Hypersil ODS C-18 column

(100 x 4.6 mm, 3 μm), isocratic mobile phase of 0.01M ammonium acetate:acetonitrile (45:55, v:v), flow rate 1.0 mL/minute, with UV (290 nm) detection (pp. 11, 13). A standard curve was generated on each day of sample analysis to determine the concentration of oryzalin in the samples (Appendix B, Figures B-1-B-7, pp. 46-52).

Identification and quantification of transformation products: Transformation products were not quantified or identified.

Detection limits (LOD, LOQ) for the parent compound: Limits of Detection (LOD) and Limits of Quantification (LOQ) were not reported.

Detection limits (LOD, LOQ) for the transformation products: Samples were not analyzed for transformation products.

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS: The temperature was reportedly maintained at 24-26°C; supporting data were not provided (p. 12). The pH ranges of the buffer solutions were 5.00-5.03, 7.04-7.07, and 8.97-9.01 throughout the study (Table 1, p. 17). No data confirming the sterility of the samples was provided.

B. MASS BALANCE: Samples were analyzed only for oryzalin. With the exception of the 33-day pH 9 samples, oryzalin concentrations were ≥96.6% of the applied in all treatments at all sampling intervals (Tables VIII-X, pp. 24-26).

Table 4: Hydrolysis of oryzalin, expressed as percentage of the applied (mean ± s.d., n = 2), at pH 5, 7 and 9.[1]

Compound	Sampling times (days)						
	0	**2**	**5**	**12**	**19**	**26**	**33**
pH 5							
Oryzalin	100.0 ± 1.6	100.0 ± 3.1	104.0 ± 0.8	104.0 ± 0.8	106.2 ± 4.0	106.2 ± 0.8	101.1 ± 6.4
pH 7							
Oryzalin	100.0 ± 1.3	105.4 ± 1.3	106.7 ± 0.6	102.7 ± 1.3	106.7 ± 0.6	106.7 ± 0.6	104.5 ± 3.7
pH 9							
Oryzalin	100.0 ± 0.6	100.9 ± 0.6	99.2 ± 0.6	98.8 ± 1.2	102.5 ± 0.6	101.3 ± 0.0	93.3 ± 0.6
All buffers							
Transformation products	Transformation products were not quantified.						
CO_2	Volatiles were not collected.						
Volatile organics	Volatiles were not collected.						
Total Recovery	Not determined.						

Means and standard deviations calculated by the reviewer using data obtained from Tables VIII-X, pp. 24-26 of the study report (DER Attachment 2).

1 Measured concentrations of oryzalin in individual samples were 0.89-0.95 µg/mL for pH 5, 1.12-1.20 µg/mL for pH 7, and 1.12-1.23 µg/mL for pH 9.

C. TRANSFORMATION OF PARENT COMPOUND: Oryzalin was stable in the pH 5 and 7 buffer solutions, with individual sample concentrations ranging from 96.6% to 109.0% (mean 103.1 ± 3.5%) of the applied at pH 5 and from 99.1% to 107.1% (mean 104.7 ± 2.7%) at pH 7 (Table VIII-IX, pp. 24-25; DER Attachment 2).

Oryzalin was relatively stable in the pH 9 buffer, but data showed temporal variability with individual sample concentrations ranging from 97.9% to 102.9% of the applied through 26 days posttreatment with no pattern of decline (Table X, p. 26). Concentrations in replicate samples were 92.9% and 93.7% of the applied at 33 days posttreatment. The overall mean concentration of oryzalin in the pH 9 buffer (0-33 days) was 99.4 ± 2.9% (DER Attachment 2).

HALF-LIVES/DT50/DT90: The study author concluded that oryzalin was stable in pH 5, 7, and 9 buffer solutions. It should be noted, however, that the data showed temporal variability.

Half-lives/DT50/DT90

pH	First order linear			Observed DT50 (days)	Observed DT90 (days)
	Half-life (days)	Regression equation	r^2		
5	Stable.			>33	>33
7	Stable.			>33	>33
9	Stable.			>33	>33

TRANSFORMATION PRODUCTS: Representative HPLC chromatograms from time 0 and 33 days posttreatment for each buffer solution showed no other peaks other than oryzalin, with the exception of a solvent peak near the void volume (p. 15; Figures 2-4, pp. 29-31).

VOLATILIZATION: Volatiles were not collected.

TRANSFORMATION PATHWAY: Based on the study results, oryzalin is stable to hydrolysis in sterilized aqueous buffered solutions at pH 5-9.

D. SUPPLEMENTARY EXPERIMENT-RESULTS: The concentration of oryzalin in the pH 5 buffer solution that was vortexed one additional time after aliquots were removed was significantly higher than the concentration of oryzalin in the aliquots that were removed (p. 16). The study author concluded that the oryzalin was not completely in solution when the sample aliquots were removed, probably a result of incomplete desorption from the surface of the mixing flask) following the evaporation of the acetonitrile from the treatment solution and addition of buffer.

III. STUDY DEFICIENCIES

No significant deficiencies were noted.

IV. REVIEWER'S COMMENTS

1. Physical and chemical properties of oryzalin, other than solubility, were not reported.

2. The measured mean, minimum and maximum sample incubation temperatures were not reported, although the study author stated that the temperature of the incubation room was continually monitored and recorded (p. 12).

3. An HPLC chromatogram of the test compound was not provided to confirm its purity.

V. REFERENCES

1. U.S. Environmental Protection Agency. 2008. Fate, Transport and Transformation Test Guidelines, OPPTS 835.2120, Hydrolysis. Office of Prevention, Pesticides and Toxic Substances, Washington, DC. EPA 712-C-08-012.

2. 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.

Attachment 1: Structure of Parent Compound

Oryzalin [OR-1; EL-119]

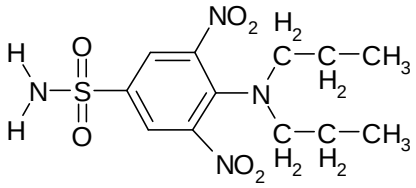
IUPAC Name: 3,5-Dinitro-4-(dipropylamino)benzenesulfonamide.
3,5-Dinitro-N^4,N^4-dipropylsulfanilamide.

CAS Name: 4-(Dipropylamino)-3,5-dinitrobenzenesulfonamide.

CAS Number: 19044-88-3.

SMILES String: CCCN(CCC)c1c(cc(cc1N(=O)=O)S(N)(=O)=O)N(=O)=O (EpiSuite version 4.0).

Empirical formula: $C_{12}H_{18}N_4O_6S$ **Molecular formula:** $C_{12}H_{18}N_4O_6S$



*** structure complexity/form was sacrificed to obtain SMILES string**