Data Evaluation Report on the Acute Dietary Toxicity of IR5878 (Orthosulfamuron) to Bobwhite quail (*Colinus virginianus*)

EPA MRID Number 46219041

Data Requirement:	PMRA DATA CODE	
	EPA DP Barcode	D304186
	OECD Data Point	
	EPA MRID	46219041
	EPA Guideline	§71-2a

Test material:		IR5878
Purity:		97.99 ± 0.39%
Common name:		Orthosulfamuron
Chemical name:	IUPAC:	Not reported
	CAS name:	Not reported
	CAS No.:	Not reported
	Synonyms:	Not reported

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Signature:
Date: 12/22/04

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Date: 7/27/06

Reference/Submission No.:

Company Code:
Active Code:
EPA PC Code: 108209

Date Evaluation Completed:

CITATION: Rodgers, M. H. and Dias, N.A. 2001. IR5878: Dietary Toxicity (LC_{50}) to the Bobwhite Quail. Unpublished study performed by Huntingdon Life Sciences, Ltd., Huntingdon, Cambridgeshire, England. Study No. IGA 002/012368. Study sponsored by ISAGRO SpA, Milano, Italy. Study initiated November 6, 2000, completed May 17, 2001.

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EXECUTIVE SUMMARY:

The acute dietary toxicity of IR5878 (Orthosulfamuron) to 14-day-old Bobwhite quail (*Colinus virginianus*) was assessed over 8 days. IR5878 (Orthosulfamuron) was administered to the birds in the diet at nominal concentrations of 0 (control), 156, 313, 625, 1250, 2500, and 5000 ppm. Mean-measured concentrations were <7.5 (LOD, control), 153, 308, 603, 1210, 2450, and 4980 ppm a.i., respectively. Mean-measured values were corrected for procedural recoveries, and represented 96-100% of nominal concentrations.

No mortality was observed during the study. The subsequent 8-day acute dietary LC_{50} was >4980 ppm a.i. (nominal 5000 ppm a.i.), the highest level tested. The toxicity of IR5878 (Orthosulfamuron) was categorized as practically non-toxic to Bobwhite quail on an acute dietary basis. No clinical signs of toxicity or treatment-related effects on body weight or food consumption were observed. Consequently, the NOEC was the highest treatment level tested (4980 ppm a.i.).

This toxicity study is scientifically sound, fulfills the guideline requirements for an avian dietary study using the Bobwhite quail (§71-2a), and is classified as ACCEPTABLE.

Results Synopsis

Test Organism Age: 14-days old
Test Organism Size: 25.6-26.9 g (group mean body weights at test initiation)

LC_{50}: >4980 ppm a.i.
NOEC: 4980 ppm a.i.
LOEC: >4980 ppm a.i.
Endpoint(s) Affected: None

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The protocol followed procedures of the U.S. EPA Subdivision E Guideline, 71-2 (1982). The following deviations from §71-2 were noted:

Some methodological details were not included in the report, including: temperature in the brooding compartment and lighting intensity.

These deviations were considered minor and did not affect the validity or acceptability of this study.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. This study was conducted in accordance with GLP standards set forth by the UK (1999), EC Commission (1999) and OECD (1997).

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A. MATERIALS:

1. Test Material IR5878 (Orthosulfamuron)

Description: Powder

Lot No./Batch No.: FCF/T/172-00 (ex 20525/03/8)

Purity: 97.99 ± 0.39%

Stability of Compound Under Test Conditions: The stability of the test material in the test feed was verified at nominal concentrations of 156 and 5000 ppm. The results indicated treated diets could be stored for 4 days at ambient temperatures following 4 days of freezer storage (p. 29, IR5878 Formulation Chemistry). In this study, the diets were prepared 4 days prior to testing. The test diets for the definitive test were prepared on November 2, 2000 and had mean-measured concentrations of <7.5 (LOD, control), 153, 308, 603, 1210, 2450, and 4980 ppm a.i. (Table 1, p. 31), respectively. The above mean-measured recoveries represented 96-100% of the nominal treatment concentrations.

Storage conditions of test chemicals: Room temperature in the dark.

2. Test organism:

Species: Bobwhite quail (*Colinus virginianus*)

Age at study initiation: 14 days

Weight at study initiation: Group means of 25.6-26.9 g (individual weights not provided)

Source: Monkfield Nutrition, Church Farm Barn, Hertfordshire, England

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding Study: None reported.

b. Definitive Study: See Table 1

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Table 1: Experimental Parameters

Parameter	Details	Remarks
Acclimation period: Conditions (same as test or not): Feeding: Health (any mortality observed):	3 days Same as test Water and Standard HRC chick diet were provided, *ad libitum*. All birds were in apparent good health at test initiation.	Diet composition was provided on p. 12. No antibiotic was used in the diet (p. 11).
Pen size and construction materials	Pens (80 x 60 x 50 cm) were constructed of print-board with a wire mesh lid.	-
Test duration	5 days with treated feed, and 3 days with "clean" feed.	-
Test concentrations nominal: measured:	0 (control), 156, 313, 625, 1250, 2500; and 5000 ppm <7.5 (LOD, control), 153, 308, 603, 1210, 2450, and 4980 ppm a.i.	Mean-measured concentrations were provided in Table 1 of Formulation Chemistry (p. 31). All measured concentrations were corrected for the mean procedural recovery (p. 32). The reviewer assumed that measured units, which were identified in the report as ppm, were equivalent to ppm a.i. IR5878 (Orthosulfamuron).
Solvent/vehicle, if used	None	-
Diet preparation and feeding	The premix was prepared by adding the test substance to the untreated diet and mixing for 5 minutes. Then, the premix was diluted and blended for an additional 5 minutes. Enough was made to last the 5-day treatment period, and the diet was presented at test initiation.	-
Feed withholding period	None	-
Indicate whether stability and homogeneity of test material in diet determined (Yes/No)	Yes	-

Parameter	Details	Remarks
Number of birds per replicate/group	Negative control: 10 Treatments: 10	-
Number of replicates/group	Negative control: 2 Treatments: 1	-
Test conditions temperature: relative humidity(%): photo-period:	 Brooder: Not reported Room: 22-24°C (means) 40% 14 hours light/10 hours dark	-
Reference chemical, if used	None used	-

2. Observations: See Table 2

Table 2: Observations

Criteria	Details
Parameters measured (mortality/body weight/ mean feed consumption/ others)	Mortality Clinical signs of toxicity Group mean feed consumption Group mean body weight
Indicate the stability and homogeneity of test chemical in the diet	Stability: The 4-day ambient stability and 4-day frozen stability of the test material in avian diet was assessed prior to test initiation at the nominal 156 (low) and 5000 ppm (high) levels (p. 30 in Formulation Chemistry). The recoveries were within 4.5% of the nominal values (p. 29). Homogeneity: Homogeneity was assessed prior to study initiation in treated feed prepared at the 156 and 5000 ppm levels (p. 29). The Coefficients of Variation were <2%.
Indicate if the test material was regurgitated	Regurgitation was not reported.
Treatments on which necropsies were performed	Gross necropsies conducted on all high-dose birds and one control replicate birds at study termination.
Observation intervals	Mortality and signs of toxicity were observed daily. Body weights were determined on Days 0 (prior to diet introduction), 5, and 8. Feed consumption was determined on Days 1-5 and 6-8.

Criteria	Details
Were raw data included?	No

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortality occurred in any control or treatment group during the 8-day study (p. 15). The 8-day LC_{50} was >4980 ppm a.i.

B. SUB-LETHAL TOXICITY ENDPOINTS:

No clinical signs of toxicity were observed in the control or any test group during the study. The study noted that the excreta of the birds appeared normal for all test groups. Mean body weight changes and food consumption per test group were reported (Table 3). No treatment related effects on body weight changes or food consumption were observed. Statistical analyses were not conducted on sub-lethal endpoints. Based on the assumption that there were no significant differences in body weight and food consumption of control groups and test groups, the NOEC was 4980 ppm a.i. and the LOEC was >4980 ppm a.i.

Table 3: Sub-lethal effects of IR5878 (Orthosulfamuron) on *Colinus virginianus*.

Treatment, ppm Mean-measured (and nominal)	Mean body weight change (g)		Food consumption (g/bird/day)	
	Day		Day	
	0-5	5-8	1-5	6-8
Control	11.8	8.5	5.5	8.0
Control	11.0	6.9	5.4	5.8
153 (156)	11.8	8.1	5.7	6.7
308 (313)	11.4	7.8	5.9	6.4
603 (625)	11.1	7.8	5.5	6.5
1210 (1250)	11.1	6.4	4.9	5.2
2450 (2500)	12.8	7.6	5.2	6.2
4980 (5000)	11.8	7.1	5.9	7.4
NOEC	4980 ppm a.i.		4980 ppm a.i.	

C. REPORTED STATISTICS:

The reported results were based on nominal concentrations. Since there were no mortalities observed in this study, the LC_{50} value was assumed to be greater than the highest concentration tested (5000 ppm). Neither body weight nor feed consumption data were statistically compared. Based on the assumption that there were no significant differences in body weight and food consumption of control groups and test groups, the NOEC was reported to be the highest concentration tested.

D. VERIFICATION OF STATISTICAL RESULTS:

The study report identified the units of measured concentrations as "ppm." The reviewer assumed that this was equivalent to ppm a.i. IR5878 (Orthosulfamuron). The reviewer converted the nominal treatment concentrations and resulting nominal toxicity values to measured values using the reported mean-measured treatment concentrations. Since there were no mortalities observed in this study, the LC_{50} value was assumed to be greater than the highest concentration tested (4980 ppm a.i.).

Neither body weight nor feed consumption data were statistically compared in the report. Body weight significance could not be statistically compared by the reviewer since body weight data for individual birds were not provided. A qualitative review of the data did not reveal any obvious concerns of significant differences in changes in mean body weights or food consumption (Table 3). Based on the assumption that there were no significant differences in body weight and food consumption of control groups and test groups, the NOEC was assumed to be the highest concentration tested.

E. STUDY DEFICIENCIES:

There were no significant deviations from U.S. EPA guideline §71-2 that affected the validity or acceptability of this study.

F. REVIEWER'S COMMENTS:

The reviewer's conclusions were consistent with those of the study authors, except that the study authors based toxicity values on the nominal concentrations, while the reviewer based them on the measured concentrations.

The toxicity category, "practically non-toxic" is defined by a LC_{50} >5000 ppm. Since the LC_{50} for this test was defined as >4980 mg a.i./kg-bw, there is some uncertainty regarding the suitability of this classification. However, since no sublethal effects were observed at 1960 mg a.i./kg-bw, it seems reasonable that an increase in the concentration of the test substance by <1% is unlikely to result in effects resulting in mortality of 50% of tested birds.

OECD requires water solubility, stability in water and light, pK_a, P_{ow}, and vapor pressure of the test compound. These OECD requirements were not reported.

G. CONCLUSIONS:

This toxicity study is scientifically sound, fulfills the guideline requirements for an avian dietary LC_{50} study using the Bobwhite quail (§71-2a), and is classified as ACCEPTABLE. No treatment-related effects on mortality were observed. No clinical signs of toxicity were observed. Qualitative observations of mean data for treatment groups indicated that body weight and food consumption were not affected during the study. The 8-day acute dietary LC_{50} was >4980 ppm a.i., the highest level tested. The NOEC was the highest treatment level tested. IR5878 (Orthosulfamuron) was classified as practically non-toxic to Bobwhite quail on an acute dietary

basis.

III. REFERENCES:

No references were cited.