

Data Evaluation Report on the Acute Oral Toxicity of IR5878 (Orthosulfamuron) on Mallard Duck (*Anas platyrhynchos*)

EPA MRID Number 46260107

Data Requirement:	PMRA DATA CODE	
	EPA DP Barcode	D304186
	OECD Data Point	
	EPA MRID	46260107
	EPA Guideline	§71-1
	OPPTS Guideline	850.2100

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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Staff Scientist, Dynamac Corporation

Signature:
Date: 12/23/2004

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Reference/Submission No.:

Company Code:
Active Code:
EPA PC Code: 108209

Date Evaluation Completed:

CITATION: Dias, N.A. 2001. IR5878: Acute oral toxicity (LD₅₀) to the Mallard duck. Unpublished study performed by Huntingdon Life Sciences, Ltd., Huntingdon, Cambridgeshire, England. Study No. IGA 003/012865. Study sponsored by ISAGRO SpA, Centro Uffici San Siro - Fabbricato D, Milano, Italy. Study initiated March 14, 2001, completed March 28, 2001.

EXECUTIVE SUMMARY:

The acute oral toxicity of IR5878 (Orthosulfamuron) to adult Mallard ducks (*Anas platyrhynchos*) was assessed over 14 days. IR5878 (Orthosulfamuron) was suspended in corn oil, and administered to the birds by oral



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gavage at nominal concentrations of 0 (vehicle control), 500, 1000, and 2000 mg/kg bw (dose levels not corrected for purity). Mean measured doses were <0.15 (LOD, control), 505, 1005 and 1960 mg a.i./kg-bw.

No mortality was observed in any of the three treatment groups; however, one control mortality occurred on day 5. The acute LD₅₀ was >1960 mg a.i./kg-bw, the highest level tested, which categorizes Orthosulfamuron as practically non-toxic to Mallard duck on an acute oral basis. No clinical signs of toxicity were observed during the study, and no treatment-related effects were observed on feed consumption, body weight change, or upon gross necropsy of the control and high-dose birds at study termination. As a result, the NOEL was 1960 mg a.i./kg-bw.

This toxicity study is scientifically sound and fulfills the guideline requirements for an acute toxicity study using the Mallard duck (§71-1). This study is classified as ACCEPTABLE.

Results Synopsis

Test Organism Age: Adult birds (age not specified)

Test Organism Size: 952-1235 g (weight range for all individual birds 2 weeks prior to dosing)

LD₅₀: >1960 mg a.i./kg-bw

NOEL: 1960 mg a.i./kg-bw

LOEL: >1960 mg a.i./kg-bw

Endpoint(s) Affected: none

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The protocol followed procedures of the U.S. EPA Pesticide Assessment Guidelines, FIFRA Subdivision E, Subsection 71-1 (1982). The following deviation from §71-1 was noted:

1. Several birds were housed individually during the study due to observations of aggressive behavior. Consumption of food was measured individually for animals which were separated.
2. The ages of the birds at test initiation was not reported

The above deviations did not affect the scientific validity or acceptability of this study.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and No 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).

A. MATERIALS:

1. Test Material IR5878 (Orthosulfamuron)

Description: Powder

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

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Purity: 97.99 ± 0.39%

Stability of Compound Under Test Conditions: N/A

Storage conditions of test chemicals: Room temperature

2. Test organism:

Species: Mallard duck (*A. platyrhynchos*)

Age at study initiation: Adult birds, age not specified

Weight at study initiation: 952-1235 g (weight range for all individual birds 2 weeks prior to dosing)

Source: In-house Huntingdon Life Sciences stock.

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding Study: An initial range-finding study was conducted with IR5878 (Orthosulfamuron) at a nominal concentration of 2000 mg/kg-bw (limit dose) using two adult Mallard ducks (one per sex). No mortality or other treatment-related effects were observed.

b. Definitive Study: See Table 1.

Table 1. Experimental Parameters.

Parameter	Details	Remarks
Acclimation period:	15 days	Diet composition is provided on p. 13. No antibiotic was used in the diet (p. 13).
Conditions (same as test or not):	Same as test	
Feeding:	Water and Standard HRC pelleted layer diet were provided, <i>ad libitum</i> .	
Health (any mortality observed):	The pre-test health of the birds (including mortality) during acclimation was not reported.	

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Parameter	Details	Remarks
Pen size and construction materials	Pens (1.84 x 1.20 m) were constructed of galvanized steel with a wire mesh floor.	According to the guideline, pens must conform to good husbandry practices and should not create crowding stress.
Test duration	14 Days	-
Dose preparation	The test substance was administered as a suspension in corn oil.	-
Mode of dose administration	Oral gavage	-
Dose levels nominal: measured:	0 (vehicle control), 500, 1000, and 2000 mg/kg-bw <0.03 (<LOD, vehicle control), 101, 201, and 392 mg a.i./mL representing a procedural recovery range of 99.1-100.5%.	The dosages were not adjusted for the purity of the test substance (p. 14). Results of test formulation analysis were presented in Table 2, p. 33. Since the amount of each dose was 5 mL/kg-bw, the dose levels for the birds were <0.15, 505, 1005 and 1960 mg a.i./kg-bw (reviewer adjusted).
Solvent/vehicle amount/bw:	Corn oil 5 mL/kg-bw	The stock solutions were administered at a constant dosing volume of 5 mL/kg-bw (p. 14).
Number of birds per groups/treatment	Control: 10 Treatments: 10/level	5 males and 5 females per treatment group. Males and females were kept in separate cages per test group.
No. of feed withholding days before dosing	Overnight (approximately 19 hours)	-
Test conditions Temperature: Relative humidity: Photo-period:	Minimum: 16°C (mean) Maximum: 18°C (mean) 55% 10-hours light/14-hours dark.	-
Reference chemical, if used	None used	-

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2. Observations: See Table 2.

Table 2: Observations.

Parameter	Details
Parameters measured	Mortality Clinical signs of toxicity Individual change in body weight Average feed consumption Necropsy
Indicate if the test material was regurgitated	None reported
Groups on which necropsies were performed	Gross necropsies conducted on all surviving control and high-dose birds at study termination.
Observation intervals	Mortality and signs of toxicity were observed daily. Body weights were determined on Days -15, -7, 0 (prior to dosing), 7, and 14. Feed consumption was determined weekly.
Were raw data included?	Yes, data for individual bodyweights were provided for days 0, 7 and 14. Data were also provided for weights taken before the test was initiated.

II. RESULTS AND DISCUSSION:

A. MORTALITY:

No mortality was observed in any of the three treatment groups. One control mortality occurred on day 5. The 14-day LD₅₀ was >2000 mg/kg-bw (nominal), the highest concentration tested. The reviewer-calculated 14-day LD₅₀ value was > 1960 mg a.i./kg-bw.

B. SUB-LETHAL TOXICITY ENDPOINTS:

No clinical signs of toxicity were observed in the control or any test group during the study. Mean body weight changes and food consumption for males and females, per test group were reported (Tables 3 and 4). No gross abnormalities were detected upon necropsy of the control and high-dose birds at study termination. 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 1960 mg a.i./kg-bw (reported as 2000 mg/kg-bw) and the LOEC was >1960 mg a.i./kg-bw.

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Table 3: Mean body weight changes of male and female mallard ducks during testing.

Treatment Dose, mg a.i./kg-bw Measured (Nominal, mg/kg-bw)	Males		Females	
	Days 0-7	Days 7-14	Day 0-7	Day 7-14
Vehicle control	+3	+5	+48	+20
505 (500)	+39	+2	+56	+12
1005 (1000)	+85	+25	+43	+8
1960 (2000)	+42	+16	+54	-7
NOEL	1960 mg a.i./kg-bw		1960 mg a.i./kg-bw	
LOEC	>1960 mg a.i./kg-bw		>1960 mg a.i./kg-bw	

Table 4: Mean daily feed consumption (g/bird/day) of male and female mallard ducks during testing.

Treatment Dose, mg a.i./kg-bw Measured (Nominal, mg/kg-bw)	Males		Females	
	Days 1-7	Days 8-14	Days 1-7	Days 8-14
Vehicle control	77	74	121	133
505 (500)	99	97	134	136
1005 (1000)	123	115	82	80
1960 (2000)	103	101	112	128
NOEL	>1960 mg a.i./kg-bw		1960 mg a.i./kg-bw	
EC ₅₀	>1960 mg a.i./kg-bw		>1960 mg a.i./kg-bw	

C. REPORTED STATISTICS:

The reported results were based on nominal concentrations, which were uncorrected for test substance purity. Since there were no mortalities observed in the treatment groups of this study, the LD₅₀ value was assumed to be greater than the highest concentration tested. 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 nominal concentration tested (2000 mg/kg-bw).

D. VERIFICATION OF STATISTICAL RESULTS:

The study report identified the units of measured concentrations as "mg/mL." The reviewer assumed that this was equivalent to mg a.i./mL IR5878 (Orthosulfamuron). The reviewer converted the nominal treatment concentrations and resulting nominal toxicity values to measured values using the reported measured

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concentrations, multiplied by the volume of test substance administered per kg-bw to achieve values in mg a.i./kg-bw. Since there were no mortalities observed in the treatment groups of this study, the LD₅₀ value was assumed to be greater than the highest concentration tested (1960 mg a.i./kg-bw.).

Neither body weight nor feed consumption data were statistically compared in the report. A qualitative review of the data did not reveal any obvious concerns of significant differences in changes in mean body weights or food consumption (Tables 3 and 4). 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 §71-1 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 for the basis of study authors toxicity values on nominal concentrations, while the reviewer based them on the measured concentrations.

The toxicity category, "practically non-toxic" is defined by a LD₅₀ >2000 mg/kg-bw. Since the LD₅₀ for this test was defined as >1960 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 2% is unlikely to result in effects resulting in mortality of 50% of tested birds.

In a previous study (IGA 004/012894), the homogeneity and stability of dose formulations was verified at nominal concentrations of 5 and 400 mg/ml. The results indicated dose formulations could be stored at ambient temperature for 4 hours and under refrigeration for 1 day (p. 25, IR5878 Formulation Chemistry).

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 and fulfills the guideline requirements for an acute toxicity study using the mallard duck (§71-1), and is classified 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 14-day acute oral LD₅₀ was >1960 mg a.i./kg-bw, the highest level tested. The NOEC was the highest treatment level tested. IR5878 (Orthosulfamuron) was classified as practically non-toxic to the mallard duck.

III. REFERENCES:

A reference list was not provided.