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

EPA MRID Number 46219040

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|---|---|---|
| **Data Requirement:** | PMRA DATA CODE | |
| | EPA DP Barcode | D304186 |
| | OECD Data Point | |
| | EPA MRID | 46219040 |
| | EPA Guideline | §71-2b |

| | | |
|---|---|---|
| **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:** 6/30/06

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Biologist, OPP/EFED/ERB-IV

**Signature:**
**Date:** 7/27/06

**Reference/Submission No.:**

**Company Code:**
**Active Code:**
**EPA PC Code:** 108209

**Date Evaluation Completed:**

**CITATION:** Dias, N.A. 2001. IR5878: Dietary Toxicity ($LC_{50}$) to the Mallard Duck. Unpublished study performed by Huntingdon Life Sciences, Ltd., Huntingdon, Cambridgeshire, England. Study No. IGA 005/012373. Study sponsored by ISAGRO SpA, Milano, Italy. Study initiated February 2, 2001, completed May 16, 2001.

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## EXECUTIVE SUMMARY:


The acute dietary toxicity of IR5878 (Orthosulfamuron) to 9-day-old Mallard duck (*Anas platyrhynchos*) 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), 161, 310, 603, 1210, 2440, and 4790 ppm a.i., respectively. Mean-measured values were corrected for procedural recoveries, and represented 96-103% of nominal concentrations.

No mortality was observed during the study. The subsequent 8-day acute dietary $LC_{50}$ was >4790 ppm a.i. (nominal 5000 ppm a.i.), the highest level tested. The toxicity of IR5878 (Orthosulfamuron) was categorized as slightly toxic ($LC_{50}$ is 1001-5000 ppm) to Mallard duck 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 (4790 ppm a.i.).

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


**Results Synopsis**

Test Organism Age: 9 days
Test Organism Size: 120-127 g (group mean body weights at test initiation)

**$LC_{50}$: >4790 ppm a.i.**
**NOEC: 4790 ppm a.i.**
**LOEC: >4790 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:

1. The following were not included in the report: temperature in the brooding compartment and lighting intensity.

2. Stability and homogeneity of the test material were not determined concurrently in treated feed prepared for this study. Stability and homogeneity were determined in the same feed for a previous study (IGA 002/012368, MRID 46219041).

The above 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).

## 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:** In a previous study (IGA 002/012368, MRID 46219041), the stability of the test material in the test diet was verified at nominal concentrations of 156 and 5000 ppm (p. 22, IR5878 Formulation Chemistry). The results indicated diets could be stored for 4 days at ambient temperature following 4 days of freezer storage. In this study, the diets were prepared 3 days prior to testing. The test diet for the definitive test was prepared on January 30, 2001 and had mean-measured concentrations of <7.5 (<LOD, negative control) 161, 310, 603, 1210, 2440, and 4790 ppm a.i. for the nominal 0 (negative control), 156, 313, 625, 1250, 2500, and 5000 ppm a.i. treatment levels (Table 1, p. 29), respectively. The above mean-measured recoveries represented 96-103% of the nominal treatment concentrations.

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

2. **Test organism:**

   **Species:** Mallard duck (*Anas platyrhynchos*)

   **Age at study initiation:** 9 days

   **Weight at study initiation:** Group means of 120-127 g

   **Source:** In-house Huntingdon Life Sciences stock.

## B. STUDY DESIGN:

1. **Experimental Conditions**

   a. Range-finding Study: None reported.

   b. Definitive Study: See Table 1

**Table 1: Experimental Parameters**

| Parameter | Details | Remarks |
|---|---|---|
| Acclimation period:<br><br>Conditions (same as test or not):<br><br>Feeding:<br><br>Health (any mortality observed): | 3 days<br><br>Same as test<br><br>Water and Standard HRC chick diet were provided, *ad libitum*.<br><br>All birds were in apparent good health at test initiation. | Diet composition is provided on p. 12.<br><br>No antibiotic was used in the diet (p. 11). |
| Pen size and construction materials | Pens (1.50 x 1.25 m) were constructed of galvanized steel with a wire mesh floor. | - |
| Test duration | 5 days with treated feed, and 3 days with "clean" feed. | - |
| Test concentrations<br>nominal:<br><br>measured: | 0 (control), 156, 313, 625, 1250, 2500, and 5000 ppm<br><br><7.5 (LOD, control), 161, 310, 603, 1210, 2440, and 4790 ppm a.i. | Mean-measured concentrations were provided in Table 1 of Formulation Chemistry (p. 30). All measured concentrations were corrected for the mean procedural recovery. 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 to nominal treatment concentrations 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 | Stability and homogeneity were determined in the same feed for a previous study (IGA 002/012368, MRID 46219041). |

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| Parameter | Details | Remarks |
|---|---|---|
| Number of birds per replicate/group | Negative control: 10<br>Treatments: 10 | - |
| Number of replicates/group | Negative control: 2<br>Treatments: 1 | - |
| Test conditions<br>temperature:<br><br>relative humidity (%):<br><br>photo-period: | <br>Brooder: Not reported<br>Room: 26-28°C (means)<br><br>45%<br><br>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<br>Clinical signs of toxicity<br>Group mean feed consumption<br>Group mean body weight |
| Indicate the stability and homogeneity of test chemical in the diet | Stability and homogeneity of the test material was not determined in this study. In a previous study (IGA 002/012368; MRID 46219041), the stability and homogeneity were verified at nominal concentrations of 156 and 5000 ppm (p. 22, IR5878 Formulation Chemistry). |
| 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 negative control replicate group of 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. |
| 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 >4790 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 4790 ppm a.i. and the LOEC was >4790 ppm a.i.

**Table 3: Sub-lethal effects of IR5878 (Orthosulfamuron) on *Anas platyrhynchos*.**

| 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 | 113 | 81 | 46 | 64 |
| Control | 122 | 83 | 50 | 64 |
| 161 (156) | 119 | 89 | 50 | 68 |
| 310 (313) | 109 | 83 | 47 | 65 |
| 603 (625) | 107 | 87 | 47 | 68 |
| 1210 (1250) | 107 | 87 | 44 | 63 |
| 2440 (2500) | 112 | 91 | 51 | 71 |
| 4790 (5000) | 102 | 87 | 45 | 64 |
| NOEC | 4790 ppm a.i. | | 4790 ppm a.i. | |
| $EC_{50}$ | Not determined | | Not determined | |

### 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 (4790 ppm a.i.). 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 (4790 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.

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 Mallard duck (§71-2b), 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 >4790 ppm a.i., the highest level tested. The NOEC was the highest treatment level tested. The toxicity of IR5878 (Orthosulfamuron) was categorized as slightly toxic ($LC_{50}$ is 1001-5000 ppm) to Mallard duck on an acute dietary basis.

## III. REFERENCES:

No references were cited.