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RPA 202248 Acute Oral Toxicity (81-1)

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DATA EVALUATION REPORT

STUDY TYPE:	Acute Oral Toxicity/Rats OPPTS 870.1100 [81-1]
EPA ID NUMBERS:	DP BARCODE: D224202 P. C. CODE: 123000 SUBMISSION NO.: S501233 MRID NUMBER: 43904810
TEST MATERIAL:	RPA 202248 Chemical Name: 2-Cyano-3-cyclopropyl-4-(2-methylsulfonyl-4-trifluoromethylphenyl)-propan-1,3-dione
STUDY NUMBER:	SA 95374
TESTING FACILITY:	Rhone-Poulenc Agrochimie, Sophia Antipolis, France
SPONSOR:	Rhone-Poulenc Ag Company, Lyon, France
TITLE OF REPORT:	RPA 202248. Oral Limit Test in the Rat
AUTHOR:	D. Bigot
REPORT ISSUED:	November 23, 1995

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID # 43904810), groups of five male and five female Sprague-Dawley rats were orally administered RPA 202248 in 0.5% methylcellulose and distilled water (20 ml/kg b.w.) at dose levels of 2000 and 5000 mg/kg. The animals were observed for mortality and clinical signs of toxicity for 15 days post-dosing. Two males and two females at 5000 mg/kg died by Day 2; the clinical signs of toxicity observed in both sexes on Day 1 included palpebral ptosis, piloerection, reduced motor activity, tremors (females) and coldness to touch (females).

The estimated acute oral LD_{50} for RPA 202248 was >5,000 mg/kg for both sexes.

The study is classified as **Acceptable** with a **Toxicity Category IV** and **satisfies** the requirements (81-1) for an acute oral toxicity study in rats.

I. MATERIALS

A. Test Material

Name: RPA 202248 (a metabolite of isoxaflutole)
Synonym: None
Chemical Name: 2-Cyano-3-cyclopropyl-4-(2-methylsulfonyl-4-trifluoromethylphenyl)propan-1,3-dione
Purity: >99%
Batch Number: DJA16-R
Description: White powder
Storage Conditions: At room temperature protected from light

The dosing formulation was prepared prior to dosing by suspending the test substance in 0.5% methylcellulose in distilled water to produce required dosing concentrations (w/v).

B. Test Animals

Species: Sprague-Dawley rats (ICO OFA SD)
Source: Iffa-Credo, L'Arbresle, France
Age: 7 weeks at initiation of dosing
Weight: Males - 187 to 225 g; Females - 140 to 157 g when dosed
Housing: Individually in stainless steel cage
Environmental Conditions: Temperature: 20-24^{0}C
Relative Humidity: 40-70%
Photoperiod: 12 hours light/dark
Air Changes: 10 to 15/hour
Food and Water: Pelleted Certified Rodent Diet A04C (from Usine d'Alimentation Rationnelle, France) and tap water *ad libitum*
Acclimation Period: 5-14 days

II. METHODS

Animals were fasted overnight prior to dosing. Each animal received a single dose of the test solution. Five male and five female rats/group were dosed with test solution (20 ml volume/kg b.w.) at 2000 or 5000 mg/kg via gavage. The animals were observed for mortality and clinical signs of toxicity on two occasions during Day 1 and daily for the remainder of the 14-day observation period. Body weights were recorded on one day prior to dosing, on the day of dosing and at 8 and 15 days post-dosing. At the end of the observation period, all animals were sacrificed and necropsied.

III. RESULTS

At 2000 mg/kg, none of the animals died during the study. No clinical signs or macroscopic postmortem findings were observed in these rats. Mortalities were noted at 5000 mg/kg on Day 1 (one female) and Day 2 (two males and one female). Palpebral ptosis, piloerection and reduced motor activity were observed in most animals, except in one male and one female. Few other clinical signs noted included bradypnea in one male, dyspnea in one female, coldness to touch in three females and tremors in two females. All surviving animals recovered by day 2. Body weights were unaffected. There were no lesions observed on gross necropsy of animals sacrificed at study termination. The estimated acute oral LD_{50} was >5000 mg/kg for males and females.

IV. COMPLIANCE

The following compliance documents were submitted: 1) signed statement by the sponsor indicating that the study was conducted in accordance with GLP Regulations; 2) signed Quality Assurance statement by the testing facility; 3) signed statement by the sponsor claiming no data confidentiality. Any deviations from the protocol were appropriately reported.

V. CONCLUSIONS

The acute oral LD_{50} for RPA 202248 in male and female rats was >5,000 mg/kg.

The study is classified as **Acceptable** with a **Toxicity Category IV** and **satisfies** the requirements (81-1) for an acute oral toxicity study in rats.

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One-Liners for RPA 202248

Study Type:	Guideline: OPP §81-1 Acute Oral Toxicity Species: Rat
Test Material:	RPA 202248
Chemical Name:	2-Cyano-3-cyclopropyl-4-(2-methylsulfonyl-4-trifluoromethylphenyl)-propan-1,3-dione
EPA MRID No.:	43904810
Testing Facility:	Rhone-Poulenc Agrochimie, Sophia Antipolis, France
Study Number:	SA 95374
Report Issued:	November 23, 1995

Executive Summary: In an acute oral toxicity study (MRID # 43904810), groups of five male and five female Sprague-Dawley rats were orally administered RPA 202248 in 0.5% methylcellulose and distilled water (20 ml/kg b.w.) at dose levels of 2000 and 5000 mg/kg. Two males and two females at 5000 mg/kg died by Day 2; the clinical signs of toxicity observed in both sexes on Day 1 included palpebral ptosis, piloerection, reduced motor activity, tremors (females) and coldness to touch (females). **The estimated acute oral LD_{50} for RPA 202248 was >5,000 mg/kg for both sexes.**

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