UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

1 February 2007

MEMORANDUM

Subject: Name of Pesticide Product: IR5878 TECHNICAL
EPA Reg. No. /File Symbol: 80289-U
DP Barcode: D331091
Decision No.: 358188
PC Code: 108209 (Orthosulfamuron: 98%)

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505P)

Byron T. Backus 2-1-2007
RJW 2-1-2007

To: Erik Kraft/James Tompkins, RM Team 25
Registration Division (7505P)

Registrant: ISAGRO S.P.A.

FORMULATION FROM LABEL:

	% by wt.
Active Ingredient(s):	
108209 Orthosulfamuron (CAS #213464-77-8)	98.0%
Inert Ingredient(s):	2.0%
Total:	100.0%

ACTION REQUESTED: The Risk Manager requests:

"Please review the attached new information in response to an initial tox review and determine the toxicity category in terms of oral exposure. New information has been provided from the company to help determine whether MRID 46578915 & 46578918 are acceptable (oral toxicity studies) after questions arose in the lst review of the tox. studies."

BACKGROUND:

In a previous review for 80289-U (memorandum dated October 31, 2005 from B. Backus to J. Tompkins for DP Barcode D319036), four studies were reviewed. Two of these studies (an acute oral toxicity study in MRID 46578915 and an acute oral study in MRID 46578918) were classified as supplementary data because no information was reported as to the chemical identities of the test materials or their relationship(s) to IR5878 technical. This information has now been provided in letters dated April 7, 2006.

COMMENTS AND RECOMMENDATIONS:

With the information as to the identity of the test materials as presented in the letters dated April 7, 2006, the two studies in MRIDs 46578915 and 46578918 are upgraded to acceptable.

Reviewer: Byron T. Backus, Ph.D.
Risk Manager: 25

February 1, 2007

STUDY TYPE: Acute Oral Toxicity (Acute Toxic Class Method) - WIST (SPF) Rat; OPPTS 870.1100; OECD 423

TEST MATERIAL: IR7825, Batch No. FCF/T/198-01 (ex 20687/38) purity 99.3%, described as a white solid; expiry date July 2005. The test material was further identified (letter from the registrant dated April 7, 2006) as a metabolite of orthosulfamuron, and by IUPAC name as (4,6-dimethoxypyrimidin-2-yl) urea, and by CA name as (4,6-dimethoxy-2-pyrimidinyl) urea, CAS 151331-81-6, with the molecular formula $C_7H_{10}N_4O_3$. For the purposes of dosage this test material was administered (as a suspension and/or solution) in Polyethylene Glycol 300 (PEG 300) with an application volume of 10 mL/kg (0.2 g test material/mL).

CITATION: Arcelin, G. (2003) IR7825: Acute Oral Toxicity Study in Rats. RCC Ltd., Wölferstrasse 4, CH-4414 Füllinsdorf, Switzerland. Study No. 848210. July 2, 2003. 20 pages. MRID 46578915. Unpublished.

SPONSOR: ISAGRO SpA, Milano, Italy

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46578915) 6 female HanBrl: WIST (SPF) 12-week-old rats (source: RCC Ltd. Laboratory Animal Services, CH-4414 Füllinsdorf, Switzerland; weights 180.4-195.8 g at dosage) were orally gavaged with a dose of 2000 mg/kg IR7825, Batch No. FCF/T/198-01 (ex 20687/38), 99.3% purity. The test material was further identified (letter from the registrant dated April 7, 2006) by IUPAC name as (4,6-dimethoxypyrimidin-2-yl) urea, and by CA name as (4,6-dimethoxy-2-pyrimidinyl) urea, CAS 151331-81-6, with the molecular formula $C_7H_{10}N_4O_3$. The test material was diluted in PEG 300 to 0.2 g/mL and the suspension/solution was administered by gavage on Day 1 at a constant dose volume of 10 mL/kg. Rats were observed for 14 days after administration. There were no clinical signs of toxicity and no mortalities. All rats gained weight from Day 1 to 8. One female showed a weight loss of 2.1% (4.1 g) from Day 8 to 15; all other rats gained in this period. Post-sacrifice necropsies showed no macroscopic findings.

Oral LD_{50} (Female rat) > 2000 mg/kg (0/6 died).

Toxicity based on the absence of mortality at the limit dose of 2000 mg/kg. EPA Toxicity Category III.

With the identification of the test material, the classification of this study is upgraded to acceptable. This study defines an EPA Toxicity Category III oral hazard potential for the test material (IR 7825, purity 99.3%), otherwise identified as [IUPAC name] (4,6-dimethoxypyrimidin-2-yl) urea, and [CA name] as (4,6-dimethoxy-2-pyrimidinyl) urea, CAS 151331-81-6, with the molecular formula $C_7H_{10}N_4O_3$. This study satisfies the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 423) in the rat for this test material.

COMPLIANCE: Signed and dated GLP (p. 3) , Quality Assurance (p. 9), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
2000	n/a	0/6	0/6

A. Mortality - as noted in table.

B. Clinical observations - All animals survived the 2000 mg/kg dose without clinical signs. All gained weight in the period from Day 1 (the day of dosage) to 8, and 5/6 gained weight in the period from Day 8 to 15. One rat had a weight loss of 4.1 g between Day 8 and 15.

C. Gross Necropsy - Post-sacrifice gross necropsy results were normal.

D. Reviewer's Conclusions: This study defines an EPA Toxicity Category III oral hazard potential for the test material (IR 7825, purity 99.3%), otherwise identified as [IUPAC name] (4,6-dimethoxypyrimidin-2-yl) urea, and [CA name] as (4,6-dimethoxy-2-pyrimidinyl) urea, CAS 151331-81-6, with the molecular formula $C_7H_{10}N_4O_3$. This study satisfies the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 423) in the rat for this test material.

Reviewer: Byron T. Backus, Ph.D.
Risk Manager: 25

February 1, 2007

STUDY TYPE: Acute Oral Toxicity (Acute Toxic Class Method) - WIST (SPF) Rat; OPPTS 870.1100; OECD 423

TEST MATERIAL: IR7863, Batch No. 20687/50, purity 97.8%, described as a white solid; expiry date July 2005. The test material was further identified (letter from the registrant dated April 7, 2006) as a metabolite of orthosulfamuron, and by IUPAC name as 2-(dimethylcarbamoylphenyl)sulfamic acid, and by CA name as 2-[(dimethylamino)carbonyl] phenylsulamic acid, CAS number not assigned, with the molecular formula $C_9H_{12}N_2O_4S$. For the purposes of dosage this test material was administered (as a suspension and/or solution) in purified water with a dosage volume of 10 mL/kg (0.2 g test material/mL).

CITATION: Ott, M. (2003) IR7863: Acute Oral Toxicity Study in Rats. RCC Ltd., Wölferstrasse 4, CH-4414 Füllinsdorf, Switzerland. Study No. 850107. September 17, 2003. 20 pages. MRID 46578918. Unpublished.

SPONSOR: ISAGRO SpA, Milano, Italy

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 46578918) 3 female and 3 male HanBrl: WIST (SPF) 12-week-old rats (source: RCC Ltd. Laboratory Animal Services, CH-4414 Füllinsdorf, Switzerland; females: 12 weeks; males: 9 weeks; weights: females: 183.0-203.1 g; males: 225.4-238.5 g at dosage) were orally gavaged with a dose of 2000 mg/kg IR7863 (97.8%), also identified as a metabolite of orthosulfamuron and by IUPAC name as 2-(dimethylcarbamoylphenyl)sulfamic acid, and by CA name as 2-[(dimethylamino)carbonyl] phenylsulamic acid, CAS number not assigned, with the molecular formula $C_9H_{12}N_2O_4S$. The test material was diluted in purified water to 0.2 g/mL and the suspension/solution was administered on Day 1 at a constant dose volume of 10 mL/kg. Rats were observed for 14 days after administration. There were no clinical signs of toxicity and no mortalities. All rats gained weight from Day 1 to 8 and again from Day 8 to 15. Post-sacrifice necropsies showed no macroscopic findings.

Oral LD_{50} (Female rat) > 2000 mg/kg (0/3 died).
Oral LD_{50} (Male rat) > 2000 mg/kg (0/3 died).

Toxicity based on the absence of mortality at the limit dose of 2000 mg/kg. EPA Toxicity Category III.

This study defines an EPA Toxicity Category III oral hazard potential for the test material (IR 7863, purity 97.8%), identified (letter from the registrant dated April 7, 2006) as a metabolite of orthosulfamuron, and by IUPAC name as 2-(dimethylcarbamoylphenyl)sulfamic acid, and by CA name as 2-[(dimethylamino)carbonyl] phenylsulamic acid, CAS number not assigned, with the molecular formula $C_9H_{12}N_2O_4S$. With this information, the study is classified as acceptable; and it satisfies the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 423) in the rat for this test material.

COMPLIANCE: Signed and dated GLP (p. 3) , Quality Assurance (p. 9), and [No] Data Confidentiality (p. 2) statements were provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined
2000	0/3	0/3	0/6

A. Mortality - as noted in table.

B. Clinical observations - All animals survived the 2000 mg/kg dose without clinical signs. All gained weight in the period from Day 1 (the day of dosage) to 8, and again from Day 8 to 15.

C. Gross Necropsy - Post-sacrifice gross necropsy results were normal.

D. Reviewer's Conclusions: The test material (IR 7863, purity 97.8%, identified (letter from the registrant dated April 7, 2006) as a metabolite of orthosulfamuron, and by IUPAC name as 2-(dimethylcarbamoylphenyl)sulfamic acid, and by CA name as 2-[(dimethylamino)carbonyl] phenylsulamic acid, CAS number not assigned, with the molecular formula $C_9H_{12}N_2O_4S$) is in EPA Toxicity Category III in terms of its oral hazard potential. This study satisfies the guideline requirement for an acute oral study (OPPTS 870.1100; OECD 423) in the rat for this test material.

ACUTE TOX ONE-LINERS

1. **DP BARCODE:** D331091
2. **PC CODE:** 108209 Orthosulfamuron
3. **CURRENT DATE:** 1 February 2007
4. **TEST MATERIALS:** IR7825; 99.3%; the test material was further identified (letter from the registrant dated April 7, 2006) as a metabolite of orthosulfamuron, and by IUPAC name as (4,6-dimethoxypyrimidin-2-yl) urea, and by CA name as (4,6-dimethoxy-2-pyrimidinyl) urea, CAS 151331-81-6, with the molecular formula $C_7H_{10}N_4O_3$ (study in MRID 46578915).

IR7863; Batch No. 20687/50; purity 97.8%, described as a white solid; expiry date July 2005. The test material was further identified (letter from the registrant dated April 7, 2006) as a metabolite of orthosulfamuron, and by IUPAC name as 2-(dimethylcarbamoylphenyl)sulfamic acid, and by CA name as 2-[(dimethylamino)carbonyl] phenylsulamic acid, CAS number not assigned, with the molecular formula $C_9H_{12}N_2O_4S$ (study in MRID 46578918).

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat/RCC Ltd., Füllinsdorf, Switzerland/Study No. 848210/JUL-2-2003	46578915	rat female LD_{50} > 2000 mg/kg; no signs of toxicity, all normal at post-sacrifice necropsy.	III	A
Acute oral toxicity/rat/ RCC Ltd., Füllinsdorf, Switzerland/Study No. 850107/SEP-17-2003	46578918	rat male and female LD_{50} >2000 mg/kg (0/3 males & 0/3 females died). No signs of toxicity, all normal at post-sacrifice necropsy.	III	A

Core Grade Key: **A =Acceptable, S = Supplementary, U = Unacceptable, W = Waived**