DATA EVALUATION RECORD

STUDY TYPE: ACUTE ORAL TOXICITY TESTING (870-1100)

PRODUCT MANAGER: 22 **REVIEWER**: M. HASHIM

TEST MATERIAL: RPA 407213,white powder, 99.8% purity. Batch No. MDA9607.

CITATION: M. Dange, Study Director. Oral LD50 in Rat. Rhone-Poulenc Agrochimie, Centre de Recherche, 355, rue Dostoievski, BP 153 F-06903 Sophia Antipolis Cedex. Study No. SA 97005 dated 6-18-97. MRID 453860-11.

SPONSOR: Rhone-Poulenc Agrochimie, 14-20, rue Pierre Baizet, BP 9163, F-69263, F-69263 Lyon Cedex 09.

EXECUTIVE SUMMARY: In an acute oral toxicity study, RPA 407213 was administered to 5 male and 5 female SD rats (wt. m 243-327, fe 168-223 g, Source Iffa-Credo, Germain-sur-L'Arbresle, France) as a single dose by gavage at 5000, 2000 (females only), 1000, 850 or 700 mg/kg of body weight. The test substance was suspended in 0.5% aqueous methylcellulose. Observations were made for signs of gross toxicity and mortality for a subsequent period of 15 days. Initial and weekly body weights and terminal necropsy findings were recorded.

Oral LD50 for male animals was >5000 mg/kg, and for females was 2028 mg/kg. TRB will use LD_{50} as > 2028 mg/kg for both sexes. The study is classified as Tox Category III.

All females that received 5000 mg/kg died on Day 1 of study. At 2000 mg/kg, two females died on Day 1. There were no deaths in male animals at any dose level or in females at 1000 or 850 mg/kg. One female at 700 mg/kg had accidental death. Males at 5000 and 1000 mg/kg showed clinical signs such as reduced motor activity. All females that died at 5000 mg/kg and the ones received 2000 mg/kg dose (2 of 5 dead) showed reduced motor activity, hunched posture, staggering gait, prostration, bradypnea and piloerection. The 2000 mg/kg group that survived recovered by Day 2. There were no clinical signs in animals receiving 1000, 850 or 700 mg/kg. Body weights were not affected in surviving animals. Necropsy findings were unremarkable.

This study (870-1100) is Acceptable in accordance with the Sub-Division F guideline.

COMPLIANCE: The study is in compliance with GLP, signed and dated. .

RESULTS:

Number of Deaths/ Total No. of animals

Dosage mg/kg	**Male**	**Female**	**Total**
5000	0/5	5/5	5/10
2000	-	2/5	2/5
1000	0/5	0/5	0/10
850	0/5	0/5	0/10
700	0/5	1/5	1/10

OBSERVATIONS: Oral LD50 for male animals was >5000 mg/kg, and for females was 2028 mg/kg. We consider LD50 to > 2028 mg/kg for both sexes for safety concerns.

All females that received 5000 mg/kg died on Day 1. Two females died on Day 1 of the study at 2000 mg/kg. There were no deaths in male animals at any dose level or in females at 1000 or 850 mg/kg. One female at 700 mg/kg had accidental death. Males at 5000 and 1000 mg/kg showed clinical signs such as reduced motor activity. All females that died at 5000 mg/kg and the ones received 2000 mg/kg (2 of 5 dead) showed reduced motor activity, hunched posture, staggering gait, prostration, bradypnea and piloerection. The 2000 mg/kg group that survived recovered by Day 2. There were no clinical signs in animals receiving 1000, 850 or 700 mg/kg. Body weights were not affected in surviving animals. Necropsy findings were unremarkable.

Necropsy Findings: Unremarkable.