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

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APR 15 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Memorandum

Subject: Review of Acute Oral Toxicity Study for Trichloromelamine (TCM)
DP Barcode D201114
Submission S461848
Case 813175
Chemical No. 077101

From: James N. Rowe, Ph.D. James N. Rowe 4/12/94
Toxicology Branch II
Health Effects Division (H7509C)

To: Ms. Bonnie Adler/Kathryn Davis (PM-52)
Accelerated Reregistration Branch
Special Review and Reregistration Division (7508W)

Thru: Marcia van Gemert, Ph.D., Chief Marcia van Gemert 4/14/94
Toxicology Branch II
Health Effects Division (H7509C)

An acute oral toxicity study (MRID No. 43165701) was reviewed for TCM. The following conclusions were noted:

In an acute toxicity study, Crl:CD^{R}(SD)BR rats (5/sex/dose level) were administered by gavage 100, 300 or 500 mg/kg of trichloromelamine in an aqueous suspension. The acute oral LD_{50} (CL) values for males and females were 413(286-596) and 387(279-538) mg/kg, respectively (combined LD_{50} (CL) values of 398(312-509) mg/kg). Clinical signs observed (primarily during the first 4 hours post dosing) included hypoactivity, staggered gait, prostration, absence of righting reflex, mydriasis, hunched posture, dyspnea and soft stool.

The study is classified as **Core Minimum Data (Acceptable)** with a **Toxicity Category II** and **satisfies** the requirement, § 81-1 for an acute oral toxicity study in rats.

Reviewed by: James N. Rowe, Ph.D. James N. Rowe 4/12/94
Section III, TB II (7509C)
Secondary Reviewer: Alberto Protzel, Ph.D. Alberto Protzel 4/12/94
Section III, TB II (7509C)

DATA EVALUATION RECORD

Study Type: Acute oral toxicity in rats
EPA Guideline 81-1

EPA Identification: EPA MRID NO. 43165701
PC Code: 077101
DP Barcode: D201114
Submission: S461848

Test Material: Trichloromelamine (TCM)

Synonyms: N/A

Study Number: HWI 31102385

Sponsor: S.C. Johnson & Son, Inc.
Racine, Wisconsin

Testing Facility: Hazleton Wisconsin, Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Title of Report: Acute oral toxicity study of trichloromelamine (TCM), #14468W46 in rats (EPA Guidelines)

Author(s): Steven M. Glaza

Report Issued: March 10, 1994

Executive Summary: In an acute toxicity study, Crl:CD^{R}(SD)BR rats (5/sex/dose level) were administered by gavage 100, 300 or 500 mg/kg of trichloromelamine in an aqueous suspension. The acute oral LD_{50} (CL) values for males and females were 413(286-596) and 387(279-538) mg/kg, respectively (combined LD_{50} (CL) values of 398(312-509) mg/kg). Clinical signs observed (primarily during the first 4 hours post dosing) included hypoactivity, staggered gait, prostration, absence of righting reflex, mydriasis, hunched posture, dyspnea and soft stool.

The study is classified as **Core Minimum Data (Acceptable)** with a **Toxicity Category II** and **satisfies** the requirement, § 81-1 for an acute oral toxicity study in rats.

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Materials:

1. Test Compound: Trichloromelamine (TCM). Description: Light yellow powder; Lot no.: #14468W46; Purity: 95.1%.

2. Test Animals: Species: rat, Strain: Crl:CD^{R}(SD)BR; Age: Stated as young; Weight (at dosing): 256-299 g (males), 223-249 g (females), definitive study; Source: Charles River Laboratories, Inc., Portage, MI; Quarantine and acclimatization: 7 days.

Methods: A range-finding study was initially performed (1/sex/dose) at 100, 500, 1000 and 5000 mg/kg with rats individually housed. The test material was mixed with distilled water (appeared to be a suspension) and administered via gavage to animals (fasted for approximately 17 to 20 hours) at a volume of 20 ml/kg of fasted body weight. The female rat died at 500 mg/kg and all rats died at higher dosages. Based upon this study, dose levels of 100, 300 and 500 mg/kg (5 rats/sex/dose) were tested.

Clinical observations including mortality checks were performed at approximately 1, 2.5 and 4 hours after administration. Once/day clinical checks and a morning and evening mortality check were performed on a daily basis thereafter for two weeks. Body weights were determined prior to test compound administration, and on day 7 and day 14. At study termination (and for animals found dead or euthanized early) gross necropsy was performed on all animals and abnormalities noted. LD_{50} values for males and females and combined sexes were determined by a computer program using a modified Behrens-Reed-Muench cumulant method.

Results: Clinical signs at 100 mg/kg were minor (first few hours of observation) and included one male with soft stool and one female with miosis. Males at 300 mg/kg exhibited limited signs of toxicity initially including soft stool (2) and dark stained urogenital region (2). No abnormal signs were noted from day 1-14. Females receiving 300 mg/kg had more severe signs of toxicity including staggered gait (2), hypoactivity (2), and lacrimation (3) as well as soft stool and dark or yellow-stained urogenital area (during the first 4 hours). Some of these signs were maintained through day 3. Three of the four high dose males died by 2.5 hours and the fourth one at four hours of observation (see Table 1 below). Toxicity signs included hypoactivity (3) , staggered gait (3), prostration (1), absence of righting reflex (1), mydriasis (1), hunched posture (1) and soft stool (5). The remaining male continued to experience a staggered gait through day 5. All HDT females died during the initial observation period, 1 female died at 1 hour, 3 at 2.5 hours and 1 at 4 hours with similar clinical signs of toxicity including dyspnea (3), prostration (3), mydriasis (1), lacrimation (1), hypoactivity

(1), absence of righting reflex (1) and soft stool (2).

All surviving animals gained weight during the observation period. The pathologist reported that the prominent findings (500 mg/kg dose group) at necropsy pertained to "contents and coloration changes in the gastrointestinal tract. These changes possibly represented test material mixed with ingesta, post mortem autolysis, or both."

Table 1. Mortality in rats after a single oral dose of trichloromelamine (from pp. 10-12 of the Study report).

Dose mg/kg	Males deaths/dosed	Females deaths/dosed
100	0/5	0/5
300	0/5	0/5
500	4/5*	5/5*
LD50(95%CL)[a] =	413(286-596) mg/kg	387(279-538) mg/kg

[a] The combined LD_{50}(95%CL) for males and females was 398(312-509) mg/kg.
* Animals were found dead on day of dosing.

Signed and dated quality assurance, GLP compliance and No Data Confidentiality Claims statements were present.