

US EPA ARCHIVE DOCUMENT

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DATA EVALUATION REPORT

ZIRAM

8/2/2000

STUDY TYPE: ACUTE ORAL TOXICITY - RAT (81-1)

Prepared for

Health Effects Division  
Office of Pesticide Programs  
U.S. Environmental Protection Agency  
1921 Jefferson Davis Highway  
Arlington, VA 22202

Prepared by

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Toxicology and Risk Analysis Section  
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Oak Ridge, TN 37831  
Task Order No. 97-22L

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Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

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Oak Ridge National Laboratory, managed by Lockheed Martin Energy Research Corp. for the U.S. Department of Energy under contract number DE-AC05-96OR22464.

ZIRAM

Acute Oral Study (OPP 81-1; OPPTS 870.1100)

EPA Reviewer: David Nixon, D.V.M., \_\_\_\_\_ Date \_\_\_\_\_  
Reregistration Branch 4 (7509C)  
Sanjivani Diwan, Ph.D. \_\_\_\_\_ Date \_\_\_\_\_  
Reregistration Branch 4 (7509C)

DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat  
OPPTS 870.1100 [S81-1]

DP BARCODE: D235025  
P.C. CODE: 034805

SUBMISSION CODE: S521512  
TOX. CHEM. NO.: 931

TEST MATERIAL (PURITY): Ziram Technical (Agrochemical grade, 98%)

SYNONYMS: Zinc dimethyldithiocarbamate

CITATION: Merriman, T. (1995) An acute oral toxicity study in rats with Ziram Technical (Agrochemical grade). Springborn Laboratories, Inc. (SLS), Life Sciences Division, 640 North Elizabeth Street, Spencerville, OH 45887 and WIL Research Laboratories, Inc., 1407 George Road, Ashland, OH 44805. SLS Study No. 3357.1 and WIL Laboratory No. WIL-205008. MRID 43701301. Unpublished.

SPONSOR: UCB Chemicals, 2000 Lake Park Drive, Smyrna, GA 30080

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 43701301) groups of five male and five female fasted young adult Sprague-Dawley [Crl:CD®BR VAF/plus®] rats were given single dose of 250, 750, 1250, or 1750 mg/kg of Ziram Technical (Agrochemical grade, 98% a.i., Lot no. 4603AA) in Mazola corn oil by gavage and observed for 14 days.

Oral LD<sub>50</sub> Males = 2719 mg/kg (95% C.I. 1414 to 5228 mg/kg)  
Females = 2060 mg/kg (95% C.I. 1331 to 3188 mg/kg)  
Males and Females Combined = 2068 mg/kg (95% C.I. 1558 to 2744 mg/kg)

Ziram is in TOXICITY CATEGORY III.

Three males (two 1250 mg/kg dose and one 1750 mg/kg dose) and three females (one 1250 mg/kg dose and two 1750 mg/kg dose) died during the study. Clinical signs of toxicity included salivation, decreased activity, mucoid/soft stools, diarrhea, decreased defecation, fecal/urine staining, rough hair coat, piloerection, dehydration, emaciation, lacrimation, eyelids partially closed and dark material around the facial area. One male and one female in the 1750 mg/kg group lost weight during the 0-7 day interval. Abnormal contents in the digestive tract, rugae absent, dark red striations and eroded areas in the stomach, and congested meningeal vessels of the brain were found in the animals that died during the study. Some animals sacrificed at study termination had

thickened stomach mucosa, dilated renal pelvis, and distended ureters.

This acute oral study is classified acceptable (guideline). This study does satisfy the guideline requirement for an acute oral study (81-1) in the rat. It should be noted that corn oil tends to limit the absorption of ziram resulting in elevated LD<sub>50</sub> values compared to other oral acute studies.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

## I. MATERIALS AND METHODS

### A. MATERIALS

1. Test material: Ziram Technical (Agrochemical grade)

Description: off white powder  
Lot/Batch #: 4603AA  
Purity: 98% a.i.  
CAS #: 137-30-4

2. Vehicle

Mazola corn oil

3. Test animals

Species: rat  
Strain: Sprague-Dawley [CrI:CD<sup>®</sup>BR VAF/Plus<sup>®</sup>]  
Age and/or weight at dosing: ~9-10 weeks; males: 192-240 g,  
females: 183-217 g  
Source: Charles River Laboratories, Inc., Portage, MI  
Acclimation period: ≥5 days  
Diet: Purina Certified Rodent Chow #5002, *ad libitum*  
Water: treated (reverse osmosis) municipal tap water, *ad libitum*  
Housing: individually in suspended stainless steel cages  
Environmental conditions:  
Temperature: 65-74°F  
Humidity: 40-68%  
Air changes: 10-12/hour  
Photoperiod: 12 hour light/dark

### B. STUDY DESIGN and METHODS

1. In life dates

Start: November 2, 1994 (experimental initiation); end:  
January 3, 1995 (experimental completion)

2. Animal assignment and treatment

Animals were assigned to the test groups noted in Table 1. Dose selection was based on a range-finding study in one male and one female. In this study, death occurred at 500 mg/kg in males;

no deaths occurred in females. In the definitive study, following an overnight fast, groups of 5 animals/sex were given single dose of 250, 750, 1250, or 1750 mg/kg of the test material in Mazola corn oil by gavage at a volume of 5 mL/kg and observed for 14 days. The animals were observed for clinical signs of toxicity at least twice on day 1 and at least daily thereafter for the remainder of the 14-day study. Mortality checks were performed twice daily. They were weighed prior to fasting (day -1), prior to dosing on day 0 and on days 7 and 14. All animals that died during the study and survivors sacrificed by carbon dioxide inhalation at study termination were necropsied.

Dose (mg/kg)	Males	Females	Combined
250	0/5	0/5	0/10
750	0/5	0/5	0/10
1250	2/5	1/5	3/10
1750	1/5	2/5	3/10

Data taken from pp. 12 and 17, MRID 43701301.

### 3. Statistics

The oral LD<sub>50</sub> and 95% confidence intervals were calculated using the method of Litchfield and Wilcoxon (1949) [J. Pharmacol. Exp. Ther., 96: 99-113.]

## II. RESULTS AND DISCUSSION

### A. MORTALITY

Mortality is given in Table 1. Two males dosed at 1250 mg/kg died on days 2 and 6; another male receiving 1750 mg/kg died on day 7. One female in the 1250 mg/kg group died on day 3; two females in the 1750 mg/kg group died on day 6.

Oral LD<sub>50</sub> Males = 2719 mg/kg (95% C.I. 1414 to 5228 mg/kg)

Females = 2060 mg/kg (95% C.I. 1331 to 3188 mg/kg)

Males and Females Combined = 2068 mg/kg (95% C.I. 1558 to 2744 mg/kg)

Ziram Technical (Agrochemical grade) is in TOXICITY CATEGORY III.

### B. CLINICAL OBSERVATIONS

The most notable clinical abnormalities in the treated animals during the 14 day study include salivation, decreased activity, mucoid/soft stools, diarrhea, decreased defecation, fecal/urine

staining, rough hair coat, piloerection, dehydration, emaciation, lacrimation, eyelids partially closed and dark material around the facial area. An abnormally high incidence of abdominal hair loss was noted in the males of the 750 and 1750 mg/kg dose groups (4/5 and 3/5, respectively).

C. BODY WEIGHT

One male and one female in the 1750 mg/kg group showed body weight loss during the day 0-7 interval. Body weight gains was noted for all other surviving animals during the study period.

D. NECROPSY

Abnormal contents in the digestive tract, rugae absent, dark red striations and eroded areas in the stomach, and congested meningeal vessels of the brain were found in the animals that died during the study. The animals sacrificed at study termination only had one incidence of thickened stomach mucosa (female at 1750 mg/kg dose) and two incidences of dilated renal pelvis (females at 250 and 750 mg/kg dose), and this 250 mg/kg dose female also had distended ureters.

E. DEFICIENCIES

No study deficiencies were identified.

ZIRAM

Acute Oral Study (OPP 81-1; OPPTS 870.1100)

SignOff Date:	8/2/00
DP Barcode:	D172447
HED DOC Number:	014277
Toxicology Branch:	RAB2