US EPA ARCHIVE DOCUMENT

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DATA EVALUATION REPORT

ZIRAM

STUDY TYPE: ACUTE INHALATION - RAT (81-3)

8/2/2000

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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Task Order No. 97-22G

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Reregistration Branch 1 (7509C)

DATA EVALUATION RECORD

STUDY TYPE: Acute Inhalation Toxicity - Rat
OPPTS 870.1300 [§81-3]

DP BARCODE: D235025
P.C. CODE: 034805

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

TEST MATERIAL (PURITY): Ziram Technical

SYNONYMS: Zinc dimethyldithiocarbamate

CITATION: Jackson, G. and C. Hardy (1989) Ziram Technical: Acute inhalation toxicity in rats - 4-hour exposure. Huntingdon Research Centre Ltd., P.O. Box 2, Huntingdon, Cambridgeshire, PE18 6ES, England. HRC Report No. UCB 314/89684, December 4, 1989. MRID 41442001. Unpublished.

SPONSOR: UCB Chemicals Corporation, 5365-A Robin Hood Road, Norfolk, VA 23513

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 41442001), groups of young adult male and female Sprague-Dawley rats (5/sex) were exposed (whole body) to Ziram Technical (98.5%, Batch no. 8331AA) for 4 hours at concentrations of 0.020, 0.029, 0.047, 0.098, or 0.145 mg/L. The Mass Median Aerodynamic Diameter (MMAD) for the particle size generated ranged from 1.3 μm to 2.7 μm with a Geometric Standard Deviation (GSD) of 2.01 to 4.30.

LC_{50} (4-hour) Males = 0.08 mg/L (SE = 0.028)
Females = 0.06 mg/L (SE = 0.017)
The Combined = 0.07 mg/L (SE = 0.011)

Ziram Technical is in TOXICITY CATEGORY II.

Four of five females exposed to 0.047 mg/L, 2/5 males and 4/5 females exposed to 0.098 mg/L, and 5/5 males and 4/5 females exposed to 1.145 mg/L died.

Clinical signs seen in all exposed rats were partial closing of the eyes and an irregular respiration rate. Wetness around the mouth was observed in rats exposed at 0.020, 0.029, or 0.145 mg/L. Other signs included pilo-erection (at 0.020 and 0.029 mg/L), reduced activity (at 0.047 and 0.098 mg/L), and a reduced respiration rate (at 0.047 mg/L). Recovery from these effects was complete in surviving rats 5-9 days following exposure.

There were moderate to marked decreases of body weight or reduced body weight gain for up to 2 days following exposure. Animals that died had congested lungs and increased lung weight to body weight ratio. Animals surviving the exposure had no macroscopic abnormalities.

This acute inhalation study is classified as acceptable (guideline). It does satisfy the guideline requirement for an acute inhalation study (81-3) in the rat.

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

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Ziram Technical

Description: creamy white powder
Lot/Batch #: 8331AA
Purity: 98.5% a.i.
CAS #: 137-30-4

2. Vehicle and/or positive control

None

3. Test animals

Species: rat
Strain: Sprague-Dawley
Age and weight at dosing: ~7 and 9 weeks; males: 196-222 g, females: 181-213 g
Source: Charles River, Portage, MI
Acclimation period: ≥five days
Diet: Biosure LAD 1, *ad libitum*
Water: tap water, *ad libitum*
Housing: 5/sex/suspended polypropylene cage with detachable wire mesh top and floor
Environmental conditions:
- Temperature: 18-24°C
- Humidity: 28-65%
- Air changes: not reported
- Photoperiod: 12 hour light/dark

B. STUDY DESIGN and METHODS

1. In life dates

Group	Start
Group 1 (Control)	2/7/89
Group 2	2/7/89
Group 3	2/9/89
Group 4	2/10/89
Group 5	2/13/89
Group 6	2/14/89

2. Exposure conditions

Temperature (22.0-24.3°C) and humidity (41-57%) were recorded at 30-minute intervals throughout the 4-hour exposure period.

3. Animal assignment and treatment

Animals were assigned to the test groups noted in Table 1. Rats were exposed to Ziram Technical by whole-body exposure for four hours. They were observed throughout the 4-hour exposure and twice daily thereafter, and weighed daily during the 14-day study. Food and water consumption were measured daily. Survivors were anesthetized by intraperitoneal injection of pentobarbitone sodium, killed by exsanguination, and a necropsy was performed. Gross necropsies were also performed on animals which died during the study. The lungs were weighed and a lung to body weight ratio calculated. The lungs were also preserved in 10% formalin for possible microscopic examination.

TABLE 1. Concentrations, exposure conditions, mortality/animals treated							
Group	Nominal Conc. (mg/L)	Analytical Conc. (mg/L)	MMAD µm	GSD µm	Males	Females	Combined
1(control)					0/5	0/5	0/10
5	0.096	0.020	2.7[b]	2.01[b]	0/5	0/5	0/10
6	(2.3)[a]	0.029	1.8	3.43	0/5	0/5	0/10
3	0.143	0.047	1.3	3.22	0/5	4/5	4/10
2	0.287	0.098	1.4	3.02	2/5	4/5	6/10
4	0.430	0.145	2.3	4.30	5/5	4/5	9/10

Data taken from pp.16, 17, 22, 23, and 24, MRID 41442001.
[a]The recorded test material usage of group 6 was 2.3 g and in excess of the theoretical possible usage. The study authors felt it was likely that there was a weighing error, and the nominal concentration for group 6 was considered invalid.
[b]In view of the small amount of material collected in the sample for group 5 the calculated MMAD and GSD should be interpreted with caution. The fact that there was no measurable amount collected on the filter will have caused the calculated MMAD to be larger than the true value.

4. Generation of the test atmosphere and description of the chamber

Exposure atmospheres were generated using a Wright's Dust Generator which was connected by an elutriation column to the inlet port of a 25 liter exposure chamber. Clean, dry air was passed across a sample of the test material in the the dust generator at a flow rate of 25 liters/min. The gear ratio of the generator mechanism was selected to give a concentration of dust of approximately 0.1 mg/L of air. The concentration of dust produced by the generator at various gear ratios was determined during preliminary trials. Time to equilibrium in the chamber was approximately 11 min.

5. Atmosphere Analyses

Five air samples of 2.5 to 5 minutes were taken from the chamber during each exposure at a rate of 4 L/min, through a weighed glass fiber filter mounted in an open-face filter holder. The filters were re-weighed to determine the concentration of the test material in the chamber air. The average results are in Table 1 above.

Two additional samples of 14 or 28 minutes duration were taken using an Andersen mini sampler and the collected

material was weighed to determine particle size distribution (Mass Median Aerodynamic Diameter) and Geometric Standard Deviation. The average results are in Table 1 above.

6. Statistics

The LC_{50} was calculated using the log probit method of Miller and Tainter (Miller, L.C. and M.L. Tainter. 1944. Proc. Soc. Exp. Bio. Med. 57(2) 261-264).

II. RESULTS AND DISCUSSION

A. MORTALITY

Mortality is given in Table 1. In Group 2 (0.098 mg/L), one male and one female died within 10 minutes post exposure. One male and two females died on day 1 and one female on day 2. In group 3 (0.047 mg/L), four females died on day 1. In Group 4 (0.145 mg/L), one male died during exposure, three males and three females died within 2 hours of post exposure, one female on day 1, and one male on day 2.

LC_{50} (4-hour) Males = 0.08 mg/L (SE = 0.028)
Females = 0.06 mg/L (SE = 0.017)
The Combined = 0.07 mg/L (SE = 0.011)

B. CLINICAL OBSERVATIONS

Clinical signs seen in all rats exposed to Ziram Technical were partial closing of the eyes and an irregular respiration rate. Wetness around the mouth (as a result of salivation) was observed in rats exposed at 0.145 mg/L, 0.020 mg/L or 0.029 mg/L (Groups 4-6). Other signs included pilo-erection (at 0.020 and 0.029 mg/L), reduced activity (at 0.047 and 0.098 mg/L), a reduced respiration rate (at 0.047 mg/L). No clinical signs of toxicity were seen following day 9.

C. BODY WEIGHT; FOOD AND WATER CONSUMPTION

There were moderate to marked decreases of body weight or reduced body weight gain for up to 2 days following exposure. Subsequently, weight gain for rats that survived exposure was similar to that of the control rats. A decrease in food and water consumption was correlated with the lowered weight gain.

D. NECROPSY

Animals that died as a result of exposure had increased lung to body weight ratios, and the lungs were congested. Some of the decedent rats had a frothy fluid in the trachea, occasional swollen appearance of the lungs and gas-filled stomachs. No treatment-related effects were found in animals that survived the observation period or in the controls.

E. DEFICIENCIES

No study deficiencies were identified.

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