[ZINC OMADINE] 8/29/1996 Acute Oral - Rat (81-1)

EPA Reviewer: John E. Whalan _____ Date: _____
Review Section I, Toxicology Branch (7509C)
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Review Section I, Toxicology Branch (7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute Oral (Gavage) - Rat (81-1)

TOX. CHEM. NO: 357

P.C.CODE.: 088002

MRID NO.: 428279-01

TEST MATERIAL: Zinc Omadine® 48% Dispersion

SYNONYMS: Zinc pyrithione, zinc pyridinethione, bis(2-pyridylthio)zinc 1,1'-dioxide, bis-(1-hydroxy-2-(1H)-pyridinethionato-O,S)zinc, De-Squaman, Vancide ZP

STUDY NUMBER: MB 85-8049 A

SPONSOR: Olin Corporation, 120 Long Ridge Road, Stamford, CT 06904

TESTING FACILITY: M B Research Laboratories, Inc., Steinsburg and Wentz Roads, P.O. Box 178, Spinnerstown, Pennsylvania 18968

TITLE OF REPORT: Single Dose Oral Toxicity in Rats/LD 50 in Rats

AUTHORS: Oscar M. Moreno, Daniel R. Cerven, Elizabeth J. Altenbach

REPORT ISSUED: February 24, 1986 (study completion date)

EXECUTIVE SUMMARY: Five male and five female Wistar rats per dose group were treated orally with a 48% dispersion of zinc omadine at 260, 329, 417, 529, and 668 mg/kg body weight and observed for 14 days. There were no control groups.

Clinical signs preceding mortality included ptosis, diarrhea, lethargy, piloerection, chromodacryorrhea, chromorhinorrhea, emaciation, soiling of body surfaces, and wetness and brown staining of the anogenital area. Clinical signs noted for survivors additionally included alopecia, ataxia, bloated abdomen and ocular abnormalities. Necropsy results of the deaths included abnormalities of the lungs, liver, spleen and gastrointestinal tract. Necropsy results of the 14-day survivors included abnormalities of the spleen and adhesions in the peritoneal cavity in all dose groups, except the 260 mg/kg group, in which necropsy results were normal. **The**

LD_{50}s and 95% confidence intervals for a 48% dispersion of zinc omadine was calculated as 630 mg/kg (438-906) in males; 460 mg/kg (352-601) in females; and 560 mg/kg (427-734) in the combined sexes.

This study satisfies the guideline requirements for an acute oral toxicity study (81-1) in rats and is classified as acceptable with a Toxicity Category of II for females and III for males and for the sexes combined. [MRID No. 428279-01]

A. MATERIALS

1. Test material: Zinc Omadine

   Description: white liquid
   Lot/Batch No.: Sample # F116A
   Purity: 48% dispersion
   Stability of compound: stable at room temperature
   CAS No.: not reported
   Structure: not reported

2. Vehicle and/or positive control

   There were neither vehicle nor negative controls used in the study.

3. Test animals

   Species: Rat
   Strain: Wistar albino
   Age and weight at study initiation: Age not given, weights: 200-300 g (males), 212-286 g (females)
   Source: Ace Animals

4. Animal care

   Housing: Rats were housed 5/sex/cage in suspended wire mesh cages.
   Transfer to clean cages: not reported
   Food: Purina Rat Chow (Diet #5012), *ad libitum*, except 16-20 hours prior to dosing
   Water: *ad libitum*
   Acclimation period: ≥5 days
   Environmental conditions:
   Temperature: controlled, temperature range not reported
   Humidity: controlled, range not reported
   Air changes: not reported
   Photoperiod: 12 hour light/dark cycle

B. METHODS

Five male or female rats were randomly assigned to each treatment group. Weight variation within groups was ±20% of the mean group weight. The test material was administered once orally using a syringe and dosing needle. The study design is presented in Table 1. Animals were observed 1, 2, and 4 hours post-dose and twice daily thereafter for 14 days for signs of mortality, toxicity, and pharmacological effects. Body weights were recorded on the day of dosing, weekly, at death, and at termination in the 14-day survivors. All animals were examined for gross pathology and any abnormal tissues preserved in 10% buffered formalin for possible future microscopic examination.

The LD_{50}, 95% confidence limits, and dose response curve were calculated by the method of Litchfield, J.T., Jr., Wilcoxon, F., JPET **96**:99 (1949).

TABLE 1. STUDY DESIGN

Dose Group (mg Zinc Omadine (48% Dispersion)/kg body weight)	No. of Animals		Dose (mg of active ingredient per kg body weight)	Volume of Dose (range in μL)
	Male	Female		
260	5	5	125	41-48
329	5	5	158	54-71
417	5	5	200	70-96
529	5	5	254	80-99
668	5	5	321	110-150

Data taken from pages 4, 6-8, MRID No. 428279-01.

C. RESULTS

1. Mortality

There were 17 deaths among the 50 animals (Table 2).

TABLE 2. MORTALITY

Dose Group (mg Zinc Omadine (48% Dispersion)/kg body weight)	Mortality (No. of Animals)		No. of Deaths (Male/Female)				
	Male	Female	Day 1	Day 2	Day 3	Day 4	Day 5
260	0	1	0/1				
329	1	1	0/1		1/0		
417	1	2	1/2				
529	2	3	1/2	1/0			0/1
668	2	4	0/3		1/1	1/0	

Data adapted from page 4, MRID No. 428279-01.

2. Clinical Observations

The deaths occurred by day 5 and were preceded by ptosis, diarrhea, lethargy, piloerection, chromodacryorrhea, chromorhinorrhea, emaciation, soiling of body surfaces, and wetness and brown staining of the anogenital area. In the survivors, observations included piloerection, lethargy, ptosis, diarrhea, chromorhinorrhea, ataxia, emaciation, bloated abdomen, alopecia, chromodacryorrhea, ocular abnormalities, alopecia of ventral surfaces, soiling of body surfaces, and wetness and brown staining of the anogenital area.

3. Body Weight

Mean group body weights for males in all dose groups increased during the 14-day observation period (Table 3). Mean group body weights for females in the 260 and 329 mg (48% dispersion zinc omadine)/kg body weight dose groups increased during the study. Mean group body weights for females in the 417 and 529 mg/kg dose groups decreased during the first week, but increased during the second week. There was one surviving female in the 668 mg/kg dose group; this female lost weight during the first week and gained weight during the second week.

TABLE 3. BODY WEIGHTS (G) AND BODY WEIGHT CHANGES

Dose Group (mg Zinc Omadine (48% Dispersion)/kg body weight)	Males				Females			
	Day 0	Day 7	Day 14	Change (Day 0-14)	Day 0	Day 7	Day 14	Change (Day 0-14)
260	218	304	366	148	223	258	279	56
329	224	292	371	147	270	306	326	56
417	280	319	384	104	228	218	262	34
529	219	285	363	144	234	224	290	56
668	220	234	309	89	260	238[a]	290[a]	30

Data adapted from pages 6-8, MRID No. 428279-01.
[a]Results are from a single animal.

4. Necropsy

Necropsy results of the deaths included abnormalities of the lungs, liver, spleen and gastrointestinal tract, as well as red and brown staining of the nose/mouth area and brown staining of the anogenital area. Six of the 17 animals that died were cannibalized before a necropsy could be performed, thus the necropsy results are from 11 animals (2 of which were partially cannibalized). Necropsy results for the survivors in the 260 mg/kg dose group were "normal," however, for the other dose groups the results included splenic abnormalities, adhesions in the peritoneal cavity, alopecia of ventral surfaces, brown staining of the anogenital area and red staining around the eyes.

5. LD_{50}

Based on the results of this study, the acute gavage LD_{50}s and 95% confidence intervals for a 48% dispersion of zinc omadine in Wistar Albino rats are: 630 mg/kg (438-906) in males; 460 mg/kg (352-601) in females; and 560 mg/kg (427-734) in the combined sexes.

D. REVIEWER'S DISCUSSION/CONCLUSIONS

None

E. Was test performed under GLPs (is a quality assurance statement present)? YES

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