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

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Zinc Omadine:** Review of an Acute Inhalation Toxicity Study in Rats.

EPA ID# 088002-001258 DP Barcode D172954
Case No. 815252 Chem. ID No. 088002

FROM: John E. Whalan, D.A.B.T., Toxicologist
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Health Effects Division (H7509C)

John E Whalan 6-8-93

TO: Bruce Sidwell (PM Team # 53)
Special Review and Reregistration Division (H7508W)

THRU: Roger L. Gardner, Section Head
Section 1, Toxicology Branch I
Health Effects Division (H7509C)

Roger Gardner 6-16-93 KB 6/21/93

Olin Corporation submitted an Acute Inhalation Toxicity Study in Rats dosed with zinc omadine powder E85656 TER (95% a.i.). This study is Acceptable, and satisfies data requirement 81-3 for an Acute Inhalation Toxicity study. At the sponsor's request, only two concentrations were used, so it was not possible to perform probit analysis. The data were nevertheless adequate to define the Toxicity Category as III.

Reviewed by: John E. Whalan JW 6-8-93
Section I, Tox. Branch I (H7509C)
Secondary reviewer: Roger L. Gardner Roger Gardner 6-16-93
Section I, Tox. Branch I (H7509C)

GUIDELINE: 81-3

DATA EVALUATION REPORT

NOTE: The introduction to the final report explained that a previous whole-body exposure study (IRDC Study No. 397-050), with a 4-hour LC_{50} of 0.14 mg/l for combined sexes, overestimated the toxicity of zinc omadine because of oral ingestion due to preening of contamined fur. It failed to mention that this study tested zinc omadine FPS (48% a.i.). The following nose-only study of the technical powder (95% a.i.) was performed with the expectation that toxicity would be reduced. It is not reasonable to compare two studies using different test articles. The new study used two groups (at the sponsor's request), so probit analysis was not possible."

STUDY TYPE: Acute Inhalation Toxicity in Rats via Nose-Only Exposure

MRID NO: 421467-03

CHEM. ID NO.: 088002

TEST MATERIAL: Zinc Omadine Powder (95% purity; white powder)

SYNONYMS: Zinc, 2-pyridinethiol-1-oxide

STUDY NUMBER(S): 397-051

SUBMITTED BY: Olin Corporation

TESTING FACILITY: International Research and Development Corporation

TITLE OF REPORT: Acute Inhalation Toxicity Evaluation on Zinc Omadine in Rats

AUTHOR(S): Charles E. Ulrich

REPORT ISSUED: October 25, 1991

CONCLUSIONS: Male and female Sprague-Dawley CD® rats were exposed nose-only for 4-hours to zinc omadine powder at analytical concentrations of 0.24 and 0.61 mg/l. Particle mass median aerodynamic diameters (and geometric standard deviations) were 1.9 (2.08) μm and 2.3 (2.11) μm, respectively. One of 10 low-concentration rats and 3 of 10 high-concentration rats were found dead the day following exposure. Since only two

concentrations were used, a probit analysis could not be performed. The mortality pattern suggests the LC_{50} is >0.61 mg/l, and probably <1 mg/l. Clinical signs included decreased activity, tremors, increased salivation, labored breathing, gasping, and staining around the mouth. Mean body weight gain was inhibited somewhat in the high-concentration females. The only dose-related gross lesion was multilobar lung congestion in the high-concentration group.

STUDY CLASSIFICATION: This study is **Acceptable**, and satisfies data requirement 81-3 for an Acute Inhalation Toxicity study. It places zinc omadine powder (95% pure) into **Toxicity Category III**. Since only two concentrations were used, it was not possible to perform probit analysis. The test article purity, which was not reported, was provided by the registrant. The Flagging Statement page was not filled out. This study received Quality Assurance review.

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PROTOCOL: Male and female Sprague-Dawley CD® rats were randomly selected for this study. Their ages at the time of exposure ranged from 56 to 75 days, and their weight ranges were 268-287 g for males, and 182-216 g for females. The rats were individually housed throughout the study. They were assigned to two groups of 5 males and 5 females. Food and water were available *ad libitum*, except during exposure.

Each group was dynamically exposed to an aerosol of the test article for 4 hours in a 40-liter stainless steel and acrylic nose-only chamber. An air micronizer was used to generate fine dust particles and dispense them into the chamber. The nominal concentrations were 2.1 and 4.3 mg/l. The analytical concentrations were measured by high pressure liquid chromatography (HPLC). Particle size distribution was measured with an Anderson® 8-stage cascade impactor and HPLC.

The rats were not observed for clinical signs during exposure, but they were examined upon removal from the chambers, and three times daily thereafter. Body weights were measured prior to exposure, on days 7 and 14, and at the time of interim death. Surviving rats were sacrificed on day 14 by sodium pentobarbital injection and exsanguination. All rats were necropsied, and their major thoracic and abdominal organs were examined.

RESULTS: The following table summarizes the nature of the chamber atmospheres:

Group*	Nominal Conc. (mg/l)	Analytical Conc. (mg/l)	MMAD (gsd) (μm)
I	4.3	0.24	1.9 (2.08)
II	2.1	0.61	2.3 (2.11)

The nominal concentrations suggest that Group I is the high-concentration group, whereas the analytical concentrations suggest that Group II is the high-concentration group. During a telephone discussion on January 29, 1993, the author explained that the nominal concentration values are not reliable since they are based on the air micronizer weights, which weighs far more than the test article contained within. Thus, the nominal concentrations should be disregarded. Thus, group II was the high-concentration group.

Four rats were found dead on post-exposure day 1. The mortality pattern was as follows:

Group*	Analytical Conc. (mg/l)	Male Deaths	Female Deaths	Combined Deaths
I	0.24	1/5	0/5	1/10
II	0.61	1/5	2/5	3/10

On the day of exposure, decreased activity was observed in 3 males and 5 females in the high-concentration group, and in 1 low-concentration male. Tremors were observed in 2 high-concentration females, and 3 males and 2 females in the low-concentration group. Increased salivation was found in half of the animals in each group, and labored breathing and staining around the mouth were observed in 1 or 2 rats from each group. Gasping and labored breathing were observed for 1 to 3 days following exposure in 3 males and 5 females in the high-concentration group. Mean body weights were as follows:

Interval	**Group I ♂**	**Group I ♀**	**Group II ♂**	**Group II ♀**
Pre-exposure	281	187	279	213
Day 7	285	205	290	210
Day 14	321	211	318	221

Mean body weight gain in the week following dosing was slowed somewhat, especially in the high-concentration females which lost a small portion of their body weight. All groups gained weight at a more normal rate during the second week.

The only gross lesions found during necropsy were multilobar reddened lungs in 1 low-concentration male, and multilobar lung congestion in 1 male and 2 females in the high-concentration group. The single case of reddened lungs could have been incidental, but the lung congestion was dose-related.