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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 a Primary Eye Irritation Study in Rabbits.

EPA ID# 088002-001258 DP Barcode D172952
Case No. 815252 Chem. ID No. 088002

FROM: John E. Whalan, D.A.B.T., Toxicologist
Section 1, Toxicology Branch I
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 a Primary Eye Irritation/Corrosion Study in Rabbits dosed with Zinc Omadine Powder E85656 TER (95 a.i.). This study is Acceptable, and satisfies data requirement 81-4 for a Primary Eye Irritation Study. The Toxicity Category is I due to severe, irreversible eye trauma.

This same study was previously submitted in December, 1991 as a FIFRA Sec. 6 (a)(2) submission (MRID No. 421546-01). The purity of the test article was not reported. TB-I was erroneous informed that Zinc Omadine Powder E85656 TER has a purity of 48%, and thus the purity was incorrectly reported in the DER (HED document No. 9304; February 24, 1992). Because of this confusion, the study was reviewed anew with the same conclusions. In order to avoid confusion regarding test article purity, this new DER should replace the earlier one.

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: 81-4

DATA EVALUATION REPORT

STUDY TYPE: Primary Eye Irritation Study in Rabbits

MRID NO: 421467-02

CHEM. ID NO.: 088002

TEST MATERIAL: Zinc Omadine Powder E85656 TER (95% a.i.; off-white powder)

SYNONYMS: Zinc, 2-pyridinethiol-1-oxide

STUDY NUMBER(S): MB 91-707 D

SUBMITTED BY: Olin Corporation

TESTING FACILITY: MB Research Laboratories, Inc.

TITLE OF REPORT: Primary Eye Irritation/Corrosion in Rabbits

AUTHOR(S): Daniel R. Cerven

REPORT ISSUED: November 25, 1991

CONCLUSIONS: Severe irritation was found in both washed and unwashed eyes as evidenced by corneal opacity, sluggish and unresponsive irises, beefy red conjunctivae, severe chemosis, and marked eye discharge. The unwashed eyes had no evidence of reversibility by day 7, so the rabbits were sacrificed for humane reasons. Pannus was found in all the washed eyes beginning on day 7. Only one of three washed eyes showed signs of reversibility by day 14. It appears that the test article is not easily washed out of the eye, and even in a well washed eye, there is great potential for severe eye trauma.

STUDY CLASSIFICATION: This study is **Acceptable**, and satisfies data requirement 81-4 for a Primary Eye Irritation study. It places zinc omadine powder E85656 TER (95% a.i.) into **Toxicity Category I**, both for washed and unwashed eyes. The test article purity, which was not reported, was provided by the registrant. This study received Quality Assurance review.

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PROTOCOL: One male and 8 female New Zealand White rabbits (2.3-2.7kg), which were free from ocular lesions, were selected for this study. They were individually housed in suspended cages. Bedding was changed twice weekly. Food and water were available *ad libitum*.

A test article dose of 0.1 ml was instilled into the conjuctival sac of the lower eyelid for one eye/rabbit, and the lids were held closed for 1 second. The contralateral eye served as a control. Two minutes after dosing, the treated eyes of three rabbits were washed with 300 ml of lukewarm water. The eyes of the remaining six rabbits were unwashed.

Eye irritation was graded by the Draize technique (Draize, J.H. *et al.*, 1944) one hour after dosing, and on days 1, 2, 3, and 7 in the unwashed eyes, and on days 1, 2, 3, 7, 14, and 21 in the washed eyes. Examination with sodium fluorescein was performed at 24 hours.

RESULTS:

Unwashed eyes - Severe chemosis made thorough observations impossible for some rabbits, most notably 1 hour after dosing, and on days 3 and 7. Eye irritation was severe and persistent, with no evidence of reversibility on day 7. The only other clinical sign found was diarrhea in one rabbit on day 7. The rabbits were sacrificed for humane reasons on day 7.

Corneal opacity at 1 hour was either absent or unobservable due to chemosis. Corneal opacity involving between 25 and 100% of the cornea (generally the latter) ranged from opalescent to opaque between days 1 and 7. Sodium fluorescein observations revealed trauma to 75-100% of the corneal area in all six rabbits 24 hours after dosing.

Iridic involvement ranged from sluggish reaction in all rabbits, to no reaction in two rabbits on day 3. The only rabbit that could be examined on day 7 had no iridic reflex.

Conjunctival redness was consistently beefy red throughout the recovery period, and was accompanied by pale areas beginning on day 1. Chemosis resulted in eyelids that ranged from half closed to completely closed. Conjunctival discharge was observed as moistening of the lids and hairs just adjacent to the lids. Test article was retained in the conjunctival sac throughout the study, and a white discharge was observed beginning on day 2 in all rabbits.

Washed eyes - No corneal involvement was observed 1 hour after exposure, but by day 1, opalescent opacity involved $<25\%$ of the cornea. The corneas were opaque on days 2 and 3. All three rabbits had pannus (corneal vascularization) on days 7, 14, and 21. Pannus may have been found in the unwashed eyes had the rabbits not been sacrificed. Sodium fluorescein observations revealed trauma to 50-100% of the corneal area 24 hours after dosing.

Sluggish irises were found in all three rabbits beginning 1 hour after dosing. This persisted through day 21 in two rabbits, but reversed by day 7 in the third.

Conjunctival redness was beefy red until day 7 when it lessened to crimson red. Chemosis resulted in eyelids that ranged from half closed to completely closed. Conjunctival discharge was observed as moistening of the lids and hairs just adjacent to the lids. Test article was retained in the conjunctival sac of one rabbit through day 3, and a white discharge was observed beginning on day 1 in all rabbits.

The fact that test article was retained in one rabbit, and reversibility of the cornea (day 14), iris (day 7), and conjunctiva (day 14) were seen in another suggests that the washing of the eyes was not consistent between animals. Even in a well washed eye, there is great potential for severe eye trauma. One rabbit had rales throughout the recovery period, and diarrhea on day 14. Another had rales on day 14 and 21.