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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Zinc Omadine:** Review of a Dermal Sensitization Study in Guinea Pigs.

EPA ID# 088002-001258 DP Barcode D172962
Case No. 815252 Chem. ID No. 088002

FROM: John E. Whalan, D.A.B.T.,Toxicologist
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John E Whalan 6-16-93

TO: Bruce Sidwell (PM Team # 53)
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THRU: Roger L. Gardner, Section Head
Section 1, Toxicology Branch I
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Roger Gardner 6-16-93 KB 6/21/93

Olin Corporation submitted a Dermal Sensitization Study in Guinea Pigs dosed with zinc omadine powder E85656 TER (95 a.i.). This study is Acceptable, and satisfies data requirement 81-6 for a Dermal Sensitization Study. Zinc omadine powder E85656 TER is a dermal sensitizer.

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

GUIDELINE: 81-6

DATA EVALUATION REPORT

STUDY TYPE: Dermal Sensitization Study in Guinea Pigs (Buehler Method)

MRID NO: 421467-05

CHEM. ID NO.: 088002

TEST MATERIALS: Zinc Omadine Powder E85656 TER (95% a.i.; off-white powder)
DNCB (positive control)

SYNONYMS: Zinc, 2-pyridinethiol-1-oxide

STUDY NUMBER(S): MB 91-707 F

SUBMITTED BY: Olin Corporation

TESTING FACILITY: MB Research Laboratories, Inc.

TITLE OF REPORT: Guinea Pig Sensitization (Buehler)

AUTHOR(S): Daniel R. Cerven

REPORT ISSUED: November 25, 1991

CONCLUSIONS: Zinc omadine powder E85656 TER is a dermal sensitizer, although it is not as potent as the positive control, DNCB.

STUDY CLASSIFICATION: This study is **Acceptable**, and satisfies data requirement 81-6 for a Dermal Sensitization study. Neither the test article purity (supplied by registrant) nor the dermal scoring reference were reported. The alcohol used to dissolve the positive control, DNCB, was not specified. This study received Quality Assurance review.

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PROTOCOL: Thirty healthy male Hartley Albino guinea pigs (319-375 g) were individually housed in suspended cages. Bedding was changed twice weekly. Food and water were available *ad libitum*.

Zinc Omadine Powder E85656 TER was formulated as 1%, 10%, and 50% mixtures in mineral oil. The positive control, DNCB, was prepared as 0.1% dilutions in alcohol (not otherwise specified) for induction dosing, and in ethyl ether for challenge dosing.

Two days prior to dosing, the dorsal trunk skin was clipped free of hair to provide 5 cm x 10 cm dosing sites (approximately 10% of the body surface area). This procedure was repeated as needed before the 3rd and 6th induction doses, and before each of the four challenge doses.

A group of 10 guinea pigs was dosed with 0.5 ml aliquots of 50% Zinc Omadine Powder E85656 TER in mineral oil on a dosing site posterior to the left shoulder. The site was covered with a Hilltop Chamber, which in turn was covered with 2 mil plastic secured with adhesive tape. The guinea pigs were then placed in a restrainer. After 6 hours of exposure, the plastic and chamber were removed. A total of 9 such induction doses were given on Wednesdays, Fridays, and Mondays over 3 consecutive weeks.

Four zinc omadine powder E85656 TER challenge doses were administered. **Challenge I** was administered 14 days after the last induction using the same dosing regimen as for induction, except that doses were applied posterior to both the left and right shoulders. **Challenge II** was similarly applied 48 hours after Challenge I.

Since irritation was observed following Challenges I and II, **Challenge III** was applied 4 days after Challenge II using a 10% dilution on previously untreated skin. **Challenge IV** was applied 7 days after Challenge III onto previously untreated skin using a 1% dilution. A naive control group of 4 previously untreated animals was also dosed with the 1% dilution.

A group of 10 male guinea pigs served as concurrent positive controls. They were dosed with a 0.1% solution of DNCB in alcohol by the same regimen as the animals treated with zinc omadine powder E85656 TER. They too were challenged four times, but always with the same formulation - 0.1% DNCB in ethyl ether.

The dosing sites of the naive controls were examined 6 and 24 hours after dosing. All other guinea pigs were examined 6, 24, and 48 hours after each induction and challenge dose. Irritation was scored by the method of Draize. A sensitizing response was defined as ≥20% of a group having an irritation score of 2 (well-defined erythema) or more. All animals were examined daily for clinical signs, and body weights were measured pretest and at termination (except for naive controls).

RESULTS: The following text describes the findings (study data tables are attached):

Zinc Omadine Powder E85656 TER (50% dilution)

No irritation was observed following the first induction dose, and only 3 guinea pigs had very

slight erythema 6 hours after the second induction dose. After the third induction dose, erythema ranged from none to well-defined. On subsequent doses, erythema was occasionally moderate to severe and there was some flaking of skin beginning after the fifth induction dose. Irritation scores varied little between each examination interval (i.e. 6, 24, and 48 hours), which means that erythema was essentially unchanged throughout the 3-week induction phase. No other clinical signs were observed in any animals. Terminal body weights were approximately double the pretest weights. Without negative control weights for comparison, it is impossible to tell whether there was a compound-related effect.

Challenge I (50% dilution), which was administered 14 days after the last induction dose, caused very slight to well-defined erythema in 7 of 10 guinea pigs dosed at the original induction sites. Although the lesions were minor, there was some evidence of progression over 48 hours, and only one case of reversal. The secondary dosing site (posterior to the right shoulder), had very slight erythema in 5 of 10 guinea pigs, with the greatest incidence at 48 hours.

Challenge II (50% dilution), which was administered 48 hours after Challenge I, evoked very slight to well-defined erythema in 9 of 10 guinea pigs at the original dosing site, and in 7 of 10 guinea pigs at the secondary dosing site. Severity was greatest at 48 hours.

Challenge III (10% dilution), which was applied 4 days after Challenge II on previously untreated skin, caused very slight to well-defined erythema in 9 of 10 guinea pigs with the greatest severity at 48 hours.

Challenge IV (1% dilution), which was applied 7 days later onto previously untreated skin, affected all guinea pigs. The response was similar to that seen after Challenge III, except that the response was faster. Nearly all guinea pigs had very slight erythema 6 hours after being challenged.

Four previously untreated guinea pigs dosed once with the 1% dilution had no erythema at 6 and 24 hours.

Positive Controls (DNCB)

After the first induction dose with 0.1% DNCB in ethyl ether, very slight erythema was seen in 5 of 10 guinea pigs. Incidence and severity increased with subsequent induction dosings. By the ninth induction dose, erythema ranged from well-defined to severe with slight eschar. No other clinical signs were observed in any animals. As with the guinea pigs treated with zinc omadine powder E85656 TER, terminal body weights for the positive controls were approximately double the pretest weights. Without negative control weights for comparison, it is impossible to tell whether there was a compound-related effect.

Challenge I, which was administered 14 days after the last induction dose, caused very slight, well-defined, and moderate to severe erythema in all guinea pigs dosed at the original and

secondary induction sites. For most of the animals, erythema was well-defined. The response was consistent 6, 24, and 48 hours after dosing.

Challenge II, which was administered 48 hours after Challenge I, evoked a similar response to Challenge I except that far more guinea pigs had moderate to severe erythema at the original dosing site (8 guinea pigs compared to 1 after Challenge I). Nearly all secondary dosing sites had well-defined erythema.

Challenge III, which was applied 4 days after Challenge II onto previously untreated skin, and **Challenge IV**, which was applied 7 days after Challenge III onto previously untreated skin, elicited responses similar to Challenge I.

These data demonstrate a positive sensitizing response in guinea pigs induced with DNCB. A positive response was also seen in guinea pigs induced with zinc omadine powder E85656 TER. Perhaps the most obvious example was Challenge IV - the latest one, and the one with the lowest challenge dose. The 1% zinc omadine powder E85656 TER dilution had no effect on untreated controls, but when induced guinea pigs received the 1% dilution, the response was very slight to well-defined erythema. Only 2 guinea pigs had no irritation at 6 hours, but by 24 hours, all were affected with 4 having very slight erythema, and 6 having well-defined erythema. There was no evidence of reversibility at 48 hours.

It is surprising that Challenges I, II, and III evoked weaker reactions than Challenge IV, which used the lowest dilution. Although DNCB evoked a stronger reaction, zinc omadine powder E85656 TER clearly was a dermal sensitizer.

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