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

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MAY 16 1995

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Zinc Omadine:** Purity Data for Three Mutagenicity Studies.

EPA ID# 088002 — DP Barcode D213333
Case No. 819310 — Chem. ID No. 088002

FROM: John E. Whalan, D.A.B.T., Toxicologist
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John E. Whalan 5-9-95

TO: Bruce Sidwell (PM Team #53)
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THRU: Roger L. Gardner, Section Head
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Roger Gardner 5/11/95 — KA 5/12/95

I. Background:

The following three mutagenicity studies were previously classified Unacceptable because they failed to describe the test article. A TB-I memorandum (John E. Whalan, May 27, 1993), which contained the Detailed Evaluation Reports (DER's), stated that these studies could be upgraded upon receipt of acceptable purity data.

84-2a *Salmonella*/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test) with a Confirmatory Assay; Study No. T9153.501014; October 19, 1990; MRID No. 419065-02.

84-2b CHO/HGPRT Mutation Assay with Confirmation; Study No. T9153.332001; September 6, 1990; MRID No. 419065-03.

84-2c Micronucleus Cytogenetic Assay in Mice; Study No. T9153.122; October 22, 1990; MRID No. 419065-01.

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Olin Corporation submitted a report (MRID No. 432833-01) describing test article purity (John E. Whalan memorandum, September 23, 1994). Lot No. 9RC-290-109ZP, a 48% zinc omadine dispersion, was formulated from two batches of zinc Omadine cake — 9RC-279-P475 and 9RC-279-P476. The purities of these lots were 97.7% and 98.8%, respectively. Lot No. 9RC-290-109ZP was used in the CHO/HGPRT Mutation Assay and the Micronucleus Cytogenetic Assay. The lot number was not reported for the Ames Assay, but the test article was described as a white, milky, semi-viscous liquid — presumably the 48% aqueous dispersion.

Thus, a 48% aqueous dispersion was used in the three mutagenicity studies, but this raised another issue. Mutagenicity studies should be performed using the technical rather than an end-use product. All previous studies had used a 95% powder as the technical. What was needed was justification for using a 48% product which contained two additives not found in the 95% powder — [redacted] Olin has responded to these issues with another submission (MRID No. 435434-01). Photocopies from this report are attached.

[redacted] No inhalation data were provided. Neither [redacted] are of toxicologic significance in the 48% aqueous dispersion. Olin's justification for using the 48% dispersion instead of the powder in the mutagenicity studies is as follows:

> The following are the reasons for using the zinc Omadine® 48% dispersion over the powder in mutagenicity evaluations for FIFRA reregistration:
>
> [redacted] is added as a dispersant to enhance homogeneity of zinc Omadine® in the dispersion. (The concentration and available toxicity data for [redacted] is provided elsewhere.)
>
> When carrying out *in vitro* mutagenicity testing, e.g. Ames Assay with a powder, it is common practice to use an innocuous vehicle that the test article is soluble in, water is used in order to dilute the test article to a non-lethal concentration and guarantee equal distribution and delivery of test article consistently throughout the test system. However, the solubility of zinc Omadine® in water is only 6 ppm. While ethanol and DMSO are two solvents considered acceptable for use, Olin preferred to use the 48% dispersion of zinc Omadine® in order to minimize confounding factors when interpreting the results. The 48% dispersion is a stable, homogenous mixture that maintains its homogeneity upon further mixing with water. In addition, zinc Omadine®, as the 48% dispersion, represents a concentrated dispersion of approximately 480,000 μ_L/ml of test article that requires further dilution to obtain the highest concentration evaluated in the Ames Assay, 333

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INERT INGREDIENT INFORMATION IS NOT INCLUDED

μg/plate. Based on the solubility of zinc Omadine®, the need of a stable homogeneous dispersion, and that the 48% dispersion is made with water, Olin chose to carry out mutagenicity testing with the zinc Omadine® dispersion over the powder.

TB-I asked Olin to declare which product(s) it considers to be the technical and end-use products. Olin has declared that, "Both the Zinc Omadine Powder and the Zinc Omadine 48% Dispersion are registered as 'End Use' products. There currently are no 'Manufacturing Use' registrations for these products." "Strictly speaking, the powder may be considered the 'Technical' material." Nevertheless, Olin considers the 48% dispersion to be preferable to the powder in some studies as described in the above justification.

II. Recommendations:

Since the only deficiency in the three mutagenicity studies was the purity data, these studies are now reclassified as **Acceptable**. Revised One-Liners are attached. Guidelines require that mutagenicity studies be performed with the technical product. TB-I concurs with Olin's explanation that the 48% aqueous dispersion can be considered equivalent to a dilution of the 95% product.

TB-I considers the 48% aqueous dispersion to essentially be an aqueous dilution of the powder because the two additives, [redacted] It is reasonable to use the 48% product instead of the powder in those cases where the addition of water is of no toxicologic consequence.

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Zinc Omadine Review

Page _____ is not included in this copy.

Pages 4 through 5 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

__✓__ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

_____ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Zinc Dimethyl Dithiocarbamate

Page 16 is not included in this copy.

Pages _____ through _____ are not included in this copy.

The material not included contains the following type of information:

✓ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

_____ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

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ATTACHMENT IV

USE OF ZINC OMADINE® 48% DISPERSION IN TOXICITY TESTING

The following are the reasons for using the zinc Omadine® 48% dispersion over the powder in mutagenicity evaluations for FIFRA reregistration:

[redacted] is added as a dispersant to enhance homogeneity of zinc Omadine® in the dispersion. (The concentration and available toxicity data for [redacted] is provided elsewhere.)

When carrying out *in vitro* mutagenicity testing, e.g. Ames Assay with a powder, it is common practice to use an innocuous vehicle that the test article is soluble in, water is used in order to dilute the test article to a non-lethal concentration and guarantee equal distribution and delivery of test article consistently throughout the test system. However, the solubility of zinc Omadine® in water is only 6 ppm. While ethanol and DMSO are two solvents considered acceptable for use, Olin preferred to use the 48% dispersion of zinc Omadine® in order to minimize confounding factors when interpreting the results. The 48% dispersion is a stable, homogenous mixture that maintains its homogeneity upon further mixing with water. In addition, zinc Omadine®, as the 48% dispersion, represents a concentrated dispersion of approximately 480,000 µg/ml of test article that requires further dilution to obtain the highest concentration evaluated in the Ames Assay, 333 µg/plate. Based on the solubility of zinc Omadine®, the need of a stable homogenous dispersion, and that the 48% dispersion is made with water, Olin chose to carry out mutagenicity testing with the zinc Omadine® dispersion over the powder.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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ATTACHMENT V

ZINC OMADINE PRODUCTS

"TECHNICAL" VS "END-USE"

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Both the Zinc Omadine Powder and the Zinc Omadine 48% Dispersion are registered as "End Use" products. There currently are no "Manufacturing Use" registrations for these products.

Please refer to Attachment I, "Zinc Omadine 48% Dispersion & Zinc Omadine Powder End Processing". This describes the point in the process where, in the case of the 48% dispersion, inert ingredients are added [redacted] or where the product is dried to the powder.

Strictly speaking, the powder may be considered the "Technical" material.

Please also see Attachment IV, "Use Of Zinc Omadine 48% Dispersion In Toxicity Testing". This is our rationale for using the material for certain tox testing.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

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