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

MEMORANDUM 001691 OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

DATE:

SUBJECT: Methoprene; Dermal Sensitization (Acc. No. 231524, ~~ID~~. No. 20954-1, Caswell No. 28AAA).

FROM: George Z. Ghali, Ph.D. G. Ghali 3/24/82
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TO: Franklin Gee
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THRU: Christine F. Chaisson, Ph.D. C.F. Chaisson 3/29/82
Review Section IV
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Registrant: Zoecon Chemical Corporation
California Avenue
Palo Alto, California 94304

Action Requested:

Review and evaluation of dermal sensitization studies with methoprene in the albino guinea pig and human volunteers.

Conclusions and Recommendations:

I. Skin Sensitizing Test by Intradermal Injection:

A positive reaction was obtained. The product may be considered a skin sensitizer in the guinea pigs under the test conditions. The test is acceptable as Core-minimal data.

II. Skin Sensitizing Test by Topical Application:

No positive reation was obtained by this route. However, the negative results of this test does not preclude the conclusion that this product may be a skin sensitizer in the guinea pigs if the skin barrier is by passed. This study is acceptable as Core-supplementary data.

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III. Human Occlusive Patch Test:

Negative for skin sensitization. C01691

IV. Epidimiology Data:

The registrant stated that no incidence of skin sensitization has ever been reported among workers or other people involving in the handling of this product.

An Overview:

The guinea pig sensitizing test performed by multiple intradermal injection of the undiluted product suggested a possible allergic contact dermatitis potential. When the test was subsequently repeated by topical application rather than intradermal injection, the results were negative.

It is a fact that many chemicals which do not sensitize when topically applied would have such an effect if the skin barrier is bypassed. Therefore, it should be emphasized that the negative results of the second test does not preclude the possible sensitizing potential obtained by the intradermal injection.

However, it should also be realized that the human exposure to this product is mainly by dermal contact, therefore, topical application best simulates potential human exposure as a result of the intended use. Furthermore, the product did not exhibit any positive reaction when tested in human volunteers by the patch test workers and other people involved in the handling of this product. In view of the above, this product may not be labeled as skin sensitizer.

Review

I - Dermal Sensitization Test in Guinea Pig by Intradermal Injection

Test Chemical:

A white liquid identified as "House Plant Spray" provided by Zoecon Corporation.

Testing Laboratory:

International Research Development Corporation, Mattawan, Michigan 49071. Report dated 5/10/77.

Procedure:

A total of twelve guinea pigs were used in this study. Eight animals were treated with the test material and the other four were used as positive controls. The positive control (0.1% 2,4-dinitro-1-chlorobenzene) or the test compound was injected intradermally into a prepared area on the back and flanks of the respective guinea pigs. The injection was made 3 times a week for a total of 10 injections. The test chemical was injected undiluted in a volume of 0.1 ml per injection.

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A new site was used for each of the ten injections. Sodium cnloride solution (0.9%) was used as a negative control. The injection sites were read and scored for diameter and intensity of erythema and hight of edema at 24 and 48 hours after each injection.

Two weeks following the tenth sensitizing dose, a challenge dose, at a volume of 0.1 ml was given by intradermal injection of either the test compound or the positive control. Reaction to the challenge dose was read and scored at 24 and 48 hours following the injection.

Results:

All animals appeared normal and exhibited normal body weight gains throughout the study.

All of the eight guinea pigs treated with the test chemical (House Plant Spray) responded to the challenge dose, in both flare and wheal reactions. All of the eight showed a flare response which was greater than the average response obtained during the sensitizing phase. The author stated that examination of the individual mean values (flare) of the sensitizing doses indicated that positive values were obtained throughout the sensitizing period. The author further stated that based on the results obtained, the test compound would be considered a skin sensitizing agent in the guinea pigs.

Three out of the four positive controls exhibited a flare response to the challenge dose that was greater than that obtained in the sensitizing doses. The negative control did not exhibit any response to the challenge dose.

Conclusion:

The test chemical is a skin sensitizer to the guinea pigs under the testing conditions.

Core-Classification:

Core-minimum.

II. Skin Sensitizing Test in Guinea Pigs by Topical Application:

Test Chemical:

The test chemical was a white liquid idntified as YOUR BRAND Insect and Mite Houseplant Mist, and provided by Zoecon.

Testing Laboratory:

The study was conducted by H. I. Maibach, Department of Dermatology, University of California, San Francisco, California. The report dated 7/27/77.

Procedure:

Fifteen female albino guinea pigs were acclimated for two weeks, their left flanks were shaved and 0.5 ml of the undiluted test chemical was applied. Animals were not individually identified (according to the author), only a single treatment and challenge reading was intended. The material was held in contact using a pad of nonwoven fabric and secured by an elestoplast bandage over the circumference of the animal's trunk. All covering was removed from the application site 24 hours later. The induction procedure including shaving was repeated on days 7 and 14 with application being made to the same site as on day 0.

On day 28 the test material was applied to a freshly shaved area on the opposit flank. The patch was removed after 24 hours. Approximately 5 hours prior to the 48 hour scoring of response to the challenge dose, the test site was chemically depilated. The treatment sites were read and scored at 24, 48 and 96 hours after the challenge. No positive or negative controls were included. However, the author stated that historically positive control groups treated with DCNB have resulted in a 100% incidence of positive response.

Results:

The investigator stated that one animal died before treatment as a result of pneumonia. Four animals died during the test and four animals died between June 15 and July 6 as a result of pneumonia.

No sensitizing reaction occured in any animal.

Conclusion:

The test material is not a skin sensitizer in the guinea pigs when topically applied and under the test conditions. However, it is obvious that the reaction here is dependent on dermal uptake of the compound.

Core-Classification:

Core-supplementary. No positive or negative controls were included (See report on Laboratory Audit conductd by the sponsor; a copy is attached).

III. Draize Human Sensitizing Test:

Test Chemical:

The test chemical was identified as YOUR BRAND Insect and Mite Houseplant Mist, a white liquid provided by Zoecon Corporation.

Testing Laboratory:

The study was conducted under the supervision of H. I. Maibach, Department of Dermatology, University of California, San Francisco, California. The report was signed on 8/25/77.

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Procedure:

The test was performed according to a standard Draize method on human subjects to determine the human contact sensitization potential of the test chemical.

The test was conducted on 231 volunteers (60% Caucasian, 35% black and 5% other). The application was made for both induction and challenge using 0.5 ml of the undiluted material. The material was held in contact with the skin using unperforated pads from Johnson and Johnson. All induction applications were made to the same site, the right dorsolateral area of the back. Challenge application was made to the dorsolateral surface of the right upper arm. Each of the 10 induction patches was removed at 48 or 72 hours and the underlying skin was read and scored.

Results:

One subject only gave an equivocal response to initial challenge. However, when the challenge was repeated, no positive response was observed.

Conclusion:

The test chemical is not a human skin sensitizer under the test conditions.

Core-Classification:

Not applicable.

IV. Human Exposure:

Zoecon's records show the following cumulative total values through May 1977.

Formulation chemists have logged 400 man hours of exposure to Houseplant Mist. 173 pints of formulated material have been shipped. In the course of assessment of efficacy it is estimated that Zoecon research entomologists and independent cooperators accumulated 350 man hours of exposure. To date, with at least 750 man hours of exposure on record, there have been no reports whatever of adverse reaction in exposed individuals. Because of the low order of toxicity of this formulation, no unusually precautionary measures have been taken in the course of handling or applying this material. We feel confident that given this much human exposure history, especially since most individuals who handled the formulation did so repeatedly, any potential for inducing delayed contact hypersensitivity would have become apparent.

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Methoprene toxicology reviews

Page _____ is not included in this copy.

Pages 6 through 8 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

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___ Sales or other commercial/financial information

___ A draft product label

___ The product confidential statement of formula

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