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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D C. 20460

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11/8/84

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORNADUM:

SUBJECT: EPA Reg. No. 11678-5; Endosulfan (Thiodan)•
Skin Sensitization
Caswell No. 420
Accession No. 252182

TO: George LaRocca
Product Manager (15)
Registration Division (TS-767)

THRU: Christine F. Chaisson, Ph.D. CF Chaisson 11/5/84
Head, Review Section IV
Toxicology Branch
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FROM: George Z. Ghali, Ph.D. G. Ghali 10/22/84
Toxicology Branch
Hazard Evaluation Division (TS-769)

Registrant: Makhteshim - Agan (America) Inc. 11/08/84
New York, NY 10016

Action Requested:

Review and evaluation of a skin sensitization study.

Conclusion and Recommendations:

Under the conditions of this study, the test chemical did not induce skin sensitization in guinea pigs.

The study is classified as Core-supplementary data. The study might be elevated to Core-minimum upon the receipt and evaluation of data on positive control.

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DATA EVALUATION RECORDS

Jung and Weigand (1983). Test for sensitization properties in female Pirbright-White guinea pigs. An unpublished report prepared by Hoechst Ag. Study No. 83.0115 submitted by Makhteshim-AGan (America) Inc. on January, 1984.

Accession Number: 252182

Laboratory: Hoechst Department of Pharmacology and Toxicology, Frankfurt, postfach 800320.

Test Material: Endosulfan technical 97.2% ai, Hoe 002671 01 A097 0003 described as brown flakes.

Protocol:

1. Female Pirbright - White guinea pigs, Hoe: DHPK(SPEL), 8-10 weeks old, weighing 309-379 gm were acclimatized at least 5 days prior to the commencement of the study.

2. According to the authors, about 24 hours before the start of the test the hair on the flank skin of each animal was removed with an electric clipper over an area of about 25 cm^2. The test substance or vehicle was applied to 2.5 x 2.5 cm cllulose patches of a specially manufactured surgical plaster (Baiersdorf AG, Hamburg), which were then fixed in place on the skin. The bodies of the animals were then wrapped round with an elastic polyurethane warp-thread bandage ("Dauerbinde F", manufactured by Lohmann).

Determination of the primary non-irritant concentration:

In order to determine the concentration of the test substance still causing primary skin irritation, 0.5 ml of various concentrations of the test substance were applied in the first preliminary study to the shaved flank skin of Pirbright-White guinea pigs, one animal being used for each concentration level. The substance Hoe 002671 01 ZD97 0003 was tested over an exposure period of 6 hours in the following concentrations:

0.1 % in polyethylene glycol 400
1.0 % in polyethylene glycol 400
10.0 % in polyethylene glycol 400
20.0 % in polyethylene glycol 400
40.0 % in polyethylene glycol 400

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Evaluation of the irritant effect took place 24 and 48 hours after application.

Based onthe results of the first preliminary study, which showed that no irritant effects occurred at any of the concentrations tested, a 40% concentration of the substance in polyethylene glycol 400 was tested on 5 Pirbright-White guinea pigs in a second preliminary study in order to determine exactly the highest concentration no longer causing primary irritation. The exposure period was 6 hours. Evaluation took place 24 and 48 hours after application.

Based on the results of this preliminary study, the concentration for use in the main study was indicated as 40 % in polyethylene glycol 400.

Study for testing sensitizing properties:

For the main test 30 Pirbright-White guinea pigs were treated. Over a period of 3 weeks 20 animals were each treated 9 times (3 times per week) epicutaneously with 0.5 ml of a 40 % concentration of Hoe 002671 OI ZD97 0003 in polyethlene glycol 400, which had been shown in the preliminary study to be the highest non-irritant concentration. As a control, 10 other animals were treated with 0.5 ml polyethylene glycol 400 only. After 6 hours exposure the patch was removed and the skin washed with warm water.

After the last application the animals remained without treatment for 16 days. This was followed by two challenge treatments at an interval of 48 hours with 0.5 ml of the 40% dilution of the test material, the highest concentration no longer causing primary irritation. The 10 control animals were also included in the challenge treatments and received 0.5 ml of the 40 % dilution of the test substance also. Evaluation of the skin reaction took place 24 and 48 hours after the two applications.

Signs of primary irritation 24 and 48 hours after application were evaluated as threshold values for significant findings.

*Parts of the methedology were taken directly from the original report.

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Results:

In the preliminary study, concentrations of upto and including 40 % of the test material wre tolerated without any signs of skin irritation.

Following the first and the second challenge treatments, there was no occurance of erythema or edema neither int he treatment nor in the control groups.

The treatment did not seem to have any effect on the body weight gain. One animal died on day 24 of the study. Macroscopic autopsy on this animal revealed tne following: dark red foci on the lung, stomach lightly filled with air, spleen light in color, lobular markings on the liver, and some kidney areas light in color. however since the autopsy of all animals killed at the end of the study revealed no macroscoic abnormalities, these findigns in the dead animals are not considered treatment-related.

Conclusion:

Under the conditions of this study the test chemical did not induce skin sensitization in guinea pigs. The mean skin sensitization score is zero. However, since no concurrent or periodical positive control data were included in this study, the test sensitivity could not be validated.

Core Classification:

Core-supplementary data. The study might be elevated to Core-minimum upon the receipt and evaluation of data on concurrent or periodical positive control.