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

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

TO: Henry Jacoby, PM # 21
Fungicide/Herbicide Branch
Registration Division TS-767C

THRU: R. Bruce Jaeger, Section Head
Rev. Sec. # 1/Toxicology Branch
Hazard Evaluation Division TS-769C

FROM: David L. Ritter, Toxicologist
Rev. Sec. # 1/Toxicology Branch
Hazard Evaluation Division TS-769C

Subject: Chlorothalonil - EPA Reg. # 50534-24.

Caswell #: 215B

Action Requested: Review Human Repeated Patch Test.

Background:

SDS Biotech Corporation submits a human repeated patch test using Daconil B (Chlorothalonil) and a product designated only as F-7463. The company finds the study using Daconil B to be invalid based on several deficiencies which they have identified in the study.

Among these are:

- The induction dosage levels were high enough to produce positive dermal reactions in 9 of 50 subjects at 1 % strength and in 20 of 50 subjects at 0.1 % strength (animal testing guidelines require no response or only a slight irritation).

- 2 subjects had a positive response following the challenge dose (4 %).

Our Response:

We concur with the company's findings that the study is not acceptable for labeling purposes.

Guidelines for dermal senstization studies in animals require that the induction dosage levels be adjusted to produce nothing more than a slight irritation. The responses in many of the test subjects in this study were often quite severe. Moreover, we do not consider that 2/50 positive responses to a challenge dose constitutes significant evidence of delayed dermal sensitivity.

Our DER of this study is attached. Since we have rated this study as "Unacceptable" due to its internal deficiencies, we do not recommend further validation of it.

A copy of this Memorandum should be sent to the IBT Validation Team in RD.

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DATA EVALUATION REPORT

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STUDY: Human Repeated Insult Patch Test

LABORATORY: Industrial Biotest, Northbrook, IL.

STUDY NUMBER & DATE: 8537-08862 8/27/76

ACCESSION NUMBER: Not Accessioned.

MATERIAL TESTED: F-7463 (not further identified) and Daconil B (Chlorothalonil)

SUBJECTS: 28 Caucasian and 1 Oriental Males; 19 Caucasian and 2 Oriental Females

METHODS:

1.5 inch patches containing the induction doses were applied on Monday, Wednesday and Thursday to either the forearm or shoulder area and left for 24 hours, then scored for irritation. Scoring was for edema and erythema on a scale of 0 - 4 for each, then the results were added for a maximum irritation score of 8/8.

The test materials were evaluated at 1 % in PEG 400 for the first three 24 hour exposure periods. Thereafter, due to the high incidence of irritation, this was reduced to 0.1 %.

In all, nine induction doses were applied, unless the irritation produced by previous exposures was too severe to permit further exposure. Following a 12 day rest period, all subjects were challenged with 0.1 % material for an additional 24 hours, then evaluated for irritation.

RESULTS:

F-7463:

8/50 subjects exhibited measurable irritation following the first induction exposure. Several subjects had reactions severe enough (score of 4/8 or better) to preclude further testing until the challenge phase. Three subjects had positive responses upon challenge.

Daconil B:

11/50 subjects showed positive irritance effects following the first exposure. Maximum irritancy response occured following the 6th exposure.

2/50 subjects demonstrated positive responses to the challenge dose 12 days after the final induction dose. Of these, one had not demonstrated any irritation during the 9 induction exposures.

CONCLUSIONS:

Clearly, the induction doses were too high for the purpose of this test. The appearance of irritation following the first induction period in significant

numbers of test subjects precludes a conclusion that the response evidenced in the challenge phase was in fact a sign of sensitivity; it could have as easily been due to a direct effect of the test material. These comments apply to both materials.

Overall, we conclude that this study contains evidence that F-7463 and Daconil B are dermal irritants in man at levels as low as 0.1%, but we cannot conclude that these materials induce delayed dermal sensitivity, due both to the excessively high doses, and due to the few subjects which responded during the challenge phase.

CORE RATING:

Since there are no requirements for human testing in the Guidelines, we cannot rate this study under CORE. However, we do find that it is Unacceptable for regulatory purposes, based on our Conclusions noted above, and based on the fact that there is no identification of the Product, F-7463.

Therefore, further validation should not be required.

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