

Revised 4/14/82

Toxicology Branch/HED Review

004479

JUN 19 1985

Caswell #: 215B

To: H. Jacoby, PM # 21.

Registration No(s): 50534-7; 50534-8 (2 actions) Petitioner SDS Biotech Corp.

Pesticide Petition No(s): _____

Chemical(s): Chlorothalonil.

Requested Action(s): Review Guinea Pig Dermal Sensitization Study; approve the label Statement, "May be a potential skin sensitizer".

Recommendation: Review of the SDS Guinea Pig Dermal Sensitization Study (Acc. # 253856) revealed a negative response to dermal sensitization in this species.

Accordingly, we have no objection to amending the label Statement.

Inert(s) cleared 180.1001: Yes. BRAVO 500.

% of ADI occupied: Existing: NA Resulting: NA

Resulting % increase in TMRC: NA

Data considered in setting the ADI: NA

Attached(?): ADI printout YES/NO: TOX "one liner": YES/NO: DER: YES/NO

Existing regulatory action against registration: None.

RPAR status: Awaiting Special Review pending receipt of new rat oncogenicity study

New Data: Guinea Pig Dermal Sensitization Study (DER attached).

Data gaps: Rat Oncogenicity study due for submission in mid-1985.

Comments: This review is based on our understanding that # 50534-7 is a follow-up to # 50534-8 and does not require comment beyond that offered here.

Reviewer: Darin Guth 6-18-85

Section Head: 6/19/85

Branch Chief: _____

JUN 19 1985

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DATA EVALUATION REPORT

004479

STUDY: Dermal Sensitization Study in the Guinea Pig.

LABORATORY: Food & Drug Research Laboratories, Inc.

STUDY DIRECTOR OR PRINCIPLE INVESTIGATOR: Nelson H. Wilson for SDS.
Joseph H. Siglin for FDRL.

DATE: 4/15/82.

STUDY NUMBER: 5TX-81-0132

ACCESSION NUMBER: 253856

MRID NUMBER: NA.

MATERIAL TESTED: Technical Chlorothalonil, purity > 97 %. (coded T-117-11).

ANIMALS: Hartley-derived Guinea Pigs, young, not sexed.

ENVIRONMENTAL PARAMETERS: Standard GLP.

HUSBANDRY: Standard GLP except: no final body weights, food or water consumption values were recorded.

METHODS:

Induction Phase

A preliminary range-finding experiment was done. Then, three groups of ten animals each were shaved dorsally with an electric clipper.

One group of animals was exposed to 0.2 gm of 100% T-117-11 in saline; another group to 0.2 ml of positive control substance (0.07 % 2,4-dinitro-1-chlorobenzene; DCNB) in ethanol during the induction phase and in acetone during the challenge phase, and the third group to physiological saline alone as the negative control substance. The test materials were applied using a 2 cm square patch. The site was occluded for 24 hours, then the areas were uncovered, cleansed and graded for dermal irritation after Draize (1959) at 24 and 48 hours. This procedure was repeated every third day until all animals had been subjected to ten exposures. Application sites were: right and left scapulae, and right and left flanks; no site was used more than once in succession for the induction exposures.

Body weights were recorded initially. Animals were observed daily for appetite, appearance, behavior and gross evidence of toxicity and mortality.

Challenge Phase

On test day 35 each animal was shaved using clippers. On test day 36 the animals received 0.2 gm or 0.2 ml of the test material to which they had been previously exposed on the left flank, with the right flank serving as the application site for the vehicle only.

The areas were then occluded and bound as before. After 24 hours the patches were removed, the treated areas wiped with clean gauze, and the sites were again scored after Draize (1959) at 1, 24 and 48 and 72 hours.

All animals dying during the study were necropsied grossly. Surviving animals were destroyed and discarded.

RESULTS:

Induction Phase

No variations were reported in initial body weights. No adverse effects were reported for appetite, appearance or toxic signs.

One animal receiving T-117-11 died on day 23 of the test, apparently of causes unrelated to treatment. All other animals survived the procedure in good health.

The authors reported that several animals exposed to T-117-11 demonstrated flaking skin over various parts of the test sites and on the feet and ears on days 10 - 21. No animals in the positive or negative control groups demonstrated this condition.

The positive control animals demonstrated some mild erythema beginning on the second day of treatment; this increased somewhat during the remainder of the study.

The vehicle control animals showed no adverse response to exposure to physiological saline.

Challenge Phase

No dermal response was reported for the T-117-11 animals or the vehicle control animals challenged once more with the original materials following the seven day rest period. The DNCB positive control animals showed evidence of irritation upon single re-exposure to the substance.

Post-Mortem Examination

One male in the T-117-11 group expired during the study. PM examination failed to determine the cause.

CONCLUSIONS

Although no terminal body weights, food and water consumption values or post-mortem examination of all animals were included in the report, we believe that the main question relative to the sensitization potential of T-117-11 has been answered satisfactorily.

We consider that the reported response of the positive control animals to both the induction and challenge phases in this study, although minimal (over-all Draize scores of ca. 1.0/8.0), nevertheless contained adequate data to show a positive response. However since the test material, T-117-11, produced no such response to the challenge exposure, we conclude that T-117-11 is not a not dermal sensitizer in this study.

It must be understood that this test (the Closed Patch Method) is of little use for detecting weak dermal sensitizers. Better methods exist for this purpose. Thus we can say that T-117-11 is not a strong sensitizer, but we cannot say that it is not a weak dermal sensitizer in guinea pigs based on data submitted in this study.

TOXICITY CATEGORY:

Not a strong sensitizing agent.

CORE RATING: Minimum data.

! Draize, J.H. Appraisal of the safety of Chemicals in Foods, Drugs and Cosmetics. Assoc. of Food & Drug Officials of the U.S. Austin, Texas. 1959.

Reviewer: D. Ritter, # 47

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