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

MAY 8 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Registration No. 8340-17 - Triphenyltin Hydroxide: Reevaluation of the Dermal Sensitization Studies and Comments on Missing Data in a 21-Day Dermal Toxicity Study and a One-Generation Reproduction and Teratology Study

TOX CHEM. No. 896E
TOX Project No. 1288
Record No. 166629

FROM: John Doherty 4/29/86
Toxicology Branch
Hazard Evaluation Division (TS-769C)

TO: Henry A. Jacoby, PM 21
Fungicide-Herbicide Branch
Registration Division (TS-767C)

THRU: Edwin Budd, Section Head
Toxicology Branch
Hazard Evaluation Division (TS-769C) 5/5/86 5/6/86

Background:

American Hoechst Corporation has previously submitted two sensitization studies with the test material triphenyltin hydroxide (TPTH). The first study (refer to review by J.D. Doherty dated August 11, 1983 for PP#3F2823/FAP#3H5384) was found to be SUPPLEMENTARY for reasons which included that no positive control was included in the study and because the study was presented in summary form only without data to confirm the procedures and support the conclusions.

The second study (refer to review by J.D. Doherty dated August 22, 1985 for EPA Registration No. 8340-15) was found to be unacceptable as a definitive study to classify TPTH as a skin sensitizer. The conclusion of the study report was that under the conditions of this study, TPTH is a sensitizer.

Because of the borderline response, Toxicology Branch (TB) requested that additional studies using one or more of the other methods to assess skin sensitization must be conducted (August 22, 1985 review).

In a letter dated December 30, 1985, from Dr. Bert Volger, Manager, Hoechst AG Products Registration and Projects Coordination to Mr. Henry Jacoby (PM 21), the registrant requests that no additional sensitization studies be required. Their rationale is that TPTH is an irritant and for this technical reason the interpretation of dermal sensitization studies is hindered.

TB Comments:

1. TB requests that additional studies with TPTH to assess potential dermal sensitization reactions be provided. In order to minimize the local irritation effects to TPTH from hindering the interpretation of the study, extra guinea pigs should be included. These guinea pigs should be treated with an equivalent dose of TPTH only at the time of ~~sensitization~~ challenge, Appropriate positive and negative controls should also be included.

The request for additional sensitization studies relates to the fact that there is already a study which the registrant's own contractor has determined to be positive. Because TB determined that this study shows only a borderline effect and is not a definitive study, TB's request to assess dermal sensitization by other study types is justified.

TB acknowledges receipt of the dermal sensitization study with the positive control agent 2,4-dinitrochlorobenzene. Presentation of this study, however, is not sufficient to upgrade the study submitted in 1983 to an acceptable level. There were other deficiencies in the reporting and presentation of the study.

2. In a previous review from TB concerning a 21-day dermal toxicity study and a rat one-generation reproduction and teratology study (see review by J. Doherty dated August 22, 1985 for EPA Registration No. 8340-17), TB made reference to items of information that could not be found in the reports available to TB for review. In Dr. Volger's letter (December 30, 1985, attached) the location of this information was provided. Inspection of the archived copy of the studies verified the presence of this missing information.

Locating this information has no negative impact on changing the conclusions of the original reviews of these studies. Reviews of the data on urinalysis from the rat teratology study (for the pups) provide further support that TPTH did not affect the function of the kidney since there were no test chemical related effects in the many parameters of urine investigated.

TB has no explanation as to why the sections could not be found in the copies of these studies available for review.

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December 30, 1985

VIA FEDERAL EXPRESS

Mr. Henry M. Jacoby
Product Manager (21)
Insecticide-Rodenticide Branch
Registration Division (TS-767C)
U. S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Dear Mr. Jacoby:

Subject: TPTH Technical
EPA Registration No. 8340-17
Your Letter Dated November 25, 1985
Review of Toxicology Studies

We have the following comments to the reviews of the toxicology studies.

1. The agency found the dermal sensitization study (EPA Accession No. 258230) to be not acceptable because of the borderline response. This is the second study we have run with TPTH. The first study was submitted in 1983 (EPA Accession No. 071364) and found supplementary because no positive control was included. Attached to this letter please find a positive control study (HAG Report No. A31443) run by Hoechst AG in the laboratory that performed the original study. We would like you to consider this positive control study and to upgrade the original study from core supplementary. The problem with these studies is that TPTH is an irritant. Because of the physical nature of the compound it is impossible to obtain a perfect suspension to use in the studies. This imperfect suspension results in small areas of irritation which cannot be distinguished from a sensitization response. We feel that if we repeat the study using other methods that the same technical problem will hinder the interpretation of the results. The two studies that have been submitted indicate that TPTH is an irritant and not a sensitizer.

2. Pretest clinical data were not found in the 21 day dermal study (EPA Accession NO. 258230). This information is located in Appendix Q, Pages 343-372.

3. Urinalysis data were not found in the one generation reproduction and teratology study (EPA Accession No. 258229). The individual data are located on pages 224 to 277. Due to the nature of this data only a summary of urine volume is provided.

4. Additional information was requested on the dermal penetration study (EPA Accession No. 258231). This information is currently being generated.

Please do not hesitate to contact me should you need any additional comments.

Very truly yours,

B Volger

Dr. Bert Volger
Manager, Hoechst AG Products
Registration & Projects Coordination

BV:ad

Attachments (3)