



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

AUG 02 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: EPA Id# 109702-000279. Cypermethrin: Response to submission of historical control data for the dermal sensitization (series 81-6) study.

TOX CHEM No.: 271DD

PC No.: 109702

TOX PROJECT No.: 2-1857/D176168

Submission No.: S414817

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THROUGH: Marion Copley, DVM, Section Head *Marion Copley 7/28/92*
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I. CONCLUSION

The historical control data are considered appropriate to consider the dermal sensitization study (series 81-6, MRID No.: 403777-01, ICI # CTL/P/866, June 1, 1984) acceptable for review. Additional reservations pertaining to the reporting of this study are noted in comment 3 below.

Since cypermethrin has been demonstrated to be a sensitizer, all products containing cypermethrin should contain the notice that it "contains a known sensitizer" and the appropriate precautionary statements.

TB-I requests that the registrant provide a comprehensive summary of the several series 81-6 (dermal sensitization) studies conducted with cypermethrin and its formulations. See item 4 below.



II. ACTION REQUESTED

The ICI Company has responded to the Phase 4 review of the dermal sensitization study with cypermethrin (MRID No.: 403777-01) which was determined to be upgradable if positive control data were submitted by providing positive control data from another study with cypermethrin technical. The registrant has provided the requested information and requests that the study be upgraded to an acceptable level and the study be used to fulfill the study data requirement (for an 81-6 study).

III. Toxicology Branch Comments

1. The study (MRID No.: 403777-01) was retrieved on microfilm from the archives. There was no DER for this study on file in the HED "one liners" for cypermethrin. The study author determined that cypermethrin was positive in this study. Following the first challenge with 50% (w/v, cypermethrin in corn oil), 12 out of 20 test animals but only 1 out of 10 control animals had mild to moderate erythema. Following rechallenge to 20 animals at 5%, 20% and 50 % (w/v), 1 at 5%, 8 at 20% but 7 at 50% showed scattered to mild and moderate erythema. The control group was consistently less than the test chemical groups except when the 5% solution was tried. Thus, there is good evidence that this study is positive.

2. In order to satisfy the Agency's request for positive control data in this strain of guinea pig using the same method of induction and challenge, the registrant provided a document entitled "First supplement to Phase 3 (summary of MRID 403777-01) Cypermethrin 70% technical material: Skin sensitization study." dated November 8, 1991 under MRID No.: 422447-01.

In this submission, data on using formaldehyde as a positive control in a guinea pig sensitization study were reported. The results indicate that 17/20 animals in the test group responded with intense redness and swelling. In the naive control group, 5/10 animals responded but the response was stated as being clearly greater in the groups dosed with formaldehyde. TB-I considers that the information demonstrate that the guinea pig strain (assumed to be the same strain and similar test conditions as the study with cypermethrin) is responsive to dermal sensitizers. Since the main study with cypermethrin was positive, TB-I does not consider additional positive control data are necessary.

3. A cursory inspection of the study report for the main study (under MRID No.: 403777-01 reveals several other deficiencies in reporting that should be required to be included if this study is eventually reformatted and submitted to satisfy the requirement

for a 81-6 dermal sensitization study. These include:

- chemical analysis of the test material (identification of the cis/trans ratio and the remaining 30% of the sample).
- individual animal data for the responses to induction and all challenge applications.
- body weight of the guinea pigs at the start of dosing and after challenge.

The registrant should refer to the recommended guidelines for submitting series 81-6 dermal sensitization studies.

4. Review of the HED 'One liners' file indicates that there are other studies with either technical grade cypermethrin and its formulations that are also positive for dermal sensitization. In this regard, the issue of whether or not the study discussed above precisely conforms to the recommended guidelines for an 81-6 study is bureaucratic. Products containing cypermethrin should be labelled "contains a known sensitizer" and appropriate precautionary statements included in the label.

Note: In order to further clarify the issue regarding potential dermal sensitization due to cypermethrin, the re-gistrant is requested to provide a summary report and comprehensive table that lists all the series 81-6 dermal sensitization studies with technical grades of cypermethrin (and cypermethrin minus) as well as its formulations. The table should contain the identification of the study, the date, strain of guinea pig, identification of the test material (% purity, isomeric ratio) method used, dose levels of test material and results.