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

FEB 12 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: EPA Id #109701. Permethrin: Phase IV Company response regarding the acceptability of a mouse cytogenetic toxicity study and dermal penetration data.

TOX CHEM No.: 652BB
PC No.: 109701
TOX PROJECT No.: 2-0840 and 2-0893
Submission No.: S408595 and S409011

FROM: John Doherty
Section IV, Toxicology Branch I
Health Effects Division (H7509C) for JD 2/4/92

TO: Christine Rice/Linda DeLouise
Product Manager #52
Special review and Reregistration Division
(H7505C)

THROUGH: Marion Copley, DVM, Section Head Marion Copley 2/4/92
Section IV, Toxicology Branch I
Health Effects Division (H7509C)

I. CONCLUSION

The structural chromosomal aberration study is not considered acceptable primarily because no females were included. A second study consistent with the genetic toxicity guidelines found in 40 CFR Part 798 is required.

TB-I has already reviewed the army dermal absorption data which the registrants plan to submit and has determined that they are SUPPLEMENTARY data and cannot be used for commercial regulatory purposes. A dermal absorption study that is consistent with current guidelines is required.

II. Action Requested.

The FMC and ICI Corporations have responded to the Phase IV review of the toxicity data base for permethrin (refer to two letters from Linda A. Dansbury of FMC and Dansbury and Robert E. Hawk of ICI both dated November 25, 1991). In particular they have requested that the structural chromosomal aberration study (84-2, MRID No.: 00054739) be reclassified as acceptable. The FMC Corporation has also advised EPA that they intend to submit dermal absorption studies conducted by the U.S. Army in order to fulfill the requirement for an 85-3 dermal absorption study. Toxicology Branch has considered the comments provided by the FMC and ICI Corporation and the following comments apply.

III. Toxicology Branch Comments.

1. 84-2. Structural chromosomal aberration study. (MRID No.:00054739 for original study and rebuttal to EPA comments in MRID No.: 421098-02).

The issue of the acceptability of this study was discussed with Dr. Kerry Dearfield, specialist in mutagenicity/ genetic toxicity (SACB, HED). The following deficiencies were noted by Dr. Dearfield.

-Major deficiency. No females were used. The current guideline for this test requires the inclusion of both sexes. While the company states there is no evidence for a sex difference, there really isn't at this time enough evidence to rule out possible sex differences either.

-Inappropriate sampling times. Neither experiment in the existing submission meets the current recommended criteria for sampling times.

In conclusion, a new study to satisfy the structural chromosomal aberration category is considered necessary. HED considers it important that there are no acceptable studies in the chromosomal aberration category. The toxicity data base for pesticides should have at least one fully acceptable study to fulfill this requirement.

2. 85-3. Dermal absorption study.

The registrant plans to submit dermal absorption studies that were conducted by the U.S. Army which were previously reviewed by TB and determined to be SUPPLEMENTARY. They are considered useful in obtaining an estimate of the dermal

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absorption of permethrin when the permethrin is applied to military fabric and the fabric is affixed to rabbit skin. The current estimate for absorption for permethrin based on this study is 30 to 70%. This wide range is considered too inexact for non-military regulatory purposes. In addition, the methods used are not consistent with the guideline procedures for dermal absorption studies.

Thus, the registrant should be advised that the army studies on dermal absorption are not considered acceptable by TB-I for supporting commercial registrations of permethrin. Studies consistent with the current dermal absorption guidelines and acceptance criteria should be conducted and submitted.

72-5 Life cycle - fish

ICI and FMC are citing an existing study which was previously submitted by FMC Corp. and classified as acceptable by the USEPA on March 7, 1987. The letter of acceptance is included in this response as Attachment 1. The study, Accession No. 096699 is titled "Chronic Toxicity of FMC 33297 to the Fathead Minnow".

72-7(a) Simul. field - aquatic orgs.

FMC Corporation and ICIA request a waiver for conducting this study. It is the belief of ICI and FMC Corporation that a new simulated aquatic field study should not be required. We believe that this data requirement should be waived for the following reasons:

An enormous body of information exists concerning the aquatic toxicity of the pyrethroids in general and permethrin in particular. We are in the process of compiling this information, together with the original references. We plan to submit this to EPA by 1/15/92.

It has come to our attention that a simulated aquatic study with permethrin has recently been conducted. This study was conducted by the Fish Pesticide Research Laboratory in Columbia, Missouri. The Senior Author for this study Tom LaPointe has previously served as a consultant to EPA. A final report is expected in approximately two months.

EPA has committed to provide a policy position for all pyrethroids by 11/92. Any information generated in an additional mesocosm study would only duplicate data already available (see above) and further, would not be available until after the EPA policy is finalized.

84-2(b) Structural Chromosome Aberration

ICI and FMC do not believe that this study materially differs from the current guidelines and respectfully suggests it should be reclassified as acceptable. ICI and FMC address each of the items raised by the EPA in the Phase 4 DCI correspondence for the Phase 3 summaries of MRID 54739, Permethrin (PP557): Cytogenetic Study in the Rat. We will also submit our response in 86-5 format.

EPA Comment: Inappropriate sampling times were used in this study.

REFERENCE
Richold M., Ashby, J., Bootman, J., Chandley, A., Gatehouse, D.G. and Henderson, L. (1990) "In vivo cytogenetic assays" In: Kirkland, D.J. (ed) "Basic Mutagenicity Tests. UKEMS recommended Procedures Cambridge University Press, pp. 115-141.

85-2 Dermal Penetration

FMC and ICI will be submitting existing studies to the EPA that fill the Dermal Penetration requirement. It has recently come to our attention that in order to obtain the use of permethrin on army uniforms, a number of studies were conducted, including a Rabbit Dermal Penetration study. These studies were not conducted by FMC or ICI; therefore, we have not previously had an opportunity to review them for submission to the EPA to support permethrin for reregistration. As this use pattern was recently approved by the EPA these studies should meet current guidelines. The studies will be submitted to the EPA by 1/15/92. If, after reviewing those studies, ICI and FMC feel that the studies that exist do not adequately address Dermal Penetration, we will at that time commit to conduct a study.

162-3	Anaerobic aquatic metabolism
162-4	Aerobic aquatic metabolism
164-2	Aquatic field dissipation

ICI and FMC request a waiver from these data requirements for the following reasons:

EPA Comment: These studies are required since permethrin has aquatic food and non-food uses.

Response: The aquatic food use on watercress will be cancelled.

Response: Some of the customers of both ICI and FMC have labels with uses for the control of adult mosquitos. We wish to emphasize that permethrin is labeled as a mosquito adulticide, which is a terrestrial use; to our knowledge, there are no labeled uses of permethrin as a mosquito larvicide, which would be an aquatic use. We know of no other use patterns registered by FMC, ICI or our distributors which would constitute an aquatic use pattern.