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

MEMORANDUM JUN 21 1982

TO: Franklin D. R. Gee, Product Manager #17
Registration Division (TS-767)

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Meeting Between Penick Representatives and Toxicology Branch Concerning Toxicity Data Base for Resmethrin.

TOX Chem. #83E

Present at the meeting:

Penick	EPA
Dr. M. L. deVries	Dr. O. E. Paynter, HED
Dr. C. King (consultant)	Dr. L. Kasza, HED
	J. Doherty, HED
	E. Budd, HED
	F. D. R. Gee, RD

The meeting was held at 1:30 P.M. in the 11th foor conference room on Thursday, May 27, 1982.

The meeting began with a presentation by Drs. deVries and King on the outcome of the reevaluation of the pathology of the rat liver. The registrants presented to EPA a report prepared by Drs. Hess, Thompson and Becci of the Food and Drug Research Laboratories which concluded that there was no oncogenic effect of resmethrin in the rat liver. Since this conclusion is in conflict with the previous reports for this study, Dr. King described the classification of the liver lesions. After some discussion of this classification system, EPA agreed to evaluate the report and to make its recommendations on the oncogenic effects in the liver (if any) after this evaluation.

Dr. deVries listed several other problems which are outlined in the attached letter dated May 25, 1982. Some of the highlights related to these problems are as follows:

1. Regarding the rat chronic feeding/oncogenic study:

The registrant was informed that there may possibly be an oncogenic effect of resmethrin in the thyroid gland. Toxicology Branch stated that a memo would be prepared describing this problem and requesting Penick to provide historical control information related to follicular adenomas and carcinomas in the thyroid. Toxicology Branch

also informed the registrant of its concern that some of the adenomas originally reported as being present in the high dose test groups were changed to cysts whereas similar changes were not reported for the control groups.

At this time (May 28, 1982) the problem of there being a possible neoplastic effect of resmethrin in the thyroid is unresolved.

As for the chronic feeding aspects of this study, the assignment of a NOEL will be addressed in a subsequent memo. The registrant was advised by EPA that 500 ppm will be assigned as the NOEL for this study for non oncogenic effects. The reduced spleen weight in the low dose test group is not considered to be related to ingestion of the test substance. This is because there was no accompanying histopathology to indicate that the spleens were affected by resmethrin. Since the spleen is a vascular organ, differences in weight may vary widely.

Note: The pathology report dated April 30, 1982 (EPA Acc. No. 247579) indicated that there was a dose related increase in "hypertrophy of hepatocytes" as 3/60, 12/60, 25/60 and 30/60 for the females in the, control, low, mid and high dose test groups respectively. This information was not available when TB agreed to assign a NOEL of 500 ppm. This type of lesions is commonly associated with increased enzymatic activity of the liver which is involved in detoxifying xenobiotics. TB does not consider this type of lesion serious enough to require additional work to establish a true NOEL. ADI determinations may, however, use a safety factor larger than the customary 100 fold.

2. Regarding the mouse oncogenesis study:

Dr. Paynter explained that Toxicology Branch would not formally assign a NOEL for amyloidosis but also explained that the amyloidosis which occurs in the low dose test group is not of toxicological and/or regulatory concern.

2

3. Regarding neurotoxicity testing:

J. Doherty advised Dr. deVries that no additional studies to assess the neurotoxicity of resmethrin are required.

4. Regarding the three-generation reproduction study:

Dr. Paynter informed the registrants that Toxicology Branch will not insist upon a clear NOEL for a reproduction study unless there are definite effects noted in a reproduction study which occur at levels significantly below levels considered as the NOEL in chronic feeding studies. Thus, the registrant was informed that a second reproduction study is not likely to be required.

The registrant was also informed that a final reply to their submission of July 27, 1981 will be delayed pending review by Toxicology Branch statistician.

5. Requirements for subchronic inhalation testing:

Dr. Paynter explained his rationale for requiring a subchronic inhalation (90-day) study for technical resmethrin.

John Doherty, Ph.D. 6/23/82 Rodd 6/23/82
Toxicology Branch
Hazard Evaluation Division (TS-769)

Attachment

cc: TOX File

OPP:HED:TOX: J.DOHERTY:sb 5/28/82 X73711 Rm. 814 #ml3