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

APR 23 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Chlordane Addendum to Pathology Reports for Chronic Toxicity Studies of Chlordane in Mice and Rats performed by the Research Institute for Animal Science in Biochemistry and Toxicology.

Accession No. 242750
EPA Registration No. 876-273

Toxicology Chem. No. 174

TO: George LaRocca, Product Manager #15
Insecticide Rodenticide Branch
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FROM: Henry Spencer, Ph.D. 4/22/85
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THRU: Albin B. Kocialski, Section Head ABK 4/23/85
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Background:

Several chronic feeding/oncogenicity studies have been completed by the Research Institute for Animal Science in Biochemistry and Toxicology, Japan, for the Velsicol Chemical Company. A mouse study using the ICR strain for 24 months (Acc. Nos. 254665, 251815) was submitted as well as a 30-month study in Fischer 344 rats (Acc. Nos. 252267 and 254667). Gary M. Williams, M.D., the consultant pathologist to Velsicol, has reviewed these studies and has submitted his opinions in this addendum (Acc. No. 242750) recieved by the Agency on January 30, 1984.

Comments:

The Toxicology Branch makes the following comments with regard to Dr. Williams' report.

1. There appear to be some inconsistencies in the addendum and we note them to be as follows:

   a. The numbers of mice or rats at risk in the studies are not necessarily the total started in each group since interim sacrifices were made.

   b. The length of treatment in Dr. Williams' report varies from that in the studies.

2. The Agency notes the comments made by Dr. Williams that:

   a. Chlordane gives weak indications of being a carcinogen.

   b. Chlordane appears to be organ specific for the liver.

   c. The possible mechanism for the oncogenicity of chlordane.

   d. The effects in mice are hepatocellular swelling in the mid-and high dose males and females; hepatic adenomas and hemangiomas in the high dose males (which were statistically significant) and that the effect in rats was a statistically significant increase in hepatocellular adenomas for high dose males.

   e. Liver hyperplasia was present in the high dose male rats tested as were liver adenomas, but that in the mouse, liver adenomas were present but no hyperplasia was reported even though hyperplasia was a separate pathological category listed in the report.

3. The Toxicology Branch is well aware of the fact that various factors may alter the response of species and strains of animals to any toxic chemical. However, it is the position of the Toxicology Branch at this time to determine whether or not there are increases in tumors as a result of exposure to the chemical as well as a decreased latency period in the appearance of tumors.

4. Dr. Williams suggests that a risk assessment for chlordane should be based on a non-genotoxic model, i.e., based on his proposed possible mechanism of oncogenicity for chlordane.

The Toxicology Branch however, finds that in evaluating oncogenic risks, the type of response data that are present usually dictate the type of model used in the assessment (personal communication with B. Fisher, statistician). As a result, if the data are supportive of genotoxic results, a model in which a best fit is made may be used in the risk assessment.

Dr. Williams' comments will be given due consideration following a complete review, evaluation and classification of these two studies.