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Study Type: Oncogenicity - Mouse (National Cancer Institute Sponsored Study)

Accession No.:

MRID No.: 73372

Sponsor: National Cancer Institute

Testing Laboratory: Gulf South Breeze Research Institute

Date: 1979

Review:

The test material used for this study was diazinon and was obtained from the Ciba-Geigy Co. The identity and purity of the batch (Lot No. F1-741308) was said to be confirmed by the Gulf-South Research Institute and the material was said to be 98 percent pure. The report stated that independent analysis of the material did not indicate changes in composition on storage for 4 years. The conditions of storage and results of analysis were not provided in the report.

The test animals used in this study were B6C3F1 mice which were obtained from the NCI Frederick Cancer Research Center. The mice were approximately 6 weeks of age when placed on the study and were dosed for 103 weeks. There were 25 of each sex for the control groups (concurrent) and 50 of each sex for the diazinon treated groups which were dosed with 100 (low dose) and 200 (high dose) ppm. The dose levels were selected based on the results of subchronic feeding studies which showed weight loss at 800 ppm and deaths for all mice at 1600 ppm and above. Diazinon was more toxic to the mice than to the rats. The mice were observed for 2 weeks after stopping the test diet, thus, the survivors were 105 weeks of age at sacrifice.

Survival: There was no trend toward dose related increases in death in either sex (Tarone test, report analysis). There were 98 percent, 90 percent, and 84 percent survivors among the males and 98 percent, 100 percent, and 96 percent survivors among the females for the high-, low-, and control groups which survived to week 76. Thus, there were nearly 45 to 50 mice of each sex per dosed group and 21 to 24 controls at risk for late developing tumors.

The body weight gains for all dosed male mice were reported as being similar to the control group. The female mice were reported to be slightly lower in weight than the controls for the last 20 weeks of the bioassay. The report also states that "hyperactivity" was noted in the dosed mice but was rare in the control groups. The was no table or summary of the incidences of hyperactivity presented.

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No hematology, clinical chemistry or urinalyses were determined. No organ weights were made.

Pathological Findings: No table summarizing the gross necropsy findings was available and since there were no individual animal pathology sheets attached, TB could not verify if gross necropsy lesions were followed up by microscopic analysis. The microscopic pathology summary tables indicate that most of the tissues/organs were examined for the mice.

The study report concluded that "histopathologic examination provided no convincing evidence for the carcinogenicity of diazinon in B6C3F1 mice under the conditions of this bioassay."

The data provided support this conclusion. Some individual organs are discussed below:

1. Liver. In the males the low-dose group had 20 incidences in 46 mice examined of hepatocellular carcinomas and the control group had only four incidences among 21 mice examined. When compared to the control group the low-dose group was statistically significant. The high-dose group had 10 incidences of 48 mice examined and was not statistically different. The higher frequency in the low-dose group is considered by TB to be incidental. Moreover, the combined incidences of hepatocellular carcinomas and adenomas was not statistically significant at either the low- or mid-dose levels.

   TB also notes that the historical control data indicate that male B6C3F1 mice have this tumor over the range of 16 to 58 percent; the 43 percent incidence noted in this study is within historical control limits.

   The other tumor types noted were commonly occurring neoplasms. There were no dose-related increases in lymphomas or leukemias.

Conclusion:

This study is CORE MINIMUM. The study report which is a summary of the original data (no original data were examined by TB) presents evidence that the mice were dosed for 103 weeks and that no indications of diazinon related neoplasia resulted. Since the study was sponsored by the National Cancer Institute, a neutral organization, TB is not requesting the original data of the study. It should be recognized that the maximum tolerated dose was not reached for the males and may have been reached only for the females. The data provide a basis for the conclusion that diazinon was not associated with increased incidences of neoplasms at dose levels up to and including 200 ppm.

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