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

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

TO: Gary Otakie
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FROM: Irving Mauer, Geneticist
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02-08-84

THRU: William L. Burnam, Chief
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SUBJECT: Trichlorfon - RS

The following oncogenicity study has just come to light:

Teichmann et al.: "Testing [TCF] for Carcinogenic Activity in Rats by Oral and Intraperitoneal Application" Arch Geschwultsforch 48(2): 112-119 (1978).

It apparently was missed in the PSD bibliography (although the companion study in mice is included therein as MRID #00069026).

A review of this study (attached) adjudged it to be INVALID DATA, due to a numbr of major deficiencies and other inadequacies.

TOXICOLOGY BRANCH: DATA REVIEW

Chemical: Trichlorfon (TCF)

Caswell No.: 385
Shaughnessey No.: 057901

Study Type: Oncogenicity in Rats

Citation: B. Teichmann, F. Hanschild and A. Eckelmann, "Testing of 0,0-dimethyl (1-hydroxy-2,2,2-trichloroethyl)-phosphonate (Trichlorphon) for Carcinogenicity Activity in Rats by Oral (Esophageal-Gastric Intubation) and Intraperitoneal Application." Arch. Geschwulsforsch., 48/2 (1978), 112-119

Accession No./MRID No.: GS0104157-2 (RS)

Sponsor/Contracting Lab.: N/A

Report No./Date: N/A

Test Material: Recrystallized (>99%), dissolved in isotonic saline for administration.

Procedures: Groups of 30 male and 35 female "albino" rats 10-weeks old were given test material twice weekly for 90 weeks by two routes: gavage at a single dose of 22 mg/kg; i.p. at a single dose of 12 mg/kg. Controls (25 male:25 female) received saline by each route. All animals dying during the treatment as well as all survivors (sacrificed at 118 weeks) were examined grossly as well as by histopathologic procedures. No statistical methods were reported.

Results: Four orally-treated and 2 parenteral animals given test substance died by 40 weeks (no statement was made in the text with respect to mortality in controls); these animals were stated to have succumbed to bronchopneumonia.

Summary statements in text as well as a single tabulation list the number, site and/or type of tumor found during the treatment period (and time to death) and/or at sacrifice, as well as other (non-tumorous) pathological changes resulting in deaths. A total of 11 animals on oral trichlorfon and 13 given test substance i.p. had tumors, compared to 14 controls each for both routes. From the single summary tabulation, there appeared to be also no differences in tumor incidences with respect to tissue type, malignant, benign or combined, by either route of administration.

Ovarian cysts were reported in 19/70 treated females (both routes combined) and "liver steatoses" (fatty degeneration) in a total of 34 treated animals (a comparable number of affected males and females by either route), versus 11/50 female and 4 (2 male:2 female) controls respectively. Average lifespan of treated rats was said to be lower than controls, but no data were presented.

Thus, the authors concluded trichlorfon "..... demonstrated ..... no carcinogenic activity ..... for either route of application in rats."

Core Classification: INVALID DATA, due to the following major deficiencies:

(1) Only summary data are presented.

(2) Only one dose level per route of administration; and that level, insufficient.

(3) Inadequate dosage schedule.

(4) Insufficient number of animals of each sex tested.

(5) Strain of rat not specified.

(6) No details given on survival, or separate tumor types, etc.

(7) List of tissues examined histologically was not provided.

The study may also be criticized on the following points:

(1) The test substance was a purified preparation (synthesized and re-crystallized, and not (preferably) the TGAI.

(2) The test substance was not administered in the feed.

(3) Although the animals were sacrificed at 118 weeks, they dosed for only 90 weeks (i.e., not a "lifetime", or at least 2 years).

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