DATA EVALUATION RECORD

TRICHLORFON

Carcinogenicity

CITATION: Gibel W, Lohs K, Widner GP, Ziebarth D. 1971. Experimental animal studies on the hepatotoxic and carcinogenic activity of organophosphorous compounds. I. Trichlorfon. Arch. Geschwulstforsch. 37(4): 303-312.

REVIEWED BY:

William L. McLellan, Ph.D.
Senior Scientist
Dynamac Corporation
11140 Rockville Pike
Rockville, MD 20852
301-468-2500

Signature: William L. McLellan Ph.D.

Date: July 28, 1983

Cipriano Cueto, Ph.D.
Program Manager
Dynamac Corporation
11140 Rockville Pike
Rockville, MD 20852
301-468-2500

Signature: Cipriano Cueto

Date: 28 July 1983

APPROVED BY:

Irving Mauer, Ph.D.
EPA Scientist

Signature: Irving Mauer

Date: 07-30-83

DATA EVALUATION RECORD

STUDY TYPE: Carcinogenicity in rats by oral gavage, carcinogenicity in rats by subcutaenous injection, and carcinogenicity in rats and mice by cutaneous application.

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ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Institute for Cancer Research, Berlin-Buch.

TEST MATERIAL: Trichlorfon, 98 percent pure after 2 times recrystallization from water, served as the test compound.

PROTOCOL:

1. The test animals were as follows:

   Species/Strain: Wistar rats and AB/Jena mice of both sexes.

   Age and Weight: The animals were two months old at initiation of dosing, but their weights were not given.

2. The compound was administered to rats:

   a. By stomach tube, 3 times a week at 30 mg/kg until death (80 rats). Maximum observation time was 705 days.

   b. Subcutaneously, 3 times a week at 30 mg/kg until death (80 rats). Maximum observation time was 720 days.

   The compound was administered cutaneously to mice three times a week for five months:

   a. One group (20 mice) received trichlorfon alone. Maximum observation time was 790 days.

   b. One group (20 mice) received trichlorfon plus croton oil (drops), weekly for six months. Maximum observation time was 781 days.

Control animals, 20 in each group were included.

The solutions (vehicle not stated) were made fresh for each dosing.

3. Animals were fed a standard diet, weighed weekly, and observed for toxic signs. Macroscopic and microscopic pathology was evaluated on animals that lived longer than 6 months.

RESULTS:

Fatty liver was found in all dosed animals in every group, but in no controls. In all these livers, lesions were present varying from anisokaryosis and moderate fatty changes, through central necrosis with hyperemia and hemorrhage, to necrotic cirrhosis. Two malignant tumors were found in mice after cutaneous application, one at 17 months after administration of trichlorfon alone, and one after administration of trichlorfon and croton oil for 14 months. A polymorphous cell sarcoma also appeared in the latter group.

CONCLUSIONS:

A long-term study (705-781 days maximum) was conducted in Wistar rats and AB/Jena mice to assess the hepatotoxic and carcinogenic activity of trichlorfon. Administration to rats was by oral gavage or by the subcutaneous routes at 30 mg/kg, 3 times a week, for lifetime. Administration to mice was cutaneously with test compound alone or with croton oil, three times a week for 5 months. The compound produced severe liver damage ranging from fatty liver to frank necrosis. Liver tumors were also found.

It could not be determined if mortality was excessive and this would have precluded evaluation of carcinogenicity. The mean observation time in the various groups was: 437 days, oral; 426 days, subcutaneous; 545 days cutaneous; 566 days cutaneous plus croton oil. Mean observation time on controls was not given and only the number of animals surviving at six months was stated. Since only one dose, was used, a dose related trend for hepatotoxicity could not be established. The data lacked sufficient detail for any quantitative assessment of the compound's effects.

← oncogenic (Qln, 07.30.83)

CORE CLASSIFICATION: ~~Invalid~~ Supplementary (Qln, 07.30.83)

The study is Core ~~Invalid~~ since only summary data were presented. The following deficiencies in the study were noted by this reviewer:

1. Deaths from massive liver necrosis may have precluded manifestations of tumors.

2. Histopathology was conducted only on animals surviving past 6 months, and the number of animals examined histologically could not be determined.

3. No data on mortality or histology of control groups was presented. A vehicle control was not included nor was there a control group of mice receiving only croton oil cutaneously.

4. Only one dose level was administered by each route, and this dose may have caused excessive mortality. Cutaneous administration was for only 5 months.

5. Survival data was given only at 6 months; evaluation of toxicity data would require survival data at 12 and 18 months.