TOXICOLOGY RANCH: DATA REVIEW

Chemical: Trichlorfon (TCF)  
Caswell No.: 385  
Shaughnessy 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. Geschwulstforsch., 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 stated to have been performed.

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 (among other inadequacies):

(1) Purified (synthesized and re-crystallized) test substances, and not the TGAI.

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

(3) Inadequate dosage schedule.

(4) Not a "lifetime" study (i.e., at least 2 yr.).

(5) Compound was not administered in feed.

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

(7) Strain of rat not specified.

(8) Only summary data presented.

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

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

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Hazard Evaluation Division (TS-769)
Jechtmann et al. (1978) - TCE in RATS

Precautions:
- Sustainably synthesized, anhydrous, chloral with dimethyl.
- Re-crystallized to > 99% a.i., dissolved in physiological saline, buffered with 5% dextrose.

Animals: Groups of 30 each

♂️ 35 female "albino" rats, 10 were treated with:

- 22 mg/kg, 2x/week
- 30♂️
- 35♀️ — i.p. 2x/week
- 12 mg/kg

Duration of Rx: 90 weeks, sac'd at 118 weeks.


Pathology: Both gross & histo. of each animal.

RESULTS:
- 4 oral-TCP + 2 i.p., died by 40 weeks Rx, of
  - Mamm CA — 1♂
  - Lp-Ad CA — 2♀
- Lung — 4♂: 6♀
- Adrenal Ad CA — 1♀
- Skeletal — 1♂
- Femoral — 1♀

Controls — Oral
- Lung Ad CA — 1♂
- Mamm CA — 2♀

Results — Injection
- Liver Ad CA — 1♀
- Lp-Ad CA — 1♀
- Mamm CA — 2♀
Other path. cts (non-tumors) (Combined oral + ip)

<table>
<thead>
<tr>
<th></th>
<th>TCF Control</th>
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<tbody>
<tr>
<td>Ovarian cysts</td>
<td>19/70</td>
</tr>
<tr>
<td>Liver (hepatos)</td>
<td>61/119</td>
</tr>
<tr>
<td></td>
<td>34*/</td>
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Life span Lower than control

Conclusions: No stat. signif. diff in tumor incidence between TCF + controls. For total mg, males, females, or combined by either route of administration.

Eval: Care (supplementary data, purified) invalid data

1) Realigned with TOA!
2) Only one dose regimen, and that dose insufficientNone lifetime study.
3) Compound was not administered.
4) Summary data presented.
5) Inadequate dosage schedule.
6) Inadequate no. of animals of each sex tested.
7) Strain of rats not specified.
8) List of tissues examined histologically not provided.