Gofmekler (1970) GS0104-069

TOXICOLOGY BRANCH: DATA REVIEW

11/15/83 Releasable

Chemical: Trichlorfon (TCF) Caswell No.: 385
Shaughnessy No.: 057901

Study Type: Inhalation Teratogenicity in Rats.

Citation: "The Effect of Trichlorfon on Embryogenesis in Rats", by V.A. Gofmekler and S.A. Tabakova, Farmakologiya i Toksikologiya (Moscow), 3: 735-737 (1970)

Accession No./MRID No.: NA/NA

Sponsor/Contractor Lab.: (Published article, tr. from Russian)

Test Material: "Chlorophos", of unstated purity and source

Procedures: Five groups of pregnant rats (total, 99 animals) weighing 170-220 g each (strain unspecified) were exposed to "chlorofos vapors" during the entire period of gestation (20 days) at concentrations of 0, 0.005, 0.02, 0.2 and 9.0 mg/m^3 (presumably, nominal, but stated to have been determined by nephelometry), and sacrificed on D-20. Reproductive and fetal indices were determined as well as "certain biochemical indexes", and fetuses examined for soft-tissue (Bouin's) and skeletal (alizarin stained) anomalies. Statistical analyses of the findings were performed, by the "peak-to-peak method" (?) and three levels of significance of differences calculated (P at 0.05, 0.01 and 0.001).

Results: No differences between any treated group and controls were stated for fertility or fetal deaths (both pre- and post-implantations), but no data were presented in the article. Dose-dependent increases in incidence and severity of skeletal variations, however, were observed by the authors (but again no data presented); these were stated to include incomplete ossification centers in paws, "spinal curvature", and "marked cartilaginous pattern in ribs", as well as incomplete ossification in spine and ribs at higher concentrations (0.2 and 9.0 mg/m^3). Soft-tissue abnormalities mentioned by the authors (no data presented) were: "Underdevelopment of the brain" (externally visualized by "cerebral enlargement"), hemorrhages in the peritoneum and "in individual organs" (not specified), "enlargement of the carotid artery, and edema". The following biochemical changes were said to have occurred (no data presented): Decreases in placental, liver and brain ascorbic acid, and increases in "nucleic acids" in organs of both dams and embryos. The authors suggest these changes were due to a "toxic effect of chlorophos on the organism of the female, and consequently, on the embryo itself" (i.e., secondary to maternal toxicity). Histopathological and histochemical changes discovered (no data) in placental of high-dose dams (0.2 and 9.0 mg/m^3) were considered by the authors to be instrumental in impairing fetal development found at these treatment levels.

Conclusions: The authors concluded that "... short-term exposure to Trichlorfon in small concentrations by female white rats during pregnancy impairs the embryonic development process".

TB Evaluation: The incompleteness of reporting in this summary article, combined with lack of detailed findings, judge this report as SUPPLEMENTARY DATA. No specific maternal effects were described, which is surprising considering the author's own statement that two of the four concentrations used (0.2 and 9.0 mg/m^3) were above the acute MTD ("maximum permissible one-time concentration in atmospheric air ..... 0.04 mg/m^3). It can be inferred from summary statements such as: "These changes suggest a toxic effect by Trichlorfon on the organism of the female, and consequently, on the the embryo itself ....." (translator's version) that fetotoxicity and development anomalies induced by trichlorfon are secondary to the chemical's effects on the dam (via the placenta, e.g.)

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