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DATA EVALUATION RECORD

TRICHLORFON

Reproduction and Fetal Metabolism Evaluation
of Orally Administered Trichlorfon In the Rabbit

CITATION: Andrashko VV, Levanyuk VF, et al. [Full citation not provided by translator]. 1975. Effect of trichlorfon on energy metabolism in placenta and organs of intrauterine fetus. Farmakologiya i Toksikologiya. 38(2):208-209 (English translation from Russian).

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DATA EVALUATION RECORD

STUDY TYPE: Reproduction and fetal metabolism evaluation of orally administered trichlorfon in the rabbit.

CITATION: Andrashko VV, Levanyuk VF, et al. [Full citation not provided by translator]. 1975. Effect of trichlorfon on energy metabolism in placenta and organs of intrauterine fetus. Farmakologiya i. Toksikologiya. 38(2):208-209 (English translation from Russian).

ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Not stated.

TEST MATERIAL: Trichlorfon. Purity and source not stated.

PROTOCOL:

1. Trichlorfon was evaluated for its reproductive toxicity and its effects on placental and fetal metabolism. The source, purity, and physical identification of the trichlorfon were not provided.
2. Sixty pregnant rabbits of an unspecified strain were utilized as the test system. The number of rabbits per treatment group was not stated.
3. An aqueous solution of trichlorfon was administered daily by oral intubation from the second day of pregnancy until sacrifice. The dose volume was 10 ml per rabbit. The trichlorfon was administered at dose levels of 50 and 75 mg/kg. A vehicle control group received distilled water.
4. An unspecified number of the rabbits were sacrificed by an air embolism on the 15th to 16th day of gestation. Twenty-nine rabbits were sacrificed by an air embolism on days 29 to 30 of gestation. The general condition of the rabbits and the number, appearance, and weight of any fetuses were determined at sacrifice. "The intensity of tissue respiration and trichlorfon content were determined by the direct manometric method of Warburg". [This reviewer is not familiar with any method of direct determination of a compound by the Warburg procedure]. The entire fetus was ground up and analyzed by a method described by Pokforsky and Ponomareva [1965, reference reported in

Russian] on days 15-16 of gestation. Tissue resorption and trichlorfon content were determined in the liver, brain, and placenta of fetuses obtained from dams sacrificed on days 29-30 of gestation by "the direct monometric method of Warburg." The authors did not state if observations, body weights, or food consumption were determined during gestation.

5. The method of statistical analysis was not described.

RESULTS:

The authors state that no "disorders in the course of pregnancy (hemorrhage, miscarriage) and anomalies in the development of 29-30 day-old fetuses that were visible to the naked eye" were "elicited". No data on maternal observations, body weights, food consumption, and the caesarean section data were provided with the exception of the number of live fetuses. At day 15-16 of gestation, the controls had a mean of 9.0 fetuses per litter. The 50 and 75 mg/kg rabbits had 7.4 and 7.0 fetuses per litter, respectively. At day 24-30 of gestation, 8.3, 7.6, and 7.5 fetuses per litter were observed among the control, 50, and 75 mg/kg groups, respectively. They were all reported to be significantly depressed when compared to controls.

"Toxic chemicals" [trichlorfon] were reported as not detected in the placenta and fetal tissues; however, no data were presented. The authors reported that respiration rates in day 15-16 of gestation fetal tissues were reduced. The respiration rate in the 75 mg/kg group was 64.4 percent of the controls. No actual values were provided. The respiration rates (in ml O₂ per 100 mg wet tissue) in tissues obtained from fetuses sacrificed on day 29-30 of gestation are presented as follows:

	Control			50 mg/kg			75 mg/kg		
	Placenta	Liver	Brain	Placenta	Liver	Brain	Placenta	Liver	Brain
Mean	35.8	49.6	48.1	24.2	26.4	41.0	24.0	31.0	32.6
N	10	10	10	10	10	10	9	9	9
Probability	-	-	-	<0.001	<0.001	<0.001	<0.001	<0.01	<0.001

Reductions in tissue respiration rates were evident in the placenta, fetal liver and fetal brain of both trichlorfon groups when compared to the controls. Although a treatment-related effect was noted, no dose-related effect was evident.

CONCLUSIONS:

Pregnant rabbits were administered 50 and 75 mg/kg trichlorfon by oral intubation daily from the second day of gestation until sacrifice. A portion [number unspecified] of the animals from each treatment group were

sacrificed on days 15-16 of gestation and 29 rabbits were sacrificed on days 29-30 of gestation. The fetuses were examined and selected fetal tissues were analyzed for trichlorfon content and respiration rate.

With the exception of the number of live fetuses per litter, no data on maternal or reproductive toxicity were presented. Administration of trichlorfon at 50 and 75 mg/kg significantly reduced the number of live fetuses per litter. This reduction in the number of live fetuses indicates that trichlorfon was a reproduction hazard (fetotoxic) in the rabbit.

The omission of data pertaining to tissue respiration rates in whole, ground fetuses (15 to 16 days of gestation) prohibits this reviewer from reaching conclusions on trichlorfon's effects on fetal metabolism for day 15-16 fetuses. Reductions in the respiration rates in gestation days 29-30 for fetal liver, brain, and placenta were observed. These data indicated that under the conditions of the study, trichlorfon significantly depressed fetal and placental metabolism.

CORE CLASSIFICATION: Supplementary Data.

The following deficiencies were noted:

- o While the Warburg procedure is an accepted procedure for determining O₂ uptake and therefore indicative of metabolic activity, this reviewer knows of no adaptation of the procedure which would allow one to determine the "trichlorfon content ... in the placenta and organs of the intrauterine fetuses, liver, and brain".
- o With the exception of the number of liver fetuses, no data on maternal or reproductive toxicity were presented.
- o No data on tissue respiration rates were provided for the days 15-16 of gestation fetuses.
- o The number of rabbits per group and their strain was not stated.
- o The purity, source, and physical description of the trichlorfon was not stated.