GS 0174-137

Scheuffler

DATA EVALUATION RECORD

TRICHLORFON

Reproductive and Teratogenic Evaluation In the Mouse
of Trichlorfon Administered by Intraperitoneal Injection

CITATION: Scheufler H. 1975. Effects of relatively high doses of dimethoate and trichlorphone on the embryogenesis of laboratory mice. Biol. Rdsch. 13(4):238-240.

REVIEWED BY:

Curt Lunchick, M.S.
Project Scientist
Dynamac Corporation
11140 Rockville Pike
Rockville, MD 20852
301-468-2500

Signature: Curt Lunchick MS
Date: 26 July 1983

John R. Strange, Ph.D.
Department Director
Dynamac Corporation
11140 Rockville Pike
Rockville, MD 20852
301-468-2500

Signature: John R. Strange
Date: 26 July 1983

APPROVED BY:

Irving Mauer, Ph.D.
EPA Scientist

Signature: Irving Mauer
Date: 07-27-83

DATA EVALUATION RECORD

STUDY TYPE: Reproductive and teratogenic evaluation in the mouse of trichlorfon administered by intraperitoneal injection.

CITATION: Scheufler H. 1975. Effects of relatively high doses of dimethoate and trichlorphone on the embryogenesis of laboratory mice. Biol. Rdsch. 13(4):238-240 [English translation from German].

ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Biologischen Institut des Bereiches Medizin, Martin Luther Universitat, Halle-Wittenberg, DDR.

TEST MATERIAL: Trichlorfon (Trichlorphone). Purity and source not stated.

PROTOCOL:

1. Trichlorfon (trichlorphone) was studied for its teratogenic and reproductive toxicity. The purity and physical description were not stated.

2. Pregnant mice from the inbred strains AB Jena-Halle, C57Bl, and DBA were used as the test system. The number of mice per treatment group is provided in Table 1.

3. The pregnant mice were administered the appropriate dose levels of trichlorfon by intraperitoneal injection. The trichlorfon was administered in a "water-base solution" at a dose volume of 0.1 ml. The vehicle controls receiving 0.1 ml physiological saline. The days of administration and dose levels are provided in Table 1.

4. The author does not state if observations, body weights, or food consumption were performed on the maternal animals. The mice were sacrificed on day 18 of gestation by an unspecified method. The numbers of corpora lutea, live and dead fetuses, and "dead embryos" [resorptions] were recorded and the live fetuses were weighed. All [live?] fetuses were treated with "caustic lye," stained with alizarian S, and examined for skeletal malformations. [The translation states that "malforma- tions on the body" were also examined after preparation for skeletal examinations. This reviewer doubts the validity of this procedure.] It was not stated that a visceral examination of the fetuses was performed.

TABLE 1. The Effect of Trichlorfon on Mice

Strain	No. of Pregnant Animals	Dose Level (mg/kg)	Administration (Days of Gestation)	Post-Implantation[a] Losses (percent)	Total[b] Losses (percent)
AB Jena-Halle					
	27	Neg. cont.	---	6.4	14.0
	27	Vehicle	1-14	4.7	29.6
	33	360	0	14.8	26.9
	25	240	1-7	10.5	26.7
	15	240	7	16.7	33.1
	23	240	7-14	43.9	50.0
	13	240	9	15.6	34.5
	30	120	1-7	19.3	27.2
	14	120	9	20.5	34.0
	13	60	9	23.3	34.2
C57B1					
	35	Neg. cont.	---	21.2	31.9
	19	Vehicle	1-14	20.0	24.6
	19	300	9	23.5	33.9
	25	150	7-14	31.0	37.6
DBA					
	65	Neg. cont.	---	10.1	22.6
	57	Vehicle	1-14	15.7	33.9
	16	240	1-7	26.9	33.0
	27	240	7-14	9.0	11.3

[a] Not defined by author. Reviewer assumes:

$$\text{post-implantation loss} = \frac{\text{No. of resorptions and dead fetuses}}{\text{No. of implantation sites}} \times 100$$

[b] Not defined by author. Reviewer assumes:

$$\text{total losses} = \frac{\text{No. of preimplantation losses + no. of postimplantation losses}}{\text{No. of corpora lutea}} \times 100$$

5. Unspecified statistical analyses were performed.

RESULTS:

No data on maternal toxicity were provided. The actual incidences of resorptions, dead fetuses, and live fetuses were not stated. The percentages of post-implantation losses and total losses are presented in Table 1. Administration of trichlorfon to the AB Jena-Halle mice increased the percentage of post-implantation losses. However, this increase was not dose related. Among the mice administered trichlorfon on day 9 of gestation, the percentage of post-implantation losses was 23.3 at 60 mg/kg, 20.5 at 120 mg/kg, and 15.6 at 240 mg/kg. Administration of trichlorfon from days 1-7 of gestation yielded 19.3 percent post-implantation losses at 120 mg/kg and 10.5 percent at 240 mg/kg. The highest percentage of post-implantation loss (43.9) occurred when trichlorfon was administered at 240 mg/kg from days 7-14 of gestation. The percentages of total losses among the AB Jena-Halle mice administered trichlorfon were comparable to the vehicle control mice with the exception of the mice administered 240 mg/kg trichlorfon from days 7-14 of gestation. Preimplantation loss (percentage) can be calculated by subtracting the postimplantation losses from the total losses. However, these values varied from 7 to 25 percent in the controls, and the test groups fell within this range. The authors stated that "preimplantary loss proved to be an unreliable measurement data after several experiments, whereby concurrently the data for the total loss was reduced as assertion."

Administration of 150 mg/kg trichlorfon to C57Bl mice from days 7-14 of gestation increased the percentage of post-implantation losses when compared to the controls. Mice administered 300 mg/kg trichlorfon on day 9 of gestation had a comparable percentage of post-implantation losses to the controls. The percentages of total losses of the trichlorfon treated mice was comparable to the negative control. The percentage was decreased in the vehicle control group.

The percentage of post-implantation losses among DBA mice administered 240 mg/kg trichlorfon from days 1-7 of gestation was increased.

The percentage of post-implantation losses among DBA mice administered 240 mg/kg trichlorfon from days 1-7 of gestation was increased compared to the vehicle control. The percentage of total losses for this group was comparable to the vehicle controls. A smaller percentage of post-implantation and total losses was observed when the DBA mice administered 240 mg/kg from days 7-14 of gestation were compared to the vehicle controls.

The fetal body weight data and teratology data were not provided. The author states the fetal body weights for AB Jena-Halle and DBA mice were less than the controls. "Major exterior malformations of the fetuses or malformations of the skeletons from trichlorphone could basically not be produced."

CONCLUSIONS:

Three different strains of pregnant mice (AB Jena-Halle, C57Bl, and DBA) were administered 60 to 260 mg/kg trichlorfon by ip injection on various days of gestation. The mice were sacrificed on day 18 of gestation and their uterine contents examined.

The failure to provide the actual incidence of corpora lutea, resorptions, dead fetuses, live fetuses, or fetal body weights prevents this reviewer from reaching a conclusion regarding the reproductive toxicity of trichlorfon in the three strains of mice. This problem is further compounded by the C57Bl and DBA treatment groups receiving either the same dose levels of trichlorfon or being administered trichlorfon on different days of gestation. The dose-reponse relationship among AB Jena-Halle mice receiving various dose levels of trichlorfon during the same periods of gestation was inverted. The more severe responses occurred in the lowest dose levels; and the severity of the response decreased with increasing dose levels of trichlorfon. The observed dose-response relationship was suggestive of external variables [a possible contaminant in the trichlorfon dose solution], and the observed response may not have been trichlorfon induced.

No data on maternal toxicity and teratogenicity were provided. This omission prohibits reaching conclusions on the maternal toxicity and teratogenicity of trichlorfon.

CORE CLASSIFICATION: Supplementary data.

The following major deficiencies were noted:

- No data on maternal toxicity and teratogenicity were provided. No trichlorfon treated mice were dosed throughout organogenesis (days 6-14 of gestation).
- No incidences of corpora lutea, resorptions, dead fetuses, and live fetuses were provided. Only the percentages of post- implantation and total losses were provided and these parameters were not defined.
- The animals were dosed by intraperitoneal injection. This is an unnatural route of exposure and does not simulate the most probable route in man.
- Each C57Bl and DBA group administered trichlorfon was dosed on days of gestation different from other groups of this respective strains.
- No trichlorfon treated group was dosed for the same duration as the vehicle control groups.