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DATA EVALUATION RECORD

TRICHLORFON

Chromosomal Aberrations in Mice (Dominant Lethal Test)

CITATION: Dedek W, Scheufler H, Fischer GW. 1975. The mutagenicity of desmethyl trichlorphon in dominant lethal test on mice. Arch. Toxicol. 33: 163-168.

REVIEWED BY:

Richard L. Hebert, M.S.
Project Scientist
Dynamac Corporation
11140 Rockville Pike
Rockville, MD 20852
301-468-2500

Signature: R L Hebert

Date: July 26, 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: Chromosomal aberrations in mice (dominant lethal test).

CITATION: Dedek W, Scheufler H, Fischer GW. 1975. The mutagenicity of desmethyl trichlorphon in dominant lethal test on mice. Arch. Toxicol. 33: 163-168.

ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Not stated.

TEST MATERIAL: Trichlorphon (1-hydroxy-2,2,2-trichloroethane phosphonic acid dimethyl ester) and desmethyl trichlorphon (sodium salt) were used [source and purity of each were not stated].

PROTOCOL:

Male and female mice of the AB Jena-Halle strain were used. In the first test, 10 male mice were each injected intraperitoneally with a 0.1-ml aliquot of an aqueous solution of desmethyl trichlorphon [concentration not stated] to yield a dose of 405 mg/kg. Beginning the next day [time after dosing not stated], each male was mated with three virgin females for 16 hours per day. Each male was bred to 3 females weekly for 8 weeks. After 8 hours of breeding, females were examined for vaginal plugs. In the second test, 10 male mice were injected intraperitoneally with daily doses of 54 mg/kg for 3 weeks. On the day after the last treatment [time after dosing not stated], the males were mated with females [number per male not stated] for 4 weeks. Females were dissected 18 days after copulation. Controls were treated in parallel with injections of 0.1 ml "bidistilled" water. Control data from different times of the spermatogenic cycle were pooled together.

RESULTS:

For the single exposure test, Table 1 shows that desmethyl trichlorphon produced a higher percentage of postimplantation loss at all weekly intervals, excepting week 3, when compared to results reported for trichlorphon [referenced from an earlier publication], and, in all cases, when compared to controls. Desmethyl trichlorphon also produced higher percentages of total loss at all intervals excepting weeks 3 and 5, when compared to trichlorphon, and in all cases when compared to controls.

For the repeated exposure test, results produced with desmethyl trichlorphon treatment for 3 weeks were compared to results produced by treating mice for 6 weeks with trichlorphon. The exposure period was shortened due to inflammation and necrosis occurring at the injection site. However, as shown in Table 1, results for desmethyl trichlorphon were greater than those produced with trichlorphon or controls with respect to both postimplantation and total percentages of embryonic loss.

CONCLUSIONS:

This study compared the mutagenic effects of desmethyl trichlorphon with those for trichlorphon that were obtained in a previous study. The trichlorphon study was not available for an independent review. Based on this comparison, it was concluded that the mutagenic activity of trichlorphon was not induced by alkylation because desmethyl trichlorphon was also mutagenic. Such a comparison is not appropriate. Furthermore, only one dose was tested, there were inadequate negative controls, and no positive controls were used in this study.

CORE CLASSIFICATION: Unacceptable.

The following deficiencies were noted:

- The purity of the test material was not stated.
- It was not stated that fresh solutions were prepared for daily doses in the second test, although the reported half-life for desmethyl trichlorphon was 137 min at 37°C in aqueous solution (Schneider and Fischer, 1977. Prakt. Chem. 319:391).
- A single dose only was tested.
- The route of administration did not simulate likely human exposure routes.
- Positive controls were not tested.
- Negative control data for the entire 8 weeks were pooled. The same control data were used for each test although the second test ran only three weeks (due to necrosis and inflammation at the injection site).
- It was not stated when mating was initiated after dosing, and if repeated matings were done with virgin females.
- Although the report stated "mutagenicity could be established with a statistical certainty with a 1 percent probability of error," statistical tests were not described.

TABLE 1. Summary of Results on Embryonic Development and Pregnancy in Mice

	Desmethyl trichlorphon			Trichlorphon[a]			Untreated control		
	N[b]	PL[c]	TL[d]	N	PL	TL	N	PL	TL
Single Exposure:									
Week 1	8	19.4	44.3	15	10.1	24.2			
Week 2	16	28.2	35.4	16	19.3	31.3			
Week 3	8	14.9	25.0	13	17.6	29.6			
Week 4	12	20.0	42.1	27	17.4	31.8			
Week 5	4	28.8	25.8	23	25.7	33.9	113	6.6	12.9
Week 6	7	22.5	45.6	29	20.2	30.6			
Week 7	12	25.1	33.8	18	19.2	29.9			
Week 8	3	14.3	26.6	20	13.8	22.7			
Multiple Exposure:									
Week 1	12	31.3	41.9	14	10.1	35	113	6.6	12.9
Week 2	19	24.2	46.7	26	14.9	29.7			
Week 3	2	23.9	42.9	12	7.3	20.8			
Week 4	24	28.4	45.8	21	22.3	37.3			

[a] Trichlorphon data were referenced from a previous publication.

[b] N = Number of pregnant females per week.

[c] PL = Postimplantation loss in percent; based on number of dead implanted embryos.

[d] TL = Total loss in percent; based on total number of embryos which failed to develop to living fetuses.