DATA EVALUATION RECORD

TRICHLORFON

Gene Mutations: 1. Salmonella typhimurium LT-2 Strains
2. Streptomyces coelicolor A3

CITATION: Carere A, Ortali VA, Cardamone G, Morpurgo G. 1978. Mutagenicity of dichlorvos and other structurally related pesticides in Salmonella and Streptomyces. Chemico-Biolog. Inter. 22(2/3):297-308.

Carere A, Ortali VA, Cardamone G, Torracca M, Raschetti R. 1978. Microbiological mutagenicity studies of pesticides in vitro. Mutat. Res. 57(3):277-286.

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: August 8, 1983

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

Signature: John R. Strange/NPH
Date: August 8, 1983

APPROVED BY:

Irving Mauer, Ph.D.
EPA Scientist

Signature: [signature]
Date: 08-09-83

DATA EVALUATION RECORD

STUDY TYPE: Gene mutations: 1. Salmonella typhimurium LT-2 strains
2. Streptomyces coelicolor A3.

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[Identical data present in both studies].

ACCESSION NUMBER: Not available.

MRID NUMBER: 05011869 and 05020822.

LABORATORY: Istituto Superiore di Sanita, Roma (Italy).

TEST MATERIAL: Trichlorphon (Dipterex), 96 percent purity, supplied by Dr. I. Camoni, Istituto Superiore di Sanita, Roma.

PROTOCOL:

Trichlorphon was dissolved in either distilled water or DMSO for assays [several pesticides screened and trichlorphon solvent not specified]. Mutation assays were conducted with Salmonella typhimurium strains TA1535, TA1536, TA1537, and TA1538, and with Streptomyces coelicolor A3 hisA1 (str-).

Assays with S. typhimurium were conducted according to the procedures of Ames et al. (1975. Mutat. Res. 31:347-364). Spot tests were also conducted with S. coelicolor on minimal media plus histidine and streptomycin, using filtered spore suspensions as inoculum, and incubating the plates for 3-5 days at 30°C. Although several concentrations of trichlorphon were assayed, only the one that "gave the maximal number of revertant colonies" was reported. In addition, liquid culture assays were conducted with S. typhimurium TA1535. Trichlorfon was incubated in a saturated aqueous solution at 37°C for up to 12 hours, then added to nutrient broth cultures at 6 or 12 mg/ml, and incubated for 1-3 hours at 37°C. For metabolic activation assays, S9 fractions were obtained from male Wistar rats treated with sodium phenobarbital. Negative controls utilized the solvent. Several positive control compounds were included

with and without S9 activation: N'-methyl-N'-nitro-N-nitrosoguanidine, N-nitrosomethylurea, methyl methanesulphonate, 2-aminofluorene, 2-acetaminofluorene, sodium nitrite, hycanthone methanesulphonate, and ICR-191. Each experiment was done with triplicate plates, and was repeated at least three times.

RESULTS:

Trichlorphon was a "doubtful mutagen" in the Ames assay, but "appeared to be more significantly mutagenic when tested in the liquid culture techniques." Data for spot tests were reported for concentrations of 0 and 2 mg/plate, with and without S9 mix. No increase in the number of revertants was seen in trichlorphon-treated plates. When trichlorphon was stored in a saturated aqueous solution at 37°C for 12 hours and added to liquid cultures (TA1535) at 6 mg/ml, the mutation rate relative to controls increased 4-fold and 5-fold after 1 and 3 hours of incubation, respectively. At 12 mg/ml, the mutation rate increased 3-fold and 5-fold after 1 and 2 hours of incubation, respectively. The spontaneous mutation rate for S. coelicolor was increased 6-fold at a trichlorphon concentration of 4 mg/plate (i.e., 9 versus 57 resistant colonies/plate). No data were reported for metabolic activation with the S. coelicolor assay or liquid culture assays.

CONCLUSIONS:

Based on previously reported chemical properties of trichlorphon, the authors concluded that with the S. typhimurium assay "the mutagenicity of trichlorphon is very likely due to its spontaneous conversion to dichlorvos." The reviewer agrees with this assessment; however if higher concentrations of trichlorphon had been tested in the plate assays (i.e., >2 mg/plate), positive mutagenic responses may have been observed. Trichlorphon at 4 mg/plate was moderately mutagenic in plate assays with S. coelicolor.

CORE CLASSIFICATION: Unacceptable.

The following deficiencies were noted:

- In the assays showing positive responses, several dose levels were tested but data for only one dose (S. coelicolor) or two doses (liquid cultures) were reported.
- Negative responses were obtained in the Ames assays, however no reason was given for not testing higher dose levels. The report did not indicate toxicity occurred at the highest dose tested (2 mg/plate).
- Data were not reported for metabolic activation with the liquid culture assays and the S. coelicolor assays.