Shirasu 65-0104-141

Releasable

Trichlorfon (TCF)

Caswell No. 385
(EPA Reg. No., 3125-9)

DATA EVALUATION RECORD

TEST CHEMICAL, or FORMULATION: Technical TCF (chemically: dimethyl-2,2,2-trichloro-1-hydroxyethylphosphonate) >99% purity.

CITATION: "Trichlorfon: Mutagenicity Test on Bacterial Systems," by Yasuhiko Shirasu, Ritsuko Koyashiki, and Masaaki Moriya, Department of Toxicology, Institute of Environmental Toxicology (Report No. 69367, October 30, 1979, Mobay Chemical Corporation, Kansas City, MO.) Accession No. 249535

TRADE SECRET CLAIM: CBI

REASON FOR REVIEW: RS - response to data call-in (received 2/23/83).

REVIEWED BY: Irving Mauer, Ph.D., Geneticist
TB/HED

04-15-83

DATE OF REVIEW: April 6, 1983

TEST TYPES: Bacterial Mutagenicity: (1) Rec-assay (DNA damage/repair) in Bacillus subtilis; (2) Reversion assays (reverse point mutation) in Escherichia coli WP-2 and Salmonella typhimurium (5 TA strains).

STUDY-1. Rec-assay: Cultures of the DNA-repair competent strain H-17 (rec +) and repair-deficient sister strain M-45 (rec-) of B. subtilis were exposed concurrently to filter paper discs soaked with 6 concentrations (20 to 2000 ug) of test chemical (TCF) dissolved in 0.02 ml DMSO, and the length of zones of inhibition measured after 24 hr incubation (37°C). Kanamycin (10 ug/disc) served as negative control (expect equal zones of inhibition in both strains), and 0.1 ug discs of mitomycin-C (MC) as positive control (greater inhibition of M-45). A solvent control (DMSO, no inhibition) was also run. [Metabolic activation is not appropriate in assays of this type.]

As shown in a tabular summary, only the two highest concentrations of RCB (1,000 and 2,000 ug) caused zones of growth inhibition (1 and 3 mm) in the M-45 strain, but no inhibition at any TCF dosage in H-17 cultures. All controls performed as expected: MC causing 5 times greater inhibition (7.5 mm) in M-45 cultures than in H-17 growth (1.5 mm);

2 pages

whereas kanamycin inhibited both strains to the same degree (4 mm), and DMSO produced none.

Hence the authors concluded that TCF was ("weakly") positive in the rec-assay with B. subtilis.

EVALUATION: The study is Acceptable, and the conclusion validly generated from the protocol.

STUDY-2. Reversion assays: Plate cultures of the standard set of auxotrophic indicator strains (S. typhimurium his-: TA 5135, TA 1537, TA 1538, TA 98, TA 100; E. coli WP-2 hcr-/ tryp-) were exposed to seven TCF concentrations (in DMSO) ranging from 50 to 20,000 ug/plate in replicate experiments, both in the absence and presence of a mammalian metabolic activation system consisting of Aroclor 1254-stimulated hepatic mixed-function oxygenases prepared from male S-D rats (S-9) plus appropriate co-factors (S-9 Mix), and revertents (his+ colonies) counted after 2 day's incubation. Positive (mutagens appropriate for each strain and mode of activation), solvent and S-9 controls were run concurrently. The highest dose (20,000 ug) was toxic (inhibited growth). As recorded in two tabular summaries, TCF induced significant increases in revertent colonies at concentrations of 5,000, 10,000 and 20,000 ug, in a roughly dose-related fashion for both the WP2 hcr- and TA 100 strains (3 to 4X DMSO control), equally both with and without S-9 activation. None of the other strains responded, even at the inhibitory dose (20,000 ug). Positive control cultures responded as expected (50 to >1,000 X DMSO controls).

The authors concluded that TCF was (weakly) mutagenic at high concentrations, probably by a base-substitution mechanism.

EVALUATION: The study is ACCEPTABLE, and the conclusion (positive mutagenicity) validly generated from the procedures employed.