

CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

ETHYLENE DICHLORIDE

SB 950-066, Tolerance #1007

October 15, 1986

Revised October 24, 1986

I. DATA GAP STATUS

Chronic rat:	Data gap, no studies on file
Chronic dog:	Data gap, no studies on file
Onco rat:	Data gap, inadequate study on file, potential adverse effect indicated
Onco mouse:	Data gap, inadequate study on file, potential adverse effect indicated
Repro rat:	Data gap, no studies on file
Terato rat:	Data gap, no studies on file
Terato rabbit:	Data gap, no studies on file
Gene mutation:	No data gap, potential adverse effects
Chromosome:	Data gap, inadequate studies, no adverse effect indicated
DNA damage:	Data gap, inadequate study, insufficient information to assess
Neurotox:	Not required

Note, Toxicology one-liners are attached

** indicates acceptable study

Bold face indicates possible adverse effect

File name 3B>SB066ETH.JG

Revised name SB066ETH.JG2

II. TOXICOLOGY ONE-LINERS AND DISCUSSION

CHRONIC, RAT

No study on file.

DOG

No study on file.

ONCOGENICITY

RAT

002 920192 (Hazleton for NCI, 1/78) Remsen, 3/19/85. Ethylene dichloride (90%) given by oral gavage for 78 weeks, 5 days/week at 0, 47, and 95 mg/kg; 50/sex/group in the treatment groups, 20/sex in vehicle (corn oil) and untreated controls; stomach squamous cell carcinomas in males at both dose levels, hemangiosarcomas in various locations at both dose levels, mammary adenocarcinomas (high dose level) and fibroadenomas (low dose level), subcutaneous tissue fibromas in males at both dose levels, kidney neoplasms in high dose group; NOEL not established; UNACCEPTABLE (insufficient number of animals due to early deaths in all groups, inadequate duration of test, only two dosing levels, no individual data, no analysis of dosing solution), NOT UPGRADEABLE.

MOUSE

002 920192 (Hazleton for NCI, 1/78) Remsen, 3/19/78. Ethylene dichloride (90%) given by oral gavage, 5 days/week for 78 weeks at 0, 97 and 195 mg/kg to males and 0, 149 and 299 mg/kg to females; 50/group in the treatment groups; 20/sex in vehicle (corn oil) and untreated controls; endometrial stromal neoplasms and adenocarcinomas at both dose levels, mammary gland adenocarcinomas at both dose levels, alveolar/bronchiolar adenomas at both dose levels--both sexes, liver carcinomas in males at the high dose level; NOEL not established; UNACCEPTABLE (insufficient number of animals due to early death in all groups, inadequate duration of test, only two dosing levels, no individual data, no analysis of dosing solution), NOT UPGRADEABLE.

REPRODUCTION

No study on file.

TERATOGENICITY, RAT

No study on file.

TERATOGENICITY

RABBIT

No study on file.

MUTAGENICITY

GNMU

Bacterial systems

50507-001 No record number (Eastman Kodak, 1981). Publication in Mutation Research 90: 31-48 (1981). JG, 10/24/86. Ethylene dichloride (no purity stated), in Salmonella strains TA1535, TA1537, TA1538, TA98 and TA100 with and without rat liver activation; tested at 0, 31.8, 63.1, 128.2 or 231.8 umoles per plate in an enclosed container designed for testing volatile solvents (EDC did not show activity when the usual plate assay procedure was used); EDC was mutagenic in TA1535 and TA100 both with and without activation with comparable activity - activation had little or no effect; there was no activity with the other three strains. UNACCEPTABLE (no repeat trial, no individual data.)

50507-001 No record number (University of Leiden, 1981). Publication in Carcinogenesis 2: 499-505 (1981). JG, 10/24/86. Ethylene dichloride (>99.5%) tested with Salmonella strain TA100 without and with the addition of S100 from rat liver; 0 to 40 mM; EDC did not show activity in the usual plate incorporation procedure but did increase the reversion rate when preincubated with TA100 for 40 minutes before plating in the presence and absence of S100. The effect of preincubation may be explained on the basis that EDC is a volatile solvent [see previous report from Eastman Kodak.] UNACCEPTABLE (one strain only, no individual plate counts - results in graphic form only.)

50507-001 27258 (New York Medical College, 1977). JG, 10/24/86. Ethylene dichloride (no purity stated); tested with Salmonella strains TA1530, TA1535 and TA1538 without activation in the plate incorporation assay; 0 to 25+ umoles per plate with TA1530 gave a concentration-dependent increase in revertants (shown graphically only); 10 umoles per plate gave a 2-fold increase with TA1535 but not TA1538. UNACCEPTABLE (strains, concentrations, data presentation.)

Mammalian systems

50507-001 11705 (Oak Ridge, 1981.) JG, 10/24/86. Ethylene dichloride (no purity stated); CHO/HGPRT with and without rat liver activation at 0 to 50 mM without activation and 0 to 3 mM with activation, 5 hours each; a concentration-dependent increase in mutation frequency was demonstrated in both instances; cytotoxicity was much greater in the presence of S9 (also true with EDB) and is NADP-mediated; UNACCEPTABLE (single trial, no purity stated.)

Miscellaneous systems

50507-001 11706 (University of Stockholm, 1980.) JG, 10/24/86. Publication in Mutation Research 76: 269-295 (1980). Review of a number of publications on EDC in microbial systems with both negative and positive results in Salmonella, positive in E. coli pol A strains but negative in B. subtilis; activity was enhanced in some investigations by activation but not others; in Drosophila, several studies report increase in sex-linked recessive lethals and chromosomal non-disjunction with the spermatids being more susceptible, as with EDB.

SUMMARY: While no single publication is acceptable, they in combination contain sufficient data to assess the toxicity/mutagenicity of EDC. EDC is a direct mutagen and the activity is enhanced in some tests by activation. It is a mutagen in microbial and mammalian systems and in Drosophila.

CHROMOSOME

50507-001 11706 (University of Stockholm, 1980.) JG, 10/24/86. Publication in Mutation Research 76: 269-295 (1980). Review of publications on EDC. Two are cited with negative results for micronuclei formation in mice at 4 mmoles/kg body weight i.p. twice or 100 mg (1.0 mmole) i.p. per kg.

DNA DAMAGE/REPAIR

50507-001 27259 (New York Medeical College, 1977). JG, 10/24/86. Ethylene dichloride (no purity stated) with E. coli pol A+ and pol A- strains at 10 ul; marginal difference in growth (8 mm versus 9 mm zone of inhibition with pol A-). Insufficient information to assess effect. UNACCEPTABLE.

NEUROTOXICITY

Not required