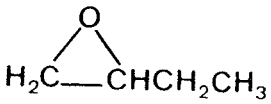
1,2-EPOXYBUTANE

1. Chemical and Physical Data

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 106-88-7
Chem. Abstr. Name: Ethyloxirane
IUPAC Systematic Name: 1,2-Butylene oxide
Synonyms: 1-Butene oxide; 1,2-butene oxide; 1,2-butylene epoxide; α-butylene oxide; 1-butylene oxide; epoxybutane; ethyl ethylene oxide; 2-ethyloxirane

1.2 Structural and molecular formulae and molecular weight



C_4H_8O

Mol. wt: 72.12

1.3 Chemical and physical properties of the pure substance:

(*a*) *Description*: Clear, colourless liquid with pungent odour (Dow Chemical Co., 1988)

(*b*) *Boiling-point*: 63.3°C (Weast, 1985)

(*c*) *Melting-point*: < -60°C (Parmeggiani, 1983)

(*d*) *Density*: 0.8312 (20°/20°C) (Hawley, 1981); 0.837 (17°C/4°C) (Weast, 1985)

(*e*) *Spectroscopy data*: Nuclear magnetic resonance and infrared spectral data have been reported (Sadtler Research Laboratories, 1980; Pouchert, 1981, 1983, 1985).

(*f*) *Solubility*: Miscible with most organic solvents (National Toxicology Program, 1988); very soluble in ethanol and diethyl ether (Weast, 1985); soluble in water (Hawley, 1981)

(*g*) *Volatility*: Vapour pressure, 140 mm Hg at 20°C (Dow Chemical Co., 1988)

(*h*) *Refractive index*: 1.3851 at 20°C (Weast, 1985)

(*i*) *Flash-point*: -22°C (closed-cup) (Dow Chemical Co., 1988)

(*j*) *Reactivity*: Extremely inflammable; reacts with water and other source of labile hydrogen, especially in the presence of acids, bases or other oxidizing substances. Reactive monomer which can polymerize exothermically. Undergoes atmospheric hydrolysis; atmospheric half-life for oxidation estimated to be six days (Hine *et al.*, 1981; National Toxicology Program, 1988; Dow Chemical Co., 1988)

(*k*) *Conversion factor:* $mg/m^3 = 2.95 \times ppm$[1]

1.4 Technical products and impurities

1,2-Epoxybutane is available at a purity of 98%, 99% or >99%. 1,2-Butanediol has been identified as an impurity (< 0.2%) (Riedel-de Haën, 1984; Aldrich Chemical Co., Inc., 1988; National Toxicology Program, 1988).

2. Production, Use, Occurrence and Analysis

2.1 Production and Use

(*a*) *Production*

1,2-Epoxybutane has been prepared by the chlorohydrin process from 1-butene (α-butene) and chlorine in water. The butylene chlorohydrin produced is dehydrochlorinated with calcium hydroxide to yield 1,2-epoxybutane, with calcium chloride as a byproduct (Considine, 1974; Hine *et al.*, 1981). A newer process based on the catalysed reaction of olefins with hydroperoxides produces high yields of epoxides and the corresponding alcohols. 1,2-Epoxybutane is reported to be produced commercially by the epoxidation of 1-butene with peroxyacetic acid (Considine, 1974; Hoff *et al.*, 1978).

It has been reported that 3.6 thousand tonnes of 1,2-epoxybutane were produced in the USA in 1978 (National Toxicology Program, 1988). Data on production elsewhere in the world were not available.

(*b*) *Use*

1,2-Epoxybutane is widely used as a stabilizer for chlorinated hydrocarbon solvents. More than 75% of 1,2-epoxybutane produced commercially is added to chlorine-containing materials such as trichloroethylene to act as an acid-scavenger (Hine *et al.*, 1981; National Toxicology Program, 1988).

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[1]Calculated from: mg/m^3 = (molecular weight/24.45) × ppm, assuming standard temperature (25°C) and pressure (760 mm Hg)

This compound is also used as a chemical intermediate for the production of butylene glycols and their derivatives (polybutylene glycols, mixed poly glycols and glycol ethers and esters), butanol-amines, surface-active agents, and other products such as gasoline additives (Hine *et al.*, 1981; Parmeggiani, 1983). It has been reported to be used as a corrosion inhibiting additive (at 0.25–0.5%) during the preparation of vinyl chloride and its copolymer resins (Hoff *et al.*, 1978).

(*c*) *Regulatory status and guidelines*

Standards for 1,2-epoxybutane have not been established by any country in the form of regulations or guidelines. However, US manufacturers have recommended a voluntary standard of 40 ppm (118 mg/m^3) for an 8-h time-weighted average threshold limit value (National Toxicology Program, 1988).

2.2 Occurrence

(*a*) *Natural occurrence*

1,2-Epoxybutane is not known to occur naturally.

(*b*) *Occupational exposure*

On the basis of a US National Occupational Exposure Survey, the National Institute for Occupational Safety and Health (1983) estimated that 47 900 workers were potentially exposed to 1,2-epoxybutane in the USA in 1981–83. No data on levels of exposure to 1,2-epoxybutane were available to the Working Group.

2.3 Analysis

In a general method for epoxides, 1,2-epoxybutane was determined spectrophotometrically after adding a colour-forming reagent, 4-(*para*-nitrobenzyl)pyridine. Maximal absorbance is observed at 574 nm (Agarwal *et al.*, 1979).

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals

(*a*) *Inhalation*

Mouse: Groups of 50 male and 50 female B6C3F1 mice, seven to nine weeks old, were exposed by inhalation to 0, 50 or 100 ppm (150 or 300 mg/m^3) 1,2-epoxybutane (purity, >99%) for 6 h per day on five days a week for 102 weeks. Survival was comparable in all

groups of males (41/50, 45/50 and 33/50 mice killed at termination) but was reduced in high-dose females after week 86 (29/50, 25/50 and 9/50 mice killed at termination). A single squamous-cell papilloma was found in the nasal cavity of a male receiving 100 ppm. Treatment-related, non-neoplastic nasal changes included inflammation, erosion, hyperplasia and squamous metaplasia of the nasal epithelium and atrophy of the olfactory sensory epithelium at both dose levels (Dunnick *et al.*, 1988; National Toxicology Program, 1988).

Rat: Groups of 50 male and 50 female Fischer 344/N rats, seven to nine weeks old, were exposed by inhalation to 0, 200 or 400 ppm (600 or 1200 mg/m^3) 1,2-epoxybutane (purity, >99%) for 6 h per day on five days a week for 103 weeks. Survival at termination of the experiment was 30/50, 18/50 and 23/50 for males and 32/50, 21/50 and 22/50 for females in the control, low-dose and high-dose groups, respectively. The incidences of papillary adenomas of the nasal cavity were 7/50 ($p < 0.05$, adjusted for differences in mortality) for high-dose males and 2/50 for high-dose females. No such tumour occurred in controls or in animals receiving the low dose. The historical background incidence of nasal papillary adenomas was 2/1977 (0.1%) in male rats. The incidences of alveolar/bronchiolar carcinomas were 0/50, 1/50 and 4/49 for males and 1/50, 0/49 and 0/50 for females in the control, low-dose and high-dose groups; and those of alveolar/bronchiolar adenomas was 0/50, 1/50 and 1/49 for males and 1/50, 0/49 and 1/50 for females, respectively. Taken together, the incidence of alveolar/bronchiolar adenomas and carcinomas in high-dose males was statistically significantly increased compared with that in controls ($p < 0.05$, adjusted for mortality); moreover, a significant positive trend was found for the incidence of adenomas and carcinomas combined ($p < 0.02$; Cochrane-Armitage test). The historical background incidence of pulmonary alveolar/bronchiolar tumours in male rats of this strain was 0.7% (2% for chamber controls in this laboratory). The neoplasms of the nose and lungs did not cause early death of the animals. Treatment-related, non-neoplastic changes in the nose included inflammation, epithelial hyperplasia and squamous metaplasia of the nasal epithelium and atrophy of the olfactory sensory epithelium at both dose levels (Dunnick *et al.*,1988; National Toxicology Program, 1988).

(*b*) *Skin application*

Mouse: A group of 30 female ICR/Ha mice, eight weeks old, received applications of 10% 1,2-epoxybutane (purity established by boiling-point: 62–64 °C) in acetone (reagent grade) on shaved dorsal skin three times per week for 77 weeks. One control group of 40 female mice received applications of 100% acetone three times a week for 85 weeks, and 100 female mice served as untreated controls. Animals in both groups were killed in week 85. No visible skin reaction and no tumour was observed in any of the groups (Van Duuren *et al.*, 1967).

(*c*) *Combined exposure*

Mouse: Groups of 50 male and 50 female Swiss ICR/Ha mice, five weeks of age, received 2400 mg/kg bw (males) or 1800 mg/kg bw (females) corn oil (control), 2400 or 1800 mg/kg bw trichloroethylene or 2400 or 1800 mg/kg bw trichloroethylene containing 0.8% 1,2-epoxybutane (97.8% pure; used as a stabilizer) up to week 35, and then half of this dose, containing 0.4% 1,2-epoxybutane, in corn oil by gavage five times per week from week 40 to

week 69. The experiment was terminated at week 106. Survival was reduced in both treated groups, but did not differ between the two groups; at week 106, six male and three female controls, no trichloroethylene-treated animal and one male and one female mouse treated with trichloroethylene plus 1,2-epoxybutane were still alive. Squamous-cell carcinomas of the forestomach occurred in 3/49 males ($p = 0.029$, age-adjusted) and 1/48 females treated with trichloroethylene plus 1,2-epoxybutane. No such tumour occurred in animals treated with trichloroethylene alone or with corn oil. Two of the tumours in males metastasized to the lung, liver or abdominal cavity. Hyperkeratosis of the forestomach was observed in groups treated with trichloroethylene and with trichloroethylene plus 1,2-epoxybutane [incidence and severity unspecified] (Henschler *et al.*, 1984). [The Working Group noted the two-fold reduction in dose to treated animals due to toxicity.]

3.2 Other relevant data

(*a*) *Experimental systems*

(i) *Absorption, distribution, excretion and metabolism*

When a single dose of 1.9 mmol (137 mg)/kg bw 1,2-epoxybutane was administered by gavage to rabbits or of 2.5 mmol (180 mg)/kg bw to rats, 4% and 11% of the dose, respectively, was excreted in the urine as 2-hydroxybutyl mercapturic acid (James *et al.*, 1968).

(ii) *Toxic effects*

The oral LD_{50} of 1,2-epoxybutane in rats has been reported to be 1.4 ml/kg bw (1.17 g/kg bw) and the dermal LD_{50}, 2.1 ml/kg bw (1.76 g/kg bw) (Weil *et al.*, 1963). Acute exposure of rats to 4000 ppm (11 800 mg/m^3) 1,2-epoxybutane by inhalation for 4 h resulted in the death of one of six animals; concentrations of 8000 ppm (23 600 mg/m^3) resulted in 100% mortality (Smyth *et al.*, 1962).

When rats received a single 4-h exposure to 500–6550 ppm (1475–19 320 mg/m^3) 1,2-epoxybutane by inhalation, all animals exposed to 6550 ppm died during the exposure period, but no death occurred in the other groups. Ocular discharge and dyspnoea were observed in males and females at 2050 and 6550 ppm (6050 and 19 320 mg/m^3) and eye irritation at 1400 ppm (4130 mg/m^3). Mice similarly exposed to 400–2050 ppm (1200–6050 mg/m^3) 1,2-epoxybutane exhibited the same toxic effects; all mice exposed to 2050 ppm, 4/5 males and 4/5 females exposed to 1420 ppm and 1/5 males exposed to 400 ppm died during the study. The 4 h-LC_{50} for mice was calculated to be about 1000 ppm (2950 mg/m^3) (National Toxicology Program, 1988).

Application of 1,2-epoxybutane to the eye of rabbits resulted in corneal injury (Weil *et al.*, 1963).

Rats and mice were exposed by inhalation to 400, 800 or 1600 ppm (1180, 2360 or 4720 mg/m^3) 1,2-epoxybutane for 6 h per day on five days per week for two weeks. All mice in the high-dose group had died by the third day of exposure; all rats exposed to this concentration survived but had pronounced retardation of growth. Inflammatory and degenerative changes in the nasal mucosa, myeloid hyperplasia in bone marrow and elevated mean white blood-cell counts were found in high-dose male and female rats; focal corneal cloudiness

was observed in high- and medium-dose rats. Similar toxic effects were observed in mice, with the exception of haematological changes. In a similar experiment, exposure of mice and rats to 75, 150 or 600 ppm (220, 440 or 1770 mg/m^3) 1,2-epoxybutane for 13 weeks did not result in treatment-related mortality; slight growth retardation was observed in high-dose female rats and mice. Inflammatory and degenerative changes in the nasal mucosa were observed in both species and myeloid hyperplasia in bone marrow in male rats only (Miller *et al.*, 1981). Similar toxic effects were observed in rats and mice exposed for 6 h on five days per week to 400–6400 ppm (1180–18 900 mg/m^3) 1,2-epoxybutane for two weeks or to 50–800 ppm (148–2360 mg/m^3) for 13 weeks (National Toxicology Program, 1988).

1,2-Epoxybutane alkylated deoxyguanosine at the *N*-7 position (Hemminki *et al.*, 1980).

(iii) *Effects on reproduction and prenatal toxicity*

Groups of 38–45 Wistar rats were exposed by inhalation to 0, 250 or 1000 ppm (738 or 2950 mg/m^3) 1,2-epoxybutane (>99% pure) for 7 h per day on five days per week during a three-week pregestational period, or for 7 h per day on days 1–19 of gestion, or were exposed during the combined pregestational and gestational period. Fetuses were examined by routine teratological techniques on day 21 of gestation. Exposure to the high dose prior to and during gestation was lethal to one of 42 females, and maternal body weight gain was depressed in all groups exposed to 1000 ppm. Fetal growth and viability were not affected by exposure to 1,2-epoxybutane, and there was no indication of dose-related malformations in the offspring (Sikov *et al.*, 1981).

Groups of 24–49 New Zealand rabbits were exposed by inhalation to 0, 250 or 1000 ppm 1,2-epoxybutane (>99% pure) for 7 h per day on days 1–24 of gestion. Fetuses were examined by standard teratological techniques on day 30 of gestation. Exposure to 1000 ppm was lethal to 14/24 does and 250 ppm to 6/48 does; no effect on maternal body weight gain was observed in survivors. An indication of decreased pregnancy rate at term was seen in the high-dose group, but this may have been a result of differential toxicity in pregnant and non-pregnant females. Litter size appeared to be reduced, and embryonic mortality was increased in the high-dose group. Of the eight surviving fetuses at this exposure level, one was stunted and had a hypoplastic tail and unilateral renal agenesis (Sikov *et al.*, 1981).

(iv) *Genetic and related effects*

The genetic activity of 1,2-epoxybutane has been reviewed (Ehrenberg & Hussain, 1981). It is a directly acting alkylating agent.

1,2-Epoxybutane has been shown to induce SOS repair activity in *Salmonella typhimurium* TA1525/pSK1002 (Nakamura *et al.*, 1987) and to produce differential killing zones in various *pol* and *rec* proficient and deficient strains of *Escherichia coli* (Rosenkranz & Poirier, 1979; McCarroll *et al.*, 1981). It produced streptomycin-resistant mutants in *Klebsiella pneumoniae* (Voogd *et al.*, 1981; Knaap *et al.*, 1982).

It was shown to be mutagenic to *E. coli* WP2 *uvr*A$^-$ in one study (McMahon *et al.*, 1979) but not in others (Dunkel *et al.*, 1984). It gave positive results only in *S. typhimurium* base-pair substituting strains (TA1535 and TA100), although frameshift tester strains were also tested both in the presence and absence of an exogenous metabolic system (Chen *et al.*, 1975;

Rosenkranz & Speck, 1975; McCann *et al.*, 1975; Speck & Rosenkranz, 1976; Henschler *et al.*, 1977; De Flora, 1979; McMahon *et al.*, 1979; Rosenkranz & Poirier, 1979; De Flora, 1981; Weinstein *et al.*, 1981; de Meester *et al.*, 1982, abstract; De Flora *et al.*, 1984; Gervasi *et al.*, 1985; Canter *et al.*, 1986; Hughes *et al.*, 1987, abstract; Rosman *et al.*, 1987; National Toxicology Program, 1988). Negative results have been reported from four laboratories in five strains (Dunkel *et al.*, 1984), and Simmon (1979a) reported negative results in six strains.

1,2-Epoxybutane induced forward mutation in *Schizosaccharomyces pombe* P1 (Migliore *et al.*, 1982) and mitotic recombination in *Saccharomyces cerevisiae* D3 (Simmon, 1979b). It was weakly mutagenic at the adenine locus in *Neurospora crassa* (Kolmark & Giles, 1955).

1,2-Epoxybutane induced sex-linked recessive lethal mutations (Knaap *et al.*, 1982; National Toxicology Program, 1988) and translocations (National Toxicology Program, 1988) in *Drosophila melanogaster* after either feeding or injection.

It produced no effect in the hepatocyte rat primary culture/DNA repair test (Williams *et al.*, 1982) but did produce differential toxicity as measured by relative growth in repair-deficient Chinese hamster ovary cells (Hoy *et al.*, 1984).

It was reported in an abstract that 1,2-epoxybutane induced mutation in L5178Y $TK^{+/-}$ mouse lymphoma cells in the absence of an exogenous metabolic system (Myhr *et al.*, 1981). In the same system, Amacher *et al.* (1980) reported positive results with a dose-reponse in the absence of an exogenous metabolic system; McGregor *et al.* (1987), the National Toxicology Program (1988), Mitchell *et al.* (1988) and Myhr and Caspary (1988) reported positive results both in the presence and absence of an exogenous metabolic system. 1,2-Epoxybutane also gave weakly positive results for the induction of 6-thioguanine-resistant mutations in L5178Y mouse lymphoma cells (Knaap *et al.*, 1982).

1,2-Epoxybutane induced chromosomal aberrations and sister chromatid exchange in Chinese hamster ovary cells with and without an exogenous metabolic system (National Toxicology Program, 1988).

It induced morphological transformation of Syrian hamster embryo cells (Pienta, 1980; Dunkel *et al.*, 1981) and increased transformation in Rauscher murine leukaemia virus-infected Fischer 344 rat embryo cells (Price & Mishra, 1980; Dunkel *et al.*, 1981). It did not induce morphological transformation in Balb/3T3 cells (Dunkel *et al.*, 1981).

(*b*) *Humans*

No data were available to the Working Group.

3.3 Case reports and epidemiological studies of carcinogenicity to humans

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Exposures

1,2-Epoxybutane is a synthetic organic liquid used primarily as a stabilizer for chlorinated hydrocarbon solvents. Other applications include its use as a chemical intermediate and corrosion inhibitor. Measurements of occupational exposure levels have not been reported.

4.2 Experimental carcinogenicity data

1,2-Epoxybutane was tested for carcinogenicity by inhalation exposure in one study in mice and in one study in rats, producing nasal papillary adenomas in rats of both sexes and pulmonary alveolar/bronchiolar tumours in male rats. It did not induce skin tumours when tested by skin application in one study in mice. Oral administration of trichloroethylene containing 1,2-epoxybutane to mice induced squamous-cell carcinomas of the forestomach, whereas administration of trichloroethylene alone did not.

4.3 Human carcinogenicity data

No data were available to the Working Group.

4.4 Other relevant data

1,2-Epoxybutane caused inflammatory and degenerative changes in the nasal mucosa and myeloid hyperplasia in the bone marrow in rats and mice. It did not cause prenatal toxicity in rats or rabbits.

1,2-Epoxybutane induced morphological transformation in cultured animal cells. It induced sister chromatid exchange, chromosomal aberrations and mutation in cultured animal cells, but did not induce DNA damage. It induced sex-linked recessive lethal mutations and translocations in *Drosophila*, mitotic recombination in yeast and mutation in yeast and fungi. 1,2-Epoxybutane induced DNA damage and mutation in bacteria. (See Appendix 1.)

4.5 Evaluation[1]

There is *limited evidence* for the carcinogenicity of 1,2-epoxybutane in experimental animals.

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[1]For definitions of the italicized terms, see Preamble, pp. 27-30.

No data were available from studies in humans on the carcinogenicity of 1,2-epoxybutane.

Overall evaluation

1,2-Epoxybutane *is not classifiable as to its carcinogenicity to humans (Group 3).*

5. References

Agarwal, S.C., Van Duuren, B.L. & Kneip, T.J. (1979) Detection of epoxides with 4-(*p*-nitrobenzyl)pyridine. *Bull. environ. Contam. Toxicol., 23*, 825–829

Aldrich Chemical Co., Inc. (1988) *Aldrich Catalog Handbook of Fine Chemicals*, Milwaukee, WI, p. 671

Amacher, D.E., Paillet, S.C., Turner, G.N., Ray, V.A. & Salsburg, D.S. (1980) Point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells. II. Test validation and interpretation. *Mutat. Res., 72*, 447–474

Canter, D.A., Zeiger, E., Haworth, S., Lawlor, T., Mortelmans, K. & Speck, W. (1986) Comparative mutagenicity of aliphatic epoxides in *Salmonella*. *Mutat. Res., 172*, 105–138

Chen, C.C., Speck, W.T. & Rosenkranz, H.S. (1975) Mutagenicity testing with *Salmonella typhimurium* strains. II. The effect of unusual phenotypes on the mutagenic response. *Mutat. Res., 28*, 31–35

Considine, D.M., ed. (1974) *Chemical and Process Technology Encyclopedia*, New York, McGraw Hill, pp. 443–445, 933

De Flora, S. (1979) Metabolic activation and deactivation of mutagens and carcinogens. *Ital. J. Biochem., 28*, 81–103

De Flora, S. (1981) Study of 106 organic and inorganic compounds in the *Salmonella*/microsome test. *Carcinogenesis, 2*, 283–298

De Flora, S., Zanacchi, P., Camoirano, A., Bennicelli, C. & Badolati, G.S. (1984) Genotoxic activity and potency of 135 compounds in the Ames reversion test and in a bacterial DNA-repair test. *Mutat. Res., 133*, 161–198

Dow Chemical Co. (1988) *Material Safety Data Sheet; 1,2-Epoxybutane*, Midland, MI

Dunkel, V.C., Pienta, R.J., Sivak, A. & Traul, K.A. (1981) Comparative neoplastic transformation responses of Balb/3T3 cells, Syrian hamster embryo cells and Rauscher murine leukemia virus-infected Fischer 34 rat embryo cells to chemical carcinogens. *J. natl Cancer Inst., 67*, 1303–1315

Dunkel, V.C., Zeiger, E., Brusick, D., McCoy, E., McGregor, D., Mortelmans, K., Rosenkranz, H.S. & Simmon, V.F. (1984) Reproducibiity of microbial mutagenicity assays: I. Tests with *Salmonella typhimurium* and *Escherichia coli* using a standardized protocol. *Environ. Mutagenesis, 6 (Suppl. 2)*, 1–254

Dunnick, J.K., Eustis, S.L., Piegorsch, W.W. & Miller, R.A. (1988) Respiratory tract lesions in F344/N rats and B6C3F1 mice after inhalation exposure to 1,2-epoxybutane. *Toxicology, 50*, 69–82

Ehrenberg, L. & Hussain, S. (1981) Genetic toxicity of some important epoxides. *Mutat. Res., 86*, 1–113

Gervasi, P.G., Citti, L., Del Monte, M., Longo, V. & Benetti, D. (1985) Mutagenicity and chemical reactivity of epoxidic intermediates of the isoprene metabolism and other structurally related compounds. *Mutat. Res., 156*, 77–82

Hawley, G.G. (1981) *Condensed Chemical Dictionary*, 10th ed., New York, Van Nostrand Reinhold, p. 165

Hemminki, K., Falck, K. & Vainio, H. (1980) Comparison of alkylation rates and mutagenicity of directly acting industrial and laboratory chemicals. Epoxides, glycidyl ethers, methylating and ethylating agents, halogenated hydrocarbons, hydrazine derivatives, aldehydes, thiuram and dithiocarbamate derivatives. *Arch. Toxicol., 46*, 277–285

Henschler, D., Eder, E., Neudecker, T. & Metzler, M. (1977) Carcinogenicity of trichloroethylene: fact or artifact? *Arch. Toxicol., 37*, 233–236

Henschler, D., Elsässer, H., Romen, W. & Eder, E. (1984) Carcinogenicity study of trichloroethylene, with and without epoxide stabilizers, in mice. *J. Cancer Res. clin. Oncol., 107*, 149–156

Hine, C., Rowe, V.K., White, E.R., Darmer, K.I., Jr & Youngblood, G.T. (1981) Epoxy compounds. In: Clayton, G.D. & Clayton, F.E., eds, *Patty's Industrial Hygiene and Toxicology*, 3rd rev. ed., Vol 2A, New York, John Wiley & Sons, pp. 2162–2165

Hoff, M.C., Im, U.K., Hauschildt, W.F. & Puskas, I. (1978) Butylenes. In: Mark, H.F., Othmer, D.F., Overberger, C.G., Seaborg, G.T. & Grayson, M., eds, *Kirk–Othmer Encyclopedia of Chemical Technology*, 3rd ed., Vol. 4, New York, John Wiley & Sons, p. 366

Hoy, C.A., Salazar, E.P. & Thompson, L.H. (1984) Rapid detection of DNA-damaging agents using repair-deficient CHO cells. *Mutat. Res., 130*, 321–332

Hughes, T.J., Simmons, D.S., Monteith, L.G., Myers, L.E. & Claxton, L.D. (1987) Mutagenicity of 31 organic compounds in a modified preincubation Ames assay with *Salmonella typhimurium* strains TA100 and TA102 (Abstract No. 123). *Environ. Mutagenesis, 9* (*Suppl. 8*), 49

James, S.P., Jeffery, D.A., Waring, R.H. & Wood, P.B. (1968) Some metabolites of 1-bromobutane in the rabbit and the rat. *Biochem. J., 109*, 727–736

Knaap, A.G.A.C., Voogd, C.E. & Kramers, P.G.N. (1982) Comparison of the mutagenic potency of 2-chloroethanol, 2-bromoethanol, 1,2-epoxybutane, epichlorohydrin and glycidaldehyde in *Klebsiella pneumoniae, Drosophila melanogaster* and L5178Y mouse lymphoma cells. *Mutat. Res., 101*, 199–208

Kolmark, G. & Giles, N.H. (1955) Comparative studies of monoepoxides as inducers of reverse mutations in *Neurospora*. *Genetics, 40*, 890–902

McCann, J., Choi, E., Yamasaki, E. & Ames, B.N. (1975) Detection of carcinogens as mutagens in the *Salmonella*/microsome test. Assay of 300 chemicals. *Proc. natl Acad. Sci. USA, 72*, 5135–5139

McCarroll, N.E., Piper, C.E. & Keech, B.H. (1981) An *E. coli* microsuspension assay for the detection of DNA damage induced by direct-acting agents and promutagens. *Environ. Mutagenesis, 3*, 429–444

McGregor, D.B., Martin, R., Cattanach, P., Edwards, I., McBride, D. & Caspary, W.J. (1987) Responses of the L5178Y tK^+/tK^- mouse lymphoma cell forward mutation assay to coded chemicals. I: Results for nine compounds. *Environ. Mutagenesis, 9*, 143–160

McMahon, R.E., Cline, J.C. & Thompson, C.Z. (1979) Assay of 855 test chemicals in ten tester strains using a new modification of the Ames test for bacterial mutagens. *Cancer Res., 39*, 682–693

de Meester, C., Mercier, M. & Poncelet, F. (1982) Comparative mutagenic activity of epoxides derived from 1,3-butadiene (Abstract No. 78). *Mutat. Res., 97*, 204–205

Migliore, L., Rossi, A.M. & Loprieno, N. (1982) Mutagenic action of structurally related alkene oxides on *Schizosaccharomyces pombe*: the influence, 'in vitro', of mouse-liver metabolizing system. *Mutat. Res., 102*, 425–437

Miller, R.R., Quast, J.F., Ayres, J.A. & McKenna, M.J. (1981) Inhalation toxicity of butylene oxide. *Fundam. appl. Toxicol., 1*, 319–324

Mitchell, A.D., Rudd, C.J. & Caspary, W.J. (1988) Evaluation of the L5178Y mouse lymphoma cell mutagenesis assay: intralaboratory results for sixty-three coded chemicals tested at SRI International. *Environ. mol. Mutagenesis, 12 (Suppl. 13)*, 37–101

Myhr, B.C. & Caspary, W.J. (1988) Evaluation of the L5178Y mouse lymphoma cell mutagenesis assay: intralaboratory results for sixty-three coded chemicals tested at Litton Bionetics, Inc. *Environ. mol. Mutagenesis, 12(Suppl. 13)*, 103–194

Myhr, B., Tajiri, D., Mitchell, A., Caspary, W. & Lee, Y. (1981) Blind evaluation of chemicals in the L5178Y/TK$^{+/-}$ mouse lymphoma forward assay (Abstract No. P55). *Environ. Mutagenesis, 3*, 324

Nakamura, S.-I., Oda, Y., Shimada, T., Oki, I. & Sugimoto, K. (1987) SOS inducing activity of chemical carcinogens and mutagens in *Salmonella typhimurium* TA1535/pSK1002: examination with 151 chemicals. *Mutat. Res., 192*, 239–246

National Institute for Occupational Safety and Health (1983) *National Occupational Exposure Survey 1981–83*, Cincinnati, OH

National Toxicology Program (1988) *Toxicology and Carcinogenesis Studies of 1,2-Epoxybutane (CAS No. 106–88–7) in F344/N Rats and B6C3F1 Mice (Technical Report No. 329; NIH Publication No. 88–2585)*, Research Triangle Park, NC, US Department of Health and Human Services

Parmeggiani, L., ed. (1983) Epoxy compounds. In: *Encyclopaedia of Occupational Health and Safety*, 3rd rev. ed., Vol. 1, Geneva, International Labour Office, pp. 770–773

Pienta, R.J. (1980) Transformation of Syrian hamster embryo cells by diverse chemicals and correlation with their reported carcinogenic and mutagenic activities. In: de Serres, F.J. & Hollaender, A., eds, *Chemical Mutagens. Principles and Methods for Their Detection*, Vol. 6, New York, Plenum, pp. 175–202

Pouchert, C.J., ed. (1981) *The Aldrich Library of Infrared Spectra*, 3rd ed., Milwaukee, WI, Aldrich Chemical Co., pp. 135H

Pouchert, C.J., ed. (1983) *The Aldrich Library of NMR Spectra*, 2nd ed., Vol. 1, Milwaukee, WI, Aldrich Chemical Co., pp. 194A

Pouchert, C.J., ed. (1985) *The Aldrich Library of FT–IR Spectra*, Vol. 1, Milwaukee, WI, Aldrich Chemical Co., pp. 228D

Price, P.J. & Mishra, N.K. (1980) The use of Fischer rat embryo cells as a screen for chemical carcinogens and the role of the nontransforming type 'C' RNA tumor viruses in the assay. *Adv. mod. environ. Toxicol., 1*, 213–239

Riedel-de Haën (1984) *Riedel-de Haën Laboratory Chemicals*, Hanover, p. 397

Rosenkranz, H.S. & Poirier, L.A. (1979) Evaluation of the mutagenicity and DNA-modifying activity of carcinogens and noncarcinogens in microbial systems. *J. natl Cancer Inst., 62*, 873–892

Rosenkranz, H.S. & Speck, W.T. (1975) Mutagenicity of metronidazole: activation by mammalian liver microsomes. *Biochem. biophys. Res. Commun., 66*, 520–525

Rosman, L.B., Gaddamichi, V. & Sinsheimer, J.E. (1987) Mutagenicity of aryl propylene and butylene oxides with Salmonella. *Mutat. Res., 189*, 189–204

Sadtler Research Laboratories (1980) *Standard Spectra Collection, 1980 Cumulative Index*, Philadelphia, PA

Sikov, M.R., Cannon, W.C., Carr, D.B., Miller, R.A., Montgomery, L.F. & Phelps, D.W. (1981) *Teratologic Assessment of Butylene Oxide, Styrene Oxide and Methyl Bromide (NIOSH Technical Report 81–124)*, Cincinnati, OH, National Institute for Occupational Safety and Health

Simmon, V.F. (1979a) In vitro mutagenicity assays of chemical carcinogens and related compounds with *Salmonella typhimurium. J. natl Cancer Inst., 62*, 893–399

Simmon, V.F. (1979b) In vitro assays for recombinogenic activity of chemical carcinogens and related compounds with *Saccharomyces cerevisiae* D3. *J. natl Cancer Inst.*, 62, 901–909

Smyth, H.F., Jr, Carpenter, C.P., Weil, C.S., Pozzani, U.C. & Striegel, J.A. (1962) Range-finding toxicity data: list VI. *Am. ind. Hyg. Assoc. J.*, *23*, 95–107

Speck, W.T. & Rosenkranz, H.S. (1976) Mutagenicity of azathioprine. *Cancer Res.*, *36*, 108–109

Van Duuren, B.L., Langseth, L., Goldschmidt, B.M. & Orris, L. (1967) Carcinogenicity of epoxides, lactones, and peroxy compounds. VI. Structure and carcinogenic action. *J. natl Cancer Inst.*, *39*, 1217–1228

Voogd, C.E., van der Stel, J.J. & Jacobs, J.J.J.A.A. (1981) The mutagenic action of aliphatic epoxides. *Mutat. Res.*, *89*, 269–282

Weast, R.C., ed. (1985) *Handbook of Chemistry and Physics*, 66th ed., Cleveland, OH, CRC Press, p. C–165

Weil, C.S., Condra, N., Haun, C. & Striegel, J.A. (1963) Experimental carcinogenicity and acute toxicity of representative epoxides. *Am. ind. Hyg. Assoc. J.*, *24*, 305–325

Weinstein, D., Katz, M. & Kazmer, S. (1981) Use of a rat/hamster S-9 mixture in the Ames mutagenicity assay. *Environ. Mutagenesis*, *3*, 1–9

Williams, G.M., Laspia, M.F. & Dunkel, V.C. (1982) Reliability of the hepatocyte primary culture/DNA repair test in testing of coded carcinogens and noncarcinogens. *Mutat. Res.*, *97*, 359–370