1,1,2,2-TETRACHLOROETHANE

Data were last reviewed in IARC (1979) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

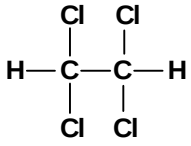
1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Serv. Reg. No.: 79-34-5
Chem. Abstr. Name: 1,1,2,2-Tetrachloroethane
IUPAC Systematic Name: 1,1,2,2-Tetrachloroethane
Synonym: Acetylene tetrachloride

1.1.2 *Structural and molecular formulae and relative molecular mass*



$C_2H_2Cl_4$ Relative molecular mass: 167.85

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Nonflammable, colourless liquid with a chloroform-like odour (Budavari, 1996)
(*b*) *Boiling-point*: 146.5°C (Lide, 1995)
(*c*) *Melting-point*: –43.8°C (Lide, 1995)
(*d*) *Solubility*: Slightly soluble in water (1 g/350 mL at 25°C); miscible with methanol, ethanol, benzene, diethyl ether, petroleum ether, carbon tetrachloride, chloroform, carbon disulfide, dimethylformamide and oils. Has the highest solvent power of the chlorinated hydrocarbons (Lide, 1995; Budavari, 1996)
(*e*) *Vapour pressure*: 665 Pa at 20°C; relative vapour density (air = 1), 5.79 (Verschueren, 1996)
(*f*) *Conversion factor:* $mg/m^3 = 6.87 \times ppm$

1.2 Production and use

1,1,2,2-Tetrachloroethane is used as a solvent, for cleansing and degreasing metals, in paint removers, varnishes, lacquers, photographic film, resins and waxes, extraction of oils and fats, as an alcohol denaturant, in organic synthesis, in insecticides, as a weed-killer and fumigant and as an intermediate in the manufacture of other chlorinated hydrocarbons (Lewis, 1993).

1.3 Occurrence

1.3.1 *Occupational exposure*

National estimates on exposure were not available.

1.3.2 *Environmental occurrence*

Most 1,1,2,2-tetrachloroethane emissions enter the atmosphere, where it is extremely stable (half-life, > 2 years). It has been detected at low levels in urban air, ambient air, drinking-water, ambient water, groundwater, wastewater and soil samples (United States National Library of Medicine, 1997).

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has recommended 6.9 mg/m^3 as the threshold limit value for occupational exposures to 1,1,2,2-tetrachloroethane in workplace air. Similar values have been used as standards or guidelines in many countries (International Labour Office, 1991).

No international guideline for 1,1,2,2-tetrachloroethane in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

The only epidemiological study available evaluated the mortality experience of Second World War army personnel engaged in treating clothing as a defence against gas warfare. In one treatment process, tetrachloroethane was the solvent used for the impregnate. Of the 3859 persons assigned to this process, 1099 whites and 124 blacks had had job duties with probable exposure to the solvent. Among these persons, no significant excess mortality from cancer occurred. Slight excesses were reported for leukaemia (standardized mortality ratio (SMR), 2.7; based on four deaths) and cancer of the genital organs (SMR, 1.6; based on three deaths) (Norman *et al.*, 1981).

3. Studies of Cancer in Experimental Animals

1,1,2,2-Tetrachloroethane was tested for carcinogenicity in one experiment in mice and in one in rats by oral administration. In male and female mice, it produced hepato-

cellular carcinomas. Although a few hepatocellular carcinomas were observed in male rats, no significant increase in the incidence of tumours was observed in animals of either sex. The compound was inadequately tested in one experiment in mice by intraperitoneal injection (IARC, 1979).

3.1 Oral administration

Rat: In a rat liver foci assay for tumour-initiating activity, groups of 10 male Osborne-Mendel rats were subjected to a two-thirds partial hepatectomy and, 24 h later, were given 1,1,2,2-tetrachloroethane or corn oil by gavage at the maximum tolerated dose in corn oil. Six days after partial hepatectomy, rats received 0.05% phenobarbital in the diet for seven weeks, then control diets for seven further days, after which they were killed and their livers were examined. The numbers of enzyme-altered foci in the liver were 0.41 ± 0.31 and 0.26 ± 0.19 foci/cm^2 in the test and control (corn oil) groups, respectively. It was concluded that 1,1,2,2-tetrachloroethane did not show initiating activity in this system (Milman *et al*., 1988).

In a promotion study, groups of 10 rats were given an intraperitoneal injection of 30 mg/kg bw *N*-nitrosodiethylamine (NDEA) 24 h after a two-thirds partial hepatectomy. Six days later, the rats received 1,1,2,2-tetrachloroethane in corn oil at the maximum tolerated dose or corn oil by gavage on five days per week for seven weeks. The rats were held for an additional seven days and then killed and the livers were examined. The numbers of enzyme-altered foci were 4.36 ± 0.85 foci/cm^2 in the treated group and 1.77 ± 0.49 foci/cm^2 in the control (corn oil) group, indicating that 1,1,2,2-tetrachloroethane shows promoting activity (Milman *et al*., 1988).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

About 97% of inhaled 1,1,2,2-tetrachloroethane was retained in the lungs 1 h after exposure (IARC, 1979).

4.1.2 *Experimental animals*

The biotransformation of 1,1,2,2-tetrachloroethane was studied in rats and mice using [^{14}C]1,1,2,2-tetrachloroethane. The metabolic disposition study was conducted after oral administration of the unlabelled compound on five days per week for four weeks, followed by a single dose of the radiolabelled compound to simulate conditions of a bioassay for carcinogenicity testing. After oral administration of 0.59 mmol/kg bw (98.5 mg/kg bw) [^{14}C]1,1,2,2-tetrachloroethane to rats and 1.19 mmol/kg bw (198.7 mg/kg bw) to mice, 7% and 9.7% of the administered radioactivity were recovered in the expired air of rats and

mice, respectively. Rats and mice excreted 46% and 30% of the administered radioactivity as metabolites, respectively, mainly in the urine. Some covalent binding of 1,1,2,2-tetrachloroethane metabolites to proteins was noted in this study (Mitoma *et al.*, 1985). The biotransformation of 1,1,2,2-tetrachloroethane is complex; dichloroacetic acid has been identified as the major urinary metabolite, along with trichloroethanol and trichloroacetic acid (Yllner, 1971). The formation of the latter two metabolites was suggested to be due to reductive biotransformation of 1,1,2,2-tetrachloroethane to give trichloroethene, which may be further oxidized to chloral hydrate by cytochrome P450 (Byington & Leibman, 1965). Trichloroethanol and trichloroacetic acid are formed from chloral hydrate by reduction and respiratory oxidation and are major urinary metabolites of trichloroethene (Daniel, 1963). Hydroxylation of 1,1,2,2-tetrachloroethane, yielding dichloroacetyl chloride, is the predominant pathway to dichloroacetic acid (Halpert & Neal, 1981).

The interaction of 1,1,2,2-tetrachloroethane with DNA, RNA and proteins of male Wistar rats and BALB/c mice *in vivo* was measured 22 h after intraperitoneal injection. The covalent binding index to liver DNA was about 500 (Colacci *et al.*, 1987).

Addition of α-naphthoflavone, metyrapone or glutathione to incubations decreased the covalent binding of 1,1,2,2-tetrachloroethane to olfactory and hepatic tissues *in vitro* (Eriksson & Brittebo, 1991).

Incubation of 1,1,2,2-tetrachloroethane with hepatic microsomes and an NADPH-generating system results in the production of chlorinated metabolites, the major ones being mono- and dichloroacetate (Ivanetich & Van Den Honert, 1981).

1,1,2,2-Tetrachloroethane also appears to be metabolized by hepatic nuclear cytochrome P450 (Casciola & Ivanetich, 1984).

Incubation of 1,1,2,2,-tetrachloro[1,2-^{14}C]ethane with a reconstituted monooxygenase system or with intact rat liver microsomes led to the formation of a metabolite capable of binding covalently to proteins and other nucleophiles. The only soluble metabolite detected upon incubation of 1,1,2,2-tetrachloroethane with a reconstituted system was dichloroacetic acid. Pronase digestion of the ^{14}C-labelled microsomal proteins indicated the presence of several derivatized amino acids, which were hydrolysed by alkali to yield dichloroacetic acid. The results are consistent with biotransformation of 1,1,2,2-tetrachloroethane by cytochrome P450 to dichloroacetyl chloride, which can bind covalently to various nucleophiles or hydrolyse to dichloroacetic acid (Halpert, 1982).

4.2 Toxic effects

The toxicity of 1,1,2,2-tetrachloroethane has been reviewed (Luotamo & Riihimäki, 1996).

4.2.1 *Humans*

Numerous deaths due to ingestion, inhalation or cutaneous absorption of 1,1,2,2-tetrachloroethane have been recorded. The solvent affects primarily the central nervous system and the liver and causes polyneuritis and paralysis. Of 380 workers exposed to the solvent, 133 (35%) exhibited tremor and other nervous symptoms. Accidental and

occupational exposure produced liver damage, ranging from severe fatty degeneration to necrosis and acute atrophy, which was frequently fatal, and gastrointestinal disorders; toxic effects were also observed in the haematopoietic system (IARC, 1979).

4.2.2 *Experimental systems*

1,1,2,2-Tetrachloroethane causes central nervous system depression and is highly hepatotoxic in mice and dogs; it produced embryotoxic effects and a low incidence of malformations in mice. A single oral dose (437 mg/kg bw) of 1,1,2,2-tetrachloroethane decreased the activity of some hepatic cytochrome P450-dependent monooxygenases and, to a smaller extent, that of UDP-glucuronosyl transferase (IARC, 1979).

A decrease in monooxygenase, UDP-glucuronosyl transferase, epoxide hydrolase and aminolaevulinic synthetase activity was observed after an intraperitoneal dose (300 or 600 mg/kg bw) to mice (Paolini *et al*., 1992). 1,1,2,2-Tetrachloroethane inactivated a phenobarbital-induced isolated rat hepatic cytochrome P450 isoenzyme but not a β-naphthoflavone-induced isoenzyme in a reconstituted system *in vitro* (Halpert *et al*., 1986). After an intraperitoneal dose of 1,1,2,2-tetrachloroethane to rats, an accentuated spectral signal of conjugated dienes was observed in extracted endoplasmic lipids, which was interpreted as indicating lipid peroxidation; generation of a nitroxide radical was observed in livers from rats treated simultaneously with the electron spin resonance probe compound, *N*-benzylidene-2-methylpropylamine-*N*-oxide (Paolini *et al*., 1992).

When 0.124 mmol/kg bw 1,1,2,2-tetrachloroethane was administered to male Fischer 344/N rats by gavage once daily, all rats died or were moribund by the termination of the experiment at 21 days. When the dose was 0.62 mmol/kg bw per day, liver weight was elevated and cytoplasmic vacuolation of hepatocytes occurred in all rats. No treatment-related effects were observed in the kidney (United States National Toxicology Program, 1996).

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Treatment of AB-Jena and DBA mice with 300–400 mg/kg bw 1,1,2,2-tetrachloroethane per day during organogenesis produced embryotoxic effects and a low incidence of malformations (exencephaly, cleft palate, anophthalmia, fused ribs and vertebrae). The effects were related to the dose and period of treatment (IARC, 1979).

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 1 for references)

1,1,2,2-Tetrachloroethane induced DNA damage in the *Escherichia coli* differential toxicity assay. It did not induce forward mutation and gave conflicting results for the induction of reverse mutation in *Salmonella typhimurium*. Only one study reported evidence of reverse mutation in strains TA100, TA104, TA98 and TA97, and these tester strains were more sensitive in the presence of an exogenous metabolic activation system. 1,1,2,2-Tetrachloroethane induced gene conversion and mutation in *Saccharomyces cerevisiae* and aneuploidy, without a requirement for exogenous metabolic activation, but not genetic crossing-over, in *Aspergillus nidulans*. It did not increase the frequency of sex-linked recessive lethal mutations in *Drosophila melanogaster*.

1,1,2,2-Tetrachloroethane did not induce chromosomal aberrations in Chinese hamster ovary cells. It induced sister chromatid exchanges in Chinese hamster ovary and mouse BALB/c 3T3 cell cultures and cell transformation in BALB/c 3T3 cells *in vitro*.

Unscheduled DNA synthesis was not induced in hepatocytes of mice given a single gavage treatment of 1,1,2,2-tetrachloroethane. Results from a single study showed that 1,1,2,2-tetrachloroethane bound covalently to DNA in liver, lung, kidney and stomach of rats and mice given a single intraperitoneal injection.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

1,1,2,2-Tetrachloroethane is used as a solvent. It has been detected at low levels in urban and ambient air and in drinking-, ground- and wastewater.

5.2 Human carcinogenicity data

The available epidemiological data are inadequate for evaluation.

5.3 Animal carcinogenicity data

1,1,2,2-Tetrachloroethane was tested in one experiment in mice and in one in rats by oral administration. In mice, it produced hepatocellular carcinomas in males and females. It was inadequately tested by intraperitoneal administration in mice. In one small experiment in rats, no initiating but promoting activity of 1,1,2,2-tetrachloroethane was found.

5.4 Other relevant data

1,1,2,2-Tetrachloroethane bound covalently to DNA but did not induce unscheduled DNA synthesis in mice *in vivo*. It induced sister chromatid exchanges and cell transformation, but not chromosomal aberrations or unscheduled DNA synthesis, in rodent cells *in vitro*. It induced gene conversion and mutation in yeast and aneuploidy, but not genetic crossing-over, in fungus. 1,1,2,2-Tetrachloroethane induced DNA damage and showed some evidence of being mutagenic in bacteria.

Table 1. Genetic and related effects of 1,1,2,2-tetrachloroethane

Test system	Results[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
ECD, *Escherichia coli* pol A, differential toxicity (spot)	+	NT	16000/disc	Brem *et al*. (1974)
SAF, *Salmonella typhimurium*, forward mutation, arabinose resistance	–	–	150	Roldán-Arjona *et al*. (1991)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	2000	Nestmann *et al*. (1980)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	500	Haworth *et al*. (1983)
SA0, *Salmonella typhimurium* TA100, reverse mutation	(+)	+	125	Strobel & Grummt (1987)
SA3, *Salmonella typhimurium* TA1530, reverse mutation	+	NT	1680/disc	Brem *et al*. (1974)
SA4, *Salmonella typhimurium* TA104, reverse mutation	–	(+)	500	Strobel & Grummt (1987)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	NT	1680/disc	Brem *et al*. (1974)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	2000	Nestmann *et al*. (1980)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	500	Haworth *et al*. (1983)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	2000	Nestmann *et al*. (1980)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	500	Haworth *et al*. (1983)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	NT	1680/disc	Brem *et al*. (1974)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	2000	Nestmann *et al*. (1980)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	2000	Nestmann *et al*. (1980)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	500	Haworth *et al*. (1983)
SA9, *Salmonella typhimurium* TA98, reverse mutation	(+)	+	5	Strobel & Grummt (1987)
SAS, *Salmonella typhimurium* TA97, reverse mutation	+	+	5	Strobel & Grummt (1987)
SCG, *Saccharomyces cerevisiae* strain D7, gene conversion, *trp*5 locus	+	NT	875	Callen *et al*. (1980)
SCH, *Saccharomyces cerevisiae* strain D7, homozygosis, *ade*2 locus	+	NT	875	Callen *et al*. (1980)
ANG, *Aspergillus nidulans* strain P1, genetic crossing-over	–	NT	640	Crebelli *et al*. (1988)
SCR, *Saccharomyces cerevisiae* strain D7, reverse mutation, *ilv*1 locus	+	NT	875	Callen *et al*. (1980)
ANN, *Aspergillus nidulans* strain P1, aneuploidy	+	NT	320	Crebelli *et al*. (1988)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	–		1500 ppm feed	Woodruff *et al*. (1985)

Table 1 (contd)

Test system	Results[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SIC, Sister chromatid exchange, Chinese hamster ovary cells *in vitro*	+	+	56	Galloway *et al.* (1987)
SIM, Sister chromatid exchange, BALB/c 3T3 cells *in vitro*	+	+	500	Colacci *et al.* (1992)
CIC, Chromosomal aberrations, Chinese hamster ovary cells *in vitro*	–	–	653	Galloway *et al.* (1987)
TBM, Cell transformation, BALB/c 3T3 mouse cells	–	NT	250	Tu *et al.* (1985)
TBM, Cell transformation, BALB/c 3T3 mouse cells	(+)	+	125	Colacci *et al.* (1990)
TBM, Cell transformation, BALB/c 3T3 mouse cells	NT	+	62.5	Colacci *et al.* (1992)
UVM, Unscheduled DNA synthesis, B6C3F_1 mouse hepatocytes *in vivo*	–		1000 po × 1	Mirsalis *et al.* (1989)
BID, DNA binding (covalent), calf thymus DNA *in vitro*	–	+	10	Colacci *et al.* (1987)
BVD, DNA binding, male BALB/c mouse liver, kidney, lung and stomach *in vivo*	+		1.46 ip × 1	Colacci *et al.* (1987)
BVD, DNA binding, male Wistar rat liver, kidney, lung and stomach *in vivo*	+		1.46 ip × 1	Colacci *et al.* (1987)
BVP, Binding to protein, male BALB/c mouse lung, liver, kidney and stomach *in vivo*	+		1.46 ip × 1	Colacci *et al.* (1987)
BVP, Binding to protein, male Wistar rat lung, liver, kidney and stomach *in vivo*	+		1.46 ip × 1	Colacci *et al.* (1987)

[a] +, positive; (+), weakly positive; –, negative; NT, not tested

[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, μg/mL; in-vivo tests, mg/kg bw/day; po, oral; ip, intraperitoneal

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of 1,1,2,2-tetrachloroethane.

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

Overall evaluation

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

6. References

American Conference of Governmental Industrial Hygienists (1997) *1997 TLVs® and BEIs®*, Cincinnati, OH, p. 37

Brem, H., Stein, A.B. & Rosenkranz, H.S. (1974) The mutagenicity and DNA-modifying effect of haloalkanes. *Cancer Res.*, **34**, 2576–2579

Budavari, S., ed. (1996) *The Merck Index*, 12th Ed., Whitehouse Station, NJ, Merck & Co., p. 1570

Byington, K.H. & Leibman, K.C. (1965) Metabolism of trichloroethylene in liver microsomes II. Identification of the reaction product as chloral hydrate. *Mol. Pharmacol.*, **1**, 247–254

Callen, D.F., Wolf, C.R. & Philpot, R.M. (1980) Cytochrome P-450 mediated genetic activity and cytotoxicity of seven halogenated aliphatic hydrocarbons in *Saccharomyces cerevisiae*. *Mutat. Res.*, **77**, 55–63

Casciola, L.A. & Ivanetich, K.M. (1984) Metabolism of chloroethanes by rat liver nuclear cytochrome P-450. *Carcinogenesis*, **5**, 543–548

Colacci, A., Grilli, S., Lattanzi, G., Prodi, G., Turina, M.P., Forti, G.C. & Mazzullo, M. (1987) The covalent binding of 1,1,2,2-tetrachloroethane to macromolecules of rat and mouse organs. *Teratog. Carcinog. Mutag.*, **7**, 465–474

Colacci, A., Perocco, P., Vaccari, M., Mazzullo, M., Albini, A., Parodi, S., Taningher, M. & Grilli, S. (1990) *In vitro* transformation of BALB/c-3T3 cells by 1,1,2,2- tetrachloroethane. *Jpn. J. Cancer Res. (Gann)*, **81**, 786–792

Colacci, A., Perocco, P., Bartoli, S., Da Via, C., Silingardi, P., Vaccari, M. & Grilli, S. (1992) Initiating activity of 1,1,2,2-tetrachloroethane in two-stage BALB/c-3T3 cell transformation. *Cancer Lett.*, **64**, 145–153

Crebelli, R., Benigni, R., Franekic, J., Conti, G., Conti, L. & Carere, A. (1988) Induction of chromosome malsegregation by halogenated organic solvents in *Aspergillus nidulans*: unspecific or specific mechanism? *Mutat. Res.*, **201**, 401–411

Daniel, J.W. (1963) The metabolism of ^{36}Cl-labelled trichloroethylene and tetrachloroethylene in the rat. *Biochem. Pharmacol.*, **12**, 795–802

Eriksson, C. & Brittebo, E.B. (1991) Epithelial binding of 1,1,2,2-tetrachloroethane in the respiratory and upper alimentary tract. *Arch. Toxicol.*, **65**, 10–14

Galloway, S.M., Armstrong, M.J., Reuben, C., Colman, S., Brown, B., Cannon, C., Bloom, A.D., Nakamura, F., Ahmed, M., Duk, S., Rimpo, J., Margolin, B.H., Resnick, M.A., Anderson, B. & Zeiger, E. (1987) Chromosome aberrations and sister chromatid exchanges in Chinese hamster ovary cells: evaluations of 108 chemicals. *Environ. mol. Mutag.*, **10** (Suppl. 10), 1–175

Halpert, J. (1982) Cytochrome P-450-dependent covalent binding of 1,1,2,2-tetrachloroethane *in vitro*. *Drug Metab. Dispos.*, **10**, 465–468

Halpert, J. & Neal, R.A. (1981) Cytochrome P-450-dpendent metabolism of 1,1,2,2-tetrachloroethane to dichloroacetic acid *in vitro*. *Biochem. Pharmacol.*, **30**, 1366–1368

Halpert, J.R., Balfour, C., Miller, N.E. & Kaminsky, L.S. (1986) Dichloromethyl compounds as mechanism-based inactivators of rat liver cytochromes P-450 *in vitro*. *Mol. Pharmacol.*, **30**, 19–24

Haworth, S., Lawlor, T., Mortelmans, K., Speck, W. & Zeiger, E. (1983) *Salmonella* mutagenicity test results for 250 chemicals. *Environ. Mutag.*, **5** (Suppl. 1), 3–142

IARC (1979) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 20, *Some Halogenated Hydrocarbons*, Lyon, pp. 477–489

IARC (1987) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Suppl. 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon, pp. 354–355

International Labour Office (1991) *Occupational Exposure Limits for Airborne Toxic Substances*, 3rd Ed. (Occupational Safety and Health Series No. 37), Geneva, pp. 378–379

Ivanetich, K.M. & Van Den Honert, L.H. (1981) Chloroethanes: their metabolism by hepatic cytochrome P-450 *in vitro*. *Carcinogenesis*, **2**, 697–702

Lewis, R.J., Jr (1993) *Hawley's Condensed Chemical Dictionary*, 12th Ed., New York, Van Nostrand Reinhold, p. 1127

Lide, D.R., ed. (1995) *CRC Handbook of Chemistry and Physics*, 76th Ed., Boca Raton, FL, CRC Press, p. 3-156

Luotamo, M. & Riihimäki, V. (1996) DECOS and NEG basis for an occupational standard. Tetrachloroethane. *Arbete och Hälsa*, **28**, 1–45

Milman, H.A., Story, D.L., Riccio, E.S., Sivak, A., Tu, A.S., Williams, G.M., Tong, C. & Tyson, C.A. (1988) Rat liver foci and in vitro assays to detect initiating and promoting effects of chlorinated ethanes and ethylenes. *Ann. N.Y. Acad. Sci.*, **534**, 521–530

Mirsalis, J.C., Tyson, C.K., Steinmetz, K.L., Loh, E.K., Hamilton, C.M., Bakke, J.P. & Spalding, J.W. (1989) Measurement of unscheduled DNA synthesis and S-phase synthesis in rodent hepatocytes following in vivo treatment: testing of 24 compounds. *Environ. mol. Mutag.*, **14**, 155–164

Mitoma, C., Steeger, T., Jackson, S.E., Wheeler, K.P., Rogers, J.H. & Milman, H.A. (1985) Metabolic disposition study of chlorinated hydrocarbons in rats and mice. *Drug chem. Toxicol.*, **8**, 183–194

Nestmann, E.R., Lee, E.G.H., Matula, T.I., Douglas, G.R. & Mueller, J.C. (1980) Mutagenicity of constituents identified in pulp and paper mill effluents using the *Salmonella*/mammalian-microsome assay. *Mutat. Res.*, **79**, 203–212

Norman, J.E., Jr, Robinette, C.D. & Fraumeni, J.F., Jr (1981) The mortality experience of army World War II chemical processing companies. *J. occup. Med.*, **23**, 818–822

Paolini, M., Sapigni, E., Mesirca, R., Pedulli, G.F., Corongiu, F.P., Dessi, M.A. & Cantelli-Forti, G. (1992) On the hepatotoxicity of 1,1,2,2-tetrachloroethane. *Toxicology*, **73**, 101–105

Roldán-Arjona, T., Garciá-Pedrajas, D., Luque-Romero, L.L., Hera, C. & Pueyo, C. (1991) An association between mutagenicity of the Ara test of *Salmonella typhimurium* and carcinogenicity in rodents for 16 halogenated aliphatic hydrocarbons. *Mutagenesis*, **6**, 199–205

Strobel, K. & Grummt, T. (1987) Aliphatic and aromatic halocarbons as potential mutagens in drinking water. III. Halogenated ethanes and ethenes. *Toxicol. environ. Chem.*, **15**, 101–128

Tu, A.S., Murray, T.A., Hatch, K.M., Sivak, A. & Milman, H.A. (1985) In vitro transformation of BALB/c-3T3 cells by chlorinated ethanes and ethylenes. *Cancer Lett.*, **28**, 85–92

United States National Library of Medicine (1997*) Hazardous Substances Data Bank (HSDB)*, Bethesda, MD [Record No. 123]

United States National Toxicology Program (1996) *NTP Technical Report on Renal Toxicity Studies of Selected Halogenated Ethanes Administered by Gavage to F344/N Rats* (National Toxicology Program Toxicity Report Series 45), Research Triangle Park, NC

Verschueren, K. (1996) *Handbook of Environmental Data on Organic Chemicals*, 3rd Ed., New York, Van Nostrand Reinhold, pp. 1671–1673

WHO (1993) *Guidelines for Drinking Water Quality*, 2nd Ed., Vol. 1, *Recommendations*, Geneva

Woodruff, R.C., Mason, J.M., Valencia, R. & Zimmering, S. (1985) Chemical mutagenesis testing in *Drosophila*. V. Results of 53 coded compounds tested for the National Toxicology Program. *Environ. Mutag.*, **7**, 677–702

Yllner, S. (1971) Metabolism of 1,1,2,2-tetrachloroethane-^{14}C in the mouse. *Acta pharmacol. toxicol.*, **29**, 499–512