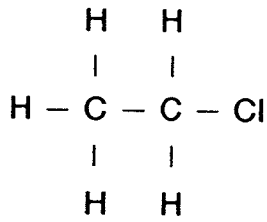
CHLOROETHANE

1. Chemical and Physical Data

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 75-00-3
Chem. Abstr. Name: Chloroethane
IUPAC Systematic Name: Chloroethane
Synonyms: Aethylis; aethylis chloridum; chlorethyl; ether chloratus; ether hydrochloric; ether muriatic; ethyl chloride; hydrochloric ether; monochlorethane; monochloroethane; muriatic ether

1.2 Structural and molecular formulae and molecular weight



C_2H_5Cl Mol. wt: 64.52

1.3 Chemical and physical properties of the pure substance

(*a*) *Description*: Gas at room temperature and pressure, with characteristic ethereal odour and burning taste (Budavari, 1989)

(*b*) *Boiling-point*: 12.3°C (Weast, 1989)

(*c*) *Melting-point*: -136.4°C (Weast, 1989)

(*d*) *Density*: 0.8978 at 20/4°C (Weast, 1989)

(*e*) *Spectroscopy data*[1]: Infrared (Sadtler Research Laboratories, 1980, prism [533], grating [36755]; Pouchert, 1985), nuclear magnetic resonance

[1]In square brackets, spectrum number in compilation

(Sadtler Research Laboratories, 1980, proton [V11]), ultraviolet (Hubrich & Stuhl, 1980) and mass spectral data [45] have been reported.

(*f*) *Solubility*: Soluble in water (5.74 g/l at 20°C), ethanol and diethyl ether (Budavari, 1989; Weast, 1989)

(*g*) *Volatility*: Vapour pressure, 1000 mm Hg at 20°C; relative vapour density (air = 1), 2.22 (Verschueren, 1983; Sax & Lewis, 1987; Budavari, 1989)

(*h*) *Reactivity*: Reacts rapidly with metals such as sodium, potassium, calcium, powdered aluminium, zinc and magnesium (Sittig, 1985)

(*i*) *Octanol/water partition coefficient (P)*: log P, 1.54 (Verschueren, 1983)

(*j*) *Conversion factor*[1]: $mg/m^3 = 2.64 \times ppm$

1.4 Technical products and impurities

Trade names: Anodynon; Chelen; Chlorene; Chloridum; Chloryl; Chloryl anesthetic; Cloretilo; Dublofix; Kelene; Narcotile

Chloroethane is available at greater than 99% purity. One technical-grade product contains water, 0.02% max; nonvolatile residue, 0.01% max; acidity (as HCl), 0.002% max; and total impurities, 0.5% max. It is also available as an anhydrous 2.0M solution in *tert*-butyl methyl ether or diethyl ether (PPG Industries, 1986; American Tokyo Kasei, 1988; Aldrich Chemical Co., 1990).

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

The dominant process for production of chloroethane in the USA involves the addition of anhydrous hydrogen chloride to ethylene (see IARC, 1987a) in the presence of an aluminium chloride catalyst. The hydrochlorination is a liquid-phase reaction, carried out at about 40°C. Reacted products are fed into a flash evaporator column, where chloroethane is separated from less volatile compounds and then purified by fractionation. Hydrochlorination of ethanol has not been used for US chloroethane production since 1980, and chlorination of ethane

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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)

(catalytically, electrolytically, thermally or photochemically) has not been used at any production facility in the USA since 1974. Chloroethane is also obtained as a by-product from the production of vinyl chloride (see IARC, 1987b) or chlorofluorocarbon, although this method accounts for only a small amount (Mannsville Chemical Products Corp., 1984; Hume, 1988).

Production of chloroethane in the USA by year is presented in Table 1. Worldwide exports and imports of chloroethane are presented in Tables 2-4.

Table 1. US production of chloroethane, 1960-88 (in thousand tonnes)[a]

Year	Quantity
1960	247
1965	311
1970	308
1975	261
1980	180
1981	147
1982	154
1983	128
1984	132
1985	77
1986	74
1987	70
1988	69

[a]From Dialog Information Services (1989); US International Trade Commission (1989)

(b) Use

Chloroethane is used in the manufacture of tetraethyllead (see IARC, 1987c) and as an alkylating agent in the production of ethylcellulose (which is used in paper coatings, printing inks, films, adhesives and moulded plastics), ethylhydroxyethylcellulose, some pharmaceuticals and as a foam-blowing agent in the manufacture of polystyrene. It is used as a local anaesthetic because of its rapid cooling effect as it vaporizes (Reynolds, 1989). Historical and minor uses include use in organic synthesis, as an alkylating agent in the production of aluminium alkyls and other metal alkyls and as a solvent for phosphorus, sulfur, fats, oils, resins and waxes (Sax & Lewis, 1987; Hume, 1988; Dow Chemical Co., 1989).

Table 2. Worldwide imports of chloroethane, 1979–88 (in tonnes)[a]

Country	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988
Belgium/Luxembourg[b]	4377	5739	5684	15 774	6168	6266	6475	5733	6166	7221
Brazil	NR[c]	168	84	127	56	15	14	158	317	NR
Canada	2029	497	936	76	10	1955	87	524	1215	3965[b]
Denmark[b]	286	435	372	361	408	396	319	326	223	NR
France	4974	509	4	415	121	1	372	123	371	4084
Germany[b]	8932	8227	8581	10 179	11 721	14 511	12 663	11 533	11 730	13 754
India	NR	5	1	NR	NR	NR	7381	3	NR	NR
Ireland[b]	509	302	277	362	478	103	161	100	243	116
Italy	3037	8923	7777	8486	8886	8877	9880	10 174	8812	NR
Japan	NR	NR	NR	NR	NR	NR	NR	NR	NR	24
Mexico	9646	10 620	10 084	10 634	8538	8739	10 496	NR	10 433	NR
Netherlands[b]	1766	2354	1725	1934	2605	3153	4002	2414	2382	2599
Pakistan	31	NR	17	2	51	2	3	3	28	NR
Portugal[b]	NR	0	0	0	54	1	22	38	0	3
Republic of Korea	55	34	2	31	5	8	11	20	19	NR
Spain	NR	NR	235	225	321	315	394	409	411	NR
UK[b]	971	1447	NR	NR	NR	NR	NR	NR	NR	NR
USA[d]	NR	1270	5030	2325	0.16	NR	1.5	NR	0.4	NR
Venezuela	0	NR	NR	0	6	36	83	51	NR	NR
Yugoslavia[e]	8732	7690	2451	1028	833	9430	51 800	36 868	117 563	1[b]

[a]From Dialog Information Services (1990)
[b]Chloromethane and chloroethane
[c]NR, not reported
[d]From US Department of Commerce (1981, 1982, 1983, 1984, 1986, 1988)
[e]Chloroethane and dichloroethane

Table 3. Countries of origin for imports of chloroethane[a]

Importing country	Year	Country of origin
Belgium/Luxembourg	1987	Federal Republic of Germany (49%), France (45%), USA (3%), Netherlands (2%), UK (1%)
	1988	Federal Republic of Germany (54%), France (42%), UK (4%)
Brazil	1986, 1987	USA (100%)
Canada	1987	USA (100%)
	1988	USA (99%), others (1%)
Denmark	1986	Federal Republic of Germany (43%), Switzerland (36%), Belgium/Luxembourg (20%), others (1%)
	1987	Federal Republic of Germany (79%), Netherlands (6%), others (15%)
Germany, Federal Republic of	1987	France (37%), UK (21%), Belgium/Luxembourg (14%), Netherlands (14%), Switzerland (14%), others (1%)
	1988	France (46%), Switzerland (20%), UK (19%), Belgium/Luxembourg (12%), Netherlands (2%), others (1%)
France	1987	Federal Republic of Germany (100%)
	1988	USSR (90%), Federal Republic of Germany (10%)
India	1985	Saudia Arabia (100%)
	1986	France (100%)
Ireland	1987	UK (55%), Federal Republic of Germany (45%)
	1988	Federal Republic of Germany (46%), Belgium/Luxembourg (38%), Netherlands (16%)
Italy	1986	Federal Republic of Germany (56%), France (44%)
	1987	Federal Republic of Germany (57%), France (43%)
Japan	1988	USA (66%), Singapore (34%)
Mexico	1987	USA (100%)
Netherlands	1987	Federal Republic of Germany (89%), France (6%), UK (3%), others (1%)
	1988	Federal Republic of Germany (87%), Belgium/Luxembourg (5%), France (4%), UK (4%)
Pakistan	1986	UK (100%)
	1987	Federal Republic of Germany (77%), UK (23%)
Republic of Korea	1986	Japan (100%)
	1987	Japan (97%), USA (3%)
Spain	1986	France (98%), Federal Republic of Germany (2%)
	1987	France (88%), Federal Republic of Germany (12%)
Yugoslavia	1987	Italy (63%), Greece (16%), Saudi Arabia (12%), USA (6%), others (3%)

[a]From Dialog Information Services (1990)

Table 4. Worldwide exports of chloroethane, 1979–88 (in tonnes)[a]

Country	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988
Belgium/Luxembourg[b]	2598	2562	2192	2073	1223	1488	1333	1598	1547	1754
Brazil	NR[c]	NR	NR	NR	NR	5	NR	NR	NR	NR
Canada[b]	NR	NR	NR	NR	NR	NR	NR	NR	NR	8118
Denmark[b]	NR	20	44	23	0	1	0	NR	0	NR
France	4994	9076	9148	9035	7603	6008	NR	NR	NR	NR
Germany, Federal Republic of[b]	16 612	19 832	15 812	18 668	20 268	20 640	24 339	33 594	46 928	34 613
India	NR	NR	1	NR	NR	NR	3	NR	NR	NR
Ireland[b]	59	51	20	45	56	60	35	49	40	104
Netherlands[b]	6	567	1268	293	201	100	463	691	896	151
Spain	NR	NR	10	7	9	1	1	NR	NR	NR
UK[b]	4197	1209	1029	1852	1963	3968	4066	3590	4362	4193
USA	12 718	11 876	12 186	12 000	9697	9112	9756	13 868	11 227	8562
Yugoslavia	NR	196[d]	NR	0	NR	NR	0	NR	0	NR

[a]From Dialog Information Services (1990)
[b]Chloromethane and chloroethane
[c]NR, not reported
[d]Chloroethane and dichloroethane

The estimated use pattern for chloroethane in the USA in 1979 was 90% as an ethylating agent in the synthesis of tetraethyllead, 5% as exports and 5% for miscellaneous uses (includes ethyl cellulose plastics, dyes and pharmaceuticals) (Anon., 1979). In 1984, the estimated use pattern for chloroethane was 80% as an ethylating agent in the synthesis of tetraethyllead, 15% in the synthesis of ethyl cellulose and 5% for miscellaneous uses (Mannsville Chemical Products Corp., 1984).

Chloroethane has been investigated as a possible substitute for chlorofluorocarbons in compression heat pumps (Narodoslawsky & Moser, 1988).

(c) *Regulatory status and guidelines*

Occupational exposure limits and guidelines for chloroethane are presented in Table 5.

Table 5. Occupational exposure limits and guidelines for chloroethane[a]

Country	Year	Concentration (mg/m^3)	Interpretation[b]
Australia	1985	2600	TWA
		3250	STEL
Austria	1987	2600	TWA
Belgium	1989	2600	TWA
Brazil	1987	2030	TWA
Canada	1986	2600	TWA
Denmark	1987	2600	TWA
Finland	1989	1300	TWA
		1625	STEL
Germany	1989	2600	TWA
Hungary	1985	50	TWA
		250	STEL
Italy	1987	1000	TWA
Japan	1987	2600	TWA
Mexico	1987	2600	TWA
Netherlands	1987	2600	TWA
Norway	1984	2600	TWA
Poland	1985	200	TWA
Romania	1985	1500	TWA
		2000	STEL
Sweden	1988	1300	TWA
		1900	STEL (15 min)
Switzerland	1987	2600	TWA

Table 5 (contd)

Country	Year	Concentration (mg/m^3)	Interpretation[b]
UK	1987	2600	TWA
		3250	STEL (10 min)
USA			
ACGIH	1989	2640	TWA
OSHA	1989	890	TWA
USSR	1982	50	MAC
Venezuela	1987	2600	TWA
		3250	Ceiling
Yugoslavia	1985	260	TWA

[a]From Cook (1987); American Conference of Governmental Industrial Hygienists (ACGIH) (1989); US Occupational Safety and Health Administration (OSHA) (1989); United Nations Environment Programme (1990)

[b]TWA, time-weighted average; STEL, short-term exposure limit; MAC, maximum allowable concentration

2.2 Occurrence

(*a*) *Natural occurrence*

Chloroethane is not known to occur as a natural product.

(*b*) *Occupational exposure*

The National Occupational Hazard Survey estimated in 1972-74 that 113 000 workers were exposed to chloroethane (National Institute for Occupational Safety and Health, 1978)

A survey at the Ethyl Corp., Pasadena, TX, in 1980 to monitor worker exposure to chloroethane during the manufacture of tetraethyllead found concentrations in personal and area air samples ranging from 274 to 1143 μg/m^3 (Ringenburg, 1983).

(*c*) *Air*

According to the US Toxic Chemical Release Inventory, total emissions of chloroethane into the air in 1987 were approximately 2000 tonnes from 42 locations. Industrial releases to other media were estimated to be 0.9 tonnes to ambient water from six locations and 0.9 kg to the land from one location (National Library of Medicine, 1989).

Estimated emissions of chloroethane in the USA in 1970 were 4800 tonnes, with hydrochlorination of ethylene contributing 3700 tonnes, hydrochlorination of ethanol, 600 tonnes, and chlorination of ethane, 500 tonnes (Processes Research, 1972).

In a later study, it was estimated that about 4500 tonnes of chloroethane are released into the atmosphere every year in the USA; the average background concentration of chloroethane at 40°N in 1981 was 26 ng/m^3. Air samples collected in seven US cities in 1980-81 contained mean chloroethane concentrations of 108-598 ng/m^3 (Singh *et al.*, 1983).

Emissions of chloroethane in 1988 from five major US sources were estimated to be 290 tonnes per year from production (process, equipment leaks, transportation and storage; four producers); 339 tonnes per year from tetraethyllead production (one producer); 982 tonnes per year from ethylene dichloride production (18 producers); 60 tonnes per year from ethyl cellulose production (two producers); and 1170 tonnes per year from its use in polystyrene foam blowing (six facilities) (Hume, 1988).

In a review of data on the presence of volatile organic chemicals in the US atmosphere between 1970 and 1980, a median concentration of 160 ng/m^3 chloroethane was reported for the 348 data points examined, 160 ng/m^3 for urban/suburban areas (337 data points) and 120 ng/m^3 (11 data points) close to industrial sources (Brodzinsky & Singh, 1983).

(*d*) *Water and sediments*

In a survey of large US water utilities, chloroethane was identified as one of 36 unregulated chemicals that were detected at the greatest frequency during routine monitoring of drinking-water (Anon., 1983).

Tap-water samples taken from two buildings in Durham, NC, USA, contained chloroethane (levels not specified); chloroethane was also identified in a purified water sample (McKinney *et al.*, 1976).

Sediment samples collected in 1980 from Lake Pontchartrain, LA, USA, contained a mean chloroethane concentration of 0.2 ng/g wet weight (Ferrario *et al.*, 1985).

(*e*) *Tissues and secretions*

In a gas chromatography-mass spectrometry screening study of human milk samples collected in four urban areas of the USA, traces of chloroethane were found in two of eight samples (Pellizzari *et al.*, 1982).

Oyster samples collected in 1980 from Lake Pontchartrain, LA, USA, contained a mean chloroethane concentration of 7.6 ng/g wet weight (Ferrario *et al.*, 1985).

2.3 Analysis

Selected methods for the analysis of chloroethane in air, breath and water are identified in Table 6. The US Environmental Protection Agency methods for analysing water (Methods 8010 and 8240) have also been applied to liquid and solid wastes. Volatile components of solid-waste samples are first extracted with methanol prior to purge-and-trap concentration and analysis by gas chromatography-electrolytic conductivity detection (Method 8010) or gas chromatography-mass spectrometry (Method 8240). The detection limit using Method 8010 is 0.5 μg/l and the practical quantification limit using Method 8240 is 10 μg/l for groundwater and soil/sediment samples (US Environmental Protection Agency, 1986a,b).

US Environmental Protection Agency Method 624 has also been adapted to the analysis of chloroethane in fish, with an estimated detection limit of 250 μg/kg (Easley *et al.*, 1981).

Table 6. Methods for the analysis of chloroethane

Sample matrix	Sample preparation[a]	Assay procedure[b]	Limit of detection[c]	Reference
Air	Adsorb on activated charcoal; desorb (carbon disulfide); inject aliquot	GC/FID	0.01 mg per sample	Eller (1985); SKC Inc. (1989)
	Collect whole air sample in neutralized stainless-steel canister	GC/FID	NR	US Environmental Protection Agency (1988a) [Method TO-14]
	Draw air through tube; compare reaction with standard chart	Colorimetric	NR	Lodge (1989a)
Breath	Collect sample in plastic bag; evacuate cell; draw sample in and scan	FT-IR	10 ppm (26.4 mg/m^3)	Lodge (1989b)
Water	Purge (inert gas); trap (OV-1 on Chromosorb-W/Tenax/silica gel); desorb as vapour (heat to 180°C, backflush with inert gas) onto packed GC column	GC/ECD	0.5 μg/l	US Environmental Protection Agency (1988b) [Method 601]
		GC/MS	NR	US Environmental Protection Agency (1988c) [Method 624]

Table 6 (contd)

Sample matrix	Sample preparation[a]	Assay procedure[b]	Limit of detection[c]	Reference
Water	Purge (inert gas); trap (OV-1 on Chromosorb-W/Tenax/silica gel); desorb as vapour (heat to 180°C, backflush with inert gas) onto capillary GC column	GC/ECD	0.1 µg/l	US Environmental Protection Agency (1988d) [Method 502.2]
		GC/MS	0.1 µg/l	US Environmental Protection Agency (1988e) [Method 524.2]

[a]GC, gas chromatograph

[b]GC/FID, gas chromatography/flame ionization detection; FT-IR, Fourier transform/infrared spectroscopy; GC/ECD, gas chromatography/electrolytic conductivity detection; GC/MS, gas chromatography/mass spectrometry

[c]NR, not reported

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

3.1 Carcinogenicity studies in animals (Table 7)

Inhalation

Mouse: Groups of 50 male and 50 female B6C3F$_1$ mice, nine weeks old, were exposed by inhalation to 15 000 ppm (39 600 mg/m^3) chloroethane (99.5% pure) by whole-body exposure for 6 h per day on five days per week for 100 weeks. Survival at 109 weeks of age was: males—control, 28/50; treated, 11/50; females—control, 32/50; treated, 2/50. Uterine neoplasms reduced the survival of treated female mice. Carcinomas of the uterus occurred in 0/49 control and 43/50 treated female mice ($p < 0.001$, logistic regression test), and the carcinomas in many female mice metastasized to a variety of organs. Hepatocellular tumours, primarily carcinomas, occurred in 3/49 control female and 8/48 treated female mice ($p = 0.025$, logistic regression test); the incidence of liver tumours in treated males was not increased (10/47 *versus* 15/50 controls). In males, alveolar/bronchiolar adenomas occurred in 3/50 control and 8/48 treated mice, and alveolar/bronchiolar carcinomas were seen in 2/50 control and 2/48 treated male mice. The proportion of treated male mice with alveolar/bronchiolar tumours was increased relative to that in controls ($p = 0.008$, logistic regression test). The incidence of lung tumours was not increased in females: controls, 5/49; treated, 4/50 (National Toxicology Program, 1989).

Rat: Groups of 50 male and 50 female Fischer 344 rats, eight weeks old, were exposed by inhalation to 15 000 ppm (39 600 mg/m^3) chloroethane (99.5% pure) by whole-body exposure for 6 h per day on five days per week for 102 weeks. Survival at 112 weeks of age was: males—control, 16/50; treated, 8/50; females—control, 31/50; treated, 22/50. Tumours of the skin occurred in 4/50 control male and 9/50 treated male rats. The distribution of tumour types was as follows: trichoepithelioma, 1/50 treated; sebaceous gland adenoma, 1/50 treated; basal-cell carcinoma, 3/50 treated; squamous-cell carcinoma, 2/50 treated; keratoacanthoma, 4/50 control and 2/50 treated. The incidences of all epithelial skin neoplasms in historical controls were 19/300 (6.3%) at the study laboratory and 100/1936 (5.2%) at all National Toxicology Program laboratories. Brain glial-cell tumours (astrocytomas) occurred in 3/50 treated female rats but not in controls; the historical incidence of these tumours in female rats at the study laboratory was 1/297 and that at all National Toxicology Program laboratories was 23/1969 (1.2%) (National Toxicology Program, 1989).

3.2 Other relevant data

(*a*) *Experimental systems*

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

The human blood serum/gas partition coefficient (K_D at 25°C) of chloroethane is 2.3 (Morgan *et al.*, 1972).

^{36}Cl-Chloroethane undergoes little (< 0.5%) dechlorination when incubated with rat hepatic microsomal fractions in the presence of NADPH and oxygen (Van Dyke & Wineman, 1971).

(ii) *Toxic effects*

The toxicology of chloroethane has been reviewed (Torkelson & Rowe, 1981).

Acute exposure of guinea-pigs by inhalation to 23-24% chloroethane vapour in air for 5-10 min and to 15.3% for 40 min resulted in some deaths, whereas all animals exposed to 9.1% for 30 min and 1% for 810 min survived (Torkelson & Rowe, 1981). A 2-h inhalation LC_{50} of 152 mg/l (57 600 ppm) chloroethane was reported for white rats [strain unspecified] (Troshina, 1964); signs of toxicity included anaesthesia, liver congestion, haemorrhage and lung oedema. The narcotic concentration of chloroethane for mice, rabbits, dogs and cats was 3.4-4.5% (Henderson & Kennedy, 1930). Cardiac arrhythmia (due to vagus stimulation and sensitization to adrenalin) were observed in dogs under chloroethane anaesthesia (Bush *et al.*, 1952; Morris *et al.*, 1953; Haid *et al.*, 1954). Exposure of male and female Fischer 344/N rats and B6C3F$_1$ mice to 4000 and 10 000 ppm (10.56 and 26.4 g/m^3) chloroethane for 6 h resulted in decreased non-protein sulfhydryl concentrations in the liver 30 min after exposure (Landry *et al.*, 1982).

Table 7. Summary of carcinogenicity studies of chloroethane in experimental animals

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Significance	Comments
					0	1	2	3		
National Toxicology Program (1989)	Mouse $B6C3F_1$	M	6 h/d, 5 d/week, inhalation, 100 weeks	Dose (ppm)	0	15 000	-	-		
				Survival (109 weeks of age)	28/50	11/50				
				Alveolar/bronchiolar						
				Adenoma	3/50	8/48			} $p = 0.008$	Increase
				Carcinoma	2/50	2/48				
		F		Dose (ppm)	0	15 000	-	-		
				Survival (109 weeks of age)	32/50	2/50				
				Uterine carcinoma	0/49	43/50			$p < 0.001$	Increase
				Hepatocellular						
				Adenoma	0/49	1/48			} $p = 0.025$	
				Carcinoma	3/49	7/48				
	Rat F344	M	6 h/d, 5 d/week, inhalation, 102 weeks	Dose (ppm)	0	15 000	-	-		
				Survival (112 weeks of age)	16/50	8/50				
				Skin						
				Trichoepithelioma	0/50	1/50			} $p = 0.016$	Increase
				Sebaceous adenoma	0/50	1/50				
				Basal-cell carcinoma	0/50	3/50				
				Squamous-cell carcinoma	0/50	2/50				
				Keratoacanthoma	4/50	2/50				
		F		Dose (ppm)	0	15 000	-	-		
				Survival (112 weeks of age)	31/50	22/50				
				Astrocytoma	0/50	3/50				Uncommon tumour

Exposure of male and female Fischer 344/N rats and male beagle dogs to 1600, 4000 or 10 000 ppm (4.2, 10.56 or 26.4 g/m^3) chloroethane for 6 h per day on five days per week for two weeks had no toxic effect except for slight increases in relative liver weights of male rats exposed to 4000 or 10 000 ppm (Landry *et al.*, 1982). Similar results were obtained when male and female B6C3F$_1$ mice were exposed to 5000 ppm (13.2 g/m^3) chloroethane for 23 h per day for 11 consecutive days; exposure to 250 or 1250 ppm (0.66 or 3.3 g/m^3) had no effect on relative liver weights (Landry *et al.*, 1989).

Exposure of male and female Fischer 344/N rats and B6C3F$_1$ mice to 2500-19 000 ppm (6.6-50.2 g/m^3) chloroethane for 6 h per day on five days per week for 13 weeks by whole-body inhalation induced no clinical sign of toxicity, and no gross pathological or histological change was observed except for reduced body weight. Increased relative liver weights were observed in male rats and female mice exposed to 19 000 ppm (National Toxicology Program, 1989). Conversely, chloroethane [purity nonspecified] at 0.57 g/m^3 (216 ppm) for 4 h per day for six months was reported to cause liver and lung damage, decreased blood pressure and reduced phagocytic activity of leukocytes in rats [sex and strain were not specified] (Troshina, 1966).

(iii) *Effects on reproduction and prenatal toxicity*

No data were available to the Working Group.

(iv) *Genetic and related effects* (Table 8)

Chloroethane was mutagenic to *Salmonella typhimurium*, but no response was observed in a cell transformation assay using cultured mammalian cells. A study reporting a positive response in *S. typhimurium* and negative responses in tests for unscheduled DNA synthesis in mouse hepatocytes and for transformation in BALB/c 3T3 cells could not be evaluated [details not given] (Milman *et al.*, 1988).

(*b*) *Humans*

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

When ^{38}Cl-chloroethane was administered by inhalation at about 5 mg/subject in a single breath [subject weight unspecified] to human volunteers, about 30% of the administered radioactivity was eliminated in the breath within 1 h. Urinary excretion of ^{38}Cl amounted to < 0.01% of the dose/min (Morgan *et al.*, 1970).

(ii) *Toxic effects*

Davidson (1926) exposed volunteers to 1.3-3.36% chloroethane vapour in air. No adverse effect was seen after exposure to 1.3% for 21 min, whereas exposure to 3.36% led to incoordination, unconsciousness and cyanosis within minutes. Decreased reaction times were observed with exposure to concentrations of 2.5%.

Table 8. Genetic and related effects of chloroethane

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation	-	+	0.0000	National Toxicology Program (1989)[a]
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	0.0000	National Toxicology Program (1989)[a]
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	0.0000	National Toxicology Program (1989)[a]
TBM, Cell transformation, BALB/c3T3 mouse cells	-	0	467.0000	Tu *et al.* (1985)[a]

[a]Closed container

The anaesthetic concentration of chloroethane in humans has been estimated to be 4% (Lawson, 1965). During anaesthesia, vagal inhibition may occur (Bush *et al.*, 1952). Deaths that occurred under anaesthesia were due mainly to very high chloroethane concentrations, which caused respiratory depression (Henderson & Kennedy, 1930; Dobkin & Byles, 1971).

Chloroethane has been shown to elicit allergic contact dermatitis (van Ketel, 1976).

(iii) *Effects on reproduction and prenatal toxicity*

No data were available to the Working Group.

(iv) *Genetic and related effects*

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 Exposure data

Chloroethane is produced by the hydrochlorination of ethylene. It is used in the manufacture of tetraethyllead, as an industrial ethylating agent, as a blowing agent in the production of polystyrene foam and as a local anaesthetic. Occupational exposure occurs during the production of tetraethyllead, and industrial emissions have led to detectable levels of chloroethane in ambient air.

4.2 Experimental carcinogenicity data

Chloroethane was tested for carcinogenicity in a two-year study in male and female B6C3F$_1$ mice and Fischer 344 rats by inhalation. It induced uterine carcinomas in mice; marginal increases occurred in the incidence of hepatocellular tumours in female mice and in the incidence of alveolar/bronchiolar tumours in male mice. There was a marginal increase in the incidence of skin tumours in male rats, and a few uncommon glial-cell tumours occurred in female rats.

4.3 Human carcinogenicity data

No data were available to the Working Group.

4.4 Other relevant data

In single studies, chloroethane was mutagenic to bacteria but did not induce transformation in cultured mammalian cells.

4.5 Evaluation[1]

There is *limited evidence* for the carcinogenicity of chloroethane in experimental animals.

No data were available from studies in humans on the carcinogenicity of chloroethane.

Overall evaluation

Chloroethane *is not classifiable as to its carcinogenicity to humans (Group 3).*

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[1]For definition of the italicized terms, see Preamble, pp. 30-33.

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