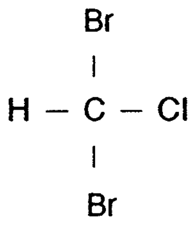
CHLORODIBROMOMETHANE

1. Chemical and Physical Data

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 124-48-1
Chem. Abstr. Name: Chlorodibromomethane
IUPAC Systematic Name: Chlorodibromomethane
Synonyms: Dibromomethanechloro; dibromomonochloromethane; monochlorodibromomethane

1.2 Structural and molecular formulae and molecular weight



$$\begin{array}{c} Br \\ | \\ H - C - Cl \\ | \\ Br \end{array}$$

$CHBr_2Cl$ Mol. wt: 208.29

1.3 Chemical and physical properties of the pure substance

(*a*) *Description*: Clear, colourless to pale-yellow liquid (Verschueren, 1983)
(*b*) *Boiling-point*: 119-120°C at 748 mm Hg (Weast, 1989)
(*c*) *Melting-point*: < -20°C (Verschueren, 1983)
(*d*) *Density*: 2.451 at 20/4°C (Weast, 1989)
(*e*) *Spectroscopy data*[1]: Infrared (Sadtler Research Laboratories, 1980, prism [1896], grating [284]; Pouchert, 1981, 1985a,b), nuclear magnetic resonance (Sadtler Research Laboratories, 1980, proton [6708], C-13 [2846]; Pouchert, 1983) and mass spectral data [1458] (Bunn *et al.*, 1975; Coleman *et al.*, 1984) have been reported.

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[1] In square brackets, spectrum number in compilation

(*f*) *Solubility*: Soluble in acetone, ethanol, benzene and diethyl ether (Weast, 1989)

(*g*) *Volatility*: Vapour pressure, 76 mm Hg at 20°C (Mabey *et al.*, 1982)

(*h*) *Reactivity*: Hydrolysis constant at 25°C and neutral pH, $K = 2.88 \times 10^{-8}$ per hour (Mabey *et al.*, 1982)

(*i*) *Octanol/water partition coefficient (P)*: log P, 2.24 (Mabey *et al.*, 1982)

(*j*) *Conversion factor*[1]: $mg/m^3 = 8.52 \times ppm$

1.4 Technical products and impurities

Chlorodibromomethane is available at > 95-98% purity (American Tokyo Kasei, 1988; Aldrich Chemical Co., 1990).

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

Chlorodibromomethane has been synthesized by the addition of dibromochloroacetone to 5N sodium hydroxide, followed by drying and distillation of the combined oil and ether extract (Barrett *et al.*, 1971). It is also formed in the reaction of a mixture of chloroform (see IARC, 1987) and bromoform (see monograph, p. 213) with triethylbenzylammonium chloride and sodium hydroxide (Fedorynski *et al.*, 1977).

(*b*) *Use*

Chlorodibromomethane has been used as a chemical intermediate in the manufacture of fire extinguishing agents, aerosol propellants, refrigerants and pesticides (Sittig, 1985). It is also used for the preparation of phenyldibromochloromethylmercury, which has been used for the generation of bromochlorocarbene (Fedoryński *et al.*, 1977).

(*c*) *Regulatory status and guidelines*

Standards for trihalomethanes (including chlorodibromomethane) have been established in drinking-water (see monograph on chlorination of drinking-water, p. 59) in several countries.

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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)

2.2 Occurrence

(*a*) *Natural occurrence*

Levels of chlorodibromomethane in tissues of temperate marine macroalgae (*Ascophyllum nodosum, Fucus vesiculosis, Enteromorpha linza, Ulva lacta, Gigartina stellata*) ranged from 150 to 590 ng/g dry weight. Chlorodibromomethane was released to seawater at rates of 150-4300 ng/g of dry algae per day (Gschwend *et al.*, 1985).

Macroalgae collected near the Bermuda Islands (*Fucales sargassum*) and at the Cape of Good Hope (*Laminariales laminaria*) showed a specific pattern of emission of volatile organohalides into the surrounding air. The main components were bromoform, bromodichloromethane and chlorodibromomethane; a minor component was bromoethane (Class *et al.*, 1986).

(*b*) *Air*

The volatilization half-time of chlorodibromomethane from rivers and streams has been estimated to range from 43 min to 17 days, depending on turbulence and temperature. A typical half-time, based on actual data, was 46 h (Kaczmar *et al.*, 1984).

Chlorodibromomethane was detected in seven of 22 air samples collected in 1978 from Bochum University and Bochum-Kemnade, Germany, at a concentration of 0.1 μg/m^3; and in five of 12 air samples from Bochum-City, at not detected to 0.9 μg/m^3 (Bauer, 1981).

Ullrich (1982) studied the organohalogen concentrations in the air of four public indoor swimming pools in western Berlin. Mean chlorodibromomethane concentrations ranged from 30 to 170 μg/m^3 in three of them.

In a review of data on the presence of volatile organic chemicals in the atmosphere of the USA in 1970-80, a median concentration of 120 ng/m^3 chlorodibromomethane was reported for the 21 urban/suburban data points examined and below the limit of detection for industrial areas (68 data points) (Brodzinsky & Singh, 1983).

In the USA, air samples collected 2 cm above the surface of five outdoor pools contained 0.4-2 μg/m^3 chlorodibromomethane; those above indoor pools contained 0.5-17 μg/m^3 and those above four spas (whirlpools or hot tubs) contained < 0.1-31 μg/m^3. Samples collected 2 m above the surface contained < 0.1 μg/m^3, < 0.1-5 μg/m^3 and < 0.1-5 μg/m^3, respectively (Armstrong & Golden, 1986).

Levels of chlorodibromomethane in air samples collected in 1982-85 over the Atlantic Ocean were 0.06-10 ppt (0.5-85.2 ng/m^3); baseline levels of biogenic chlorodibromomethane in air were 0.1-0.5 ppt (0.9-4.3 ng/m^3). Air samples collected in 1985 from a forest area in southern Germany contained 0.4 ppt (3.4 ng/m^3) chlorodibromomethane (Class *et al.*, 1986).

(*c*) *Water and sediments*

The formation of trihalomethanes in drinking-water (see also the monograph on chlorinated drinking-water, p. 56 *et seq.*) and the effects of temperature and pH have been discussed extensively (Williams, 1985). The formation of chlorodibromomethane during drinking-water chlorination depends on the presence of bromine in untreated water.

Chlorodibromomethane has been measured or detected in many drinking-water systems, both in samples collected at treatment facilities or along the distribution system (Table 1) and in samples collected from natural and untreated water sources (Table 2). Concentrations in treated drinking-water typically ranged from 1 to 20 μg/l (with higher or lower values in some locations), compared with concentrations in untreated (natural) waters which are typically less than 1 μg/l.

Table 1. Chlorodibromomethane concentrations in treated[a] drinking-water, 1973-89

Location, date[b]	Sample site/raw water source[c]	Concentration (μg/l)[d]	Reference
NS, 1973, 1974 NS, 1974	NS/surface NS/well	< 0.1–2.0 0.8–0.9	Bellar *et al.* (1974a,b)
80 US cities (NORS), 1975	NS/ground and surface	ND–100	Symons *et al.* (1975)
113 Public water supplies, 1976	Water supplies/NS	Mean, 14; median, 3.5	Brass *et al.* (1977)
945 US sites, 1981–82	T/ground	2.1–4.6[e] (max., 63)	Westrick *et al.* (1984)
13 US community systems, 1984–85	T and D/NS	< 0.2–27	Reding *et al.* (1989)
10 US utilities, 1985	T/ground and surface	> 10– < 100 (2 sites) < 10 (8 sites)	Stevens *et al.* (1989)
35 US sites	T/ground and surface	Median	Krasner *et al.* (1989)
Spring 1988		2.6	
Summer 1988		4.5	
Autumn 1988		3.8	
Winter 1989		2.7	
Durham, North Carolina, 1975	D/surface	2.16–3.40	McKinney *et al.* (1976)
15 Kentucky cities, 1977	T/surface	ND–trace	Allgeier *et al.* (1980)

Table 1 (contd)

Location, date[b]	Sample site/raw water source[c]	Concentration (μg/l)[d]	Reference
20 Tennessee sites	T/ground and surface		Minear & Morrow (1983)
Autumn 1980		1–96 ng/l	
Winter 1980		7–291 ng/l	
Spring 1981		10–152 ng/l	
Summer 1981		19–373 ng/l	
Miami, Florida	NS/ground		Loy *et al.* (1976)
January 1975		35	
July 1975		37	
Southwestern US city, 1975	NS/ground	7.53–42.8	Henderson *et al.* (1976)
East Texas, 1977	NS/surface (14 sites) NS/ground (11 sites)	trace–183.7 ND–173.1	Glaze & Rawley (1979)
Houston, Texas, summer 1978 to winter 1980	NS/surface NS/ground	max., 46 max., 7	Cech *et al.* (1982)
40 Michigan utilities, NS	T/surface (22 sites) T/ground (18 sites)	ND–39.6 ND–3.1	Furlong & D'Itri (1986)
Old Love Canal, NY, 1978	D/NS	ND–6.8	Barkley *et al.* (1980)
5 Pennsylvania sites, 1987	T surface	3.2–4.7	Smith (1989)
5 Virginia sites, 1987		0.3–1.49 (range of means)	
3 Puerto Rican cities, NS	D/ground and surface	6.1–11 ng/l	Rodriguez-Flores (1983)
70 Canadian cities, 1976–77	D and T/ground and surface	0–6.2 (median, 0.1)	Health & Wefare Canada (1977)
30 Canadian sites,	T/ground and surface		Otson *et al.* (1982)
Aug.–Sep. 1979		mean, < 1; max., 4	
Nov.–Dec. 1979		mean, < 1; max., 3	
Burlington, Ontario, Canada, 1981	D/NS	0.91	Comba & Kaiser (1983)
Niagara Falls, Ontario, 1981		1	
Port Robinson, Ontario, 1981		4	
Chippawa, Ontario, 1981	D/surface	2.1	Kaiser & Comba (1983)
10 Ontario cities, 1981	T/surface D/surface	0.1–2.9 0.1–4.8	Oliver (1983)
10 Canadian Great Lakes sites, Ontario	T/ground and surface		Otson (1987)
Summer 1982		mean, 1.8	
Winter 1983		mean, 1.4	
Spring 1983		mean, 1.9	

Table 1 (contd)

Location, date[b]	Sample site/raw water source[c]	Concentration (μg/l)[d]	Reference
Lancashire–Cheshire, UK, 1974	D/NS	< 0.01–3 μg/kg	McConnell (1976)
Southeastern UK, NS	D/ground and surface	2.3	Trussell *et al.* (1980)
Southampton, UK, 1977–78	D/surface	pumping station mean, 1.50 reservoir mean, 2.29	Brett & Calverley (1979)
5 Belgian utilities, 1977–78	T/surface	0.3–14.6	Quaghebeur & De Wulf (1980)
	D/surface	0.4–12.8	
9 Belgian utilities, 1977–78	T/ground	0–10.4	
	D/ground	0–5.5	
100 German cities, 1977	NS/NS	< 0.1–17.1 (mean, 0.4)	Bauer (1981)
37 German sites, 1976	NS/NS	mean, 0.3	
Bremen and Leverkusen, Germany, NS	NS/NS	0.1–1.5	
12 German cities, 1978	NS/NS	ND–19.8 (mean, 2.2)	Eklund *et al.* (1978)
9 German cities, 1978–79	D/NS	1.2–9.6	Lahl *et al.* (1982)
Gothenberg, Sweden, 1977	D/surface	0.6	Eklund *et al.* (1978)
Southern China, NS	D/local catchments	13	Trussell *et al.* (1980)
Southern Philippines, NS	D/ground and surface	1.2	Trussell *et al.* (1980)
Northern Philippines, NS	D/surface	1.5	Trussell *et al.* (1980)
Northern Egypt, NS	D/surface	ND	Trussell *et al.* (1980)
Southern Indonesia, NS	D/surface	0.7	Trussell *et al.* (1980)
Southeastern Australia, NS	D/surface	ND	Trussell *et al.* (1980)
Southern Brazil, NS	D/surface	ND	Trussell *et al.* (1980)
Eastern Nicaragua, ND	D/surface	1.1	Trussell *et al.* (1980)
Northern Venezuela, NS	D/surface	ND	Trussell *et al.* (1980)
Eastern Peru, NS	D/ground and surface	2.7	Trussell *et al.* (1980)

[a] Treatment not always specified

[b] NORS, National Organics Reconnaissance Survey; NS, not specified

[c] D, distribution system; T, treatment plant

[d] Unless otherwise noted; ND, not detected

[e] Range of median values for randomly and nonrandomly selected water supplies serving fewer than and more than 10 000 people

Table 2. Chlorodibromomethane concentrations in untreated (natural) water, 1973-89

Location, date	Sample source	Concentration (ng/l)[a]	Reference
Northern Taiwan, NS	Well	ND	Trussell *et al.* (1980)
Rhine River, Germany, 1976	River	< 0.1–0.3	Bauer (1981)
New Jersey, USA, 1977–79	Ground Surface	2.4 μg/l 8.2 μg/l	Page (1981)
30 Canadian sites, 1979	River, lake and ground	mean, < 1 μg/l	Otson *et al.* (1982)
Lake Ontario, Canada, 1981	Lake	ND–630	Kaiser *et al.* (1983)
Niagara River, Ontario, Canada, 1981	River	trace–15 (mean, 4)	
Welland River watershed, Ontario, Canada	Surface (river)		Kaiser & Comba (1983)
Summer 1980		ND–15	
Spring 1981		ND–800	
10 Canadian Great Lakes sites	Ground and surface		Otson (1987)
Summer 1982		mean, < 100	
Winter 1983		0	
Spring 1983		mean, 100	
North and South Atlantic 1985	Seawater	0.1–2.2 (baseline, 0.12)	Class *et al.* (1986)
Ulm, Germany, NS	Rainwater	0.7	Class *et al.* (1986)

[a] ND, not detected

Rook (1974) demonstrated that chlorodibromomethane, observed at concentrations ranging from 1.7 to 13.3 μg/l following chlorination of stored surface waters, was a product of chlorination of the humic substances in natural waters.

Chlorodibromomethane was detected (but not quantified) by headspace analysis in two of ten Pacific seawater headspace samples collected in 1983 (Hoyt & Rasmussen, 1985).

Chlorodibromomethane was found in water samples collected at various stages of water treatment: not detected (< 0.1 μg/l) in raw river water; 0.7 μg/l in river water treated with chlorine and alum; 1.1 μg/l in three-day-old settled water; 2.4 μg/l in water flowing from settled areas to filters; 1.7 μg/l in the filter effluent; and 2.0 μg/l in finished water (Bellar *et al.*, 1974a,b).

In the 1975 US National Organics Reconnaissance Survey of water supplies from 80 US cities, chlorodibromomethane was not found in any of the raw water samples (minimum quantifiable concentration, 0.4 μg/l) (Symons *et al.*, 1975).

According to the US Environmental Protection Agency STORET system, chlorodibromomethane concentrations in 130 samples of surface water in 1970-79 ranged from 0.1 to 1.0 μg/l in 80% of the samples and 1 to 10 μg/l in 20% of the samples (Perwak *et al.*, 1980).

The US Environmental Protection Agency estimated that 204 tonnes of chlorodibromomethane were generated in the USA in 1978 by water chlorination. On the basis of the 1976 National Organic Monitoring Survey, the general population was estimated to be exposed to 7 μg chlorodibromomethane per day from drinking-water, assuming a median concentration of 4 μg/l and a water intake of 1.65 l per day; assuming a maximal concentration of 290 μg/l and an intake of 2.18 l per day, the daily exposure increased to 600 μg per day (Perwak *et al.*, 1980). In a later investigation by the US Environmental Protection Agency STORET data base, analysis of 18 616 water samples revealed a mean chlorodibromomethane concentration of 10.09 μg/l (range, 0-10133 μg/l); analysis of 590 sediment samples revealed a mean of 11.3 μg/kg (range, 0-237 μg/kg) (US Environmental Protection Agency, 1985).

In the 1982 US Nationwide Urban Runoff Program, chlorodibromomethane was detected in samples from one of the 15 reporting cities at a concentration of 2 μg/l (Cole *et al.*, 1984).

Tap-water samples collected between January 1977 and March 1978 in Osaka, Japan, contained chlorodibromomethane at levels of 1.6, 2.6 and 4.3 μg/l at seasonal mean water temperatures of 7.4°C, 15.8°C, and 25.4°C, respectively. An increase of approximately 0.5 in pH to control pipe corrosion resulted in chlorodibromomethane concentrations of 2.4, 3.4 and 4.9 μg/l at similar mean water temperatures (Kajino & Yagi, 1980).

Chlorodibromomethane levels in tap water collected at four locations in a Swedish community ranged from 0.87 to 1.3 μg/l; when the treatment facility briefly changed the disinfectant from chlorine to chlorine dioxide, chlorodibromomethane was not detected (detection limit, 0.006 μg/l) (Norin *et al.*, 1981).

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

Samples of water were collected between August and October 1980 from four supply systems in São Paulo State, Brazil. Mean levels of chlorodibromomethane were 1.3-3.4 µg/l in treated water (after treatment), 1.8-6.4 µg/l in treated water from the reservoir and 2.2-80 µg/l in treated tap water (de Fernicola & de Azevedo, 1984).

Water samples were collected from five outdoor pools, four indoor pools, and four spas (whirlpools or hot tubs) in Lubbock, TX, USA. The concentration of chlorodibromomethane in the outdoor pools, which used chlorine-based materials for chlorination, were < 0.1-8 µg/l. Two of the indoor pools in which only chlorination was used had chlorodibromomethane levels of 0.3-11 µg/l; one indoor pool in which only bromination (sodium hypobromite) was used had levels of 8-30 µg/l; and the fourth indoor pool, in which chlorination and bromination were alternated, had levels of 9-26 µg/l. The spa in which only chlorination was used had levels of < 0.1-5 µg/l; the two spas in which only bromination was used had levels of 0.6-48 µg/l; and the spa in which the combination was used had levels of 11-26 µg/l. The average concentration of chlorodibromomethane in Lubbock, TX, tap water was 0.43 µg/l (Armstrong & Golden, 1986).

Water samples were collected in 1978-79 from eight covered swimming pools in Bremen, Germany, to determine the concentration of chlorodibromomethane. The source of fresh water was mixed river and groundwater for four pools and groundwater for four pools. The level of chlorodibromomethane in the pools with mixed sources was 7.0 and for the pools with groundwater, 0.4 µg/l. The range of means of chlorodibromomethane in the four pools with a mixed water source was 6-28 µg/l (total range, 0.1-140 µg/l); that in the four pools with a groundwater source was 4-10 µg/l (total range, 0.2-140 µg/l) (Lahl *et al.*, 1981).

The concentrations of chlorodibromomethane in three thermal spas in western Germany in which the initial bromide concentration was 0.5-0.7 mg/l were 13.6-32.2 µg/l (Weil *et al.*, 1980).

Scotte (1984) studied the concentrations of organohalogen compounds in the water of 10 covered swimming pools in France. The mean concentrations of chlorodibromomethane were 2.4 µg/l in the four pools treated with Surchlor GR 60 (anhydrous sodium dichloroisocyanurate), 2.5 µg/l in the two treated with gaseous chlorine and 4.5 µg/l in the two treated with sodium hypochlorite and the two treated with bromine.

Kaminski and von Loew (1984) found an average concentration of 2.3 µg/l (max, 6.7 µg/l) chlorodibromomethane in 26 indoor pools in western Germany.

Effluents from a wastewater treatment plant on Boston Harbor, MA, USA, sampled in 1984 and 1985, contained a mean chlorodibromomethane level of 3.34 µg/l (range, 0.20-12.16) and had an estimated mass input rate of 2.98 kg per day (Kossik *et al.*, 1986).

Heating water to prepare food has been shown to eliminate a large part of trihalomethanes in the water, as a function of temperature and heating time. Chlorodibromomethane levels were reduced from 42.3 μg/l in tap water to 24.1 μg/l after heating at 80°C for 1 min, to 14.4 μg/l after heating to 100°C, to 12.3 μg/l after boiling for 1 min and to 5.5 μg/l after boiling for 5 min (Lahl *et al.*, 1982).

(*d*) *Food and beverages*

The mean concentration of chlorodibromomethane in 12 milk products (ice cream, yoghurt, curds, buttermilk) was 0.1 μg/kg fresh weight. The maximal level found was 0.3 μg/kg (Bauer, 1981).

(*e*) *Tissues and secretions*

The mean concentrations (micrograms per kilogram fresh weight) of chlorodibromomethane in human tissues samples collected in 1978 from the Ruhr District of Germany were: kidney capsule fat, 5.1 (max, 40.1); hypodermis fat, 0.9; lung, 0.7; liver, 0.4; and muscle, 1.3 (Bauer, 1981).

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

Chlorodibromomethane was detected at concentrations of 0.6 ± 0.02 (SD) in human kidney and 0.06 ± 0.01 μg/kg in human lung tissues collected at surgery or during pathological examination (Kroneld, 1989).

(*f*) *Other*

Chlorodibromomethane was detected in cosmetic products (face wash and shaving lotion) bought in shops in Bochum, Germany, at a concentration of 0.2 μg/l; it was detected in one of seven cough mixtures at a concentration of 0.9 μg/kg (Bauer, 1981).

2.3 Analysis

Selected methods for the analysis of chlorodibromomethane in air, water and other media are given in Table 3. A variety of analytical methods exist for measuring chlorodibromomethane in water. The commonly used methods are based on extraction with solvent, followed by gas chromatography-electron capture detection (Standing Committee of Analysts, 1980; US Environmental Protection Agency, 1988f), purge-and-trap and flame ionization detection and microcoulometric gas chromatography (Bellar *et al.*, 1974a,b; US Environmental Protection Agency, 1988g) and gas chromatography-mass spectrometry and headspace analysis (Otson *et al.*, 1982).

Table 3. Methods for the analysis of chlorodibromomethane

Sample matrix	Sample preparation[a]	Assay procedure[b]	Limit of detection[c]	Reference
Air	Collect cryogenically into stainless-steel bottle; inject sample	GC/EC-FI-FPD/GC/MS	NR	Hoyt & Rasmussen (1985)
Seawater	Collect in vacuum extraction flask; pressurize with zero air; inject headspace sample	GC/EC-FI-FPD/GC/MS	NR	Hoyt & Rasmussen (1985)
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 GC/MS	0.09 μg/l 3.1 μg/l	US Environmental Protection Agency (1988a) [Method 601] US Environmental Protection Agency (1988b) [Method 624]
	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 GC/MS	0.3 μg/l 0.05 μg/l	US Environmental Protection Agency (1988c) [Method 502.2] US Environmental Protection Agency (1988d) [Method 524.2]
	Add internal standard (isotope-labelled chlorodibromomethane); purge; trap and desorb as above	GC/MS	10 μg/l	US Environmental Protection Agency (1988e) [Method 1624]
	Extract in pentane; inject onto GC	GC/EC (>50 μg/l) GC/MS (<50 μg/l)	0.5 μg/l	US Environmental Protection Agency (1988f) [Method 501.2]
Adipose tissue	Purge from liquefied fat at 115°C; trap on silica gel; desorb thermally	GC/HSD	2.1 μg/l	Peoples *et al.* (1979)
Blood serum	Purge from water-serum mixture containing anti-foam reagent at 115°C; trap on Tenax/silica gel; thermally desorb	GC/ECD	2.1 μg/l	Peoples *et al.* (1979)

[a] GC, gas chromatograph

[b] GC/EC-FI-FPD, gas chromatography/electron capture-flame ionization-flame photometric detection; GC/ECD, gas chromatography/electrolytic conductivity detection; GC/MS, gas chromatography/mass spectrometry; GC/HSD, gas chromatography/halide selective detection

[c] NR, not reported

The US Environmental Protection Agency methods for analysing water (Methods 8010 and 8240) have also been used for 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 method detection limit using Method 8010 is 0.09 μg/l, and the practical quantification limit using Method 8240 is 5 μg/l for groundwater and for soil/sediment samples (US Environmental Protection Agency, 1986a,b).

US Environmental Protection Agency Method 624 has also been adapted to the analysis of chlorodibromomethane in fish, with an estimated detection limit of 10 μg/kg (Easley *et al.*, 1981).

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

3.1 Carcinogenicity studies in animals (Table 4)

Oral administration

Mouse: Groups of 50 male and 50 female B6C3F$_1$ mice, eight weeks old, were given chlorodibromomethane (> 98% pure) in corn oil by gavage at 50 or 100 mg/kg bw on five days per week for 105 weeks. Survival at 107 weeks was: males—vehicle control, 44/50; low-dose, 7/50; high-dose, 29/50; females—control, 32/50; low-dose, 27/50; high-dose, 36/50. The poor survival of low-dose males was caused by an accidental overdose which killed 35 rats in weeks 58-59. Hepatocellular adenomas occurred in 14/50 control and 10/50 high-dose male mice, whereas hepatocellular carcinomas occurred in 10/50 vehicle control and 19/50 high-dose males. Although the proportion of high-dose male mice with carcinomas was significantly increased relative to controls ($p = 0.03$, incidental tumour test), the overall proportion with hepatocellular adenomas or carcinomas combined was not. In female mice, hepatocellular adenomas occurred in 2/50 control, 4/49 low-dose and 11/50 high-dose animals; hepatocellular carcinomas occurred in 4/50 control, 6/49 low-dose and 8/50 high-dose females. The proportion of high-dose female mice with hepatocellular adenoma or carcinoma was significantly greater than in controls ($p = 0.004$, pairwise comparison; $p = 0.003$, trend test, incidental tumour test). The proportion of high-dose male mice with lymphomas was significantly smaller than in controls (vehicle control, 9/50; high dose, 0/50; $p = 0.006$, incidental tumour test) (National Toxicology Program, 1985).

Groups of male and female CBA × C57Bl/6 hybrid mice [age unspecified] were given chlorodibromomethane [purity unspecified] at 0.04 mg/l (50 males, 50 females), 4 mg/l (50 males, 50 females) or 400 mg/l (55 males, 55 females) in the drinking-water for 104 weeks. Seventy-five males and 50 females served as controls. The numbers of animals surviving to the appearance of the first tumour were: males—control, 63; low-dose, 13; medium-dose, 33; and high-dose, 39; females—control, 34; low-dose, 27; medium-dose, 40; and high-dose, 32 [average survival time and number of terminal survivors unspecified]. No tumour occurred at increased incidence in treated mice (Voronin *et al.*, 1987). [The Working Group noted the incomplete reporting of the study.]

Rat: Groups of 50 male and 50 female Fischer 344 rats, eight weeks old, were given chlorodibromomethane ($>$ 98% pure) in corn oil by gavage at 40 or 80 mg/kg bw on five days per week for 104 weeks. Survival at 106 weeks was: males—vehicle control, 34/50; low-dose, 38/50; high-dose, 43/50; females—control, 39/50; low-dose, 37/50; high-dose, 41/50. No tumour occurred in a significantly greater proportion of rats receiving chlorodibromomethane than in controls. The incidences of stromal polyps of the uterus and fibroadenomas of the mammary gland were significantly lower in high-dose female rats than in controls (stromal polyps—control, 14/50; low-dose, 8/50; high-dose, 5/50; $p = 0.021$, incidental tumour test; fibroadenomas—control, 18/50; low-dose, 12/50; high-dose, 4/50; $p < 0.001$, incidental tumour test) (National Toxicology Program, 1985).

3.2 Other relevant data

(*a*) *Experimental systems*

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

The blood/gas partition coefficient (at 37°C) of chlorodibromomethane in rats was 116 (Gargas *et al.*, 1989), which predicts that it will be readily absorbed by inhalation.

^{14}C-Chlorodibromomethane at 0.48 mmol/kg (16 μCi/kg; 100 mg/kg bw) administered orally in corn oil to rats by gavage was absorbed and eliminated in the expired air as bromodichloromethane (48% of dose) or as ^{14}C-carbon dioxide (18% of dose) in 8 h; radiolabel amounting to about 1% of the dose was eliminated in the urine, and about 1% of the dose was retained in body tissues. ^{14}C-Chlorodibromomethane (0.72 mmol/kg; 32 μCi/kg; 150 mg/kg bw) administered similarly to mice was absorbed and eliminated in the expired air as unchanged chlorodibromomethane (12% of dose) or as ^{14}C-carbon dioxide (72% of dose) in 8 h; about 2% of the administered radiolabel was eliminated in the urine, and 5% was retained in body tissues (Mink *et al.*, 1986). Chlorodibromomethane is metabolized to carbon monoxide *in vivo* (Anders *et al.*, 1978) and *in vitro* (Ahmed *et al.*, 1977).

Table 4. Summary of carcinogenicity studies of chlorodibromomethane in experimental animals

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Significance	Comments
					0	1	2	3		
National Toxicology Program (1985)	Mouse B6C3F$_1$	M	5 d/week, gavage, corn oil, 105 weeks	Dose (mg/kg)	0	50	100	-		
				Survival (107 weeks)	44/50	7/50	29/50			Accidental overdose
				Hepatocellular						
				Adenoma	14/50	5/50	10/50			Increase (but combined tumours NS)
				Carcinoma	10/50	9/50	19/50		$p = 0.03$	
				Lymphoma	9/50	4/50	0/50		$p = 0.06$	Decrease
		F		Dose (mg/kg)	0	50	100	-		
				Survival (107 weeks)	32/50	27/50	36/50			
				Hepatocellular						
				Adenoma	2/50	4/49	11/50		$p = 0.003$	Increase
				Carcinoma	4/50	6/49	8/50			
Voronin *et al.* (1987)	Mouse CBA × C57Bl/6	M/F	Ad lib. in drinking-water	Dose (mg/l)	0	0.04	4.0	400		
				Survival M	63/75	13/50	33/50	39/55		
				F	34/50	27/50	40/50	32/55		
				Tumours	-	-	-	-		
National Toxicology Program (1985)	Rat F344	M	5 d/week, gavage, corn oil, 104 weeks	Dose (mg/kg)	0	40	80	-		
				Survival (106 weeks)	34/50	38/50	43/50			
		F		Dose (mg/kg)	0	40	80	-		
				Survival (106 weeks)	39/50	37/50	41/50			
				Uterine stromal polyp	14/50	8/50	5/50		$p = 0.021$	Decrease
				Mammary fibroadenoma	18/50	12/50	4/50		$p < 0.001$	Decrease

(ii) *Toxic effects*

The single-dose oral LD_{50} of chlorodibromomethane (Emulphor:ethanol: saline, 1:1:8) was 800 mg/kg bw in male and 1200 mg/kg bw in female ICR Swiss mice (Bowman *et al.*, 1978). Oral LD_{50} values (corn oil) of 1186 and 848 mg/kg bw were reported in male and female Sprague-Dawley rats, respectively, in one study (Chu *et al.*, 1980, 1982a), and of 1.08 ml/kg bw in males in another (Hewitt *et al.*, 1983). Signs of acute toxicity included sedation, prostration, anaesthesia, ataxia, muscular weakness, increased blood cholesterol and reduction in the number of peripheral lymphocytes.

Daily oral treatment by gavage of male CD-1 mice with 250 mg/kg bw chlorodibromomethane (Emulphor:ethanol:saline, 1:1:8) for 14 days resulted in body weight reduction, liver damage, depression of humoral and cellular immunity and reduced spleen and thymus weights (Munson *et al.*, 1982). Oral treatment by gavage of male CD-1 mice with 147 mg/kg bw chlorodibromomethane in corn oil for 14 days led to morphological and functional kidney lesions (Condie *et al.*, 1983).

Daily oral administration by gavage of 500 and 1000 mg/kg bw chlorodibromomethane in corn oil was lethal after a few days to 3/5 male and to all female Fischer 344/N rats, whereas a few male and female $B6C3F_1$ mice survived treatment with 500 mg/kg bw for 14 days. Mottled livers and renal alterations were observed at necropsy (National Toxicology Program, 1985). In a 13-week study, male and female Fischer 344/N rats and $B6C3F_1$ mice were administered 15-250 mg/kg bw chlorodibromomethane in corn oil by gavage on five days per week. In the highest dose groups, treatment was lethal to 9/10 male and 9/10 female rats and resulted in fatty changes and centrilobular necrosis in the liver and proximal tubular-cell degeneration and regeneration in the kidney. Lesions of the salivary gland were inflammation and squamous metaplasia. $B6C3F_1$ mice were less sensitive. Fatty metamorphosis of the liver and tubular degeneration of the kidney were observed in 5/10 of the males but not the females in the high-dose groups (Dunnick *et al.*, 1985; National Toxicology Program, 1985).

Male and female Sprague-Dawley rats received 5-2500 mg/l chlorodibromomethane in drinking-water for 90 days. The highest dose, which corresponded to an approximate daily intake of 55 mg/rat, resulted in some deaths, moderate liver damage, reduction in the number of blood lymphocytes and mild changes in the thyroid (Chu *et al.*, 1982b).

Administration of chlorodibromomethane in corn oil for two years (see section 3.1) resulted in fatty changes of the liver in rats and mice of each sex in all treatment groups; cytomegaly and necrosis were observed only in livers of high-dose male mice. Nephrosis was observed in female rats and male mice at low and high doses. Furthermore, follicular-cell hyperplasia of the thyroid gland was observed in female but not male mice in all treatment groups (Dunnick *et al.*, 1985; National Toxicology Program, 1985).

(iii) *Effects on reproduction and prenatal toxicity*

As reported in an abstract, multigeneration reproduction and dominant lethal studies were conducted in ICR Swiss mice administered chlorodibromomethane in drinking-water at 0, 0.1, 1.0 or 4.0 g/l (Borzelleca *et al.*, 1980). There appeared to be dose-dependent effects on survival and weight gain of pups and on viability and lactation indices in the multigeneration study. [The Working Group noted that the data presented were insufficient to allow assessment of the design of this study.]

As reported in an abstract, no apparent teratogenic effect was observed in ICR Swiss mice given chlorodibromomethane at 0, 0.1, 1.0 or 4.0 g/l in drinking-water (Borzelleca *et al.*, 1980). [The Working Group noted that the data presented were insufficient to allow assessment of the design of this study.]

Sprague-Dawley rats were given chlorodibromomethane daily in corn oil by gavage at 0, 50, 100 or 200 mg/kg bw on gestation days 6-15. Group sizes were 10-12 pregnant dams at the time of caesarean section. Maternal weight gain was significantly decreased from control values at the highest dose level. There was no increase in the incidence of resorptions or change in litter size or fetal body weight or in the incidence of external, visceral or skeletal malformations (Ruddick *et al.*, 1983). [The Working Group noted that the selection of dose levels appears to be appropriate but that the small number of animals per group gives this study a low power for detecting changes in the proportion of malformed fetuses.]

(iv) *Genetic and related effects* (Table 5)

Chlorodibromomethane was mutagenic to *Salmonella typhimurium* in some reported studies; experiments performed in closed containers generally gave positive results. In *Saccharomyces cerevisiae*, there was an increase in the frequency of gene conversion, but no mutation was observed. Chromosomal aberrations were induced in Chinese hamster CHL cells and sister chromatid exchange in human lymphocytes *in vitro*. Sister chromatid exchange but not micronuclei was induced in mouse bone marrow *in vivo*. As reported in an abstract, dominant lethal effects were not induced in male mice (Borzelleca *et al.*, 1980).

(*b*) *Humans*

No data were available to the Working Group.

3.3 Case reports and epidemiological studies of carcinogenicity to humans

A single correlation study (Isacson *et al.*, 1983), described in the monograph on chlorinated drinking-water (p. 113), mentioned chlorodibromomethane, but the information could not be used to evaluate the carcinogenicity of this compound individually.

Table 5. Genetic and related effects of chlorodibromomethane

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	0	0.0000	Simmon *et al.* (1977)[a]
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	500.0000	National Toxicology Program (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	0.0000	Khudoley *et al.* (1987)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	+	8.0000	Varma *et al.* (1988)
SA0, *Salmonella typhimurium* TA100, reverse mutation	0	+	0.0000	Khudoley *et al.* (1989)[a]
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	0.0000	Mersch-Sunderman (1989)[b]
SA2, *Salmonella typhimurium* TA102, reverse mutation	–	–	0.0000	Mersch-Sunderman (1989)[c]
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	5000.0000	National Toxicology Program (1985)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	8000.0000	Varma *et al.* (1988)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	1667.0000	National Toxicology Program (1985)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	+	+	8.0000	Varma *et al.* (1988)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	1667.0000	National Toxicology Program (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	0.0000	Khudoley *et al.* (1987)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	+	8.0000	Varma *et al.* (1988)
SA9, *Salmonella typhimurium* TA98, reverse mutation	0	+	0.0000	Khudoley *et al.* (1989)[a]
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	0.0000	Mersch-Sunderman (1989)[b]
SAS, *Salmonella typhimurium* TA97, reverse mutation	–	–	0.0000	Mersch-Sunderman (1989)[b]
SCG, *Saccharomyces cerevisiae* D7, gene conversion	+	(+)	245.0000	Nestmann & Lee (1985)
SCR, *Saccharomyces cerevisiae* XVI85-14C, reverse mutation	–	–	1225.0000	Nestmann & Lee (1985)
CIC, Chromosomal aberrations in Chinese hamster CHL cells	–	+	100.0000	Ishidate (1987)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	+	0	80.0000	Morimoto & Koizumi (1983)
SVA, Sister chromatid exchange, ICR/SJ mouse bone-marrow cells	+	0	25.0000	Morimoto & Koizumi (1983)
MVM, Micronucleus test, ddY mice *in vivo*	–	0	1000.0000	Hayashi *et al.* (1988)

[a] Closed container
[b] Standard assay, closed container or spot test
[c] Standard assay or spot test

4. Summary of Data Reported and Evaluation

4.1 Exposure data

Chlorodibromomethane has limited commercial use but is used industrially as a chemical intermediate. It is found in chlorinated drinking-water as a consequence of the reaction between chlorine, added during drinking-water treatment, and natural organic substances in the presence of bromide. The major route of human exposure is *via* drinking-water. Chlorodibromomethane has been detected in chlorinated drinking-water in many parts of the world; it is not normally present in untreated water. It is a major component of organohalide emissions from marine algae.

4.2 Experimental carcinogenicity data

Chlorodibromomethane was tested for carcinogenicity in two-year studies by oral gavage in male and female B6C3F$_1$ mice and Fischer 344 rats and in a lifetime study in CBA × C57Bl/6 hybrid mice by administration in drinking-water. In B6C3F$_1$ mice, it produced a significant increase in the incidence of hepatocellular neoplasms in females and a marginal increase in males. Chlorodibromomethane did not increase the proportion of rats with tumours at any site relative to that in controls. There was no increase in tumour incidence in CBA × C57Bl/6 hybrid mice given chlorodibromomethane in drinking-water.

4.3 Human carcinogenicity data

No relevant data were available to the Working Group.

4.4 Other relevant data

Chlorodibromomethane was mutagenic to bacteria. In single studies, it induced mitotic recombination, but not mutation, in yeast, chromosomal aberrations in cultured mammalian cells and sister chromatid exchange in cultured human cells. Sister chromatid exchange but not micronuclei were observed in rodents treated *in vivo*.

4.5 Evaluation[1]

There is *inadequate evidence* for the carcinogenicity of chlorodibromomethane in humans.

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

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

Overall evaluation

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

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