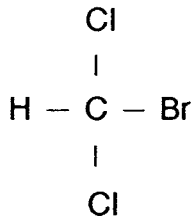
BROMODICHLOROMETHANE

1. Chemical and Physical Data

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 75-27-4
Chem. Abstr. Name: Bromodichloromethane
IUPAC Systematic Name: Bromodichloromethane
Synonyms: Dichlorobromomethane; dichloromonobromomethane; monobromodichloromethane

1.2 Structural and molecular formulae and molecular weight



$CHBrCl_2$ Mol. wt: 163.83

1.3 Chemical and physical properties of the pure substance

(*a*) *Description*: Colourless liquid (Verschueren, 1983)
(*b*) *Boiling-point*: 90.1°C (Weast, 1989)
(*c*) *Melting-point*: -57.1°C (Weast, 1989)
(*d*) *Density*: 1.980 at 20/4°C (Weast, 1989)
(*e*) *Spectroscopy data*[1]: Infrared (Sadtler Research Laboratories, 1980, prism [1898], grating [18024]; Pouchert, 1981, 1985a,b), nuclear magnetic resonance (Sadtler Research Laboratories, 1980, proton [6709], C-13

[1]In square brackets, spectrum number in compilation

[4023]; Pouchert, 1974, 1983) and mass spectral data [1026] (Bunn *et al.*, 1975; Coleman *et al.*, 1984) have been reported.

(*f*) *Solubility*: Soluble in water (4.5 g/l at 20°C) (Mabey *et al.*, 1982), acetone, ethanol, benzene, chloroform and diethyl ether (Weast, 1989)

(*g*) *Volatility*: Vapour pressure, 50 mm Hg at 20°C (Mabey *et al.*, 1982)

(*h*) *Reactivity*: Hydrolysis rate at neutral pH, 25°C, K = 5.76×10^{-8} per hour (Mabey *et al.*, 1982)

(*i*) *Octanol/water partition coefficient (P)*: log P, 2.10 (Chemical Information Systems, 1990)

(*j*) *Conversion factor*[1]: $mg/m^3 = 6.70 \times ppm$

1.4 Technical products and impurities

Bromodichloromethane is available at > 97-98% purity, and may be stabilized with potassium carbonate or ethanol (Riedel-de Haën, 1986; American Tokyo Kasei, 1988; Aldrich Chemical Co., 1990).

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

Bromodichloromethane has been prepared by treating a mixture of chloroform (see IARC, 1987) and bromoform (see monograph, p. 213) with triethylbenzylammonium chloride and sodium hydroxide (Fedoryński *et al.*, 1977).

(*b*) *Use*

Bromodichloromethane can be used in organic synthesis, such as in the preparation of phenylbromodichloromethylmercury, which has been widely used for the generation of dichlorocarbene (Fedoryński *et al.*, 1977; Sittig, 1985).

Bromodichloromethane is currently used only as a standard in the analysis of drinking-water (Strobel & Grummt, 1987).

(*c*) *Regulatory status and guidelines*

Standards have been established for trihalomethanes (including bromodichloromethane) in drinking-water (see monograph on Chlorinated 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*

Mean levels of bromodichloromethane in the tissues of a number of temperate marine microalgae (*Ascophyllum nodosum, Fucus vesiculosis, Enteromorpha linza, Ulva lacta, Gigartina stellata*) ranged from 7 to 22 ng/g dry weight; the algae release this compound into seawater, from which it may be released to the atmosphere (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 emissions of volatile organohalides into the surrounding air. The main components were bromoform, bromodichloromethane, chlorodibromomethane; a minor component was bromoethane (Class *et al.*, 1986).

(*b*) *Multimedia exposure assessment*

In a study of exposures to volatile organic compounds on two US university campuses in 1980, bromodichloromethane levels in personal breathing-zone air samples ranged from not detected to 3.7 μg/m^3 for 11 students at Lamar University, Texas, and from not detected to 4.3 μg/m3 for six students at the University of North Carolina. It was detected in the ambient air of 64% of the Lamar University samples at a mean concentration of 1.23 μg/m^3 and in 17% of the University of North Carolina samples at 0.83 μg/m3. It was not detected in any of the collected breath samples. Tap-water samples contained mean bromodichloromethane levels of 21 ng/ml (range, 13-44) for the Lamar University students and 17 ng/ml (range, 15-20) for those at the University of North Carolina. The authors concluded that drinking-water was an important contributor to total intake of bromodichloromethane from air and water, assuming daily intakes of 10 m^3 of air and 1 litre of drinking-water. The water accounted for 76% of the bromodichloromethane intake (Wallace *et al.*, 1982).

Nine volunteers in New Jersey and three in North Carolina were monitored for exposure to bromodichloromethane in personal air samples, drinking-water, food and breath from July to December 1980. Bromodichloromethane was detected at 0.10-13.40 μg/m^3 in 28 (16 at trace) of the 164 breathing zone air samples in New Jersey and at 0.10-3.66 μg/m^3 in 12 (seven at trace) of the 60 samples in North Carolina. It was detected in none of the exhaled breath samples: 49 in New Jersey (limit of detection, 0.17-0.20 μg/m^3) and 17 in North Carolina (limit of detection, 0.14-2.20 μg/m^3). The drinking-water of the New Jersey volunteers contained bromodichloromethane levels ranging from 4.40 to 42.00 μg/l in home samples and from 0.02 to 37.00 μg/l in workplace samples; it was present in all of the 75 home

samples at a median concentration of 18.00 μg/l and in 44 of the 45 workplace samples at a median concentration of 13.0 μg/l. In North Carolina, home drinking-water samples contained bromodichloromethane levels ranging from 12.0 to 20.0 μg/l and those in the workplace from 0.02 to 20.0 μg/l; it was present in all of the 30 home samples at a median concentration of 16 μg/l and in 17 of the 18 workplace samples at a median concentration of 14 μg/l. Bromodichloromethane was detected in composite beverage samples at 1.0 μg/l; it was not detected in composite dairy, meat or fatty food samples. The authors conclude that at least 75% of the volunteers' exposure to bromodichloromethane was contributed by drinking-water and that beverages supplied a significant fraction of the intake (Wallace *et al.*, 1984).

(c) *Air*

The volatilization half-time of bromodichloromethane from rivers and streams has been estimated to range from 33 min to 12 days, depending on turbulence and temperature. A typical half-time, based on actual data, was 35 h (Kaczmar *et al.*, 1984).

Air samples were collected in 1978-79 from eight covered swimming pools in Bremen, Germany, to determine the concentration of bromodichloromethane. The range of means, measured from the surface up to 2 m, in the four pools in which a mixed water source was used was 0.2-22 μg/m^3 (total range, 0.1-38 μg/m^3). The range of means in the four pools in which a groundwater source was used was 0.6-22 μg/m^3 (total range, 0.1-39 μg/m^3). Release of volatile compounds into the air depended on water and air temperature, concentration in the water, and intensity of air circulation (Lahl *et al.*, 1981).

Ullrich (1982) studied the organohalogen compound concentrations in the air of four public indoor swimming pools in western Berlin. Mean concentrations of bromodichloromethane ranged from 36 to 210 μg/m^3.

In the USA, air samples collected 2 cm above the surface of five outdoor pools contained 1-7 μg/m^3 bromodichloromethane; those above four indoor pools contained 1-14 μg/m^3; and those above four spas (whirlpools or hot tubs) contained < 0.1-90 μg/m^3. Samples collected 2 m above the surface contained < 0.1 μg/m^3, < 0.1-10 μg/m^3 and < 0.1-10 μg/m^3, respectively (Armstrong & Golden, 1986).

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 1.2 μg/m^3 bromodichloromethane was reported for the 17 urban/suburban data points examined and 0.11 μg/m^2 for industrial areas (nine data points) (Brodzinsky & Singh, 1983).

Bromodichloromethane levels in air samples collected in 1982-85 over the Atlantic Ocean were 0.1-1 ppt (0.7-6.7 ng/m^3); baseline levels of biogenic bromodichloromethane in air were 0.2-0.6 ppt (1.3-4.0 ng/m^3). Air samples collected in 1985 from a forest area in southern Germany contained 0.5 ppt (3.4 ng/m^3) bromodichloromethane (Class *et al.*, 1986).

According to the Toxic Chemical Release Inventory (National Library of Medicine, 1989), 115 kg of bromodichloromethane were released to ambient air in one US location. No release to media other than air was reported.

(d) Water and sediments

The formation of trihalomethanes in drinking-water and the effects of temperature and pH have been discussed extensively (Williams, 1985; see also the monograph on Chlorinated drinking-water, pp. 56 *et seq.*).

Bromodichloromethane 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 50 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. Bromodichloromethane concentrations in treated[a] drinking-water, 1973–89

Location, date[b]	Sample site/ raw water source[c]	Concentration (µg/l)[d]	Reference
USA, 1974	NS/surface	2.9–20.8	Bellar *et al.* (1974a,b)
USA, 1974	NS/well	1.1–1.9	
80 US cities (NORS), 1974	Water supplies/ground and surface	ND–116 (mean, 6)	Symons *et al.* (1975)
113 Public water supplies, 1976	Water supplies/NS	Mean, 18; median, 14	Brass *et al.* (1977)
945 US sites, 1981–82	T/ground	1.4–2.2[e] (max., 110)	Westrick *et al.* (1984)
13 US community systems, 1984–85	T and D/ground (3) and surface (10)	< 0.2–58	Reding *et al.* (1989)
10 US utilities, 1985	T/ground and surface	> 10 – < 100 (5 sites) < 10 (5 sites)	Stevens *et al.* (1989)
35 US sites	T/ground and surface	Median 6.9	Krasner *et al.* (1989)
Spring, 1988		10	
Summer, 1988		5.5	
Autumn, 1988		4.1	
Winter, 1989			

Table 1 (contd)

Location, date[b]	Sample site/ raw water source[c]	Concentration (μg/l)[d]	Reference
Durham, North Carolina, 1975	D/surface	10.99–11.60	McKinney *et al.* (1976)
15 Kentucky cities, 1977	T/surface	trace–15	Allgeier *et al.* (1980)
20 Tennessee sites	T/ground and surface		Minear & Morrow (1983)
Autumn, 1980		0.012–0.287	
Winter, 1980		0.012–0.402	
Spring, 1981		0.051–0.299	
Summer, 1981		0.070–0.480	
Miami, Florida	Water supplies	78	Loy *et al.* (1976)
January, 1975	ground	63	
July, 1975			
Southwestern US city, 1975	Municipal water/ ground	0.69–7.76	Henderson *et al.* (1976)
Lamar University, Texas, 1980	D/NS	13–44 (mean 21)	Wallace *et al.* (1982)
University of North Carolina, 1980		15–20 (mean, 17)	
East Texas, 1977	NS/surface (14 sites)	9.3–89.8	Glaze & Rawley (1979)
	NS/ground (11 sites)	ND–53.4	
Houston, Texas, Summer 1978 to winter 1980	NS/surface	max., 39	Cech *et al.* (1982)
	NS/ground	max., 5	
Huron, South Dakota, 1976	T/surface	0–25	Harms & Looyenga (1977)
	D[f]/surface	22–44	
	D[g]/surface	24–57	
	D[h]/surface	29–47	
40 Michigan utilities, NS	T/surface (22 sites)	2.0–54.2	Furlong & D'Itri (1986)
	T/ground (18 sites)	ND–3.2	
Old Love Canal, NY, 1978	D/NS	1.8–10	Barkley *et al.* (1980)
5 Pennsylvania sites, 1987	T/surface	12.3–16.3	Smith (1989)
5 Virginia sites, 1987		2.7–10 (range of means)	
3 Puerto Rican cities, NS	D/ground and surface	0.003–0.011	Rodriguez-Flores (1983)
70 Canadian cities, 1976–77	D and T/ground and surface	0–33 (median, 1.4)	Health & Welfare Canada (1977)
3 Canadian utilities, 1977–78	T/raw water	< 0.1	Otson *et al.* (1981)
	filter effluent	0.44–0.64	
	plant effluent	0.59–0.98	
	D/surface	0.91–1.15	

Table 1 (contd)

Location, date[b]	Sample site/ raw water source[c]	Concentration (μg/l)[d]	Reference
30 Canadian sites Aug.–Sep. 1979 Nov.–Dec.. 1979	T/ground and surface	 mean, 3; max., 16 mean, 2; max., 12	Otson *et al.* (1982)
Burlington, Ontario, Canada, 1981	D/NS	3.8	Comba & Kaiser (1983)
Niagara Falls, Ontario, Canada, 1981		11	
Port Robinson, Ontario, Canada, 1981		160	
Chippawa, Ontario, Canada, 1980–81	D/surface	2.6	Kaiser & Comba (1983)
10 southern Ontario cities, 1981	T/surface D/surface	1.5–9.1 2.2–12	Oliver (1983)
Calgary, Alberta, Canada, 1983	T/surface	0.2–3.0	Hargesheimer (1985)
10 Canadian Great Lakes sites Summer 1982 Winter 1983 Spring 1983	T/ground (1) and surface (9)	Mean 4.4 2.8 4.1	Otson (1987)
Lancashire–Cheshire, UK, 1974	D/NS	1–27	McConnell (1976)
Southeastern UK, NS	D/ground and surface	6.4	Trussell *et al.* (1980)
Southampton, UK, 1977–78	D/surface pumping station reservoir	 mean, 8.66 mean, 12.58	Brett & Calverley (1979)
5 Belgian utilities, 1977–78 9 Belgian utilities, 1977–78	T/surface D/surface T/ground D/ground	9.4–56.0 2.4–38.1 0.1–4.1 0.2–5.3	Quaghebeur & De Wulf (1980)
100 German cities, 1977 37 German sites, 1976	NS/NS	ND–7.3 (mean, 0.7)	Bauer (1981)
Bremen and Leverkusen, Germany, NS	NS/NS	mean, 0.6	
	NS/NS	ND–2.3	
12 German cities, 1978	NS/NS	ND–19.6 (mean, 3.4)	Eklund *et al.* (1978)
Tübingen, Germany, 1981	D/NS D/surface	0.10–0.47 (mean, 0.26) 0.78–1.27 (mean, 1.05)	Hagenmaier *et al.* (1982)
9 German cities, 1978–79	D/ground (1) and surface (8)	0.6–13.1	Lahl *et al.* (1982)

Table 1 (contd)

Location, date[b]	Sample site/ raw water source[c]	Concentration (μg/l)[d]	Reference
Gothenberg, Sweden	D/surface		Eklund *et al.* (1978)
1977		2.2	
February 1978		1.4	
Southern Brazil, NS	D/surface	4.4	Trussell *et al.* (1980)
Eastern Nicaragua, NS	D/surface	ND	
Northern Venezuela, NS	D/surface	10	
Eastern Peru, NS	D/ground and surface	5.7	
Southern China, NS	D/local catchments	7.6	Trussell *et al.* (1980)
Southern Philippines, NS	D/ground and surface	2.3	
Northern Philippines, NS	D/surface	1.7	
Northern Egypt, NS	D/surface	ND	
Southern Indonesia, NS	D/surface	3.0	
Southeastern Australia, NS	D/surface	4.1	

[a]Treatment not always specified

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

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

[d]ND, not detected

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

[f]Short residence time

[g]Medium residence time

[h]Long residence time

Rook (1974) demonstrated that bromodichloromethane, observed at concentrations ranging from 4.2 to 20 μg/l following chlorination of stored surface waters, was a product of chlorination of the humic substances in natural waters.

Bromodichloromethane was detected (but not quantified) by headspace analysis of six of ten Pacific seawater samples collected in 1983; it was not detected in the corresponding marine air samples (Hoyt & Rasmussen, 1985).

Bromodichloromethane was found in water samples collected at various stages of water treatment: not detected (< 0.1 μg/l) in raw river water; 6.3 μg/l in river water treated with chlorine and alum; 18.0 μg/l in three-day-old settled water; 21.9 μg/l in water flowing from settled areas to filters; 18.0 μg/l in the filter effluent; and 20.8 μg/l in finished water (Bellar *et al.*, 1974a,b).

Table 2. Bromodichloromethane concentrations in untreated (natural) water, 1973–89

Location, date[a]	Sample source	Concentration (μg/l)[b]	Reference
80 US cities (NORS), 1975	River, lake and ground	ND–0.8	Symons *et al.* (1975)
Northern Taiwan, NS	Well	ND	Trussell *et al.* (1980)
30 Canadian sites, 1979	River, lake and ground	mean, < 1; max., 13	Otson *et al.* (1982)
Campbellville, Ontario, Canada, 1981	Well	0.004	Comba & Kaiser (1983); Kaiser *et al.* (1983)
Waterdown, Ontario, 1981	Well	0.027	
Burlington, Ontario, 1981	Well	0.016	
	Well	0.025	
Beamsville, Ontario, 1981	Lake	0.02	
Crawford Lake, Ontario, 1981	Lake	ND–0.02 (mean, 0.002)	
Lake Ontario, Ontario, 1981	Spring	0.006	
Ancaster, Ontario, 1981	River	Trace–0.025 (mean, 0.006)	
Niagara River, Ontario, 1981			
Welland River watershed; Ontario	Surface (river)		Kaiser & Comba (1983)
Summer 1980		0.005–0.02	
Spring 1981		0.015–0.45	
10 Canadian Great Lakes sites	Ground and surface		Otson (1987)
Summer 1982		mean, 0.2	
Winter 1983		0	
Spring 1983		mean, 0.3	
North and South Atlantic, 1985	Seawater	0.0001–0.001 (baseline, 0.0001)	Class *et al.* (1986)
Ulm, Germany, NS	Rainwater	0.0004	Class *et al.* (1986)

[a]NORS; National Organics Reconnaissance System; NS, not specified

[b]ND, not detected

According to the US Environmental Protection Agency STORET system, concentrations of bromodichloromethane in 143 samples of surface water in 1970-79 ranged from 0.1 to 1 μg/l in 66% of the samples, 1-10 μg/l in 31% of the samples and 10-100 μg/l in 3% of the samples (Perwak *et al.*, 1980).

The US Environmental Protection Agency estimated that 832 tonnes of bromodichloromethane 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 20 μg bromodichloromethane per day from drinking-water, assuming a median concentration of 14 μg/l and a water intake of 1.65 l per day; assuming a maximal concentration of 180 μg/l and an intake of 2.18 l per day, the daily exposure increased to 400 μg per day (Perwak *et al.*, 1980). In a later investigation by the US Environmental Protection Agency STORET data base, analysis of 19 550 water samples revealed a mean bromodichloromethane concentration of 11.14 μg/l (range, 0-10 133 μg/l); analysis of 581 sediment samples revealed a mean of 10.8 μg/kg (range, 0-55 μg/kg) (US Environmental Protection Agency, 1985).

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

Samples of finished water collected in 1976 from the clear well storage area at the Huron, South Dakota, USA, water-treatment plant contained 42 μg/l bromodichloromethane. Changing the location of the prechlorination dose (from the presedimentation/chemical addition station to the recarbonation basin) or changing the pH did not substantially affect the bromodichloromethane concentration (Harms & Looyenga, 1977).

Although the levels found were not reported, a detection frequency of 10% for concentrations > 1 μg/l was reported for bromodichloromethane in water samples collected in 1976 from the Delaware, Schuylkill and Lehigh Rivers in the USA. Levels in raw water at treatment plants in Trenton, Torresdale-Philadelphia and Queenslane-Philadelphia increased from < 1 μg/l to 1, 10 and 6 μg/l, respectively, as a result of the chlorination process (DeWalle & Chian, 1978).

Tap-water samples collected between January 1977 and March 1978 in Osaka, Japan, contained bromodichloromethane at levels of 5.8, 7.5 and 14.0 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 bromodichloromethane concentrations of 7.8, 9.6 and 14.6 μg/l at similar mean water temperatures (Kajino & Yagi, 1980).

Bromodichloromethane levels in tap water collected at four locations in a Swedish community ranged from 0.84 to 1.2 μg/l; when the treatment facility briefly changed the disinfectant from chlorine to chlorine dioxide, the levels ranged from 0.021 to 0.023 μg/l (detection limit, 0.005 μg/l) (Norin *et al.*, 1981).

Samples of water were collected between August and October 1980 from four supply systems in São Paulo State, Brazil. Mean levels of bromodichloromethane were 6.8-15.8 μg/l in treated water (after treatment), 9.8-23.3 μg/l in treated water from the reservoir and 11.5-27.8 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 concentrations of bromodichloromethane in the outdoor pools, which used chlorine-based materials for disinfection were 1-72 μg/l. Two of the indoor pools in which only chlorination was used had levels of 1.5-90 μg/l; one indoor pool in which only bromination (sodium hypobromite) was used had levels of 1-11 μg/l; and the fourth indoor pool, in which chlorination and bromination were alternated, had levels of 1-8 μg/l. The spa in which only chlorination was used had levels of 1-105 μg/l; the two spas in which only bromination was used had levels of < 0.1-21 μg/l; and the spa in which the combination was used had levels of 0.7-13 μg/l. The average concentration of bromodichloromethane in Lubbock, TX, tap water was 1.0 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 bromodichloromethane. The source of fresh water was mixed river and groundwater for four pools and groundwater for four pools. The level of bromodichloromethane in the pools with mixed sources was 1.5 and that in the pools with groundwater, 1.0 μg/l. The range of means of bromodichloromethane in the four pools with a mixed water source was 15-60 μg/l (total range, 4-150 μg/l); that in the four pools with a groundwater source was 0.1-25 μg/l (total range, 0.1-76 μg/l) (Lahl *et al.*, 1981).

Kaminski and von Loew (1984) found an average concentration of 0.8 μg/l (max, 2.0 μg/l) bromodichloromethane in 26 indoor pools in western Germany. The concentrations of bromodichloromethane in two thermal spas in which the initial bromide concentration was 0.5-0.7 mg/l were 2.3-23.8 μg/l (Weil *et al.*, 1980).

Scotte (1984) studied the concentrations of organohalogens in the water of 10 covered swimming pools in France. The mean concentrations of bromodichloromethane were 4.5 μg/l in the four pools treated with Surchlor GR 60 (anhydrous sodium dichloroisocyanurate); 11.10 μg/l in the two treated with gaseous chlorine, 14.18 μg/l in the two treated with sodium hypochlorite and 0.5 μg/l in the two treated with bromine.

Effluents from a wastewater treatment plant on Boston Harbor, MA, USA, sampled in 1984 and 1985, contained a mean bromodichloromethane concentration

of 4.5 μg/l (range, 0.96-10.3) and had an estimated mass input rate of 4.1 kg/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. Levels of bromodichloromethane were reduced from 44.6 μg/l in tap water to 24.1 μg/l after heating at 80°C for 1 min, to 13.5 μg/l after heating to 100°C, to 10.8 μg/l after boiling for 1 min, and to 4.6 μg/l after boiling for 5 min (Lahl *et al.*, 1982).

(*e*) *Food and beverages*

Entz *et al.* (1982) purchased 39 different food items at retail markets in three geographical areas in the USA and analysed 20 food composites, comprising four groups (dairy, meats, oils-fats, beverages), for bromodichloromethane. It was detected in one dairy composite (milk, ice-cream, cheese and butter) at a concentration of 1.2 μg/l and in two beverage composites at concentrations of 0.3 and 0.6 μg/l. Subsequent analysis of the components of the composites revealed concentrations of 2.3, 3.4 and 3.8 μg/l in three cola soft drinks and 7 μg/kg in butter.

Abdel-Rahman (1982) analysed various US soft drinks for the presence of bromodichloromethane. Cola beverages had mean ranges of 0.9-5.9 μg/l, while other soft drinks had levels of 0.1-3.3 μg/l. Municipal water supplies from which the soft drinks were manufactured were found to contain less than 20 μg/l trihalomethanes.

Uhler and Diachenko (1987) analysed process water and food products from 15 food processing plants located in nine states in the USA, representing 39 food products. Bromodichloromethane was found in seven process waters at levels ranging from < 1 to 14.1 μg/kg, in three soft drinks from one plant at 1.2-2.3 μg/kg and in three ice creams from one plant at 0.6-2.3 μg/kg. The ice-cream plant was the only location at which bromodichloromethane was found in both the process water and the associated food products.

2.3 Analysis

Selected methods for the analysis of bromodichloromethane in air and water are given in Table 3. A variety of analytical methods exist for measuring bromodichloromethane in water. The commonly used methods are based on extraction with solvent followed by gas chromatograph-electron capture detection (US Environmental Protection Agency Method 501-2) (Standing Committee of Analysts, 1980), purge-and-trap, flame ionization detection and microcoulometric gas chromatography (Bellar *et al.*, 1974a,b; Method 501-1), gas chromatography-mass spectrometry and headspace analysis (Otson *et al.*, 1982).

Table 3. Methods for the analysis of bromodichloromethane

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	0.10 µg/l	US Environmental Protection Agency (1988a) [Method 601]
		GC/MS	2.2 µg/l	US Environmental Protection Agency (1988b) [Method 624]
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/ED	0.02 µg/l	US Environmental Protection Agency (1988c) [Method 502.2]
		GC/MS	0.08 µg/l	US Environmental Protection Agency (1988d) [Method 524.2]
	Add internal standard (isotope-labelled bromodichloromethane); 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	0.8 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; desorb thermally	GC/HSD	0.8 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/MS, gas chromatography/mass spectrometry; GC/ECD, gas chromatography/electrolytic conductivity detection; 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 detection limit for bromodichloromethane using Method 8010 is 0.10 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 bromodichloromethane 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)

(*a*) *Oral administration*

Mouse: Groups of 50 male and 50 female B6C3F$_1$ mice, eight weeks old, were given bromodichloromethane (> 99% pure) in corn oil by gavage at 25 or 50 mg/kg bw (males) and 75 or 150 mg/kg bw (females) on five days per week for 102 weeks. Survival at 104 weeks was: males—vehicle control, 34/50; low-dose, 32/50; high-dose, 42/50; females—control, 26/50; low-dose, 13/50; high-dose, 15/50. Decreased survival in female mice was associated in part with tubo-ovarian abscesses (control, 8/50; low-dose, 19/47; high-dose, 18/49). Tubular-cell adenomas of the kidney occurred in 1/49 vehicle control, 2/50 low-dose and 6/50 high-dose male mice and tubular-cell adenocarcinomas occurred in 4/50 high-dose male mice. The proportion of high-dose male mice with renal tubular-cell neoplasms was significantly greater than that in controls ($p = 0.022$, incidental tumour test). Renal tubular-cell neoplasms were uncommon in control male mice of this strain (historical incidences: study laboratory, 2/299 (0.7%); all National Toxicology Program laboratories, 5/1490 (0.3%)). Hepatocellular adenomas occurred in 1/50 control, 13/48 low-dose and 23/50 high-dose female mice; hepatocellular carcinomas occurred in 2/50 control, 5/48 low-dose and 10/50 high-dose female mice. The proportion of low- and high-dose female mice with hepatocellular neoplasms was significantly greater than that in controls ($p < 0.001$, incidental tumour test; pairwise comparisons and trend test). Adenomas of the anterior

pituitary gland occurred at significantly lower incidence in high-dose female mice (control, 17/44; low-dose, 8/43; high-dose, 3/38; $p = 0.006$, pairwise comparison, incidental tumour test). Follicular-cell hyperplasia of the thyroid was significantly more common in treated mice, principally in those given the high dose (males: control, 0/48; low-dose, 3/44; high-dose, 5/49; females: vehicle control, 6/50; low-dose, 18/45; high-dose, 21/48) (National Toxicology Program, 1987).

Groups of male and female CBA × C57Bl/6 hybrid mice [age unspecified] were given bromodichloromethane [purity unspecified] at 0.04 mg/l (50 males, 50 females), 4.0 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 number of animals surviving to the appearance of the first tumour were: males—control, 63; low-dose, 35; medium-dose, 16; and high-dose, 45; females—control, 34; low-dose, 45; medium-dose, 18; and high-dose, 13 [average survival time and numbers 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 bromodichloromethane (> 99% pure) in corn oil at 50 or 100 mg/kg bw by gavage on five days per week for 102 weeks. Survival at 104 weeks was: males—vehicle control, 28/50; low-dose, 36/50; high-dose, 28/50; females—vehicle control, 34/50; low-dose, 27/50; high-dose, 41/50. Adenomatous polyps of the large intestine occurred in 0/50 control, 3/50 low-dose and 33/50 high-dose males; adenocarcinomas of the large intestine occurred in 0/50 control, 11/50 low-dose and 38/50 high-dose males. The proportion of male rats receiving 50 or 100 mg/kg bw bromodichloromethane that had neoplasms of the large intestine was significantly greater than in controls ($p < 0.001$, incidental tumour test, pairwise comparisons and trend test). Tubular-cell adenomas of the kidney occurred in 0/50 control, 1/50 low-dose and 3/50 high-dose male rats, whereas tubular-cell adenocarcinomas occurred in 10/50 high-dose males. The proportion of high-dose male rats with renal tubular-cell neoplasms was significantly greater than in controls ($p < 0.001$, incidental tumour test, pairwise comparison and trend test). Renal tubular-cell neoplasms were uncommon in control male rats of this strain (historical incidences: study laboratory, 1/250 (0.4%); all National Toxicology Program laboratories, 8/1448 (0.6%)). Cytomegaly of renal tubular epithelial cells occurred at high incidence in treated male rats but not in control male or treated or control female rats. The proportion of high-dose male rats with adrenal medullary phaeochromocytomas (benign or malignant) was lower than that in controls: control, 18/50; low-dose, 14/50; high-dose, 5/50 ($p = 0.003$, pairwise comparison by incidental tumour test). Adenomatous polyps of the large intestine occurred in 0/46 control, 0/50 low-dose and 7/47 high-dose female rats, while adenocarcinomas

occurred in 0/46 control, 0/50 low-dose and 6/47 high-dose rats. The proportion of high-dose female rats with neoplasms of the large intestine was significantly greater than in controls ($p < 0.001$, incidental tumour test, pairwise comparisons and trend test). Renal tubular-cell adenomas occurred in 0/50 control, 1/50 low-dose and 6/50 high-dose females, and tubular-cell adenocarcinomas occurred in 9/50 high-dose female rats. The proportion of high-dose female rats with renal tubular-cell neoplasms was significantly greater than in controls ($p < 0.001$, incidental tumour test, pairwise comparison and trend test). Increased incidences of non-neoplastic lesions of the liver seen in treated females included clear-cell, eosinophilic cytoplasmic, focal cellular and fatty changes. The incidences of neoplasms of the anterior pituitary and of fibroadenomas of the mammary gland were significantly lower in high-dose female rats than in controls (anterior pituitary neoplasms: control, 31/49; low-dose, 20/49; high-dose, 14/49; $p < 0.001$, incidental tumour test and life table test, pairwise comparison and trend; mammary gland fibroadenomas: control, 20/50; low-dose, 15/50; high dose, 1/50; $p < 0.001$, incidental tumour test, pairwise comparison and trend) (National Toxicology Program, 1987).

Groups of 58 male and 58 female weanling Wistar rats received bromodichloromethane [purity unspecified] at 2.4 g/l (approximately the maximal acceptable level) in the drinking-water for 72 weeks followed by 1.2 g/l for the remainder of their life [average survival time not given]. Twenty-six male and 22 female rats received drinking-water without bromodichloromethane and served as controls. Neoplastic nodules of the liver occurred in 0/18 control and 17/53 treated female rats ($p < 0.001$, Fisher's exact test). Adenofibrosis of the liver was also observed in 12/53 treated female and 1/47 treated male rats, but not in controls. The proportion of treated rats with lymphosarcomas in comparison to controls was decreased in treated males and increased in treated females (males: control, 14/22; treated, 9/47; $p < 0.001$, Fisher's exact test; females: control, 2/18; treated, 9/53; $p < 0.01$, Fisher's exact test). The proportion of treated female rats with pituitary gland or mammary gland tumours [types unspecified] was decreased relative to controls (pituitary tumours: controls, 6/18; treated, 5/53; $p < 0.03$, Fisher's exact test; mammary gland tumours: controls, 8/18; treated, 3/53; $p < 0.001$, Fisher's exact test) (Tumasonis *et al.*, 1985). [The Working Group noted that survival-adjusted statistics were not given and the controversial nature of the lesion diagnosed as adenofibrosis.]

(*b*) *Intraperitoneal administration*

Mouse: In a screening assay based on the enhanced induction of lung tumours, groups of 20 male strain A/St mice, six to eight weeks old, were injected intraperitoneally three times per week with bromodichloromethane (> 95% pure) in tricaprylin at 20, 40 or 100 mg/kg bw (maximum tolerated dose) for a total of 18 or

24 injections (total doses, 360, 960 or 2400 mg/kg bw). Twenty males receiving tricaprylin only were used as controls. Twenty-four weeks after the first injection, all surviving animals were killed; these were 15/20 of the controls, 15/20 at the low dose, 16/20 at the mid-dose and 13/20 at the high dose. The average numbers of lung adenomas per mouse were 0.27 ± 0.015 (SE) in controls, 0.20 ± 0.11 at the low dose, 0.25 ± 0.11 at the mid-dose and 0.85 ± 0.27 at the high dose [proportion of mice with tumours not given]. In a positive control group given a single intraperitoneal injection of urethane at 1000 mg/kg bw, the average number of lung tumours per mouse was 19.6 ± 2.4 (Theiss *et al.*, 1977).

3.2 Other relevant data

(*a*) *Experimental systems*

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

^{14}C-Bromodichloromethane (0.61 mmol/kg bw; 16 μCi/kg bw; 100 mg/kg bw) administered orally in corn oil to rats by gavage was absorbed and eliminated in the expired air as unchanged bromodichloromethane (42% of dose) or as ^{14}C-carbon dioxide (14% of dose) in 8 h; radiolabel amounting to about 1% of the dose was eliminated in the urine, and about 3% of the dose was retained in body tissues. ^{14}C-Bromodichloromethane (0.92 mmol/kg bw; 32 μCi/kg bw; 150 mg/kg bw) administered similarly to mice was absorbed and eliminated in the expired air as unchanged bromodichloromethane (7% of dose) or as ^{14}C-carbon dioxide (81% of dose) in 8 h; about 2% of the administered radiolabel was eliminated in the urine, and 3% was retained in body tissues (Mink *et al.*, 1986). Bromodichloromethane is also metabolized to carbon monoxide *in vivo* (Anders *et al.*, 1978) and *in vitro* (Ahmed *et al.*, 1977).

Rats given bromodichloromethane at 0.5 or 5 mg by gavage in corn oil once daily for 25 days showed an average serum concentration of 1 or 23 μg/l and an average fat concentration of 51 or 1800 ng/g (Pfaffenberger *et al.*, 1980); three to five days after dosing had ended, the average serum concentration was 1 μg/l and the average fat concentration was 3-4 ng/g fat for both dose levels.

(ii) *Toxic effects*

The single-dose oral LD_{50} of bromodichloromethane (in Emulphor:ethanol: saline 1:1:8) was 450 mg/kg bw in male and 900 mg/kg bw in female ICR Swiss mice (Bowman *et al.*, 1978). Oral LD_{50} values (in corn oil) of 916 and 969 mg/kg bw were reported in male and female Sprague-Dawley rats (Chu *et al.*, 1980, 1982a), of 651 and 751 mg/kg bw in male and female Fischer 344/N rats and of 300-600 and 651 mg/kg bw in male and female $B6C3F_1$ mice (National Toxicology Program, 1987). Signs of acute toxicity in rats included sedation, prostration, lethargy, laboured

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

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group 0	1	2	3	Significance	Comments
National Toxicology Program (1987)	Mouse $B6C3F_1$	M	5 d/week, gavage, corn oil, 102 weeks	Dose (mg/kg)	0	25	50	-		
				Survival (104 weeks)	34/50	32/50	42/50			
				Renal tubular-cell						
				Adenoma	1/49	2/50	6/50		$p = 0.022$	Increase
				Adenocarcinoma	0/50	0/50	4/50			
		F		Dose (mg/kg)	0	75	150	-		Tubo-ovarian abscesses
				Survival (104 weeks)	26/50	13/50	15/50			
				Hepatocellular						
				Adenoma	1/50	13/48	23/50		$p < 0.001$	Increase
				Carcinoma	2/50	5/48	10/50			
				Anterior pituitary adenoma	17/44	8/43	3/38		$p = 0.006$	Decrease
Voronin *et al.* (1987)	Mouse CBA × C57Bl/6	M&F	Ad lib. in drinking-water	Dose (mg/l)	0	0.04	4.00	400		
				Survival M	63/75	35/50	16/50	45/55		
				F	34/50	45/50	18/50	13/55		
				Tumours	No increase					
Theiss *et al.* (1977)	Mouse strain A/St	M	3 d/week, i.p. inj., tricaprylin, 18 or 24 doses	Dose (mg/kg)	0	20	40	100		Screening test in strain in which lung adenomas common; ± SE
				Total dose (mg/kg)	0	360	960	2400		
				Survival (24 weeks)	15/20	15/20	16/20	13/20		
				Lung adenomas per mouse	0.27 ± 0.015	0.20 ± 0.11	0.25 ± 0.11	0.85 ± 0.27		

Table 4 (contd)

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Significance	Comments
					0	1	2	3		
National Toxicology Program (1987)	Rat F344	M	5 d/week, gavage, corn oil, 102 weeks	Dose (mg/kg)	0	50	100	–		
				Survival (104 weeks)	28/50	36/50	28/50			
				Large intestine						
				Adenomatous polyp	0/50	3/50	33/50		$p < 0.001$	Increase
				Adenocarcinoma	0/50	11/50	38/50			
				Renal tubular-cell						
				Adenoma	0/50	1/50	3/50		$p < 0.001$	Increase
				Adenocarcinoma	0/50	0/50	10/50			
				Adrenal medullary phaeochromocytoma	18/50	14/50	5/50		$p = 0.003$	Decrease
		F		Dose (mg/kg)	0	50	100	–		
				Survival (104 weeks)	34/50	27/50	41/50			
				Large intestine						
				Adenomatous polyp	0/46	0/50	7/47		$p < 0.001$	Increase
				Adenocarcinoma	0/46	0/50	6/47			
				Renal tubular-cell						
				Adenoma	0/50	1/50	6/50		$p < 0.001$	Increase
				Adenocarcinoma	0/50	0/50	9/50			
				Anterior pituitary adenoma	31/49	20/49	14/49		$p < 0.001$	Decrease
				Mammary gland fibroadenoma	20/50	15/50	1/50		$p < 0.001$	Decrease

Table 4 (contd)

Reference	Species/ strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Significance	Comments
					0	1	2	3		
Tumasonis *et al.* (1985)	Rat Wistar	M	Ad lib. drinking-water; 2.4 g/l for 72 weeks; 1.2 g/l for remainder of life	Dose (g/l)	0	2.4	-	-		
				Survival	NS/26	NS/58				
				Hepatic 'adenofibrosis'	0/22	1/47				
				Neoplastic nodules	5/22	6/47				
				Lymphosarcoma	14/22	9/47			$p < 0.001$	Decrease
		F		Dose (g/l)	0	2.4	-	-		
				Survival	NS/22	NS/58				
				Hepatic 'adenofibrosis'	0/18	12/53				
				Neoplastic nodules	0/18	17/53			$p < 0.001$	Increase
				Lymphosarcoma	2/18	9/53			$p < 0.01$	Increase
				Mammary tumour	8/18	3/53			$p < 0.001$	Decrease

NS, not stated

breathing, ataxia, muscular weakness, anaesthesia and reduction in the number of peripheral lymphocytes (Chu *et al.*, 1980, 1982a; National Toxicology Program, 1987); in mice, sedation and anaesthesia, liver damage including fatty infiltration, kidney lesions and haemorrhage in the adrenal glands, lung and brain were seen (Bowman *et al.*, 1978).

Daily oral treatment of CD-1 mice with 50-250 mg/kg bw bromodichloromethane (in 10% Emulphor in water) for 14 days resulted in decreases in serum glucose in males and increases in transaminases (ALAT and ASAT) and blood urea nitrogen in both males and females treated with 250 mg/kg bw. Decreases in body weight, spleen weight, humoral and cellular immunity and blood fibrinogen as well as increases in liver weight were observed with the highest dose in animals of each sex; some of these effects were also observed with 125 mg/kg bw (Munson *et al.*, 1982). Oral treatment of male CD-1 mice with 37-148 mg/kg bw bromodichloromethane in corn oil for 14 days also led in a dose-dependent fashion to liver damage, as shown by morphological changes, and to increases in serum transaminases (ALAT) at the highest dose level. Morphological and functional changes were observed in the kidney after treatment with the two highest doses (Condie *et al.*, 1983).

Daily oral administration of 150 mg/kg bw bromodichloromethane in corn oil for 14 days was lethal to male but not female $B6C3F_1$ mice, whereas male and female Fischer 344/N rats survived treatment at 600 mg/kg bw. In a 13-week study, male and female Fischer 344/N rats were administered 19-300 mg/kg bw, male $B6C3F_1$ mice were administered 6.25-100 mg/kg bw and female $B6C3F_1$ mice were administered 25-400 mg/kg bw bromodichloromethane in corn oil by gavage on five days per week. In the highest dose groups, treatment was lethal to some rats and resulted in reductions in body weight. Liver and kidney lesions were observed in some of the animals. Atrophy of the thymus, spleen, lymph nodes, seminal vesicles and prostate was observed in rats, the toxicity being less pronounced in females than in males (National Toxicology Program, 1987).

Male and female Sprague-Dawley rats received 5-2500 mg/l bromodichloromethane in drinking-water for 90 days [approximate daily intake, 0.14-49 mg/rat]. The highest concentration resulted in some deaths, mild-to-moderate liver damage, reduction in body weight gain and the number of peripheral lymphocytes and mild changes in the thyroid (Chu *et al.*, 1982b).

Administration of bromodichloromethane in corn oil by gavage for two years (see section 3.1) resulted in kidney damage and fatty changes in the liver in male and female rats (50 or 100 mg/kg bw) and in male (25 or 50 mg/kg bw) but not female (75 or 150 mg/kg bw) mice in all treatment groups. Liver-cell necrosis was observed only in male rats (National Toxicology Program, 1987).

(iii) *Effects on reproduction and prenatal toxicity*

Sprague-Dawley rats were administered bromodichloromethane in corn oil by gavage at daily doses of 0, 50, 100 or 200 mg/kg bw on gestation days 6-15 (Ruddick *et al.*, 1983). Maternal weight gain was significantly decreased at the high-dose level; maternal liver weight was significantly increased at all dose levels, and kidney weight was increased at the highest dose level. There was no difference in the incidence of resorptions, litter size or mean fetal weight. There was no increase in the incidence of external or visceral malformations, but aberrations of the sternum were more prevalent at 100 and 200 mg/kg bw than at 50 mg/kg bw.

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

Bromodichloromethane induced positive responses in some *Salmonella typhimurium* reverse mutation assays, particularly with strain TA100. Conflicting results were observed in these studies when an exogenous metabolic system was incorporated into the incubation mixture. Generally, the positive results were observed after modifications to the standard assay procedure that resulted in higher doses of the compound reaching the cells, such as exposure in a closed container, a preincubation period or use of a bacterial spot test.

A weak positive response was observed in yeast in a mutation and a gene conversion assay. A mutagenic response was also obtained in L5178Y cells. No sister chromatid exchange was induced in Chinese hamster cells, whereas chromosomal aberrations were observed in two out of three studies. Sister chromatid exchange was observed in one study in human lymphocytes *in vitro*. Sister chromatid exchange but not micronuclei was induced in mouse bone marrow *in vivo*.

(*b*) *Humans*

No data were available to the Working Group.

3.3 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 bromodichloromethane, but the information could not be used to evaluate the carcinogenicity of this chemical individually.

4. Summary of Data Reported and Evaluation

4.1 Exposure data

Bromodichloromethane is found in chlorinated drinking-water as a consequence of the reaction between chlorine, added during water treatment, and

Table 5. Genetic and related effects of bromodichloromethane

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,b]
SA0, *Salmonella typhimurium* TA100, reverse mutation	-	-	500.0000	Mortelmans *et al.* (1986)
SA0, *Salmonella typhimurium* TA100, reverse mutation	-	-	0.0000	Khudoley *et al.* (1987)
SA0, *Salmonella typhimurium* TA100, reverse mutation	-	+	5.0000	Strobel & Grummt (1987)
SA0, *Salmonella typhimurium* TA100, reverse mutation	-	-	170.0000	Varma *et al.* (1988)
SA0, *Salmonella typhimurium* TA100, reverse mutation	-	+	0.0000	Mersch-Sunderman (1989)[c]
SA0, *Salmonella typhimurium* TA100, reverse mutation	0	+	0.0000	Khudoley *et al.* (1989)[a]
SA2, *Salmonella typhimurium* TA102, reverse mutation	-	-	0.0000	Mersch-Sunderman (1989)
SA4, *Salmonella typhimurium* TA104, reverse mutation	(+)	(+)	125.0000	Strobel & Grummt (1987)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	-	-	500.0000	Mortelmans *et al.* (1986)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	-	-	170.0000	Varma *et al.* (1988)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	-	-	500.0000	Mortelmans *et al.* (1986)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	+	-	130.0000	Varma *et al.* (1988)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	500.0000	Mortelmans *et al.* (1986)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	0.0000	Khudoley *et al.* (1987)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	(+)	500.0000	Strobel & Grummt (1987)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	170.0000	Varma *et al.* (1988)
SA9, *Salmonella typhimurium* TA98, reverse mutation	+	+	0.0000	Mersch-Sunderman (1989)[c]
SA9, *Salmonella typhimurium* TA98, reverse mutation	0	+	0.0000	Khudoley *et al.* (1989)[a]
SAS, *Salmonella typhimurium* TA97, reverse mutation	-	+	5.0000	Strobel & Grummt (1987)
SAS, *Salmonella typhimurium* TA97, reverse mutation	-	+	0.0000	Mersch-Sunderman (1989)[c]
SZG, *Saccharomyces cerevisiae* D7, gene conversion	(+)	-	10.0000	Nestmann & Lee (1985)
SGR, *Saccharomyces cerevisiae* (XV185-14C), reverse mutation	(+)	-	20.0000	Nestmann & Lee (1985)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus	-	+	180.0000	McGregor *et al.* (1988)
SIC, Sister chromatid exchange, Chinese hamster FAF cell line	-	0	8.0000	Strobel & Grummt (1987)

Table 5 (contd)

Test system	Result		Dose LED/HID	Reference
	Without exogenous metabolic system	With exogenous metabolic system		
SIC, Sister chromatid exchange, Chinese hamster CHO cells	–	–	5000.0000	National Toxicology Program (1987)
CIC, Chromosomal aberrations, Chinese hamster FAF cell line	+	0	8.0000	Strobel & Grummt (1987)
CIC, Chromosomal aberrations, Chinese hamster CHO cells	–	–	5000.0000	National Toxicology Program (1987)
CIC, Chromosomal aberrations, Chinese hamster CHO cells	(+)	+	240.0000	Ishidate (1987)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	+	0	65.0000	Morimoto & Koizumi (1983)
SVA, Sister chromatid exchange, mouse bone-marrow cells *in vivo*	+	0	50.0000	Morimoto & Koizumi (1983)
MVM, Micronucleus test, ddY mice *in vivo*	–	0	500.0000	Hayashi *et al.* (1988)

[a]Closed container
[b]Closed container +, standard –
[c]Spot test +, standard –

natural organic substances in the presence of bromide. The major route of human exposure to bromodichloromethane is *via* drinking-water. It has been detected in chlorinated drinking-water in many parts of the world; it has also been detected in some untreated waters, but at much lower levels. Bromodichloromethane is a major component of the organohalides produced by marine algae.

4.2 Experimental carcinogenicity data

Bromodichloromethane was tested for carcinogenicity in two-year studies in male and female Fischer 344 rats and B6C3F$_1$ mice by oral gavage, in life-span studies in male and female Wistar rats and in CBA × C57Bl/6 hybrid mice by administration in drinking-water. In the gavage studies, bromodichloromethane increased the incidences of adenomatous polyps and adenocarcinomas of the large intestine and of tubular-cell adenomas and adenocarcinomas of the kidney in male and female rats, of tubular-cell adenomas and adenocarcinomas of the kidney in male mice and of hepatocellular adenomas and carcinomas in female mice. In the study by administration in drinking-water, it induced neoplastic nodules and adenofibrosis of the liver in rats; no increase in tumour incidence was seen in mice. In a screening test for lung adenomas by intraperitoneal injection, bromodichloromethane did not increase the incidence of lung tumours in strain A mice.

4.3 Human carcinogenicity data

No relevant data were available to the Working Group.

4.4 Other relevant data

Repeated exposure of rats and mice to bromodichloromethane resulted in toxic effects in several organs, including the liver and kidney.

A study of developmental toxicity in rats given bromodichloromethane throughout the period of major organogenesis showed skeletal variations in the presence of maternal toxicity but no teratogenic effect.

Bromodichloromethane induced mutations in some studies with bacteria and, in a single study, in cultured mammalian cells. Chromosomal aberrations but not sister chromatid exchange were observed in cultured mammalian cells. In single studies, sister chromatid exchange was observed in cultured human cells and in mouse bone marrow *in vivo*. In one study, bromodichloromethane did not induce micronuclei in bone-marrow cells of mice treated *in vivo*.

4.5 Evaluation[1]

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

There is *sufficient evidence* for the carcinogenicity of bromodichloromethane in experimental animals.

Overall evaluation

Bromodichloromethane *is possibly carcinogenic to humans (Group 2B).*

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

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