

Dibromochloromethane; CASRN 124-48-1

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

STATUS OF DATA FOR Dibromochloromethane

File First On-Line 09/30/1987

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	yes	09/30/1987
Inhalation RfC (I.B.)	not evaluated	
Carcinogenicity Assessment (II.)	yes	11/01/1990

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Dibromochloromethane

CASRN — 124-48-1

Last Revised — 09/30/1987

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this

substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Hepatic lesions	NOEL: 30 mg/kg/day (converted to 21.4 mg/kg/day)	1000	1	2E-2 mg/kg/day
Rat, Subchronic Gavage Bioassay	LOAEL: 60 mg/kg/day (converted to 42.9 mg/kg/day)			
NTP, 1985				

*Conversion Factors -- Dose adjusted for gavage schedule (5\days/week).

I.A.2. Principal and Supporting Studies (Oral RfD)

NTP (National Toxicology Program). 1985. Toxicology and Carcinogenesis Studies of Chlorodibromomethane in F344/N Rats and B6C3F1 mice (gavage studies). NTP TR282.

Groups of 10 F344/N rats of each sex and 10 B6C3F1 mice of each sex were administered 0, 15, 30, 60, 125, or 250 mg DBCM/kg/day by gavage for 5\days/week for 13 weeks. At 250 mg/kg/day, male mice showed increased incidence of vacuolar change (fatty metamorphosis) in the liver and toxic nephrosis. Both sexes of rats showed increased incidences of liver vacuolar change, centrilobular necrosis, toxic nephropathy, and salivary gland inflammation and squamous metaplasia at 250 mg/kg/day. Vacuolar changes in the livers of lower-dose male rats were also increased. A Fisher Exact test showed that incidences of these liver lesions at doses of 60 mg/kg/day or above were elevated relative to the vehicle controls, thus 30 mg/kg/day is the NOEL.

In the chronic bioassay portion of the NTP (1985) study, 50 F344/N rats of each sex were administered 0, 40, or 80 mg DBCM/kg/day by gavage for 104 weeks and 50 B6C3F1 mice of each sex were similarly treated with 0, 50, or 100 mg DBCM/kg/day for 105 weeks. Treatment was 5 days/week. A dose-related increase in liver fatty changes and ground glass cytoplasmic changes in treated rats of both sexes was reported. Treated female rats also had higher incidences of kidney nephrosis. Treated mice of both sexes exhibited higher incidences of hepatomegaly, fatty metamorphosis, calcification, and liver necrosis. The incidence of nephrosis was increased

in dosed males and thyroid follicular cell hyperplasia was increased in dosed female mice. The LOAELS for this portion of the study are 40 mg/kg/day for rats and 50 mg/kg/day for mice.

The results in these chronic bioassays support the subchronic studies used as a basis of the RfD. In this case, the choice of the subchronic NOAEL as the basis of the RfD rather than the chronic LOAEL (either choice normally requires a 1000 UF, and the resulting RfDs are similar), reflects the slightly greater confidence in the subchronic NOAEL versus the chronic LOAEL that was associated with several adverse effects.

I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — Factors of 10 each were employed for use of a subchronic assay, for extrapolation from animal data, and for protection of sensitive human subpopulations.

MF — None

I.A.4. Additional Comments (Oral RfD)

No adequate data on the teratogenic or reproductive effects of trihalomethanes are available.

I.A.5. Confidence in the Oral RfD

Study — Medium

Database — Medium

RfD — Medium

The NTP (1985) subchronic bioassays utilized adequate numbers of animals of both sexes of two species; multiple endpoints were measured, including complete histopathology; thus confidence in the chosen study is medium. NTP also published supporting chronic studies of dibromochloromethane, but without adequate reproductive or teratology bioassays, the database is given medium confidence. Medium confidence in the RfD follows.

I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — U.S. EPA, 1985

The 1985 Drinking Water Criteria Document for Trihalomethanes is currently undergoing Agency Review.

Other EPA Documentation — None

Agency Work Group Review — 12/02/1985, 02/05/1986, 05/14/1986, 08/13/1987

Verification Date — 08/13/1987

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfD for Dibromochloromethane conducted in September 2002 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Dibromochloromethane
CASRN — 124-48-1

Not available at this time.

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Dibromochloromethane
CASRN — 124-48-1
Last Revised — 11/01/1990

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document.

IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Classification — C; possible human carcinogen

Basis — Based on inadequate human data and limited evidence of carcinogenicity in animals; namely, positive carcinogenic evidence in B6C3F1 mice (males and females), together with positive mutagenicity data, and structural similarity to other trihalomethanes, which are known animal carcinogens.

II.A.2. Human Carcinogenicity Data

Inadequate. There are no epidemiologic studies of dibromochloromethane alone. Dibromochloromethane is one of several trihalomethanes (including chloroform, bromodichloromethane, and bromoform) which are formed from the interaction of chlorine with the organic materials found in water. Several ecologic studies (Cantor et al., 1978; Aldrich and Peoples, 1982; Isacson et al., 1983) and case-control studies (Young and Kanarek, 1983; Cantor et al., 1987) suggest a positive correlation between drinking chlorinated water and the incidence of several human cancers, particularly bladder, rectal and colon cancer. Although both types of studies have design limitations, which might include lack of individual information; misclassification of exposure; or no controls for diet, smoking, or alcohol consumption, the agreement of findings in several independent studies strengthens the association between drinking chlorinated water and cancer (Cantor, 1983; Crump, 1983; Crump and Guess, 1982). In all studies, the cases were exposed to a mixture of compounds, including chloroform, which is considered to be a probable human carcinogen. The data collected are inadequate for assessing the carcinogenic potential of dibromochloromethane.

II.A.3. Animal Carcinogenicity Data

Limited. In a 2-year carcinogenicity study, 50 F344/N rats/sex/dose were treated by gavage with dibromochloromethane (>98% pure) in corn oil at 0, 40, or 80 mg/kg, 5 days/week for 104 weeks (NTP, 1985). Groups of B6C3F1 mice (50/sex/dose) were similarly gavaged at doses of 0, 50, or 100 mg/kg, 5 days/week for 105 weeks. In rats, the final survival rates of all groups were comparable (approximately 76%); mean body weights were also comparable between dose groups in each sex, except for a decrease in the high-dose males after week 20. No compound-

related clinical signs were seen, and no evidence for carcinogenicity was seen in rats under these study conditions.

In mice, the mean body weights of both male and female high-dose groups were lower than those of their respective controls throughout the study. Mean body weight of the low-dose male mice was lower than the control group after both low-dose groups received an overdose of chemical in week 58. Survival of low- and high-dose males was significantly lower than the control group; the percent survival was 88, 14, and 58% in the control, low-, and high-dose groups, respectively (70% of the low-dose males were accidentally killed). The survival rate in females was comparable for all groups (approximately 63%). In female mice, the incidence of hepatocellular adenomas and the combined incidence of hepatocellular adenomas and carcinomas were statistically significantly increased in the high-dose group. The incidence of adenomas was 2/50, 4/49, and 11/50; the incidence of carcinomas was 4/45, 6/49, and 8/50; and the combined incidence was 6/50, 10/49, and 19/50 for female mice in the 0, 50, and 100 mg/kg dose groups, respectively. In high-dose male mice, there was a significantly increased incidence of hepatocellular carcinomas; however, the combined incidence of hepatocellular adenomas and carcinomas was only marginally increased. The incidence of adenomas was 14/50, 5/50, and 10/50; the incidence of carcinomas was 10/50, 9/50, and 19/50; and the combined incidence of adenomas and carcinomas was 23/50, 14/50, and 27/50 for the 0, 50, and 100 mg/kg dose groups, respectively. Under the conditions of this study, NTP (1985) determined that there was equivocal evidence of carcinogenicity of dibromochloromethane in male mice, and some evidence of carcinogenicity in female mice.

Voronin et al. (1987) observed no significant tumor increases in groups of 50 CBAx57B1/6 mice/sex treated with dibromochloromethane in the drinking water at concentrations of 0, 0.04, 4.0, or 400 mg/L (0, 0.008, 0.76, or 76 mg/kg/day) for 104 weeks.

Preliminary results of an unpublished 2-year dietary study using groups of 40 SPF Wistar rats reported no increase in gross tumors in male rats treated with dibromochloromethane at doses of 10, 39, or 210 mg/kg/day, or in female rats treated at doses of 17, 66, or 350 mg/kg/day. Control groups consisted of 70 rats/sex. Only 5 or 7 rats/sex/dose group were examined following 18 or 24 months of exposure (Tobe et al., 1982).

II.A.4. Supporting Data for Carcinogenicity

Dibromochloromethane has been shown to produce reverse mutations in *Salmonella typhimurium* strain TA100 in a vapor-phase test performed in a desiccator (Simmon et al., 1977). Results were not positive when plate incorporation (Simmon et al., 1977) or preincubation (NTP, 1985; Zeiger et al., 1987) methods were used. Nestmann and Lee (1985) reported positive results for gene conversion in *Saccharomyces cerevisiae* strain D4 without, but not with, hepatic homogenates, and negative results for mutation in strain XV185-14C both with and without

hepatic homogenates. Dibromochloromethane produces sister chromatid exchange in cultured human lymphocytes and in bone marrow cells of mice treated orally (Morimoto and Koizumi, 1983).

Dibromochloromethane is structurally similar to known animal carcinogens such as bromodichloromethane, bromoform, and chloroform (B2, probable human carcinogens).

II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

II.B.1. Summary of Risk Estimates

Oral Slope Factor — $8.4E-2$ per (mg/kg)/day

Drinking Water Unit Risk — $2.4E-6$ per (ug/L)

Extrapolation Method — Linearized multistage procedure, extra risk

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	$4E+1$ ug/L
E-5 (1 in 100,000)	$4E+0$ ug/L
E-6 (1 in 1,000,000)	$4E-1$ ug/L

II.B.2. Dose-Response Data (Carcinogenicity, Oral Exposure)

Tumor Type: hepatocellular adenoma or carcinoma

Test animals: mouse/B6C3F1, female

Route: gavage

Reference: NTP, 1985

Administered Dose (mg/kg/day)	Human Equivalent Dose (mg/kg/day)	Tumor Incidence
0	0	6/50
50	35.71	10/49
100	71.43	19/50

II.B.3. Additional Comments (Carcinogenicity, Oral Exposure)

The unit risk should not be used if the water concentration exceeds 4E-3 mg/L, since above this concentration the slope factor may differ from that stated.

II.B.4. Discussion of Confidence (Carcinogenicity, Oral Exposure)

An adequate number of animals of both sexes were treated for an adequate duration of exposure at two dose levels. Comprehensive histopathological and statistical analyses were performed. The compound was given by gavage rather than in feed or drinking water; exposure to a chemical through oral gavage is different from exposure through drinking water. Exposure could be overestimated leading to an underestimate of potency.

II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

Not available.

II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

II.D.1. EPA Documentation

Source Document — U.S. EPA, 1988

The 1988 Health and Environmental Effects Document for Dibromochloromethane is an external draft for review purposes. It has received OHEA review.

II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 09/07/1989

Verification Date — 09/07/1989

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the cancer assessment for Dibromochloromethane conducted in September 2002 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at hotline.iris@epa.gov or (202)566-1676.

II.D.3. EPA Contacts (Carcinogenicity Assessment)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Dibromochloromethane
CASRN — 124-48-1

VI.A. Oral RfD References

NTP (National Toxicology Program). 1985. Toxicology and Carcinogenesis Studies of Chlorodibromomethane in F344/N Rats and B6C3F1 mice (gavage studies). NTP TR282.

U.S. EPA. 1985. Drinking Water Criteria Document for Trihalomethanes. Office of Drinking Water, Washington, DC. External Review Draft.

VI.B. Inhalation RfD References

None

VI.C. Carcinogenicity Assessment References

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VII. Revision History

Substance Name — Dibromochloromethane

CASRN — 124-48-1

Date	Section	Description
11/01/1990	II.	Carcinogen assessment on-line
12/03/2002	I.A.6., II.D.2.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Dibromochloromethane

CASRN — 124-48-1

Last Revised — 09/30/1987

- 124-48-1
- Chlorodibromomethane
- Dibromochloromethane
- Dibromomonochloromethane
- Methane, dibromochloro-
- Monochlorodibromomethane